Glossary

acid: a molecule or chemical group that donates a proton, either to water or to some other base. (2-12)

acid-base catalysis: catalysis in which a proton is transferred in going to or from the transition state. When the acid or base that abstracts or donates the proton is derived directly from water (H^+ or OH^-) this is called specific acid-base catalysis. When the acid or base is not H^+ or OH^-, it is called general acid-base catalysis. Nearly all enzymatic acid-base catalysis is general acid-base catalysis. (2-12)

activation energy: the energy required to bring a species in a chemical reaction from the **ground state** to a state of higher free energy, in which it can transform spontaneously to another low-energy species. (2-6)

activation-energy barrier: the higher-energy region between two consecutive chemical species in a reaction. (2-6)

activation loop: a stretch of polypeptide chain that changes conformation when a kinase is activated by phosphorylation and/or protein binding. This segment may or may not be the one containing the residue that is phosphorylated to activate the kinase. Usually, in the inactive state, the activation loop blocks access to the active site. (3-13)

activation segment: see **activation loop**.

active site: asymmetric pocket on or near the surface of a macromolecule that promotes chemical catalysis when the appropriate **ligand** (substrate) binds. (2-1)

affinity: the tightness of a protein–ligand complex. (2-4)

alignment: procedure of comparing two or more sequences by looking for a series of characteristics (residue identity, similarity, and so on) that match up in both and maximize conservation, in order to assess overall similarity. (4-1)

allosteric activator: a ligand that binds to a protein and induces a conformational change that increases the protein's activity. (3-5)

allosteric inhibitor: a ligand that binds to a protein and induces a conformational change that decreases the protein's activity. (3-5)

allostery: the property of being able to exist in two structural states of differing activity. The equilibrium between these states is modulated by ligand binding. (3-5)

alpha/beta barrel: a parallel beta barrel formed usually of eight strands, each connected to the next by an alpha-helical segment. Also known as a **TIM barrel**. (1-18)

alpha/beta domain: a protein domain composed of beta strands connected by alpha helices. (1-17)

alpha+beta domain: a protein domain containing separate alpha-helical and beta-sheet regions. (1-17)

alpha/beta twist: a twisted parallel beta sheet with a saddle shape. Helices are found on one side of the sheet for the first half and the other side for the second half. (1-18)

alpha domain: a protein domain composed entirely of alpha helices. (1-17)

alpha helix: a coiled conformation, resembling a right-handed spiral staircase, for a stretch of consecutive amino acids in which the backbone –N–H group of every residue n donates a hydrogen bond to the C=O group of every residue n+4. (1-5)

alternative splicing: the production of different versions of the final protein sequence from a gene sequence by the removal during RNA processing of portions of the RNA containing or affecting coding sequences. (1-2)

amide bond: a chemical bond formed when a carboxylic acid condenses with an amino group with the expulsion of a water molecule. (1-3)

amphipathic: having both polar and nonpolar character and therefore a tendency to form interfaces between **hydrophobic** and **hydrophilic** molecules. (1-1)

amphipathic alpha helix: an alpha helix with a hydrophilic side and a hydrophobic side. (1-6)

anisotropic: behaving differently in different directions; dependent on geometry and direction. (2-4)

antiparallel beta sheet: a beta sheet, often formed from contiguous regions of the polypeptide chain, in which each strand runs in the opposite direction from its immediate neighbors. (1-7)

atomic coordinate: the position in three-dimensional space of an atom in a molecule relative to all other atoms in the molecule. (5-1)

autophosphorylation: phosphorylation of a protein kinase by itself. Autophosphorylation may occur when the active site of the protein molecule to be phosphorylated catalyzes this reaction (*cis* autophosphorylation) or when another molecule of the same kinase provides the active site that carries out the chemistry (*trans* autophosphorylation). Autophosphorylation *in trans* often occurs when kinase molecules dimerize, a process that can be driven by ligand binding as in the receptor tyrosine kinases. (3-13)

backbone: the regularly repeating part of a polymer. In proteins it consists of the amide –N–H, alpha carbon –C–H and the carbonyl –C=O groups of each amino acid residue in the **polypeptide** chain. Residues are linked to each other by means of **peptide bonds**. (1-0, 1-3)

base: (in a nucleic acid) the aromatic group attached to the sugar of a **nucleotide**. (1-2)

