Edexcel

AS Level

Biology

CODE: (WBI11)

Topic 2

Membranes, proteins and DNA Gene expression

1A – Cell membranes

MEMBRANES IN CELLS

There are many membranes within cells, such as those that surround **organelles** like the nucleus and mitochondria. But the most obvious membrane is the cell surface membrane (outer cell membrane) which forms the boundary of the cell. Anything that leaves or enters the cell must pass through this membrane.

Enzymes and all the factors that are needed to make the reactions happen, are held closely together so that the process can go easily from one reaction to the next.

Chemical secretions made by the cell are contained in membrane bags, called **vesicles**, which must be able to combine with the cell surface membrane to release their contents.

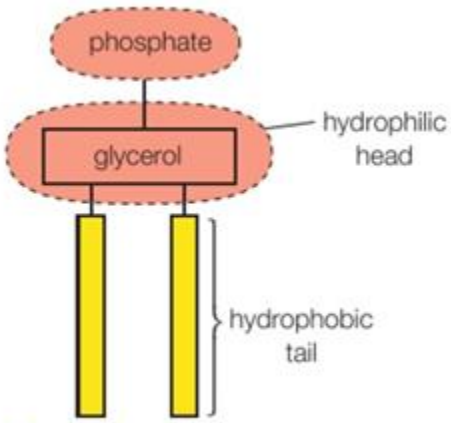
THE STRUCTURE OF MEMBRANES

Our current model of the structure of membranes has been developed over many years. In the future, there will probably be further adjustments to the model presented here but overall, the ideas are unlikely to change much. The membrane is composed of mainly two types of molecules - **phospholipids** and proteins - arranged in a very specific way.

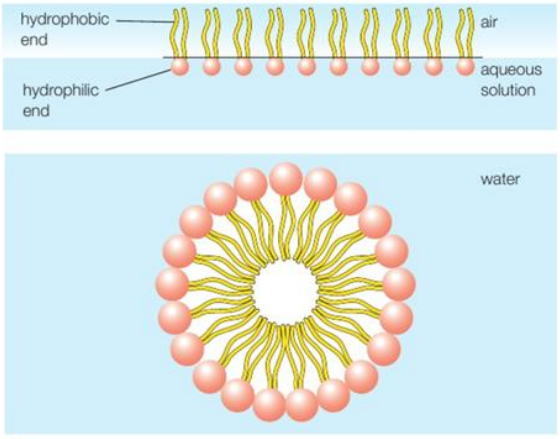
THE PHOSPHOLIPID BILAYER

The lipids in the membrane are called **polar lipids**. These are lipid molecules with one end joined to a polar group. Many of the polar lipids in the membrane are phospholipids, with a phosphate group forming the polar part of the molecule (see fig A).

When the phospholipids contact water, the two parts of the molecule behave differently. The polar phosphate part is **hydrophilic** (water-loving) and dissolves easily in water. The lipid tails are **hydrophobic** (water-hating) and insoluble in water. If the molecules are tightly packed in water they form either a **monolayer**, with the hydrophilic heads in the water and the hydrophobic lipid tails in the air, or clusters which are called **micelles**. In a micelle, all the hydrophilic heads point outwards and all the hydrophobic tails are hidden inside (see fig B).



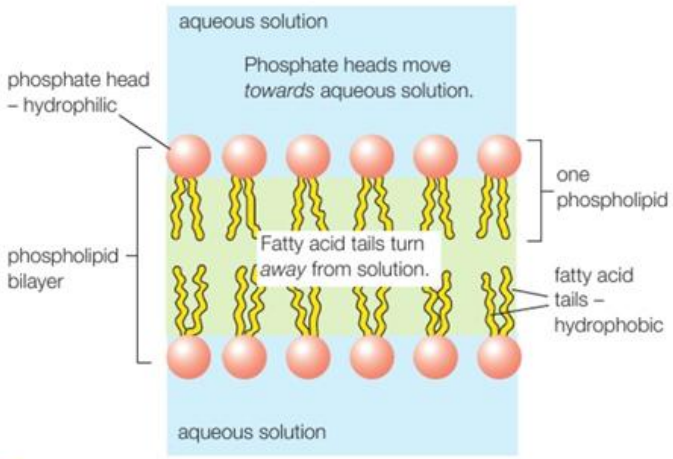
▲ **fig A** A phospholipid molecule



▲ **fig B** Phospholipids form a monolayer at an air/water junction and a micelle when water surrounds them.

With water on each side the phospholipid molecules form a **bilayer**, with the hydrophilic heads pointing into the water while the hydrophobic tails are protected in the middle (see fig C). This structure, the **unit membrane**, is the basis of all membranes.

A simple phospholipid bilayer allows fat-soluble organic molecules to pass through it, but many vital molecules needed in cells are ionic. While these dissolve in water, they cannot dissolve in or pass through lipids, even polar lipids.



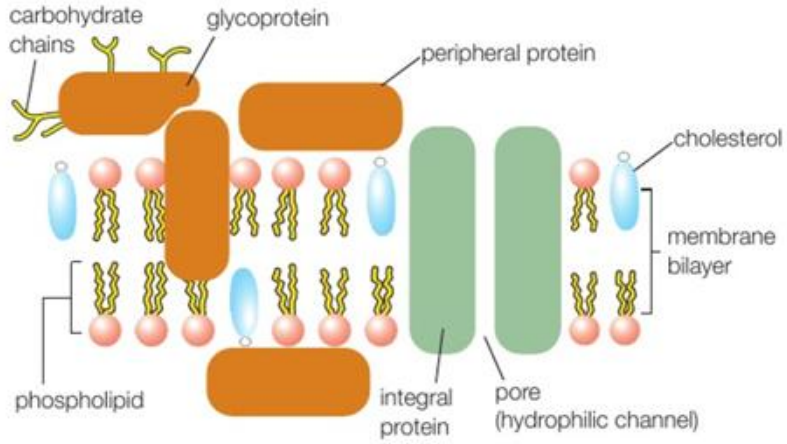
▲ **fig C** A phospholipid bilayer is the key structure of all membrane structures in a cell.

THE FLUID MOSAIC MODEL OF THE CELL MEMBRANE

The proportion of phospholipids containing unsaturated fatty acids (see Section 1A.4) in the bilayer seems to affect how freely the proteins move within the membrane. Another important lipid in the cell membrane is cholesterol (see Chapters 1B and 1C in relation to heart disease).

Cholesterol is a more rigid molecule than many of the phospholipids and so makes the membrane more stable and stronger. This makes it harder for small molecules and ions to pass

Some proteins go all the way through the lipid bilayer, while others are only in part of the bilayer. This model of floating proteins in a lipid sea is known as the **fluid mosaic model** and it was first proposed by S. Jonathan Singer and Garth Nicholson in 1972.



▲ **fig D** The fluid mosaic model of the cell membrane – a phospholipid sea with associated proteins, which may be floating or anchored within the membrane.

One of the main functions of the membrane proteins is to help substances move across the membrane. The proteins may make pores or channels - some permanent, some temporary - which allow specific molecules to move through the membrane. Some of these channels can be open or shut, depending on conditions in the cell. These are known as **gated channels**.

Proteins may act as specific receptor molecules - for example, making cells sensitive to a specific hormone. They may be enzymes, particularly on the internal cell membranes, to control reactions linked to that membrane. Some membrane proteins are **glycoproteins**, proteins with a carbohydrate part added to the molecule.

BUILDING A MODEL OF THE MEMBRANE

Our ideas about membrane structures have developed over many years from scientific observations. These observations have changed as the technology available has changed. Here is a summary of the story of where our ideas of the cell membrane have come from.

• The first indications that lipids are important components of cell membranes came at the end of the 19th century when Charles Ernest Overton (1865-1933) made a series of observations on how easily substances passed through cell membranes. Lipid-soluble substances entered more easily than any others, so he concluded that a large part of the membrane structure must be lipid.

• The idea that cell membranes are not rigid but are fluid structures came from observations of the behaviour of cell surface membranes when cells join, together with the way in which most membranes seal themselves if they are punctured with a fine needle.

• In 1917, Irving Langmuir (1881-1957) demonstrated the lipid monolayer mentioned earlier. In collaboration with Katharine Blodgett, he also developed a piece of equipment for collecting lipid monolayers called the Langmuir-Blodgett trough.

• In 1925, two Dutch scientists, Evert Gorter and François Grendel, decided to measure the total size of the monolayer film formed by lipids extracted from human red blood cells (erythrocytes).

• By 1935, Hugh Davson and James Danielli had produced a further model of the membrane with a lipid centre coated on each side by protein. This is the basis of our current ideas.

• The Davson-Danielli hypothesis was backed up in the 1950s by work on the electron microscope by James D. Robertson. He found ways of staining the membrane which revealed it as a three-layered structure - two distinct lines with a gap in the middle.

• More recently, techniques such as X-ray diffraction and new electron microscopy methods have added to our knowledge of the structure of cell membranes.

SUBJECT VOCABULARY

cell membrane the selectively permeable membrane which surrounds the cytoplasm of a cell, acting as a barrier between the cell contents and their surroundings
organelles sub-cellular bodies found in the cytoplasm of cells
enzymes proteins that act as biological catalysts for a specific reaction or group of reactions
vesicles membrane 'bags' that hold secretions made in cells
phospholipids chemicals in which glycerol bonds with two fatty acids and an inorganic phosphate group
polar lipids lipids with one end attached to a polar group (e.g. a phosphate group) so that one end of the molecule is hydrophilic and one end is hydrophobic
hydrophilic a substance with an affinity for water that will readily dissolve in or mix with water
hydrophobic a substance that tends to repel water and that will not mix with or dissolve in water
monolayer a single closely packed layer of atoms or molecules
micelles a spherical aggregate of molecules in water with hydrophobic areas in the middle and hydrophilic areas outside
bilayer a double layer of closely packed atoms or molecules
unit membrane a lipoprotein membrane which is composed of two protein layers enclosing a less dense lipid
fluid mosaic model the current model of the structure of the cell membrane including floating proteins forming pores, channels and carrier systems in a lipid bilayer
gated channels protein channels through the lipid bilayer of a membrane that are opened or closed, depending on conditions in the cell
glycoproteins conjugated proteins with a carbohydrate prosthetic group

2.Cell transport and diffusion

THE MAIN TYPES OF TRANSPORT ACROSS MEMBRANES

Substances are transported into, out of and around cells by a variety of different mechanisms. **Passive transport** takes place when there are concentration, pressure or electrochemical gradients, and it involves no energy from the cell. **Active transport** involves moving substances into or out of the cell by using adenosine triphosphate (ATP) which is produced during cellular respiration.

PASSIVE TRANSPORT MECHANISMS

There are three main types of passive transport in cells.

• **Diffusion** - the movement of particles in a liquid or gas down a concentration gradient. They move from an area where they are at a relatively high concentration to an area where they are at a relatively low concentration by random movements. Cell membranes are no barrier to the diffusion of small particles such as the gases oxygen and carbon dioxide.

• **Facilitated diffusion**- diffusion that takes place through carrier proteins or protein channels. The protein-lined pores of the cell membrane make facilitated diffusion possible.

• **Osmosis** - a specialised form of diffusion that involves the movement of solvent molecules (in cells, this is free water molecules) down a water potential gradient through a **partially permeable membrane**. You will learn more about water potential gradients in Section 2A.3. The partially permeable nature of the cell membrane means **solutes** (dissolved substances) can be accumulated either side of the membrane and this results in the movement of water by osmosis across the membrane.

ACTIVE TRANSPORT MECHANISMS

Active transport is the movement of substances across the membrane of cells using ATP as an immediate source of energy. Active transport always involves a **carrier protein** which carries molecules or ions through the membrane using energy supplied by the breakdown of ATP.

There are two other mechanisms for moving substances into and out of cells. These also use energy from ATP. They are:

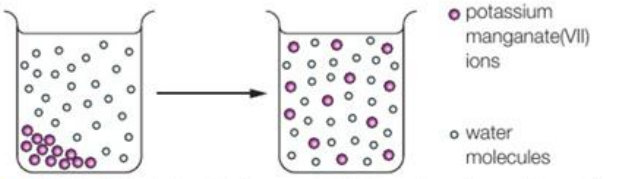
• **Endocytosis** - the movement of large molecules into cells through vesicle formation. The fluid nature of the cell membrane makes it possible to form vesicles.

• **Exocytosis** - the movement of large molecules out of cells through fusion of vesicles to the membrane.
You will learn more about active transport, endocytosis and exocytosis in Section 2A.4.

▲ **fig A** The rapid movements of the sensitive plant *Mimosa pudica* are the result of different types of transport within the cells of the plant.

DIFFUSION

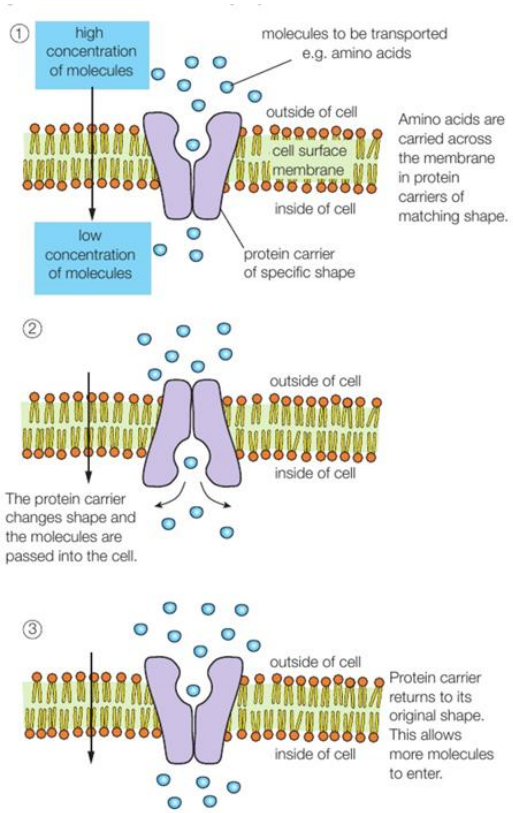
In physical terms, diffusion is the movement of the molecules of a liquid or gas from an area where they are at a high concentration to an area where they are at a lower concentration. We say that they move down their concentration gradient (see Section 1B.1). This happens because of the random motion of molecules due to the energy they have, which depends on the temperature. If you have many molecules tightly packed together, random motion means that they spread out and eventually reach a uniform distribution.



▲ **fig B** If the beaker is left to stand, diffusion takes place as the random movement of both the water and the potassium manganate(VII) ions ensures that they become evenly mixed.

FACILITATED DIFFUSION

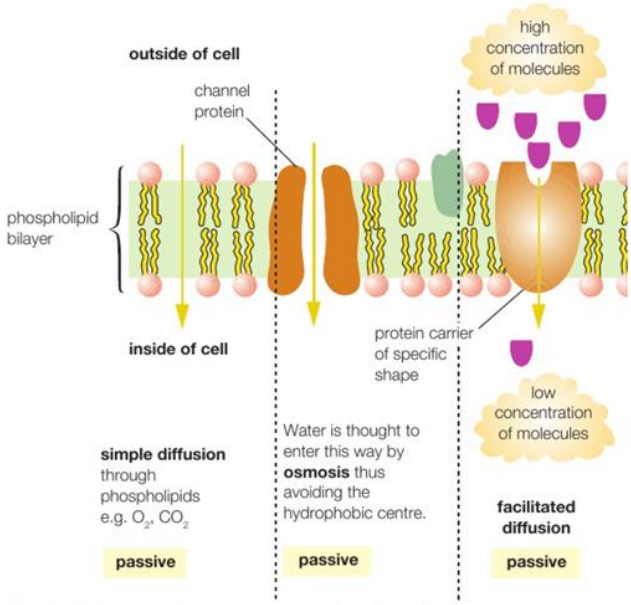
Substances with a strong positive or negative charge and large molecules cannot cross cell membranes by simple diffusion. Nevertheless, they may move into and out of the cell down a concentration gradient by a specialised form of diffusion. Facilitated diffusion involves proteins in the membrane that allow specific substances to move passively down their concentration gradient (see fig C). The proteins may be channel proteins that form pores through the membrane. Each type of channel protein allows one particular type of molecule to pass through; this depends on the molecule's shape and charge.



▲ **fig C** Facilitated diffusion acts as a ferry across the lipid membrane sea. It is not an active process, so it can only work when the concentration gradient is in the right direction.

IN SUMMARY

The three types of passive transport are summarised in fig D.



