APPLICATION CHEMISTRY:

CHEMISTRY OF LIFE

Proteins

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Proteins

- **Antibodies, enzymes and haemoglobin**, are **water-soluble molecules**
- **Collagen and keratin**, are insoluble and aggregate to form very **tough and resistant structures**
- Proteins make up 18% of the mass of the average person.
- Proteins are **unbranched polymer chains made by linking together large numbers** (from hundreds to several thousand) **of amino acid monomer** units **by peptide bonds**.
- Such chains are often referred to as polypeptide chains

Proteins

Table 1.1: Some proteins and their functions

Protein(s)	Function	Location
myosin actin	muscle contraction	muscle tissue
chymotrypsin	digestive enzymes	small intestine
pepsin		stomach
insulin	hormone	blood
immunoglobulins	antibodies	blood
collagen	structural proteins	skin, tendon
keratin		hair
haemoglobin	transport	blood
ferritin	storage	bone marrow, liver, spleen

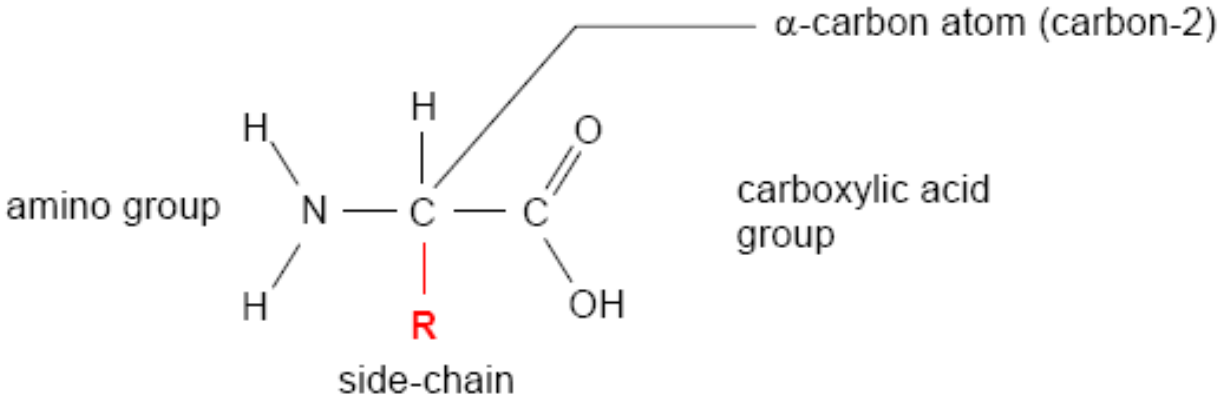
Amino Acids

- Protein chains are synthesized from **twenty different amino acids**.

- Nineteen of these molecules contain **two functional groups**: a **carboxylic acid group (-COOH)** and a **primary amino group (-NH_2).**

- All have **one common feature**: **the two functional groups are both attached to the same carbon atom**

Amino Acids



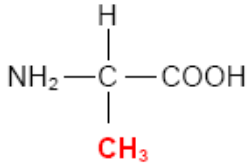
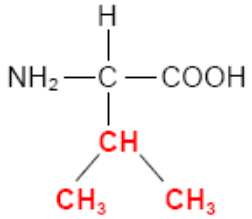
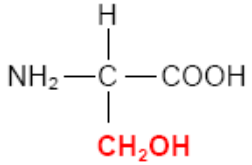
- The **carbon atom of an acid group** is always **counted as the first in the structure**
- **Amino group** is always **attached to the second carbon** atom (C-2)
- This carbon atom is also sometimes known as the **α-carbon atom**
- These important molecules are therefore all 2-amino acids (or α-amino acids).

