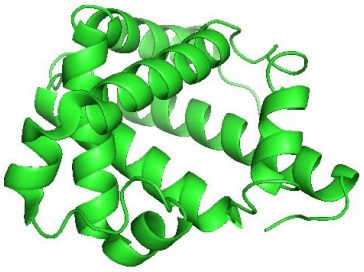
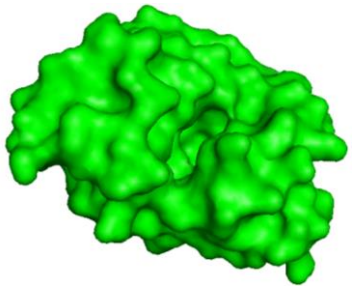
TA5 - Tertiary and Quaternary Structures





The tertiary structure of 112m_Tertiary_Structure_Myoglobin_Sperm_Whale shown in the cartoon and surface representations

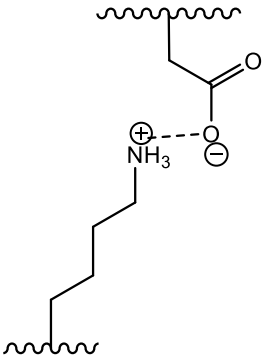
TERTIARY STRUCTURE AND PROTEIN FOLDING

As well as their secondary structure, proteins have a higher order of **folding** called the **tertiary structure**. The tertiary structure describes how the whole polypeptide chain, including the secondary structural features, folds itself into a **3D structure**. This tertiary structure is held together by the interactions between the side chains of the amino acids which make up the primary structure. The interactions cause **protein folding**, where the polypeptide chain **self-assembles** into a specific 3D structure.

In the myoglobin protein shown, you can see the α-helices which comprise the secondary structure. The secondary structures combine to form the tertiary structure, this is the **overall arrangement of the polypeptide chain in space**. This is better represented by the surface view of the polypeptide shown.

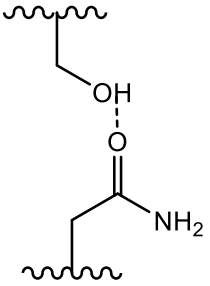
THERE ARE **FOUR KEY INTERACTIONS** TO BE AWARE OF:

IONIC INTERACTIONS



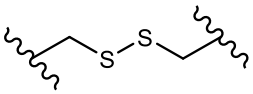
Some amino acids, such as aspartic acid contain a carboxylic acid in their side chain. These can lose protons to give a negatively charged COO^-. Equally, some amino acids, such as lysine, contain positively charged NH_3^+ groups. Proteins can fold in such a way that these **oppositely charged groups** can form an ionic bond.

HYDROGEN BONDING



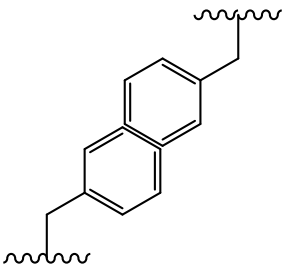
Hydrogen bonds are important in primary and secondary structures. This is because many amino acids contain side chains with **OH** or **NH** groups which can form hydrogen bonds. For example, serine contains an alcohol group, which can hydrogen bond with the amide in asparagine.

DISULFIDE BRIDGES



These are strong interactions which occur when two **cysteine** residues are near each other, and they form a **strong covalent bond** between the **sulfur** atoms.

HYDROPHOBIC INTERACTIONS



When two **non-polar, hydrophobic side chains** are brought together, they will **repel water** and other polar groups. This causes an **overall attraction** to each other. Hydrophobic side chains are typically made from hydrocarbons, and don't contain any oxygen, sulfur or nitrogen atoms.