base: (in chemistry) a molecule or chemical group that accepts a proton, either from water or from some other acid. (2-12)

beta barrel: a beta sheet in which the last strand is hydrogen bonded to the first strand, forming a closed cylinder. (1-7)

beta domain: a protein domain containing only beta sheet. (1-17)

beta sandwich: a structure formed of two antiparallel beta sheets packed face to face. (1-17)

beta sheet: a **secondary structure** element formed by backbone hydrogen bonding between segments of extended polypeptide chain. (1-5)

beta turn: a tight turn that reverses the direction of the polypeptide chain, stabilized by one or more backbone hydrogen bonds. Changes in chain direction can also occur by loops, which are peptide chain segments with no regular conformations. (1-5)

bifunctional: having two distinct biochemical functions in one gene product. Bifunctional enzymes catalyze two distinct chemical reactions. (2-15)

BLAST: a family of programs for searching protein and DNA databases for sequence similarities by optimizing a specific similarity measure between the sequences being compared. (4-2)

catalyst: a substance that accelerates the rate of a reaction without itself being permanently altered. (2-6)

catalytic triad: a set of three amino acids that are hydrogen bonded together and cooperate in catalysis. (2-14)

cavity: a completely enclosed hole in the interior of a protein. Cavities may contain one or more disordered water molecules but some are believed to be completely empty. (2-3)

chameleon sequence: a sequence that exists in different conformations in different environments. (4-14)

chaperone: a protein that aids in the folding of another protein by preventing the unwanted association of the unfolded or partially folded forms of that protein with itself or with others. (1-9)

chromatin: the complex of DNA and protein that comprises eukaryotic nuclear chromosomes. The DNA is wound around the outside of highly conserved histone proteins, and decorated with other DNA-binding proteins. (3-20)

co-activator: a regulatory molecule that binds to a gene activator protein and assists its binding to DNA. (3-5)

codon: three consecutive **nucleotides** in a strand of DNA or RNA that represent either a particular amino acid or a signal to stop translating the transcript of the gene. The formula for translating the codons is given by the genetic code. (1-2)

coenzyme: a cofactor that is an organic or organometallic molecule and that assists catalysis. (2-13)

cofactor: a small, non-protein molecule or ion that is bound in the functional site of a protein and assists in ligand binding or catalysis or both. Some cofactors are bound covalently, others are not. (1-13, 2-13)

coiled coil: a protein or a region of a protein formed by a dimerization interaction between two alpha helices in which hydrophobic side chains on one face of each helix interdigitate with those on the other. (1-19)

competitive inhibitor: a species that competes with substrate for binding to the active site of an enzyme and thus inhibits catalytic activity. (3-0)

conservative substitution: replacement of one amino acid by another that has similar chemical and/or physical properties. (1-2)

conserved: identical in all sequences or structures compared. (4-1)

convergent evolution: evolution of structures not related by ancestry to a common function that is reflected in a common structure. (1-16, 4-5)

cooperative binding: interaction between two sites on a protein such that the binding of a ligand to the first one affects the properties—usually binding or catalytic—of the second one. (3-4)

cooperativity: interaction between two sites on a protein such that something that happens to the first one affects the properties of the second one. (3-4)

coordinate covalent bond: a bond formed when a lone pair of electrons from an atom in a ligand is donated to a vacant orbital on a metal ion. (1-13)

co-repressor: a regulatory molecule that binds to a gene repressor protein and assists its binding to DNA. (3-5)

cross-linked domain: a small protein domain with little or no secondary structure and stabilized by disulphide bridges or metal ions. (1-17)

decarboxylation: removal of carbon dioxide from a molecule. (2-11)

degenerate: having more than one **codon** for an amino acid. (1-2)

denaturant: a chemical capable of unfolding a protein in solution at ordinary temperatures. (1-12)

denatured state: the partially or completely unfolded form of a biological macromolecule in which it is incapable of carrying out its biochemical and biological functions. (1-12)

dimer: an assembly of two identical (homo-) or different (hetero-) subunits. In a protein, the subunits are individual folded polypeptide chains. (1-19)

dipole moment: an imaginary vector between two separated charges that may be full or partial. Molecules or functional groups having a dipole moment are said to be polar. (1-3)

disulfide bridge: a covalent bond formed when the reduced –S–H groups of two cysteine residues react with one another to make an oxidized –S–S– linkage. (1-4)

divergent evolution: evolution from a common ancestor. (4-5)

