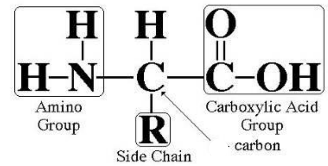
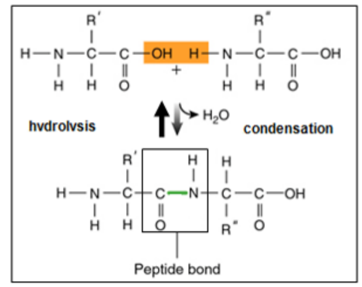
Proteins

Describe the structure and properties of an amino acid and describe the formation and breakage of a peptide bond



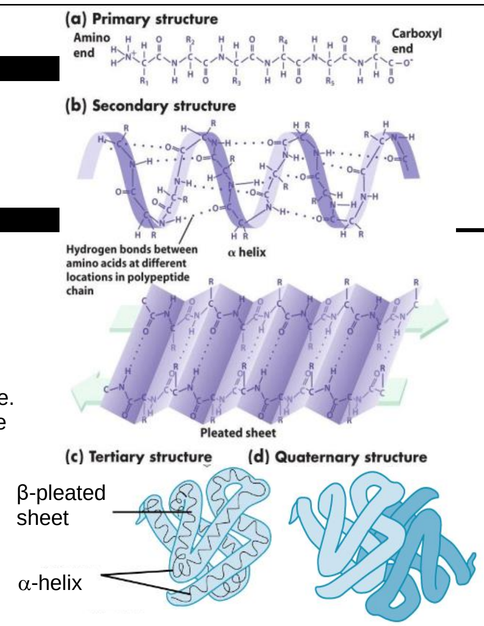
- **Amino Acids – Basic structural unit of proteins**
  - **Structure**
    - consists of an α-**carbon atom** covalently bonded to 4 groups
      1) **hydrogen atom**, 2) **amino group (-NH_2),** 3) **carboxyl group (-COOH),** 4) **variable R group**
  - **Properties of amino acids**
    - Classified according to their R groups as **uncharged (non-polar or polar)** or **charged**
    - Exist as zwitterions in solution – carry both positive and negative charges
    - Act as buffers
      - Can donate or accept H^+, therefore able to act as an acid or as a base – **amphoteric**
      - Essential in biological systems – sudden change in pH could adversely affect performance of proteins like enzymes



- **Polypeptides**
  - Amino acids are joined by a **peptide bond** via a **condensation reaction** with the **removal of one water molecule**.
  - Further addition of amino acids results in the formation of a **linear** polymer called a **polypeptide**
    - Regularly repeating part, the main chain, is referred to as the **backbone**.
    - Variable part comprises the distinctive **variable R groups**
  - polypeptide folds into a **specific three-dimensional shape / conformation**

- The nucleotide **sequence in DNA** determines **amino acid sequence** in polypeptide which determines **types** and **locations of R groups** which determines **R group interactions** which determines **3D structure** and **function of protein. (See picture with 4 R gp bonds / interactions below)**

Explain *primary structure, secondary structure, tertiary structure* and *quaternary structure* of proteins, and describe the types of bonds (hydrogen, ionic, disulfide and hydrophobic interactions) that hold the molecule in shape.



- 4 levels of organization in the structure of proteins

(a) Primary structure

- Refers to the **number and sequence of amino acids** in a single polypeptide chain.
- Linear structure maintained by **peptide bonds**
- The **sequence of amino acids** (and their **R groups**) in a polypeptide chain determines the **type and location of chemical bonds/interactions**, and hence the **3D conformation** and **characteristics** of a particular protein.