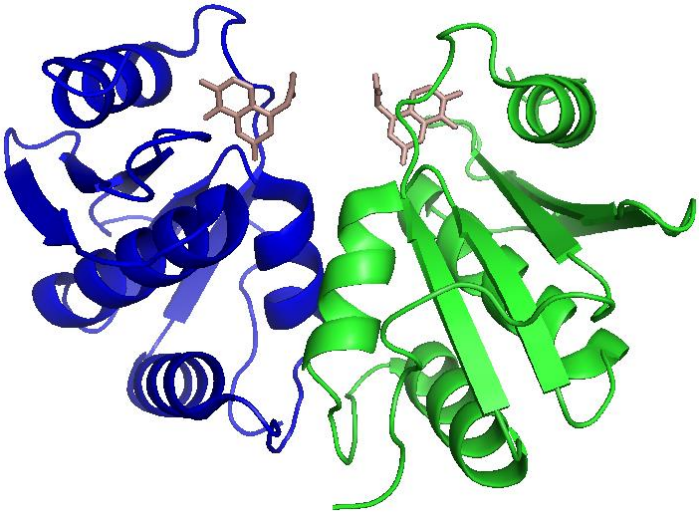
Produced by Lucy Jakubecz at Newcastle University as part of an MChem project.
Edited by Adam Stubbs at Newcastle University as part of a summer outreach project.

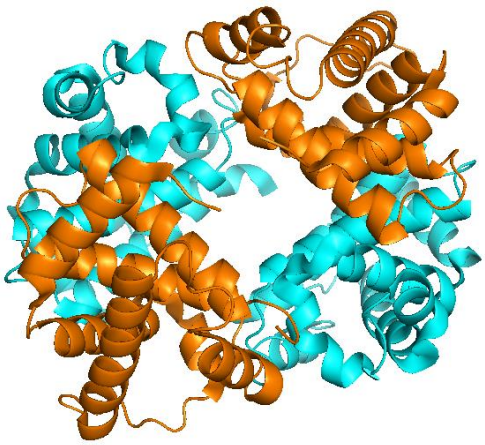
QUATERNARY STRUCTURES

The quaternary structure of a protein describes how **multiple polypeptide chains** come together and arrange in 3D. The interactions which hold them in place are the same as in the tertiary structure. Except this time, they are **inter-chain** (between two different chains), rather than intra-chain (between residues of the same chain).

Some quaternary structures are made up of two or more identical chains.

HIV protease (PDBe entry 4je2) exists as a dimer – two subunits of the same polypeptide. Both of the chains have an identical primary structure, the exact same amino acid sequence. Therefore, the two chains are identical. Together, they form the quaternary structure of HIV protease.





Quaternary structures can be made from multiple non-identical chains too. An example of this is hemoglobin (PDBe entry 2m6z).

In this structure, there is a group of α-subunits (shown in orange), and a pair of β-subunits (shown in blue). Together the two different pairs combine to form a tetrameric quaternary structure. Each subunit binds a heme ligand, which contains a Fe^{2+} ion. The ions bind to O_2 and allow oxygen to be transported around the body in the bloodstream.

HOW DO GENES INFLUENCE PROTEIN STRUCTURE?

As proteins build up from the basic constituents, they are heavily influenced by changes in DNA. DNA codes for specific amino acids, through **codons**, sets of **three DNA nucleotides** in the **triplet code**. These amino acids then join in a series of condensation reactions to give a polypeptide chain. The order of amino acids is known as the **primary structure**. The different side-chains on the amino acids interact with each other, and create **secondary structures** such as **α-helices** and **β-sheets** which are held together by **hydrogen bonds**. These secondary structures then interact, again through the amino acid residues, to form an overall 3D arrangement known as the **tertiary structure**, held together by interactions such as **ionic** and **hydrogen bonds**, **hydrophobic interactions**, and **disulfide bonds**. These tertiary structures can form enzymes, which have very specific active sites which catalyse reactions. The structure of these proteins can be traced back to the DNA code which builds them, and therefore any changes in the DNA code, such as a mutation, can affect the overall protein structure. It is the overall protein structure which determines its function and effectiveness.

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