

# 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, Dessenhofer 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

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

**$\alpha$  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.

**$\beta$  sheet** collection of  $\beta$  strands assembled into planar sheet like structure held together by hydrogen bonds.

**3d<sub>10</sub> 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  $\alpha$  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  $\beta$  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 archaeobacteria.

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

**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 $_{\alpha}$ -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  $^{12}\text{C}$  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  $\phi$  is defined by  $\text{C}'\text{--N--C}_\alpha\text{--C}'$ .

**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 inert 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  $\text{pH} = \text{p}K_a + \log ([\text{A}^-]/[\text{HA}])$ .

**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 nonwetable 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  $\alpha$  and  $\beta$  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  $I = 1/2 \sum m_i z_i^2$

**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.

**pI** 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.

**pK** 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.

**Porphyryns** 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 ( $\sim 4.6 \times 10^9$ – $3.6 \times 10^9$  years ago)

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

**Preprotein** 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  $\phi$  against  $\psi$ .

**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  $\beta$  bend.

**Ribozyme** an 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.

**Serp**in 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.

**$v_0$**  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

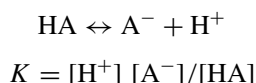
Frequently when discussing protein structure bond lengths will be expressed in nanometres (nm). For example, the average distance between two carbon atoms in an aliphatic side chain is  $\sim 0.14$  nm or  $0.14 \times 10^{-9}$  m. Occasionally a second (non SI) unit is used and is named after the Swedish 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	$k$	$1.380658 \times 10^{-23}$ J K <sup>-1</sup>
Elementary charge	$e$	$1.60217733 \times 10^{-19}$ C
Avogadro number	$N$	$6.0221367 \times 10^{23}$ particles/mol
Speed of light	$c$	$2.99792458 \times 10^8$ ms <sup>-1</sup>
<sup>1</sup> H gyromagnetic ratio		$2.67515255 \times 10^8$ T s <sup>-1</sup>
Atomic mass unit	amu	$1.66057 \times 10^{-27}$ kg
Gas constant	$R$	$8.31451$ J mol <sup>-1</sup> K <sup>-1</sup>
Faraday constant	$F$	$96485.3$ C mol <sup>-1</sup>

## 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.



Rearranging this equation leads to

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

and by taking negative logarithms this leads to

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

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

$$\text{pH} = \text{p}K - \log [\text{HA}]/[\text{A}^-]$$

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

$$\text{pH} = \text{p}K + \log [\text{A}^-]/[\text{HA}]$$

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

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

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  $\text{p}K_a$ 's are known. Alternatively this equation can be used to calculate the molar ratio of donor and acceptor given the pH and  $\text{p}K$ , or to calculate the  $\text{p}K$  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

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### Enzyme classes and subclasses

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#### 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<sub>2</sub> 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<sub>2</sub> 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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# Bibliography

## General reading

- Alberts B., Bray, D., Lewis, J., Raff, M., Roberts, K. & Watson J.D. *Molecular Biology of the Cell*, 3rd edn. Garland Publishing, New York, 1994.
- Barrett, G. C. *Chemistry and Biochemistry of Amino Acids*. Chapman & Hall, London, 1985.
- Branden, C. & Tooze, J. *Introduction to Protein Structure*. Garland Publishing, New York, 1991.
- Cornish-Bowden, A. *Fundamentals of Enzyme Kinetics*. Butterworths, Oxford, 1979.
- Creighton, T. E. *Proteins Structures and Molecular Properties*, 2nd edn. W.H. Freeman, London, 1993.
- Darnell, J., Lodish, H. & Baltimore, D. *Molecular Cell Biology*, 2nd edn. Scientific American Books, New York, 1990.
- Fersht, A. *Enzyme Structure and Mechanism*, 2nd edn. W.H. Freeman, New York, 1985.
- Frausto da Silva, J. J. R. & Williams, R. J. P. *The Biological Chemistry of the Elements*. Oxford University Press, Oxford, 1991.
- Gutfreund, H. *Enzymes: Physical Principles*. Wiley-Interscience, New York, 1972
- Lehninger, A., Nelson, D. L. & Cox, M. M. (eds) *Principles of Biochemistry*, 3rd edn. Worth Publishers, New York, 2000.
- Lippard, S. J. & Berg, J. M. *Principles of Bioinorganic Chemistry*. University Science Books, 1994.
- Voet, D. Voet, J. G. & Pratt, C. W. *Fundamentals of Biochemistry*. John Wiley & Sons, Chichester, 1999.
- Watson, J. D. *et al. Molecular Biology of the Gene*. Benjamin Cummings, New York, 1988.
- Kendrew, J. *The Thread of Life*. G. Bell, 1966.
- Mirsky, A. E. The discovery of DNA. *Sci. Am.* 1968, **218**, 78–88.
- Olby, R. E. *The Path to the Double Helix: the Discovery of DNA*. Dover Publications, 1995.
- Rutherford, N. J. *A Documentary History of Biochemistry 1770–1940*. Fairleigh Dickinson University Press, 1992.
- Schrodinger, E. *What is Life?* Cambridge University Press, Cambridge, 1944.

## Chapter 2

- Barrett, G.C. (ed) *Chemistry and Biochemistry of amino acids*. Chapman & Hall, New York, 1985.
- Barrett, G.C. & Elmore, D.T. *Amino Acids and Peptides*. Cambridge University Press, 1998.
- Creighton, T.E. *Proteins: Structure and molecular properties*, 2nd edn. Chapters 1–7. W.H. Freeman, New York, 1993.
- Creighton, T.E. (ed) *Protein Function: A practical approach*. IRL Press, Oxford, 1989.
- Hirs, C.H.W. & Timasheff, S.N. (eds) Enzyme Structure part 1. *Methods Enzymology*, 91. Academic Press, 1983.
- Jones, J. *Amino Acids and Peptide Synthesis (Oxford Chemistry Primers)*. Oxford University Press, 2002.
- Lamzin, V.S., Dauter, Z. & Wilson, K.S. How nature deals with stereoisomers. *Curr. Opin. Struct. Biol.* 1995, **5**, 830–836.
- Means, G.E. & Feeney, R.E. *Chemical Modification of Proteins*. Holden-Day, 1973.

## Chapter 3

- Berman, H.M., Westbrook, J., Feng, Z., Gilliland, G., Bhat, T.N., Weissig, H., Shindyalov, I.N. & Bourne, P.E. The Protein Data Bank. *Nucl. Acids Res.* 2000, **28**, 235–242.

## Chapter 1

- Ingram, V. A case of sickle-cell anemia. *Biochem. Biophys. Acta* 1989, **1000**, 147–150.

- Davies, D.R., Padlan, E.A. & Sheriff, S. Antibody-antigen complexes. *Annu. Rev. Biochem.* 1990, **59**, 439–473.
- Doolittle, R.F. Proteins. *Sci. Am.* 1985, **253**, 88–96.
- Goodsell, D.S. & Olson, A.J. Soluble proteins: Size, shape and function. *Trends Biochem. Sci.* 1993, **18**, 65–68.
- Kuby, J. *Immunology*. W.H. Freeman, London, 1997.
- Lesk, A.M. *Introduction to protein architecture*. Oxford University Press, 2001.
- Perutz, M.F. *Hemoglobin structure and respiratory transport*. *Sci. Am.* 1978, **239**, 92–125.
- Richardson, J.S. The anatomy and taxonomy of protein structure. *Adv. Prot. Chem.* 1981, **34**, 167–339.
- Trabi, M., & Craik, D.J. Circular proteins – no end in sight. *Trends Biochem. Sci.* 2002, **27**, 132–138.
- ### Chapter 4
- Baum, J. & Brodsky, B., Folding of peptide models of collagen and misfolding in disease. *Curr. Opin. Struct. Biol.* 1999, **9**, 122–128.
- Downing, A. K., Knott, V., Werner, J. M., Cardy, C. M., Campbell, I. D., & Handford, P. A. Solution structure of a pair of Ca<sup>2+</sup> binding epidermal growth factor-like domains: implications for the Marfan syndrome and other genetic disorders. *Cell* 1996, **85**, 597–605.
- Glover, J. N., Harrison, S. C. Crystal structure of the heterodimeric bZIP transcription factor *c-Fos c-Jun* bound to DNA. *Nature* 1995, **373**, 257.
- Handford, P. A. Fibrillin-1, a calcium binding protein of extracellular matrix. *Biochim. Biophys. Acta* 2000, **1498**, 84–90.
- Kaplan, D., Adams, W. W., Farmer, B. & Viney, C. *Silk Polymers*. American Chemical Society, 1994.
- Lupas, A. Coiled coils new structures and new functions. *Trends Biochem. Sci.* 1996, **21** 375–382.
- Martin, G. R. Timple, R., Muller, P. K. & Kuhn, K. The genetically distinct collagens. *Trends Biochem. Sci.* 1985, **10**, 285–287.
- O’Shea, E. K. Rutkowski, R. & Kim, P. S. Evidence that the leucine zipper is a coiled coil. *Science* 1989, **243**, 538–542.
- Parry, D. A. D. The molecular and fibrillar structure of collagen and its relationship to the mechanical properties of connective tissue. *Biophys. Chem.* 1988, **29**, 195–209.
- Porter, R. M. & Lane E. B. Phenotypes, genotypes and their contribution to understanding keratin function. *Trends Genet.* 2003, **19**, 278–285.
- Prockop, D. J. & Kivirikko, K. I. Collagens – molecular-biology, diseases, and potentials for therapy. *Annu. Rev. Biochem.* 1995, **64**, 403–434.
- Royce, P.M. & Steinmann, B. (eds) *Connective Tissue and Its Heritable Disorders: Molecular, Genetic, and Medical Aspects*. John Wiley & Sons, 2002.
- Van der Rest, M. & Bruckner, P. Collagens: Diversity at the molecular and supramolecular levels. *Curr. Opin. Struct. Biol.* 1993, **3**, 430–436.
- ### Chapter 5
- Benz R. (ed) *Bacterial and Eukaryotic Porins: Structure, Function, Mechanism*. John Wiley & Sons, 2004.
- Blankenship, R.E. *Molecular Mechanism of Photosynthesis*. Blackwell Science, 2001.
- Capaldi, R.A & Aggeler, R. *Mechanism of the F<sub>1</sub>F<sub>0</sub>-type ATP synthase, a biological rotary motor*. *Trends Biochem. Sci.* 2002, **27**, 154–160.
- Gennis, R.B. *Biomembranes*. Springer Verlag, New York, 1989.
- Hamm, H.E. The many faces of G protein signaling. *J. Biol. Chem.* 1998, **273**, 669–672.
- Lehninger, A. *Principles of Biochemistry*. 3rd edn. (Nelson, D.L. and Cox, M.M., eds.) *Oxidative Phosphorylation and Photophosphorylation*, pp. 659–690. Worth Publishers
- Nicholls, D.G. & Ferguson, S.J. *Bioenergetics 2*, Academic Press, 1992.
- Scheffler, I.E. *Mitochondria*. John Wiley & Sons Inc, 1999.
- Vance, D.E. & Vance, J.E. *Biochemistry of lipids, lipoproteins and membranes*. 4th edn. Elsevier, 2002.
- Torres, J., Stevens, T.J. & Samsó, M. *Membrane proteins: the ‘Wild West’ of structural biology*. *Trends Biochem. Sci.* 2003, **28**, 137–144.
- Von Jagow, G., Schaeffer, H., & Hunte, C. (eds) *Membrane Protein Purification and Crystallization: A Practical Guide*. Academic Press, 2003.
- ### Chapter 6
- Baxevanis, A.D. & Ouellette, B.F.(eds) *Bioinformatics: A practical guide to the analysis of genes and proteins*. John Wiley & Sons Inc, 2004.
- Findlay, J.B.C. & Geisow, M.J. (eds) *Protein Sequencing. A practical approach*. IRL press 1989.
- Margulis, L & Sagan, C. *What is Life*. Simon & Schuster, New York, 1995.
- Miller, S.J. & Orgel, L.E. *The Origins of Life*. Prentice-Hall, New Jersey, 1975.
- Mount, D.W. *Bioinformatics: Sequence and Genome Analysis*. Cold Spring Harbor Laboratory Press, 2001.
- Orengo, C.A., Thornton, J.M & Jones, D.T. *Bioinformatics (Advanced Texts Series)*. BIOS Scientific Publishers, 2002.

- Primrose, S.B. *Principles of Genome Analysis: A Guide to Mapping and Sequencing DNA from Different Organisms*. Blackwell Science, 1998.
- Sanger, F. *Sequences, sequences, sequences*. *Annu. Rev. Biochem.* 1988, **57**, 1–28.
- Volkenstein, M.V. *Physical Approaches to Biological Evolution*. Springer Verlag, Berlin, 1994.
- Webster, D.M. *Protein Structure Prediction: Methods and Protocols*. Humana Press, 2000.
- Trends Biochem. Sci.* 1997, **22**, 371–410. Issue devoted to proteasome and proteolytic processes.
- Watson, J.D. *The Double Helix: Personal Account of the Discovery of the Structure of DNA*. Penguin 1999.
- Zwickl, P. & Wolfgang Baumeister, W. *The Proteasome-Ubiquitin Protein Degradation Pathway*. Springer Verlag, Berlin, 2002.

## Chapter 7

- Bairoch, A. The enzyme databank. *Nucl. Acids. Res.* 1994, **22**, 3626–3627.
- Fersht, A.R. *Structure and Mechanism in Protein Science: Guide to Enzyme Catalysis and Protein Folding*. W.H. Freeman and Company, New York, 1999.
- Gutfreund, H. *Kinetics for the Life Sciences: Receptors, Transmitters and Catalysts*. Cambridge University Press, Cambridge, 1995.
- Kovall, R.A. & Matthews, B.W. Type II restriction endonucleases: structural, functional and evolutionary relationships. *Curr. Opin. Chem. Biol.* 1999, **3**, 578–583.
- Kraut, J. How do enzymes work? *Science* 1988, **242**, 533–540.
- Martins, L.M. & Earnshaw, W.C. Apoptosis: Alive and kicking in 1997. *Trends Cell Biol.* 1997, **7**, 111–114.
- Moore, J.W. & Pearson, R.G. *Kinetics and Mechanism*. John Wiley & Sons, Chichester, 1981.
- Vaux, D.L. & Strasser, A. The molecular biology of apoptosis. *Proc. Natl. Acad. Sci. USA* 1996, **93**, 2239–2244.
- Wold, F. & Moldave, K. Posttranslational modifications. *Methods Enzymol.* **106** and **107**. Academic Press, 1985.

## Chapter 8

- Dodson, G. & Wlodawer, A. Catalytic triads and their relatives. *Trends Biochem. Sci.* 1998, **23**, 347–352.
- Kornberg, A., & Baker, T.A. *DNA Replication*, 2d ed. W. H. Freeman, San Francisco, 1992.
- Murray A.W., & Hunt T, eds. *The Cell Cycle: An Introduction*. Oxford University Press. 1993.
- Norbury C, & Nurse P. Animal Cell Cycles and Their Control. *Annu. Rev. Biochem.* 1992, **61**, 441–470.
- Spirin, A.S. *Ribosomes*. Kluwer Academic, New York, 1999.
- Stein G. S, (ed.) *The Molecular Basis of Cell Cycle and Growth Control*. John Wiley & Sons Inc, New York, 1999.
- Stillman, B. (ed.) *The Ribosome*. Cold Spring Harbor Symp. **66**. Cold Spring Harbor Laboratory Press, 2001.

## Chapter 9

- Brown, T.A. *Gene Cloning and DNA Analysis: An Introduction*. Blackwell, 4th edn, 2001.
- Deutscher, M.P., Colowick, S.P. & Simon, M.I. (eds). Guide to protein purification. *Methods Enzymol.* **182**. Academic Press, London, 1990.
- Dunn, B.M. Speicher, D.W., Wingfield, P.T. & John E. Coligan, J.E. (eds) *Short Protocols in Protein Science*. John Wiley & Sons, 2003.
- Freifelder, D. *Physical Biochemistry: Applications to Biochemistry and Molecular Biology*. W.H. Freeman, 1982.
- Hames, B.D. & Rickwood. (eds) *Gel Electrophoresis of Proteins, A practical approach*, 2nd edn. IRL press, 1990.
- Jansen, J-C. & Ryden, L. (eds) *Protein Purification: Principles, High Resolution Methods and Applications*. John Wiley & Sons Inc, 1998.
- Meyer, V.R. *Practical High-Performance Liquid Chromatography*, 4th edn. John Wiley & Sons, 2004.
- Scopes, R. *Protein purification: Principles and Practice*. Springer-Verlag, Berlin, 1993.
- Tanford, C. *The hydrophobic effect; formation of micelles and biological membranes*, 2nd edn. John Wiley & Sons, Chichester, 1980.
- Voet, D., Voet, J.G. & Pratt, C.W. *Fundamentals of Biochemistry*, John Wiley & Sons, Ltd, Chichester, 1999.

## Chapter 10

- Campbell, I.D. & Dwek, R. *Biological Spectroscopy*. Benjamin Cummings, New York, 1984.
- Cavanagh, J., Fairbrother, W.J., Palmer III, A.G. & Skelton, N.J. *Protein NMR spectroscopy: Principles and Practice*. Academic Press, 1996.
- Chang, R. *Chemistry*. 8th edn. McGraw-Hill Education, 2004.
- Drenth, J. *Principles of Protein X-ray Crystallography*. Springer-Verlag, New York, 1994
- Fasman, G.D. (ed) *Circular Dichroism and the Conformational Analysis of Biomolecules*. Plenum Publishers, 1996.
- Ferry, G. *Dorothy Hodgkin: A life*. Granta Books, 1999.

- Harrison, S.C. Whither structural biology? *Nat. Struct. Mol. Biol.* 2004, **11**, 12–15.
- Nat. Struct. Biol.* 1997, **4**, 841–865 and *Nat. Struct. Biol.* 1998, **5**, 492–522. (Series of short NMR reviews)
- Rhodes, G. *Crystallography made crystal clear*. Academic Press 2nd edn, San Diego, 2000.
- Wider, G. & Wüthrich, K. NMR spectroscopy of large molecules and multimolecular assemblies in solution. *Curr. Op. Struct. Biol.* 1999, **9**, 594–601.
- Chapter 11**
- Caughey, B. (ed) Prion Proteins. *Adv. Protein Chem.* **57**. Academic Press, 2001
- Creighton, T.E. *Protein Folding*. W.H. Freeman, New York, 1992.
- Daggett, V. & Fersht, A.R. Is there a unifying mechanism for protein folding? *Trends Biochem. Sci.* 2003, **28**, 18–25.
- Horwich, A.L. (ed) Protein folding in the cell. *Adv. Protein Chem.* **59**. Academic Press, 2001.
- Dobson, C.M. Protein Misfolding, *Evolution and Disease Trends Biochem. Sci.* 1999, **24**, 329–332.
- Ladbury, J.E & Chowdhry, B.Z. (eds) *Biocalorimetry: Applications of Calorimetry in the Biological Sciences*. John Wiley & Sons, Chichester, 1998.
- Matthews, B.W. Structural and genetic analysis of protein stability. *Annu. Rev. Biochem.* 1993, **62**, 139–160.
- Matthews, C.R. (eds) Protein Folding Mechanisms. *Adv. Protein Chem.* 2000, **53**.
- Pain, R. (ed) *Mechanisms of Protein Folding* (Frontiers in Molecular Biology Series). Oxford University Press, 2000.
- Saibil, H.R. & Ranson, N.A. The chaperonin folding machine. *Trends Biochem. Sci.* 2002, **27**, 627–632.
- Chapter 12**
- Crystal, R. G. The  $\alpha_1$ -antitrypsin gene and its deficiency states. *Trends Genet.* 1989, **5**, 411–417.
- Culotta, E. & Koshland, D. E., Jr. p53 sweeps through cancer research. *Science* 1993, **262**, 1958–1959.
- Fauci, A. S. HIV and AIDS: 20 years of science. *Nature Medicine* 2003, **9**, 839–843. (and subsequent articles)
- Lane, D. & Lain, S. Therapeutic exploitation of the p53 pathway. *Trends Molec. Med.* 2002, **8**, S38–S42.
- Gouras, G.K. Current theories for the molecular and cellular pathogenesis of Alzheimer's disease. *Expert Rev. Mol. Med.* 2001. <http://www.expertreviews.org/01003167h.htm>
- Perutz, M.F. *Protein Structure: New Approaches to Disease and Therapy*. W.H. Freeman, 1992.
- Rowland-Jones, S.L. AIDS pathogenesis: what have two decades of HIV research taught us? *Nature Rev. Immunol.* 2003, **3**, 343–348.
- Prusiner, S. Prion diseases and the BSE crisis. *Science* 1997, **278**, 245–251.
- Varmus, H. Retroviruses. *Science* 1988, **240**, 1427–1435.
- Wiley, D.C. & Skehel, J.J. The Structure and Function of the Haemagglutinin Membrane Glycoprotein of Influenza Virus. *Annu. Rev. Biochem.* 1987, **56**, 365–394.