(b) Secondary structure

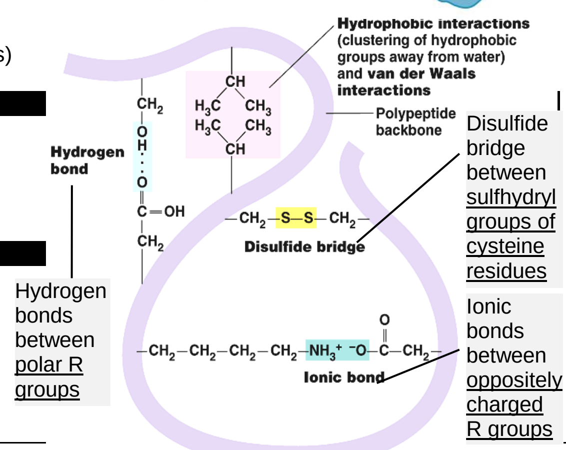
- Structure formed by **regular coiling or pleating** of a **single polypeptide** chain.
- Maintained by **hydrogen bonds**
  - between **C=O and N-H** groups of the **polypeptide backbone**.
  - **R groups are <u>not</u> involved**
- Examples of secondary structures:
  - **α-helix**
    - Made up of a **single polypeptide** chain which is wound into a **coiled/spiral** structure.
    - A **hydrogen bond** forms between the **C=O group** of one amino acid residue and the **N-H group** of another amino acid residue **four amino acids away** along the backbone of a **single polypeptide**
    - There are **3.6** amino acid residues in **every turn** of the helix
  - **β-pleated sheet**
    - **Two or more regions/segments** of a **single polypeptide chain** lying side by side are linked together by **hydrogen bonds**
    - A **hydrogen bond** forms between the **C=O group** of an amino acid residue and a **N-H group** of another amino acid residue on an **adjacent segments** along the backbone of a **single polypeptide**
    - Chains may run **parallel** (same direction) or **anti-parallel** (opposite directions)
    - Forms **flat sheet** which becomes folded

(c) Tertiary structure

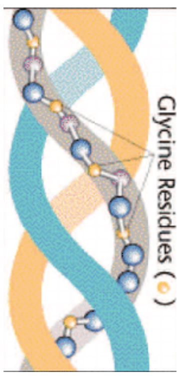
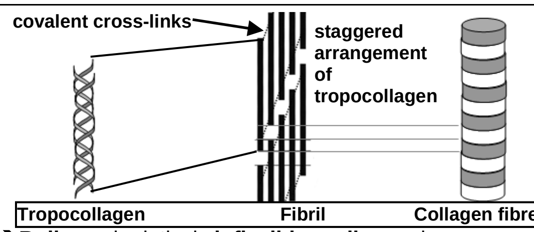
- Structure formed by **further extensive folding and bending** of a **single polypeptide chain**, giving rise to the **specific 3D conformation** of a protein
- Maintained by all **4** types of interactions
  - **hydrogen bonds**, **ionic bonds**, **hydrophobic interactions** and **disulfide bonds**
  - formed **between R groups** of amino acid residues **within a polypeptide**

(d) Quaternary structure

- Refers to the association of **two or more polypeptide** chains into one functional protein molecule
- Maintained by all **4** types of interactions
  - **hydrogen bonds**, **ionic bonds**, **hydrophobic interactions** and **disulfide bonds**
  - formed **between R groups** of amino acid residues of **different** polypeptides
- Constituent chains of a multimeric protein can be identical or different.



Describe the molecular <u>structure</u> of the haemoglobin and collagen and explain how the structure of each protein <u>relates to the function</u> it plays:

Example	Structure	Function
Haemoglobin (**globular** protein) ➔transports oxygen in the blood **(The binding of successive O_2 molecules facilitates binding of the next. Binding of the 1st O_2 molecule increases the affinity of haemoglobin for oxygen and hence facilitates the binding of the 2nd O_2 molelcule. Binding of the 2nd O_2 molecule facilitates the binding of the 3rd O_2 molecule and so on.)	1. Haemoglobin has a **quaternary** structure made up of **4 polypeptide subunits**: **2 α-globin** subunits and **2 β-globin** subunits. Each subunit is made of globin polypeptide and a prosthetic (non-protein) component called **haem group.** Each haem group consists of a **porphyrin ring** and **an iron ion (Fe^{2+})**	➔**Fe^{2+} of haem group binds temporarily to O_2**, so **1 Hb molecule can carry up to 4 O_2,** at a time forming oxyhaemoglobin
	2. Each subunit is arranged so that most of its **hydrophilic amino acid side chains** are on **external surface** while its **hydrophobic amino acid side chains** are buried in **interior**	➔Thus haemoglobin is **soluble in an aqueous environment** and can be transported in the blood while carrying O_2 from lungs to tissues vice versa
	3. The 4 subunits held together by **intermolecular interactions formed between R groups** (hydrogen bonds, ionic bonds and hydrophobic interactions). No disulfide bridges.	➔As a result binding of one oxygen molecule to one haemoglobin subunit induces a **conformational change** in remaining 3 subunits so that their **affinity for oxygen increases.** This is known as the **<u>**cooperative binding</u> of oxygen.**
Collagen (**fibrous** protein) ➔ an essential component of connective tissue in the human body. 	1. A **tropocollagen molecule** consists of **three helical polypeptide chains** (loose helices, not α-helices) wound around each other like a rope. (has quaternary but no tertiary structure) 2. Each chain contains about 1000 amino acids and contain a repeating sequence, usually a repeating tripeptide unit: **glycine-X-Y,** where X is usually **proline,** Y is usually **hydroxyproline.** The tropocollagen molecule can form a **tight, compact coil** as almost every third amino acid in each polypeptide chain is a **glycine**, the **smallest amino acid.** This allows it to fit into the restricted space in the center of the **triple helix**.	 ➔**Bulky** and relatively **inflexible proline** and hydroxy**proline** residues confer **rigidity** on the molecule.
	3. Extensive **hydrogen bonds** form **between amino acid residues of adjacent polypeptides,** hence interaction with water molecules are limited.	➔**Increases tensile strength** (ability to resist snapping due to stretching) and makes the molecule **insoluble in water**
	4. Adjacent tropocollagen molecules are arranged in a **staggered** manner	➔**Staggered/overlapping arrangement minimizes points of weaknesses along fibrils**
	5. **Covalent cross-links** between **lysine residues** at **C and N ends** of adjacent tropocollagen molecules results in the formation of fibrils.	➔Greatly **increases tensile strength**.
	6. Bundles of **fibrils** unite to form **long** collagen **fibres**.	➔Large size of collagen makes it **insoluble**, an important property for a structural molecule

	Fibrous protein (e.g. collagen)	Globular protein (e.g. haemoglobin, amylase)
Shape	Made up of long polypeptide chains forming **long, straight fibres**	Made up of polypeptide chains folded into **roughly spherical** shape
Solubility in H_2O	**Insoluble in water** ➔ as it is a l**arge molecule** and **extensive hydrogen bonds** have already formed **between residues** in different polypeptides	**Soluble in water** ➔ as **polar R groups** can form hydrogen bonds with water molecules in the **aqueous** environment
Amino acid sequence	**Less variety of amino acids** are used to construct the protein. i.e. consists of **repetitive regular sequence** of amino acids. (eg tripeptide, gly-X-Y repeats in collagen)	**More variety of amino acids** are used to construct the protein i.e. consists of non-repetitive amino acid sequence
Length of polypeptide	**Length of polypeptide** may **vary slightly** between two samples of the same protein, yet protein is still functional.	**Length of polypeptide** is **always identical** between two samples of the same protein, or else protein may not be functional.
Function	**Structural role**	Protein with **metabolic role** e.g. **enzyme**

Carry out Biuret test for proteins

Test	Procedure	Observations and Deduction
Biuret Test (A test for **peptide bonds**)	1. Place 2cm^3 of test solution in a test-tube 2. Add equal volume of 5% KOH solution and shake the mixture well 3. Add two drops of 1% copper sulphate solution, shaking well after each drop.	Presence of protein indicated by a **purple colour** developing slowly.

Denaturation of proteins

<u>3D shape of a protein may be changed by</u>: (a) Heat (affect hydrogen bonds, hydrophobic interactions) (b)Acids/Alkalis (affect hydrogen and ionic bonds)

NB: Strength of bonds: **hydrophobic interaction<H bonds<ionic bonds <disulfide bridges <peptide bonds**