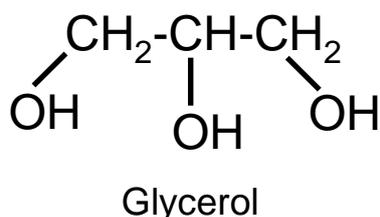


# Macromolecules

1. Proteins: polymers of **amino acids** joined together by covalent **peptide links** (polypeptides) in a **condensation reaction**. There are about 20 different types of amino acid used in proteins, e.g. glycine, methionine. Proteins contain C, H, O, N and S. Only methionine and cysteine contain sulphur (S).

2. Lipids: a variety of substances are classed as lipids. **Triglycerides** are molecules of glycerol with three long fatty acid chains attached. **Glycerol** is a small alcohol with three alcohol, -OH, groups. A fatty acid is a long chain of C-atoms (with attached H atoms) with a carboxylic acid group: -COOH. This acid group reacts with the alcohol group to form a covalent link (a **condensation reaction**). Since glycerol has three alcohol groups, three fatty acid chains can be added to form a triglyceride. The three fatty acid chains may differ in length, but are typically from 8 to 30 C atoms long. Lipids contain C, H and O.

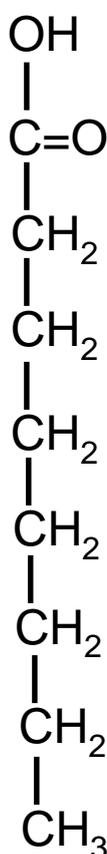
3. Phospholipids: a type of lipid formed by replacing one of the fatty acid chains of a triglyceride with a **phosphate group** (-PO<sub>4</sub><sup>3-</sup>) attached in place of one of the fatty acids to form the head of the molecule. Since the phosphate group is electrically charged (**polar**) it is attracted to water (it is water-loving or **hydrophilic**) – it forms a **polar head**. Two fatty acids remain attached to the glycerol back-bone and form fat-soluble, water-avoiding **hydrophobic non-polar tails**.



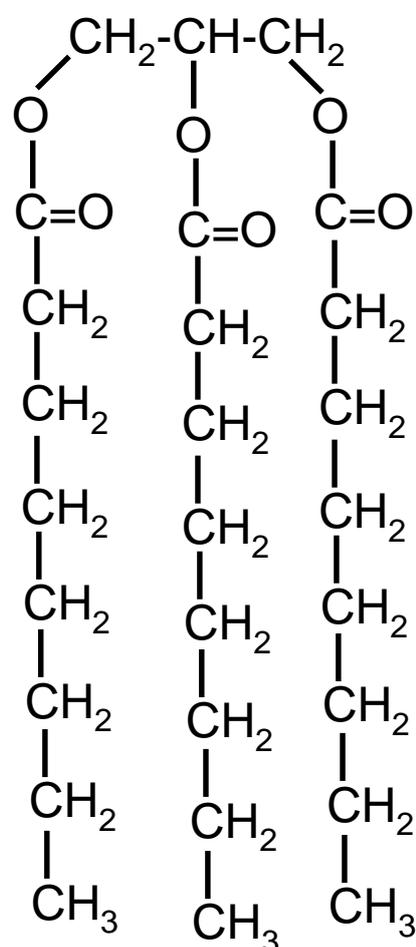
The long hydrocarbon chains or tails of the triglyceride make it insoluble in water!

To form a phospholipid from the triglyceride, simply remove one of the three tails and add a phosphate group. The fatty acid tails may be **unsaturated**, that is contain C=C double bonds, which places a kink in the tail and lowers the melting point. Margarine contains more unsaturated fats than butter and so is softer as it melts at a lower temperature and is more fluid. A **polyunsaturated** fat contains many C=C bonds.