DNA microarray: an ordered array of nucleic acid molecules, either cDNA fragments or synthetic oligonucleotides, where each position in the array represents a single gene. (4-4)

domain: a compact unit of protein structure that is usually capable of folding stably as an independent entity in solution. Domains do not need to comprise a contiguous segment of peptide chain, although this is often the case. (1-14)

domain fold: the particular topographical arrangement of secondary structural elements that characterizes a single domain. Examples are an antiparallel arrangement of four helices in a four-helix bundle, or an open twisted beta sandwich with a particular sequence that binds nucleotides. (1-15)

domain swapping: the replacement of a structural element of one subunit of an oligomer by the same structural element of the other subunit, and vice versa. The structural element may be a secondary structure element or a whole domain. (2-4)

dominant-negative: dominant loss of function due to a single mutant copy of a gene. This can occur when the mutant subunit is able to oligomerize with normal subunits to form a non-functional protein, thereby producing a loss-of-function phenotype even in the presence of a normal copy of the gene. (1-20)

effector: a species that binds to a protein and modifies its activity. Effectors may be as small as a proton or as large as a membrane and may act by covalent binding, noncovalent binding, or covalent modification. (3-0)

effector ligand: a ligand that induces a change in the properties of a protein. (3-4)

electron density map: a contour plot showing the distribution of electrons around the atoms of a molecule. (5-1)

electrostatic interactions: noncovalent interaction between atoms or groups of atoms due to attraction of opposite charges. (1-4)

enthalpy: a form of energy, equivalent to work, that can be released or absorbed as heat at constant pressure. (1-12)

entropy: a measure of the disorder or randomness in a molecule or system. (1-12)

equilibrium: the state at which the rate of the forward reaction and the rate of the reverse reaction in a chemical transformation are equal. At equilibrium, the relative concentrations of reactants and products no longer change, although the reaction continues to occur. (2-6)

equilibrium constant: the ratio of the product of the concentrations of reaction products to the product of the concentrations of reaction reactants. For a reaction of the general form A + B = C + D, the equilibrium constant K_{eq} is [C][D]/[A][B], where [X] is the concentration of X, usually in moles per liter. This definition is a simplification that neglects effects at high concentrations. (2-6)

E-value: the probability that an **alignment** score as good as the one found between two sequences would be found in a comparison between two random sequences; that is, the probability that such a match would occur by chance. (4-1)

evolutionary distance: the number of observed changes in nucleotides or amino acids between two related sequences. (4-1)

exon: coding segment of a gene. The coding DNA of many eukaryotic genes is interrupted by segments of non-coding DNA (**introns**). (1-2)

extein: the sequences flanking an intein and which are religated after **intein** excision to form the functional protein. (3-17)

family: a group of homologous proteins that share a related function. Usually these will also have closely related sequences. Members of the same enzyme family catalyze the same chemical reaction on structurally similar substrates. (4-8)

four-helix bundle: a structure of four antiparallel alpha helices. Parallel bundles are possible but rare. (1-17)

free energy: a function, designed to produce a criterion for spontaneous change, that combines the **entropy** and **enthalpy** of a molecule or system. Free energy decreases for a spontaneous process, and is unchanged at equilibrium. (1-12)

functional motif: sequence or structural **motif** that is always associated with a particular biochemical function. (1-16, 4-2)

gated binding: binding that is controlled by the opening and closing of a physical obstacle to substrate or inhibitor access in the protein. (2-7)

gene knockout: inactivation of the function of a specific gene in a cell or organism, usually by recombination with a marker sequence but sometimes by antisense DNA, RNA interference, or by antibody binding to the gene product. The phenotype resulting from the knockout can often provide clues to the function of the gene. (4-4)

genetic code: the relationship between each of the 64 possible three-letter combinations of A, U, G and C (which stand for the RNA bases adenine, uracil, guanine and cytosine, respectively) and the 20 naturally occurring amino acids that make up proteins. U is the RNA equivalent of T (thymine) in DNA. (1-2)

genomics: the study of the DNA sequence and gene content of whole genomes. (4-0)

globin fold: a predominantly alpha-helical arrangement observed in certain heme-containing proteins. (1-17)

glycosylation: the post-translational covalent addition of sugar molecules to asparagine, serine or threonine residues on a protein molecule. Glycosylation can add a single sugar or a chain of sugars at any given site and is usually enzymatically catalyzed. (1-13, 3-18)

glycosylphosphatidylinositol anchor: a complex structure involving both lipids and carbohydrate molecules that is reversibly attached to some proteins to target them to the cell membrane. (3-19)

