

BIOL213 – Principles in Biochemistry – EXAM NOTES

Amino Acids

- Structure:
 - Alpha carbon
 - Hydrogen atom
 - Amino group
 - Carboxylic acid
 - R side chain – variable and unique to each amino acid
- Chirality
 - Enantiomers = non-superimposable, mirror images
 - Exist as either D (Clockwise) or L (anticlockwise) form
 - Proteins only contain the L form
 - Achiral = can be rotated & superimposed on its mirror image.
- Classification by R group
 - Nonpolar, aliphatic
 - Hydrophobic, not water-soluble
 - Includes Glycine, alanine, valine, isoleucine, leucine, proline, methionine.
 - Polar, uncharged
 - Hydrophilic, weakly polar, soluble in water
 - Includes: Glutamine, asparagine, cysteine, serine, threonine
 - Aromatic
 - Absorb UV light at 270-28nm = pi bonds in benzene ring + conjugation (resonance structure).
 - Hydrophobic, varying polarity
 - Include: phenylalanine, Tyrosine, Tryptophan.
 - Positively charged (basic) at physiological pH
 - Strongly polar
 - Includes: histidine, Lysine, Arginine
 - Negatively charged (acidic) at physiological pH
 - Strongly polar
 - Includes: Aspartate, Glutamate
- Acid/base characteristics of amino acids
 - Equilibrium constant (K_a) = tendency of any acid to lose a proton
 - Stronger acids have high K_a's and low pK_a.
 - Henderson-Hasselbach equation = finding pH of a buffer
 - $\text{pH} = \text{pK}_a + \log [\text{base}/\text{acid}]$
 - When $[\text{base}] = [\text{acid}]$, then $\text{pH} = \text{pK}_a$
 - Concentration of charged and uncharged forms are equal.
 - Buffer capacity = pK_a +/- 1 pH unit
 - Ionization of amino acids
 - Amphoteric (ampholytes) = dual acid/base nature within one molecule.
 - Acidic pH = COOH & NH₃⁺ (positive charge)
 - $\text{pI} > \text{pH}$
 - Neutral pH = COO⁻ & NH₃⁺ (neutral charge)
 - $\text{pI} = \text{pH}$

- Basic pH = COO^- & NH_2 (negative charge)
 - $\text{pI} < \text{pH}$
- Inflection point = pK_a is the pH at which the concentration of the charged group is equal to the concentration of the uncharged group.
- Isoelectric point (pI) = pH at which the amino acid has a net neutral charge.
 - Without ionisable R group – $\text{pI} = (\text{pK}_1 + \text{pK}_2)/2$
 - With ionisable R group – $\text{pI} = (\text{pK}_{\text{R group}} + \text{pK}_2) / 2$

Peptides and Proteins

- Structure of proteins
 - Structure of Peptide bonds (covalent, dehydration reaction)
 - Resonance – partial sharing of 2 pairs of electrons between the carbonyl O & amide N.
 - Decrease reactivity of peptide bond
 - Exhibits a large dipole moment in favour of the Trans (E) configuration.
 - Carbonyl O = partial negative charge
 - Amide N = partial positive charge
 - Rigid and planar
 - Peptide bonds have some double-bond character due to resonance and cannot rotate.
 - Rotation around bonds connected to the alpha-carbon is permitted.
 - Rules that define structural patterns of proteins
 - Hydrophobic residues are buried in protein interior, away from aqueous environment.
 - The number of hydrogen bonds and ionic interactions within the proteins are maximized.
 - Levels of protein structure
 - Primary structure
 - Formation of peptide chain via covalently linked peptide bonds between amino acids.
 - Ultimately dictates function.
 - Secondary structures
 - Local spatial arrangement of the polypeptide backbone.
 - Common arrangements:
 - Alpha helix
 - stabilized by hydrogen bonds between $\text{C}=\text{O}$ & $\text{N}-\text{H}$ residues of peptide bonds 4 AAs apart.
 - Polypeptide backbone winds tightly around a longitudinal axis
 - Right-handed helix with 3.6 residues per turn.
 - R groups stick outward from helical backbone.

- Sequence affects helix stability
 - Small hydrophobic residues such as Ala & Leu are strong helix formers.
 - Several Glutamate residues in a row repel one another & untwist = all negatively charged
 - Bulky AAs won't fit closely together in the chain.
 - Pro is a helix breaker = rotation around N-C_{alpha} bond is impossible.
 - Gly is a helix breaker = tiny R-group gives too much flexibility
 - Beta sheet
 - Extended length of polypeptide backbone = composed of several beta strands that run alongside each other.
 - Stabilized by hydrogen bonds between adjacent segments that can be nearby or distant, or occur between different chains.
 - Exist as parallel or antiparallel beta sheets
 - Parallel – H-bonded strands run in the same direction
 - Results in bent H-bonds, which are weaker.
 - Antiparallel – H-bond strands run in opposite directions
 - Results in linear H-bonds = stronger.
 - Beta-turns occur whenever strands in beta sheets change direction
 - Can also link alpha-helices to beta-sheets or to each other.
 - Random coil = irregular arrangement of polypeptides
 - Looping regions.
- Tertiary structure
 - Overall spatial arrangement of atoms in a protein
 - Forms 3D structure that dictates function
 - Involves interactions between R groups.
 - Most proteins require assistance to fold into native conformation = chaperones
- Quaternary structure
 - Occurs in proteins that contain 2 or more separate polypeptide chains, which may be identical or different.

- Formed by assembly of individual polypeptides (subunits) into a larger functional cluster (multimers).
 - Stabilized by numerous weak interactions between R group side chains
 - Largely hydrophobic and polar interactions
 - Further stabilized by disulfide (covalent) bonds
 - Interacting AAs are not necessarily next to each other in the primary sequence.
 - E.g. Insulin (2 subunits – alpha & beta), hemoglobin (4 subunits – 2x alpha & 2x beta).
- Major classes of proteins
 - Protein Motifs = basis of protein structural classification
 - Specific arrangement of several secondary structure elements
 - All alpha-helix
 - All beta-sheet
 - Combination
 - Can be found as reoccurring structures in numerous proteins
 - Proteins are made from different motifs folded together
 - Examples:
 - Beta-barrel = twisted beta-sheet
 - Helix-loop-helix
 - Beta-alpha-beta loop
 - Fibrous proteins
 - Polypeptide chains arranged in long, linear strands/sheets
 - Made from a single type of secondary structure – either alpha-helix OR beta-sheets.
 - Provide support, shape, external protection
 - Examples:
 - Alpha-keratin
 - Tough, rigid, hard
 - Hair, nails, horns
 - Structure = cross-linked alpha-helices
 - Silk fibroin
 - Soft, flexible, non-stretchy
 - Main protein in silk from moths & spiders
 - Structure: non-covalently held beta-sheets with numerous weak interactions.
 - Consists of layers of antiparallel beta-sheets rich in Ala (allow close packing to give strong structure) & Gly
 - Globular proteins
 - Polypeptide chains arranged in globe-like bundles
 - Often contain several types of secondary structure – combinations of alpha-helices and beta-sheets.
 - Tend to be enzymes & regulatory proteins

- Water-soluble globular proteins – e.g. hemoglobin
- Lipid-soluble membranous proteins.