A fatty acid  
(octanoic acid)

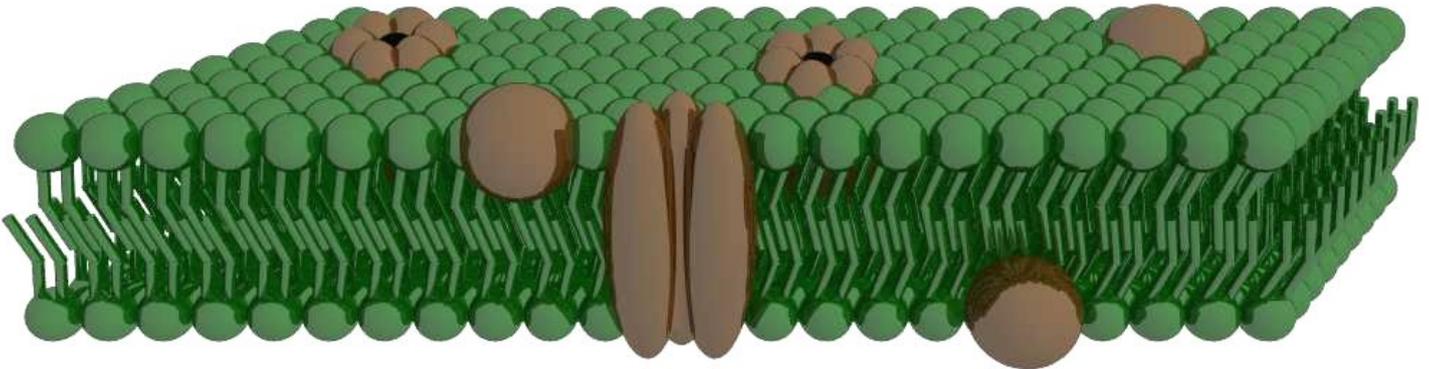


A triglyceride



**Cell membranes** are formed from phospholipids (shown in green). The ball represents the phosphate-group or hydrophilic polar head and the two tails are the fatty acid chains. Notice that the phospholipids form two layers or leaflets with the hydrophobic non-polar tails pointing into the middle of the membrane, which is almost completely free of water, whilst the polar head groups align so as to face the water on either side of the **bilayer phospholipid membrane**.

Water outside cell



Water inside cell

Proteins (brown) float around in this sea or **fluid mosaic** of phospholipids. This is called the fluid-mosaic model of the membrane. In reality membranes are slightly more complex – another lipid, **cholesterol**, is dispersed throughout the membrane to give it extra stiffness. A layer of carbohydrates (sugar chains) covers the external surface, forming a slimy **glycocalyx**. The carbohydrates may be attached to some of the phospholipids (forming **glycolipids**) or to some of the proteins (forming **glycoproteins**). (Only some of the phospholipids and proteins have sugar chains attached).

The membrane is also attached at intervals to the cytoskeleton of the cell.

The more unsaturated the fatty acid tails of the phospholipids, the more kinked the tails become and the less tightly the phospholipids pack together and the more liquid the membrane becomes. This means that the membrane freezes at a lower temperature. If the membrane freezes then the cell will die. Ectothermic organisms adapted to cold climates have more unsaturated phospholipids to stop their membranes freezing (ectotherms do not generate enough heat to keep their bodies warm in the cold, e.g. the ice fish in Antarctica has a body temperature of  $-2^{\circ}\text{C}$ !). Phospholipids contain C, H, O and P.

4. Carbohydrates: some carbohydrates are small molecules, such as simple sugars like glucose and fructose (monosaccharides) or sucrose (a disaccharide). However, polymers of sugars form long-chain carbohydrates, e.g. starch, glycogen and cellulose. The sugar units are joined together by covalent **glycosidic bonds** in a **condensation reaction**. Starch acts as a store of glucose in plants, glycogen is a store of glucose in animals and cellulose is the main component of plant cell walls. These are  $\alpha(1\rightarrow4)$  bonds in starch and glycogen,  $\beta(1\rightarrow4)$  bonds in cellulose. Carbohydrates contain C, H and O.

