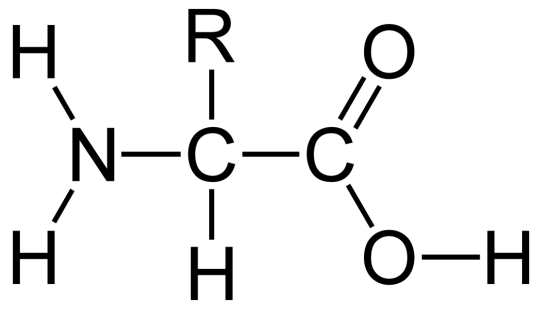
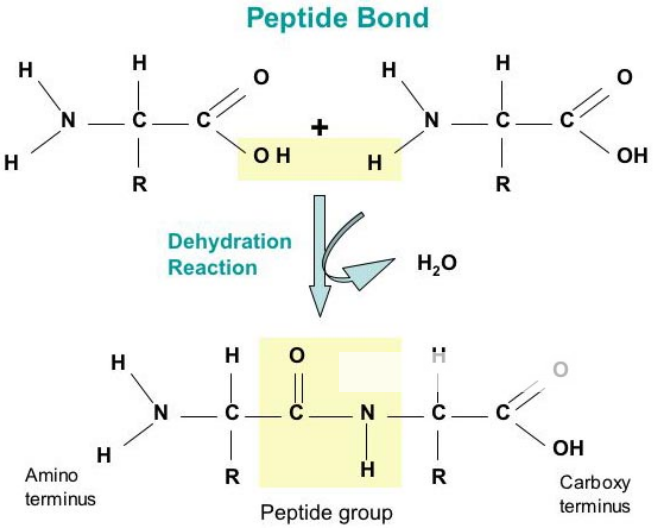
Proteins

Amino acids



- *Structure:
  - 1 α-carbon covalently bonded to 1 H atom, 1 amino group (-NH_2), 1 carboxyl group (-COOH) and 1 variable R group
  - R group can be non-polar, polar, acidic or basic
- Exist as zwitterions in solution = Carry both +ve and -ve charge
- Act as buffers
  - Due to amphoteric property (amino group acts as base; carboxyl group acts as acid)
  - Essential in biological systems as sudden changes in pH could adversely effect enzymes

Polypeptides



- Formation of **peptide bond**
  - Amino acids joined via **condensation** reactions with removal of 1 water molecule for every peptide bond formed

    - OH group from carboxyl group and H atom from amino group contribute to the formation of water molecule
    - Draw and label peptide bond
    - Reaction is catalysed by **peptidyl transferase** in large ribosomal subunit of **ribosomes**
- Peptide bond broken by **hydrolysis** reaction with addition of 1 water molecule per peptide bond broken
- Regularly repeating part referred to as polypeptide backbone

Proteins
Structure of Proteins

- **Primary Structure** = Specific number and sequence of amino acids in a single polypeptide chain maintained by **peptide** bonds
- Secondary, tertiary and quaternary structures are direct consequences of primary structure
- **Secondary Structure** = Regular coiling and folding/pleating of the polypeptide maintained by **hydrogen bonds** at regular intervals between CO and NH groups of the polypeptide backbone
    - **α-helix** = Regular coiling of a polypeptide chain with turns linked by **hydrogen bonds** formed between CO group of one amino acid residue and NH group of another amino acid **4** amino acids away
        - **3.6** amino acid residues in every turn of α-helix
    - **β-pleated sheet** = Flat sheet with **hydrogen bonds** formed between CO group of amino acid residues on one region and NH group of amino acid residues on adjacent region of single polypeptide chain
- **Tertiary Structure** = Further extensive folding and bending of a single polypeptide chain into specific 3D conformation maintained by hydrogen bonds, ionic bonds, hydrophobic interactions and disulfide bonds formed between R groups of amino acid residues within the same polypeptide
    1. Hydrogen bond
        - Formed between R groups of polar amino acids at tertiary structure
        - Individually weak but collectively strong
    2. Ionic bond
        - Formed between oppositely-charged R groups of amino acids
    3. Hydrophobic interaction
        - Formed between non-polar R groups which are hydrophobic as they cluster at the core of the protein to avoid water, causing the polypeptide to fold such that the hydrophobic R groups are shielded from the aqueous environment
    4. Disulfide bridge
        - Formed between 2 **cysteine** amino acid residues by oxidation of sulfydryl groups
        - Strong covalent bonds that contribute to the stability of proteins to heat denaturation
- **Quaternary Structure** = Association of 2 or more polypeptide chains into one functional protein molecule held together by the same R group interactions as in the

tertiary structure

- Significance of different R groups to protein structure
    - Sequence of amino acids and their R groups ⇒ Type and location of R group interactions ⇒ Specific tertiary structure ⇒ Specific 3D conformation ⇒ Function of the protein
    - Non-polar R groups of different amino acids cluster to form hydrophobic interactions
    - R groups containing sulphur are able to form disulphide bonds
    - R groups containing -NH and -OH groups have electronegative O and N atoms as well as electropositive H atoms covalently bonded to O or N, allowing them to form hydrogen bonds
    - Charged acidic and basic R groups are able to form ionic bonds
    - The presence of R groups that are too large may hinder the formation of the secondary structure

Globular Proteins - e.g. Haemoglobin

- Location: RBC of vertebrates
- Function: Transport oxygen in the blood (i.e. transport protein)
- Structure:
    - Secondary structure → Only α-helix, no β pleated sheet
    - Tertiary structure → No disulfide bonds
    - Quaternary structure with 4 polypeptide subunits → 2 α-globin subunits and 2 β-globin subunits each associated with an inorganic haem group