G protein: a member of a large class of proteins with GTPase activity that act as molecular switches in many different cellular pathways, controlling processes such as sensory perception, intracellular transport, protein synthesis and cell growth and differentiation. They undergo a large conformational change when a bound GTP is hydrolyzed to GDP. (3-6)

Greek-key motif: an arrangement of antiparallel strands in which the first three strands are adjacent but the fourth strand is adjacent to the first, with a long connecting loop. (1-17)

ground state: a species with low free energy; usually, the non-activated state of any substance. (2-6)

ground-state destabilization: raising the free energy, (relative to some reference state), of the ground state, usually referring to the bound substrate in the active site before any chemical change has occurred. Geometric or electronic strain are two ways of destabilizing the ground state. (2-8)

GTPase-activating protein (GAP): a protein that accelerates the intrinsic GTPase activity of switch GTPases. (3-7)

guanine-nucleotide-binding protein: see **G protein**.

guanine-nucleotide exchange factor (GEF): a protein that facilitates exchange of GDP for GTP in switch GTPases. (3-7)

hairpin turn: another name for **beta turn**.

helical parameters: set of numerical values that define the geometry of a helix. These include the number of residues per turn, the translational rise per residue, and the main-chain torsional angles. (1-6)

helix dipole: the macrodipole that is thought to be formed by the cumulative effect of the individual peptide dipoles in an alpha helix. The positive end of the dipole is at the beginning (amino terminus) of the helix; the negative end is at the carboxyl terminus of the helical rod. (1-6)

heptad repeat: a sequence in which hydrophobic residues occur every seven amino acids, a pattern that is reliably indicative of a **coiled-coil** interaction between two alpha helices in which the hydrophobic side chains of each helix interdigitate with those of the other. (1-19)

heterotetramer: an assembly of four subunits of more than one kind of polypeptide chain. (1-19)

heterotrimeric G protein: a GTPase switch protein composed of three different subunits, an α subunit with GTPase activity, and associated β and γ subunits, found associated with the cytoplasmic tails of G-protein-coupled receptors, where it acts to relay signals from the receptor to downstream targets. Exchange of bound GDP for GTP on the α subunit causes dissociation of the heterotrimer into a free α subunit and a $\beta\gamma$ heterodimer; hydrolysis of the bound GTP causes reassociation of the subunits. (3-8)

hexamer: an assembly of six identical or different subunits. In a protein the subunits are individual folded polypeptide chains. (1-19)

Hidden Markov Model: a probabilistic model of a sequence **alignment**. (4-1)

homologous: describes genes or proteins related by divergent evolution from a common ancestor. Homologous proteins, or homologs, will generally have similar sequences, structures and biochemical functions, although the sequence and/or functional similarity may be difficult to recognize. (4-1)

homology: the similarity seen between two gene or protein sequences that are both derived by evolution from a common ancestral sequence. (4-1)

homology modeling: a computational method for modeling the structure of a protein based on its sequence similarity to one or more proteins of known structure. (4-6)

homotrimer: an assembly of three identical subunits: in a protein, these are individual folded polypeptide chains. (1-19)

hydride ion: a hydrogen atom with an extra electron. (2-9)

hydrogen bond: a noncovalent interaction between the **donor atom**, which is bound to a positively polarized hydrogen atom, and the acceptor atom, which is negatively polarized. Though not covalent, the hydrogen bond holds the donor and **acceptor atom** close together. (1-4)

hydrolysis: breaking a covalent bond by addition of a molecule of water. (1-3)

hydrophilic: tending to interact with water. Hydrophilic molecules are polar or charged and, as a consequence, are very soluble in water. In polymers, hydrophilic **side chains** tend to associate with other hydrophilic side chains, or with water molecules, usually by means of hydrogen bonds. (1-1)