## 5. DNA (deoxyribonucleic acid) and RNA (ribonucleic acid)

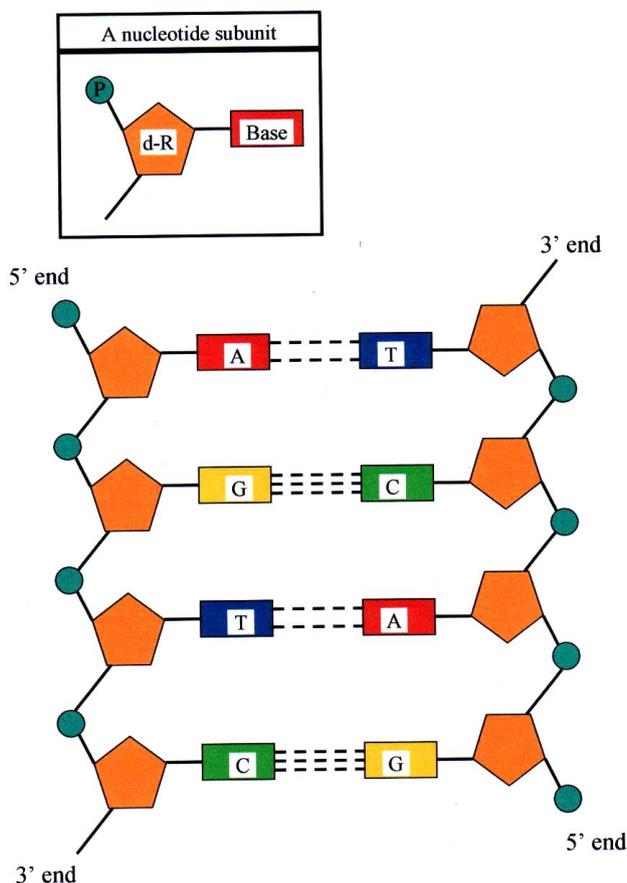
DNA is a **double helix** – that is a molecule of DNA consists of two helical strands wound together. Each of these strands is a **polymer of nucleotides** and the two strands are connected to one another by bonds (**hydrogen bonds**) which are much like the rungs of a ladder. Nucleotides within each strand are joined by **covalent phosphodiester bonds** (-O-P-O-) in a **condensation reaction**.

Each nucleotide subunit is made of a modified **ribose sugar** molecule (called deoxyribose as it has lost an oxygen) joined to a **phosphate group** and one of **four bases** (adenine, A; guanine, G; cytosine, C; and thymine, T). In the double helix, each base pairs up with another base to form a base pair (bp).

**A always pairs with T and C with G.**

These four bases are the 'letters' of the genetic code. These letters make up 'words' each of which is three nucleotides (or 3 bases) long – a single 'word' codes for one of about 20 different amino acids. These 'words' are grouped into 'sentences' or **genes**, each of which encodes the sequence of amino acids that make up a single protein (proteins are made of amino acids!). One strand of the DNA molecule will contain the necessary code for the proteins the cell needs to make, this is the **sense strand (coding strand)**, the other strand is complementary to the sense strand (the antisense or non-coding strand).

You do not need to remember the structures of the bases, but cytosine and thymine are single rings, guanine and adenine are double-rings and these rings all contain nitrogen (N). Ribose and deoxyribose are 5C monosaccharide sugars. Thus, DNA contains C, H, O, N and P (but NOT S).



Left: each strand of the double-stranded DNA molecule is a polymer of nucleotides. Each nucleotide contains a deoxyribose molecule (orange), a phosphate group (green) and a base. The dashed lines forming the rungs of the ladder that connect the strands together are hydrogen bonds. Hydrogen bonds are weaker than ionic or covalent bonds, allowing the double helix to be unzipped during DNA replication or **transcription of mRNA**, but they are strong enough and numerous enough to keep the molecule stable. Note that each strand has a 5' (5-prime) end where the phosphate is on the 5<sup>th</sup> C of the deoxyribose and a 3' (3-prime) end at the 3<sup>rd</sup> C of deoxyribose.