Amino Acids

- The 20 different amino acids that cells use to build proteins **differ in the nature of the R-group**

- Simplest, where **R** is **hydrogen atom** –
  2-aminoethanoic acid (glycine)

- The **20 different amino acids can** usefully **be** categorized **into separate sub-groups according to the nature of the R-group**
- There are **three broad categories depending on** whether the **side-chain** group is **non-polar**, **polar**, or **can be ionised (charged)** under appropriate conditions

sub-group (based on type of R-group)	example	structure
non-polar	alanine (ala)	
	valine (val)	
polar	serine (ser)	

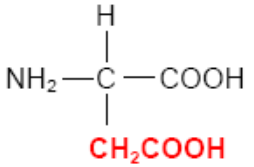
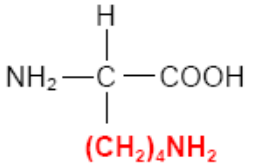
sub-group (based on type of R-group)	example	structure
electrically-charged (acidic or basic side-chains)	aspartic acid (asp)	
	lysine (lys)	

Figure 1.9 – examples of the 20 different amino acids found in proteins

Ionisation of Amino Acids

- Amino acid molecule – **amphoteric**
- X-ray crystallography of crystalline amino acids has shown that amino acids exist in the **zwitterionic** form in the solid.
- Physical properties characteristic of ionic compounds: **white solids** that are **soluble** in **water**.

Ionisation of Amino Acids

- Amino acids such as **glycine or alanine**, with **non-polar R-groups**, **will have no net charge at pH 7** (overall charge = 0)

- **Aspartic acid** will have an **overall charge of –1** because of the additional **acid group** in its side-chain.

- These **differences in charge** can be **used to separate amino acids** by **electrophoresis** or **ion exchange chromatography**.

Amino Acids

- The nature of the R-groups in these amino acids is of crucial importance.

- Once the amino acids have condensed together to form a **polypeptide chain**, the **R-group is the remaining feature of a particular amino acid** which is still distinctive.

- **Interactions between the different R-groups** profoundly **influence the folding of the polypeptide chain**, and hence the **shape of the final protein.**

Structure

Condensation Polymerisation of amino acids

- When many amino acids react to form a polymer they produce a condensation polymer – a protein (or polypeptide chain).

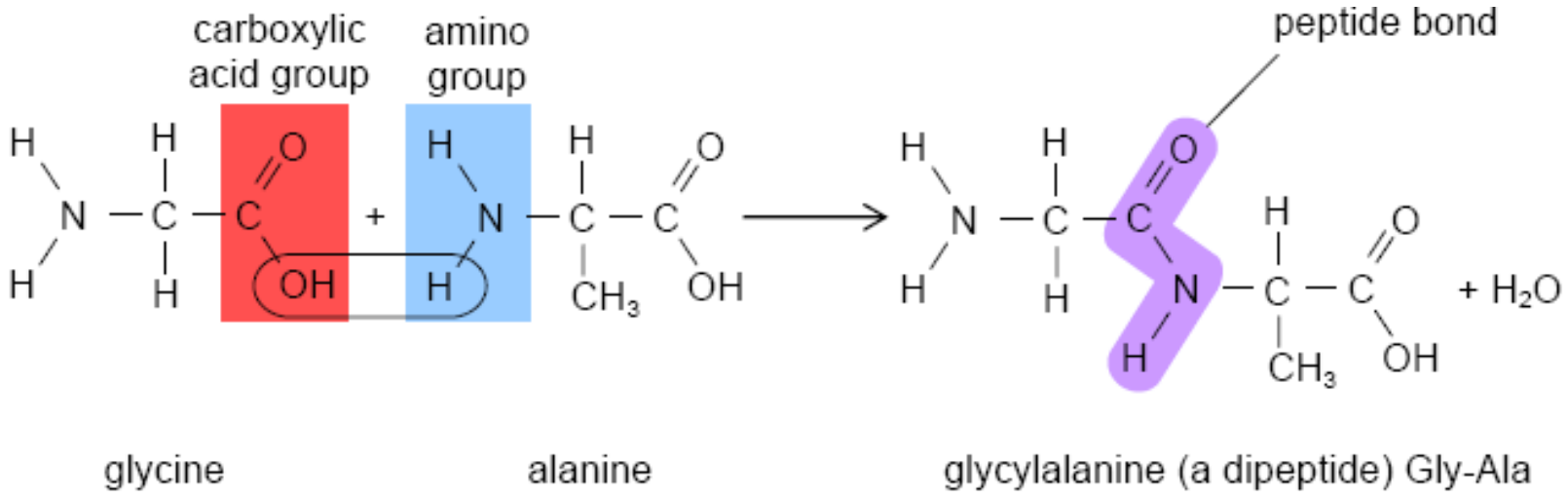


Figure 1.10 – Diagram showing the formation of a gly-ala dipeptide

- Additional amino acids can react with the dipeptide to form first a tripeptide and then eventually a polypeptide. In this way a protein can be put together.