hydrophobic: tending to avoid water. Hydrophobic molecules are nonpolar and uncharged and, as a consequence, are relatively insoluble in water. In polymers, hydrophobic **side chains** tend to associate with each other to minimize their contact with water or polar side chains. (1-1)

hydrophobic effect: the tendency of nonpolar groups in water to self-associate and thereby minimize their contact surface area with the polar solvent. (1-9)

induced fit: originally, the change in the structure of an enzyme, induced by binding of the substrate, that brings the catalytic groups into proper alignment. Now generalized to the idea that specific ligands can induce the protein conformation that results in optimal binding interactions. (1-22, 2-2)

intein: a protein intron (intervening sequence). An internal portion of a protein sequence that is post-translationally excised in an autocatalytic reaction while the flanking regions are spliced together, making an additional protein product. (3-17)

interaction domain: a protein that recognizes another protein, usually via a specific recognition motif. (3-1)

intermediate: a species that forms transiently along the path from substrate to product. (2-6)

intron: an intervening sequence in a gene that does not correspond to any portion of the final protein sequence and is spliced out of the RNA transcript before translation. (1-2)

jelly roll fold: a beta sandwich built from two sheets with topologies resembling a Greek key design. The sheets pack almost at right-angles to each other. (1-17)

K_d: the dissociation constant for the binding of a ligand to a macromolecule. Typical values range from 10^{-3} M to 10^{-10} M. The lower the K_d, the tighter the ligand binds. (1-13)

ligand: small molecule or macromolecule that recognizes and binds to a specific site on a macromolecule. (2-1)

ligand-binding site: site on the surface of a protein at which another molecule binds. (2-1)

limited proteolysis: specific cleavage by a protease of a limited number of the peptide bonds in a protein substrate. The fragments thus produced may remain associated or may dissociate. (1-13)

lipid anchor: lipid attached to a protein that inserts into a membrane, thereby anchoring the protein to the bilayer. (3-2)

lipidation: covalent attachment of a fatty-acid group to a protein. (3-19)

lipid bilayer: the structure of cellular membranes, formed when two sheets of lipid molecules pack against each other with their hydrophobic tails forming the interior of the sandwich and their polar headgroups covering the outside. (1-6)

local alignment: alignment of only a part of a sequence with a part of another. (4-2)

mesophilic: favoring moderate temperatures. Mesophilic organisms normally cannot tolerate extremes of heat or cold. Mesophilic enzymes typically denature at moderate temperatures (over 40 ºC or so). (1-12)

messenger RNA (mRNA): the RNA molecule transcribed from a gene sequence after removal of **introns** and editing. (1-2)

metastable: only partially stable under the given conditions. In the case of protein structures, a metastable fold exists in equilibrium with other conformations or with the unfolded state. (4-15)

methylation: modification, usually of a nitrogen or oxygen atom of an amino-acid side chain, by addition of a methyl group. Some bases on DNA and RNA can also be methylated. (3-20)

mixed beta sheet: beta sheet containing both parallel and antiparallel strands. (1-7)

monomer: a single subunit: in a protein, this is a folded peptide chain. (1-19)

motif: characteristic sequence or structure that in the case of a **structural motif** may comprise a whole domain or protein but usually consists of a small local arrangement of secondary structure elements which then coalesce to form domains. **Sequence motifs**, which are recognizable amino-acid sequences found in different proteins, usually indicate biochemical function. Structural motifs are less commonly associated with specific biochemical functions. (1-16)

multifunctional: having a number of distinct biochemical functions in one gene product. (2-15)

multiple sequence alignment: alignment of more than two sequences to maximize their overall mutual identity or similarity. (4-1)

myristoylation: irreversible attachment of a myristoyl group to a protein via an amide linkage. (3-19)