**RNA** contains ribose instead of deoxyribose, is usually single-stranded and has **uracil** (U) instead of thymine.

## Carbohydrates (saccharides)

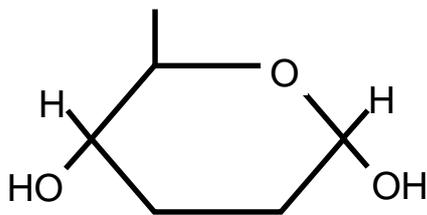
Carbohydrates are made up of carbon, oxygen and hydrogen (literally hydrated carbon or carbon with added water) - a carbon skeleton with attached hydroxyl groups (-OH), H-atoms and a ketone or aldehyde group.

### Functions:

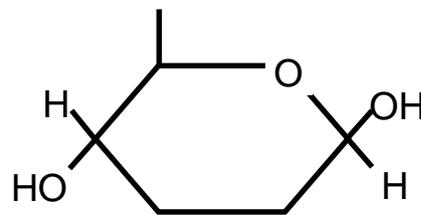
- Storage of energy, e.g. starch in plants, glycogen in animals.
- Transport of energy, e.g. glucose in the blood of mammals, sucrose in the sap (phloem) of plants.
- Structural components, e.g. cellulose in plant cell walls, chitin in the cuticle of insects.

### Structure:

**Monosaccharides** are the simplest – these are single sugar units, e.g. glucose, galactose, fructose, basic formula:  $(C.H_2O)_n$  where n is at least 3 and is the number of carbon atoms in one molecule of the sugar. Ribose is a 5C monosaccharide,  $(C.H_2O)_5$  or  $C_5H_{10}O_5$ . For glucose, galactose and fructose, n = 6. Many monosaccharides consist of rings of C atoms (and one O atom):

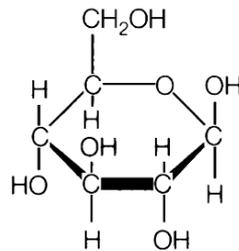


$\alpha$ -glucose



$\beta$ -glucose

Above: two isomers of glucose  $(C.H_2O)_6$  or  $C_6H_{12}O_6$  (isomers are molecules with the same formula but different arrangements of atoms). Note: in alpha-glucose the C atom to the right of the O atom has the -OH group pointing down (below the ring). Note that the structures above are simplified. The H atom on the rightmost C is above the ring for alpha-glucose and below the ring in beta-glucose.

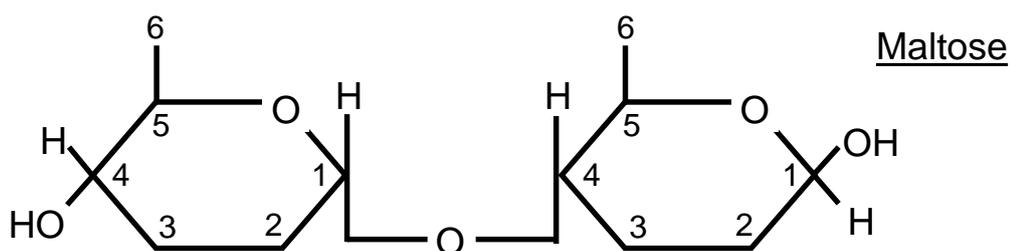


Left: the complete formula for beta-glucose.

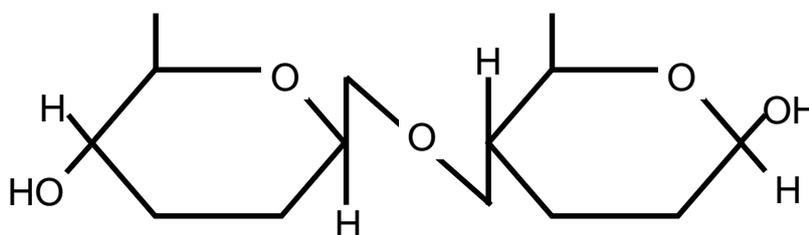
Monosaccharide units can be joined together by forming a special type of covalent bond between them, called a glycosidic bond – two monosaccharides joined together form a **disaccharide** sugar, e.g. sucrose is made up of one glucose and one fructose joined together. Monosaccharides and disaccharides are together called sugars.