Structure

Condensation Polymerisation of amino acids

- The **peptide bond consists of** the group **–CONH-** in which the four atoms lie in one plane, with all **bond angles being about 120°.**
- *Biochem pg 12*

- Each protein chain is a linear polymer built from its own unique selection from the amino acid pool.

- The sequence is genetically determined and characterizes that particular protein.

Structure

Condensation Polymerisation of amino acids

- The structure of a single protein chain in its functional form can be considered on three levels:

  • **Primary structure** – the **sequence of amino acids in a polypeptide chain** – the direct product of the coding sequence in the gene.

  • **Secondary structure** – regular structural arrangements of the polypeptide chain that result from **hydrogen-bonding between peptide bond** regions of the chain.

  • **Tertiary structure** – the **overall folding of a polypeptide** chain that arises from **interactions** between the amino acid **side-chains**.

Primary Structure

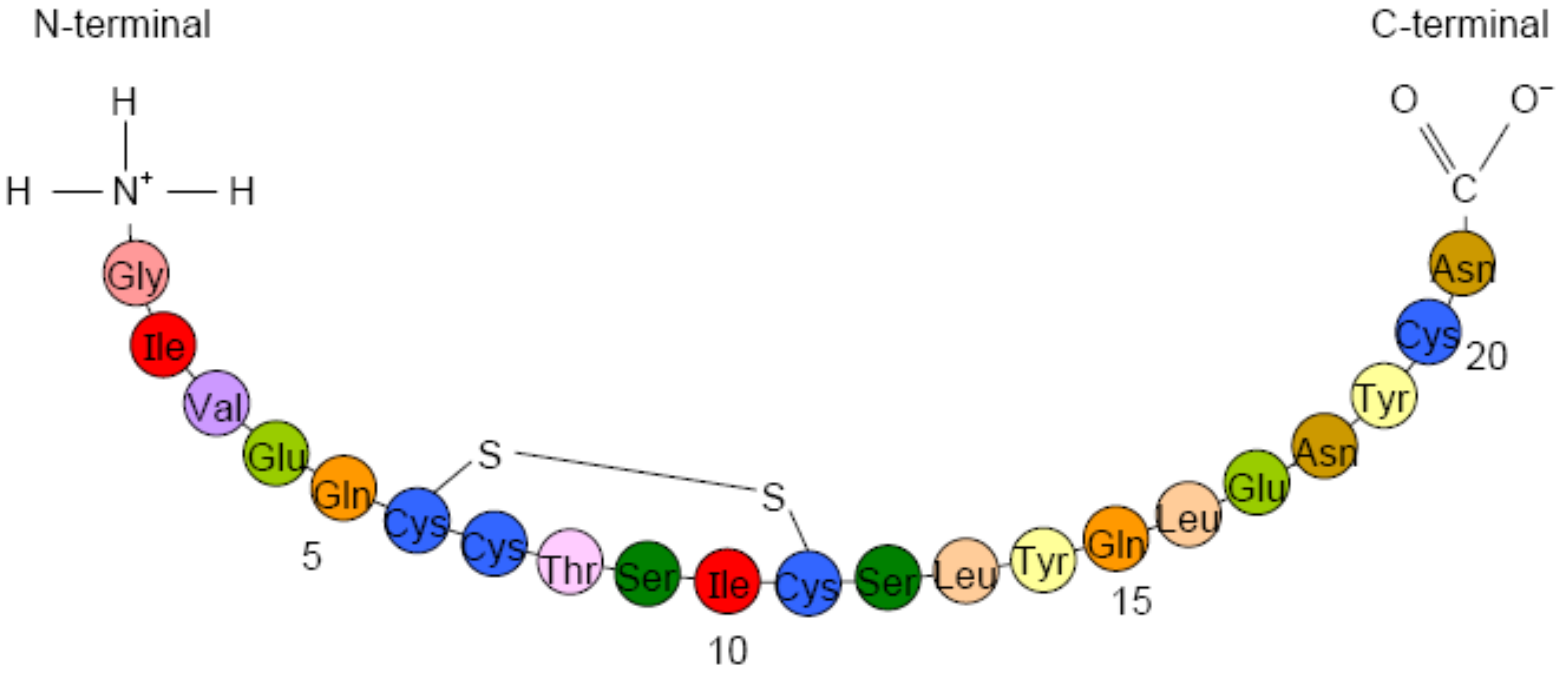


Figure 1.11 – The primary sequence of the insulin A chain, a short polypeptide of 21 amino acids