# References

- Abrahams, J. P., Leslie, A. G. W., Lutter, R. & Walker, J. E. Structure at 2.8 Å resolution of F1-ATPase from bovine heart mitochondria. *Nature* 1994, **370**, 621–628.
- Abramson, J., Svensson-Ek, M., Byrne, B. & Iwata, S. Structure of cytochrome *c* oxidase: a comparison of the bacterial and mitochondrial enzymes *Biochim. Biophys. Acta* 2001, **1544**, 1–9.
- Agarrarberes, F. A., & Dice, J. F. Protein translocation across membranes. *Biochim. Biophys. Acta* 2001, **1513**, 1–24.
- Agarwal, M. L., Taylor, W. R., Chernov, M. V., Chernova, O. B. & Stark, G. R. The p53 network. *J. Biol. Chem.* 1998, **273**, 1–4.
- Aguzzi, A., Glatzel, M., Montrasio, F., Prinz, M. & Heppner, F. L. Interventional strategies against prion diseases. *Nature Rev. Neurosciences* 2001, **2**, 745–749.
- Aguzzi, A., Montrasio, F., & Kaeser, P. S. Prions: Health scare and biological challenge. *Nature Reviews Molecular Cell Biology* 2002, **2**, 118–126.
- Albright, R. A., & Matthews, B. W. How Cro and λ repressor Distinguish Between Operators: The Structural Basis Underlying a Genetic Switch. *Proc. Natl. Acad. Sci USA* 1996, **95**, 3431–3436.
- Allen, T. D., Cronshaw, J. M., Bagley, S. Kiseleva, E. & Goldberg, M. W. The nuclear pore complex: mediator of translocation between nucleus and cytoplasm. *J. Cell Sci.* 2000, **113**, 1651–1659.
- Als-Nielsen, J. & McMorrow, D. *Elements of Modern X-ray Physics*. John Wiley & Sons, Chichester, 2001.
- Altman, S. & Kirsebom, L. Ribonuclease P. in Gesteland, R. F., Cech, T. R. and Atkins, J. F. (eds), *The RNA World*. Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York 1999.
- Altschul, S. F. Amino acid substitution matrices from an information theoretic perspective. *J. Mol. Biol.* 1991, **219**, 555–665.
- Amit, A. G., Mariuzza, R. A., Phillips, S. E. V. & Poljak, R. J. Three dimensional structure of an antigen-antibody complex at 2.8Å resolution. *Science* 1986, **233**, 747–750.
- Andrade, C., A peculiar form of peripheral neuropathy: familial atypical generalised amyloidosis with special involvement of peripheral nerves. *Brain* 1952, **75**, 408–427.
- Andrews, D. W. & Johnson, A. E. The translocon: more than a hole in the ER membrane? *Trends Biochem. Sci.* 1996, **21**, 365–369.
- Anfinsen, C. B. Principles that govern the folding of protein chains. *Science* 1973, **181**, 223–230.
- Arakawa, T & Timasheff, S. N. Theory of protein solubility. *Methods Enzymol.* 1985, **114**, 49–77, Academic Press.
- Babcock, G. & Wikström, M. Oxygen activation and the conservation of energy in cellular respiration. *Nature* 1992, **356**, 301–309.
- Baldwin, R. L. & Rose, G. D, Is protein folding Hierarchic? I. Local structure and peptide folding. *Trends Biochem. Sci.* 1999 **24**, 26–33 II. Folding Intermediates and transition states. *Trends Biochem. Sci.* 1999 **24**, 77–83.
- Baltimore, D. Our genome unveiled. *Nature* 2001, **409**, 814–816.
- Ban, N. Nissen, P., Hansen, J., Moore, P. B. & Steitz, T. A. The complete atomic structure of the large ribosomal subunit at 2.4 Å resolution. *Science* 2000, **289**, 905–920.
- Barber, M & Quinn, G. B. High-Level Expression in *Escherichia coli* of the Soluble, Catalytic Domain of Rat Hepatic Cytochrome *b*<sub>5</sub> Reductase. *Protein expression and purification* 1996, **8**, 41–47.
- Bardwell, J. C. A. & Beckwith, J. The bonds that tie: catalyzed disulfide bond formation *Cell* 1993, **74**, 769–771.
- Batey, R. T., Sagar M. B., & Doudna J. A. Structural and energetic analysis of RNA recognition by a universally



- conserved protein from the signal recognition particle. *J. Mol. Biol.* 2001, **307**, 229–246.
- Baum, J. & Brodsky, B. Folding of peptide models of collagen and misfolding in disease. *Curr. Opin. Struct. Biol.* 1999, **9**, 122–128.
- Baumeister, W. & Steven, A. C. Macromolecular electron microscopy in the era of structural genomics. *Trends Biochem. Sci.* 2000, **25**, 625–631.
- Bax, A. Multi-dimensional nuclear magnetic resonance methods for protein studies. *Curr. Opin. Struct. Biol.* 1994, **4**, 738–744.
- Bergfors, T. *Protein Crystallization Techniques, Strategies, and Tips. A Laboratory Manual* 1999.
- Berry, E. A., Guergova-Kuras, M., Huang, L. -S. & Antony R. Crofts, A. R. Structure and function of cytochrome bc complexes *Annu. Rev. Biochem.* 2000, **69**, 1005–1075.
- Billeter, M., Kline, A. D., Braun, W., Huber, R., & Wüthrich, K. Comparison of the High-Resolution Structures of the  $\alpha$ -Amylase Inhibitor Tendamistat Determined by Nuclear Magnetic Resonance in Solution and by X-ray Diffraction in Single Crystals. *J. Mol. Biol.* 1989, **206**, 677–687.
- Blobel, G. & Dobberstein, B. Transfer of proteins across membranes. I. Presence of proteolytically processed and unprocessed nascent immunoglobulin light chains on membrane-bound ribosomes of murine myeloma, *J. Cell Biol.* 1975, **67**, 835–851.
- Bockaert, J., & Pin, J. P. Molecular tinkering of G protein-coupled receptors: an evolutionary success. *EMBO J.* 1999, **18**, 1723–1729.
- Bokman S. H., Ward W. W. Renaturation of *Aequorea* green fluorescent protein. *Biochem. Biophys. Res. Commun.* 1981, **101**, 1372–1380.
- Bolton, W. & Perutz, M. F. Three dimensional Fourier synthesis of horse deoxyhaemo-globin at 2.8 Å resolution. *Nature* 1970, **228**, 551–552.
- Booth, P., Templer, R. H., Curran, A. R. & Allen, S. J. Can we identify the forces that drive the folding of integral membrane proteins? *Biochem Soc. Trans.* 2001, **29**, 408–413.
- Boriack-Sjodin, P. A., Zeitlin, S., Chen, H. -H., Crenshaw, L., Gross, S., Dantanarayana, A., Delgado, P., May, J. A., Dean, T. & Christianson, D. W. Structural analysis of inhibitor binding to human carbonic anhydrase II. *Protein Science* 1998, **7**, 2483–2489.
- Bowie, J. U., Clarke, N. D., Pabo, C. O. & Sauer, R. T. Deciphering the message in protein sequence: tolerance to amino acid substitutions. *Science* 1990, **247**, 1306–1310.
- Boyer, P. D. The binding change mechanism for ATP synthase – Some probabilities and possibilities. *Biochim. Biophys. Acta* 1993, **1140**, 215–250.
- Boyer, P. D., The ATP synthase – a splendid molecular machine, *Annu. Rev. Biochem.* 1997, **66**, 717–749.
- Braig, K., Menz R. I., Montgomery M. G., Leslie A. G., & Walker J. E. Structure of bovine mitochondrial F<sub>1</sub>-ATPase inhibited by Mg<sup>2+</sup> ADP and aluminium fluoride. *Structure* 2000, **8**, 567–573.
- Braig, K., Otwinowski, Z., Hegde, R., Boisvert, D. C., Joachimiak, A., Horwich, A. L & Sigler, P. B. The crystal structure of the bacterial chaperonin GroEL at 2.8 Å. *Nature* 1994, **371**, 578–586.
- Brandts, J. F., Halvorson, H. R., & Brennan, M. Consideration of the possibility that the slow step in protein denaturation reactions is due to *cis-trans* isomerism of proline residues. *Biochemistry* 1975, **14**, 4953–4963.
- Brandts, U. Bifurcated ubihydroquinone oxidation in the cytochrome bc 1 complex by protongated charge transfer. *FEBS Lett.* 1996, **387**, 1–6.
- Brejč, K., Sixma, T. K., Kitts, P. A., Kain, S. R., Tsien, R. Y., Ormo, M., Remington, S. J. Structural basis for dual excitation and photoisomerization of the *Aequorea victoria* green fluorescent protein. *Proc. Natl. Acad. Sci U S A* 1997, **94**, 2306–2311.
- Brenner, S., Jacob, F. & Meselson, M. An unstable intermediate carrying information from genes to ribosomes for protein synthesis. *Nature* 1961, **190**, 576–581.
- Brodersen, D. E., Carter, A. P., Clemons Jr, W. M., Morgan-Warren, R. J., Murphy IV, F. V. Ogle, J. M., Tarry, M. J. Wimberley, B. T. & Ramakrishnan, V. Atomic Structures of the 30S Subunit and Its Complexes with Ligands and Antibiotics. *Cold Spring Harbor Symp.* 2001, **66**, 17–32.
- Browner, M. F. & Fletterick, R. J. Phosphorylase: a Biological Transducer. *Trends Biochem. Sci.* 1992, **17**, 66–71.
- Burley, S. K. The TATA box binding protein. *Curr. Opin. Struct. Biol.* 1996, **6**, 69–75.
- Butler, P. J. G., Klug, A. The assembly of a virus. *Sci. Amer.* Nov. 1978
- Byrne, B. & Iwata, S. Membrane protein complexes. *Curr. Opin. Struct. Biol.* 2002, **12**, 239–243.
- Cahn, R. S., Ingold, C. K. & Prelog, V. Specification of Molecular Chirality. *Angew. Chem.* 1966, **78**, 413–447.
- Cammack, R. & Cooper, C. E. Electron paramagnetic resonance spectroscopy of iron complexes and iron-containing proteins. *Methods Enzymol.* 1993, **22**, 353–384, Academic Press.
- Campbell, I. D. & Dwek, R. *Biological Spectroscopy*. Benjamin Cummings, New York, 1984.
- Capaldi, R. A. Structure and function of cytochrome oxidase. *Annu. Rev. Biochem.* 1990, **59**, 569–96.



- Carter, C. W. Cognition, Mechanism, and Evolutionary Relationships in Aminoacyl-tRNA Synthetases. *Ann. Rev. Biochem.* 1993, **62**, 717–748.
- Cavanagh, J., Fairbrother, W. J., Palmer III, A. G. & Skelton, N. J. *Protein NMR spectroscopy: Principles and Practice*. Academic Press, 1996.
- Chaddock, J. A., Herbert, M. H., Ling, R. J., Alexander, F. C. G., Fooks, S. J., Revell, D. F., Quinn, C. P., Shone, C. C. & Foster, K. A. Expression and purification of catalytically active, non-toxic endopeptidase derivatives of *Clostridium botulinum* toxin type A. *Protein Expression and Purification* 2002, **25**, 219–228.
- Chalfie, M., Tu, Y., Euskirchen, G., Ward W. W., Prasher D. C. Green fluorescent protein as a marker for gene expression. *Science* 1994, **263**, 802–805.
- Cheetham, G. M., Jeruzalmi, D. & Steitz, T. A. Structural basis for initiation of transcription from an RNA polymerase- promoter complex *Nature* 1999, **399**, 80–84.
- Chen, S., Roseman, A. M., Hunter, A. S., Wood, S. P., Burston, S. G., Ranson, N. A., Clarke, A. R. & Helen R. Saibil, H. R. Location of a folding protein and shape changes in GroEL–GroES complexes imaged by cryo-electron microscopy *Nature* 1994, **371**, 261–264.
- Chevet, E., Cameron, P. H., Pelletier, M. F., Thomas D. Y. & Bergeron, J. J. M. The endoplasmic reticulum: integration of protein folding, quality control, signaling and degradation. *Curr. Opin. Struct. Biol.* 2001, **11**, 120–124.
- Cho, Y., Gorina, S., Jeffrey, P. D., Pavletich, N. P. Crystal structure of a p53 tumor suppressor-DNA complex: understanding tumorigenic mutations. *Science* 1994, **265**, 346–355.
- Chothia, C & Finkelstein, A. V. The classification and origins of protein folding patterns. *Annu. Rev. Biochem.* **59**, 1007–1039, 1990.
- Chou, P. Y. & Fasman, G. D. Empirical Predictions of Protein Conformation. *Annu. Rev. Biochem.* 1978, **47**, 251–276.
- Cingolani, G., Petosa, C., Weis, K., & Müller, C. W. Structure of importin- $\beta$  bound to the IBB domain of importin- $\alpha$ . *Nature* 1999, **399**, 221–229.
- Cohen, C. & Parry, D. A. D.  $\alpha$  helical coiled coils and bundles: how to design an  $\alpha$  helical protein. *Prot. Struct. Funct. Genet.* 1990, **7**, 1–15.
- Cohen, F. E. & Prusiner, S. B. Pathologic conformations of prion proteins. *Annu. Rev. Biochem.* 1998, **67**, 793–819.
- Collinge, J. Human prion diseases and bovine spongiform encephalopathy (BSE). *Hum. Mol. Genet.* 1997, **6**, 1699–1705.
- Coux, O., Tanaka, K. & Goldberg, A. L. Structure and Functions of the 20S and 26S Proteasomes. *Annu. Rev. Biochem.* 1996, **65**, 801–847.
- Cowan, S. W., Schirmer, T., Rummel, G., Steiert, M., Ghosh, R., Pauptit, R. A., Jansonius N. J. & Rosenbusch, J. P. Crystal structures explain functional properties of two *E. coli* porins. *Nature* 1992, **358**, 727–733.
- Crick, F. H. C. The packing of  $\alpha$  helices: simple coiled coils. *Acta Cryst.* 1953, **6**, 689–697.
- Crick, F. H. C., Barnett, L., Brenner, S. & Watts-Tobin, R. J. General nature of the genetic code for proteins. *Nature* 1961, **192**, 1227–1232.
- Crystal, R. G. The  $\alpha_1$ -antitrypsin gene and its deficiency states. *Trends Genet.* 1989, **5**, 411–417.
- Cserzo, M., Wallin, E., Simon, I., von Heijne, G. & Elofsson, A. Prediction of transmembrane  $\alpha$  helices in prokaryotic membrane proteins: the Dense Alignment Surface method. *Prot. Eng.* 1997, **10**, 673–676.
- Cullen, B. R. Nuclear RNA export pathways. *Mol. Cell. Biol.* 2000, **20**, 4181–4187.
- Dalbey, R. E., Chen, M. Y., Jiang, F. & Samuelson, J. C. *In vivo* Assembly of Transporters and other Membrane Proteins. *Curr. Opin. Cell Biol.* 2000, **12**, 435–442.
- Dalbey, R. E. & Robinson, C. Protein translocation into and across the bacterial plasma membrane and the plant thylakoid membrane. *Trends Biochem. Sci.* 1999, **24**, 17–24.
- Danna, K. & Nathans, D. Specific cleavage of Simian virus 40 DNA restriction endonuclease of *Haemophilus influenzae*. *Proc. Natl. Acad. Sci. USA* 1971, **68**, 2913–2917.
- Davie, E. W. Introduction to the blood clotting cascade and the cloning of blood coagulation factors. *J. Prot. Chem.* 1986, **5**, 247–253.
- Davies, D. R. The structure and function of the aspartic proteinases. *Ann. Rev. Biophys. Biophys. Chem.* 1990, **19**, 189–215.
- Davies, D. R. & Chacko, S. Antibody structure. *Acc. Chem. Res.* 1993, **26**, 421–427.
- Dayhoff, M. The origin and evolution of protein superfamilies. *FASEB J.* 1976, **35**, 2132–2138.
- Dayhoff, M. O., R. M. Schwartz and B. C. Orcutt. 1978. A model of evolutionary change in proteins. In *Atlas of Protein Sequence and Structure* Vol. 5 suppl. 2 (ed. M. O. Dayhoff), 345–352. National Biomedical Research Foundation, Washington DC.
- DeBondt, H. L., Rosenblatt, J., Jancarik, J., Jones, H. D., Morgan, D. O. & Kim, S. H. Crystal structure of cyclin-dependent kinase 2. *Nature* 1993, **363**, 595–602.
- Deisenhofer, J., Epp, O., Miki, K., Huber, R. & Michel, H. Structure of the protein subunits in the photosynthetic reaction centre of *R. viridis* at 3 Å resolution. *Nature* 1985, **318**, 618–624.

- Deisenhofer, J., Epp, O., Miki, K., Huber, R. & Michel, H. X-ray structure analysis of a membrane protein complex. Electron density map at 3 Å resolution and a model of the chromophores of the photosynthetic reaction center from *Rhodospseudomonas viridis*. *J. Mol. Biol.* 1984, **180**, 385–398.
- Deisenhofer, J., Epp, O., Sinning, I. & Michel, H. Crystallographic refinement at 2.3 Å resolution and refined model of the photosynthetic reaction centre from *Rhodospseudomonas viridis*. *J. Mol. Biol.* 1995, **246**, 429–457.
- DeRose, V. J. & Hoffman, B. M. Protein structure and mechanism studied by electron nuclear double resonance spectroscopy *Methods Enzymol.* 1995, **246**, 554–589 Academic Press.
- Dill, K. A. & Chan, H. S. From Levinthal to pathways to funnels. *Nature Struct. Biol.* 1997, **4**, 10–19.
- Dill, K. A. Dominant Forces in Protein Folding. *Biochemistry* 1990, **29**, 7133–7155.
- Dinner, A. R. & Karplus, M. The roles of stability and contact order in determining protein folding rates. *Nature Struct. Biol.* 2001, **8**, 21–22.
- Ditzel, L., Löwe, J., Stock, D., Stetter, K. -O., Huber, H., Huber, R. & Steinbacher, S. Crystal structure of the thermosome, the archaeal chaperonin and homolog of CCT. *Cell* 1998, **93**, 125–138.
- Dobson, C. M. Protein Misfolding, Evolution and Disease *Trends Biochem. Sci.* 1999, **24**, 329–332.
- Dobson, C. M., Evans, P. A., & Radford, S. E. Understanding How Proteins Fold: The Lysozyme Story so Far, *Trends Biochem. Sci.* 1994, **19**, 31–37.
- Dodson, G. & Wlodawer, A. Catalytic triads and their relatives. *Trends Biochem. Sci.* **23**, 347–352, 1998.
- Dohlman *et al* *Biochemistry* 1987, **26**, 2660–2666.
- Doolittle, R. F. The multiplicity of domains in proteins. *Annu. Rev. Biochem.* 1995, **64**, 287–314.
- Doudna, J. A. & Batey, R. T. Structural insights into the signal recognition particle. *Annu. Rev. Biochem.* 2004, **73**, 539–557.
- Downing, A. K., Knott, V., Werner, J. M., Cardy, C. M., Campbell, I. D., & Handford, P. A., Solution structure of a pair of Ca<sup>2+</sup> binding epidermal growth factor-like domains: implications for the Marfan syndrome and other genetic disorders. *Cell* 1996, **85**, 597–605.
- Drenth, J. *Principles of Protein X-ray Crystallography*, Springer-Verlag. New York 1994
- Dunbrack, Jr. R. L., & Karplus, M. Conformational analysis of the backbone-dependent rotamer preferences of protein sidechains. *Nature Struct. Biol.* **1**, 334–340, 1994.
- Eckert, D. M. & Kim, P. S. Mechanisms of viral membrane fusion and its inhibition. *Annu. Rev. Biochem.* 2001, **70**, 777–810.
- Edman, P. & Begg, G. A protein sequenator. *Eur. J. Biochem.* 1967, **1**, 80–91.
- Eisenberg, D. The discovery of the α-helix and β-sheet, the principal structural features of proteins. *Proc. Natl. Acad. Sci. USA.* 2003, **100**, 11207–11210.
- Ellenberger, T. E., Brandl, C. J., Struhl, K. & Harrison, S. C. The GCN4 basic region leucine zipper binds DNA as a dimer of uninterrupted alpha helices: crystal structure of the protein-DNA complex. *Cell* 1992, **71**, 1223–1237.
- Ellis, R. J. Chaperone substrates inside the cell. *Trends Biochem. Sci.* 2000, **25**, 210–212.
- Elrod-Erickson, M., Benson, T. E., Pabo, C. O.: High-resolution structures of variant Zif268-DNA complexes: implications for understanding zinc finger-DNA recognition. *Structure* 1998, **6**, 451–464.
- Englander S. W., Mayne, L., Bai, Y. & Sosnick T. R. Hydrogen exchange: the modern legacy of Linderström-Lang. *Protein Sci.* 1997, **6**, 1101–1109.
- Englander, S. W. & Kallenbach, N. R. Hydrogen exchange and structural dynamics of proteins and nucleic acids. *Quart. Rev. Biophys.* 1984, **16**, 521–655.
- Evans, J. N. S. *Biomolecular NMR spectroscopy*. Oxford University Press. 1995.
- Evans, P. R. Structural aspects of allostery. *Curr. Opin. Struct. Biol.* 1991, **1**, 773–779.
- Farquhar, M. G. Progress in Unraveling Pathways of Golgi Traffic. *Annu. Rev. Cell Biol.* 1985, **1**, 447–488.
- Ferguson, M. A. J. & Williams, A. F. Cell surface anchoring of proteins via glycosyl-phosphatidylinositol structures. *Annu. Rev. Biochem.* 1988, **57**, 285–320.
- Ferre-D'Amare, A. R., Prendergast, G. C., Ziff, E. B., Burley, S. K. Recognition by Max of its cognate DNA through a dimeric b/HLH/Z domain. *Nature* 1993, **363**, 38–45.
- Ferrell, K. Wilkinson, C. R. M., Dubiel, W., & Gordon. C. Regulatory subunit interactions of the 26S proteasome, a complex problem *Trends Biochem. Sci.* 2000, **25**, 83–88.
- Fersht, A. R. Protein folding and stability: the pathway of folding of barnase. *FEBS Lett.* 1993, **325**, 5–16.
- Fersht, A. R., Knill-Jones, J. W., Bedouelle, H., & Winter G. Reconstruction by site-directed mutagenesis of the transition state for the activation of tyrosine by the tyrosyl-tRNA synthetase: A mobile loop envelopes the transition state in an induced-fit mechanism. *Biochemistry* 1988, **27**, 1581–1587.
- Fersht, A. R., Matouschek, A. & Serrano, L. Folding of an enzyme: Theory of protein engineering of stability and pathway of protein folding. *J. Mol. Biol.* 1992, **224**, 771–782, 783–804, 805–818, 819–835, 836–846, 847–859.
- Findlay, J. B. C. & Geisow, M. J. (eds) *Protein Sequencing. A practical approach* IRL press 1989.