Many monosaccharides can join together by forming glycosidic bonds into chains called **polysaccharides**, e.g. starch (plants) and glycogen (animals). **Starch** is a polymer of glucose with  $\alpha(1\rightarrow4)$  glycosidic bonds, comprising **amylopectin** (branched chains, branches due to  $\alpha(1\rightarrow6)$  glycosidic bonds) and **amylose** (straight chains). **Glycogen** is similar to amylopectin and is branched.

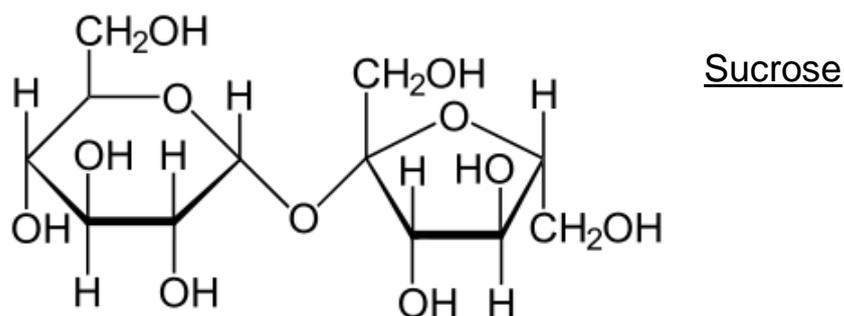
## Disaccharides and glycosidic bonds



Above: an  **$\alpha$ -glycosidic bond** (-O-) formed when the monosaccharide on the left is an  $\alpha$ -sugar, i.e. the -OH group on the C atom right of the O atom in the ring points down below the plane of the ring. Here we have an  $\alpha$ -glucose on the left joined to a  $\beta$ -glucose on the right. The numbers are the C atoms, ordered clockwise from the ring O atom by convention. This glycosidic bond joins C1 of the glucose on the left to C4 of the right-hand sugar and so it is an  $\alpha(1\rightarrow4)$  glycosidic bond.

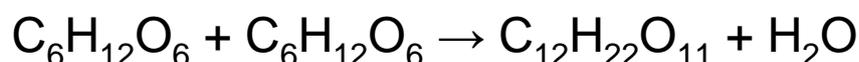


The disaccharide above shows a beta-glucose on the left joined by a glycosidic bond to a beta glucose on the right. This is a  **$\beta$ -glycosidic bond** (as the left hand monosaccharide is a beta-monosaccharide) and it is a  $\beta(1\rightarrow4)$  glycosidic bond.



Above: sucrose is a disaccharide formed from an alpha-glucose on the left joined to a fructose molecule on the right. Fructose is a 6C monosaccharide, like glucose, but it has a five-membered ring. The bond between these sugars is an  **$\alpha$ -glycosidic bond**.

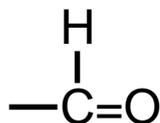
When two monosaccharides join together to form a disaccharide one water molecule is lost in the formation of the glycosidic bond – a process called a **condensation reaction**:



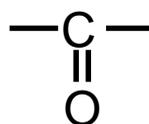
monosaccharide + monosaccharide  $\rightarrow$  disaccharide + water

## Food Tests for Carbohydrates

1. Reducing sugars are sugars which have an exposed aldehyde or ketone group:



aldehyde group



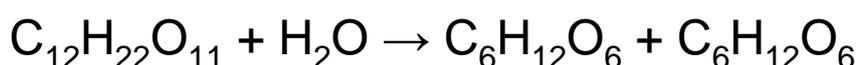
ketone group

Looking at the ring structures of glucose and fructose we see no C=O but only –H and –OH groups. However, in solution some of the rings spontaneously open up and the first C atom, C1, will then contain a C=O as the O atom from the ring bonds with C1 twice instead of with C1 once and C5 once as it does in the ring.

It is this aldehyde or ketone group that reacts with Fehling's solution or Benedict's solution in the test for monosaccharides. Fehling's and Benedict's solutions contain Cu<sup>2+</sup> (blue) and the aldehyde/ketone group on monosaccharides (when their rings open) reduces the blue Cu<sup>2+</sup> to a red precipitate (solid) of Cu<sub>2</sub>O (copper (I) oxide) and so these sugars are called reducing sugars.