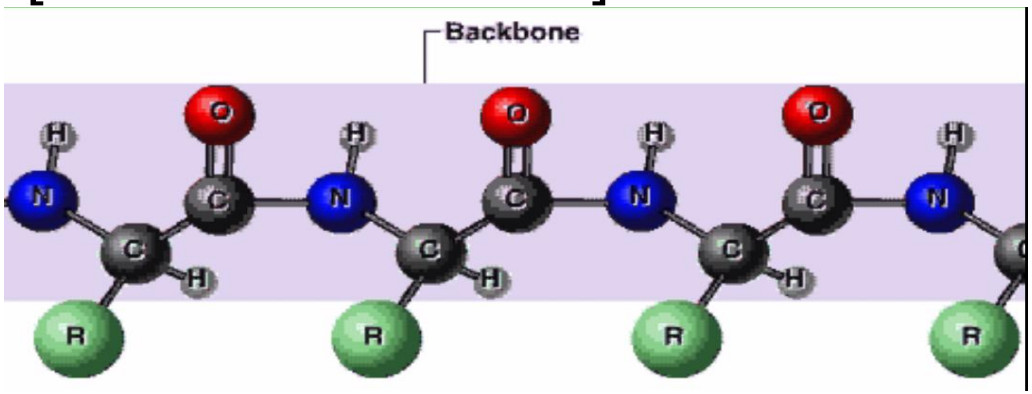
- **Each polypeptide chain is a linear polymer of amino acids** and as such has an amino- (or N-) terminal end and a carboxy- (or C-)terminal end

Primary Structure

- Each polypeptide has direction and the sequence of amino acid residues in a chain is known as the primary structure of the polypeptide.
- In the cell, a **polypeptide chain is always synthesized from the N-terminal end to the C-terminal end**.
- when writing out the primary sequence of a polypeptide chain the **amino acids are numbered from the N-terminal end**.
- Primary structure of a polypeptide chain is **genetically controlled**
- the positions of any **cysteine** residues, will determine the possible formation of **disulphide bridges** to stabilise the **3D-tertiary** structure of the protein.

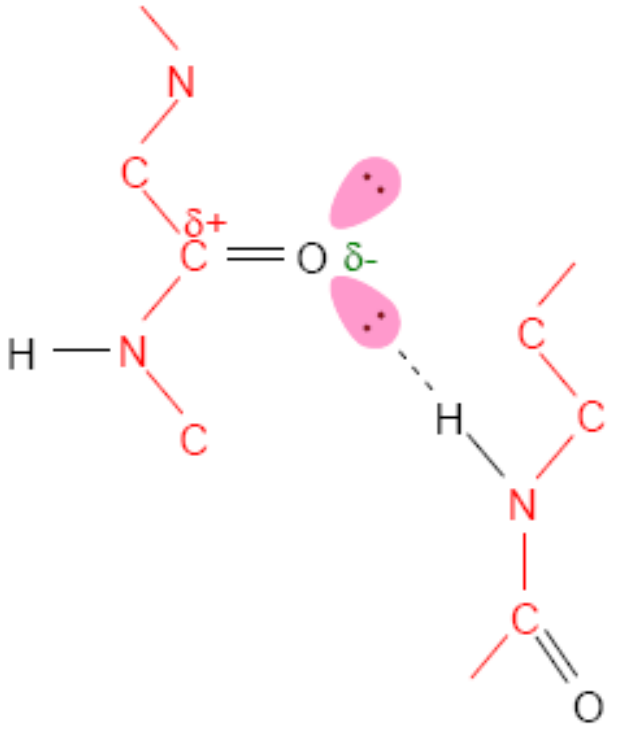
Secondary Structure

- Each polypeptide has a ‘backbone’
- This backbone is essentially the same for all protein chains [-C-C-N-C-C-N- etc].



- Polypeptide **backbone is flexible and in certain regions** of the **protein can fold in a regular manner**, known as **secondary structure**.
- These **structures are stabilized by hydrogen bonding** between the peptide bond regions of the chain’s backbone.

