



Proteins

Describing and explaining how the different bonds and intermolecular interactions maintain the different levels of protein structures

Explaining

- Hydrogen bonds can be formed between a hydrogen is attached to a highly electronegative atom such as nitrogen and atom making the hydrogen carry a partial positive charge, and a electronegative atom such as oxygen and nitrogen
- Ionic bonds are formed between oppositely charged R groups of amino acids
- Hydrophobic interactions is formed between hydrophobic non-polar R groups of amino acids
- Disulfide bond or bridges are formed only between two cytesine amino acids by oxidation of sulfydryl, -SH groups which contains sulphur
- In collagen, covalent cross links form between lysine residues at C and N ends of adjacent parallel tropocollagen molecules

Describing

Primary structure:

- The single polypeptide chain contains a **precise number, type and sequence of amino acids** held together by **peptide bonds** within each chain, which determines the chemical interactions and bonds of R groups

Secondary structure:

- The polypeptide chain **coils and folds into the regular repeating secondary structures** (α-helices/ beta pleated sheets) held together by hydrogen bonds between C=O and -NH groups (of peptide linkages) of the amino acids in the main chain (R group not involved)

Tertiary structure:

- The polypeptide chain further bends, coils and folds, to form a 3D shape / specific tertiary structure, maintained by intramolecular ionic bonds, hydrogen bonds, disulfide bonds and hydrophobic interactions between R groups of amino acids

Questions regarding the amino acid residue cysteine

(ii) "Cysteine is found to be more common than most other amino acids in the *Thermotoga maritima* enzyme compared to those found in other species".

Suggest why this may be so.

.....
.....
.....
..... [2]

1. Cysteine is the only amino acid that has an -SH R group (explains more common than most other amino acids); capable of forming disulfide bridges between their R-groups which are strong covalent bonds.
2. Covalent bonds contribute to high thermal stability, and are unaffected by pH, thereby allowing the maintenance of globular, 3D structure of the enzyme at much higher temperature. *OWTTE

▼ Tips

- Note that only cysteine has a -SH R group, making it the only one being able to form disulfide bridges with another cysteine molecule
- Disulfide bridges unaffected by temperature and PH
- For temperature, only hydrogen bonds and hydrophobic interactions are disrupted (aka weak intermolecular forces between covalent molecules)
- For pH, only hydrogen and ionic bonds affected
 - Ionic as there is charge, can affect the charge
 - Hydrogen bonds as there it can release H⁺

- (ii) Suggest why the amylase molecules of some species of bacteria are able to work at higher temperatures than others.

1 due to presence of more disulfide bridges

which are strong covalent bonds;

2 formed between sulfhydryl/ SH R groups

of cysteine amino acids within polypeptide chain;

3 higher temperatures, higher energy required

to break disulfide bridges to lose its 3D configuration shape;

[3]

[Total: 10]

Compare hydrogen bonds in tropocollagen and alpha helix secondary structure

- (iii) Compare between the hydrogen bonds within tropocollagen and within an alpha helix of a protein.

Similarities:

- Both are between N-H and C=O of the polypeptide backbone::
- Both are occurring at regular intervals throughout the helix::

Max. 1m

Differences:

Feature	Triple helix	Alpha helix
1. Location of hydrogen bonds	Between different polypeptide chain	Within the same polypeptide chain;;
2. Amino acids forming the hydrogen bonds	Between glycine & hydroxlysine OR proline	Between any amino acids;;
3. AVP;;		

Max. 1m

▼ Notes

- Do not write hydrogen bonds in tropocollagen formed between R groups (very vague)
- Tropocollagen also forms hydrogen bonds with C=O and N-H groups in its secondary structure

Structure and properties of haemoglobin

- Common mistake:
 - Consist of 2 alpha helices and 2 beta sheets
 - Consist of 2 alpha globin and 2 beta globin

Structure	Properties
It is a globular protein and has a quaternary structure comprising of 4 polypeptide subunits consisting of 2 alpha globin subunits and 2 beta globin subunits tightly packed into a tetrahedral conformation,	making the structure compact, allowing many haemoglobin molecules to be packed
Made up of 4 polypeptides packed in a tetrahedral conformation and held by weak hydrogen bonds which each carry a haem group	The bonds result in the ability of the polypeptide chains to move with respect to each other. Hence, the binding of an oxygen molecule to one subunit induces a conformational change in the remaining subunits to increase the affinity for oxygen in these subunits, allowing cooperative binding and facilitate the effective loading and unloading of oxygen at the lungs and body tissues respectively, allows high capacity for carrying oxygen. At high CO ₂ concentration caused by lots of respiration, haemoglobin can bind to carbon dioxide which causes a conformational change in haemoglobin, decreasing affinity for oxygen and facilitating the release of oxygen (function)
Each subunit is arranged so that most of the hydrophilic amino acid side chains are on external surface while hydrophobic amino	making it soluble in aqueous environment and Can be transported and carry oxygen