<u>Structure → Function of Haemoglobin</u>

- Function of haemoglobin is to transport oxygen in the blood

Structure	Function
Each subunit arranged such that its hydrophilic amino acid side chains are on the external surface while its hydrophobic amino acid side chains are buried in the interior	Soluble in aqueous environment allowing it to be transported and carry O_2 from lungs to tissues and vice versa
<u>4 polypeptide subunits</u>: 2 α-globin subunits and 2 β-globin subunits. Each subunit made up of a **globin**	Allows each haemoglobin molecule to carry up to 4 O_2 at a time, forming

polypeptide and a prosthetic component called **haem group** consisting of a porphyrin ring and Fe^{2+} which binds temporarily to O_2	oxyhaemoglobin ⇒ Allows haemoglobin to transport oxygen in the blood
4 subunits held together by weak intermolecular interactions (ionic bonds, hydrophobic interactions and hydrogen bonds) formed between R groups allows movement that influences their affinity for oxygen	Allows for **cooperative binding** of oxygen where the binding of one oxygen molecule to one haemoglobin subunit induces a conformational change in the remaining 3 subunits that increases their affinity for oxygen

Fibrous Proteins - e.g. Collagen

- Function: Structural protein
- Structure:
    - Made up of chain of amino acids linked by peptide bonds
    - Polypeptide chains have repeating tripeptide unit: glycine-X-Y where X is usually proline and Y is usually hydroxyproline
    - NO tertiary structure
    - Quaternary structure with 3 loose helical polypeptide chains held together by hydrogen bonds, wound together to form a tropocollagen molecule
    - Covalent cross-linking between lysine residues of adjacent staggered tropocollagen molecules to form collagen fibril
    - Bundles of collagen fibril form collagen fibre
    - Polypeptide chains → Tropocollagen → Fibrils → Collagen fibres

Structure	Function
Each chain has repeating tripeptide unit: glycine-X-Y where X is usually proline and Y is usually hydroxyproline	Bulky and relatively inflexible proline and hydroxyproline residues confer rigidity Small glycine residues allow the formation of a very compact triple helical structure
Extensive hydrogen bonding between amino acid residues of adjacent polypeptides chains Fibrous structural protein that has 3 helical polypeptide chains wound together to form a compact **tropocollagen** molecule	Insoluble in water as intramolecular hydrogen bonding limits ability to form hydrogen bonds with water molecules High tensile strength

Covalent cross-linking between lysine residues of adjacent tropocollagen molecules results in formation of fibrils Bundles of fibrils form large and long collagen fibres Staggered arrangement of tropocollagen molecules	High tensile strength Minimises weak fault lines along fibrils

Point of comparison	**Fibrous Proteins**	**Globular Proteins**
Shape	Made up of long polypeptide chains forming long, straight fibres	Made up of polypeptide chains folded into roughly spherical shape
Solubility in water	Insoluble in water since extensive hydrogen bonds already formed between residues in different polypeptides	Soluble in water since polar R groups, which are exposed to water molecules in the aqueous environment, can form hydrogen bonds with water
Constituent amino acids	Less variety of amino acids are used to construct the protein with a repetitive regular sequence of amino acids	More variety of amino acids are used to construct the protein (i.e. no repetitive regular sequence)
Length of polypeptide	Length of polypeptide and sequence of amino acids may vary slightly but protein is still functional	Length of polypeptide and sequence of amino acids are always identical or else protein may not be functional
Function	Structural proteins	Perform metabolic roles

Biuret Test
Procedure:

1. Mix 2cm^3 of test solution with equal volume of 5% KOH
2. Add 2 drops of 1% $CuSO_4$ and mix

Observations:

- Purple colour slowly develops if polypeptides are present (tests for peptide bonds)

Functions of Proteins

- Enzymatic catalysis
    - e.g. Amylase
    - Polypeptide chain folds to form active sites that are complementary in shape and charge to the specific substrate
    - Specific catalytic R groups in different active sites interact with the specific substrate forming a temporary association
    - Active site is flexible, being able to adjust its shape to better fit the substrate
    - Enzyme may interact with allosteric regulators that causes shape changes that affect its affinity for the substrate
- Transport
    - e.g. Haemoglobin
    - Different proteins may be associated with different prosthetic groups
    - For example, Fe^{2+} in each harm group in each of the 4 subunits of haemoglobin is able to bind reversibly to oxygen, allows haemoglobin to be an oxygen carrier
    - The binding of an oxygen molecule enhances the conformation of the next subunit to bind to another oxygen (positive co-operativity)
    - e.g. Membrane transport proteins
    - Protein is folded such that the hydrophilic amino acids are along the channel to allow the charged particles to pass through (ion channel)
    - Some transport proteins may have binding sites for molecules being transported. When the molecule binds to the transport protein, it induces a conformational change that translocates the molecule across the membrane
- Immunity
    - e.g. Antibodies
- Structural support
    - e.g. Collagen
    - In collagen, almost every 3rd amino acid is glycine, allowing the close fit of the 3 polypeptide chains to form a compact coil
    - Covalent cross-links between lysine residues at the C and N terminus of adjacent tropocollagen molecules and their staggered arrangement allows for the formation of fibrils, thus giving collagen high tensile strength
- Growth and differentiation
    - e.g. Insulin/Glucagon
- Coordination of motion
    - e.g. Proteins involved in muscle contraction

Things to Note

- Points of comparison between biological molecules
    - Monomers
    - Bonds involved
    - Shape/Conformation
    - Types of elements present
    - Solubility in water
    - Number of monomers - Varied or fixed