**Glossary of biochemical terms**

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| **Term** | **Definition** |
| acetazolamide | An inhibitor of carbonic anhydrase. |
| activation loop | A sequence of a protein, typically a kinase, that is modified, allowing the enzyme to be "turned on". Kinase function is initiated by specific residues in the activation loop being phosphorylated. |
| aliphatic | An organic molecule consisting of unbranched or open chains. In amino acids, it refers to a hydrocarbon side group. |
| alpha helix | A common secondary structure motif of a protein, consisting of a right-handed repetitive loop (helix). The shape is maintained by hydrogen bonds between the amino (NH) group in a peptide bond with the carbonyl (CO) group in a peptide bond three or four residues earlier.  |
| amidic | Of a molecule, containing an amide (-CONH2) group. |
| amiloride | A diuretic, and sodium/potassium ATPase inhibitor. It acts by selectively blocking sodium transport. |
| amino acid | The monomer that proteins are composed from. All amino acids have a central (or alpha) carbon, with four constituents covalently bonded to it: hydrogen, an amino (NH2) group, a carboxyl (COOH) group and a side group of varying composition. The amino and carboxyl groups from adjacent amino acids condense to form a peptide bond (CONH) whereas the side group is responsible for chemical differences between amino acid residues.  |
| anhydrous | When referring to macromolecules or minerals, the form that does not have any water molecules bound to it. |
| antibody | A protein that marks pathogens (for destruction by immune cells) by binding to them. In immunohistochemistry labelling, an antibody is created (“raised”) that specifically binds to a protein of interest. The protein’s location can then be visualised through a “tag” that is covalently bonded to the antibody. |
| antiserum | A blood serum that contains protein-specific antibodies. |
| aragonite | A calcium carbonate mineral polymorph. It has orthorhombic geometry, where each calcium ion is coordinated to nine oxygen atoms. |
| aromatic | In organic molecules, refers to containing a flat, ring of resonance bonds. A resonant bond is one where one or more electrons is delocalised, being shared over the whole molecule. Benzene is an example of an aromatic organic molecule.  |
| ATPase | A class of enzyme that catalyses the conversion of adenosine triphosphate (ATP) into free phosphate and adenosine diphosphate (ADP). This process yields energy which is often used by the enzyme to drive additional chemical reactions such as active transport.  |
| basement membrane | Also called the basal lamina. It is a form of extracellular matrix whose function is to provide structure to epithelial cells and to anchor them to the underlying connective tissue. |
| basic | In organic molecules, refers to containing a functional group that can receive protons (H+). In amino acids, basicity is the result of side groups with one or more amino groups. |
| Basic Local Alignment Search Tool (BLAST) | An algorithm that allows for the comparison of a target primary sequence with a database of chosen sequences, looking for regions of local similarity.  |
| Beta sheet | A motif of protein secondary structure. In a beta street, beta strands of three to ten amino acids in length form a pleated, twisted sheet structure. Individual beta strands are held together laterally by hydrogen bonds. |
| BLASTN | A BLAST analysis where a target nucleotide (DNA or RNA) sequence is compared with a chosen nucleotide database. |
| BLASTP | A BLAST analysis where a target peptide sequence is compared with a chosen protein database. |
| BLASTX | A BLAST analysis where a target nucleotide sequence is translated into all possible amino acid sequences and then compared with a chosen peptide database.  |
| C1q | An abbreviation of complement component 1q, a conserved protein domain. Proteins with the C1q domain have sequences that are structurally similar to collagen types VIII and X.  |
| calcite | A calcium carbonate mineral polymorph. It has trigonal geometry, where each calcium ion is coordinated to six oxygen atoms. |
| carboxylate | In organic molecules, the ion created when a carboxylic acid group (COOH) loses a proton (H+) to form COO-. |
| cDNA | Complementary DNA. A single-stranded DNA sequence synthesised through enzyme-mediated reverse transcription of messenger RNA.  |
| chaperone, chaperonin | A class of protein responsible for the correct folding of other proteins. Chaperonins produce the conditions that encourage proper folding, and often additionally prevent misfolding. Some chaperonins are involved in protection against extreme temperatures, are referred to as Heat Shock Proteins (HSPs). |
| co-factor | A molecule or metal ion necessary for the correct functioning of an enzyme.  |
| collagen | A superfamily of proteins that are the main structural constituents of extracellular matrices and connective tissues.  |