- Fischmann, T. O., Bentley, G. A., Bhat, T. N., Boulout, G., Mariuzza, R. A., Phillips, S. E. V., Tello, D., & Poljak, R. J. Crystallographic Refinement of the Three-dimensional Structure of the FabD1.3-Lysozyme Complex at 2.5-Å Resolution. *J. Biol. Chem.* 1991, **266**, 12915–12920.
- Frankel, A. D. & Young, J. A. T. HIV-1: Fifteen Proteins and an RNA. *Annu. Rev. Biochem.* 1998, **67**, 1–25.
- Gesteland, R. F., Cech, T. R., & Atkins, J. F. *The RNA World*. Cold Spring Harbor Press, New York 1999.
- Gether, U. Uncovering Molecular Mechanisms Involved in Activation of G Protein-Coupled Receptors. *Endocrine Rev.* 2000, **21**, 90–113.
- Gething, M. J. & Sambrook, J. Protein folding in the cell. *Nature* 1992, **355**, 33–45.
- Glover, J. N., & Harrison, S. C., Crystal structure of the heterodimeric bZIP transcription factor *c-Fos c-Jun* bound to DNA. *Nature* 1995, **373**, 257–260.
- Gorlich, D. & Rapoport, T. A, Protein translocation into proteoliposomes reconstituted from purified components of the endoplasmic reticulum membrane. *Cell* 1993, **75** 615–630.
- Gould, K. L. & Nurse, P. Tyrosine phosphorylation of the fission yeast *cdc2*<sup>+</sup> protein kinase regulates entry into mitosis. *Nature* 1991, **342**, 39–45.
- Green, A. A., *J. Biol. Chem.* 95, **47**, 1932.
- Griffiths, W. J., Jonsson, A. P., Liu, S., Rai, D. K. & Wang, Y. Electrospray and tandem mass spectrometry in Biochemistry. *Biochem. J.* 2001, **355**, 545–561.
- Grigorieff, N., Ceska, T. A., Downing, K. H., Baldwin, J. M. & Henderson, R. Electron-crystallographic refinement of the structure of bacteriorhodopsin. *J. Mol. Biol.* 1996, **259**, 393–421.
- Guidotti, G. Membrane proteins. *Annu. Rev. Biochem.* 1972, **41**, 731–752.
- Guijarro, J. I. Guijarro, I., Sunde, M., Jones, J. A., Campbell, I. D. & Dobson, C. M. Amyloid fibril formation by an SH3 domain. *Proc. Natl. Acad. Sci. USA.* 1998, **95**, 4224–4228.
- Hames, B. D. & Rickwood, D. (Eds.), *Gel Electrophoresis of proteins. A Practical Approach* (2<sup>nd</sup> Ed). 1990 IRL press.
- Handford, P. A. Fibrillin-1, a calcium binding protein of extracellular matrix. *Biochim. Biophys. Acta*, 2000, **1498**, 84–90.
- Hansen, J. C., Lebowitz, J. & Demeler, B. Analytical ultracentrifugation of complex macromolecular systems. *Biochemistry* 1994, **33**, 13155–13163.
- Hartl F. U. & Hayer-Hartl, M. Molecular chaperones in the cytosol: from nascent chain to folded protein. *Science* 2002, **295**, 1852–1888.
- Hartl. F. U. Molecular chaperones in cellular protein folding *Nature* 1996, **381**, 571–580.
- Heijne, von G. Patterns of amino acids near signal cleavage sites. *Eur. J. Biochem.* 1983, **133**, 17–21.
- Henderson, R. & Unwin, P. N. T. Three-dimensional model of purple membrane obtained by electron microscopy. *Nature* 1975, **257**, 28–32.
- Henderson, R., Baldwin, J. M., Ceska, T. A., Zemlin, F., Beckmann, E. & Downing, K. H. Model for the Structure of Bacteriorhodopsin Based on High-Resolution Electron Cryo-microscopy. *J. Mol. Biol.* 1990, **231**, 899–929.
- Henikoff, S. & Henikoff, J. G. Amino acid substitution matrices from protein blocks. *Proc. Natl. Acad. Sci. USA* 1992, **89**, 10915–10919.
- Hensley, P. Defining the structure and stability of macromolecular assemblies in solution: the re-emergence of analytical ultracentrifugation as a practical tool. *Structure* 1996, **4**, 367–373. 1996.
- Hershko, A., & Ciechanover, A. The ubiquitin system. *Annu. Rev. Biochem.* 1998, **67**, 425–479.
- Hill, A. F., Desbruslais, M., Joiner, K., Sidle, C. L., Gowland, I., Collinge, J., Doey, L. J. & Lantos, P. The same prion strain cause nvCJD and BSE. *Nature* 1997, **389**, 448–450.
- Hochstrasser, M. Ubiquitin-dependent protein degradation. *Annu. Rev. Genet.* 1996, **30**, 405–439.
- Hofmeister, F. On the understanding of the effects of salts. *Arch. Exp. Pathol. Pharmacol. (Leipzig)* 1888, **24**, 247–260.
- Holley, R. W., Everett, G. A., Madison, J. T. & Zamir, A. Nucleotide sequences in yeast alanine transfer RNA. *J. Biol. Chem.*, 1965, **240**, 2122–2127.
- Homans, S. W. A dictionary of concepts in NMR. Oxford Science Publication. 1992.
- Hong, L., Turner, R. T., Koelsch, G., Shin, D., Ghosh, A. K. & Tang, J. Crystal Structure of Memapsin 2 (β-Secretase) in Complex with Inhibitor Om00-3 *Biochemistry* 2002, **41**, 10963–10967.
- Hubbard, S. R. & Till, J. R. Protein tyrosine kinase structure and function *Annu. Rev. Biochem.* 2000, **69**, 373–398.
- Huffman, J. L. & Brennan, R. G. Prokaryotic transcription regulators: more than just the helix-turn-helix motif. *Curr. Opin. Struct. Biol.* 2002, **12**, 98–106.
- Hunkapiller, M. W., Strickler, J. E., & Wilson, K. E. Contemporary methodology for protein structure determination. *Science* 1984, **226**, 304–311.
- Ingram, V. A case of sickle-cell anemia. *Biochem. Biophys. Acta* 1989, **1000**, 147–150.
- Iwata, S., *et al.* Complete structure of the 11-subunit bovine mitochondrial cytochrome bc<sub>1</sub> complex. *Science* 1998, **281**, 64–71.

- Iwata, S., Ostermeier, C., Ludwig, B., & Michel, H. Structure at 2.8 Å resolution of cytochrome c oxidase from *Paracoccus denitrificans*. *Nature* 1998, **376**, 660–669.
- Jackson, S. E. & Fersht, A. R. Folding of chymotrypsin inhibitor 2, 1: Evidence for a two-state transition. *Biochemistry* 1991, **30**, 10428–10435.
- Jeffrey, P. D., Russo, A. A., Polyak, K., Gibbs, E., Hurwitz, J., Massague, J. & Pavletich, N. P.: Mechanism of CDK activation revealed by the structure of a cyclinA-CDK2 complex. *Nature* 1995, **376**, 313–320.
- Jencks, W. P. Economies of enzyme catalysis. *Cold Spring Harbor Symp. Quant. Biol.* 1987, **52**, 65–73.
- Jimenez, J. L., Tennent, G., Pepys, M. & Saibil, H. R. Structural Diversity of *ex vivo* Amyloid Fibrils Studied by Cryo-electron Microscopy. *J. Mol. Biol.* 2001, **311**, 241–247.
- Johnson L. N. Jenkins J. A. Wilson K. S. Stura E. A. & Zanotti G. Proposals for the catalytic mechanism of glycogen phosphorylase b prompted by crystallographic studies on glucose 1-phosphate binding. *J. Mol. Biol.* 1980, **140**, 565–580.
- Johnson, W. C. Jr. Protein secondary structure and circular dichroism. A practical guide. *Proteins Struct. Funct. Genet.* 1990, **7**, 205–214.
- Jones, D. T., Taylor, W. R. & Thornton. J. M. The rapid generation of mutation data matrices from protein sequences. *Computer Applied Biosciences* 1992, **8**, 275–282.
- Jordan, P., Fromme, P., Witt, H. T., Klukas, O., Saenger, W., & Krauss, N. Three-dimensional structure of cyanobacterial photosystem I at 2.5 Å resolution. *Nature* 2001, **411**, 909–917.
- Kalies, K. -U. & Hartmann, E. Protein translocation into the endoplasmic reticulum (ER) Two similar routes with different modes. *Eur. J. Biochem.* 1998, **254**, 1–5.
- Karwaski, M. F., Wakarchuk, W. W. & Gilbert, M. High-level expression of recombinant *Neisseria* CMP-sialic acid synthetase in *Escherichia coli*. *Protein Expression and Purification* 2002, **25**, 237–240.
- Kauzmann, W. Some factors in the interpretation of protein denaturation. *Adv. Prot. Chem.* 1959, **14**, 1–63.
- Kay, L. E., Clore, G. M., Bax, A. & Gronenborn, A. M. Four-dimensional heteronuclear triple-resonance NMR spectroscopy of interleukin – 1β in solution. *Science* 1990, **249**, 411–414.
- Kay, L. E., D. Marion, D. & Bax, A. Practical aspects of three-dimensional heteronuclear NMR of proteins. *J. Magn. Reson.* 1989, **84**, 72–84.
- Kay, L. E., Ikura, M., Tschudin, R. & Bax, A. Three-dimensional triple resonance NMR spectroscopy of isotopically enriched proteins. *J. Magn. Reson.* 1990, **89**, 496–514.
- Keenan, R. J., Freymann, D. M., Stroud, R. M., & Walter, P. The signal recognition particle. *Annu. Rev. Biochem.* 2001, **70**, 755–775.
- Keleti, T. Two rules of enzyme kinetics for reversible Michaelis-Menten mechanisms. *FEBS Lett.* 1986, **208**, 109–112.
- Kelly, J. W. Alternative conformations of amyloidogenic proteins govern their behavior, *Curr. Opin. Struct. Biol.* 1996 **6**, 11–17.
- Kelly, J. W. Towards an understanding of amyloidosis. *Nature Struct. Biol.* 2002, **5**, 323–324.
- Kendrew, J. C., Bodo, G., Dintzis, H. M., Parrish, R. G., Wyckoff, H., and Phillips, D. C. A Three-Dimensional Model of the Myoglobin Molecule Obtained by X-ray Analysis. *Nature*, 1958, **181**, 662.
- Kim P. S. & Baldwin R. L. Intermediates in the Folding Reactions of Small Proteins *Annu Rev. Biochem.* 1990, **59**, 631–660.
- King, R. W., Deshaies, R. J., Peters, J. M. & Kirschner, M. W. How proteolysis drives the cell cycle. *Science* 1996, **274**, 1652–1659.
- Kirby, A. J. The lysozyme mechanism sorted – after 50 years. *Nat. Struct. Biol.* 2001, **8**, 737–739.
- Knoll, A. H. The early evolution of eukaryotes: A geological perspective, *Science* 1992, **256**, 622–627.
- Knowles, J. R. & Albery, W. J. Perfection in enzyme catalysis, the energetics of triose phosphate isomerase. *Acc. Chem. Res.* 1977, **10**, 105–111.
- Knowles, J. R. Tinkering with enzymes: what are we learning? *Science* 1987, **236**, 1252–1257.
- Kohlstaedt, L. A., Wang, J., Friedman, J. M., Rice, P. A. & Steitz, T. A. Crystal structure at 3.5 Å resolution of HIV-1 reverse transcriptase complexed with an inhibitor. *Science* 1992, **256**, 1783–1790.
- Kraut, J. How do enzymes work? *Science* 1988, **242**, 533–540.
- Kwong, P. D., Wyatt, R., Majeed, S., Robinson, J. Sweet, R. W., Sodroski, J. & Hendrickson, W. A. Structures of HIV-1 Gp120 Envelope Glycoproteins from Laboratory-Adapted and Primary Isolates. *Structure* 2000, **8**, 1329–133X.
- Kyte J., Doolittle R. F. A simple method for displaying the hydrophobic character of a protein. *J. Mol. Biol.* 1982, **157**, 105–132.
- Ladbury, J. E & Chowdhry, B. Z. (eds) *Biocalorimetry: Applications of Calorimetry in the Biological Sciences*. John Wiley & Sons Chichester 1998.
- Laemmli, U. K. Cleavage of structural proteins during the assembly of the head of bacteriophage T4. *Nature* 1970, **227**, 680–685.



- Lander, E. S. Linton, L. M., Birren, B. *et al.* International Human Genome Sequencing Consortium. Initial sequencing and analysis of the human genome. *Nature* 2001, **409**, 860–921.
- Lander, E. S. The new genomics: global view of biology. *Science* 1996, **274**, 536–539.
- Larrabee, J. A. & Choi, S. Fourier transform infrared spectroscopy. *Methods Enzymol.* 1993, **226**, 289–305, Academic Press.
- Lashuel, H. A., Lai, Z. & Kelly, J. W. Characterization of the transthyretin acid denaturation pathways by analytical ultracentrifugation: implications for wild-type, V30M, and L55P amyloid fibril formation, *Biochemistry* 1998, **37**, 17851–17864.
- Leatherbarrow, R. J., Fersht, A. R., & Winter, G. Transition-state stabilization in the mechanism of tyrosyl-tRNA synthetase revealed by protein engineering. *Proc. Natl. Acad. Sci. USA* 1985, **82**, 7840–7844.
- Lee, A. G. A calcium pump made visible. *Curr. Opin. Struct. Biol.* 2002, **12**, 547–554.
- Lemmon M. A., Flanagan J. M., Treutlein H. R., Zhang J., & Engelman D. M. Sequence specificity in the dimerization of transmembrane alpha-helices *Biochemistry* 1992, **31**, 12719–12725.
- Lin. L. N. & Brandts, J. F. Isomerization of proline-93 during the unfolding and refolding of ribonuclease A. *Biochemistry* 1983, **22**, 559–563.
- Lipschutz, R. J. & Fodor, S. P. A. Advanced DNA technologies. *Curr. Opin. Struct. Biol.* 1994, **4**, 376–380.
- Lipscomb, W. N. Aspartate Transcarbamylase from *Escherichia Coli*: Activity and Regulation *Adv. Enzymol.* 1994, **73**, 677–751.
- Ludwig, S., Pleschka, S., Planz, O., & Wolff, T. Influenza virus induced signalling cascades: targets for antiviral therapy? *Trends Mol. Medicine* 2003, **9**, 46–52.
- Luecke, H., Schobert, B., Richter, H. T., Cartailler, P. & Lanyi, J. K. Structure of bacteriorhodopsin at 1.55 Å resolution. *J. Mol. Biol.* 1999, **291**, 899–911.
- Luecke, H., Schobert, B., Richter, H. T., Cartailler, P. & Lanyi, J. K. Structural changes in bacteriorhodopsin during ion transport at 2 Å resolution. *Science* 1999, **286**, 255–260.
- Luong, C., Miller, A., Barnett, J., Chow J., Ramesha C., & Browner M. F. Flexibility of the NSAID binding site in the structure of human cyclooxygenase-2. *Nature Struct. Biol.* 1996, **3**, 927–933.
- Lupas, A. Coiled coils new structures and new functions. *Trends Biochem. Sci.* 1996, **21**, 375–382.
- Lynch, D. R. & Synder, S. H. Neuropeptides: multiple molecular forms, metabolic pathways and receptors. *Annu. Rev. Biochem.* 1986, **55**, 773–799.
- Malkin, D., Li, F. P., Strong, L. C., Fraumeni, J. F., Jr., Nelson, C. E., Kim, D. H., Kassel, J., Gryka, M. A., Bischoff, F. Z., Tainsky, M. A. & Friend, S. H. Germ line p53 mutations in a familial syndrome of breast cancer, sarcomas, and other neoplasms. *Science* 1990, **250**, 1233–1238.
- Mallucci, G. R., Ratte, S., Asante, E. A., Linehan, J., Gowlan, I., Jefferys, J. G. R., Collinge, J. Post-natal knockout of prion protein alters hippocampal CA1 properties, but does not result in neurodegeneration. *EMBO J.* 2002, **21**, 202–210.
- Mann, M., Hendrickson, R. C & Pandey, A. Analysis of proteins and proteomes by mass spectrometry. *Annu. Rev. Biochem.* 2001, **70**, 437–473.
- Margulis, L & Sagan, C. *What is Life.* Simon & Schuster. 1995.
- Marquart, M., Walter, J., Deisenhofer, J., Bode, W., & Huber, R. The Geometry of the Reactive Site and of the Peptide Groups in Trypsin, Trypsinogen and its Complexes with Inhibitors *Acta Crystallogr., Sect. B* 1983, **39**, 480–484.
- Martin, G. R., Timple, R., Muller, P. K. & Kuhn, K. The genetically distinct collagens. *Trends Biochem. Sci.* 1985, **10**, 285–287.
- Martoglio, B. & Dobberstein, B. Snapshots of membrane-translocating proteins. *Trends Cell Biol.* 1996, **6**, 142–147.
- Masters, C. L.; Simms, G.; Weinman, N. A.; Multhaup, G.; McDonald, B. L.; Beyreuther, K. Amyloid plaque core protein in Alzheimer disease and Down syndrome. *Proc. Nat. Acad. Sci. USA* 1985, **82**, 4245–4249.
- McPherson, A. *Crystallization of Biological Macromolecules.* Cold Spring Harbor Laboratory Press, 1999.
- McRee, D. E. *Practical Protein Crystallography.* 2<sup>nd</sup> edn. Academic Press. 1999.
- Meselson, M. & Stahl, F. The replication of DNA in *Escherichia coli.* *Proc. Natl Acad. Sci. USA* 1958, **44**, 671–682.
- Michel, H. Three dimensional crystals of a membrane protein complex. The photosynthetic reaction centre from *Rhodospseudomonas viridis.* *J. Mol. Biol.* 1982, **158**, 567–572.
- Miller, S. *Cold Spring Harbor Symp. Quant Biol.* 1988, **52**, 17–28.
- Miller, S. J. & Orgel, L. E. *The Origins of Life,* Prentice-Hall, New Jersey, 1975.
- Miranker, A., Radford, S. E., Karplus, M., & Dobson, C. M. Demonstration by NMR of Folding Domains in Lysozyme. *Nature*, 1991, **349**, 633–636.
- Miranker, A., Robinson, C. V., Radford, S. E., Aplin R. T., Dobson C. M. Detection of Transient Protein Folding Populations by Mass Spectrometry. *Science* 1993, **262**, 896–900.

- Moore, P. B. & Steitz, T. A. The structural basis of large ribosomal subunit function. *Annu. Rev. Biochem.* 2003, **72**, 813–850.
- Moore, P. B. The ribosome at atomic resolution. *Biochemistry* 2001, **40**, 3243–3250.
- Morgan, D. A. Cyclin dependant kinases: Engines, Clocks, and Microprocessors. *Ann Rev. Cell Dev. Biol.* 1997, **13**, 261–291.
- Morgan, D. G., Menetret, J. F., Neuhof, A., *et al*, Structure of the Mammalian Ribosome–Channel Complex at 17 Å Resolution. *J. Mol. Biol.* 2002, **324**, 871–886.
- Morimoto, R., Tissieres, A & Georgopoulos, C, (eds). *The biology of heat shock proteins and molecular chaperones*. Cold Spring Harbour Laboratory Press 1994.
- Morise, H., Shimomura, O., Johnson, F. H., & Winant, J. Intermolecular energy transfer in the bioluminescent system of *Aequorea*. *Biochemistry* 1974, **13**, 2656–2662.
- Mullan, M., Crawford, F., Axelman, K., Houlden, H., Lilius, L., Winblad, B. & Lannfelt, L. A pathogenic mutation for probable Alzheimer’s disease in the APP gene at the N-terminus of  $\beta$ -amyloid. *Nature Genet.* 1992, **1**, 345–347.
- Newman, M., Strzelecka, T., Dorner, L. F., Schildkraut, I. & Aggarwal, A. K. Structure of restriction endonuclease *Bam*HI and its relationship to *Eco*RI, *Nature* 1994, **368**, 660–664.
- Nikolov, D. B. & Burley, S. K. RNA polymerase II transcription initiation: A structural view. *Proc. Natl. Acad. Sci.* 1997, **94**, 15–22.
- Nissen, P., Hansen, J., Ban, N., Moore, P. B. & Steitz, T. A. The structural basis of ribosome activity in peptide bond synthesis. *Science* 2000, **289**, 920–930.
- Noel, J. P. Hamm, H. E. & Sigler, P. B. The 2.2 Å crystal structure of transducin- $\alpha$  complexed with GTP $\gamma$ S. *Nature* 1993, **366**, 654–658.
- Nogales, E., Wolf, S. G. & Downing, K. H. Structure of the  $\alpha\beta$ -tubulin dimer by electron crystallography. *Nature* 1998, **391**, 199–203.
- Nogales, E. Structural insight into microtubule function. *Annu. Rev. Biophys. Biomol. Struct.* 2001, **30**, 397–420.
- Noiva, R., & Lennarz, W. J. Protein Disulfide Isomerase – A Multifunctional Protein Resident in the Lumen of the Endoplasmic Reticulum. *J. Biol. Chem.* 1992, **267**, 3553–3556.
- Nugent, J. H. A. Oxygenic photosynthesis: electron transfer in photosystem I and photosystem II. *Eur. J. Biochem.* 1996, **237**, 519–531.
- Nurse, P. Genetic control of cell size at cell division in yeast. *Nature* 1975, **256**, 547–551.
- O’Farrell, P. H. High resolution two dimensional electrophoresis. *J. Biol. Chem.* 1975, **250**, 4007–4021.
- O’Shea, E. K. Rutkowski, R. & Kim, P. S., Evidence that the leucine zipper is a coiled coil. *Science* 1989, **243**, 538–542.
- Oliver, J., Jungnickel, B., Gorlich, D., Rapoport, T., & High S. The Sec61 complex is essential for the insertion of proteins into the membrane of the endoplasmic reticulum. *FEBS Lett.* 1995, **362**, 126–30.
- Onuchic, J. N., Wolynes, P. G., Luthey-Schulten, Z. & Socci, N. D. Towards an Outline of the Topography of a Realistic Protein-Folding Funnel. *Proc. Natl. Acad. Sci. USA* 1995, **92**, 3626–3630.
- Orengo, C. A., Michie, A. D., Jones, S., Jones, D. T., Swindells, M. B., & Thornton, J. M. CATH – A Hierarchic Classification of Protein Domain Structures. *Structure* 1997, **5**, 1093–1108.
- Orgel, L. E. Molecular replication. *Nature* 1992, **358**, 203–209.
- Orlov, E. V. & Saibil, H. R. Structure determination of macromolecular assemblies by single-particle analysis of cryo-electron micrographs. *Curr. Opin Struct. Biol.* 2004, **14**, 584–590.
- Pace, C. N. Conformational stability of proteins. *Trends Biochem. Sci.* 1990, **15**, 14–17.
- Pace, C. N., and Scholtz, J. M. A Helix Propensity Scale Based on Experimental Studies of Peptides and Proteins. *Biophys. J.* 1998, **75**, 422–427.
- Padlan, E. Anatomy of the Antibody Molecule. *Molecular Immunology* 1994, **31**, 169–178.
- Parry, D. A. D. The molecular and fibrillar structure of collagen and its relationship to the mechanical properties of connective tissue. *Biophys. Chem.* 1988, **29**, 195–209.
- Passner, J. M., Ryoo, H. D., Shen, L., Mann, R. S. & Aggarwal, A. K. Structure of a DNA-bound Ultrathorax-Extradenticle homeodomain complex. *Nature* 1999, **397**, 714–719.
- Pauling, L. & Corey, R. B. Atomic Coordinates and Structure Factors for Two Helical Configurations of Polypeptide Chains. *Proc. Natl. Acad. Sci. USA* 1951, **37**, 235–240.
- Perl, D. Welker, C., Schindler, T., Schroder, K., Marahiel, M. A., Jaenicke, R., and Schmid, F. X. Conservation of rapid two-state folding in mesophilic, thermophilic and hyperthermophilic cold shock proteins. *Nature Structural Biology* 2000, **7**, 380–383.
- Perutz, M. F., Rossmann, M. G., Cullis, A. F., Muirhead, H., Will, G. & North, A. C. T. Structure of haemoglobin. A three-dimensional Fourier synthesis at 5.5 Å resolution, obtained by X-ray analysis. *Nature* 1960, **185**, 416–422.
- Perutz, M. F., Wilkinson, A. J., Paoli, M., & Dodson, G. The stereochemical mechanism of cooperative effects in