**Fehling's reagent is a test for reducing sugars (e.g. monosaccharides) and turns from a blue solution to a red precipitate.**

Sucrose will not ordinarily react as its rings cannot open up as two rings are bonded together by a glycosidic bond which is stable. However, boiling sucrose with some HCl (hydrochloric acid) solution will break up the sucrose by adding water back to the glycosidic bond – a process called (acid) **hydrolysis**:



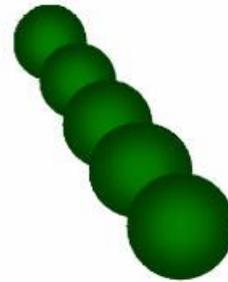
sucrose + water → glucose + fructose

Some of the glucose and fructose rings will then form will open out to form reactive aldehyde / ketone groups and so will act as reducing sugars and give a red precipitate with Fehling's reagent.

**Test for non-reducing sugars: Sucrose reacts tests positive with Fehling's or Benedict's reagent only after boiling with acid for about 5 minutes as sucrose is a non-reducing sugar.**

2. Test for starch: starch will react with **iodine** dissolved in KI (potassium iodide – iodine dissolves poorly in water so we dissolve it in KI) to form a blue-black colour. Starch reacts either not at all or very poorly with Benedict's and Fehling's solutions.

## Proteins

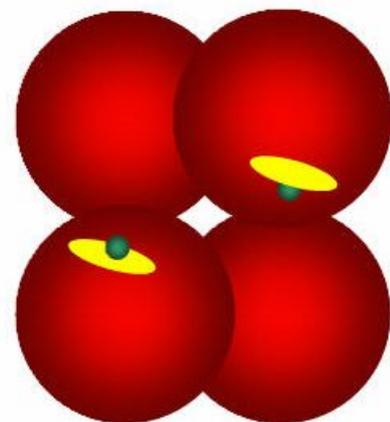


## Cytoskeleton

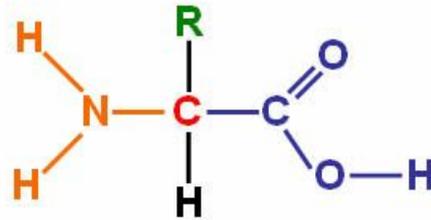
Left and above: many globular subunits may join together in a long chain to form a helix which forms a tubular protein. Smaller filamentous proteins may consist of a simple chain of protein subunits. These proteins act as struts, columns and beams that support the cell, maintain its shape and move it about.

Collagen and elastin are important filamentous or fibrous proteins that are secreted by cells to form a tough matrix that gives tissues their strength (collagen) and elasticity (elastin).

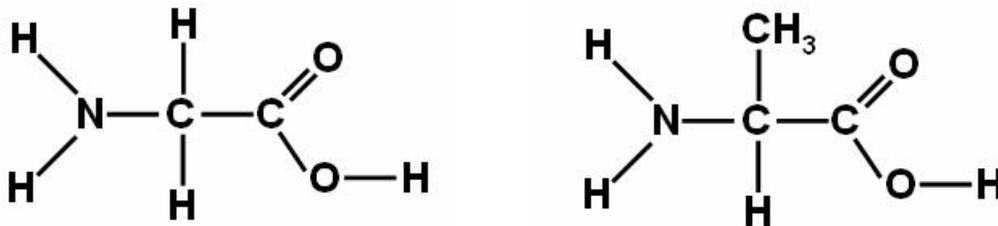
Right: globular proteins are made up of one or more globular subunits and include proteins involved in transport and enzymes. Shown here is haemoglobin – the protein that carries oxygen in the blood of vertebrates and gives human blood its red colour. Each spherical subunit (a globin) has a haem group (yellow ring) joined to it which contains a central iron atom (green sphere) which binds oxygen. Four such subunits form one haemoglobin protein.