| collagenase | A group of enzymes that catalyse the digestion of collagen proteins.  |
| collectin | Also called collagen-containing C-type lectin. Members of this family of lectins are both Ca2+-dependent and collagenous. |
| conserved | In DNA, RNA and proteins, refers to a sequence that is either identical or extremely similar between different taxa.  |
| cristae | Plural abbreviation of *crista ampullaris*. Organ of the inner ear found in the semicircular canals, responsible for detection of rotation. |
| crystal polymorph | In a mineral, the geometry of its solid form. Minerals can be arranged in different geometries. For example, calcium carbonate may exist as trigonal (calcite), orthorhombic (aragonite), or hexagonal (vaterite) crystal polymorph. |
| C-terminal | In polypeptides, the end of the chain that terminates with a free carboxyl (-COOH) functional group.  |
| dimer | In proteins, a complex formed by two protein monomers. The monomers are usually not bound by covalent bonds to each other. |
| disulfide crosslink | A covalent bond (-S-S-) formed by the reaction of the thiol groups (-SH) of two cysteine residues.  |
| disulfonate stilbene | An inhibitor that blocks anion transport such as the exchange of chloride and bicarbonate ions. |
| domain | A sequence in a protein with a discrete biological function and/or structure. Domains are often conserved sequences between taxa. |
| EF-hand | A structural domain often found in calcium-binding proteins. EF-hand consists of two alpha helices connected by a short loop. |
| enzyme cascade | A series of successive enzyme-catalysed reactions. In a cascade, each enzyme activated catalyses the activation of the enzyme that immediately follows it. |
| extracellular matrix | A three-dimensional network of proteins, glycoproteins and other macromolecules that provides structure to adjacent cells.  |
| family | A group of proteins that share a common evolutionary ancestor. Members of a family often have similar domains, sequences, structures and functions. |
| fibril | In proteins, a thin rod-like, linear arrangement. Collagen is often arranged into fibrils, which are then bundled together. |
| fold | A three-dimensional arrangement of secondary structure elements of a protein (e.g. alpha helices, beta sheets) that form part of its tertiary structure.  |
| folding | The mechanism by which a protein’s secondary structure is arranged into its functional, three-dimensional, tertiary structure. An incorrectly folded protein is referred to as “misfolded”.  |
| follistatin | A family of glycoproteins that are neutralisers of a family of cell regulatory proteins, transforming growth factor beta (TGFβ). |
| frictional ratio | A measurement indicating the shape and relative asymmetry of a protein. It is a dimensionless ratio of a protein’s observed translational frictional coefficient (a measurement of the resistance to movement of a molecule) to that of an anhydrous spherical molecule of equivalent mass and density. Proteins with larger frictional ratios tend to be more asymmetrical. |
| genome | The complete set of genetic material in an organism. |
| glycogen | A multi-branched polymer of glucose produced by eukaryotes. It is typically an energy storage carbohydrate but can play roles in other intra- and extracellular processes.  |
| glycoprotein | A protein that has been post-translationally modified through the covalent bonding of one or more carbohydrates to its peptide chain. |
| glycosaminoglycan | A long unbranched polysaccharide that consists of a repeating disaccharide with amino (-NH2­) groups. Also called a mucopolysaccharide. One or more glycosaminoglycans can attach to a core protein to form a proteoglycan. |
| heparan sulfate | A glycosaminoglycan that often occurs in extracellular matrices and at the cell surface. In heparan sulfate, the disaccharide subunit is variously sulfated. |
| HEXXH | A zinc binding sequence motif. Specifically, the motif is histidine-glutamic acid-(any amino acid)-(any amino acid)-histidine. |
| homolog | In proteins or nucleic acids, two sequences that have significant similarity are said to be homologs. High homology is often taken as evidence that two sequences have the same ancestor and are the product of divergent evolution. |
| hydrophilic | Of molecules or parts of molecules, readily interacting with water and other polar solvents. Typically, a hydrophilic region will be either charged or a permanent dipole, and capable of forming hydrogen bonds.  |
| hydrophobic | In molecules or parts of molecules, refers to the tendency to exclude water and other polar solvents. Typically, a hydrophobic region will be non-polar. |
| in situ hybridization | The process by which a single stranded nucleic acid anneals to a complementary strand of DNA or RNA in a specific tissue. This technique can allow for visualisation of protein expression by employing a labelled fragment of DNA or RNA termed an DNA/RNA probe. |
| integrin | A family of proteins that act to facilitate adhesion of the extracellular matrix to cells.  |