Structure	Properties
acid side chains are buried in interior	from lungs to tissue and vice versa
Each subunit is made of globin polypeptide and associated with haem prosthetic group held in the hydrophobic pocket of the polypeptide chains consisting of a porphyrin ring and an iron ion	allowing haemoglobin to bind reversibly to oxygen..

Role of bonds in haemoglobin

- the two polypeptide chains in each dimer are held together by ionic bonds, hydrogen bonds and hydrophobic interactions between R groups so as to stabilise the alpha beta dimers
- The two dimers held together weakly by hydrogen bonds between R groups results in the ability of the two dimers to move with respect to each other in order to increase the affinity of haemoglobin to oxygen, increasing efficiency of loading and unloading of oxygen

Explain the significance of R groups of different amino acids to protein structure

- R groups of different amino acids have different properties such as non-polar, polar, acidic and basic
- Interactions between R groups of amino acids constituting the protein can form hydrogen bonds, ionic bonds, disulphide bonds and hydrophobic interactions
- These interactions between R groups are required to maintain specific three dimensional conformation of the tertiary and quaternary structures of proteins
- The hydrophobic interactions between the hydrophobic R groups of amino acids will cause the protein to fold in a way that keeps most hydrophobic R groups shielded from the aqueous environment

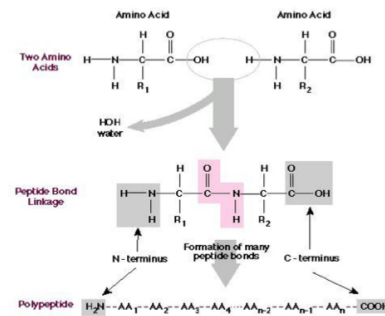
- Cytosine which has a sulfhydryl group allows formation of disulfide bridges contribute greatly to the stability of protein structure as it increases resistance to high temperatures extreme pH changes
- Acidic and basic R groups of amino acids can be attracted to each other, forming ionic bonds that play a part in determining the tertiary/quaternary protein structure
- Polar R groups such as amide groups and hydroxyl groups allow formation of hydrogen bonds that play a part in determining the tertiary/quaternary structure

Structure and properties of collagen

Structure	Properties
Mostly comprises of glycine in the alpha chains of the tropocollagen as every 3rd amino acid is glycine. Glycine has the smallest R group of all amino acids (importance of abundance of glycine in its function)	This allows the alpha chains of tropocollagen to be able to wind tightly together and fit into the restricted space between alpha chains to allow formation of hydrogen bonds causing an increase in tensile strength of collagen making it suitable structural protein
Each alpha chain of the tropocollagen molecules has a repetitive sequence has a repetitive sequence of Gly-X-Y where X mainly being proline and Y is often hydroxyproline	1. Proline and glycine have non-polar R groups and will not be able to form hydrogen bonds with water molecules, contributing to the insolubility of collagen. Hydroxyproline is a polar amino acid but the OH group is used to form hydrogen bonds with other polar amino acids in adjacent alpha chains of tropocollagen hence not able to form hydrogen bonds with water molecules making it insoluble 2. Hydroxylation of proline(hydroxyproline) allows for formation of hydrogen bonds with adjacent alpha chains of the tropocollagen molecules to further stabilise the tropocollagen structure and these tropocollagen molecules can then form covalent bonds with adjacent tropocollagen molecules to form collagen fibrils in order to