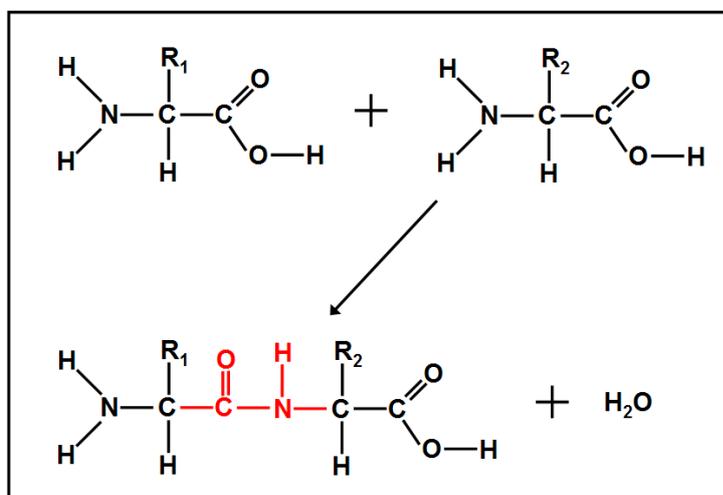
Polypeptides are polymers of amino acids. A polymer is a long chain molecule formed by chemically bonding many subunit monomers together end-to-end. Starch and glycogen are polymers of glucose, DNA is a polymer of nucleotides and polypeptides are polymers of amino acids. One long polypeptide or more than one polymer that are bonded together make up a protein. Plastics like polyethylene (polythene) are polymers (in this case of ethene) and proteins are rather like plastics.



Above: a single amino acid – the subunit monomer of polypeptides and proteins. The orange  $\text{-NH}_2$  is the amine group and the blue  $\text{-COOH}$  is the carboxylic acid group. The green R is a side-chain which is different for each of the 20 or so amino acids found in proteins.



Above: left, the simplest amino acid is glycine with  $\text{R} = \text{H}$ ; right, in alanine  $\text{R} = \text{CH}_3$ ; in other amino acids R is more complex and may be an electrically charged group that is attracted to water (it is polar or hydrophilic) or it may be a water-insoluble (fat-soluble) side-chain (which is non-polar or hydrophobic). The nature of the side-chains determines the chemical properties of each amino acid and thus the shape into which the polypeptide folds and so the properties of the protein.



Left: two amino acids join together to form a dipeptide by a condensation reaction (a reaction that yields water). The amine  $\text{-NH}_2$  group is a base (like an alkali) and reacts with the acidic  $\text{-COOH}$  group to neutralise it (acid + base = salt + water, but in this case the 'salt' is a dipeptide). The bond between the two amino acids is covalent and is called a **peptide link/bond** and is shown in red.

# The Structure of Proteins

## Primary Structure

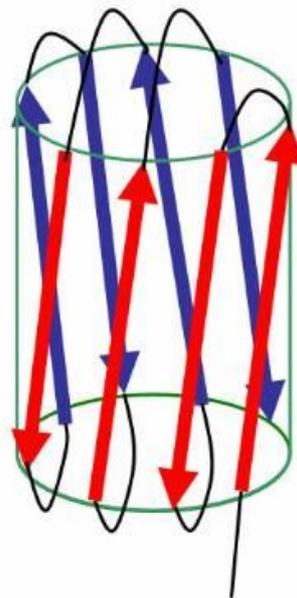
The primary structure is simply the sequence of amino acids in each polypeptide. The amino acid sequence is critical in determining how the polypeptide will fold, since the various amino acid side-chains (R-groups) of the amino acids will form different types of bonds with one another. This sequence is encoded for in the DNA of the genes.