| intrinsically disordered protein | A protein that partially or completely lacks an ordered three-dimensional structure. |
| ion-exchange chromatography | A method used to purify proteins. Ion-exchange chromatography works by attracting charged molecules in the solute (i.e. peptides, proteins) to an oppositely charged solid-phase.  |
| ionocyte | A specialised cell found in the inner ear epithelium responsible for transporting ions into the extracellular space. |
| isoform | A variant of a protein. Isoforms of a protein generally are the result of the same gene or gene family and have slight differences in their amino acid sequences. As a result, isoforms tend to be functionally identical while not having 100% sequence homology. |
| isozyme | A member of a set of enzymes that differ in amino acid sequence but have the same catalytic function. |
| kilobase (kb) | The unit for expressing length of nucleic acids. One kb represents one thousand nucleotide base pairs. |
| kilodalton (kDa) | The common unit for expressing mass of proteins and other macromolecules. A kilodalton is equivalent to one thousand atomic mass units. The scale is based on 1 atom of 12C being assigned a mass of 12 Da, or 0.012 kDa. |
| kinase | A class of enzyme that catalyzes the transfer of one or more phosphate (-PO43-) groups from a donor (such as ATP) to a substrate (such as a protein). After the phosphates have covalently bonded, the substrate is said to be phosphorylated. |
| kinocilia | A specialised form of cilia that protrude from the apices of hair cells in the maculae of the inner ear. Kinocilia are essential for mechanoreception.  |
| knockdown | In genetic manipulation studies, the reduction of a gene’s expression.  |
| knockout | In genetic manipulation studies, the complete removal of a gene’s expression.  |
| lectin | A carbohydrate-binding protein family. |
| ligand | A molecule or ion that donates a pair of electrons to a central, positively charged, metal atom, forming a coordinate bond. The resulting complex of ligands and metal atom is called a coordination complex. For example, in hemoglobin, each protein subunit contains a heme group (porphyrin), which acts as a ligand for one iron atom.  |
| ligase | An enzyme that can catalyze the bonding of two large molecules. DNA ligase, for example, catalyzes the joining of two DNA strands. |
| lipoprotein | A complex made of a lipid and a protein. Lipoproteins are often involved in triglyceride and cholesterol transport. |
| lobe | A type of shape made by a protein’s tertiary structure. |
| lumen | The inside space of a structure. In the context of this review, the inside of the otic vesicle. |
| lysis | The act of breaking down or splitting. |
| macromolecule | A molecule with a high molecular weight. It is often a polymer. In biology, "macromolecule" typically refers to either proteins, nucleic acids or polysaccharides. |
| macula | The sensory portion of the inner ear. It has numerous hair cells for mechanoreception.  |
| Mascot search | Mascot is a search tool created by Matrix Science that allows for protein identification, characterisation and quantitation. It facilitates the searching of collected protein mass spectrometry data against large nucleotide or peptide databases. |
| Matrix Assisted Laser Desorption/Ionization-Time of Flight-Mass Spectrometry (MALDI-TOF-MS) | A technique used in protein analysis. In MALDI, a matrix is bound to the sample which allows for large molecular ions to be created when hit with a ionization laser. This system is coupled with TOF-MS, an approach where the ions are separated and then determined based on the time taken for them to reach the detector. |
| matrix protein | In otoliths, this refers to those proteins that are responsible for creating the scaffold of fibres that are necessary for proper mineralisation to occur. Broadly speaking, the discontinuous zone is dominated by matrix proteins, whereas the incremental zone is dominated by mineral. |
| metalloproteinase | An enzyme that catalyzes the breakdown of other proteins and has a metal as part of its mechanism. In biomineral systems, matrix metalloproteinases are common. These often have zinc as part of their structures and catalyze the breakdown of collagens. |
| morpholino | More properly called a morpholino oligomer (MO), these molecules are involved in gene expression studies. They act by binding to specific mRNA sequences, blocking or decreasing protein translation. |
| motif | In proteins, a motif can be either a structural motif or a sequence motif. A structural motif is used to explain how different secondary structures are connected. For example, two alpha helices can be connected by a loop, creating the “helix-loop-helix” motif. As a result, motifs are considered supersecondary structures, assembling secondary structures into the overall three-dimensional tertiary structure of the protein. In contrast to this, a sequence motif is a common pattern of amino acids that is thought have biological significance. Glycine-(any amino acid)-(any other amino acid) is a sequence motif of collagens. |