▲ **fig D** The main passive transport routes through a cell surface membrane

SUBJECT VOCABULARY

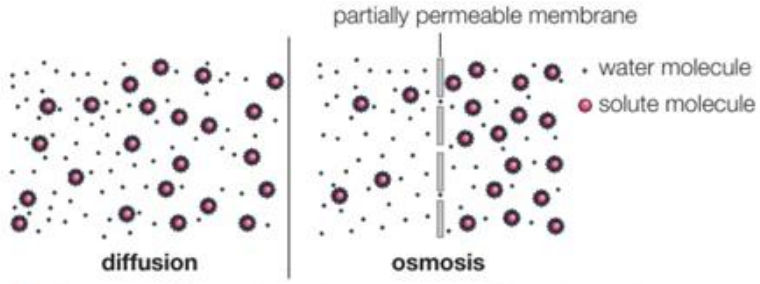
passive transport transport that takes place as a result of concentration, pressure or electrochemical gradients and involves no energy from a cell
active transport the movement of substances into or out of the cell using ATP which is produced during cellular respiration
diffusion the movement of the particles in a liquid or gas down a concentration gradient from an area where they are at a relatively high concentration to an area where they are at a relatively low concentration
facilitated diffusion diffusion that takes place through carrier proteins or protein channels
osmosis a specialised form of diffusion that involves the movement of solvent molecules down their water potential gradient
partially permeable membrane a membrane which only allows specific substances to pass through it
solute a substance in a solution, dissolved in the solvent
carrier protein a protein that moves a substance through the membrane in active transport using energy from the breakdown of ATP or in passive transport such as facilitated diffusion down a concentration gradient
endocytosis the movement of large molecules into cells through vesicle formation
exocytosis the movement of large molecules out of cells by the fusing of a vesicle containing the molecules with the surface cell membrane; the process requires ATP

2A – 3 Osmosis: A special case of diffusion

WHAT IS OSMOSIS?

Osmosis in cells can be defined as the net movement of free water molecules through a partially permeable membrane, down a water potential gradient. In living organisms, the solvent is always water, and membranes in cells are generally partially permeable. This means that they let some molecules through, but not others. But what is a water potential gradient? The **water potential** of a solution measures the concentration of free water molecules - in other words, the water molecules that are not associated with solute molecules. More free water molecules mean a higher water potential.

If the opposite is true and the solution bathing the cell has a higher concentration of solute than the cell contents, the water potential gradient will be from the inside to the outside and free water molecules will move out of the cell. The **osmotic concentration** of a solution concerns only those solutes that have an osmotic effect.



▲ **fig A** In diffusion, the random movement of particles results in an even distribution of both solute and solvent particles. In osmosis, a partially permeable membrane means only solvent molecules and very small solute particles can move freely.

MODELLING OSMOSIS IN CELLS

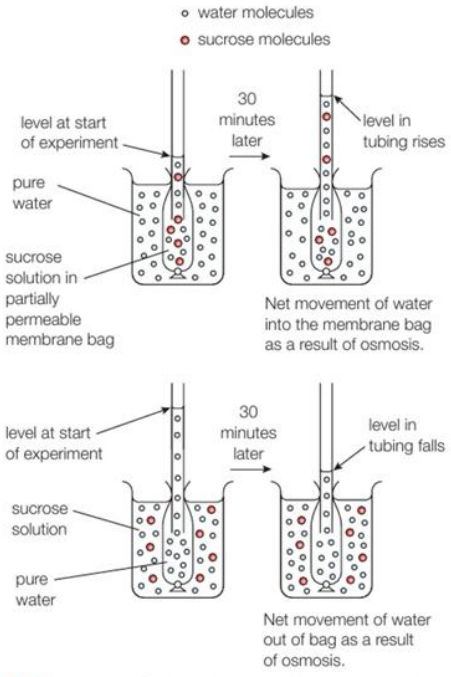
You can make a model cell using an artificial membrane that is permeable to water molecules and impermeable to others such as sucrose. There are many experiments showing the movement of water in these circumstances, and one of the simplest is illustrated in fig B. The presence or absence of sucrose in the different regions of the model can be shown by carrying out Benedict's test for non-reducing sugars on the solutions (see Section 1A.2).

OSMOTIC CONCENTRATIONS

During osmotic experiments, cells are often immersed in solutions of different osmotic concentration. The osmotic concentration of a solution is a measure of only those dissolved substances that have an osmotic effect.

• In an **isotonic** solution, the osmotic concentration of the solutes in the solution is the same as that in the cells.

• In a **hypotonic** solution, the osmotic concentration of solutes in the solution is lower than that in the cytoplasm of the cells.



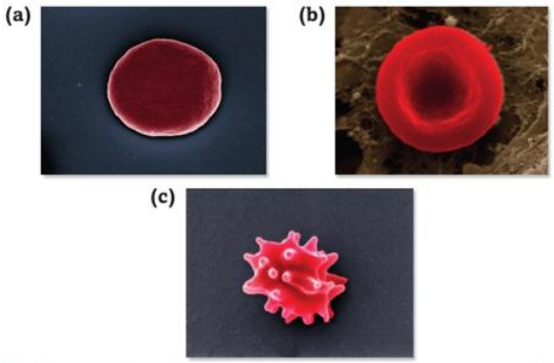
▲ **fig B** The artificial partially permeable membrane in this experiment provides a model for the cell surface membrane. It allows water molecules to pass through freely, but not the solute molecules.

• In a hypertonic solution, the osmotic concentration of solutes in the solution is higher than that in the cytoplasm.

OSMOSIS IN ANIMAL CELLS

Osmosis needs to be carefully controlled in animal cells. The net movement of water in or out needs to be kept to a minimum.

When too much water moves in, the cells burst; when too much moves out, the cells shrivel as the concentrated cytoplasm loses its internal structure (**see fig C**). This means that the chemical reactions that normally take place in the cell stop working.



▲ **fig C** The effects of osmosis on red blood cells show why the systems of the body that maintain solute concentrations and water balance are so important. **(a)** In hypotonic solution, water moves in and the cell swells and bursts; **(b)** in isotonic solution the red blood cell maintains its normal shape; **(c)** in hypertonic solution, water moves out and the cell shrivels.

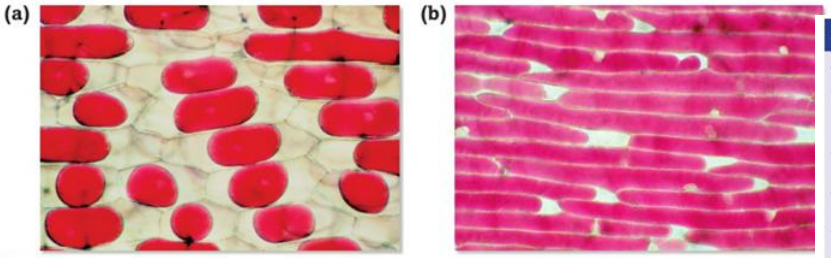
OSMOSIS IN PLANT CELLS

If the surrounding fluid is hypotonic to the cytoplasm of a plant cell, water will enter the cell by osmosis - but not indefinitely. As the cytoplasm swells and presses on the cell walls, it generates **hydrostatic pressure**.

The inward pressure of the cell wall on the cytoplasm increases until it cancels out the tendency for water molecules to move in. This inward pressure is called the pressure potential. When the osmotic force moving water into the plant cell is balanced by the pressure potential forcing it out, the plant cell is rigid, in a state known as **turgor**.

If plant cells are put in a solution which is slightly hypertonic, water moves out of the cell by osmosis and turgor is lost. The cell membrane begins to pull away from the cell wall as the protoplasm shrinks. This is called **incipient plasmolysis**.

plasmolysed and 50% are not. This is the concentration that is equivalent to the solute potential of the cell sap. If the cell is placed in a hypertonic solution, so much water will leave the cell that the vacuole will be reduced and the protoplasm will shrink away from the cell walls completely - the cells suffer **plasmolysis**.



▲ **fig D** Plant cells from red beet showing **(a)** plasmolysis; and **(b)** turgor.

SUBJECT VOCABULARY

water potential a measure of the potential for water to move out of a solution by osmosis
osmotic concentration a measure of the concentration of the solutes in a solution that have an osmotic effect
isotonic solution a solution in which the osmotic concentration of the solutes is the same as that in the cells
hypotonic solution a solution in which the osmotic concentration of solutes is lower than that in the cell contents
hypertonic solution a solution in which the osmotic concentration of solutes is higher than that in the cell contents
hydrostatic pressure the pressure exerted by a fluid in an equilibrium
turgor the state of a plant cell when the solute potential causing water to be moved into the cell by osmosis is balanced by the force of the cell wall pressing on the protoplasm
incipient plasmolysis the point at which so much water has moved out of the cell by osmosis that turgor is lost and the cell membrane begins to pull away from the cell wall as the protoplasm shrinks
plasmolysis the situation when a plant cell is placed in hypertonic solution when so much water leaves the cell by osmosis that the vacuole is reduced and the protoplasm is concentrated and shrinks away from the cell walls

2A 4 Active transport

HOW DOES ACTIVE TRANSPORT WORK?

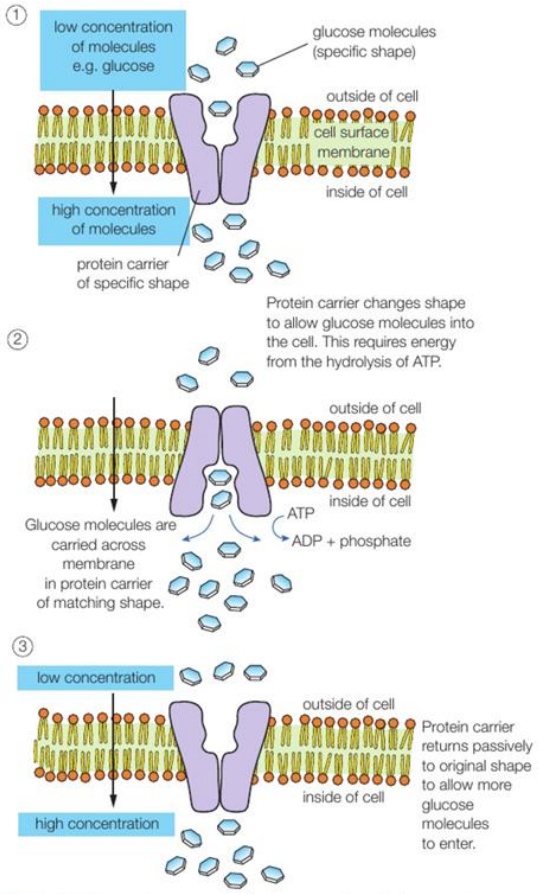
The energy needed for active transport is provided by molecules of adenosine triphosphate (ATP). Cells that carry out a lot of active transport generally have many mitochondria to supply the ATP they need. The active transport carrier system in the membrane involves the enzyme **ATPase**. This enzyme catalyses the hydrolysis of ATP by breaking one bond and forming two more. This provides the energy needed to move carrier systems in the membrane or to release the transported substances and return the system to normal.

Endocytosis and exocytosis

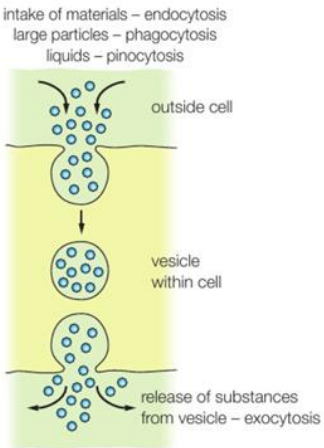
Membrane-bound vesicles can surround and take up materials in a process known as endocytosis (see fig B). This can occur on a relatively large scale, for example the ingestion of bacteria during **phagocytosis** (cell eating). It also happens at a microscopic level, when tiny amounts of the surrounding fluid are taken into minute vacuoles. This is known as **pinocytosis** (cell drinking). Electron microscope studies have shown that pinocytosis is very common as cells take in the extracellular fluid as a source of minerals and nutrients (see fig C).

SUBJECT VOCABULARY

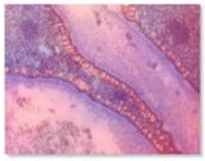
ATPase an enzyme that catalyses the hydrolysis of ATP, releasing energy to move carrier systems and drive metabolic reactions
cyanide a metabolic poison that stops mitochondria working
phagocytosis the active process when a cell engulfs something relatively large such as a bacterium and encloses it in a vesicle
pinocytosis the active process by which cells take in tiny amounts of extracellular fluid by tiny vesicles



▲ **fig A** Using active transport, cells can move selected substances into or out of the cell, even when the concentration gradient is in the wrong direction.



▲ **fig B** The properties of the cell membrane allow cells to take in large particles or release secretions.



▲ **fig C** The mass of tiny vesicles along these cell membranes show pinocytosis.

2A – 5 The need for gas exchange surfaces

GAS EXCHANGE IN SMALL ORGANISMS

Section 1B.1 discussed the surface area: volume ratio principles, which determine whether an organism requires a mass transport system or specialized gas exchange system. Single-celled organisms have a large ratio, allowing them to obtain oxygen through their outer body surface. As organisms grow, their ratio decreases, necessitating specialized systems.

GAS EXCHANGE IN LARGE ORGANISMS

Larger organisms consist of billions of cells organized into specialized tissues and organs, with substances needing long distances to reach the cytoplasm. They have higher metabolic rates, allowing them to be active and control their body temperature. Complex organisms have evolved specialized systems to exchange gases, such as in humans, fish, insects, and plants, with gas exchange taking place in the lungs, gills, tracheal system, and leaves.

fig A This *Hydra* is less than 15 mm long, and has only two layers of cells. The Arabian horse is around 155 cm tall at the shoulder, and contains billions of cells. The surface area : volume ratio of the *Hydra* means it can get the oxygen it needs by simple diffusion. The surface area : volume ratio of the horse is very small – it needs lungs, organs specially adapted for gas exchange.

KEY PROPERTIES OF GAS EXCHANGE SYSTEMS

Gas exchange systems are specialised for the exchange of oxygen and carbon dioxide between the body of the organism and the environment. These gases are exchanged by simple diffusion. The rate of diffusion across a membrane is controlled by several factors.

- The surface area - the bigger the surface area, the more particles can be exchanged at the same time.
- The concentration gradient of the particles diffusing - particles diffuse from an area where they are at a relatively high concentration to an area where they are at a relatively low concentration. This means that the more particles there are on one side of a membrane compared with the other, the faster they move across.
- The thickness of the exchange surfaces - the shorter the diffusion distance, the faster diffusion can take place.

You can use this information to calculate the rate at which substances of a given size will diffuse at a known temperature. This relationship is known as Fick's Law of Diffusion:

$$\text{rate of diffusion} = \frac{\text{surface area} \times \text{concentration difference}}{\text{thickness of exchange membrane or barriers}}$$

2A 6 The mammalian gas exchange system

EFFECTIVE GAS EXCHANGE

Effective gas exchange systems have several features in common.

• A large surface area giving sufficient gas exchange to supply all the needs of the organism - it has to compensate for the relatively small surface area: volume ratio of the whole organism.

• Thin layers to minimise the diffusion distances from one side to the other.

• In animals, a rich blood supply to the respiratory surfaces. The blood is involved in the transport of the respiratory gases to and from the site of gas exchange and helps to maintain a steep concentration gradient.

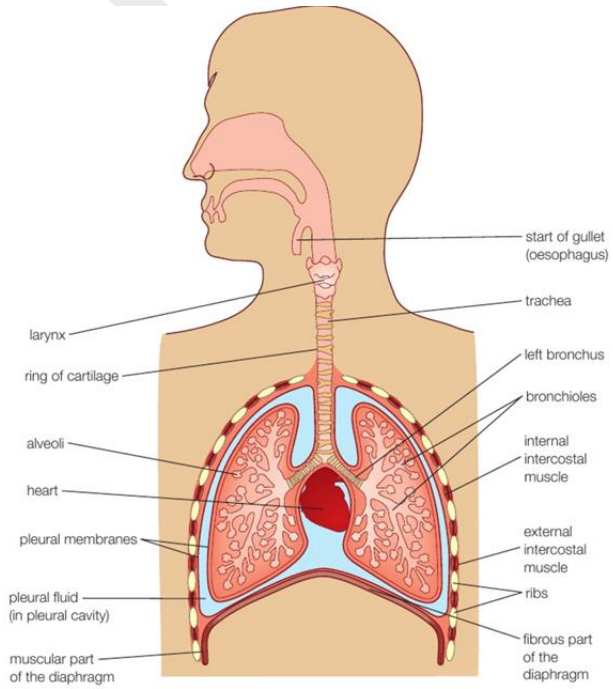
• Moist surfaces because diffusion takes place with the gases in solution.