Secondary Structure



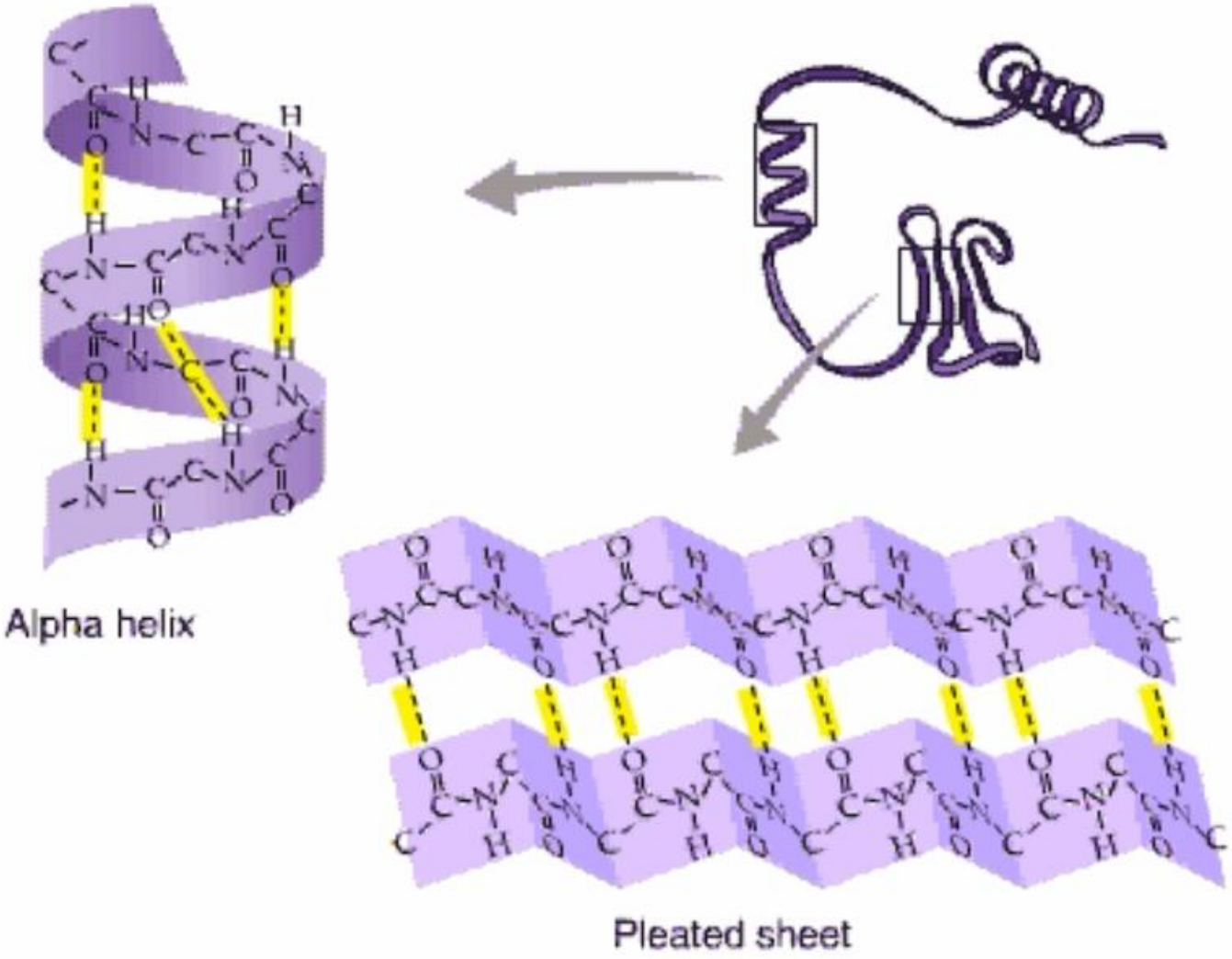
- Collectively this level of structural organisation is known as secondary structure.

Secondary Structure

- Two of the most stable arrangements at this level of protein folding are the **α-helix** and the **β-pleated sheet**.

- In both these structures the chain folds on itself in a very stable arrangement because of the many hydrogen bonds formed between adjacent peptide bond regions.

Secondary Structure



Tertiary Structure

- **Interactions between the R-groups** of the different amino acid residues in a protein chain

- The **three-dimensional shape** or conformation of a protein chain is **maintained by** a series of mainly **non-covalent, intramolecular interactions between the R-groups of the amino acids making the chain**.