Structure	Properties
	prevent tropocollagen molecules to slide against each other due to the unstability, increasing tensile strength (importance of hydroxylation of amino acids)
It is a fibrous protein. has secondary and quaternary structure and comprises of 3 polypeptide chains coiled around each other, forming a loose triple left handed helix	Gives rise to high tensile strength which means can stretch without breaking Triple helix allows greater surface area for cross linking/hydrogen bonds formation And also allows 3 polypeptide to wind around each other more tightly, needing more force to break them
The triple helices are arranged in a staggered pattern	to minimise points of weaknesses along the length of the fibrils
hydroxyproline and proline which have bulky and inflexible R group, contributing to the rigidity of the polypeptide chains	Rigidity, provide support for muscles
covalent cross links between different tropocollagen molecules forming collagen fibril which further assembles to fibre,	structure has a higher tensile strength, can stretch without breaking
The 3 helical chains are held together by hydrogen bonds between -NH and -C=O of peptide bonds in adjacent polypeptide chains,	making collagen insoluble due to extensive hydrogen bonding between chains, limiting interactions with water, won't dissolve easily and can function as a structural protein

How amino acids are joined together



1. Amino acids undergo **condensation*** to form polypeptides with **removal of 1 water molecule**;
2. **OH group from carboxyl group** and **H atom from amino group** contribute to formation of water molecule (*showing OH and H in diagram coming together*);
3. Box up and label **peptide bond***;
4. Correct structure and label of **amino acids**;
5. Box up and label **amino terminus** and **carboxyl terminus**;
6. **Polypeptide** formed from condensation;
7. This reaction is **catalysed*** by enzyme, **peptidyl transferase***, at **ribosomes***;

Describe the levels of protein

Primary structure:

- Refers to specific number and sequence of amino acids joined by peptide bonds in a polypeptide chain
- Peptide bonds are formed by condensation reaction between amino group of one amino acid and one carboxyl group of another amino acid with the elimination of a molecule of water
- Sequences of amino acids determine the type and location of chemical interactions and hence the pattern of folding which confers the specific 3D conformation of a particular protein
- Sequence of amino acids is determined by sequence of DNA in the cell

Secondary:

- consists of repeated coiling or folding of a polypeptide chain in a specific pattern
- Maintained by hydrogen bonds between oxygen of C=O in a peptide bond and hydrogen of N-H in a peptide bond
- Side chains or R groups not involved
- Regions of polypeptide chains without a regular secondary structure are described to have a random coil or loop conformation

- Two types: alpha helix, beta pleated sheets
- Alpha helix:
 - Right handed spiral with 3.6 amino acids residues per turn
 - Maintained by hydrogen bonds between groups at every 4th peptide bond or between the O of c=O of one amino acids and hydrogen of n-h four amino acids away in a single polypeptide chain
 - Each successive turn of the α -helix is held to adjacent turns by three to four hydrogen bonds, conferring significant stability on the overall structure;
- Beta pleated sheets:
 - Each β -pleated sheet consists of **two or more β -pleated strands aligned side by side** and held together by **hydrogen bonds**;
 - β -pleated sheet is maintained by hydrogen bonds between the **-C=O of an amino acid on one region/segment and the -N-H group of an amino acid on an adjacent region/segment** of a single polypeptide chain;
 - The β -pleated strands may run **parallel** (same) or **anti-parallel** (opposite) directions, forming a β -pleated sheet;

Tertiary structure:

- The tertiary structure of a protein refers to the **unique three-dimensional conformation** formed by further coiling and folding of a single polypeptide;
- As a result of the coiling and folding, amino acids that are far apart in the primary structure and in different types of secondary structure may interact within the completely folded Protein;
- Tertiary structure is stabilised by four types of interactions (name as least 2): **hydrogen bonds, ionic bonds, hydrophobic interactions, and disulfide bonds between R groups of amino acids**;
- [marked once] Hydrogen bonds are formed between **an electronegative atom and a hydrogen atom bonded to an electronegative atom** / between **polar R groups** of amino acids;

- [marked once] Ionic bonds are **electrostatic attractions** formed between **oppositely charged R groups** (e.g. COO⁻ of acidic amino acids and NH₃⁺ of basic amino acids);
- [marked once] Hydrophobic interactions are caused by the **exclusion of non-polar substances by water** / formed between **non-polar R groups** which interact and cluster at the core of the protein to avoid contact with water;
- [marked once] Disulfide bonds are strong covalent bonds between **sulfhydryl (-SH) groups of two cysteine** residues which are brought close together by the folding of polypeptide;

Quaternary structure:

- The quaternary structure refers to the association of **two or more polypeptide chains** to form one functional protein;
- Each polypeptide forms a subunit, and the subunits are held together by (name at least 2) **hydrogen bonds, ionic bonds, hydrophobic interactions, and disulfide bonds between R groups of amino acids** to form a multimeric protein