• Permeable surfaces that allow free passage of the respiratory gases.

Mammals, including humans, have very efficient gas exchange systems.

THE HUMAN GAS EXCHANGE SYSTEM

The human gas exchange system is primarily located in the chest, connected to the outside world through the mouth and nose. The alveoli, with large surface areas and good blood supply, filter out dust, particles, and pathogens, protecting the lungs from damage and infection. The moist surfaces increase water vapor levels and raise air temperature, minimizing internal environmental impact.



▲ **fig A** The human gas exchange system including the lungs

HOW DOES IT WORK?

The different parts of the breathing system of a mammal, represented here by a person, are all adapted to their roles. The whole breathing system has evolved to make sure gas exchange takes place as rapidly as possible in the lungs.

- Nasal cavity: this is the main route by which air enters the gas exchange system.
- Mouth: air can enter the respiratory system here, but misses out on the cleaning, warming and moistening effects of the nasal route.
- Epiglottis: a flap of tissue that closes over the glottis in a reflex action when food is swallowed. This prevents food from entering the gas exchange system.
- Larynx: the voice box, which uses the flow of air across it to produce sounds.

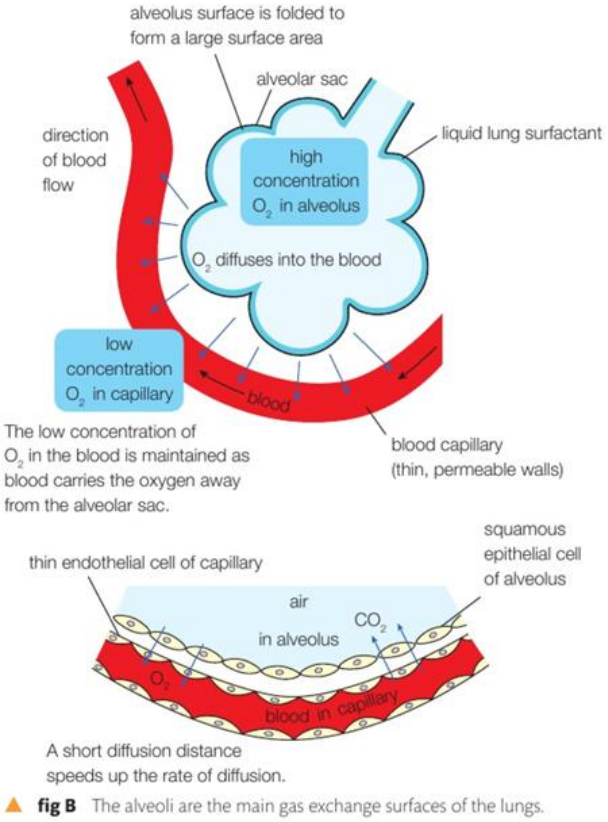
- Trachea: the major airway to the bronchi, lined with cells including mucus-secreting goblet cells. Cilia on the surface of the trachea move mucus and any trapped microorganisms and dust away from the lungs.
- Incomplete rings of cartilage: these prevent the trachea and bronchi from collapsing but allow food to be swallowed and moved down the oesophagus.
- Left and right bronchi: these tubes lead to the lungs and are similar in structure to the trachea but narrower. They divide to form bronchioles.
- Bronchioles: small tubes that spread through the lungs and end in alveoli. Their main function is still as an airway, but some gas exchange may occur.
- Alveoli: the main site of gas exchange in the lungs.
- Ribs: protective bony cage around the gas exchange system.
- Intercostal muscles: found between the ribs and important in breathing, which moves air into and out of the lungs to maintain a steep concentration gradient for rapid gas exchange.
- Pleural membranes: surround the lungs and line the chest cavity forming a sterile, sealed unit.
- Pleural cavity: space between the pleural membranes, usually filled with a thin layer of lubricating fluid that allows the membranes to slide easily with breathing movements.
- Diaphragm: broad sheet of tissue made of tendon and muscle that forms the floor of the chest cavity, also important in breathing movements.

GAS EXCHANGE IN THE ALVEOLI

The capillaries that run close to the alveoli also have a wall that is only one cell thick. Between the two is a layer of elastic connective tissue holding everything together. The elastic tissue helps to force air out of the lungs, which are stretched when you breathe in. This is known as the elastic recoil of the lungs. The alveoli have a natural tendency to collapse, but this is prevented by a special phospholipid known as **lung surfactant** that coats the alveoli and makes breathing easier.

LARGE SURFACE AREA

The alveoli provide an enormous surface area for the exchange of gases in the human body. Recent calculations have shown that an average adult human has around 480-500 million alveoli in their lungs. This means the surface area for gas exchange is around 40-75 m2 packed into your chest - that is the surface area of between 10 and 18 table tennis tables.



▲ **fig B** The alveoli are the main gas exchange surfaces of the lungs.

STEEP CONCENTRATION GRADIENT

Blood is continuously flowing through the capillaries past the alveoli, exchanging gases. The continuous flow of the blood maintains the concentration gradient on the capillary side. The air within the alveoli is constantly being refreshed with air from outside by breathing (see table A). Movement of gases into and out of the alveoli is mainly by diffusion, but movement of air into and out of the lungs is by a mass transport system (see fig C).

GAS	PERCENTAGE OF GAS IN:		
	INSPIRED AIR	ALVEOLAR AIR	EXPIRED AIR
oxygen	20.70	13.20	14.50
carbon dioxide	0.04	5.00	3.90
nitrogen	78.00	75.60	75.40
water vapour	1.24	6.20	6.20

table A The composition of the gases in the human gas exchange system

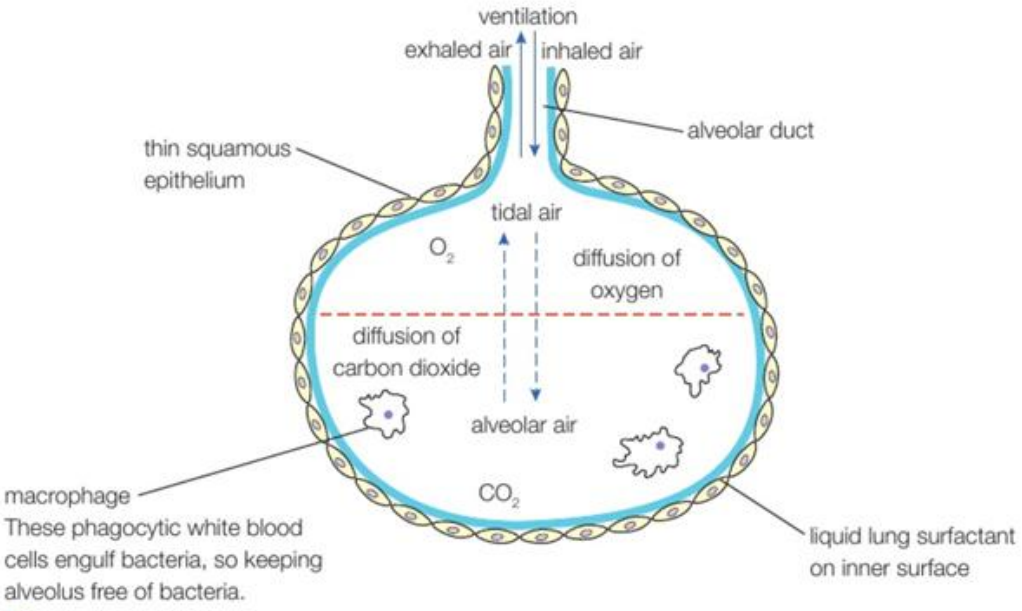


fig C Diffusion across the alveolar surfaces provides the blood with oxygen and disposes of carbon dioxide.

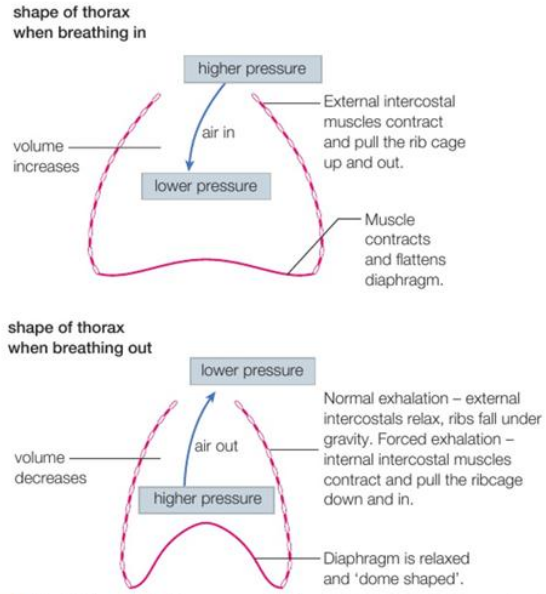
SHORT DIFFUSION DISTANCE

The walls of the alveoli are only one cell thick, as are the walls of the capillaries that run beside them. This means the distance that diffusing gas molecules need to travel between them is only around 0.5-1.5 µm (micrometres, microns, 10-6 m). This makes it as easy as possible for diffusion to take place rapidly and effectively.

BREATHING (VENTILATION)

The exchange of gases at the alveolar surfaces in the lungs happens by passive diffusion alone, but moving air between the lungs and the external environment is an active process known as **breathing** or **ventilation**. This is key to rapid gas exchange taking place in the alveoli. By delivering air rich in oxygen, and removing air loaded with waste carbon dioxide, breathing maintains a steep concentration gradient for diffusion between the blood in the capillaries and the air in the lungs. There are two parts to the process of breathing: taking air into the chest, called **inhalation**, and breathing air out again, called **exhalation**.

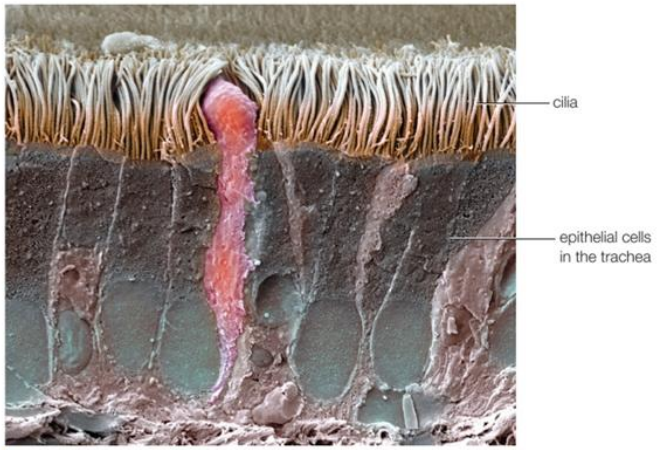
Forced exhalation is a method of increasing chest cavity pressure by contracting internal intercostal and abdominal muscles. It is used by singers and free divers to maintain long notes and fill lungs with air, while coughing is an exaggerated form.



▲ **fig D** You can feel the movements of your ribs during inhalation and exhalation, but the movements of your diaphragm are less obvious.

PROTECTING THE LUNGS

The gas exchange system exchanges oxygen and carbon dioxide, while air contains tiny particles and microscopic organisms like bacteria and viruses. To reduce lung damage and infection, the respiratory system produces mucus to line airways and trap these particles. Mucus is easily moved up airways and swallowed by the stomach, where it is digested by stomach acid and digestive enzymes.



▲ **fig E** The cilia in your trachea and bronchi beat constantly to move mucus with its load of pathogens and dirt out of your gas exchange system.

SUBJECT VOCABULARY

lung surfactant a special phospholipid that coats the alveoli and prevents them from collapsing
breathing (ventilation) the process in which physical movements of the chest change the pressure so that air is moved in or out
inhalation breathing in
exhalation breathing out
pathogens microorganisms that cause disease

2B 1 Enzymes

WHAT IS AN ENZYME?

A **catalyst** is a substance that changes the rate of a reaction without changing the substances produced. The catalyst is unaffected at the end of the reaction and can be used again. **Enzymes** are biological catalysts, which control the rate of the reactions that occur in individual cells and in whole organisms.

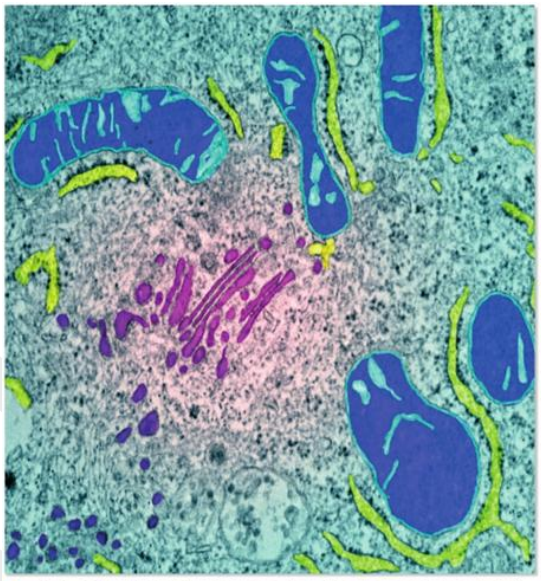


fig A Each cell contains several hundred different enzymes to control all the reactions going on inside.

Enzymes are globular proteins (see Section 1B.5) which are produced during protein synthesis as mRNA transcribed from the DNA molecule is translated (see Section 2B.6). They have a very specific shape as a result of their primary, secondary, tertiary and quaternary structures (see Section 1B.5). This means that each enzyme will only catalyse a specific reaction or group of reactions. We say enzymes show great **specificity**.

Within any cell, many chemical reactions are going on at the same time. Those reactions that build up new chemicals are known as **anabolic reactions** ('ana' means up, as in 'build up'). Those that break substances down are **catabolic reactions** means down, as in 'break down'). The combination of these two processes is **metabolism**. Most of the reactions of metabolism occur as part of a sequence of reactions known as a **metabolic chain or metabolic pathway**.

NAMING ENZYMES

In the study of biology, in medicine, in cellular and genetic research and in industries that use biotechnology, it is important to be able to refer to the action of specific enzymes.

Many of the enzymes found in animals and plants work inside the cells. The enzymes that catalyse reactions inside cells are known as **intracellular enzymes**; examples include DNA polymerase and DNA ligase (see Section 2B.4).

The enzymes that catalyse reactions outside the cells are called extracellular enzymes. The digestive enzymes and lysozyme, the enzyme in your tears, are good examples of these.

SUBJECT VOCABULARY

catalyst a substance that speeds up a reaction without changing the substances produced or being changed itself
enzymes proteins that act as biological catalysts for a specific reaction or group of reactions
specificity the characteristic of enzymes that means that each enzyme will catalyse only a specific reaction or group of reactions; this is due to the very specific shapes which come from the tertiary and quaternary structures
anabolic reaction a reaction that builds up (synthesises) new molecules in a cell
catabolic reaction a reaction which breaks down substances within a cell
metabolism the sum of the anabolic and catabolic processes in a cell
metabolic chain (metabolic pathway) a series of linked reactions in the metabolism of a cell
intracellular enzymes enzymes that catalyse reactions within the cell
extracellular enzymes enzymes that catalyse reactions outside of the cell in which they were made

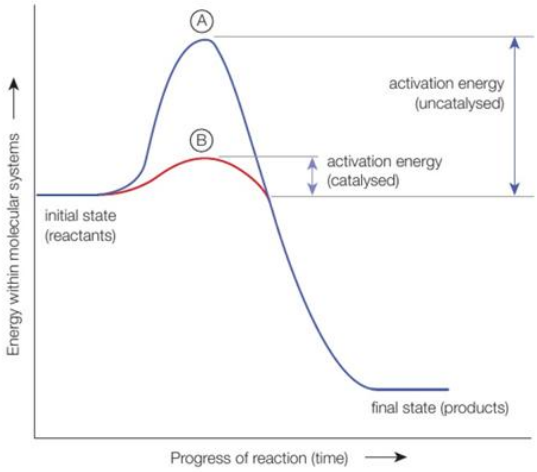
Most enzymes - both intracellular and extracellular - have several names including:

- a relatively short, recommended name, which is often the name of the molecule that the enzyme works on (the substrate) with '-ase' on the end, or the substrate with an indication of what it does (e.g. creatine kinase)
- a longer systematic name describing the type of reaction being catalysed (e.g. ATP: creatine phosphotransferase)
- a classification number (e.g. EC 2.7.3.2).