- The chemical nature of the different R-groups becomes particularly significant.

Tertiary Structure

- Some of these interactions are relatively easily disrupted, others not so, and include:

  • **van der Waals' forces** between ***non-polar*** side-chains,

  • **hydrogen bonding** between ***polar*** R-groups,

  • **ionic bonds** (salt bridges) between ***ionised*** R-groups, and

  • **covalent disulphide bridges** formed between ***cysteine*** residues at different locations in the primary sequence (Figure 1.15)

Tertiary Structure

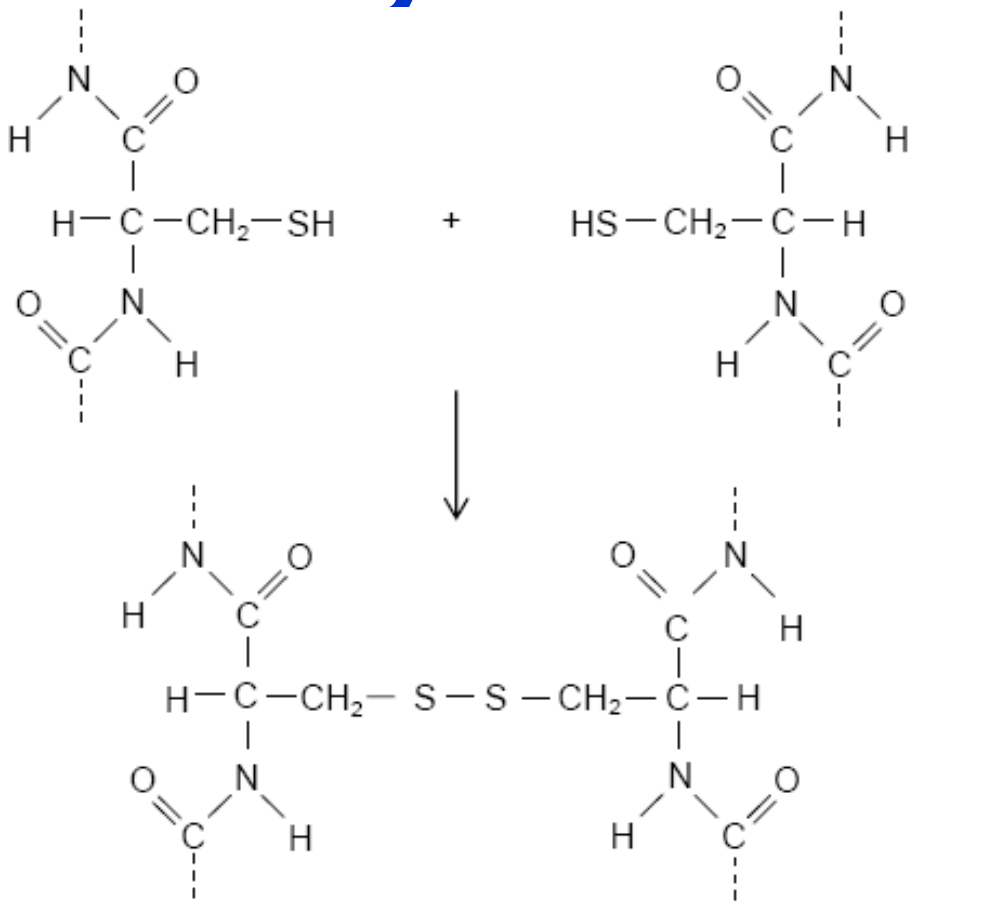


Figure 1.15 – diagram showing the formation of a disulphide bridge

Because of their covalent nature disulphide bonds can have the effect of **locking** a particular tertiary structure in place.