| mucopolysaccharide | See glycosaminoglycan, above. |
| N-glycosylation | The attachment of a sugar (usually an oligo- or polysaccharide) to a nitrogen atom in the side group of an Asparagine of a protein. Other glycosylation events are possible e.g. O-glycosylation, the binding of sugars to an oxygen in the side group of serine or threonine. |
| node | In a protein, a sequence that acts as a hub. |
| N-terminal | In polypeptides, the end of the chain that terminates with a free amino (-NH2) functional group.  |
| nucleation | The first, or initial, stage in crystal formation. |
| oligomerise | To form a complex made up of a few repeating subunits. Oligomers are often formed by proteins binding non-covalently, and are typically dimers (two subunits), trimers (three subunits) or tetramers (four subunits). Contrast this with a polymer, where the number of repeating subunits is potentially infinite.  |
| order/disorder | In proteins, order refers to having locally organised secondary structures (e.g. alpha helices, beta sheets) whereas disorder refers to a total or partial absence of three-dimensional structure. Residues are considered either “order-promoting” (e.g. cysteine) or “disorder-promoting” (e.g. proline). |
| osteoblast | The cell type responsible for secreting matrix proteins and synthesizing tissue in bone. |
| osteoclast | The cell type responsible for absorbing, breaking down and recycling bone tissue. |
| otic placode | In the embryo, the thickening of the outer ectoderm that leads to the formation of the inner ear. |
| otic vesicle | In embryonic development, the otic vesicle is a sac-like structure formed from the otic placode. The otic vesicle will eventually form the entire labyrinth of the inner ear. |
| ouabain | A chemical inhibitor of Na+/K+-ATPase. |
| paracellular | In transport, refers to the transferring of material through the space between two epithelial cells. |
| peptide | Refers to the covalent bonding of two or more amino acids. The carboxyl (-COOH) functional group of one amino acid reacts with the amine (-NH2) functional group of a different amino acid to create a peptide, or amide, bond (-CONH-). A peptide chain refers to many amino acids linked in this way. |
| phospholipase | An enzyme that catalyzes the breakdown of phospholipids into fatty acids and other products. A phospholipid is a lipid that has a phosphate group attached to it.  |
| phosphorylation | A post-translational modification where a phosphate (PO43-) is covalently bonded to one or more residues in a polypeptide. Most phosphorylation occurs at serine, threonine or tyrosine residues. |
| polyanionic | A complex or molecule that has multiple negatively charged sites. |
| post-translational modification | A change made to the secondary sequence of a protein after its assembly at the ribosome (translation). Examples of post-translational modifications can include the addition to residues of sugars (glycosylation) or phosphates (phosphorylation). |
| primary sequence | The specific order of monomers in a biological polymer. In proteins, it is the order of amino acids in a polypeptide, whereas in DNA and RNA it refers to the order of nucleotides. |
| primary structure | In proteins, the order of amino acids in a polypeptide. |
| primordium | The initial, organic, complex structure of the otolith.  |
| protease | An enzyme that catalyzes the breakdown of proteins. |
| proteinaceous | Consisting of protein; protein-rich. |
| proteoglycan | A heavily glycosylated protein. Proteoglycans consist of a small protein core covalently bonded to glycosaminoglycan chains. |
| proteolysis | The breakdown of proteins into amino acids or smaller peptide units. |
| proteome | The complete suite of proteins produced by a single cell, tissue, organ or whole organism at a specific point in time. |
| proton pump | A membrane protein that establishes a pH gradient through proton (H+ ion) transport. |
| quaternary structure | The interaction of several polypeptides (called protein subunits) to form a larger protein complex. For example, hemoglobin’s quaternary structure consists of four subunits: 2 alpha chains and 2 beta chains.  |
| regulation | In the context of proteins, a change in activity or expression through interaction or binding with a molecule or ion.  |
| residue | In macromolecules, this refers to the specific monomers in the polymer sequence. For example, a peptide that is 30 amino acids long can be said to be 30 residues in length. |
| RNA probe | A variable length fragment of RNA that binds to a target nucleotide sequence. |
| screening | A methodical search and identification of relevant DNA sections according to specific criteria. For example, in differential screening, an entire cDNA library is compared with a reference library and sequences that differ are identified. |