2B 2 How enzymes work

For a chemical reaction to occur, the reacting molecules must have enough energy to break the chemical bonds that hold them together. A simple model is that the reaction must get over an 'energy hill', known as the **activation energy**, before it can get started.

Raising the temperature increases the rate of a chemical reaction by giving more molecules sufficient energy to react. However, living cells could not survive the temperatures which are needed to make many cellular reactions fast enough – and the energy demands to produce the heat would be enormous. Enzymes solve the problem by lowering the activation energy needed for a reaction to take place (see **fig A**).



(A) = Energy of transition state in uncatalysed reaction.

(B) = Energy of transition state, i.e. enzyme/substrate complex, during catalysed reaction.

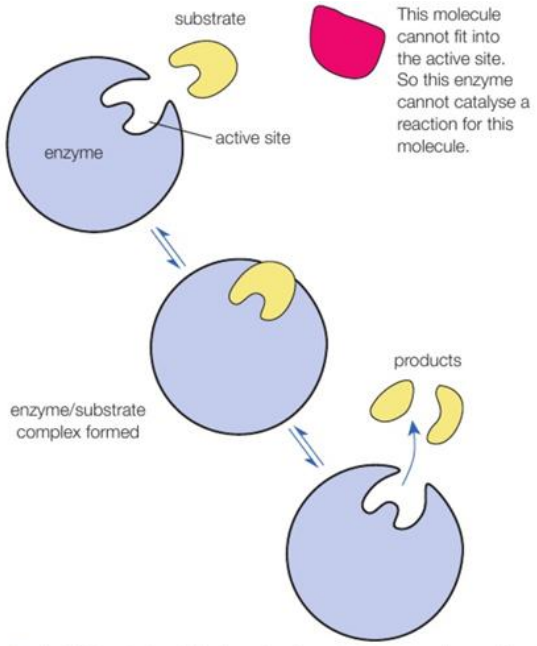
▲ **fig A** Energy diagram showing the difference between an uncatalysed and a catalysed reaction.

HOW DO ENZYMES WORK?

To lower the activation energy and catalyse a reaction, enzymes form a complex with the substrate or substrates of the reaction. A simple model of enzyme action in a catabolic reaction is:

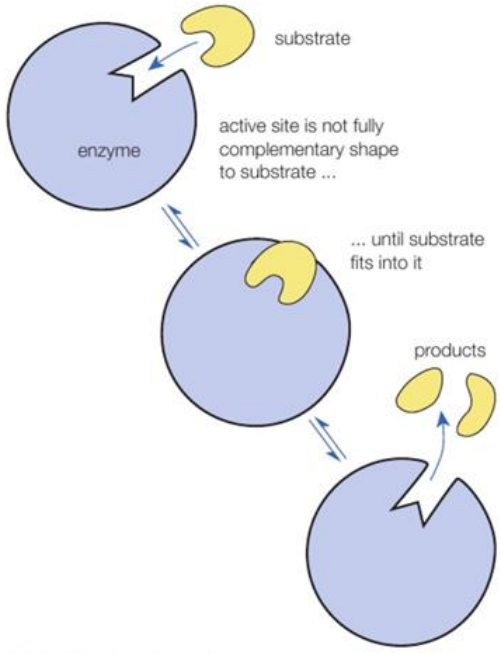
substrate + enzyme ⇆ enzyme–substrate complex
⇆ enzyme + products

The lock- and-key hypothesis gives us a simple model that helps us understand what happens (see fig B). Within the globular protein structure of each enzyme is an area known as the **active site** that has a very specific shape. Only one substrate or type of substrate will fit the shape of the active site, and it is this that gives each enzyme its specificity.



▲ **fig B** The lock-and-key hypothesis underpins our understanding of how enzymes work.

The **induced-fit hypothesis** is generally accepted as the best current model of enzyme action. In this, the active site still has a distinctive shape and arrangement, but it is a flexible one. After the substrate enters the active site, the shape of the site is modified around it to form the active complex. Once the products have left the complex, the enzyme returns to its inactive, relaxed form until another substrate molecule binds (see fig C).



▲ **fig C** The induced-fit theory of enzyme action proposes that the catalytic groups of the active site are not brought into their most active positions until a substrate is bound to the site, inducing a change in shape.

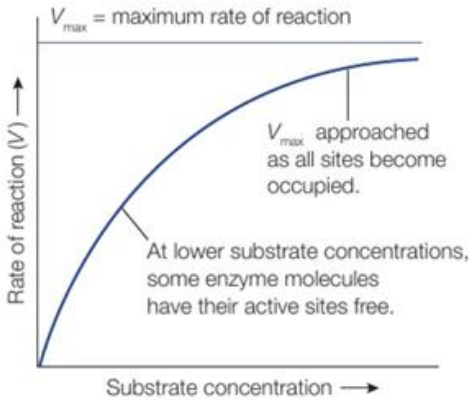
WHAT DO WE KNOW ABOUT ENZYMES?

Enzymes are globular proteins with an active site that is crucial for their function. The shape of the protein molecule affects its ability to function, indicating the importance of the three-dimensional nature of the molecule. Enzymes only change the rate of a reaction, act as catalysts, and do not affect the equilibrium of the reaction.

EVIDENCE FOR THE RELATIONSHIP BETWEEN THE STRUCTURE AND FUNCTIONS OF ENZYMES

Enzymes speed up reactions so much that only very small amounts of them are needed to catalyse the reaction of many substrate molecules into products. This is described by the **molecular activity** or **turnover number** of an enzyme, which measures the number of substrate molecules transformed per minute by a single enzyme molecule.

The number of substrate molecules present (the concentration of the substrate) affects the rate of an enzyme-catalysed reaction. Take a simple reaction where substrate A is converted to product Z. If the concentration of A increases, the rate of the enzyme- catalysed reaction A→ Z increases - but only for a limited period. Then the enzyme becomes saturated - all of the active sites are occupied by substrate molecules - and a further increase in substrate concentration will not increase the rate of the reaction further (see fig D). At this point, only an increase in enzyme concentration will increase the rate of the reaction.



▲ **fig D** The effect of substrate concentration on an enzyme-catalysed reaction, showing how the enzyme becomes saturated with substrate molecules.

Temperature affects the rate of an enzyme-catalysed reaction in a characteristic way (see fig E). Temperature affects all reactions because the number of successful collisions leading to a reaction increases at higher temperatures. The effect of temperature on the rate of any reaction can be expressed as the temperature coefficient, Q_{10}. This is expressed as:

$$Q_{10} = \frac{\text{rate of reaction at } (x + 10)\,^{\circ}\text{C}}{\text{rate of reaction at } x\,^{\circ}\text{C}}$$

Enzymes, including most proteins, **denature** at temperatures over 40°C, causing the shape of the active site to change, resulting in a decrease in the rate of enzyme-catalyzed reactions in human beings. This leads to a loss of their ability to catalyze reactions.

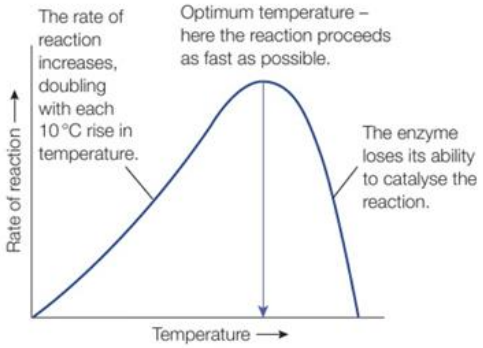


fig E The effect of temperature on the rate of a typical enzyme-catalysed reaction. All other factors must be kept constant.

pH also has a major effect on enzyme activity by affecting the shape of protein molecules. Different enzymes work in different ranges of pH (see **fig F**). This is because changes in pH affect the formation of the hydrogen bonds and disulfide bonds that hold the three-dimensional structure of the protein together. The optimum pH for an enzyme is not always the same as the pH of its normal surroundings. This seems to be one way in which cells control the effects of their intracellular enzymes, increasing or decreasing their activity by very small changes in the pH.

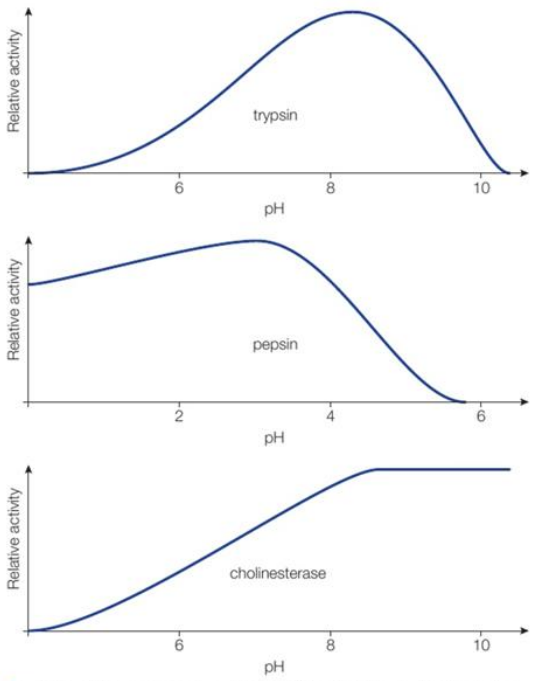


fig F Different enzymes work best at different pH levels. All other factors must be kept constant.

SUBJECT VOCABULARY

activation energy the energy needed for a chemical reaction to get started
substrate the molecule or molecules on which an enzyme acts
lock-and-key hypothesis a model that explains enzyme action by an active site in the protein structure that has a very specific shape; the enzyme and substrate slot together to form a complex in the same way as a key fits in a lock
active site the area of an enzyme that has a specific shape into which the substrate(s) of a reaction fit
induced-fit hypothesis a modified version of the lock-and-key model of enzyme action where the active site is considered to have a more flexible shape; after the substrate enters the active site, the shape of that site changes around it to form the active complex; after the products have left the complex, the enzyme returns to its inactive, relaxed form
molecular activity (turnover number) the number of substrate molecules transformed per minute by a single enzyme molecule
temperature coefficient (Q_{10}) the measure of the effect of temperature on the rate of a reaction
denaturation the loss of the three-dimensional shape of a protein (e.g. caused by changes in temperature or pH)
initial rate of reaction the measure taken to compare the rates of enzyme-controlled reactions under different conditions

2B 3 The structure of DNA and RNA

MONONUCLEOTIDES

Mononucleotides are key molecules in biology. They provide the energy currency of cells in the form of **adenosine triphosphate (ATP).** They also provide the building blocks for the mechanism of inheritance in the form of **deoxyribonucleic acid (DNA**) and **ribonucleic acid (RNA**).

Each nucleotide has three parts:

- a 5-carbon pentose sugar
- a nitrogen-containing base
- a phosphate group.

The pentose sugar in RNA is **ribose**, and in DNA is **deoxyribose**. Deoxyribose, as its name suggests, contains one fewer oxygen atom than ribose (see fig A).

The most common types of nucleotide have either a **purine base**, which has two nitrogen-containing rings, or a **pyrimidine base**, which has only one. The most common purines are **adenine** (A) and **guanine** (G) and the most common pyrimidines are **cytosine** (C), **thymine** (T) and **uracil** (U).

POLYNUCLEOTIDES

Nucleic acids, also known as **polynucleotides**, are the information molecules of the cell. They carry all the information needed to make new cells. They are polymers, consisting of many mononucleotide monomer units. The chromosomes in the nucleus of eukaryotic cells like our own store the genetic information; but in prokaryotes (e.g. bacteria), the DNA is found floating freely in the cytoplasm of the cells.

BUILDING THE POLYNUCLEOTIDES

Nucleic acids are chains of nucleotides linked together by condensation reactions that produce **phosphodiester bonds** between the sugar on one nucleotide and the phosphate group of the next nucleotide (see fig B). These nucleic acids can be millions of nucleotide units long. Both DNA and RNA have this sugar-phosphate backbone.

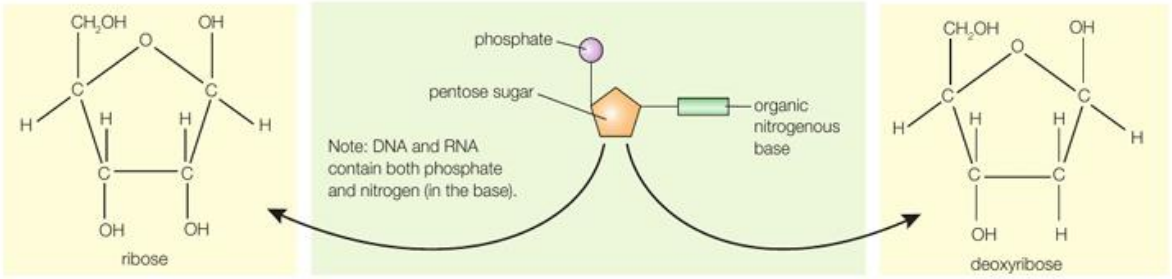


fig A The structure of a mononucleotide. The properties of mononucleotide molecules are crucial to the roles of ATP, DNA and RNA.

RNA molecules form single polynucleotide strands. These can either fold into complex shapes, held in place by hydrogen bonds, or remain as long thread-like molecules. DNA molecules consist of two polynucleotide strands twisted around each other. The sugars and phosphates form the backbone of the molecule and, pointing inwards from the two sugar-phosphate backbones, are the bases which make pairs in specific ways. A purine base always pairs with a pyrimidine base. In DNA, adenine pairs with thymine, and cytosine pairs with guanine. This results in the famous DNA double helix, a massive molecule that is the same shape as a spiral staircase (see fig C).

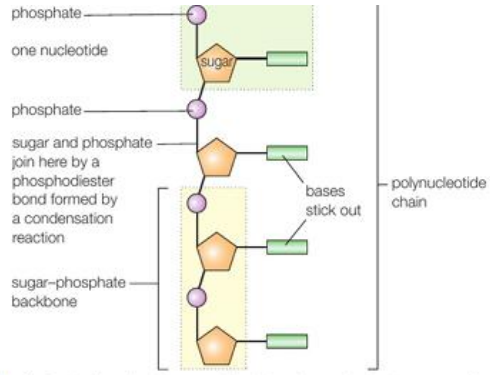


fig B A polynucleotide strand like this makes up the basic structure of both DNA and RNA.

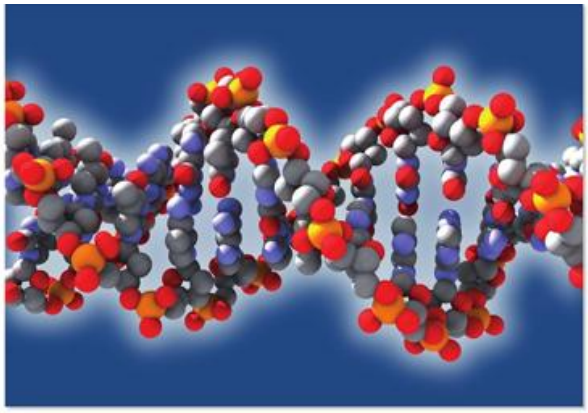


fig C The double helix structure of a DNA molecule is not just an iconic image of science – it is vital to the role of DNA in cells.

The two strands of the DNA double helix are held together by hydrogen bonds between the **complementary base pairs** (see fig D). These hydrogen bonds form between the amino and the carbonyl groups of the purine and pyrimidine bases on the opposite strands. There are three hydrogen bonds between C and G but only two between A and T. There are 10 base pairs for each complete twist of the helix.