Tertiary Structure

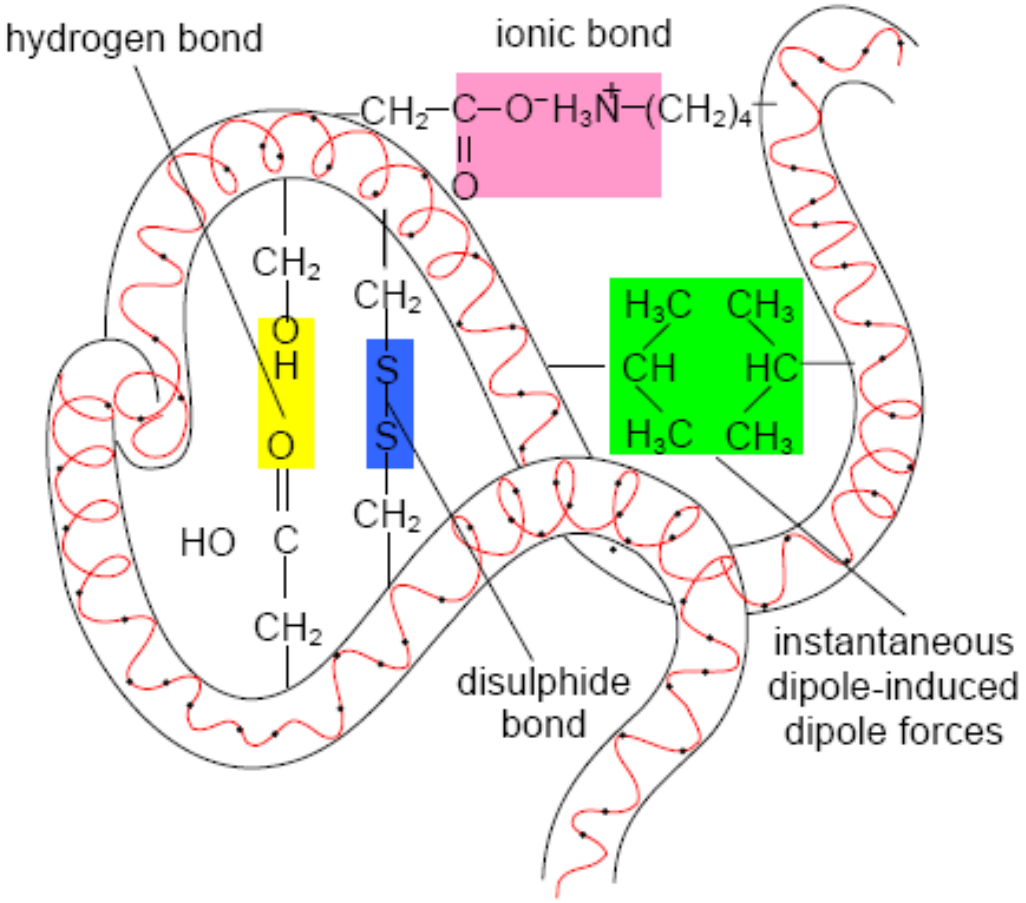


Figure 1.16 – diagram illustrating the nature of the interactions responsible for protein tertiary structure

Haemoglobin

- **Consists of two pairs of identical protein chains** (subunits) known as **α- and β-chains**. (quaternary structure)

- These assemble together to form the functional, oxygen-carrying protein in our red blood cells (Figure 1.17).

- The human globin α- and β-chains are different polypeptide chains coded for by different genes.

- When folded, each of the globin chains has a high degree (about 70%) of **α-helical** secondary structure.

