Name:
Date:

QA3 - Intramolecular forces within polypeptides

Intermolecular forces are those which occur between **different molecules/macromolecules**. The forces which join two polypeptide chains to make the **quaternary structure** of a protein are intermolecular forces.
Intramolecular forces are those which occur between parts of the **same molecule/macromolecule**. These are the forces which fold the polypeptide chain into a specific shape, producing **secondary, and tertiary structure**, by interactions between the amino acid residues.

1. What makes the intramolecular forces within a protein so important to its overall function?
   The intramolecular forces give the protein a very **specific tertiary structure**. It is the tertiary structure of a protein which determines the **overall effectiveness of a protein**, whether the protein consists of a single polypeptide chain, or whether multiple chains combine to form a quaternary structure. Proteins such as **hormones, enzymes, and structural proteins all rely on having a very specific shape and structure to work effectively**. This structure is **determined by the intramolecular forces within individual polypeptide chains**.

2. What makes the intermolecular forces within a protein so important to its overall function?
   Some proteins need to exist as a supramolecular unit – i.e. one which is made from multiple molecules/macromolecules. These are the proteins which have a **quaternary structure**. Some more complex proteins can only **work effectively as a quaternary structure** with **multiple polypeptide chains**. The intermol**ecular forces which connect the polypeptide chains** are crucial in giving the overall protein a **very specific quaternary structure**.

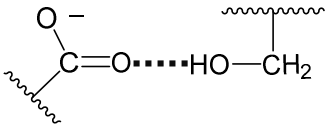
3. Describe a type of protein complex which requires intermolecular interactions, but which doesn't have a quaternary structure.
   Some **conjugated proteins**. These are proteins where a **polypeptide chain is bound to a non-polypeptide group**, such as **ions** or other **small molecules**, called a **prosthetic group**.

4. State four types of interactions which could be present within a protein structure
   Hydrogen bonding. **Ionic** bonding. **Disulfide** bonding. **Hydrophobic interactions**.

Produced by Rebecca Kirkley at Emmanuel College as part of an extracurricular project.
Edited by Adam Stubbs at Newcastle University as part of a summer outreach project.

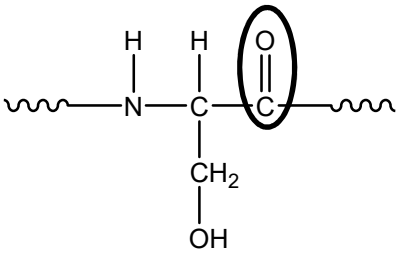
5. Explain what causes a protein's secondary structure to be different to its primary structure.
The **primary structure** of a protein is the **sequence of amino acids**. These amino acids can **interact** with each other, **forming hydrogen bonds between the residues**. As these hydrogen bonds form, they force the **polypeptide chain to fold** into specific and localised shapes – the **secondary structures**. They include the α-helices and β-sheets.

6. Using the following diagram, explain how these two groups could interact and make a polypeptide chain fold. Draw the interaction.



The carbonyl group on the left has a very electronegative oxygen atom. This means that it pulls some of the electron density from the carbon atom, and the **oxygen becomes electron-rich**. The alcohol group on the right has a very electronegative oxygen atom too. In this case, it pulls electron density away from the hydrogen atom, making the **hydrogen very electron-poor**. This allows the **electron-rich oxygen in the carbonyl group to donate electron density to the electron-poor hydrogen atom on the alcohol group**, forming a **hydrogen bond**.
As hydrogen bonds like this form, they will **force the polypeptide chain to fold and bend**, to allow the bonding to occur.

7. The amino acid residue serine is shown below. Using your knowledge of intramolecular interactions, explain how a serine residue could interact with another part of a polypeptide chain.



Serine residues have a hydroxy (-**OH**) group. This group is capable of **hydrogen bonding**, as shown in Q6. For the hydrogen atom to take part in hydrogen bonding, it must be able to interact with an **electron rich group**. This could occur in two ways, either by interacting with **another amino acid residue** which has an electron rich atom, such as the **carboxylic acid group** in Q6. Or it could interact with the **electron-rich oxygen atoms on the carbonyl groups** visible **along the core of the polypeptide chain** – such as the one circled above.

8. Why can secondary structures be easily disrupted by gentle heating or changes in pH?
Heating a system will **add energy** to the protein. This extra energy can be enough to cause the structure to **vibrate** rapidly, and **destabilise** the secondary structures. The **hydrogen bonds** which hold the structures together can be **broken** by this excess energy, causing the polypeptide chains to change shape and **denature**.
Altering the pH of a protein system can have a similar effect. In this case however, the change in pH will change the **concentration** of **H^+ ions**. **These ions will interfere with the hydrogen bonding** that occurs in secondary structures, and by adding or removing hydrogen ions, the bonds can easily become **less stable**, causing the secondary structures to **denature**.

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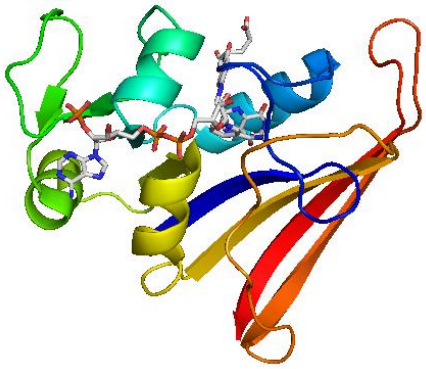
9. State what happens to the α-helices and β-sheets to form a tertiary structure.
α-helices and β-sheets are types of **secondary structures**. They can **interact** with each other along the polypeptide chain, and **fold** into a tertiary structure. The tertiary structure is the **overall 3D structure** of a **polypeptide chain** in space.

10. In a protein's tertiary structure, where do ionic bonds occur?
Between residues with **ionic groups** as **side chains**, specifically **-COO^-** and **-NH_3^+** groups.

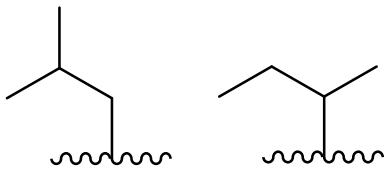
11. The enzyme dihydrofolate reductase is shown below, PDBe entry 7dfr. Identify the types of protein structure which are visible.
Primary structure: not technically visible, but you could argue that it is visible in that it is the sequence of amino acids which make up the visible chains.
Secondary structure: visible as α-helices and β-sheets.
Tertiary structure: visible as the overall shape of the polypeptide. i.e. the collection of secondary structural features as a whole.



12. Which type of interaction is unique to cysteine residues, which have the side chain -CH_2SH?
Disulfide bonding. This occurs because two cysteine groups can condense, eliminating H_2 and forming an S-S bond.

13. The above interaction between cysteine residues can be either intramolecular or intermolecular. Explain why.
Whether an interaction is intermolecular or intramolecular depends purely on whether it occurs between residues of the same chain or not. **Two cysteine groups on the same chain can interact, giving an intramolecular interaction, or two cysteine groups on different chains can interact, giving an intermolecular interaction**.

14. The two amino acid residues shown below are leucine and isoleucine respectively. Which type of interaction can they exclusively take part in?
Hydrophobic interactions. These are when two hydrophobic groups, such as hydrocarbon chains, repel polar groups such as water. This causes the hydrophobic groups to have a net attraction to each other.



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