## Secondary Structure

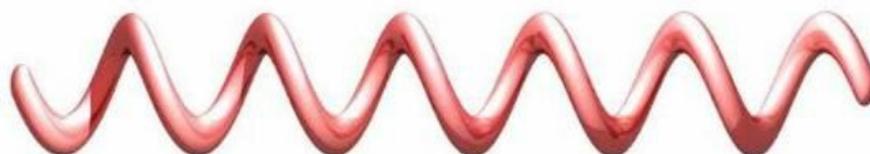
This is formed when the R side-chains of the amino acids bond to one-another, causing the polypeptide to fold into a specific shape. Each polypeptide then is made up of one or more folded structures or motifs – such as the **alpha-helix**, the **beta-pleated sheet** or the **beta-barrel**. Alpha-helices form rod-like sections of proteins (that may act as levers, ropes or springs), beta-pleated sheets are shaped like sheets of corrugated iron and these may roll up to form hollow cylinders or beta-barrels. Beta-barrels may form pores in the cell membrane, e.g. aquaporins are protein pores that allow water to diffuse more easily across cell membranes (facilitated diffusion and osmosis).



Above: a beta-pleated sheet containing three antiparallel polypeptide strands.



Above: a beta-barrel formed from 8 antiparallel strands.

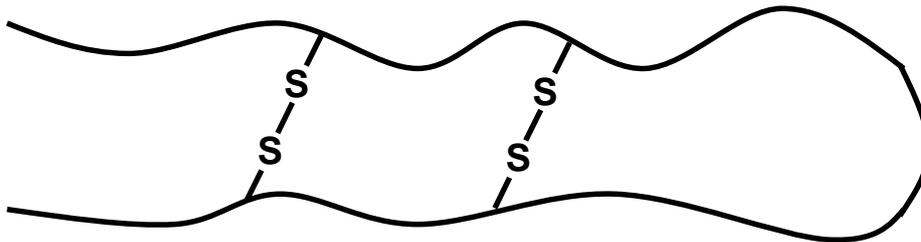


Above: an alpha-helix (a right-handed helix motif).

## Tertiary Structure

This is determined by longer-range interactions between the amino-acid side-chains in the polypeptide, such as the formation of **disulphide bridges** –S-S- between two cysteine amino acid residues (an amino acid residue is the name given to an amino acid that is part of a polypeptide) – cysteine has a R = –CH<sub>2</sub>SH side-chain and two such side-chains can react to form disulphide bridges. Other long-range bonds involved include **hydrogen-bonds**.

These form domains, or large 3D structures (containing several motifs) such as the elongated zinc finger domain which acts like a finger that fits into the groove of the DNA helix and allows certain proteins to grab hold of DNA.



## Quaternary Structure

Some proteins only have tertiary structure, however, many are made up of several polypeptides (called protein subunits) joined together by long-range bonds, including disulphide bridges (-S-S-) between two polypeptides, hydrogen bonds and others. Haemoglobin is a good example of a protein with quaternary structure as it contains four polypeptides joined together.

## How does DNA encode the primary structure or amino acid sequence?

First of all enzymes copy or transcribe the message from the DNA into **messenger RNA (mRNA)** – a process called **transcription**. In this DNA message, which is coded on only one of the two strands of the double helix (the **sense or coding strand**) groups of three bases (adenine, A; thymine, T; cytosine, C and guanine, G) called **codons** code for one amino acid. Transcription occurs in the cell nucleus and the mRNA moves out into the cytoplasm where it can be read and translated by **ribosomes** into polypeptides – a process called **translation** and which involves **transfer RNAs (tRNAs)** each with an **anticodon** (a region of three nucleotides that recognise and bind to the codon on the mRNA) and a region which binds the correct amino acid.

e.g. a codon for the amino acid threonine is ACT on the sense strand of the DNA and TGA on the antisense strand which transcribes to the codon UGA on the mRNA (all Ts become Us, or uracils, on the RNA) when the mRNA is produced by transcription (the enzyme RNA polymerase reads the message from the antisense strand, or non-coding strand, of the DNA and creates the correct mRNA molecule).

When the ribosome translates the mRNA code and reaches the codon UGA it waits for the correct tRNA with the ACU anti-codon carrying the correct amino acid, threonine, to attach to the mRNA (by its anti-codon pairing with the codon) and deliver the threonine amino acid which the ribosome then adds to the growing polypeptide by enzymically catalysing the formation of a peptide bond between the polypeptide and the threonine.