- hemoglobin revisited. *Annu Rev. Biophys. Biomol. Structure* 1998, **27**, 1–34.
- Pfanner, N. & Neupert, W. The mitochondrial protein import apparatus. *Annu. Rev. Biochem.* 1990, **59**, 331–353.
- Phillips, M. A. & Fletterick, R. J. Proteases. *Cur. Opinion. Struct. Biol.* 1992, **2**, 713–720.
- Picot, D., Loll P. J., & Garavito R. M. The X-ray crystal structure of the membrane protein prostaglandin H2 synthase-1. *Nature* 1994, **367**, 243–249.
- Plaxco, K. W., Simons, K. T., & Baker, D. Contact order, transition state placement and the refolding rates of single domain proteins. *J. Mol. Biol.* 1998, **277**, 985–994.
- Pognard, P., Saphire, E. O., Parren, P. W. H. I. & Burton, D. R. GP120: Biologic Aspects of Structural Features. *Annu. Rev. Immunol.* 2001, **19**, 253–74.
- Ponder, J. W. & F. M. Richards. Tertiary templates for proteins. Use of packing criteria in the enumeration of allowed sequences for different structural classes. *J. Mol. Biol.* 1987, **193**, 775–791.
- Popot, J.-L. & Engelman, D. M. Helical membrane protein folding, stability and evolution *Annu. Rev. Biochem.* 2000, **69**, 881–922.
- Privalov, P. L. Stability of proteins: Small globular proteins. *Adv. Protein Chem.* 1979, **33**, 167–241.
- Privalov, P. L. & Gill, S. J. Stability of protein structure and hydrophobic interaction. *Adv. Prot. Chem.* 1988, **39**, 191–234.
- Prusiner, S. B., Novel proteinaceous infectious particles cause scrapie. *Science* 1982, **216**, 136–144.
- Radford, S. Protein folding: progress made and promise ahead. *Trends Biochem. Sci.* 2000, **25**, 611–618.
- Ramachandran, G. N. & Sasiskharan, V. Conformation of polypeptides and proteins. *Adv. Protein Chem.* 1968, **23**, 283–437.
- Ramakrishnan, V. & Moore, P. B. *Curr. Opin. Struct. Biol.* 2001, **11**, 144–154, 2001
- Rao, S. T. & Rossmann M. G. Comparison of super-secondary structure in protein *J. Mol. Biol.* 1973, **76**, 241–256.
- Rapoport, T. A., Jungnickel, B. & Kutay, U. Protein transport across the eukaryotic endoplasmic reticulum and bacterial inner membranes, *Annu. Rev. Biochem.* 1996, **65**, 271–303.
- Rappsilber, J. & Mann, M. What does it mean to identify a protein in proteomics? *Trend Biochem. Sci.* 2002, **27**, 74–78.
- Rath, V. L., Silvian, L. F., Beijer, B., Sproat, B. S., Steitz, T. A. How glutaminyl-tRNA synthetase selects glutamine. *Structure* 1997, **6**, 439–449.
- Rechsteiner, M. & Rogers, S. W. PEST sequences and regulation by proteolysis. *Trends Biochem. Sci.* 1996, **21**, 267–271.
- Riek, R., Hornemann, S., Wider, G., Billeter, M., Glockshuber, R. & Wüthrich, K. NMR structure of the mouse prion protein domain PrP (121–231). *Nature* 1996, **382**, 180–184.
- Roder, H., Elöve, G., & Englander, S. W. Structural characterization of folding intermediates in cytochrome c by H-exchange labeling and proton NMR. *Nature* 1888, **335**, 700–704.
- Roeder, R. G. The role of general initiation factors in transcription by RNA polymerase II. *Trends Biochem. Sci.* 1996, **21**, 327–335.
- Rose, G. N. Turns in peptides and proteins *Adv. Protein Chem.* 1985, **37**, 1–109.
- Rosenberg, J. M. Structure and function of restriction endonucleases. *Curr. Opin. Struct. Biol.* 1991, **1**, 104–113.
- Rould, M. A., Perona, J. J., Soll, D., & Steitz, T. A. Structure of E. coli glutaminyl-tRNA synthetase complexed with tRNA(Gln) and ATP at 2.8 Å resolution. *Science* 1989, **246**, 1135–1141.
- Rowland-Jones, S. L. AIDS pathogenesis: what have two decades of HIV research taught us? *Nature Rev. Immunol.* 2003, **3**, 343–348.
- Rupp, B., <http://www-structure.llnl.gov>.
- Russell, P. & Nurse, P. cdc25+ functions as an inducer in the mitotic control of fission yeast. *Cell* 1986, **45**, 145–153.
- Russo, A. A., *et al.* *Nat. Struct. Biol.* **3**, 696–XXX 1996
- Rutherford, A. W. & Faller, P. The heart of photosynthesis in glorious 3D. *Trends Biochem. Sci.* 2001, **26**, 341–344.
- Saibil, H. Molecular chaperones: containers and surfaces for folding, stabilizing or unfolding proteins. *Current Opinion in Struct. Biol.* 2000, **10**, 251–258.
- Sambrook, J. & Russell, D. *Molecular Cloning: A laboratory manual.* Cold Spring Harbor Laboratory Press, 2001
- Sambrook, J., Fritsch, E. F. & Maniatis, T. *Molecular Cloning.* Cold Spring Harbor Laboratory Press, 1989.
- Sanger, F. Sequences, sequences, sequences. *Annu. Rev. Biochem.* 1988, **57**, 1–28.
- Saraiva, M. J. M. Hereditary transthyretin amyloidosis: molecular basis and therapeutical strategies. *Expert Rev. Mol. Med.* 2002. <http://www.expertreviews.org/02004647h.htm>
- Schekman, R. Dissecting the membrane trafficking system. *Nature Medicine* 2002, **8**, 1055–1058.
- Schellman, J. A. The thermodynamic stability of proteins. *Ann. Rev. Biophys. Biophys. Chem.* 1987, **16**, 115–137.
- Schmid F. X., Mayr L. M., Mucke, M., & Schonbrunner, E. R. Prolyl isomerases: role in protein folding. *Adv. Prot. Chem.* 1993, **44**, 25–66.
- Schopf, J. W. Microfossils of the early Archaean Apex chert: New evidence of the antiquity of life. *Science* 1993, **260**, 640–646.

- Schramm, V. L. Enzyme transition states and transition state analog design. *Annu. Rev. Biochem.* 1998, **67**, 693–720.
- Schulz, G. E. Structure of porin refined at 1.8 Å resolution. *J. Mol. Biol.* 1992, **227**, 493–509.
- Schuster, T. M. & Toeddt, J. M. New revolutions in the evolution of analytical ultracentrifugation. *Curr. Opin. Struct. Biol.* 1996, **6**, 650–658.
- Scopes, R. *Protein purification: principles and practice.* Springer-Verlag, Berlin 1993.
- Selkoe, D. J. Amyloid β-protein and the genetics of Alzheimer's disease. *J. Biol. Chem.* 1996, **271**, 18295–18298.
- Shine, J. & Dalgarno, L. The 3' terminal sequence of *E. coli* 16S rRNA : Complementary to nonsense triplets and ribosome binding sites. *Proc. Natl. Acad. Sci USA* 1974, **71**, 1342–1346.
- Sidransky, D & Hollstein, M. Clinical implications of the p53 gene. *Annu. Rev. Med.* 1996, **47**, 285–30.
- Siebert, F. Infrared spectroscopy applied to biochemical and biological problems. *Methods Enzymol.* 1995, **246**, 501–526 Academic Press.
- Sigler, P. B., Xu, Z. Rye, H. S. Burston, S. G. , Fenton, W. A & Horwich, A. L. Structure and function in GroEL-mediated protein folding *Annu. Rev. Biochem.* 1998, **67**, 581–608.
- Silver, P. A. How proteins enter the nucleus. *Cell* 1991, **64**, 489–497.
- Silverman, G. A. *et al.* The Serpins Are an Expanding Superfamily of Structurally Similar but Functionally Diverse Proteins. *J. Biol. Chem.* 2001, **276**, 33293–33296.
- Simons K. T., Ruczinski, I., Kooperberg, C., Fox, B., Bystroff, C., & Baker, D. Improved Recognition of Native-like Protein Structures using a Combination of Sequence-dependent and Sequence-independent Features of Proteins. *Proteins* 1999, **34**, 82–95.
- Singer, S. J. The molecular organization of membranes. *Annu. Rev. Biochem.* 1974, 805–833.
- Singer, S. J. & Nicolson, G. The fluid mosaic model of the structure of cell membranes. *Science* 1972, **175**, 720–731.
- Skehel, J. J., Bayley, P. M., Brown, E. B., Martin, S. R., Waterfield, M. D., White, J. M., Wilson, I. A., and Wiley, D. C. Changes in the conformation of influenza virus haemagglutinin at the pH optimum of virus-mediated membrane fusion *Proc. Natl. Acad. Sci. USA* 1982, **79**, 968–972.
- Skehel, J. J. & Wiley, D. C. Receptor binding and membrane fusion in virus entry: the influenza haemagglutinin. *Annu. Rev. of Biochem.* 2000, **69**, 531–569.
- Smith, W. L., DeWitt, D. L. & Garavito, R. M. Cyclooxygenase: Structural, Cellular, and Molecular Biology *Annu. Rev. Biochem.* 2000, **69**, 145–182.
- Song, L., Hobaugh, M. R., Shustak, C., Cheley, S., Bayley, H., & Gouaux J. E. Structure of staphylococcal α-hemolysin, a heptameric transmembrane pore, *Science* 1996, **274**, 1859–1866.
- Steinhauer, D. A. & Skehel, J. J. Genetics of influenza viruses. *Annu. Rev. Genet.* 2002, **36**, 305–332.
- Steitz, T. A. & Schulman, R. G. Crystallographic and NMR studies of the serine proteases. *Annu. Rev. Biophys. Bioenerg.* 1982, **11**, 419–464.
- Stock, D., Gibbons, C., Arechaga, I., Leslie, A. G. W. & Walker, J. E. The rotary mechanism of ATP synthase. *Curr. Opin. Struct. Biol.* 2000, **10**, 672–679.
- Stock, D., Leslie, A. G. W., & Walker, J. E. Molecular Architecture of the Rotary Motor in ATP Synthase. *Science* 1999, **286**, 1700–1705.
- Stoeckenius, W. Bacterial rhodopsins: Evolution of a mechanistic model for the ion pumps *Prot. Sci.*, 1999, **8**, 447–459.
- Storey, A., Thomas, M., Kalita, A., Harwood, C., Gardiol, D., Mantovani, F., Breuer, J., Leigh, I. M., Matlashewski, G., & Banks, L. Role of a p53 polymorphism in the development of human papilloma-virus-associated cancer. *Nature* 1998, **393**, 229–234.
- Studier, F. W., Rosenberg, A. H., Dunn, J. J., & Dubendorff, J. W. Use of T7 RNA polymerase to direct expression of cloned genes. *Methods in Enzymology* 1990, **185**, 60–89, Academic Press.
- Sunde, M., Serpell, L. C., Bartlam, M., Fraser, P. E., Pepys, M. B., & Blake C. C. Common core structure of amyloid fibrils by synchrotron X-ray diffraction. *J. Mol. Biol.* 1997, **273**, 729–739.
- Tanford, C. The Hydrophobic Effect; formation of micelles and biological membranes. 2<sup>nd</sup> ed. Wiley 1980.
- Tarn W.-Y. & Steitz. J. A. Pre-mRNA splicing: the discovery of a new spliceosome doubles the challenge *Trends Biochem. Sci.* 1997, **22**, 132–137.
- Taylor, K. A. & Glaeser, R. M. Electron diffraction of frozen, hydrated protein crystals *Science* 1974, **186**, 1036–1037.
- Toyoshima, C., Nakasako, M., Nomura, H. & Ogawa, H. Crystal structure of the calcium pump of sarcoplasmic reticulum at 2.6 Å resolution. *Nature* 2000, **405** 647
- Trabi, M., & Craik, D. J. Circular proteins – no end in sight. *Trends Biochem. Sci.* 2002, **27**, 132–138.
- Tsukihara, T. Aoyama, H., Yamashita, E., Tomizaki, T., Yamaguchi, H., Shinzawa-Itoh, K., Nakashima, R., Yaono, R., & Yoshikawa, S. The whole structure of the 13-subunit oxidized cytochrome c oxidase at 2.8 Å. *Science*, 1996, **272**, 1136–1144.
- Tugarinov, V., Hwang, P. M. & Kay, L. E. Nuclear magnetic resonance spectroscopy of high-molecular weight proteins. *Annu. Rev. Biochem.* 2004, **73**, 107–146.

- Turner, B. G. & Summers, M. F. Structural biology of HIV. *J. Mol. Biol.* 1999, **285**, 1–32.
- Unger, V. M. Electron cryomicroscopy methods. *Curr. Opin. Struct. Biol.* 2001, **11**, 548–554.
- Vane, J. R. Inhibition of prostaglandin synthesis as a mechanism of action for the aspirin-like drugs. *Nature*, 1971, **231**, 232–235.
- Varghese, J. N., Colman, P. M., van Donkelaar, A., Blick, T. J., Sahasrabudhe, A., & McKimm-Breschkin, J. L. Structural evidence for a second sialic acid binding site in avian influenza virus neuraminidases. *Proc Natl Acad Sci USA* 1997, **94**, 11808–11812.
- Varghese, J. N., McKimm-Breschkin, J. L., Caldwell, J. B., Kortt, A. A. & Colman, P. M. The structure of the complex between influenza virus neuraminidase and sialic acid, the viral receptor. *Proteins* 1992, **14**, 327–332.
- Varghese, J. N. & Colman, P. M. Three-dimensional structure of the neuraminidase of influenza virus A/Tokyo/3/67 at 2.2 Å resolution. *J. Mol. Biol.* 1991, **221**, 473–486.
- Varghese, J. N., Laver, W. G. & Colman P. M. Structure of the influenza virus glycoprotein antigen neuraminidase at 2.9 Å resolution. *Nature* 1983, **303**, 35–40.
- Varshavsky, A., The ubiquitin system. *Trends Biochem. Sci.* 1997, **22**, 383–387.
- Verméglio, A & Joliot, P. The photosynthetic apparatus of *Rhodobacter sphaeroides* *Trends Microbiol.* 1999, **7**, 435–440.
- Viadiu, H., & Aggarwal, A. K. The role of metals in catalysis by the restriction endonuclease BamHI. *Nat. Struct. Biol.* 1998, **5**, 910–6.
- Vogelstein, B., Lane, D. & Levine, A. J. Surfing the p53 network. *Nature* 2000, **408**, 307–310.
- Voges, D., Zwickl, P. & Baumeister, W. The 26S proteasome: a molecular machine designed for controlled proteolysis *Annu. Rev. Biochem.* 1998, **68**, 1015–1068.
- Voos, W. Martin, H., Krimmer, T. & Pfanner, N., Mechanisms of protein translocation into mitochondria *Biochim. Biophys. Acta*, 1999, **1422**, 235–254.
- Walter, P. & Johnson, A. E. Signal sequence recognition and protein targeting to the endoplasmic reticulum membrane. *Annu. Rev. Cell Biol.* 1995, **10**, 87–119.
- Wang, J., Smerdon, S. J., Jager, J., Kohlstaedt, L. A., Rice, P. A., Friedman, J. M., Steitz, T. A. Structural basis of asymmetry in the human immunodeficiency virus type 1 reverse transcriptase heterodimer. *Proc Natl Acad Sci USA* 1994, **91**, 7242–7246.
- Wang, Y. & van Wart, H. E. Raman and resonance Raman spectroscopy *Methods Enzymol.* 1993, **226**, 319–373, Academic Press.
- Warren, A. J. Eukaryotic transcription factors. *Curr. Opin. Struct. Biol.* 2002, **12**, 107–114.
- Watson J. D. & Crick. F. H. C. Molecular structure of nucleic acids: a structure for deoxyribose nucleic acid. *Nature* 1953, **171**, 737–738.
- Weis, W., Brown, J. H., Cusack, S., Paulson, J. C., Skehel, J. J., & Wiley, D. C. Structure of the influenza virus haemagglutinin complexed with its receptor, sialic acid *Nature* 1988, **333**, 426–431.
- Weis. K. Importins and exportins: how to get in and out of the nucleus *Trends Biochem. Sci.* 1998, **23**, 185–189.
- Weiss M. S., Olson, R., Nariya, H., Yokota, K., Kamio, Y., & Gouaux, E. Crystal structure of Staphylococcal Lukf delineates conformational changes accompanying formation of a transmembrane channel. *Nat. Struct. Biol.* 1999, **6**, 134–140.
- Weissmann, C., Enari, M., Klöhn, P.-C., Rossi, D. & E. Flechsig. E. Transmission of prions. *Proc. Natl. Acad. Sci. USA* 2002, **99**, 16378–16383.
- Weissmann, C., Molecular Genetics of Transmissible Spongiform Encephalopathies. *J. Biol. Chem.* 1999, **274**, 3–6.
- Wetlaufer, D. B. Ultraviolet spectra of proteins and amino acids. *Adv. Prot. Chem.* 1962, **17**, 303–390.
- White, S. H. & Wimley, W. C. Membrane protein folding and stability: Physical principles. *Ann. Rev. Biophys. Biomol. Struct.* 1999, **28**, 319–6.
- Wiley D. C., & Skehel J. J. The structure and function of the haemagglutinin membrane glycoprotein of influenza virus. *Annu. Rev. Biochem.* 1987, **56**, 365–94.
- Wilmot, C. M. & Thornton, J. M. Analysis and prediction of the different types of beta-turn in proteins. *J. Mol. Biol.* 1988, **203**, 221–232.
- Wimberley, B. T., Brodersen, D., Clemons, W., Morgan-Warren, R., Carter, A., Vornrhein, C., Hartsch, T. & Ramakrishnan, V. Structure of the 30S Ribosomal Subunit. *Nature* 2000, **407**, 327–339.
- Wimley, W. C. The versatile  $\beta$ -barrel membrane protein *Curr. Opin. Struct. Biol.* 2003, **13**, 404–411.
- Wlodawer. A. & Erickson, J. W. Structure based inhibitors of HIV-1 proteinase. *Annu. Rev. Biochem.* 1993, **62**, 543–585.
- Woody, R. W. Circular dichroism. *Methods Enzymol.* 1995, **246**, 34–71, Academic Press.
- Wower, J. Rosen, K. V., Hixson, S. S. & Zimmermann, R. A. Recombinant photoreactive tRNA molecules as probes for cross-linking studies. *Biochimie* 1994, **76**, 1235–1246.
- Wuthrich, K. NMR of Proteins and Nucleic Acids. John Wiley & Sons. 1984.
- Xu, Z., Horwich A. L., & Sigler P. B. The crystal structure of the asymmetric GroEL-GroES-(ADP)<sub>7</sub> chaperonin complex. *Nature*. 1997, **388**, 741–750.
- Yates. J. R. Mass spectrometry: from genomics to proteomics. *Trends Genet.* 2000, **16**, 5–8.

- Yoshida, M., Muneyuki, E., & Hisabori, T. ATP synthase—a marvellous rotary engine of the cell. *Nat. Rev. Mol. Cell Biol.* 2001, **2**, 669–77.
- Yoshikawa, S. Beef heart cytochrome oxidase. *Curr. Opin. Struct. Biol.* 1997, **7**, 574–579.
- Zahn, R., Liu, A., Luhrs, T., Riek, R., von Schroetter, C., López García, F., Billeter, M., Calzolari, L., Wider, G. & Wüthrich, K. NMR solution structure of the human prion protein. *Proc. Natl. Acad. Sci USA* 2000, **97**, 145–150.
- Zhang, D., Kiyatkin, A., Bolin, J. T. & Low, P. S. Crystallographic Structure and Functional Interpretation of the Cytoplasmic Domain of Erythrocyte Membrane Band 3. *Blood* 2000, **96**, 2925–2933.
- Zouni, A., Horst-Tobias, W., Kern, J., Fromme, P., Krauss, N., Saenger, W., & Orth, P. Crystal structure of photosystem II from *Synechococcus elongatus* at 3.8 Å resolution. *Nature* 2001, **409**, 739–743.

# 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;  $\beta$  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.

- A site, 273  
A $\beta$  protein, 430, 468–470  
AAA superfamily, 308  
*Ab intio*, 186  
Abrin, 228  
Absorbance, 379–381  
  aromatic amino acids, 381  
  Beer-Lambert's Law, 32  
  data on aromatic amino acids, 30  
  excitation and emission, 380  
  heme groups, 67  
  spin multiplicity, **380**  
  vibrational states, 380  
  wavenumber, 381  
Acetazolamide, 205  
Acetylation, 270, 292  
Acetylcholinesterase, **191**  
  specificity constant, **201**  
Acid base catalysis, 203–204  
Acid base properties of amino acids,  
  14–15  
Acquired immune deficiency syndrome,  
  443–457  
  recognition and identification, 443  
Acrylamide, 335, 381  
Activated state (complex), 196  
Activation energy, 195–196  
Active site  
  Gln-tRNA synthetase, 221  
  lysozyme, 210  
  serine proteases, 212  
  triose phosphate isomerase, 216  
  tyrosyl tRNA synthetase, 219  
Acyl chains, **107**  
  unsaturation, 106  
Acyl-enzyme intermediate, 214  
Adenine, 247  
  A76, 269–270  
  A2451, 279  
  A2439, 279  
  A2486, 282  
Adenosine monophosphate  
  pK of N1 atom, 280  
  structure of AMP, 282  
Adenosine triphosphate, synthesis  
  allosteric activation, 234  
  transition state analogue, 148  
Adenylate cyclase, 116–117, 439–440  
  signaling pathway, 120  
Adenylation, 292  
5-adenyl-imidophosphate, 148  
Adiabatic chamber, 399  
Adrenaline, 116  
*Aequorea victoria*, 383–384  
Aerobic, 126  
Affinity chromatography, 332–334  
  types of ligands, **334**  
Affinity labeling, 216, 279  
Aggregation, 416–417  
  in disease states, 427–428  
Agonists, 116  
AIDS, *see* Acquired immune deficiency  
  syndrome  
Alanine  
  chemical properties, 24  
  D isomer, 35  
  data, **18**  
  genetic code specification, 268  
  helix/sheet propensity, **41**  
  hydropathy index, **112**  
  optical rotation, **34**  
  prevalence in secondary structure,  
    **180**  
  spatial arrangement of atoms, 16  
  stereoisomers, 34  
  titration curve, 14  
Albumin, 1, 33  
Aldol condensation, 97  
Alignment methods, 172–173  
Aliphatic amino acids, 24  
Alkaline phosphatase, 207, 339  
Allele, 475, 476  
Allosteric regulation, 72–74, 231–237  
Allostery, 189  
Allysine, 97  
 $\alpha$  helix, 41–45  
  dihedral angles, 43  
  dimensions, **43**  
  dipole moment, 56  
  formation, 409  
  hydrogen bonding, 41–43  
  side chains, 42–43  
  space-filling view, 4  
  structure, 42  
 $\alpha$ -secretase, 469  
 $\alpha_1$ -antitrypsin, 475–478  
 $\alpha$ -haemolysin, 130–131  
Alveoli, 475  
Alzheimer's disease, 422, 427, 430,  
  468–470  
  diagnostic markers, 468  
  genetic basis, 468–470  
Amidation, 292  
Amide exchange, 411–412  
Amide, 25–26, 43, **56**  
Amino acid residue, 17  
Amino acids  
  acid-base properties, 14–15  
  chemical and physical properties, 23–32  
  detection of, 32–34  
  formation of peptide bonds, 16–17  
  genetic code specification, 268  
  non-standard, 35–36  
  optical rotation, **34**