***N*-acetylation:** covalent addition of an acetyl group from acetyl-CoA to a nitrogen atom at either the amino-terminus of a polypeptide chain or in a lysine side-chain. The reaction is catalyzed by *N*-acetyltransferase. (1-13, 3-20)

native state: the stably folded and functional form of a biological macromolecule. (1-9)

negative cooperativity: binding of one molecule of a ligand to a protein makes it more difficult for a second molecule of that ligand to bind at another site. (3-4)

nitrosylation: modification of the –SH group of a cysteine residue by addition of nitric oxide produced by nitric oxide synthase. (3-20)

northern blot: technique for detecting and identifying individual RNAs by hybridization to specific nucleic acid probes, after separation of a complex mixture of mRNAs by electrophoresis and blotting onto a nylon membrane. (4-4)

nucleophile: a group that is electron-rich, such as an alkoxide ion ($-O^-$), and can donate electrons to an electron-deficient center. (2-14)

nucleotide: the basic repeating unit of a nucleic acid polymer. It consists of a **base** (A, U [in RNA, T in DNA], G or C), a sugar (ribose in RNA, deoxyribose in DNA) and a phosphate group. (1-2)

nucleotide-binding fold: an open parallel beta sheet with connecting alpha helices that is usually used to bind NADH or NADPH. It contains a characteristic sequence motif that is involved in binding the cofactor. Also known as the Rossmann fold. (1-18)

oligomer: an assembly of more than one subunit: in a protein, the subunits are individual folded polypeptide chains. (1-19)

oxidation: the loss of electrons from an atom or molecule. (2-10)

oxyanion hole: a binding site for an alkoxide in an enzyme active site. The "hole" is a pocket that fits the $-O^-$ group precisely, and has two hydrogen-bond-donating groups that stabilize the oxyanion with $-O^-\cdots H-X$ hydrogen bonds. (2-14)

packing motif: an arrangement of secondary structure elements defined by the number and types of such elements and the angles between them. The term motif is used in structural biology in a number of contexts and thus can be confusing. (1-10)

pairwise alignment: alignment of two sequences. (4-1)

palmitoylation: reversible attachment of a palmitoyl group to a protein via a thioester linkage. (3-19)

parallel beta sheet: a beta sheet, formed from non-contiguous regions of the polypeptide chain, in which every strand runs in the same direction. (1-7)

partner swapping: exchange of one protein for another in multiprotein complexes. (2-4)

pentamer: an assembly of five identical or different subunits: in a protein, these are individual folded polypeptide chains. (1-19)

peptide bond: another name for **amide bond**, a chemical bond formed when a carboxylic acid condenses with an amino group with the expulsion of a water molecule. The term peptide bond is used only when both groups come from amino acids. (1-3)

percent identity: the percentage of columns in an **alignment** of two sequences that contain identical amino acids. Columns that include gaps are not counted. (4-1)

phase problem: in the measurement of data from an X-ray crystallographic experiment only the amplitude of the wave is determined. To compute a structure, the phase must also be known. Since it cannot be determined directly, it must be determined indirectly or by some other experiment. (5-2)

phi torsion angle: see **torsion angle**.

phosphate-binding loop: see **P-loop**.

phosphorylation: covalent addition of a phosphate group, usually to one or more amino-acid side chains on a protein, catalyzed by protein kinases. (1-13)

phylogenetic tree: a branching diagram, usually based on the evolutionary distances between sequences, that illustrates the evolutionary history of a protein family or superfamily, or the relationships between different species of organism. (4-1)

pK_a value: strictly defined as the negative logarithm of the equilibrium constant for the acid-base equation. For ranges of pK_a between 0 and 14, it can be thought of as the pH of an aqueous solution at which a proton-donating group is half protonated and half deprotonated. pK_a is a measure of the proton affinity of a group: the lower the pK_a, the more weakly the proton is held. (2-12)

pleated sheet: another name for **beta sheet**.

P-loop: a conserved loop in GTPase- and ATPase-based nucleotide switch proteins that binds to phosphate groups in the bound nucleotide. (3-6)

polypeptide: a polymer of amino acids joined together by **peptide bonds**. (1-3)

positive cooperativity: binding of one molecule of a ligand to a protein makes it easier for a second molecule of that ligand to bind at another site. (3-4)

prenylation: irreversible attachment of either a farnesyl or geranylgeranyl group to a protein via thioether linkage. (3-19)

primary structure: the amino-acid sequence of a polypeptide chain. (1-2)

primary transcript: the RNA molecule directly transcribed from a gene, before removal of introns or other editing. (1-2)

profile: a table or matrix of information that characterizes a protein family or superfamily. It is typically composed of sequence variation or identity with respect to a reference sequence, expressed as a function of each position in the amino-acid sequence of a protein. It can be generalized to include structural information. Three-dimensional profiles express the three-dimensional structure of a protein as a table which represents the local environment and conformation of each residue. (4-2)

propinquity factor: another term for **proximity factor**.

