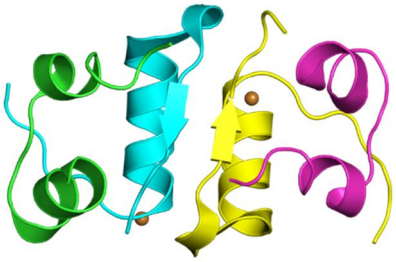
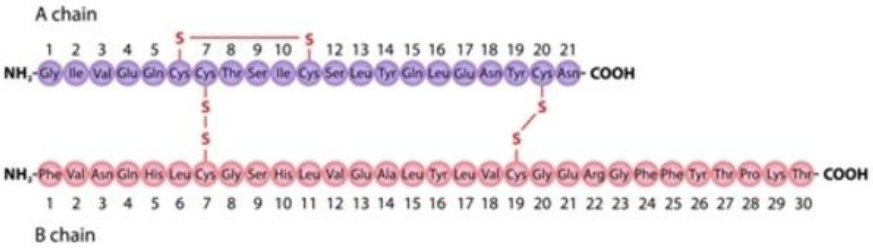
TA11 – Insulin: Structure and Bonding

Insulin is a hormone produced in the pancreas which allows the body to absorb glucose from food or to store glucose in the liver for release when blood sugar is low. Insulin is an incredibly important hormone within the human body, and a lack of this vital protein can lead to disease, such as diabetes. Consequently, it is very important for us to be able to understand the structure and bonding of this protein so we can manipulate this hormone and ensure that insulin-based medicines are as effective as possible.

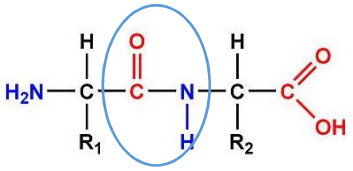


PRIMARY STRUCTURE



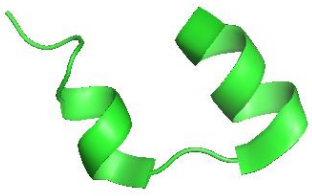
The primary structure of a protein is the sequence of amino acids which make up its long polypeptide chain. Insulin consists of two polypeptide chains: 'A' and 'B'. Chain A contains 21 amino acid residues, whilst chain B is slightly longer containing 30. Between each amino acid is a bond called a peptide link which holds the residues together. Polypeptide chains are formed through condensation reactions, since water is produced when amino acid 'monomers' are joined together. Because of this, proteins can be described as condensation polymers.

Peptide link



SECONDARY STRUCTURES

The secondary structure of a protein describes the way regions of a polypeptide chain are organised into regular structures. Some of the amino acids in insulin's polypeptide chain can form hydrogen bonds with each other. These hydrogen bonds occur between the N-H from the amino group of one amino acid in the chain and the C=O from the carboxyl group of another 3 or 4 amino acids along. This causes the chain to coil together into a shape called an α-helix (pronounced 'alpha helix'). Chain A of human insulin consists of two sections of α-helix connected by a fairly flat section of chain. This flat section means that the two helices can lie alongside each and experience instantaneous dipole-induced dipole forces between them.

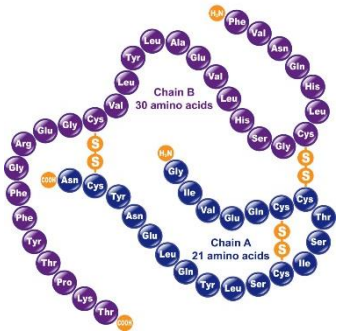


PDBe entry 4ins: human insulin, chain A.

Illustration of the formation of hydrogen bonds in an α-helix.

Produced by Anna McKie at Newcastle University as part of a Nuffield Research Placement.

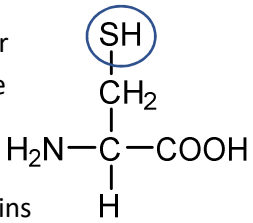
TERTIARY STRUCTURES



Disulphide bridges are show here in orange.

The tertiary structure of a protein describes the way the secondary structure folds itself into its overall 3-dimentional shape. The tertiary structure affects the properties of a protein and determines where on the molecule the active sites are located, a fact which is particularly important as far as medicines are concerned.

Thiol group



The two chains of insulin, A and B, are linked together in two places by 'disulfide bridges'. In addition to this, there is another disulfide bridge within chain A which twists it into shape. These sulfur-sulfur bonds form between molecules of the amino acid cysteine. Cysteine contains a thiol group (S-H), which causes the formation of these bonds. The disulfide bridge forms when two sulfur atoms in nearby cysteine molecules bond covalently, holding polypeptide chains together and, in this case, giving insulin its tertiary structure. In addition to this, there are instantaneous dipole-induced dipole forces between non-polar side groups which also contribute to the tertiary structure of insulin.

QUATERNARY STRUCTURES

The quaternary structure of a protein describes the way that several peptide chains cluster together. The picture below shows a final insulin hexamer. A hexamer is a protein made up of six tertiary structures. Note that not all proteins possess a quaternary structure. In the centre are two zinc ions ligated to the protein by histidine residues.