SUBJECT VOCABULARY

mononucleotides molecules with three parts – a 5-carbon pentose sugar, a nitrogen-containing base and a phosphate group – joined by condensation reactions
adenosine triphosphate (ATP) a molecule that acts as the universal energy supply molecule in cells; it is made up of the base adenine, the pentose sugar ribose and three phosphate groups
deoxyribonucleic acid (DNA) a nucleic acid that is the genetic material in many organisms
ribonucleic acid (RNA) a nucleic acid which is the genetic material in some organisms and is involved in protein synthesis
ribose a pentose sugar that is part of the structure of RNA
deoxyribose a pentose sugar that is part of the structure of DNA
purine base a base found in nucleotides that has two nitrogen-containing rings
pyrimidine base a base found in nucleotides that has one nitrogen-containing ring
adenine a purine base found in DNA and RNA
guanine a purine base found in DNA and RNA
cytosine a pyrimidine base found in DNA and RNA
thymine a pyrimidine base found in DNA
uracil a pyrimidine base found in RNA
nucleic acids/polynucleotides polymers made up of many nucleotide monomer units that carry all the information needed to form new cells
phosphodiester bond bond formed between the phosphate group of one nucleotide and the sugar of the next nucleotide in a condensation reaction
complementary base pairs complementary purine and pyrimidine bases which align in a DNA helix, with hydrogen bonds holding them together (C–G, A–T)
genome the entire genetic material of an organism

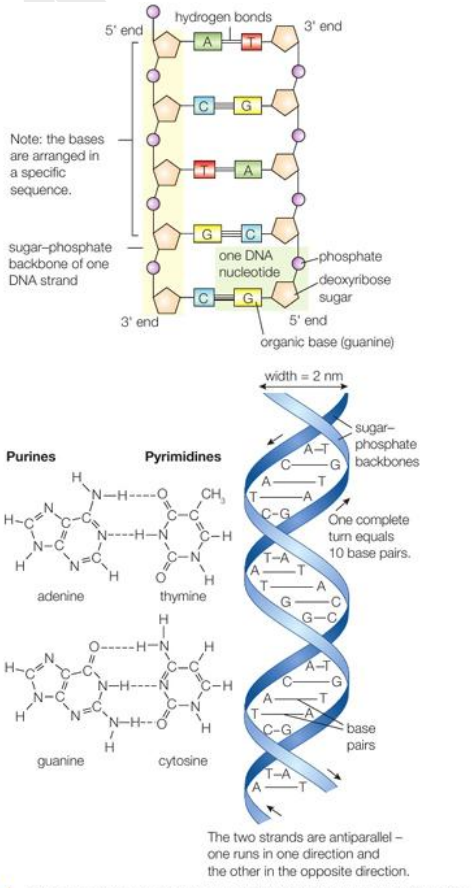


fig D The double helix structure of DNA depends on the hydrogen bonds that form between the base pairs.

2B 4 How DNA works

UNCOVERING THE MECHANISM OF REPLICATION

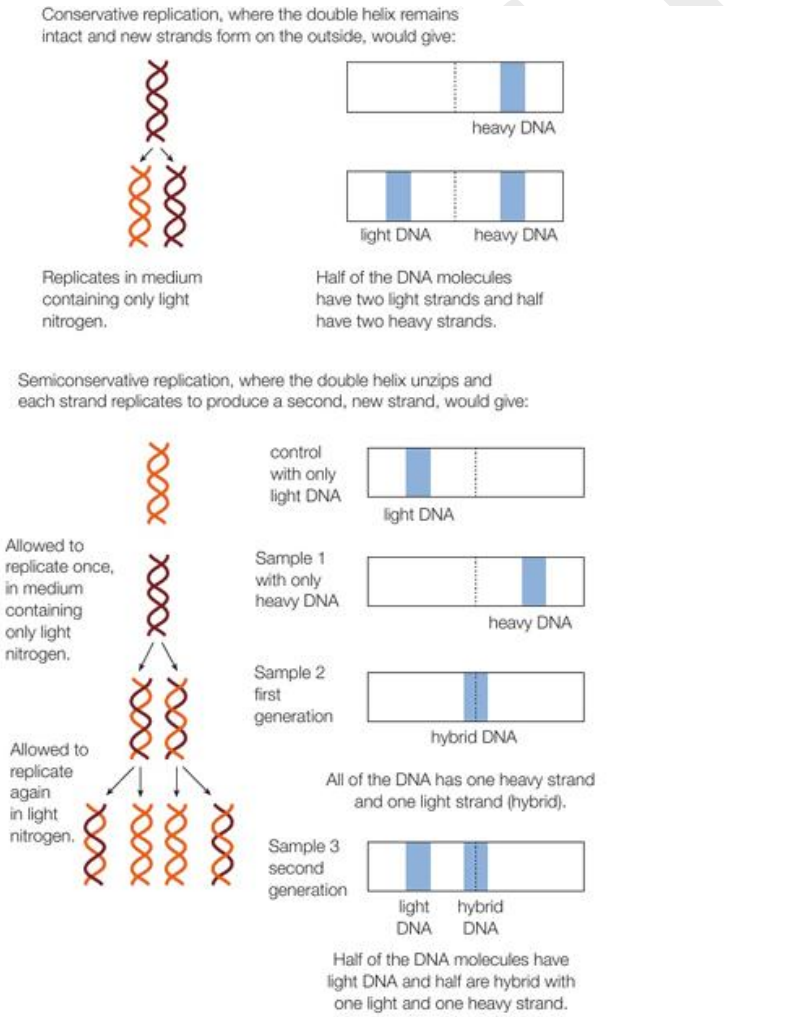
After Watson and Crick had produced their double helix model for the structure of DNA, it took scientists some years to work out exactly how the molecule replicates itself.

There were two main ideas about how replication happens: **conservative replication** and **semiconservative replication**. In the conservative replication model, the original double helix remained intact and in some way instructed the formation of a new, identical double helix, made up entirely of new material.

EXPERIMENTAL EVIDENCE

Matthew Meselson (1930-) and Franklin Stahl (1929-) carried out an elegant set of experiments in the late 1950s at the California Institute of Technology, USA. These led to semiconservative replication becoming the accepted model of DNA replication.

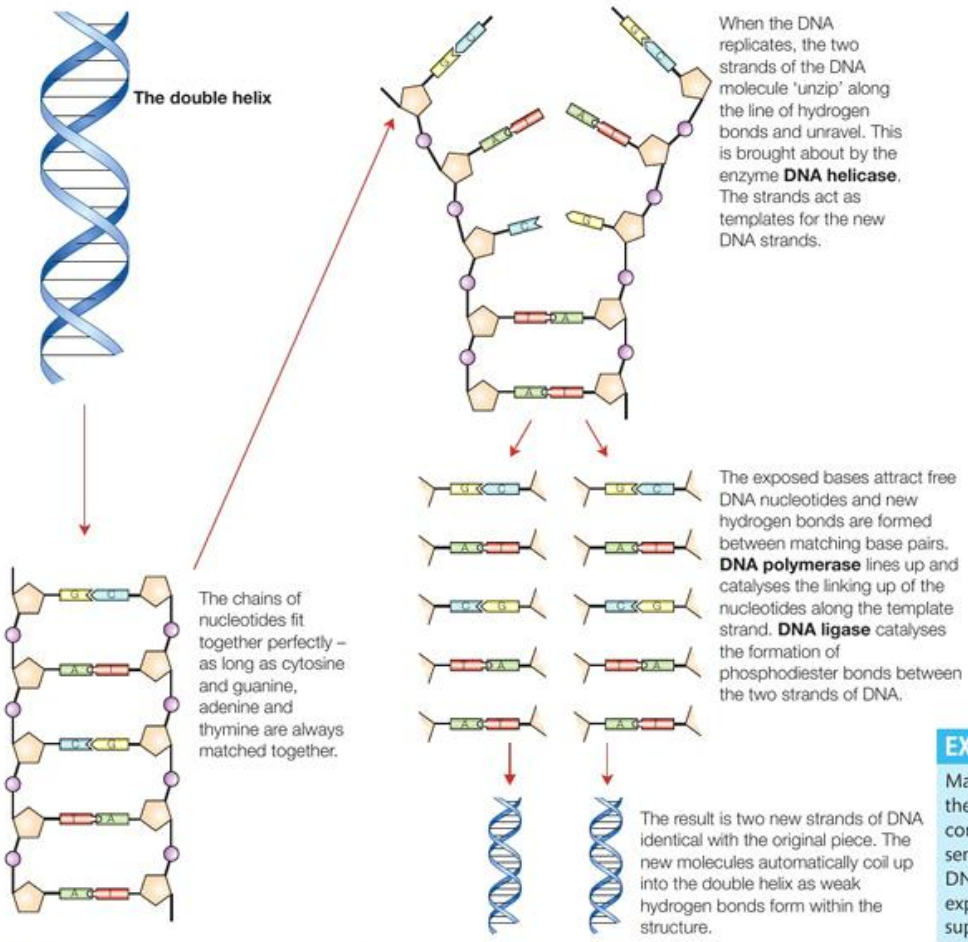
They grew several generations of the gut bacteria Escherichia coli (E. coli) in a medium where their only source of nitrogen was the radioactive **isotope** ^{15}N from $^{15}NH_4Cl$.



▲ **fig A** The results of these experiments by Meselson and Stahl confirmed the model of semiconservative replication of DNA – and at the same time put an end to the theory of conservative replication.

HOW DNA MAKES COPIES OF ITSELF

A careful look at the process of the semiconservative replication of DNA shows clearly how important the structure and properties of the DNA molecule are to its role as the genetic material of the cell. The complete process depends on three enzymes. **DNA helicase** unzips the two strands of the DNA. **DNA polymerase** lines up the new nucleotides along the DNA template strands, and **DNA ligase** catalyses the formation of the phosphodiester bonds between the new nucleotides. This is shown in **fig B**.



▲ **fig B** The semiconservative replication of DNA

EXAM HINT

Make sure you are clear about the difference between conservative and semiconservative models of DNA replication and can explain how the evidence supports the second model.

SUBJECT VOCABULARY

conservative replication a model of DNA replication which suggests that the original double helix remains intact and in some way instructs the formation of a new, identical double helix made up entirely of new material
semiconservative replication the accepted model of DNA replication in which the DNA 'unzips' and new nucleotides align along each strand; each new double helix contains one strand of the original DNA and one strand made up of new material
isotopes different atoms of the same element, with the same number of protons but a different number of neutrons; isotopes have the same chemical properties
DNA helicase an enzyme involved in DNA replication that 'unzips' the two strands of the DNA molecules
DNA polymerase an enzyme involved in DNA replication that lines up the new nucleotides along the DNA template strands
DNA ligase an enzyme involved in DNA replication that catalyses the formation of phosphodiester bonds between the nucleotides

2B 5 The genetic code

Proteins are made up of amino acids. Using the DNA code, the 20 naturally occurring amino acids are joined together in countless combinations to make an almost infinite variety of proteins. This process of **translation** happens on the surface of the **ribosomes** (see protein synthesis in Section 2B.6).

WHAT IS THE GENETIC CODE?

In the DNA double helix, the components that vary are the bases. So scientists guessed that it was the arrangement of the bases that carries the genetic code - but how? There are only four bases, so if one base coded for one amino acid there could be only four amino acids. Even a combination of two bases does not give enough amino acids - the possible arrangements of four bases into groups of two is 4 x 4 = 16. However, a **triplet code** of three bases gives 4 x 4 x 4 = 64 possible combinations - more than enough for the 20 amino acids that are coded for.

CRACKING THE CODE

The genetic code is based on genes. We can define a **gene** as a sequence of bases on a DNA molecule which codes for a sequence of amino acids in a polypeptide chain. This polypeptide affects a characteristic in the phenotype of the organism. By the early 1960s, it had been proved that a triplet code of bases was the cornerstone of the genetic code.

A sequence of three bases on the DNA or RNA is called a **codon**. The codons of the DNA are difficult to work out because the molecule is so large, so most of the work was done on the codons of the smaller molecule **messenger RNA** (**mRNA**). This mRNA is formed as a **complementary strand** to the DNA, so it is like a reverse image of the original base sequence. When we know the RNA sequence, we can work out the DNA sequence because of the way bases always pair: T and U with A, and G with C.

So, for example, the codon to start a polypeptide chain is TAC. This is also the codon for methionine - so the first amino acid in a polypeptide chain is always methionine. We now know that the genetic code is not only a triplet code, it is also a **non-overlapping code and degenerate code.**

A NON-OVERLAPPING CODE ...

After scientists had worked out that the genetic code was based on triplets of DNA bases, they wanted to find out how the code was read. Do the triplets of bases follow each other along the DNA strand like beads on a necklace, or do they overlap? For example, the mRNA sequence UUUAGC could code for two amino acids, phenylalanine (UUU) and serine (AGC). Alternatively, if the code overlaps, it could code for four: phenylalanine (UUU), leucine (UUA), a nonsense or stop codon (UAG) and serine (AGC).

Scientists rely on experimental observations to help decide whether the genetic code is overlapping or not. If a codon consists of three nucleotides and is completely overlapping, and a single nucleotide is altered by a **point mutation**, then three amino acids will be affected by that single change.

SUBJECT VOCABULARY

translation the process by which proteins are produced, via RNA, using the genetic code found in the DNA; it takes place on the ribosomes
ribosomes the site of protein synthesis in the cell
triplet code the code of three bases that is the basis of the genetic information in the DNA
gene a sequence of bases on a DNA molecule; it contains coding for a sequence of amino acids in a polypeptide chain that affects a characteristic in the phenotype of the organism
codon a sequence of three bases in DNA or mRNA
messenger RNA (mRNA) the RNA formed in the nucleus that carries the genetic code out into the cytoplasm
complementary strand the strand of RNA formed that complements the DNA acting as the coding strand
non-overlapping code a code where each codon codes for only one thing with no overlap between codons
degenerate code a code containing more information than is needed
point mutation a change in a single base of the DNA code

... AND A DEGENERATE CODE

When you look at the genetic code, it seems that the code is degenerate, also known as redundant. In other words, it contains more information than it needs. If you look carefully at **table B,** you will see that often only the first two of the three nucleotides in a codon seem to determine which amino acid results.

2B 6 DNA and protein synthesis

DIFFERENT TYPES OF RNA

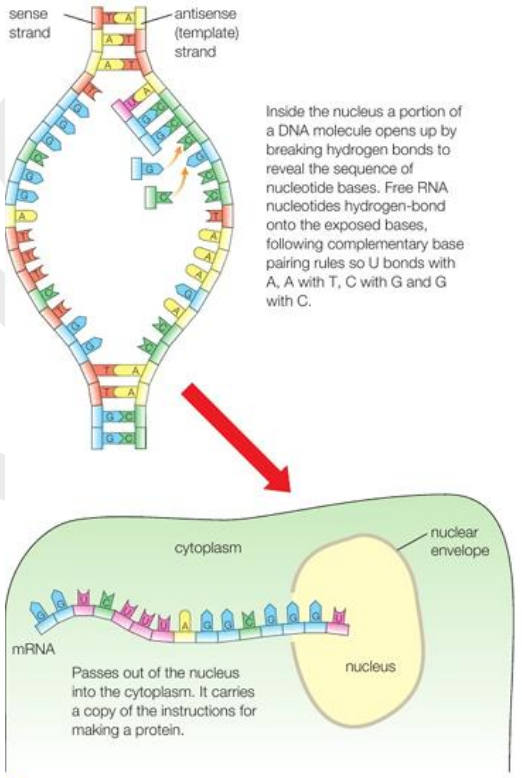
RNA is closely related to DNA (see Section 2B.4). However, it contains a different sugar (ribose) and a different base (uracil instead of thymine). It consists of a single helix and does not form enormous and complex molecules like DNA. The sequence of bases along a strand of RNA relates to the sequence of bases on a small part of the DNA in the nucleus. RNA enables DNA to act as the genetic material. It carries out three main functions in the process of protein synthesis:

- it carries the instructions for a polypeptide from the DNA in the nucleus to the ribosomes where proteins are made
- it picks up specific amino acids from the protoplasm and carries them to the surface of the ribosomes
- it makes up the bulk of the ribosomes themselves.

MESSENGER RNA

Messenger RNA (mRNA) is formed in the nucleus. A piece of mRNA usually has instructions for one polypeptide. This is different from the double helix of DNA which carries information about a vast array of proteins. The **sense strand** of the DNA strand carries the code for the protein to be formed, but the messenger RNA forms on the **antisense strand** of the DNA, also called the **template strand**.

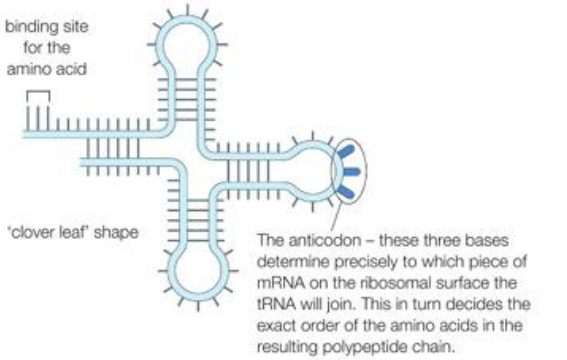
Part of the DNA unravels and unzips, exposing the bases which act as a template. Beginning at a **start codon**, which is also the code for methionine (see the codons in tables A and B, Section 2B.5), RNA nucleotides align along the exposed sequence of DNA bases in the normal complementary fashion. Then **RNA polymerase** joins the chain of RNA nucleotides together. The process ends when the chain reaches a **stop codon** and the mRNA chain separates from the DNA template, allowing the DNA chains of the double helix to re-join.