proteasome: a multiprotein complex that degrades ubiquitinated proteins into short peptides. (3-11)

protein kinase: enzyme that transfers a phosphate group from ATP to the OH group of serines, threonines and tyrosines of target proteins. Kinases that phosphorylate carboxylates and histidines also occur as part of **two-component systems** in prokaryotes, fungi and plants, but not in animals. (3-2)

protein phosphatase: enzyme that specifically removes phosphate groups from phosphorylated serines, threonines or tyrosines on proteins. (3-12)

proteolytic cascade: a sequential series of protein cleavages by proteases, each cleavage activating the next protease in the cascade. (3-16)

protomer: the asymmetric repeating unit (or units) from which an oligomeric protein is built up. (1-21)

proximity factor: the concept that a reaction will be facilitated if the reacting species are brought close together in an orientation appropriate for chemistry to occur. (2-8)

pseudosymmetric: having approximate but not exact symmetry. A protein with two non-identical subunits of very similar three-dimensional structure is a pseudosymmetric dimer. (1-21)

psi torsion angle: see **torsion angle**.

quaternary structure: the subunit structure of a protein. (1-19)

Ramachandran plot: a two-dimensional plot of the values of the backbone torsion angles phi and psi, with allowed regions indicated for conformations where there is no steric interference. Ramachandran plots are used as a diagnosis for accurate structures: when the phi and psi torsion angles of an experimentally determined protein structure are plotted on such a diagram, the observed values should fall predominantly in the allowed regions. (1-5)

reaction sub-site: that part of the active site where chemistry occurs. (2-7)

redox reactions: reactions in which oxidation and reduction occur. (2-10)

reducing environment: a chemical environment in which the reduced states of chemical groups are favored. In a reducing environment, free –S–H groups are favored over –S–S– bridges. The interior of most cells is a highly reducing environment. (1-4)

reduction: the gain of electrons by an atom or molecule. (2-10)

residue: the basic building block of a polymer; the fragment that is released when the bonds that hold the polymer segments together are broken. In proteins, the residues are the amino acids. (1-1)

resolution: the level of detail that can be derived from a given process. (5-1)

resonance: delocalization of bonding electrons over more than one chemical bond in a molecule. Resonance greatly increases the stability of a molecule. It can be represented, conceptually, as if the properties of the molecule were an average of several structures in which the chemical bonds differ. (1-3)

reverse turn: another name for **beta turn**.

RGS protein: regulator of G-protein signaling protein; protein that binds to the free GTP-bound α subunit of a **heterotrimeric G protein** and stimulates its GTPase activity. (3-8)

RNA editing: enzymatic modification of the mRNA base sequence. It may involve changes in the bases or the insertion of entirely new stretches of bases. RNA editing produces a protein sequence that does not correspond precisely to the sequence of amino acids that would be predicted from the gene sequence by the genetic code. (1-2)

RNA interference (RNAi): abolition of the expression of a gene by a small (~22 base pair) double-stranded RNA. (4-4)

***S*-acylation:** reversible attachment of a fatty-acid group to a protein via a thioester linkage; **palmitoylation** is an example of *S*-acylation. (3-19)

salt bridge: a **hydrogen bond** in which both donor and acceptor atoms are fully charged. The bonding energy of a salt bridge is significantly higher than that of a hydrogen bond in which only one participating atom is fully charged or in which both are partially charged. (1-4)

scaffold protein: a protein that serves as a platform onto which other proteins assemble to form functional complexes. (2-5)

secondary structure: folded segments of a polypeptide chain with repeating, characteristic phi, psi backbone torsion angles, that are stabilized by a regular pattern of hydrogen bonds between the peptide –N–H and C=O groups of different residues. (1-5)

side chain: a chemical group in a polymer that protrudes from the repeating backbone. In proteins, the side chain, which is bonded to the alpha carbon of the backbone, gives each of the 20 amino acids its particular chemical identity. Glycine has no side chain, and the end of the side chain of proline is fused to the nitrogen of the backbone, creating a closed ring. (1-1)

single-nucleotide polymorphism (SNP): a mutation of a single base in a codon, usually one that does not affect the identity of the amino acid that it encodes. (1-2)