Haemoglobin

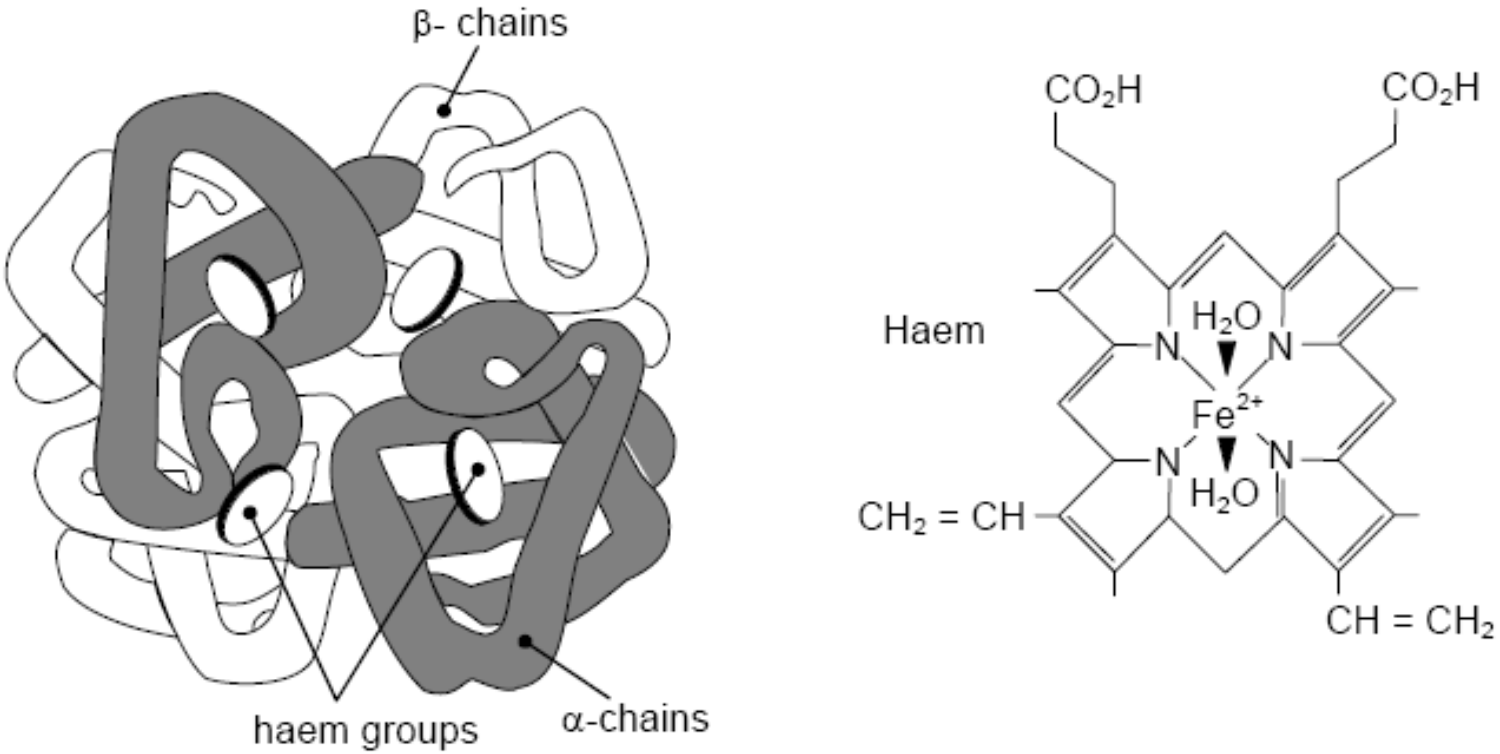


Figure 1.17 – (a) the structure of haemoglobin showing the α and β chains; (b) the structure of the haem group.

Haemoglobin

- Each of the protein subunits in one molecule is also bound to a non-protein **haem group** containing an iron(II) ion (**Fe^{2+}**).

- The **iron(II) ions** in the haem groups **bind oxygen** and enable the molecules to perform their function of transporting oxygen around the body.

- The non-covalent interactions similar to those involved in tertiary structure bind these haem groups in place in the structure.

Haemoglobin

- Overall structure of the whole molecule changes as oxygen binds to the haem groups.
- There is a favoured sequence for the attachment and detachment of oxygen from the molecule.
- Either all four subunits have oxygen attached to their haem groups, or none of them do.

Denaturation of protein

- Denaturation ➔ disruption of protein structure.
- Weaker interactions that holds the shape of the protein is disrupted.
- Protein losses its unique 3-D shape.
- 4 factors :

1) pH of solution
2) Temperature
3) Chemicals

Change in pH

- Drastic change in pH can alter the **protonation** or **ionisation** of R groups.
- Eg :

At low pH: - COO^-

- NH_2

At high pH : - COOH

- NH_3^+

- Everyday example :

Curdling of milk protein when milk turns sour or mixed with vinegar.

Temperature

- Increase temperature gives molecules more energy.
- → **increase vibrational motion** of molecules
- → weak interactions (such as **van der Waal's forces**) that holds the 3D shape of the molecules are disrupted.

- Irreversible denaturation occurs when secondary and tertiary structure are disrupted to produce random coils.
- The chains are so unraveled that they tangle with each other (occurs between 60 – 70°C).

- E.g : Eggs turned solid when cooked.

Chemical denaturation

a) **Metal ions**

- Disrupts **ionic interactions**
- E.g :

b) **Urea**

- **Urea denatures proteins by disrupting the hydrogen bonds** that maintain the secondary and tertiary structure of proteins.