- Amino acids (*continued*)  
 pK values for ionizable groups, **15**  
 quantification, 34  
 reaction with tRNA,  
 single letter codes, 40  
 solubility, 13  
 stereochemical representation, 15  
 stereoisomerism, 34–35  
 three letter codes, 40
- Amino acyl AMP, 268
- Amino acyl tRNA synthetases, 218,  
 268–269  
 catalysis, 268  
 class I and class II tRNA synthetases, **220**  
 classification, **220**, **269**  
 glutamyl tRNA synthetase, 220–221  
 transition state analogue, 221  
 tyrosyl tRNA synthetase, 218–220
- AMP, *see* Adenosine monophosphate,
- Amphiphiles, 122
- Ampicillin, 315
- Amplification (PCR), 169–170
- Amplitude, 353–354
- AMP-PNP, *see* 5-adenylyl-imidophosphate
- Amyloid precursor protein, 469
- Amyloid, 427  
 structure of fibril, 431  
 plaques, 468
- Amyloidogenesis, 427–431  
 diseases arising from, **428**  
 involving transthyretin, 428–430  
 prion based, 431–435
- Anacystis sp.*, 164
- Analytical centrifugation, 322–323
- Anfinsen cage, 420
- Anfinsen, C., 402, 416, 423
- Angiotensin, 287
- Angstrom, **18**
- Angstrom, A.J., 478
- Anisotropy, 383
- Ankyrin, 111
- Anoxygenic photosynthesis, 128
- Antagonists, 116
- Antechambers, 306
- Antibiotics, 278–279,  
 selection of transformants, 315  
 studying ribosomal structure, 279
- Antibody, 75–80 *see* immunoglobulins
- Anticodon loop, 268–269
- Anticodon, 283
- Antigen, 75  
 flu virus antigens, 464
- Antigenic determinants, 77
- Antigenic drift, 464
- Antigenic shift, 464
- Antigenic sub-types, 465
- Antimycin A, 134
- Antiport, 154
- Apoenzyme, 192
- Apoptosis, 238–239, 310, 471
- APP *see* amyloid precursor protein,  
 468–469
- Aquaporin, 377
- Arabidopsis thaliana*, 169
- Arachidonic acid, **107**, 229–230
- Arber, W., 221
- Archae, 128, 304, 309, 417, 422
- Archaeobacteria *see* archae
- Arginine  
 charge-charge interactions, 55–56  
 chemical properties, 28–29  
 data, **18**  
 genetic code specification, 268  
 helix/sheet propensity, **41**  
 hydrophathy index, **112**  
 optical rotation, **34**  
 prevalence in secondary structure, **180**  
 trypsin substrate, 227
- Armadillo motifs, 301
- Aromatic amino acids,  
 Aromatic residues, 30
- Arrhenius equation, 195
- Arrhenius, S.A., 195
- Arylation, 29
- Ascorbate, 289
- Asparagine chemical properties, 25  
 data, **18**  
 helix/sheet propensity, **41**  
 hydrophathy index, **112**  
 genetic code specification, 268  
 prevalence in secondary structure, **180**  
 location in turns, 47–48  
 N linked glycosylation, 98, 290
- Aspartate  
 binding domain in ATCase, 236  
 chemical properties, 25  
 data, **18**  
 genetic code specification, 268  
 helix/sheet propensity, **41**  
 hydrophathy index, **112**  
 in HIV protease, 450–452  
 in lysozyme catalysis, 211–212  
 in T7 RNA polymerase, 256  
 prevalence in secondary structure, **180**
- Aspartate transcarbamoylase, 6, 234–237  
 allosteric behaviour, 234  
 binding of carbamoyl phosphate, 234  
 conformational change, 237  
 feedback inhibition, 235  
 quaternary structure, 235
- Aspartic acid *see* aspartate
- Aspartyl protease, 450–452, 470
- Aspirin, 228–230
- AspN, 166
- Astbury, W.T., 92
- Astrocytosis, 434
- Asymmetric centres, 37
- Ataxia, 433
- Atherosclerosis, 99
- ATP synthase, *see* ATP synthetase
- ATP synthetase, 132, 144–152, 173  
 Boyer model, 146  
 chemical modification, 146, 151  
 composition, **145**  
 conformational changes in, 146–148  
 cooperativity, 146  
 $\gamma$  subunit, 150  
 mechanism of ATP synthesis, 146–147  
 nucleotide binding site, 149  
 proton translocation, 149  
 structure of F<sub>1</sub> ATPase, 147–151  
 structure of F<sub>0</sub>, 150–152  
 yeast enzyme, 156
- ATP, *see* adenosine triphosphate
- ATPase family, 152–156, 308
- Autolysis, 238, 449
- Aval, 222
- 3'-azido-3-deoxythymidine, *see* AZT
- AZT, 453
- Azurin, 359
- B cells, 75
- BACE, *see*  $\beta$  secretase
- Bacillus caldolyticus*, 397–398
- Bacillus subtilis*, 397–398
- Bacterial reaction centre, 119–126  
 crystallization, 123  
 cytochrome subunit, 125  
 electron transfer, 121–122  
 transmembrane helices, **125**
- Bacteriochlorophyll, 121  
 protein crystallization of, 359
- Bacteriophage  $\lambda$ , 64  
 defective groE operon, 416
- Bacteriophage T4, 266
- Bacteriophage T7, 256
- Bacteriorhodopsin, 114–115  
 light driven pump, 115  
 protein folding, 422–425  
 structure, 117  
 transmembrane organization, 116
- Baldwin, R., 414
- BamHI, 222  
 signature sequence, 224
- Band 3 protein, 111
- Barnase, 405–408
- Beer Lamberts Law, quantification of amino  
 acids, 32
- Benzamidine, 227
- Benzene, 55
- Benzopyrene, 454
- Bernal, J.D., 353
- Berzelius, J. J., 1
- $\beta$  adrenergic receptor, 117
- $\beta$  barrel, 47, 180  
 GFP, 383  
 gp120 454–455  
 Gro-ES, 417  
 $\alpha$ -haemolysin, 130–131



- ODCase, 205  
 porins, 128–132  
   triose phosphate isomerase, 47  
 $\beta$  blocker, 116  
 $\beta$  endorphin, 289  
 $\beta$  helix, 61–62, 430–431  
 $\beta$  lactamase, 181  
 $\beta$  lipotrophin, 289  
 $\beta$  meander, 59, 61, 222  
 $\beta$  propeller motif, 61, 180, 463  
 $\beta$  sandwich, 59, 180  
   gp120, 454–455  
   p53, 472  
 $\beta$  scaffold, 430  
 $\beta$  secretase, 469–470  
 $\beta$  sheet, 45–47  
 $\beta$  strand, 45–46  
   dimensions, **43**  
 $\beta$  turn, 47  
 $\beta$ -*N*-oxalyl L- $\alpha$ ,  $\beta$ -diamino propionic acid, 36  
 B factor, 357  
 Bilayers, 107–109  
 Bimolecular reactions, 194–195, 208, 382  
 Bioinformatics, 50, 184–187  
 Biotin, 193  
 2,3-bisphosphoglycerate, 73, 74  
 Bisacrylamide, 335  
 Biuret, 33  
 Blobel, G., 293  
 Bloch, F., 360  
 BLOCKS database, 175  
 Blood clotting cascade, 237, 239  
 Blood clotting factors, 318, 239  
 BLOSUM, 175  
 Blue green algae, 126  
 Boat conformation, 211  
 Bohr effect, 74  
 Bohr, C., 74  
 Boltzmann distribution, 380  
 Boltzmann's constant, 196, 323  
*Bombyx mori*, 92, 93  
*Bordetella pertussis*, 440  
 Bovine pancreatic trypsin inhibitor, 53, 224, 468  
 Bovine serum albumin, 33  
 Bovine spongiform encephalopathy, 466–468  
 Boyer, P.D., 146  
 BPTI, *see* Bovine pancreatic trypsin inhibitor  
 Bragg, W.H., 349  
 Bragg, W.L., 349  
 Branch point, 266  
 Brandts, J.F., 414  
 Bravais Lattices, 352  
 Brenner, S., 266  
 Briggs, G.E., 199  
 Bromelain, 459, 460  
 Bromoaspirin, 228  
 Brønsted equation, 407  
 Brownian diffusion, 320, 382  
 Browsers, 185  
 BSA, *see* bovine serum albumin  
 BSE, *see* bovine spongiform encephalopathy  
 Buchner, E., 2, 189  
 Buoyant density, 320  
 Burley, S.K., 259  
 Burnet, M., 75  
 Bursa of Fabricius, 75  
 C peptide, 456  
*Caenorhabditis elegans*, collagen genes, 93  
   genome, 169  
 Cahn Ingold Prelog, 34  
 Calcium binding domains, 101, 415  
 Calmodulin, 25  
 Calorimetry, 109  
   differential scanning, 399–400  
 Canavanine, 36  
 Cancer, 11, 441  
   cdk-cyclin complex regulation, 252–253  
   cervical, 475  
   involvement of p53, **474**  
   Kaposi's sarcoma, 445  
 Cannibalism, 433  
 Capsid, 377  
   TMV, 443  
   HIV, 445, 446  
   p17, 446–447  
 Carbamoyl phosphate, 234  
 Carbonic anhydrase, 74, **179**  
   catalysis by, 204–207  
   imidazole ligands in active site, 206  
   pH dependent catalysis, 205  
   specificity constant, **201**  
 Carboxypeptidase A, 25, 192, 193  
 Cardiac glycosides, 154  
 Cargo proteins, 300  
 Carotenoids, 121  
 Cartoon representation, 13, 46  
 Cascade, 237, 239  
 CASP, 186  
 Caspases, 238–239, 310  
 Catabolism, 189  
 Catalase, sedimentation coefficient, 324  
   specificity constant, **201**  
 Catalysts, 197  
 Catalytic mechanisms, 202–209  
   acid-base catalysis, 202–203  
   covalent catalysis, 203  
   electrostatic catalysis, 205  
   metal ion catalysis, 204–205  
   preferential binding of transition state, 207–209  
   proximity and orientation effects, 206–207  
   rate enhancements, 197  
 Catalytic triad, 213  
 CBCA(CO)NH, 373  
 CBCANH, 373  
 CCD, *see* charge coupled device  
 CCK motif, 81  
 CCM, *see* common core motif  
 CD4, 446  
 cdc genes, 249  
 Cdks *see* Cyclin dependant kinases,  
 Celebrex<sup>®</sup> 231  
 Cell cycle, 247–250  
   DNA replication, 253  
   mitosis, 247  
 Cell disruption, 319  
 Cell division, 249, 253  
 Cell membrane, 110  
 Centrifugation, 320–323,  
 Chair conformation, 211  
 Chaotropes, 326  
 Chaperones, 416–422  
   catalytic cycle, 419–422  
   crystal structure, 420  
   domain movements, 418  
   electron microscopy, 417–419  
   GroEL-GroES, 417–422  
   mitochondrial, 297–298  
   organization, 418  
   small heat shock proteins, 417  
   thermosome, 422  
 Chaperonin, 416  
 Charge coupled devices, 170, 349  
 Charge-charge interactions, 55–56  
 Checkpoints, 249  
 Chemical kinetics, 192–195  
 Chemical modification, 29, 205  
   in RNase A, 202  
 Chemical shift, 362  
   table of <sup>13</sup>C chemical shifts, 372  
   table of <sup>15</sup>N chemical shifts, 371  
   table of <sup>1</sup>H chemical shifts, 366  
 Chemiosmosis, 145  
 Chevron plot, 405  
    $\chi$  angle, 43  
 Chiral, 19, 34–35  
 Chitinase, 319  
 Chloroamphenicol, 278, 279  
 Chlorophyll, 121  
   in photosystem II, 127  
   special pair, 125  
   voyeur, 125  
 Chloroplast  
   lipid:protein ratios, 109  
   RNA polymerases, **257**  
   schematic diagram, 299  
   sorting and targeting, 299  
   stromal proteins, 299  
   Tic system, 299  
   Toc complexes, 299  
 Cholera toxin, 120, 439–440

- Cholera, 439
- Chou, P.Y., 182
- Chou-Fasman algorithm, 183–184
- Chromatography, 326–333
  - affinity, 332–333
  - cation exchange, 167,
  - gel filtration principle, 330
  - hydrophobic interaction, 331
  - ideal separation, 327
  - ion exchange, 329–330
  - molecular mass estimation, 331
  - protein hydrolysate, 167
  - reverse phase, 331–332
  - size exclusion, 330–331
  - system and instrumentation, 328
- Chromophore, 33, 121
- Chromosome, 247
- Chronic obstructive pulmonary disease, (COPD) 475
- Chymotrypsin, 46, 287
  - active site substrate specificity, 212
  - arrangement of catalytic triad, 213
  - hydrolysis of esters, 201
  - inhibitor, 406
  - PDB file, 51
  - proteolytic activation, 237–238
  - structural homology, 177, 179
  - TPCK binding, 213
- cI repressor, 64
- CIP family, 252
- circe effect, 205
- Circular dichroism, 385–387
  - folding of bacteriorhodopsin, 423
  - folding of OmpA, 424
  - for studying protein folding, 404, 409
  - magnetic circular dichroism, 387
  - spectra, 387
- cis* isomer
- cis* ring, 418, 419
- Cis-trans peptidyl proline isomerase, 59
  - in protein folding, 415–416
  - parvulins, 416
  - FK506 binding proteins, 416
- Citric acid cycle, 190
- Citrulline, 38
- CJD *see* Creutzfeldt Jacob disease
- Clathrates, 54
- Clathrin coated vesicles, 297
- Cleland's reagent, *see also* dithiothreitol, 28
- Cloning, 314–316
- Clostridium, 166
- Cloverleaf structure, 268, 269
- CMC, *see* critical micelle concentration
- Cobalt, 193
- Codon, 268,
- Coelenterazine, 383
- Coenzyme Q, 193, *see also* ubiquinone
- Co-factors, 192–193
- Coiled coil, 86–90
  - ATP synthetase, 147, 150
  - gp41 of HIV, 456
  - haemagglutinin, 456
  - non-keratin based motifs, 90
  - parallel and antiparallel coils, 87
- Cold shock proteins, 398
- Collagen, 92–100
  - abundance, 93
  - biosynthesis, 97–99
  - connective tissue, 93
  - dimensions, 94
  - disease states associated with, 99–100
  - genes, 93
  - hydroxylation, 289
  - processing, 98
  - procollagen, 289
  - related disorders, 100–102
  - structure and function, 94–97
  - thermal denaturation, 96
  - triple helix, 95
  - types, 94
- Common core motif, 222
- Competent cells, 315
- Competitive enzyme inhibition, 225–226, 453
- Complementarity determining regions (CDRs), 77
- Complex I, *see* NADH-ubiquinone oxidoreductase
- Complex II, *see* succinate dehydrogenase
- Complex III, *see* cytochrome bc<sub>1</sub> complex
- Complex IV, *see* cytochrome oxidase
- Conformational stability, 396–404
  - estimations from ideal denaturation curves, 401
  - linear extrapolation method, 402
  - table of selected proteins, 402
- Connective tissue disorders,
- Conotoxins, 178
- Conserved residues, 172
- Contact order, 410
- Conus, 178
- Convergent evolution, 179
- Coomassie Blue, 33, 336
- Cooperative binding curve, 69–70, 396
- Cooperativity, 70,
- Copper, 7
  - binuclear cluster, 139
  - co-factor role, 193
- Correlation time, 363
- Coulomb's Law, 55
- Coupling constants, 363
- Covalent catalysis, 204
- Covalent modification, 237–241
- Cowpox, 75
- Cox, G.B., 146
- COX-1, *see also* cyclo-oxygenases, 230
- COX-2, *see also* cyclo-oxygenases, 230
- CPK models, 13
- Creutzfeldt, H.G., 433
- Creutzfeldt-Jakob disease, 433
- Crick, F.H.C., 2, 87, 247, 266, 267
- Critical micelle concentration, 107–108
- Cro repressor, 66
- Crowther, R.A., 377
- Cryoelectron microscopy, 375–379
  - amyloid fibril structure, 430–431
  - ATP synthetase, 149
  - hepatitis B capsid, 377
  - instrumentation, 376
  - proteasome, 308, 309, 418
  - ribosome, 271
  - sample preparation, 376–377
  - tubulin structure, 377–379
- Crystal lattices, 352
- Crystal violet, 319
- Crystallization, 358–360
- Crystallography, 349–360
- Cu, 9
  - centres in cytochrome oxidase, 138
- Cyanide, 228
- Cyanobacteria, 126, 164
- Cyanogen bromide, 26
- Cyclic AMP, 439–440
  - in signaling, 116–119
- Cyclic GMP, 118
- Cyclic nucleotides, 202
- Cyclic proteins, 81
- Cyclin dependant kinases, 249–253
  - ATP binding, 251
  - conformational changes, 251–252
  - inhibitors, 252
  - interaction with p53, 471
  - regulation, 252
  - structure and function, 250–253
  - T loop activation, 251–252
- Cyclins, 248–249
  - binding with cdk, 251–252
  - conformational changes, 251–252
  - cyclin boxes, 249
  - cyclin-cdk complexes in cell cycle, 250
  - regulation, 252
  - tertiary structure, 252
  - threonine phosphorylation, 252
- Cyclohexane, 53
- Cyclo-oxygenases, 228–230
  - active site, 230
  - tertiary structure, 229
  - isoforms, 230
- Cyclophilin, 416
- Cyclosporin A, 81, 416
- Cyclotides, 81
- Cysteine
  - active site of *caspases*, 310
  - chemical properties, 26–28
  - data, 19
  - genetic code specification, 268
  - helix/sheet propensity, 41
  - hydrophathy index, 112

- ligands in Zn fingers, 261, 263  
location in turns, 47  
optical rotation, **34**  
prevalence in secondary structure, **180**  
reaction with Ellman's reagent, 28
- Cystic Fibrosis, 9, 426–427
- Cytochrome b, 132–137  
absorbance maxima, 133  
ligands, 137  
redox potential, 133  
separation distances, 137  
subunit mass, **137**
- Cytochrome b<sub>5</sub>, 58, 60, **173**, 181, 401
- Cytochrome b<sub>562</sub>, 59
- Cytochrome bc complex, *see* cytochrome bc<sub>1</sub> complex
- Cytochrome bc<sub>1</sub> complex, 132–137  
crystal structure, 136  
cytochrome c<sub>1</sub>, 136  
cytochrome b, 137  
electron transfer reactions, 135  
gating, 137  
inhibitor binding studies, 133–134  
Q cycle in, 135  
Reiske protein, 133, 136  
subunit composition, **137** subunit mass, **137**  
ubiquinone, 134
- Cytochrome c  
prokaryotic, 176  
sequence homology, 175  
sorting pathway, 299  
structural homology, 176
- Cytochrome c<sub>1</sub>, 132–137  
orientation, 136  
signal sequence, 299  
sorting pathway, 299  
subunit mass, **137**
- Cytochrome oxidase, 138–144  
catalytic cycle, 138–139  
channels, 144  
Cu<sub>A</sub> centre, 139  
Cu<sub>B</sub> center, 140  
enzyme from *P.denitrificans*, **141**  
isoforms, 141  
mammalian enzyme, 140–141  
mitochondrial coded subunits, 139  
monomeric core, 141  
oxygen binding site, 143  
proton pump, 142–143  
subunit structure, **141**
- Cytochrome P450, 241
- Cytosine, 247
- Cytoskeleton, 111  
role of tubulin, 377
- Cytotoxic T lymphocytes, 79
- D amino acids, 34, 36, 321
- Dansyl chloride, 33, 167
- Databases, **184**
- Dayhoff, M.O., 174
- ddATP, 171
- ddCTP, 171
- ddGTP, 171
- ddl, 453
- ddTTP, 171
- Deamidation, 25
- Death effector domains, 239
- Debye, P., 325
- Debye-Huckel Law, 324–325
- Degradation, *see* protein degradation
- ΔC<sub>p</sub>, 55  
measurements, 399–400  
table for selected proteins, 401
- Denaturant  
concentration dependence, 400–401  
guanidine hydrochloride, 396  
solubility of amino acids, 397  
thermal, 96  
urea, 396
- Denaturation in PCR, 169
- Denaturation, 396–398  
ideal curves, 401  
linear extrapolation method, 402
- Deoxyadenosine, 170
- Detergents, 122, 425  
amphiphiles, 122  
critical micelle concentration, 107–108  
SDS binding, 335  
use of LDAO, 121
- Dextrorotatory, 34
- 2/3'-dideoxyinosine, *see* ddl
- Diabetes, 422, type-I, 441
- Dialysis, 333, 359
- Dideoxyadenosine, 170
- Dideoxynucleotide, 169–170, 171, 453
- Diesenhofer, J.E., 126
- Differential scanning calorimetry, 399  
profiles, 400
- Diffusion controlled rate, 195, 201
- DIFP, *see* Diisopropylfluorophosphate
- Dihedral angle, 41, 43, 46
- Dihydrouridine, 268
- Diisopropylfluorophosphate, 212, 228
- Dipalmitoylphosphatidylcholine, 107
- DIPF *see* di-isopropylphosphofluoridate
- Dipole moment, 41, 56
- D-isoglutamate, 35
- Dissociation of weak acids, 478–479
- Distal histidine, 68
- Disulfide, bond formation, 288–289  
bridges in keratin, 91–92  
bridges in prions, 433  
bridges, 53  
chemical properties, ribonuclease, neuraminidase, 463  
oxidoreductase, protein disulfide isomerase, 288–289  
thioredoxin, 288
- Dithiothreitol, 27–28
- DNA binding proteins, 64–66, 258–261  
arc repressor, 261  
cro repressor, 66  
eukaryotic transcription factors, 261–265  
met repressor, 261  
molecular saddle, 259–260  
recognition helix, 65  
restriction endonucleases, 221–224  
sequence homology, 66
- DNA gyrase, 253
- DNA ligase, 254  
ligation, 315
- DNA polymerase, 253–254  
cloning, 314–315  
enzyme nomenclature, 191  
PCR, 170  
specificity constant, **201**
- DNA replication, 253–254,  
semi-conservative model,
- DNA sequencing, 168–170  
profiles from, 171
- DNA structure, 248  
major groove, 222
- dNTP, 170
- Domains  
b<sub>5</sub>-like proteins, 60  
death effector, 239  
definition, 58–59  
EGF-like, 101  
extracellular domains in receptor tyrosine kinases, 240  
folding domains in lysozyme, 415  
gp120 inner and outer, 454–455  
Gro-EL, 418  
immunoglobulin domain, 77  
non receptor tyrosine kinases, 240  
nucleotide binding, 62, 148, 155  
p53, 471  
tyrosine kinases, 240
- Donnan effect, 333
- Dopamine, 36
- Double helix, 247–248
- Double reciprocal plot,
- DPPC, *see* dipalmitoylphosphatidylcholine
- Drosophila melanogaster*, 168, 263, 308
- Drug resistance, 454
- Drugs, 205, 228, 231, 451, 453, 454
- Dsb family, 288
- E site, 272, 286
- Eadie Hofstee plot, 199, 225
- Earth, 127
- EcoRI, 221–224  
cleavage site, **222**  
DNA distortion, 223  
major groove binding, 223  
role of divalent ions in catalysis, 223  
sequence specificity and hydrogen bonding, 223