▲ **fig A** The transcription of the DNA message. Any mistakes in this process can have fatal consequences for the cell or even the whole organism if the wrong protein is made.

TRANSFER RNA

Transfer RNA (tRNA) is found in the cytoplasm. It has a complex shape that enables it to carry out its function (see fig B). This shape is the result of hydrogen bonding between different bases. One part of the tRNA molecule has a sequence of three bases that matches the genetic code of the DNA and corresponds to one specific amino acid. This sequence of three bases is called the **anticodon**.



▲ **fig B** There are 61 types of tRNA molecule available to carry all the necessary amino acids to the surface of the ribosomes ready for synthesis into protein molecules.

RIBOSOMES

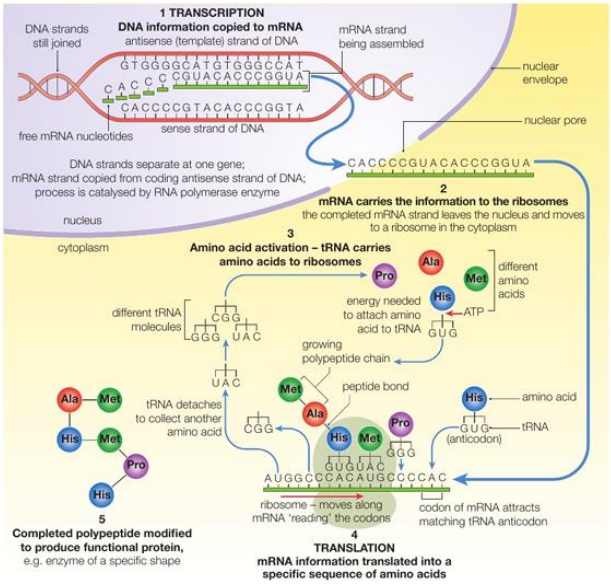
Ribosomes are made up of a combination of ribosomal RNA (rRNA) and proteins. They consist of a large and a small subunit. Ribosomes surround and bind to the parts of the mRNA that are being actively **translated**, and then move along to the next codon.

PROTEIN SYNTHESIS

In the process of protein synthesis, the genetic code of the DNA of the nucleus is **transcribed** onto messenger RNA. This mRNA moves out of the nucleus into the cytoplasm and becomes attached to a ribosome. Molecules of transfer RNA carry individual amino acids to the surface of the ribosome.

MASS PRODUCTION

The cytoplasm of cells contains many **polysomes**. These are groups of ribosomes joined by a thread of mRNA and they are used to mass-produce specific proteins. Ribosomes attach in a steady stream to the mRNA and move along one after the other producing lots of identical polypeptides.
This is how the genetic code carried on the DNA is translated into living material by the synthesis of proteins.



▲ **fig C** A simplified diagram to show how the information held in the DNA sequence in the nucleus is translated into a sequence of amino acids in a polypeptide chain. The mRNA strand always begins with the code for methionine and ends with a stop codon. Both the mRNA strand and the amino acid chain may be thousands of units long.

SUBJECT VOCABULARY

sense strand the DNA strand that carries the code for the protein to be produced
antisense strand (template strand) the DNA strand which acts as a template for an mRNA molecule
start codon the sequence of bases which indicates the start of an amino acid chain – TAC; this is the code for the amino acid methionine
RNA polymerase the enzyme that polymerises nucleotide units to form RNA in a sequence determined by the antisense strand of DNA
stop codon one of three sequences of bases which indicate the end of an amino acid chain
transfer RNA (tRNA) small units of RNA that pick up specific amino acids from the cytoplasm and transport them to the surface of the ribosome to align with the mRNA
anticodon a sequence of three bases on tRNA that are complementary to the bases in the mRNA codon
translation the process by which the DNA code is converted into a protein from the mRNA strand made in the nucleus
transcription the process by which the DNA sequence is used to make a strand of mRNA in the nucleus
polysomes groups of ribosomes, joined by a thread of mRNA, that can produce large quantities of a particular protein

2C Gene expression and genetics

2C 1 Gene mutation

The genetic code carried on the DNA is translated into living cellular material through protein synthesis. Consequently, the whole polypeptide chain and the final protein may be altered. A change like this is known as a mutation. A mutation is a permanent change in the DNA of an organism. A **mutation** can happen when the **gametes** (sex cells) form, although they also occur during the division of body cells.

DIFFERENT TYPES OF MUTATION

Some mutations occur when just one, or a small number of nucleotides, are miscopied during replication (see fig A). These are **point mutations or gene mutations**. If you think of the amino acids produced from the codons as similar to letters of the alphabet, the result of a **point mutation** is like changing a letter in one word. It may still make an acceptable word, but the meaning will probably be different. These gene mutations include the following types:

- substitution, where one base substitutes for another
- deletion, where a base is completely lost from the sequence
- insertion, when an extra base is added, which may be a repetition of one of the bases already there or a different base entirely.

You can see examples of these different types of mutation in fig A.

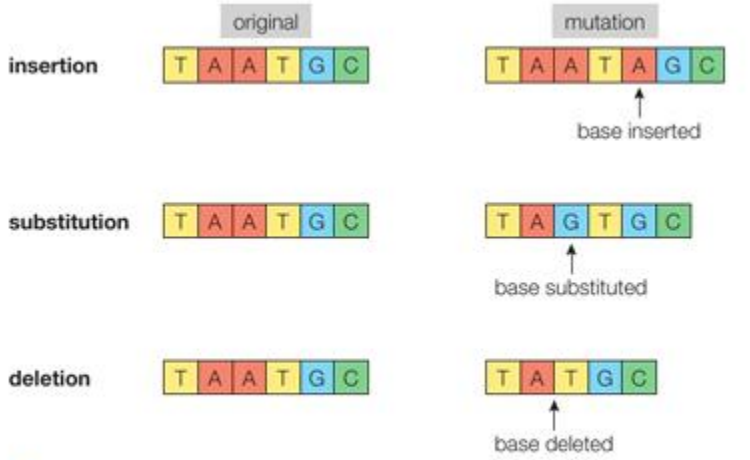


fig A Three of the most common types of point mutation in a chromosome

Chromosomal mutations involve changes in the positions of whole genes within the chromosomes. Think of this as rearranging the words within a sentence - if you are lucky, the rearranged words will still make sense, but it will not mean the same as the original sentence. Finally, there are **whole-chromosome mutations**, where an entire chromosome is either lost during meiosis (cell division to form the sex cells) or duplicated in one cell by errors in the process.

HOW GENE MUTATIONS CAN AFFECT THE PHENOTYPE

Mutations can produce **variation** within an organism. If the different arrangements of nucleotides code for the same amino acid (see Section 2B.6), a point mutation will have no effect. Very occasionally, a mutation occurs that produces a new and superior protein. This may help the organism gain a reproductive advantage so that it leaves more offspring than other individuals of that species, particularly if environmental conditions change. Most mutations are neutral,

which means that they neither improve nor worsen the chances of survival. Some mutations cause much damage, disrupting the biochemistry of the whole organism. If a harmful mutation is in a protein that is important to the function of a cell - for example, the active site of an enzyme - the effect can be catastrophic (see fig B on p130). Random mutations in the genetic material of the gametes are the cause of many human genetic diseases. Examples include:

- thalassaemia, in which the blood proteins are not manufactured correctly
- cystic fibrosis, in which a membrane protein does not function properly (see Section 2C.4). Mutations in the somatic cells of the body as they divide result in many different types of cancer, depending on where in the body they occur.

However, most mutations will have no observable effects on the organism. This may be because:

- the mutations occur in part of the non-coding DNA which does not affect the way the genetic code is read
- the code is degenerate (see Section 2B.5), and one small change in the code may not alter the amino acid coded for.

SICKLE CELL DISEASE: WHEN THE CODE GOES WRONG

Sickle cell disease is a genetic disease that affects the protein chains of the haemoglobin in the red blood cells. It is the result of a point mutation. A change of one base in one codon changes a single amino acid in a chain of 147 amino acids - but that change alters the nature of the protein (see table A).

SEQUENCE FOR HEALTHY HAEMOGLOBIN								
ATG	GTG	CAC	CTG	ACT	CCT	GAG	GAG	TCT
Start	Val	His	Leu	Thr	Pro	Glu	Glu	Ser
SEQUENCE FOR SICKLE CELL HAEMOGLOBIN								
ATG	GTG	CAC	CTG	ACT	CCT	GTG	GAG	TCT
Start	Val	His	Leu	Thr	Pro	Val	Glu	Ser

table A This table shows the change in the single codon that causes sickle cell disease (only the first nine codons are shown). This shows the 'sense' or 'coding' strand sequence.

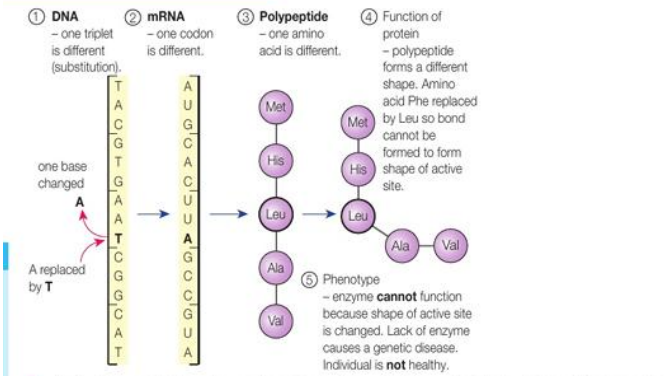


fig B This example shows how a change in a single nucleotide can affect the structure and function of the protein formed.

The most damaging mutations occur in the gametes because they will be passed on to future offspring. These are the mutations that lead to genetic diseases. X-rays, ionising radiation and certain chemicals are called **mutagens** because exposure to them increases the rate at which mutations occur. It is best to avoid exposure to mutagens whenever possible.

SUBJECT VOCABULARY

mutation a permanent change in the DNA of an organism
gametes haploid sex cells that fuse to form a new diploid cell (zygote) in sexual reproduction
point mutation (gene mutation) a change in a single base of the DNA code
substitution a type of point mutation in which one base in a gene is substituted for another
deletion a type of point mutation in which a base is completely lost
insertion a type of point mutation in which an extra base is added into a gene, which may be a repeat or a different base
chromosomal mutations changes in the position of entire genes within a chromosome
whole-chromosome mutations the loss or duplication of a whole chromosome
variation differences between organisms which may be the result of different genes or the environment they live in
mutagen anything that increases the rate of mutation

2C 2 Patterns of inheritance

GENETICS: THE BASIS OF INHERITANCE

The physical and chemical characteristics that make up the appearance of an organism are known as its **phenotype**. Examples include the size of an olive, the colour of a flower, the shape of a nose. The phenotype is partly the result of the **genotype** (the combination of alleles) passed from parents to their offspring and partly the effects of the environment in which the organism lives.
Differences in the genotype between individuals of a species are due to:

- rearrangement of genes during meiosis (see Section 3B.3)
- inheritance of genes from two different individuals in sexual reproduction.

Half the chromosomes are inherited from the female parent and the other half come from the male parent. The two sets can be arranged as matching pairs, called **homologous pairs.**

Along each chromosome are hundreds of genes. Each gene is a different segment of DNA coding for a particular protein or polypeptide. The chromosomes in a homologous pair carry the same genes - except for the sex chromosomes. The gene for any particular characteristic is always found in the same position or **locus**, which means that you usually carry two genes for each characteristic.

Each gene exists in slightly different versions called **alleles**. For example, at the locus for the gene for the height of a pea plant, the allele may code for a tall plant or for a dwarf plant.

If both alleles that code for a particular characteristic are identical, then the individual is homozygous for that characteristic - it is a **homozygote** ('homo' means 'the same'). If the two alleles coding for a characteristic are different, the individual is heterozygous for that characteristic and is called a **heterozygote** ('hetero' means 'different').
Some phenotypes are **dominant**: their effect is always expressed (shown) whether the individual is homozygous or heterozygous for the allele. If one allele for the dominant phenotype is present

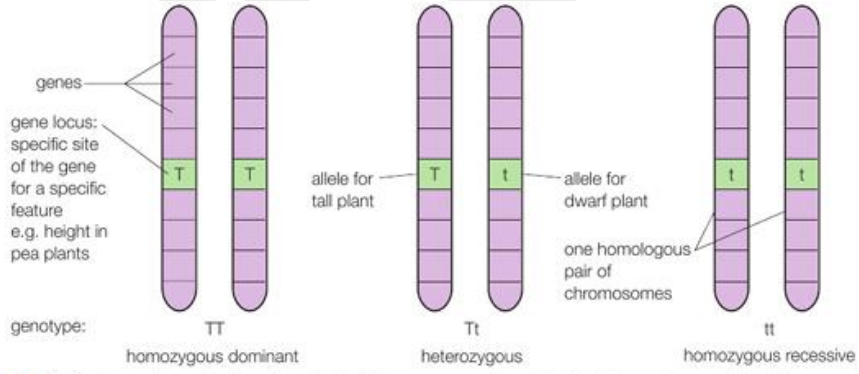


fig A In sexual reproduction, the variants of the genes passed on determine the genotype and, therefore, eventually an aspect of the phenotype of the offspring.

it will be expressed even if an allele for the **recessive** phenotype is there. Recessive phenotypes are only expressed when there are two alleles coding for the recessive feature, in other words, when the individual is homozygous recessive. In genetic diagrams, the alleles coding for dominant phenotypes are usually represented by a capital letter and those for recessive phenotypes by the lower-case version of the same letter.

MONOGENIC (MONOHYBRID) CROSSES

Homozygotes are referred to as **true breeding**, because if you cross two individuals that are homozygous for the same characteristic, all the offspring of all the generations that follow will show this same characteristic in their phenotype (unless a mutation occurs). Heterozygotes are not true breeding. If two heterozygotes are crossed, the offspring will include homozygous dominant, homozygous recessive and heterozygous types and at least two different phenotypes.

When genes are considered individually in a genetic cross, it is called a **monohybrid cross**. We can represent these crosses using simple diagrams called Punnett squares. A Punnett square shows you the potential alleles inherited from both parents, and the potential offspring that result. For example, **fig C** shows a cross between a pea plant homozygous for the dominant round pea seed shape and a pea plant homozygous for the recessive wrinkled pea (see **fig B**). The first generation of this cross is called the F_1 (first filial generation) and you can see that they all have the same genotype for the characteristic and they are heterozygous. They also all have the same phenotype – round pea shape because the round allele is dominant. There is no sign of the wrinkled pea allele. If we cross individuals from the F_1 generation we call the next generation the F_2 (second filial generation). In **fig C** you can see that theory predicts the ratio of the genotypes to be 1 homozygous dominant : 2 heterozygous dominant : 1 homozygous recessive. In terms of the phenotypes that would result from these genotypes, you would expect to see three round peas for every wrinkled one. The recessive trait of wrinkled peas has become visible again, after being 'hidden' in the F_1 generation.

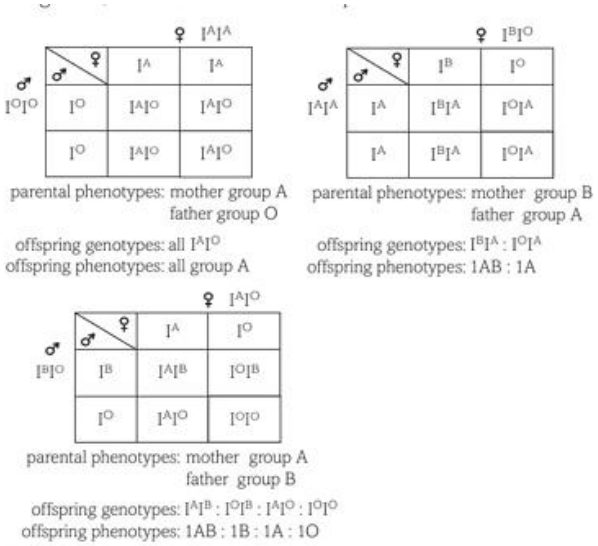
TEST CROSS

As you can see from fig C, individuals that are homozygous dominant or heterozygous have identical dominant phenotypes. For a plant or animal breeder this can cause many difficulties. A breeder often needs to know that the stock will breed true, in other words, that it is homozygous for the desired feature. If the feature is a recessive phenotype, then any plant showing the feature in the phenotype must be homozygous.