specificity sub-site: that part of the active site where recognition of the ligand takes place. (2-7)

stop codon: a codon that signals the end of the coding sequence and usually terminates **translation**. (1-2)

stress-response proteins: proteins whose synthesis is induced when cells are subjected to environmental stress, such as heat. (3-11)

structural domain: a compact part of the overall structure of a protein that is sufficiently independent of the rest of the molecule to suggest that it could fold stably on its own. (2-3)

substrate: the molecule that is transformed in a reaction. (2-6)

sumoylation: modification of the side chain of a lysine residue by addition of a small ubiquitin-like protein (SUMO). The covalent attachment is an amide bond between the carboxy-terminal carboxylate of SUMO and the NH_2 on the lysine side chain of the targeted protein. (3-20)

superfamily: proteins with the same overall fold but with usually less than 40% sequence identity. The nature of the biochemical functions performed by proteins in the same superfamily are more divergent than those within families. For instance, members of the same enzyme superfamily may not catalyze the same overall reaction, yet still retain a common mechanism for stabilizing chemically similar rate-limiting transition-states and intermediates, and will do so with similar active site residues. (4-8)

switch I region: a conserved sequence motif in GTPase- and ATPase-based nucleotide switch proteins that, with the **switch II region**, binds the terminal gamma-phosphate in the triphosphate form of the bound nucleotide and undergoes a marked conformational change when the nucleotide is hydrolyzed. (3-6)

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temperature-sensitive: losing structure and/or function at temperatures above physiological or room temperature. A temperature-sensitive mutation is a change in the amino-acid sequence of a protein that causes the protein to inactivate or fail to fold properly at such temperatures. (1-12)

temperature-sensitive mutants: organisms containing a genetic mutation that makes the resulting protein sensitive to slightly elevated temperatures. The temperature at which the mutant protein unfolds is called the restrictive temperature. The term is also used for the protein itself. (3-11)

tertiary structure: the folded conformation of a protein, formed by the condensation of the various secondary elements, stabilized by a large number of weak interactions. (1-10)

tetramer: an assembly of four identical or different subunits. (1-19)

thermophilic: favoring high temperatures. A thermophilic organism is one that requires high temperatures (above approximately 50 °C) for survival. A thermophilic enzyme is one that functions optimally and is stable at temperatures at which **mesophilic** proteins denature. (1-12)

TIM barrel: another name for the alpha/beta barrel fold. (1-18)

torsion angle: the angle between two groups on either side of a rotatable chemical bond. If the bond is the C_α–N bond of a peptide backbone the torsion angle is called **phi**. If the bond is the C_α–C backbone bond, the angle is called **psi**. (1-3)

transcription: the synthesis of RNA from the coding strand of DNA by DNA-dependent RNA polymerase. (1-2)

transition state: the species of highest free energy either in a reaction or a step of a reaction; the highest region on the **activation-energy barrier**. (2-6)

translation: the transfer of genetic information from the sequence of **codons** on **mRNA** into a sequence of amino acids and the synthesis on the ribosome of the corresponding polypeptide chain. (1-2)

trimer: an assembly of three identical or different subunits. (1-19)

two-component systems: signal transduction systems found in bacteria and some eukaryotes involving a membrane-bound histidine kinase and a cytoplasmic response regulator protein that is activated by phosphorylation. (3-15)

ubiquitin: a small protein that when attached to other proteins (**ubiquitination**), targets them for degradation to the **proteasome**. Sometimes ubiquitin tagging targets a protein to other fates such as endocytosis. (3-11)

ubiquitination: the attachment of ubiquitin to a protein. (3-11)

up-and-down structural motif: a simple fold in which beta strands in an antiparallel sheet are all adjacent in sequence and connectivity. (1-17)

van der Waals interaction: a weak attractive force between two atoms or groups of atoms, arising from the fluctuations in electron distribution around the nuclei. Van der Waals forces are stronger between less electronegative atoms such as those found in hydrophobic groups. (1-4)

yeast two-hybrid: a method for finding proteins that interact with another protein, based on activation of a reporter gene in yeast. (4-4)

zinc finger: a small, irregular domain stabilized by binding of a zinc ion. Zinc fingers usually are found in eukaryotic DNA-binding proteins. They contain signature metal-ion binding sequence motifs. (1-18)