| secondary structure | In proteins, the local three-dimensional structure of a sequence or segment. The most common secondary structures are alpha helices and beta sheets. Secondary structures form as the result of attraction (e.g. hydrogen bonds) between non-adjacent amino acids. |
| side group | A group of atoms attached to the core part of the molecule. In proteins, amino acids are differentiated by their side groups. The side group gives an amino acid (and thus a peptide sequence) its chemical properties. Also called a “side chain”. |
| size exclusion chromatography (SEC) | A fractionation method in which large molecules (often macromolecules) in a mixture are separated by size and/or molecular weight. In SEC, a mixture is suspended in a buffer which is loaded into a chromatography column packed with porous beads. Macromolecules of different sizes navigate through the column at different rates, resulting in the fractionation of the mixture. |
| spacer | The region between two nodes in a protein. |
| sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) | A method that allows protein or peptide separation by mass. Sodium dodecyl sulfate (SDS) is a detergent employed in protein analysis. It binds to the surface of proteins, swamping their intrinsic charge. The SDS-treated proteins are then injected into wells on a gel bed, made of polyacrylamide, with a constant electric field applied. As proteins have been treated with SDS, they have comparable mass-to-charge ratios, and thus all move towards the anode relative to their overall molecular weights. |
| squamous  | Referring to the shape of epithelial cells, flattened and wide. |
| stereocilia | Specialised hair cells that surround the kinocilium in an inner ear hair bundle. |
| Stokes radius | A measurement of molecular size in gel separation techniques such as size exclusion chromatography (SEC). A macromolecule’s Stokes radius is the radius of a hard, perfect sphere, that diffuses through a chromatography column at the same rate as the macromolecule in question. Also called Stokes-Einstein radius or hydrodynamic radius. It can be used to estimate molecular weight.  |
| subcupular | Of structures, being found beneath the cupula of the inner ear. In the inner ear, the cupula is a gelatinous mass that covers the *crista ampullaris.*  |
| substrate | In biochemistry, the target molecule/s of an enzyme. The enzyme binds to the substrate/s, catalyzing a specific reaction. For example, in phosphorylation, a kinase will have both ATP and a target protein as substrates. |
| tandem mass spectrometry (MS/MS) | A common method of analysis of macromolecules. In MS/MS, there are two stages. First, peptides (precursor ions) are separated based on their mass-to-charge ratio (MS1). Then, precursor ions of a specified mass-to-charge ratio are broken, and the resulting fragments (product ions) are further separated based on mass-to-charge ratio (MS2). This produces mass spectra that can be used to determine a peptide’s primary sequence.  |
| tectorial membrane | An acellular membrane in the vertebrate inner ear. In mammals, the tectorial membrane is in the cochlea. |
| tertiary structure | In proteins, the overall three-dimensional structure. |
| tether cell | A specialised hair cell in the fish inner ear. During early development, the otolith precursor particles attach to a tether cell, eventually resulting in the formation of the primordium. |
| thiocyanate | A chemical inhibitor of cellular ion transport. It particularly affects the sodium-iodide transport pathway. |
| transcriptome | The sum of mRNA molecules in a cell, tissue or organism. A transcriptome often takes the form of a cDNA library assembled from reverse transcription of mRNA. |
| transitional epithelial cell | A type of epithelial cell that can expand or contract, changing from squamous to cuboidal. They can function as a barrier between the lumen and the bloodstream. Transitional epithelial cells are connected by tight junctions – virtually impenetrable junctions that seal together the cell membranes, preventing reabsorption of toxins and/or pathogens. They are usually impermeable to water and salts. |
| trimer | An oligomer consisting of three subunits.  |
| urea/hydroxylamine | A digestion method used in early protein analyses. Urea can denature proteins, whereas hydroxylamine is a chemical agent that cleaves peptide bonds. |
| V-type ATPase | Vacuolar-type H+-ATPase. An evolutionarily conserved enzyme, it uses the energy from hydrolysis of ATP to pump protons across both plasma and intracellular membranes. For this reason, it is often considered the opposite of ATP synthase (which uses the energy from a pH gradient to create ATP). It is found in a wide variety of cell types in all eukaryotes.  |
| vaterite | A calcium carbonate mineral polymorph. It has hexagonal geometry. |
| von Willebrand factor type D | A protein domain found in many glycoproteins. It is found in fibrillar collagens, integrins and extracellular proteins. |
| zona pellucida | A protein domain originally found in mammalian oocytes. It facilitates membrane adhesion. |