▲ **fig B** Round or wrinkled peas may not seem very exciting, but they show genetic characteristics that are easy to identify and have been studied since the earliest days of genetics.

CODOMINANCE

IA and IB are **codominant**. This means both alleles are expressed and produce their proteins, which act together without mixing. So an individual who inherits IA and IB (IAIB) will have both antigen A and antigen B on the surface of their erythrocytes and they will have the blood group AB. The A and B antigens will act in just the same way as if they were there individually - there is no blending in the phenotype. This is the key feature in codominance.



▲ **fig E** The genetics of the ABO blood group system

SAMPLING ERRORS

The theoretical ratios of phenotypes that are predicted by a genetic cross are usually seen (approximately) in real genetic experiments. However, the numbers are never precise. There are several reasons for this.

• Reproduction is a result of chance. The combination of alleles in each gamete is completely random and so is the joining of particular gametes. However, the theoretical diagrams that we draw do not show this.

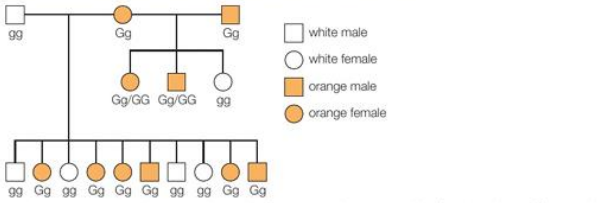
• Some offspring die before they can be sampled. For example, some seeds do not germinate and some embryos miscarry.

• Inefficient sampling techniques. For example, it is very easy to allow a few Drosophila to escape.

GENETIC PEDIGREE DIAGRAMS

Genetic diagrams, like Punnett squares, show how traits can be passed on and the likelihood of different offspring. Family trees or genetic pedigree diagrams provide insight into reality over time. They highlight carriers of recessive phenotypes, helping predict carriers of genetic mutations like thalassaemia and cystic fibrosis. These diagrams also help identify **sex-linked traits**, as family trees indicate males and females in the family.

Genetic pedigree diagrams are also widely used wherever people selectively breed animals. For example, pedigrees are extremely important in the breeding of thoroughbred racehorses, and in specific breeds of animals such as dogs, cats, cattle and sheep. They can also track mutations in rare animals such as white Bengal tigers. Normal tigers have black stripes on a golden orange coat. White tigers have black stripes on a white coat. This is the result of a mutation in a single gene. The white phenotype is recessive, so we know that any white tiger is homozygous recessive. You can see how a genetic pedigree works by looking at the family tree for a group of tigers shown in **fig H**.



▲ **fig H** This genetic pedigree shows you the results of two crosses between a golden female and two different male tigers. You can see the phenotypes of the cubs, and work out possible genotypes. The dominant allele for golden/orange coat is shown as **G**; the recessive allele for white coat is shown as **g**

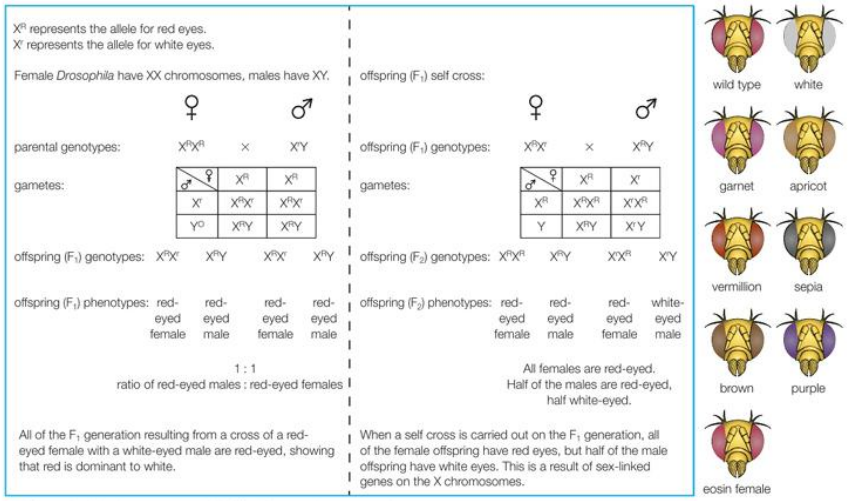
2C 3 Sex linkage

SEX DETERMINATION

The **autosomes** are all except one of the homologous pairs of chromosomes. They carry information about the general body cells and their biochemistry. The remaining pair of chromosomes are not a homologous pair. They are the X chromosome and the Y chromosome, known together as the sex chromosomes. They carry information about the sex of the individual. In mammals, the female has two large X chromosomes. Therefore, all of her eggs contain an X chromosome and she is **homogametic**. The male has one X chromosome and one much smaller Y chromosome. Half of his sperm will each contain an X chromosome and the other half will each contain a Y chromosome. Males are **heterogametic**.

SEX LINKAGE

Sex-linked genes on the X chromosome are passed down from a female parent to male offspring, with recessive or mutant alleles expressed in the phenotype. Sex linkage was first discovered in Drosophila by Thomas Morgan and is present in various organisms. Eye color in Drosophila is sex-linked, with red being the most common.



▲ **fig B** Sex-linked genes in *Drosophila* affect the eye colours seen in the insects.

SEX LINKAGE IN HUMANS

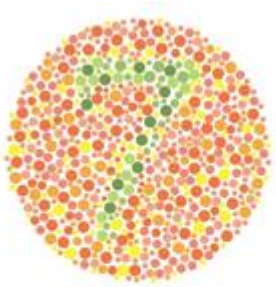
Human genetics work in the same way as the genetics of the peas and fruit flies that you have been studying. In people, as in most organisms, few characteristics are the result of single genes. Almost every aspect of your phenotype results from interactions between variants of multiple genes, together with **transcription factors and epigenetics.** Studying the inheritance of some single human genes can still be helpful, especially in understanding some of the more common inherited diseases that affect people around the world.

SUBJECT VOCABULARY

phenotype the physical traits, including biochemical characteristics, expressed as a result of the interactions of the genotype with the environment
genotype the genetic make-up of an organism with respect to a particular feature
homologous pairs matching pairs of chromosomes in an individual which both carry the same genes, although they may have different alleles
locus the site of a gene on a chromosome
alleles versions of a gene, variants
homozygote an individual where both alleles coding for a particular characteristic are identical
heterozygote an individual where the two alleles coding for a particular characteristic are different
dominant a characteristic which is expressed in the phenotype whether the individual is homozygous or heterozygous for that allele
recessive a characteristic which is only expressed when both alleles code for it; in other words, the individual is homozygous for the recessive trait
true breeding a homozygous organism which will always produce the same offspring when crossed with another true-breeding organism for the same characteristic
monohybrid cross a genetic cross where only one gene for one characteristic is considered
codominance in heterozygotes, where both alleles at a gene locus are fully expressed in the phenotype
sex-linked traits characteristics which are inherited on the sex chromosomes

SEX-LINKED DISEASES IN HUMANS

Sex-linked genes occur in humans just as they do in other organisms. A mother always donates an X chromosome to her sons. The father always donates the Y chromosome. Any mutations in a gene on the X chromosome will affect the phenotype of the offspring, even if the characteristic it codes for is recessive. This is because the Y chromosome is small and carries only genes which code for traits associated with maleness. It follows that sex linkage in humans leads to a variety of conditions known as **sex-linked diseases**. Some of these are relatively minor. Some are life-threatening or even fatal.

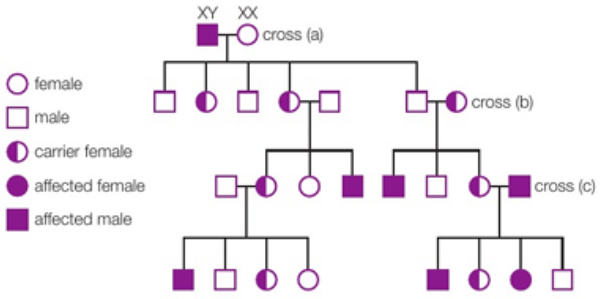


▲ **fig C** Tests like this can demonstrate colour blindness – if you have normal colour vision you will see a 7 in this image.

RED-GREEN COLOUR BLINDNESS

Many of these genes are found on the X chromosome. Mutations in these genes can affect our ability to see in colour, causing different types of colour blindness. **Red-green colour blindness** is the result of one of these mutations. People affected still see red and green colours, but can have difficulty seeing the difference between some tones of colour (see fig C).

Red–green colour blindness is usually an inconvenience but nothing more. It is caused by a recessive mutation of a gene on the X chromosome. It is much more common in men than in women because the condition is sex linked. However, colour blindness does occasionally occur in women (see **fig D**) because the gene does not markedly affect the chances of survival of an individual, and because the homozygous form is not lethal. In many populations, around 7–8% of males are affected by red–green colour blindness, but fewer than 1% of females. In the genetic pedigree in **fig D**, symptom-free carriers are shown as half-shaded circles.



X^C represents the allele for normal vision.
X^c represents the allele for colour blindness.

cross (a)

parental genotypes:	X^CY	×	X^CX^C
gametes:	X^C	X^C	
	X^c	X^CX^c	X^CX^c
	Y	X^CY	X^CY
offspring genotypes:	X^CX^c	X^CX^c	X^CY X^CY
offspring phenotypes:	carrier females		normal males

cross (b)

parental genotypes:	X^CY	×	X^CX^c	
gametes:	X^C	X^c		
	X^C	X^CX^C	X^CX^c	
	Y	X^CY	X^cY	
offspring genotypes:	X^CX^C	X^CX^c	X^CY	X^cY
offspring phenotypes:	normal female	carrier female	normal male	colour blind male

cross (c)

parental genotypes:	X^CX^c	×	X^cY	
gametes:	X^C	X^c		
	X^c	X^CX^c	X^cX^c	
	Y	X^CY	X^cY	
offspring genotypes:	X^CX^c	X^CY	X^cX^c	X^cY
offspring phenotypes:	carrier female	normal male	colour blind female	colour blind male

▲ **fig D** These genetic diagrams show how the colour blindness genes are transmitted through a family tree.

HAEMOPHILIA

Colour blindness is usually only an inconvenience. **Haemophilia** is a much more severe sex-linked trait in which one of the proteins needed for blood to clot is missing. The components of the blood- clotting process (see Section 1B.2) are coded for by multiple genes. Many of these genes are carried on the X chromosome, so problems with blood clotting are often sex-linked diseases. One of the most common and best understood forms of haemophilia is haemophilia A

(see fig E). This is a sex-linked condition in which clotting factor VIII is missing. It is also known as factor VIII deficiency. Globally, the condition affects between 1 in 4000 and 1 in 5000 live male births. The severity of the disease varies, but it can be fatal if not treated.

X^H represents the normal allele.
X^h represents the haemophiliac allele.

parental genotypes:	X^HX^h	×	X^HY	
gametes:	♂ \ ♀	X^H	X^h	
	X^H	X^HX^H	X^hX^H	
	Y	X^HY	X^hY	
offspring genotypes:	X^HX^H	X^HY	X^hX^H	X^hY
offspring phenotypes:	normal female	normal male	carrier female	haemophiliac male

▲ **fig E** It only takes one recessive allele for haemophilia to affect a family with this sex-linked disease.

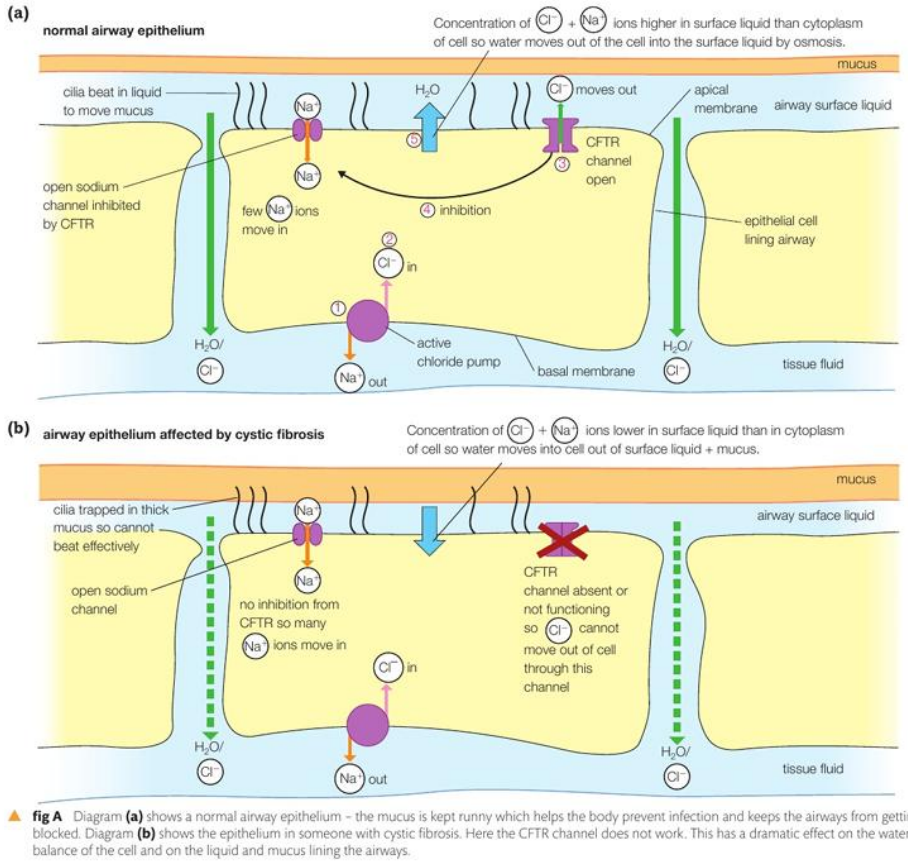
SUBJECT VOCABULARY

autosomes chromosomes which carry information about the body but do not determine the sex of an individual
homogametic an individual who produces gametes that contain only one type of sex chromosome – in humans this is the female
heterogametic an individual who produces two types of gamete each containing different types of sex chromosome – in humans this is the male
transcription factors proteins that bind to the DNA in the nucleus and affect the process of converting, or transcribing, DNA into RNA
epigenetics the study of changes in gene expression (active versus inactive genes) that does not involve changes to the underlying DNA sequence but affects how cells read genes
sex-linked diseases genetic diseases that result from a mutated gene carried on the sex chromosomes – in human beings, on the X chromosome
red–green colour blindness a sex-linked genetic condition which affects the ability to distinguish tones of red and green
haemophilia a sex-linked genetic disease in which one of the factors needed for blood to clot is not made in the body

2C 4 Cystic fibrosis: A genetic disease

CYSTIC FIBROSIS

Cystic fibrosis (CF) is a serious genetic disease which affects people all over the world. It is a life-threatening condition that causes severe respiratory and digestive problems as well as very salty sweat. It also often causes infertility. The chloride transport systems of the **exocrine glands** don't function properly leading to production of a thick sticky mucus.



▲ **fig A** Diagram **(a)** shows a normal airway epithelium – the mucus is kept runny which helps the body prevent infection and keeps the airways from getting blocked. Diagram **(b)** shows the epithelium in someone with cystic fibrosis. Here the CFTR channel does not work. This has a dramatic effect on the water balance of the cell and on the liquid and mucus lining the airways.

THE INHERITANCE OF CYSTIC FIBROSIS

Cystic fibrosis is very common in Europe – for example, in the UK about 1 person in 25 carries a faulty CF allele – that's between 2 and 3 million people – and cystic fibrosis occurs in about 1 in 2500 babies born to white Europeans. It is much less common in other ethnic groups – for example in 2017, only 62 patients were diagnosed in the UAE outside of Dubai – but it occurs everywhere in the world and it is often under-diagnosed. Early diagnosis is vital to take advantage of the various treatments now available to affected children and adults. Cystic fibrosis is caused by a recessive allele, which means that many people carry the mutation without knowing it. These carriers are phenotypically normal and usually have no idea that they are carrying the cystic fibrosis mutation. It is only if two carriers have children together that the problems show (see **fig B**). Even then, because the allele is recessive, there is only a 1 in 4 chance that any child of these parents will develop cystic fibrosis.