- EcoRI (*continued*)  
 signature sequence, 224  
 tertiary structure, 223
- Ectodomain, 455–456
- Edelman, G., 76
- Edman degradation, 165, 340
- Edman, P., 165
- EF-G, 275, 279
- EF-Ts, 275,
- EF-Tu, 274–275  
 regeneration, 277  
 structure with Phe-tRNA, 278
- EGF, *see* epidermal growth factor
- Ehlers-Danos syndrome, 99–100
- Eighteen 18S rRNA, 257
- Elastase  
 active site substrate specificity, 212  
 emphysema, 476  
 structural homology, 177
- Elastin, 101
- Electromagnetic spectrum, 348
- Electron density, 108, 356, 358
- Electron microscope, 376
- Electron microscopy, *see also* cryoelectron  
 microscopy, nuclear pore complex, 303
- Electron spin resonance, 390–392  
 ENDOR, 392  
 ESEEM, 392  
 iron sulfur proteins, 391
- Electron, 31
- Electrophile, 205  
 in covalent catalysis, 203–205
- Electrophoresis, 333–340  
 isoelectric focusing, 339  
 SDS-PAGE, 335–338  
 two dimensional electrophoresis, 339
- Electroporation, 315
- Electrospray ionization, **340**
- Electrostatic catalysis, 205–207
- Elements, 9
- ELISA, 337–338
- Ellipticity, 386
- Ellman's reagent, 27, 28, 33
- Elongation factors, *see also* EF-G, EF-Tu  
 and EF-Ts, 274–277
- Eluate, 327
- Emphysema, 475–478
- Enantiomers, 34
- Encounter complex, 195
- Endergonic process, 195
- Endocytosis, 98, 458–459, 459
- Endoplasmic reticulum, 164  
 collagen processing, 97–99  
 disulfide bond formation, 288–289  
 hydroxylation reactions, 289–290  
 insulin processing, 287–288  
 lumen, 295, 296, 427  
 translocon/SRP interaction, 424–425  
 unwanted transfer, 426
- Endoproteolysis, 469
- Endosomes, 460
- Enediol intermediate, 208
- Energy transfer, 382, 383
- Engelman, D., 423
- Engrailed, 263
- Enteropeptidase, 237
- Enthalpy, 54
- Entropy, 54  
 activation parameters, 397–398
- Enzymes, 188–245  
 allosteric regulation, 231–237  
 catalytic efficiency, **201**  
 catalytic mechanisms, 202–209  
 covalent modification, 237–241  
 databases, 192  
 inhibition and regulation, 224–228  
 irreversible inhibition, 227–231  
 isoenzymes, 241–242  
 kinetics, 197–202  
 multicatalytic activities, 305–308  
 nomenclature, **189**, 478–479  
 preferential binding of transition state,  
 207–209  
 purification, **343**  
 rotary motion, 146  
 steady state approximation, 199–200  
 subsites, 208
- Epidermal growth factor, 101–102, **369**
- Epitopes, 77, 272
- Equilibrium constant, 194
- Equilibrium dialysis, 359
- Ernst, R., 360
- Error rate, 169
- Erythrocyte, 110–114  
 band, 3  
 protein, 111  
 glycophorin, 112–114  
 lipid: protein ratio, **109**  
 membrane organization, 110–114
- Erythromycin, 278
- Escherichia coli*  
 ATP synthetase, 144–145  
 cell division, 247  
 competent cells, 315  
 expression host, 313  
 genome, 9  
 K12 strain, 168  
 lac operon, 317  
 met repressor, 261  
 OmpA, 425  
 OmpF, 425  
 phosphofructo-kinase, 232  
 porins, 128–132  
 protein expression, 314  
 protein purification, **343**  
 replication of DNA, 253  
 restriction endonucleases from, 222  
 ribosomes, 270  
 RNA polymerase, **254**  
 SRP54 M domain, 295
- ESR *see* Electron spin resonance
- Ethanolamine, 106
- Eukaryotic cells, 164
- Eukaryotic RNA polymerases, 257–261  
 basal transcription factors, **258**  
 role and location, **257**  
 processing, 257
- Evolution, 164
- EX1 mechanism, 412
- EX2 mechanism, 412
- Excited state, 380
- Exergonic reaction, 195
- Exocytosis, 98
- Exon, 267
- Exonuclease activity, 254
- Exportins, 300
- Expression vectors, 316–318
- Extinction coefficient, *see* Molar  
 absorptivity coefficient
- Extrinsic proteins, 110
- Eye, damage in glaucoma, 205
- Eyring, H., 195
- F<sub>1</sub> complex, 146  
 structure, 147–150
- F<sub>ab</sub> fragments, 76–79
- Fabry disease, 308
- FAD, *see* flavin adenine dinucleotide
- Familial amyloidotic neuropathy, 428
- FAP mutations, 430
- FAP, *see* familial amyloidotic neuropathy
- Fasman, G.D., 182
- FASTA, 175
- Fatal familial insomnia, **428**, 434–435, 465
- Fatty acids, 105–109
- F<sub>c</sub>, 76
- Feedback mechanisms, 189
- Fenn, J., 340
- Ferredoxin, 128, 299  
 types of clusters, 391
- Ferredoxin-NADP reductase, 299
- Ferrimyoglobin, 68
- Fersht, A.R., 405
- Fibrillin, 101–102  
 modular organization, 102
- Fibrils, transthyretin based, 430
- Fibrin, 238–239
- Fibrinogen, 239  
 sedimentation coefficient, 324
- Fibroins, 92
- Fibrous proteins, 85–103  
 amino acid composition, **86**  
<sup>15</sup>N, 253,
- 50S subunit, *see* large subunit, 279–282
- First order reaction, 192–194
- Fischer, E., 2, 189
- 5.8S rRNA, 257
- 5S rRNA, 261, 269  
 secondary structure prediction, 280

- FK506 binding proteins, 416  
 Flavin adenine dinucleotide, 9, 132–133, 162  
 Flavin, 380  
 Flavodoxin, 181, 359  
 Flu, *see* influenza  
 Fluid mosaic model, 109–110  
 Fluorescamine, 33  
 Fluorescence, 381–385  
   emission anisotropy, 383  
   Green fluorescent protein, 383–385  
   instrumental setup, 382  
   Perrin equation, 383  
   profile from DNA sequencing, 171  
   Stern-Volmer analysis, 382  
   collisional quenching, 382  
   Stokes shift, 381  
 Fluorescein, 167, 170  
 Flurodinitrobenzene, 33, 37  
 F<sub>0</sub>, 145,  
 Folding, *see* protein folding  
 Folic acid, **193**  
 Folin-Ciocalteu's reagent, 33  
 Folin-Lowry method, 33  
 Formylmethionine, 273–274  
 Forster energy transfer, 382  
 4.5S rRNA, 294  
 Fourier transform, 354, 360, 389  
 Franck, J., 377  
 Franklin, R., 2, 247  
 Free energy, 195–197  
   contributions to protein folding, 403  
   transition state profile, 196  
 Free induction decay, 361–362  
 Fructose-6-phosphate, 232–233  
 FtsY, 295  
 Fumarase, specificity constant, **201**  
 Fumaroles, 162  
 Funnel, 411  
 Fusogenic peptide, 455, 457
- G protein coupled receptor, 115–121  
   cDNA isolation, 115  
 G protein, 117–119  
   heterotrimeric, 118  
   G $\alpha$  structure, 119  
   G $\beta$ /G $\gamma$ , 118, 120, 439  
   EF-Tu, 274  
   Ran, 302  
   Ran binding proteins, 302  
 G<sub>1</sub> phase, of cell cycle, 247–248  
 G<sub>2</sub> phase, of cell cycle, 247–248  
 GABA, *see*  $\gamma$  amino butyric acid  
 GAL4, transcription factor, 262–263  
 Galactolipids, 107  
 Gallo, R., 443  
 $\gamma$  crystallin, 59  
 $\gamma$  secretase, 469  
 $\gamma$  turn, 46–48
- $\gamma$  amino butyric acid, 36  
 $\gamma$  lipotrophin, 289  
 Gamow, G., 266  
 Garavito, R., 228  
 Gaucher's disease, 310  
 GCN4, transcription factor, 263–264  
 Gel electrophoresis, 333–340  
   enzyme linked immunosorbent assay, 337  
   instrumentation, 337  
   polyacrylamide SDS, 336  
   two dimensional, 339  
   Western Blotting, 337–338  
 Gel state, 109  
 Gene fusion, 181  
 Gene,  
   amyloid precursor protein, 469  
   seven transmembrane helices receptors, 118  
   cdc, 249  
   defective, 441  
   engrailed, 263  
   *env,gag,pol*, 445–446  
   globin cluster, 442  
   p53 location, 471  
   PNRP, 433, 435  
   screening, 441  
   tumour suppressor, 470  
   secretion, 424  
 Genetic code, 268  
   in organelles, 268  
   translation of synthetic nucleotides, **267**  
   start codon, 169,  
 Genetic engineering, 222  
 Genomes, 168–169  
   *Haemophilus influenzae*, 168  
   *Helicobacter pylori*, 168  
   pathogens, 395  
   RNA based, 444  
   segmented, 444, 457  
   sequencing projects, 168, 185  
 Genomics, 183  
 Germ line mutations, 473  
 Gerstmann–Straussler–Scheinker, 434–435  
 GFP, *see* green fluorescent protein.  
 Ghost membranes, 110  
 Glaesser, R., 376  
 Glaucoma, 205  
 Gln-tRNA synthetase, 220  
   active site pocket with analogue, 221  
   discrimination between substrates, 220  
   transition state analogue, 221  
 Globin evolution, 182  
 Globin gene cluster, 442  
 Glucokinase, 200  
 Glucose isomerase, specificity constant, **201**  
 Glucose-6-phosphate, 241  
 Glutamate, 25  
   chemical properties, 25  
   data, **19**  
   genetic code specification, 268  
   helix/sheet propensity, **41**  
   optical rotation, **34**  
   prevalence hydropathy index, **112**  
   prevalence in secondary structure, **180**  
 Glutamine, 25–26  
   chemical properties, 25–26  
   data, **19**  
   genetic code specification, 268  
   helix/sheet propensity, **41**  
   hydropathy index, **112**  
   prevalence in secondary structure, **180**  
 Glutamyl tRNA synthetase, 220–221  
 Glutathione binding proteins, 334  
 Glutathionine-S-transferase, 334,  
   SDS-PAGE, 337  
 Glycerol backbone, 105  
 Glycerophospholipid, 106  
 Glycine  
   chemical properties, 24  
   data, **19**  
   genetic code specification, 268  
   helix/sheet propensity, **41**  
   hydropathy index, **112**  
   prevalence in secondary structure, **180**  
   in collagen structure, 94–96  
   location in turns, 47  
   poly(Gly), 48  
 Glycogen phosphorylase, 231, 241  
 Glycogen storage diseases, 309–310  
 Glycogen, 241  
 Glycolysis, 190  
 Glycophorin, 113  
   domain labeling, 113–114  
   dimerization, 114  
 Glycophosphatidyl inositol, *see* GPI anchors  
 Glycoprotein  
   amyloid precursor protein, 469  
   prion protein, 433  
   transmembrane receptors, 239  
   variant surface, 290  
 Glycosidic bonds, 210, 211  
   cleavage by neuraminidase, 462–463  
 Glycosylation, 98–99, 290–292  
   adrenergic receptor, 115  
   glycophorin, 113  
   N-linked glycosylation, 98  
   prion, 434  
 GM1, 439  
 GM2, 310  
 Golgi apparatus, 99, 292, 296  
 gp120  
   domain organization, 455  
   env gene product, 446  
   function, 447  
   interactions with CD4 receptor, 455  
   location within HIV, 446  
   structure, 449  
   surface glycoproteins of HIV, 454–455  
   vaccine development, 455



- gp41, 90  
 ectodomain region, 456–457  
 env gene product, 446  
 function, 447  
 structure, 449  
 fusogenic sequence, 456  
 location within HIV, 446  
 trimer of hairpins, 457
- GPCR, *see* G protein coupled receptor
- GPI anchors, 291  
 in prion protein, 433
- Gradient gel electrophoresis, 336
- Gram negative, 128, 319
- Gram positive, 35, 319
- Gramicidin A, 36
- Greek key motif, 59, 61
- Green fluorescent protein, 383–385
- GroEL-ES, 417–422  
 catalytic cycle, 419–421  
 domain movements, 418–419  
 hydrophobic interactions, 420–421  
 negative staining EM, 417  
 tripartite structure, 418
- GroES structure, 418
- Ground state, 380
- GTP  
 analogue, 275  
 GTP binding proteins, 295  
 hydrolysis of GTP, 274, 294–295, 378  
 use in capping, 265
- Guanidine hydrochloride, 396–397, 400, 412
- Guanidinium thiocyanate, 326
- Guanidino, 28
- Guanine, 247
- H subunit (Reaction centre), 124
- H/D exchange, 413
- HAART, *see* highly active retroviral therapy
- Haemoglobin, 69–74  
 absorbance spectra, 67  
 allosteric regulation of, 72–74  
 $\alpha$  subunit, 70, 172  
 $\beta$  subunit, 70, 172  
 Bohr effect, 74  
 conformational change, 71–72  
 cooperativity, 72–73  
 deoxy state, 71  
 evolution of globin chains, 181–182  
 haemoglobin S, 441  
 hydrophobic pocket, 441  
 lamprey protein crystals, 359  
 mechanism of oxygenation, 71–72  
 met form, 67  
 R state, 73  
 sequence homology, 172  
 spin state changes, 71  
 structural homology, 172  
 solubility of, 325
- Haemophilus influenzae*, 168
- Hair, *see* keratins
- Hairpin, 456–457
- Haldane, J.B.S., 199
- Half-chair conformation, 211
- Half-life, 193–194, 305
- Haloarcula marismortui*, 272
- Halobacterium halobium*, 114
- Halophile, 114
- Hanging-drop, 359
- Haplotype, 442
- Harker construction, 356–357
- Hartwell, L., 249
- Heat capacity, 55  
 changes in protein folding
- HEAT motifs, 301
- Heat shock proteins, 298, 416
- Heavy chain, 76
- Heavy metal derivatives, 357
- Heisenberg, W., 349
- Helicases, 253, 258
- Helicobacter pylori*, 168
- Helix, 41–45  
 $\alpha$  helix, 41–44  
 other conformations, 45  
 $\pi$  helix, 44  
 PSTAIRE, 250–251  
 reaction center, 115, 125  
 restriction endonucleases, 222–223
- Helix loop helix motif, 263, 264
- Helix propensity, 41
- Helix turn helix motif, 64–66  
 eukaryotic, 263–265
- Helper T cells, 445, 446
- Haemagglutinin, 459–462  
 antigenic subtypes, 465  
 comparison of membrane bound and protease treated forms, 460  
 conformational changes, 462  
 crystal structure, 461  
 HA1 monomer, 461  
 HA2 monomer, 461  
 low pH forms, 462  
 organization, 460  
 sialic acid binding and the active site, 460–462
- Heme a, 133, 138
- Heme a<sub>3</sub>, 133, 138, 140
- Heme, 9, 66, 67  
 complex III, 132–133  
 cytochrome oxidase, 138  
 edge to edge distance, 137
- Henderson, R., 114, 376
- Henderson-Hasselbalch equation, 14, 477–478
- Hepatitis B, 377
- Heptad repeat, 87, 89, 263
- Hess' Law, 406–407
- Heteronuclear NMR spectroscopy, 370–373
- Heterotropic effector, 234
- Hexokinase, 191, 200
- Hierarchy, 180
- Highly active retroviral therapy, 454
- Hill coefficient, 231
- Hill equation, 231
- HindIII, 222
- Hippocrates, 228
- His-tags, 333–334
- Histamine, 36
- Histidine  
 acid catalysis in RNaseA, 203  
 chemical modification in ribonuclease, 202  
 chemical properties, 29–30  
 data, 20  
 general base catalysis, 202–203  
 genetic code specification, 268  
 helix/sheet propensity, 41  
 hydrophathy index, 112  
 imidazole ligand in globins, 68  
 imidazolite form in catalysis, 215–217  
 optical rotation, 34  
 prevalence in secondary structure, 180  
*pros* and *tele*, 30  
 reaction with TPCK in chymotrypsin, 213  
 tagged proteins, 333–334  
 Zn fingers, 261
- Histone, 250
- HIV protease, 446, 449–452  
 bond specificity, 449  
 catalytic mechanism, 450  
 inhibitors, 452  
 structure, 451  
 substrates, 451
- HIV *see* human immunodeficiency virus
- HLH motif, *see* Helix loop helix motif
- HNCA, 373
- HNCO, 373
- Hodgkin, D., 353
- Hofmeister series, 325–326
- Hofmeister, F., 2, 325
- Holley, R.W., 268
- Holoenzyme, 260
- Homedomains, 264
- Homeobox, 265
- Homeostasis, 189
- Homology, 170–175
- Homopolymer, 40
- Homoserine lactone, 27
- Homotropic effector, 234
- Hooke's Law, 388
- Hormone, 116, 228, 287
- Horseradish peroxidase, 338, 339
- Host-guest interaction, 40
- HTH, *see* Helix turn helix motif
- Huber, R., 51, 126, 370
- Huckel, E., 325
- Human diseases and disorders, 10–11, 428  
 Alzheimer's, 468–470



- amyloidogenesis, 427–431  
 cancer, 10, 470–475  
 cervical carcinoma, 475  
 cholera, 439–440  
 collagen based, 99–100  
 Creutzfeldt-Jakob disease, 433  
 cystic fibrosis, 10, 416–427  
 diabetes, 441  
 emphysema, 475–477  
 familial amyloidotic polyneuropathy, 428–430  
 folding diseases, **428**  
 glaucoma, 205  
 HIV, 10, 443–457  
 influenza, 457–465  
 kuru, 433  
 misfolding and disease, 426–435  
 neurodegenerative disease, 441, 465–470  
 p53 based, 470–474  
 prion based diseases, 431–435, 466–468  
 sickle cell anemia, 10 441–442  
 skin cancer, 445
- Human Genome Sequencing project, 9
- Human immunodeficiency virus, 11, 443–457  
 epidemic, 445  
 gene products, **447**  
 genome organization, 446  
 gp120, 454–455  
 gp41 structure, 455–457  
 helper T cells, 445  
 history, 444–445  
 HIV-2, 446  
 opportunistic infections, 445  
 protease, 63, 449–452  
 reverse transcriptase, 452–454  
 role of Vpu, Vif, Vpr, 448  
 structural proteins, 448–449  
 structure and function of Rev, Nef, Tat, 447–448  
 surface glycoproteins, 454–457  
 virus, 446
- Hybridization, 31
- Hydration layer, 324
- Hydrogen bonding, 56  
 examples in proteins, **56**  
 helices, 41–44  
 in  $\beta$  sheets, 45–46  
 restriction endonuclease specificity, 223  
 substrate discrimination in tRNA synthetases, 220
- Hydrogen exchange, 379
- Hydrolases, **191**, 308
- Hydrolysis, 202  
 bromophenol esters, 206–208  
 of acyl enzyme intermediate, 214–215  
 of ATP, 152  
 of NAG-NAM polymers, 211
- Hydropathy index, **112**
- Hydropathy plot, 111–113
- Hydrophobic effect, 53–55  
 energetics, 54  
 folding, 410  
 in chromatography, 331  
 interactions in proteins, 54–55, 403, 410–411
- Hydrophobic interaction chromatography, 331
- Hydroxylation, 29, 289–290
- Hydroxylysine, 97, 289–290
- Hydroxyproline, 96, 289
- Hyperbolic binding curve, 69, 232
- Hyperthermophile, 306
- Hypervariable regions, 77
- Iatrogenic transmission, 433, 467
- Ibuprofen, 228
- Ice, 54
- IF-1, 275
- IF-2, 274, 275
- IF-3, 274, 275
- IgG, 76–80
- Imidazole, 29, 30  
 catalytic mechanism of triose phosphate isomerase, 216–217  
 groups in nucleophilic reactions, 203  
 increased basicity, 214  
 ligands in active site of carbonic anhydrase, 206
- Immune response, 74–76
- Immunity, 76
- Immunoblotting, 337–339
- Immunoglobulins, 74–81  
 CDRs, 77  
 classes, 78–80  
 disulfide bridges, 76  
 heavy and light chains, 74  
 hypervariable regions, 77  
 immunoglobulin fold, 77  
 interaction with lysozyme, 78–79  
 monoclonal antibody, 79  
 structure, 76–78  
 $V_L$  and  $V_H$  domains, 77
- Importins, 300–302  
 interaction between  $\alpha$  and  $\beta$  301  
 schematic representation, 300
- Indole, 32
- Influenza, 457–465  
 avian strains, 465  
 classification, 458  
 entry into cells, 459  
 epitopes, 464  
 genome, **458**  
 haemagglutinin, 459–462  
 Hong Kong strain, 465  
 neuraminidase, 462–464  
 segmented RNA genome and coding of proteins, **458**  
 organization, 457
- strategies to combat influenza pandemics, 464–465  
 symptoms, 457  
 virus, 457
- Infrared spectroscopy, 387–389  
 amide bands, 389  
 fingerprint region, 389  
 regions of interest, **388**  
 spectrum of water, 388
- Infrared, 348  
 frequency range and measurement, **349**
- Ingram, V., 10, 441
- Inhibition, of enzyme activity, 224–228
- Initiation factors, 274–275
- INK4 family, 252
- Inositol, 106
- Insulin, 6,  
 disulfide bridge formation, 287  
 proteolytic processing, 287  
 expression, 318
- Integral proteins, 109–110
- Integrase, 445
- Interleukin- $1\beta$ , structure, 374–375
- Intermediate filaments, 88–89  
 classification of, **89**
- Intermembrane space, 298, 299
- Interphase, 247
- Intracellular messengers, 116–119
- Intrinsic pathway, 239
- Intrinsic proteins, 109–111
- Introns, 265–267
- Invariant residues, 39
- Iodide, 381
- Ion exchange chromatography, 329–330
- Ion pumps, 152–156
- Ion, solvation, 324–325
- Ionic atmosphere, 325
- Ionic strength, 324–325
- IPTG, *see* Isopropylthiogalactoside
- Iron sulfur protein, 132  
 ESR spectra, 391
- Iron, 7, 8, 58  
 observation by ESR, 391
- Islets of Langerhans, 441
- Isoalloxine, 9
- Isoelectric focusing, 339
- Isoelectric point, 14
- Isoenzymes, 205, 241–242
- Isoleucine  
 chemical properties, 24  
 data, **20**  
 genetic code specification, 268  
 helix/sheet propensity, **41**  
 hydropathy index, **112**  
 occasional use as start codon, **268**  
 optical rotation, **34**  
 prevalence in secondary structure, **180**
- Isomerases, **191**

- Isomorphous, 26  
 Isoprenoid units, 134  
 Isopropylthiogalactoside, inducer, 317  
 Isozymes, 205 *see also* isoenzymes  
 IUPAC, 107,  
 Ivanofsky, D., 442  
 Iwata, S., 132
- Jakob, A., 433  
 Jelly roll motif, 61  
 Jencks, W.P., 205  
 Jenner, E., 75  
 Jerne, N., 75
- Kanamycin, 316  
 Kaposi's sarcoma, 445  
 Karplus Equation, 363  
 $k_{cat}/K_m$  *see* specificity constant, 201  
 KDEL sequence, 296  
 Kendrew, J., 2, 358  
 $K_{eq}$ , (equilibrium constant), 194  
 in oxygen binding, 69  
 Keratins, 86–92  
 acidic, 88  
 $\alpha$ -keratin, 86–87  
 basic, 88  
 $\beta$ -keratin, 88  
 coiled coils, 87–89  
 Distribution of type I and II, 92  
 mutations in, 91  
 structural organization, 89
- Kevlar<sup>®</sup>, 92  
 Khorana, H.G., 422  
 Killer T cells, 79  
 Kinase, 172  
 Kinetic analysis, 192–195  
 of protein folding, 405  
 heterogeneity, 414  
 Kinetic techniques, 413  
 Kinetics, 192–195  
 Klenow fragment, 254, 452  
 Klug, A. 376  
 $K_m$ , Michaelis constant, 200  
 $k_{obs}$ , 195  
 Kohler, G., 75  
 Kosmotropes, 326  
 Kuru, 432, 433, 465
- L isomers, 34–35  
 L subunit (reaction centres), 124–125  
*Lac* operon, 317  
*Lac* repressor, 263, 317  
 Lactate dehydrogenase, 61, 191, 241–242  
 clinical diagnosis, 242  
 different isoenzymes, 242  
 sedimentation coefficient, 324  
 Lactocystin, 308  
 Laevorotatory, 34  
 $\lambda$ -repressor, 59, 65
- Lane, D.P., 470  
 Large (50S) ribosomal subunit, 279–282  
 peptidyl transferase mechanism, 283  
 sedimentation coefficient, 324  
 structure of globular proteins, 282  
 tertiary structure, 281  
 transition state analogue, 280, 282  
 23S rRNA structure, 280  
 Lariat structure, 267  
 Larmor frequency, 361–362  
 Lathyrism, 36  
 Lauryl, 107  
 LDAO, 121  
 Lecithin, 105  
 Leder, P., 267  
 Lentivirus, 448  
 Leonard-Jones potential, 57  
 Leucine, 24  
 chemical and physical properties, 24  
 data, 20  
 genetic code specification, 268  
 helix/sheet propensity, 41  
 hydrophathy index, 112  
 optical rotation, 34  
 prevalence in secondary structure, 180  
 Leucine zipper, 87, 263  
 in DNA binding, 264  
 Leucocyte, 476  
 Levine, A.P., 470  
 Levinthal's paradox, 403–404, 410  
 Lewis acid, 224  
 Lewis, G.N., 325  
 Li-Fraumeni syndrome, 441, 473–474  
 Ligands, 262  
 in affinity chromatography, 334  
 in bacterial reaction center, 125  
 in reverse phase chromatography, 332  
 Ligases, 191, 254  
 Ligation, 315  
 Light (L) chain, 76  
 Light harvesting chlorophyll complexes,  
 121, 127, 299  
 Light, 118  
 Linderström-Lang, K., 412  
 Lineweaver-Burk plot, 199  
 inhibition, 225–226  
 Linoleic acid, 107  
 Linolenic acid, 107  
 Lipid,  
 phase transition temperatures, 109  
 protein ratio, 109  
 fluidity, 109–109  
 bilayer, 108  
 Lipid:protein ratios, 109  
 Lipscomb, W., 234  
 Liquid crystalline state, 110  
 Long terminal repeats (LTRs), 446  
 Longitudinal relaxation time, 363  
 Loop-sheet polymerization, 476–477  
 Lumen, 296, 303
- Luminescence, 384  
 Lyases, 191  
 Lymphocytes, 75–76, 443  
 B cells, 75  
 CD4 bearing, 446  
 Lysine  
 chemical properties, 28–29  
 cofactor binding in bacteriorhodopsin,  
 114  
 crosslinks, 96–97  
 data, 20  
 genetic code specification, 268  
 helix/sheet propensity, 41  
 hydrophathy index, 112  
 hydroxylation, 97, 289–290  
 in collagen structure, 96–97  
 oxidation of side chain, 97  
 prevalence in secondary structure, 180  
 Lysogenic phase, 64  
 Lysosome, 296, 308–310  
 Lysozyme, 79  
 catalysis, 209–212  
 cell disruption, 319  
 folding domains, 415  
 glycosyl intermediate, 212  
 interaction with antibody, 78–79  
 neutron diffraction, 379  
 specificity constant, 201  
 systemic amyloidogenesis, 428  
 tertiary structure, 210  
 Lysyl hydroxylase, 290  
 Lysyl oxidase, 97  
 Lytic phase, 64
- M subunit, 124–125  
 Macrophages, 445, 454  
 Mad cow disease, 466  
 Magnesium, 221, 271  
 in cytochrome oxidase, 139–140  
 Magnetic moment, 391  
 Magnetic nuclei, 360  
 Magnetogyric ratio, 360  
 Malaria, 442  
 Malate synthase, 372  
 MALDI-TOF, 341–343  
 Malonate, 226–227  
 Maltose binding protein, 334  
 Manganese, 193  
 Marfan's syndrome, 100–102  
 Martin, A.J.P., 326  
 Mass spectrometry, 340–343  
 Matrix protein, 446, 447  
 structure, 448  
 in influenza virus, 458  
 Matrix protein, 446–449, 457  
 Mdm2, 475  
 Measles, 442  
 Membrane proteins, 105–159  
 bacteriorhodopsin, 423–424

- crystallography, 119–123  
 expression, 314, 344  
 folding, 422–426  
 integral, 110,  
 OmpA, 424  
 peripheral, 110  
 porins, 128–132  
 respiratory complexes, 132–144  
 topology, 110  
 two stage model, 423  
 with globular domains, 111–114
- Membranes, 105–110  
 fluid mosaic model, 109–110  
 ghosts, 110  
 molecular organization, 105–108
- Memory cells, 75
- Menaquinone, 125
- Menten, M., 198  
 $m_{eq}$ , dependence of  $\Delta G$  on denaturant concentration, 400–402, 405  
 table for selected proteins, **401**
- Mercaptoethanol, 27
- Meselson, M., 254
- Meselson-Stahl experiment, 254
- Messenger RNA capping, 265  
 methylaton, 265  
 viral, 443  
 plus (+)strand, 443
- Metal ion catalysis, 204–205
- Metal ions, **6, 8**,  
 activity of restriction endonucleases, 221, 223  
 carbonic anhydrase, 205 ribosome assembly, 271  
 catalysis, 204–205  
 co-factors, 192, **193**
- Metalloenzyme, **193**, 204
- Metalloproteinase, 99, 136, 469
- Metarhodopsin II, 118
- Metazoa, 133
- Methanococcus jannaschii*, 417
- Methanol, 55
- Methionine, 26–28  
 alternative genetic code, 268  
 chain initiation, 273–274  
 chemical and physical properties, 26–27  
 data, **21**  
 genetic code specification, 268  
 helix/sheet propensity, **41**  
 hydrophathy index, **112**  
 interactions with heavy metal derivatives, 26  
 prevalence in secondary structure, **180**  
 reaction with cyanogens bromide, 27  
 side chain oxidation, 26  
 SRP54, 294
- Methylation, 29, 292  
 by restriction endonucleases, 221  
 lysine sidechains, 28  
 RNA transcripts, 265  
 7-methylguanylate, 265
- Metmyoglobin, 68
- Micelles, 107
- Michaelis, L., 198
- Michaelis-Menten equation, 199
- Michel, H., 120, 126
- Microfibril, 88, 89, 101
- Microwaves, 348  
 frequency range and measurement, **349**  
 use in ESR, 391
- Miller, S., 162
- Milstein, C., 75
- Mitchell, P., 145
- Mitochondria, 132–144  
 complex I, 132–133  
 complex II, 133  
 cristae, 145  
 cytochrome  $bc_1$  complexes, 132–137  
 cytochrome oxidase, 138–144  
 inner mitochondrial membrane translocase system, **298**  
 inter-membrane space, 133  
 lipid:protein ratio, **109**  
 matrix, 133  
 outer-membrane, 133  
 proteases, 298  
 respiratory complexes, 132–144  
 RNA polymerases, **257**  
 targeting, 297–299
- Mitosis, 247–248
- Mixed disulfide, 28
- Molar absorptivity coefficient, 32,
- Molar extinction coefficients, 30–31, 385  
 globins, 67
- Molecular evolution, 161–165, 189
- Molecular graphics, 52, 478
- Molecular mass, 7
- Molecular medicine, 441
- Molecular orbitals, 31  
 theory, 380
- Molecular saddle, 259–260
- Molecular weight, *see* molecular mass
- Molten globule, 409–410
- Molybdenum, 7, 58, 193  
 in sulfite oxidase, 181
- Monochromators, 355, 404
- Monod, Wyman and Changeaux (MWC) model, 71
- Montagnier, L., 443
- Moore, P., 272
- Moore's Law, 185
- Motifs, 173
- mRNA *see* messenger RNA
- Mulder, G. J., 1
- Multiple anomalous dispersion, 357
- Mumps, 442
- Mutagenesis, 307, 406–408
- Mutational hot spots, 474
- Myelin sheath, **109**
- Myoglobin, 67–69  
 absorbance spectrum, 67  
 evolution of globins, 181–182  
 human and sperm whale, 40  
 oxygen binding curve, 69  
 sedimentation coefficient, 324  
 structure, 67  
 superposition of polypeptide chains, 70
- Myristoylation, 240, 292  
 of Nef, 447
- Myxathiazol, 134, 135
- N acetyl glucosamine, 209–210, **321**
- N acetyl muramic acid, 209–210, **321**
- N peptide, 456
- N terminal nucleophile hydrolases, 303
- N terminal *see* Amino terminal
- $Na^+K^+$  ATPase, 153–155  
 reaction stoichiometry, 153  
 subunit composition, 153  
 transport of ions, 154  
 use of cardiac glycosides, 154
- N-acetyl neuraminic acid, 462
- NAD<sup>+</sup>, *see* Nicotinamide adenine dinucleotide
- NADH/NADPH, 132
- NADH-ubiquinone oxidoreductase, 132–133
- NAG, *see* N acetyl glucosamine
- NAM, *see* N acetyl muramic acid
- Nathans, D., 221
- N-bromosuccinimide, 32
- NcoI, 222, 317
- NdeI, 317
- Nef, 446–448
- Nestin, 87
- Neuraminidase, 61, 462–464  
 active site, 464  
 crystal structure, 463  
 enzyme activity, 462  
 tetrameric state, 463
- Neurodegenerative disease, 441, 465–470  
 Alzheimer's, 468–470  
 BSE, 466  
 Lou Gehrig's disease, 441  
 scrapie, 466  
 vCJD, 467
- Neurotoxicity, 212
- Neurotoxins, 212
- Neutron diffraction, 379
- Nevirapine, 454
- Niacin, **193**
- Nicolson, G., 109
- Nicotinamide adenine dinucleotide, 9, 162, **193**, 439–440
- 19S regulatory complex, 308
- Ninhydrin, 33, 167
- Nirenberg, M., 267
- Nitrate reductase, **173**, 181

- Nitrocellulose, 337, 339  
 Nitrothiobenzoate, 27  
 Nitrotyrosine, 32  
 N-linked glycosylation, 290  
 NMR structures, BUSI IIa, 370  
   interleukin 1 $\beta$ , 375  
   tendamistat, 370  
   thioredoxin, 375  
 NMR, *see* Nuclear magnetic resonance spectroscopy  
*N*-myristoyltransferase, 292  
 Nobel Prize, 2, 4–5, 126, 340  
 NOE, *see also* Nuclear Overhauser effect, 364  
   regular secondary structure, **369**  
 Non steroidal anti-inflammatory agents, 230  
 Non Watson-Crick base pairs, 268  
 Non-competitive enzyme inhibition, 226–227  
 Non-competitive inhibition, 226,  
 Non-covalent interactions, 403  
 Non-nucleoside inhibitors, 454  
 Nonsense codons, 268  
*Nostoc sp.*, 164  
 NSAIDs, *see* non steroidal anti-inflammatory agents  
 NTN hydrolases, *see* N terminal nucleophile hydrolases  
 Nuclear envelope, 299,  
 Nuclear localization signals, **300**  
 Nuclear magnetic resonance spectroscopy, 360–375  
   <sup>13</sup>C chemical shifts for amino acid residues, **372**  
   <sup>15</sup>N 2D connectivity patterns, **368**  
   <sup>1</sup>H chemical shifts for amino acid residues, **366**  
   amide exchange, 411–412  
   assignment problem, 364–370  
   chemical shifts for amino acid residues, **371**  
   COSY, 368  
   generating protein structures, 373–375  
   heteronuclear methods, 370–373  
   instrumentation, 365  
   magnetogyric ratio, 360  
   national facilities, 392  
   NOESY, 368  
   nuclear Overhauser effect, 364, 373–374  
   practical biomolecular NMR, 364  
   relaxation, 363–364  
   spectra, 367, 371  
   structure calculations in, 374–375,  
   TOCSY, 367–368  
   triple resonance experiments, **373**  
 Nuclear Overhauser effect, 364  
 Nuclear pore complexes, 302–303  
 Nucleation,  
   crystal formation, 359  
   helix formation, 409  
 Nuclei, **360**  
 Nucleocapsid, 443  
 Nucleocytoplasmic transport, 299–302  
   importin  $\alpha$  structure, 301  
   importin  $\beta$  structure, 301  
   involvement of Ran binding proteins, 302  
   localization signals, **300**  
   pores, 299, 302–303  
   Ran-GDP structure, 302  
 Nucleophile, 32, 202–205  
 Nucleoplasmin, 299–300  
 Nucleoporins, 302–303  
 Nucleoprotein, 457  
 Nucleoside analogues, 453  
 Nucleoside inhibitors, 453  
 Nucleotides, 169  
 Nucleus, 299  
 Nups, *see* nucleoporins  
 Nurse, P., 249  
 O linked glycosylation, 290–291  
 Octapeptide repeat, 434, 436  
 ODAP *see*  $\beta$ -*N*-oxalyl L- $\alpha$ ,  $\beta$ -diamino propionic acid  
 ODCase, *see* Orotidine 5-monophosphate decarboxylase  
 Okazaki fragments, 254–255  
 Oleic acid, **107**  
 Oligomerization domain, 473  
 Oligomycin, 145  
 OmpA, 424  
 OmpF, 129–131  
 Oncogene, 470  
 Oncoprotein, 250  
 Operon, 317  
 Opiomelanocortin, 288  
   processing of, 289  
 Opsin, 117  
 Optical isomers, **34**  
 Optical rotation, **34**  
 Optical spectroscopy, 379–390  
   absorbance, 381–385  
   absorbance spectra, 67, 381  
   circular dichroism, 385–387  
   fluorescence, 381–385  
   fluorescence polarization, 382–383  
   Raman, 389–390  
 Orbitals, 31, 380  
 Organization, 37  
 Orientation effects, 206–207  
 Orotidine 5-monophosphate decarboxylase, 205  
 Osteogenesis imperfecta, *100*, 428  
 Osteoporosis, 99  
 Oubain, 154  
 Oxidoreductases, **191**  
 Oxygen, 8,  
   binding site in cytochrome oxidase, 143  
   binding to myoglobin, 69  
   binding to hemoglobin, 69  
   oxidation of methionine side chains, 26  
   production from water splitting, 126  
 Oxygenic photosynthesis, 126–128  
 Ozone, 32  
 P site, 273  
 p17, 446–449  
 P22 tail spike protein, *61*  
 p51, *see* reverse transcriptase  
 p53, 11, 265, 470–475  
   crystal structure, 472–473  
   domain structure, 472  
   function, 471  
   Li Fraumeni syndrome, 473–474  
   linked to cancer, 474  
   malfunctions, **474**  
   mutation, 474  
   organization, 471  
   primary sequence, 472  
   regulation, 474  
   smoking, 474  
   transcription factor, 265  
 p66, *see* reverse transcriptase  
 P870, 121  
 PALA, 235–236  
 Palindromic sequence, 222  
 Palmitic acid, **107**  
 Palmitoyl transferase, 292  
 Palmitoylation, 240, 292  
 PAM matrices, 174  
 Pancreas, 237, 287, 441  
 Pandemics, 443, 445, 457  
 Papain, 76  
 Para substitution, 31  
*Paracoccus denitrificans*, 138, 140  
   cytochrome oxidase, 141, 144  
 Parvalbumin, 415  
 Parvulins, 416  
 Pasteur, L., 75  
 Pauling, L. 14, 41, 67  
 Pavletich, N., 472  
 pBR322, *316*  
 p-bromophenylacetate, 206  
 PCR, *see* polymerase chain reaction,  
 PDI *see* protein disulfide isomerase,  
 Penicillin, 228  
 Pepsin, 237, 287  
   catalytic mechanism, *450*  
   specificity constant, 201  
   structure, 449–450  
 Peptide bond formation, 16–17  
   cis/trans isomerization, 23  
   ribosome, properties, 17–23  
 Peptide fragments, 166  
 Peptidoglycan layer, *320*, 321  
 Peptidomimetic, 451  
 Peptidyl proline isomerase, 415–416

- Peptidyl transferase, 273, 275  
inhibition of, 280  
mechanism, 282
- Periodic table of elements, 8
- Peripheral proteins, 110
- Periplasm, 121, 288, 320
- Perrin equation, 383
- Pertussis toxin, 440
- Perutz, M.F., 2, 71, 352, 356, 358
- PEST sequences, 305
- pET vector, 319
- PFK, *see* phosphofructokinase
- PGH synthase, 229
- pH, 14–15
- Phase angle, 353–354
- Phase problem, 356–357
- Phenylalanine  
absorbance spectrum, 381  
chemical properties, 31  
data, **21**  
DNA distortion, 259  
genetic code specification, 268  
helix/sheet propensity, **41**  
hydropathy index, **112**  
mutation in CFTR gene, 427  
optical rotation, **34**  
 $\pi$ - $\pi$  interactions, 31  
secondary structure preference, **180**  
spectroscopic properties, **30**
- Phenylalanine ammonia lyase, **191**
- Phenylisothiocyanate, 165–166
- Pheophytin, 121, 124
- Phe-tRNA, 278
- $\phi$  angle, 41–44
- Phillips, D., 210
- 2-phosphoglycolate, 209, 233
- Phosphatase, 258, 290
- Phosphatidylcholine, 105
- Phosphatidylethanolamine, 105
- Phosphatidylglycerol, 105
- Phosphatidylinositol, 105, 291
- Phosphatidylserine, 105
- Phosphodiester bond, 267  
cleavage, 224
- Phosphodiesterase, 118
- Phosphoenolpyruvate, 233
- Phosphofructokinase, 231–234  
domain organization and movement, 232–233  
regulation by ATP/ADP, 232–233  
transition state analogue, 232
- Phosphorylase *a*, 241
- Phosphorylase *b*, 241
- Phosphorylation, 153–154  
as post translational event, 290  
enzyme, 241
- Phosphoserine, 25, 290  
in glycogen phosphorylase, 241
- Phosphotyrosine, 25, 241, 290
- Photobleaching, 115
- Photocycle, 115
- Photon, 121
- Photosynthetic reaction centres, 119–128  
bacterial reaction center, 123–126  
chromophores, 121  
cytochrome subunit, 125  
electron transfer pathway, 122, 125  
fractionation with detergents, 121  
H subunit, 123–124  
kinetics, 122  
L and M subunits, 124–125  
organization, 121  
photosystems I and II, 126–128  
special pair, 121, 125  
structure, 123–126
- Photosystem I, 126–127
- Photosystem II, 126
- $\pi$  helix, 43–44
- pI, *see* isoelectric point
- Pichia pastoris*, expression system, 314
- Pigment, 115
- Ping-pong mechanism, 215
- Pituitary, 288
- pK, 14–15
- Planck's constant, 196, 348
- Planck's Law, 348
- Plaques, 431, 432, 434
- Plasma membrane, 109, 164, 320
- Plasmids, 315–316
- Plasmodium falciparum*, 442
- Plastocyanin, 59, 299, 369
- Pneumonia, 445, 457
- Polarization, 382–383
- Polyacrylamide gel electrophoresis, 335–338  
polymerization reactions, 335
- Polyalanine, 40
- Polymerase chain reaction, 169–170
- Polymorphism, 442
- Polypeptide, 39–50  
cleavage by enzymes, 166–167  
folding kinetics, 408–410  
hydrolysis, 167  
permutations, 40
- Polyprotein, 289, 445, 448, 449
- Polysaccharide coat, 319
- Pompe disease, 308
- Porins, 128–132  
biological unit, 130  
channel selectivity, 128  
constriction site, 130  
folding properties, 424  
hydrophobic residues, 129  
OmpA, 424  
OmpF, 129–130  
PhoE, 130  
secondary structure, 129  
trimeric unit, 130
- Porter, R., 76
- Post translational modification, 287–293  
covalent modification, 237–241
- Ppi, *see* peptidyl proline isomerase
- Pre-steady state, 200
- Prebiotic synthesis, 161–163  
demonstration of, 162  
yields of biomolecules from, **162**
- Precipitation, 343
- Pre-initiation complex, 258–260
- Preproprotein, 287, 402
- Preproteins, 287  
N terminal sequences, 293
- Presenilins, 470
- Pribnow box, 64, 256
- Primary sequence, 39–40  
cytochromes *c*, 175  
haemoglobin, 172  
myoglobins, 40  
unknown, 167  
ubiquitin, 304
- Primase, 254
- Primers, 169–170
- Primosome, **254–255**
- Prion, 431–435  
cellular, 433–434  
glycosylation sites, 434  
knockout mice, 435  
mutations of PNRP gene, **435**  
primary sequence, 434  
scrapie, 433–434  
structural properties, **433**  
structure, 434
- Prokaryotic cells
- Proline chemical properties, 29  
cis-trans isomerization, 412–415  
collagen structure, 94–96  
data, **21**  
genetic code specification, 268  
globin helices, 68  
helix/sheet propensity, **41**  
hydropathy index, **112**  
hydroxylation, 96, 289  
location in turns, 47  
peptidyl isomerases, 415–416  
poly(Pro), 48  
prolyl hydroxylase, 289  
pyrrolidone ring, 94, 289  
transmembrane helices, 124
- Promoter, 256  
inducible, 317  
prokaryotic, 64–66
- Proof reading, 169, 275
- Propranolol, 116
- Pros*, 30
- Prostaglandins, 228–239
- Protease inhibitors, 451–452, 476
- Proteasome, 305–308  
heptameric ring structures, 306  
multiple catalytic activities, 305



- Proteasome (*continued*)  
 mutagenesis, 307  
 19S regulatory complex, 308  
 regulation of activity, 308  
 structural organization, 309  
 subunit structure, 307  
 three dimensional structure, 307
- Protein crystallization, 358–360
- Protein DataBank, 50–51, 105, 180, 347
- Protein databases, 180–181
- Protein degradation, lysosomal, 308–310  
 proteasome, 305–308  
 ubiquitin, 305
- Protein disulfide isomerase, 288–289  
*in vivo* protein folding, 416  
 sorting pathway, 296
- Protein evolution,  
 convergent, **179**  
 gene duplication, 181  
 rates of, **178**
- Protein expression, 313–318
- Protein folding, 395–438  
*ab initio*, 185–186  
 amide exchange, 411–412  
 barnase, 405–408  
 Brønsted equation, 407  
 databases, 180  
 denaturant dependence, 405  
 diversity, 161–187  
 energy landscapes, 411  
 GroEL-ES mediated, 417–422  
 Hess' Law, 406–407  
*in vivo*, 415–422  
 intermediates, 415  
 kinetics, 404–406  
 membrane proteins, 422–426  
 misfolding and disease, 426–435  
 models, 408–411  
 molten globule, 409–410  
 motifs, **173**  
 stopped flow kinetics, 404  
 structure prediction, 186  
 techniques, **413**  
 temperature dependence, 400
- Protein purification, 313–346  
 affinity chromatography, 332–333  
 centrifugation, 320–323  
 chromatography, 326–333  
 dialysis, 333  
 electrophoresis, 333–340  
 ion-exchange chromatography, 328–329  
 reverse phase methods, 331–332  
 salting-out, 323–326  
 size exclusion chromatography, 330–331  
 ultrafiltration, 333
- Protein solubility, 325
- Protein sorting and targeting, 293–303  
 chloroplast, 299  
 mitochondrion, 297–299  
 nuclear targeting, 299–302
- Protein stability  
 conformational stability of proteins,  
**402**  
 contributions to free energy, 403  
 factors governing, 403
- Protein synthesis,  
 chain initiation, 273–274  
 elongation, 274–277  
 molecular mimicry in, 277  
 outline of reaction, 273  
 role of soluble factors, 275  
 termination, 277–278
- Protein turnover, 303–310  
 half-lives, 303–304
- Protein/lipid ratio, **108**
- Proteinase K, 467
- Proteinase, *see* protease
- Proteins,  
 cyclic, 81  
 estimation of, 33  
 function, 5–6  
 isolation and characterization, 313  
 size, **6**
- Proteolysis, 304  
 limited proteolysis, 237–239
- Proteolytic processing, 287
- Proteomics, 184, 339
- Protofilaments, 88, 89, 431
- Proton pumping, 114–115, 142–144
- Protonation, 30
- Protoporphyrin IX, 9, 66–67
- Proximal histidine, 68
- Prusiner, S., 433
- Pseudomonas aeruginosa*, 168
- $\psi$  angle, 41–44
- PTC, *see* phenylisothiocyanate
- Pterin, 9
- Purcell, E., 360
- Puromycin, 278, 279, 282
- Purple membrane, 114
- Pyridoxal phosphate, 29, **193**
- Pyrimidine biosynthesis, 207, 234
- Pyrrrolidine ring, 16, 21, 29
- Q cycle, 135
- Quality control, 296
- Quantum mechanics, 379
- Quantum yield, **30**
- Quaternary structure of proteins, 62–81  
 hemoglobin, 70  
 aspartate transcarbamoylase, 235
- Quench cooling, 355, 377
- Quenching, 381–382
- Quinone, 105, 124–125,
- R factor, 358
- R group, 23–32  
 properties, 18–22
- R state, 71, 235
- R/S isomers, 24, 34, 38
- Racker, E., 114
- Radiation, 348
- Radio waves, 348
- Ramachandran plot, 48, 186
- Ramachandran, G.N. 48
- Ramakrishnan, V., 283
- Raman spectroscopy, 389–390
- Raman, C.V., 389
- Ran binding proteins, 302
- Ran, 302
- Random coil, 396
- Rapoport, T., 424
- Rate constant, 192  
 first order, 193  
 pseudo-first order, 195  
 second order, 195
- Rayleigh scattering, 389
- RCF, 322
- Reaction centres, type I and type II, 128
- Reaction controlled rate, 195
- Reaction coordinate, 195–196
- Reaction rate, 194  
 enhancement of, 202–209
- Reactive center loop, 476–477
- Receptor, 115  
 acetylcholine, 377  
 adrenergic, 115  
 bacterial, 295  
 chemokine, 454  
 genes, 119  
 hormone binding, 119  
 seven transmembrane, 115  
 tyrosine kinases, 239–240  
 SRP54, 295
- Recognition helix, 263
- Recombinant DNA technology, 313–318
- Red blood cell, *see* erythrocyte
- Redox reactions, **193**  
 and metal ion catalysis, 203
- Reiske protein, 126, 133–137  
 targeting sequence, 299
- Relaxation times, 363–364
- Release factors, *see* RF-1, RF-2 RF-3
- Replication origin, 316, 318
- Repressor, *see also* DNA binding proteins,  
 64–66
- Residue, 17
- Resins, 326  
 polystyrene, 332
- Resolving gel, 336
- Resonance, 23, 28
- Respiratory complexes, 132–144
- Restriction endonucleases, 221–224  
 cleavage sites, 315  
 multicloning sites, 317  
 signature sequence, 224  
 table of selected enzymes with cleavage  
 sites, **222**  
 type II in cloning, 314



- Retinal, 114  
 isomerase, 118  
 11-*cis*, 117–118  
 trans, 117–118
- Retinol binding protein, 428, 429
- Retrovirus, 443
- Rev, 446–448
- Reverse phase chromatography, 331–332
- Reverse transcriptase, 452–454  
 AZT binding, 453  
 p51 crystal structure, 453  
 p66 crystal structure, 452
- RF-1, 278
- RF-2, 278
- RF-3, 278
- Rheumatoid arthritis, 99
- Rhodamine 6G, 170
- Rhodobacter viridis*, 120
- Rhodopsin, 117–119
- Riboflavin, 193
- Ribonuclease, 6, 288  
 active site chemistry, 202–203  
 protein folding, 402–403  
 sedimentation coefficient, **324**  
 structure, 203
- Ribonucleoprotein, 265, 458
- Ribosomal RNA, 257, 261
- Ribosome, 269–287  
 A site, 273  
 affinity labeling and footprinting, 279  
 anatomical features, 271  
 assembly, 271  
 complex with SRP, 293  
 composition of prokaryotic, 269–271,  
 composition of eukaryotic, 269–270  
 E site, 272, 286  
 18S rRNA, 257  
 electron microscopy of, 272  
 5.8S rRNA, 257  
 5S rRNA, 269  
*Haloarcula marismortui*, 272  
 large and small subunit, 282–287  
 mechanism of protein synthesis, 208–282  
 P site, 273,  
 peptidyl transferase site, 273–275  
 RNA recognition motifs, 270  
 role of antibiotics, 278–279  
 sedimentation coefficient, **324**  
 16S rRNA, 269  
 soluble factors interacting with, **275**  
 surface epitopes, 272  
*Thermus thermophilus*, 272  
 transition state analogue, 282  
 28S rRNA, 257  
 23S rRNA, 269,
- Ribosylation, 439
- Ribozymes, 162, 192, 242, 287
- Ricin, **228**
- RNA binding protein, 271
- RNA hydrolysis, 202
- RNA polymerase, 64  
 T7 enzyme, 256  
 eukaryotic, **257**
- RNA recognition motif, 270  
 conserved sequences, 271
- RNA transcript, 265
- RNase A, *see* ribonuclease
- RNase H, 452–453
- Roeder, R.G., 259
- Röntgen, W., 349
- Rossmann fold, 58, 148, 180, 218, 220, 378
- Rossmann, M. 60
- Rotamer, 43, libraries, 49–50
- Rotary motion, 146
- Rotational states, 380
- rRNA, *see* ribosomal RNA
- RS (Cahn Ingold Prelog) system, 34
- S (Svedburg), 323
- S phase, of cell cycle, 247
- Sabatini, D., 293
- Saccharomyces cerevisiae*,  
 expression system, 314  
 genome sequencing, 9  
 secretion mutants, 424
- Salicylate, 230
- Salt bridges, in chymotrypsin, 55
- Salting in, 323–326
- Salting out, 323–326
- Sanger, F., 169
- Saquinavir, 452
- Sarcoplasmic reticulum, 155  
 Ca<sup>2+</sup> transport, 155–156  
 lipid:protein ratio, 109
- Saturation curve, 198, 325
- Scalar coupling, 363
- Scattering, 351
- Schiff base, 29, 203
- Schizosaccharomyces pombe*, 249
- Scissile bond, 212
- Scrapie, 433–434, 466
- Scurvy, 289
- SDS PAGE, 111, 335–337  
 identification of vCJD, 467  
 purification using, 344  
 principles of, 335–336  
 use with mass spectrometry, 342
- SDS, use in protein folding, 396, 423
- Sea urchin, 248
- Sec61, 295, 424–426
- Second messengers, 119
- Second order reaction, 195
- Secondary structure, 37–50  
 additional, 48  
 $\alpha$  helix, 41  
 $\beta$  strand, 45  
 dihedral angles, **43**  
 other helical conformations, 44  
 prediction, 181–183
- Ramachandran plot, 48
- regular NOEs and distances, **369**
- supersecondary, 58  
 translation distance, **43**  
 turns as elements of, 46
- Secretory granules, 287
- Sedimentation coefficient, 323–324  
 identification of rRNA, 269
- Sedimentation velocity, 323
- Selectable markers, 318
- Selection rules, 380
- Selenomethionine, 357
- Semi-conservative model, 253
- Semiquinone, 134
- Sequence homology, 170–176  
 c type cytochromes, 175  
*cro* repressor, 66
- Sequence identity, 222
- Sequencing, protein, 165–168  
 DNA, 168–171
- Serine  
 active site serine in cyclo-oxygenases,  
 230  
 catalytic triad, 25, 177, 179, 212–213  
 chemical properties, 25  
 covalent catalysis by, 214  
 genetic code specification, 268  
 helix/sheet propensity, **41**  
 hydropathy index, **112**  
 lipid headgroup, **106**  
 location in turns, 47  
 nucleophile, 25, 214  
 O linked glycosylation, 290–291  
 phosphorylation, 25  
 proteases, 212–215  
 secondary structure preferences, **180**
- Serine carboxypeptidase II, **179**
- Serine proteases, 25, 177, 212–215  
 active site, 212  
 catalytic mechanism, 214–215  
 catalytic triad, 212  
 convergent evolution, 179  
 inactivation by DIPF, 213  
 reaction of chymotrypsin with TPCK,  
 213  
 studied using neutron diffraction, 379  
 superposition, 177
- Serpinopathies, 478
- Serpins, 224, 238
- 7S rRNA, 294
- Seven transmembrane helices, 115
- SH2 domains, 241
- SH3 domains, 172, 241, 433  
 formation of amyloid fibrils, 431
- Shine-Dalgarno sequence, 273–274,  
 317
- SI units, 477
- Sialic acid, 458, 464
- Sickle cell anemia, 9, 441–442  
 haplotypes, 442

- Sigler, P., 417
- Sigmoidal binding curve, 69, 231, 232, 234
- Signal hypothesis, 293
- Signal peptidase, 295–296
- Signal peptide, 288, 293  
SRP54 binding, 294
- Signal recognition particle, 293–295  
E.coli homologue, 294  
pathway, 293  
receptor structure and function, 295  
signal peptide, 293
- Signal sequence peptidase, **293**, 295–296
- SRP54, 294–295  
structure and organization, 294  
translocon interaction, 424–426
- Signature sequence, 224
- Silk, 86, 92–93
- Silver staining, 337
- Simian immunodeficiency virus, 447, 456
- Sinapinic acid, 341
- Singer, S.J., 109
- Single particle analysis, 377
- Singlet, 380
- SIV, *see* simian immunodeficiency virus
- 16S rRNA, 269  
complementarity, 318  
helix44, 279  
the 530 loop, 279,  
helix34, 279  
secondary structure, 284  
tertiary structure, 284  
surface location of ends of molecule, 272
- Size exclusion chromatography, 330–331
- Skehel, J., 459
- Sleeping sickness, 290
- Smal, 222
- Small subunit (30S), 282–286  
anatomical features, 284  
decoding process, 286  
functional activity, 285–287  
IF-3 binding, 283  
protein composition, 284–286  
16S rRNA structure, 284
- Smallpox, 75, 442
- Smith, H.O., 221
- Smoking, effects on p53, 474  
emphysema, 478
- S<sub>N</sub>2-type reaction, 211
- snRNPs, 265
- Sorting, *see* protein sorting and targeting
- Southern Blotting, 337
- Southern, E.M., 337
- Soyabean lipoxygenase, 44
- Spanish flu, 457
- Special pair, 121
- Specificity constant, 201
- Sphingolipids, 107
- Spin multiplicity, 380
- Spin state, 71
- Spin-forbidden transitions, 380
- Spin-lattice relaxation time, 363, 391
- Spin-spin relaxation time, 363–364
- Splice sites, 266
- Spliceosome, 265–267  
branch point, 266  
composition, 265  
consensus sequence, 266  
lariat structure, 267
- SR Ca<sup>2+</sup> ATPase, 155–156
- Src homology domains, 172
- SRP, *see* signal recognition particle
- SRP54, 294–295
- Stacking gel, 336
- Stahl, F., 254
- Stanley, W.M., 443
- Staphylococcus aureus*, 35, 130  
hemolysin structure, 130–131
- Start codon, 268, 273–274
- Start sequences, 426–427
- Steady state approximation, 199–200
- Stearic, **107**
- Steitz, T., 272
- Stem loop structure, 269
- Stereochemistry, 15–16, 34–35
- Stereogenic, 35
- Stern-Volmer equation, 382
- Steven, A.C. 377
- Sticky ends, 222, 314
- Stigmatellin, 135, 137
- Stoeckenius, W., 114
- Stokes Law, 323, 363  
radius, 330
- Stokes shift, 381
- Stop codons, 268, 318
- Stop transfer sequences, 426–427
- Stopped flow analysis, 404–405  
double mixing experiments, 415
- Streptomycin, 278
- Stroma, 128, 299
- Structural homology, 175–177
- Structure factor, 355
- Subsites, 208, 212
- Substitution reactions, 32
- Substrate discrimination, 220
- Subtilisin, 179, 402
- Succinate dehydrogenase, 226
- Succinate, 227
- Sulfation, 292
- Sulfite oxidase, 58, 181
- Sulfolipids, 107
- Sulfonamide, 205
- Sulfone, 26
- Sulfoxide, 26
- Sumner, J., 358
- Super secondary structure, 37, 58
- Superconducting magnet, 364
- Superfamily, 180
- Superoxide dismutase, 193,
- SV40 T antigen, **299**
- Svedburg constant, 323
- Svedburg, T., 323
- Swiss roll motif, 61, 460
- Symmetry-forbidden transitions, 380
- Symport, 154
- Synchrotron, 357
- Synechococcus sp.*, 164  
photosystem structure, 126
- Synge, R.L.M., 326
- Syrian hamster, 434
- T cells, 75, 443, 445
- T loop, 251
- T state, 71
- T<sub>1</sub>, 363
- T<sub>2</sub>, 363–364
- T4 DNA ligase, **191**
- T7 RNA polymerase, 256, 313  
structure, 256
- Tanaka, K., 340
- Tanford, C., 396
- Taq polymerase, 169
- Targeting, *see* protein sorting and targeting
- Tat, 446–448
- TATA binding protein (TBP), 258–261
- TATA box, 64, 256  
recognition by transcription factors, **258**
- Tautomerization, 202
- Taxol, 378–379
- Taylor, K., 376
- Tay–Sachs disease, 309–310, 428, 441
- TCA cycle, *see* citric acid cycle
- tele*, 30
- Template, 169
- Tertiary structure, 50–62  
globular proteins, 52  
hydrogen bonding, 56  
hydrophobic effect, 53–55  
reformation, 402  
stabilizing interactions, 53–58  
van der Waals interactions, 56–58
- Tetracycline, 315
- Tetrahedral intermediates, 214
- Tetramerization domain, 473
- Tetrapyrrole,  
TFIIA, 258–261  
TFIIB, 258–261  
TFIID, 258–261  
TFIIE, 258–261  
TFIIF, 258–261  
TFIIH, 258–261  
TFIIIA, **173**, 262
- Thermal denaturation, 97
- Thermoplasma acidophilum*, 306  
thermosome, 422
- Thermosome, 422–423
- Thermus aquaticus*, 169  
Fth subunit, 295  
M domain, 295
- Thermus thermophilus*, 272

- Thiamine, *see* vitamin B1
- Thiol, 26–28, 288  
 formation of mixed disulfides, 27  
 ionization, 27
- Thiolate, 27
- Thioredoxin, 59, **369**, 375, **401**  
 conserved motif, 416  
 30S subunit, *see also* small subunit, 282–286
- Thomson, J.J., 340
- Threading, 185
- $3_{10}$  helix, 43–44  
 in glycogen phosphorylase, 241
- Threonine  
 [2S-3R], **35**  
 chemical properties, 25  
 data, **22**  
 genetic code specification, 268  
 helix/sheet propensity, **41**  
 hydrophathy index, **112**  
 O linked glycosylation, 290–291  
 optical rotation, **34**  
 phosphorylation in cdk, 251–252  
 secondary structure preference, **180**  
 use as nucleophile in catalysis, 303
- Thrombin, 212, 238–239
- Thylakoid membrane, 128, 299
- Thymine, 247
- Thyroxine, 36, 428
- TIM, *see* triose phosphate isomerase
- $T_m$ , *see* transition temperature
- Tobacco mosaic virus, 443
- Topogenic sequences, 426–427
- Topoisomerases, 253
- Torsion angle, 41, 48–49
- Tosyl-L-phenylalanine chloromethylketone, 211, **228**
- Toxin, 228
- TPCK, *see* tosyl-L-phenylalanine chloromethylketone
- Trace elements, **7**
- trans* ring, 419
- Transaminase, 193
- Transcription factors, **258**  
 basal components, 258–261  
 structures, 261–265  
 TBP, 258–261
- Transcription, 254–265  
 control in prokaryotes, 64–65  
 cI repressor, 64  
 cro repressor, 66  
 terminators, 318
- Transducin, 118–119
- Transfer RNA (tRNA), 267–270  
 acceptor stem, 268–269  
 anticodon, 269  
 binding to amino acyl tRNA CCA region, 220, 270  
 D arm and loop, 269  
 discrimination against, 286  
 structure, 267–269  
 synthetases, 220  
 variable loop, 268–269
- Transferases, **191**
- Transformation, 315
- Transition metals, **7**, **26**, **193**
- Transition state analogue, 209, 221, 233, 282
- Transition state, 195–197  
 bond energies, 207  
 preferential binding to enzymes, 207–209  
 two stage reactions, 197
- Transition temperature, 108  
 phase changes for diacyl-phospholipids, **109**  
 protein denaturation, 397–398,
- Transitions, 380  
 in CD spectra, 386
- Translation distance, 94
- Translation, 266–287  
 arrest, 424  
 of synthetic polynucleotides, 267
- Translocases, 297–299  
 tom, 297  
 tim, 298  
 tic, 299  
 toc, 299
- Translocon, 295, 424–426  
 organization, 426
- Transmissible spongiform encephalopathies, 431, 434  
 BSE, 466–468  
 incidence in UK, 467  
 inherited forms associated with PNRP mutations, **435**  
 UK advisory committee, 467
- Transport, 153
- Transthyretin, 428–430  
 mutations and disease progression, 430  
 complex with RBP, 429
- Tricarboxylic acid cycle (TCA) *see* Citric acid cycle
- Triglycerides *see* Triacylglycerols
- Triose phosphate isomerase, 179, 215–218  
 catalytic fine tuning, 218  
 catalytic reaction, 209  
 imidizolate in catalysis, 215–217  
 mechanism of conversion of DHAP, 217  
 pH dependence of catalysis, 216  
 transition state analogues, 208
- Triple helices, 94–97  
 cross-linking, 97  
 thermal denaturation, 96  
 structure, 95
- Triple resonance experiments, **373**
- Triplet, 380  
 of genetic code, 268
- tRNA, *see* transfer RNA
- Tropocollagen, 6, 94
- Trypanosoma brucei*, 290
- Trypsin, 287  
 activation of other proteolytic enzymes, 238  
 active site substrate specificity, 212  
 catalytic mechanism, 212–215  
 inhibitor, 224  
 protein sequencing, 166, 167  
 structural homology, 177
- Tryptophan  
 absorbance spectrum, 381  
 anisotropy, 383  
 blue shift, 381  
 chemical properties, 32  
 data, **22**  
 fluorescence, 381  
 genetic code specification, 268  
 helix/strand propensity, **41**  
 hydrophathy index, **112**  
 optical rotation, **34**  
 secondary structure preference, **180**  
 spectroscopic properties, **30**
- TSEs *see* transmissible spongiform encephalopathies
- Tuberculosis, 445
- Tubulin, 377–379
- Tumour suppressor genes, 252, 470, 474
- Turns, 46–48  
 $\beta$ -bends, 48  
 $\gamma$ -turns, 47
- 28S rRNA, 257
- 23S rRNA, 269  
 secondary structure prediction, 280  
 tertiary structure, 281
- Two dimensional gel electrophoresis, 270
- Two dimensional NMR spectroscopy, 365–370  
 H/D exchange measurements, 412–413
- Twort, F., 443
- Tyrosine kinases, 239–241
- Tyrosine  
 absorbance spectrum, 381  
 chemical properties, 31–32  
 data, **22**  
 formation of tyrosyl adenylate, 218  
 genetic code specification, 268  
 helix/strand propensity, **41**  
 hydrophathy index, **112**  
 phosphorylation, 239  
 reaction with nucleophiles, 31  
 secondary structure preference, **180**  
 spectroscopic properties, **30**
- Tyrosyl tRNA synthetase, 218–221  
 active site structure, 219  
 binding affinities for substrates, 218–219  
 characteristic motifs, 219–220  
 mutagenesis of critical residues, 219  
 three dimensional enzyme structure, 218

- U1-snRNA, 265, 270  
 U2-snRNA, 265  
 U4/U6-snRNA, 265  
 U5-snRNA, 265  
 Ubiquinol-cytochrome c oxidoreductase, *see*  
   also cytochrome bc<sub>1</sub> complex,  
   132–137  
 Ubiquinone, 133–134, 193  
 Ubiquitin, 304–305  
   addition to CFTR, 427  
   ATP dependent activation, 305  
   E1 enzymes, 304  
   E2 enzymes, 304  
   E3 enzymes, 304  
   NMR spectrum, 367  
   sequence, 304  
   tertiary structure, 304  
 Ultracentrifugation, 322–323  
 Ultrafiltration, **333**  
 Uncertainty principle, 349  
 Unimolecular reaction, 192, 195, 208  
 Uniport, 154  
 Unit cell, 351  
 Unsaturation, 107  
 Unwin, N., 114, 376  
 Urea, 193, 396, 400  
 Urease, 207, 358  
 Urey, H., 162  
 Uridine monophosphate, 207  
  
 Vaccination, 75, 440  
 Valine  
   chemical properties, 24  
   data, **22**  
   genetic code specification, 268  
   helix/strand propensity, **112**  
   hydropathy index, **41**  
   secondary structure preference, **180**  
 Van der Waals interactions, 53, 56–58  
   in collagen structure, 95  
 Van der Waals volume, **18–22**  
 Vapour diffusion, 359  
 Variable domain, in gp120, 454–455  
 Variable loop, 268–269  
 Variant CJD, 466–468  
 vCJD, *see* variant CJD  
  
 Vectors, 313–319  
   pBR322, 316  
   pET, 319  
 Vibrational states, 380  
*Vibrio cholerae*, 439  
 Vif, 446, 448  
 Viral fusion, 456–457,  
 Viruses, 442–443  
   Baltimore classification, **444**  
   flu virus, 458  
   human papilloma, 475  
   tobacco mosaic, 443  
 Viscosity, 383  
 Visual cycle, 118  
 Vitamin B<sub>6</sub> (pyridoxine), 29, **193**  
 Vitamin C and scurvy, 193, 429  
 Vitamin K<sub>3</sub>, 105, **193**  
 Vitamins, **193**  
 Vitrified water, 377  
 V<sub>max</sub>, maximal enzyme catalysed velocity,  
   198–202  
   competitive inhibition, 225–226  
   non-competitive inhibition, 226–227  
 Vogelstein, B., 470  
 Voyeur chlorophylls, 125  
 Vpr, 446, 448  
 Vpu, 446, 448  
  
 Walker, J.E., 147  
 Water elimination of, 16  
 Water splitting reaction, **193**  
 Water, metastable form, 377  
 Watson, J.D., 2, 247  
 Wavelength, 348  
 Wavenumber, 381  
 Waves, 353–354  
 Western Blotting, 337, 465  
 WHO, *see* world health organization  
 Whooping cough, *see* pertussis,  
 Wiley, D., 459  
 Wilkins, M.F., 2, 247  
 Wilm's tumour, 265  
 Wilson, I., 459  
 Wohler, F., 1  
 World Health Organization, 11,  
   465  
  
 World wide web, 185  
 Wuthrich, K., 369  
  
 Xenopus laevis, 261, 308  
 X-ray crystallography, 349–359  
   Bravais lattices and unit cells, 351–352  
   experimental set-up, 350  
   frequency range and measurement, **349**  
   isomorphous replacement, 356–357  
   multiple anomalous dispersion, 357  
   national facilities, 392  
   phase problem, 356–357  
   protein crystallization, 358–360  
   R factor, 358  
   refinement of structures, 357–358  
   synchrotron radiation, 357  
   wavelengths, 350  
 X-ray, 348  
  
 Yarus inhibitor, 280  
 Yeast genome sequencing, 9  
   flavocytochrome b<sub>2</sub>, 299  
   secretion mutants, 424  
   tRNA structure, 269  
*Yersenia pestis*, 168  
 YO<sub>2</sub> (fractional saturation with O<sub>2</sub>), 68–70  
 Yonath, A., 283  
 Yoshikawa, S., 138  
  
 Zanamivir, 464, 465  
 Zif268, 262  
 Zinc fingers, 261–263  
   HIV proteins, 449  
   primary sequence, 262  
 Zinc ion  
   carbonic anhydrase, 206  
   carboxypeptidase, 192, 193  
   cytochrome oxidase, 139  
   p53, 472  
   proteases, 136  
   regulation of activity of aspartate  
     trans-carbamoylase, 235  
   tubulin assembly, 377–379  
 Zn fingers, 261  
 Zwitterion, 13, 15  
 Zymogens, 237–238, 287, 310