SYMPTOMS OF CYSTIC FIBROSIS

If someone inherits two alleles for cystic fibrosis it will affect many body systems. This is because it affects the mucus that lines the tubes in these systems.

THE RESPIRATORY SYSTEM

The thick, sticky mucus which is typical of cystic fibrosis builds up in the tiny airways of the lungs and reduces the flow of air into the alveoli. It often obstructs the smaller bronchioles completely, preventing air flow in the bronchioles. The reduced airflow means there is a smaller concentration gradient between the air and the blood in the lungs which reduces gas exchange.

THE DIGESTIVE SYSTEM

The gut is badly affected in 85-90% of people with cystic fibrosis. Your digestive system makes enzymes that break down the large complex food molecules (carbohydrates, proteins and fats) into smaller molecules. These can then be absorbed into your blood through the lining of your small intestine, which is covered in finger-like projections called **villi**.

The enzymes from the pancreas are very important in the breakdown of carbohydrates, proteins and fats in the top part of your small intestine (the **duodenum**).

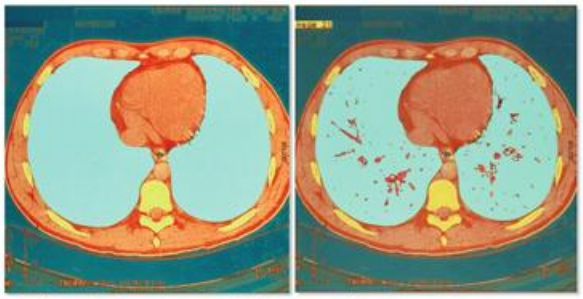


fig D The lung tissue on the left is clear and healthy. The lung tissue on the right shows blocked, damaged, mucus-filled airways from someone affected by cystic fibrosis.

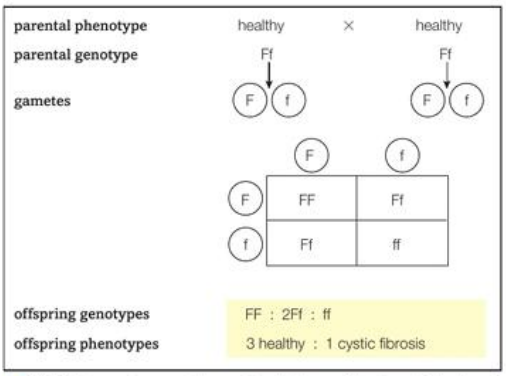


fig B Two carrier parents have a 1 in 4 chance of having a child who will have cystic fibrosis.

Once the disease has appeared in a family, other family members become aware they may carry the faulty allele (see **fig C**). They will often be offered genetic counselling before they have children.

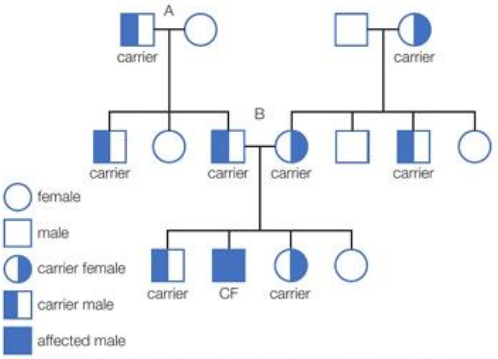


fig C This genetic pedigree shows how the faulty cystic fibrosis allele can be passed on through families for generations until, by chance, two carriers have an affected child.

The enzyme passes from the pancreas into your duodenum along a tube known as the **pancreatic duct**. Thin mucus is produced by the cells lining this tube in the same way that the airways of the lungs produce it. A faulty CFTR protein means that the mucus produced in the pancreatic duct is also very thick and sticky. It often blocks the pancreatic duct, so that the enzymes do not reach the duodenum. This has two damaging effects.

If the digestive enzymes do not reach your gut, you cannot digest your food properly. This means you do not get enough nutrients from the food. Also, the digestive enzymes trapped in the pancreas may start to digest and damage the cells of the pancreas.

If they affect the cells which make the hormone **insulin**, then the person may also develop diabetes. Not only does the thick mucus stop enzymes getting to the gut to digest food, it also makes it more difficult for any digested food to be absorbed into the blood.

THE REPRODUCTIVE SYSTEM

The thick, sticky mucus produced in cystic fibrosis can have a damaging effect on the reproductive system. In women, the mucus in the reproductive system normally changes through the menstrual cycle. When the woman is fertile it becomes thinner to help the sperm get through the cervix and along the oviducts. Women with cystic fibrosis usually produce fertile eggs, but the thick mucus can block the cervix so sperm cannot reach them. It can also block the oviducts, making fertilisation even less likely.

THE SWEAT GLANDS

The faulty CFTR protein means that people with cystic fibrosis usually have sweat that is more concentrated and salty than normal. Sweat is mainly salty water that is produced in your sweat glands. Normally, as the sweat passes along the duct of a sweat gland, salt (sodium chloride) is reabsorbed, largely as a result of the CFTR protein moving chloride ions into the cells.

SUBJECT VOCABULARY

cystic fibrosis (CF) a serious genetic disease caused by a recessive allele which affects the production of mucus by epithelial cells
exocrine glands glands which produce substances and secrete them to where they are needed through a small tube called a duct
villi finger-like projections of the lining of the duodenum and small intestine which increase the surface area for the absorption of digested food
duodenum the first part of the gut after the stomach
pancreatic duct the duct from the pancreas which carries digestive enzymes made in the pancreas into the duodenum
insulin a hormone made in the pancreas involved in the regulation of blood sugar levels

2C 5 Genetic screening

SCREENING BEFORE AND AFTER BIRTH

For some genetic diseases, whole populations are tested. This is known as **genetic screening**. Globally, about 7 in 100000 babies are born the genetic **condition phenylketonuria (PKU**).

▲ **fig A** This baby is being tested for PKU and other genetic diseases at University Hospital, Sharjah.

Genetic diseases like cystic fibrosis are currently uncurable, so early diagnosis is crucial for survival and overall health. Genetic screening can be done during pregnancy or on newborn babies to identify problems and provide the best treatment. PKU, a recessive autosomal disease, affects 7 in 100,000 babies globally. If left untreated, the baby's amino acid buildup can cause irreversible brain and nervous system damage. Early diagnosis can lead to a healthy diet and better survival.

IDENTIFYING CARRIERS

If one member of a family is born with a genetic disease such as PKU or cystic fibrosis, other members of the family will be offered genetic testing. For example, it is possible to detect the cystic fibrosis allele in a carrier who has no symptoms. A sample of blood, or some cells from the inside of the mouth, can be used to carry out a simple test to identify the allele.

PRENATAL SCREENING

Couples who find they are at risk of having children with a serious genetic condition have several options open to them. They can go ahead and have a family as usual, hoping that they are lucky and that their children inherit healthy genes.

The third option is to go ahead with pregnancies but to have screening during each pregnancy (**prenatal screening).**

Ideally, prenatal screening is used to try and discover if a fetus is affected by a serious condition early in the pregnancy. The information gained from prenatal screening is used differently in different countries. In some parts of the world it is used to prepare parents for the fact that their child has a genetic disorder which is not compatible with life, so their child will die before or at birth, or that the child has a serious genetic defect which will mean it has serious health problems.

Amniocentesis involves removing about 20 cm3 of the amniotic fluid which surrounds the fetus using a needle and syringe. This is done at about the 16th week of pregnancy. Fetal epithelial cells and blood cells can be recovered from the fluid after spinning it in a centrifuge. The cells are cultured for 2-3 weeks and then a number of genetic defects and the sex of the baby can be determined from examination of the chromosomes.
Amniocentesis has the following disadvantages.

- It can only be carried out relatively late in the pregnancy making it very difficult for the parents if termination of the pregnancy is necessary.
- The results are not available until 2-3 weeks after the test.
- It carries a 0.5-1% risk of spontaneous abortion after the procedure, regardless of the genetic status of the fetus.

In **chorionic villus sampling**, a small sample of embryonic tissue is taken from the developing placenta. This makes a much bigger sample of fetal tissue available for examination. The cells can be tested for a wide range of genetic abnormalities.

There are two disadvantages to chorionic villus sampling.

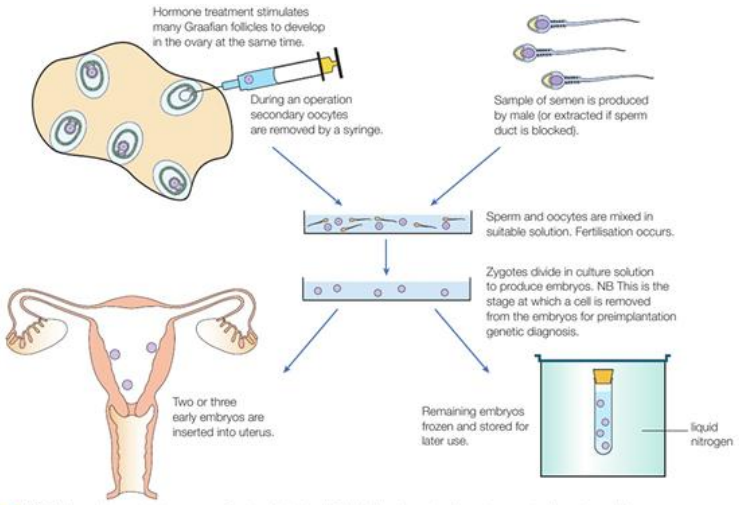
• There is a 0.5-1% risk that the embryo may spontaneously abort after the tissue sample is taken, though the risk of miscarriage at this stage of pregnancy is high anyway.

• All paternal X chromosomes are inactivated in fetal placental cells so any problems in the genes on that chromosome cannot be detected by this technique.

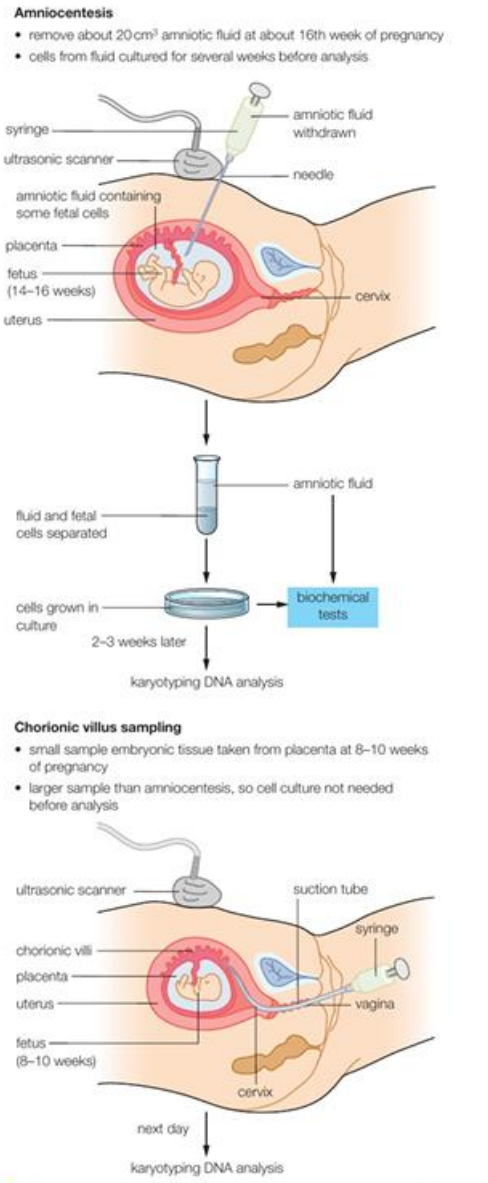
PREIMPLANTATION GENETIC DIAGNOSIS

Can parents who know they are carriers avoid having a child with cystic fibrosis without going through amniocentesis or chorionic villus sampling?

As a result of major developments in human infertility treatments over the last 30 years, sophisticated ways of genetically screening an early embryo before it is implanted in the uterus have been introduced. This technique, called **preimplantation genetic diagnosis**, is based on the technique of IVF (in vitro fertilisation) (see fig C). In this technique, the egg and sperm are fertilised outside the body.



▲ **fig C** The main steps in the process of *in vitro* fertilisation (IVF) which makes preimplantation genetic diagnosis possible.



▲ **fig B** Prenatal diagnostic techniques such as amniocentesis and chorionic villus sampling make an accurate diagnosis of serious genetic disorders possible before birth.

DIFFICULT DECISIONS

Genetic screening raises ethical issues due to personal beliefs and societal moral codes. Parents may reject screening due to religious beliefs, while others see scientific advances as beneficial. False positives and false negatives can occur, and tests like amniocentesis and chorionic villus sampling can cause miscarriages, highlighting the need for parents to weigh the potential consequences.

GENETIC COUNSELLING

For most people, finding out about genetic diseases in their family is very traumatic. All the issues discussed above - decisions concerned with having children or not, who to tell - are suddenly of immediate and personal relevance. Genetic counsellors are trained to help people to understand and come to terms with the situation of carrying a faulty allele that can cause a genetic disease.

SUBJECT VOCABULARY

genetic screening when whole populations are tested for a genetic disease
phenylketonuria (PKU) a recessive genetic disorder where those affected lack the enzyme needed to digest the amino acid phenylalanine; the amino acid builds up in the blood and causes severe brain damage
prenatal screening screening of an embryo or fetus before birth
amniocentesis a type of prenatal screening which involves removing a sample of amniotic fluid at around 16 weeks of pregnancy, culturing the fetal cells found and analysing them for genetic diseases
chorionic villus sampling a type of prenatal screening where a small sample of embryonic tissue is taken from the developing placenta and the cells tested for genetic diseases
preimplantation genetic diagnosis testing the cells of an embryo produced by IVF to check for genetic diseases before it is implanted into the uterus of the mother

Revision questions

Q1.

The cell membrane is important in the control of which substances can enter and leave the cell.

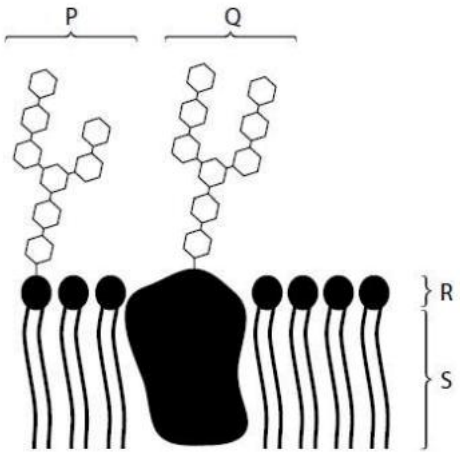
(a) The cell membrane consists of a phospholipid bilayer.

(i) Why do phospholipids form a bilayer?

(1)

- ☐ **A** the hydrophobic heads dissolve in the aqueous (water) environment
- ☐ **B** the hydrophobic heads move away from the aqueous (water) environment
- ☐ **C** the hydrophobic tails dissolve in the aqueous (water) environment
- ☐ **D** the hydrophobic tails move away from the aqueous (water) environment

(ii) This diagram shows part of a cell membrane.



Which letter represents a membrane glycoprotein?

(1)

- ☐ **A** P
- ☐ **B** Q
- ☐ **C** R
- ☐ **D** S

(b) State what is meant by the term **osmosis.**

(1)

(c) Compare and contrast exocytosis and endocytosis.

Q2.

The photographs show two mammals, an elephant and a mouse.

Magnification ×0.02

(a) The height of a mouse is 3 cm.

Calculate how many times taller an elephant is than a mouse.

Use the white line drawn on the photograph of the elephant to calculate this value.

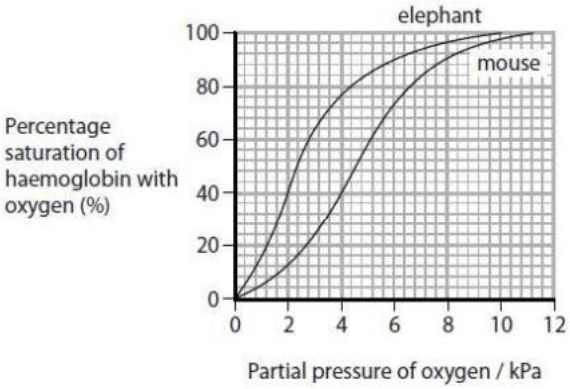
(b) The respiratory system of an elephant is different from that of other mammals.

The lungs are attached to the chest cavity wall and diaphragm by collagen fibres.

Describe how the lungs of an elephant are adapted for gas exchange.

* (c) Graph 1 shows the oxygen dissociation curve of haemoglobin for a mouse and for an elephant.

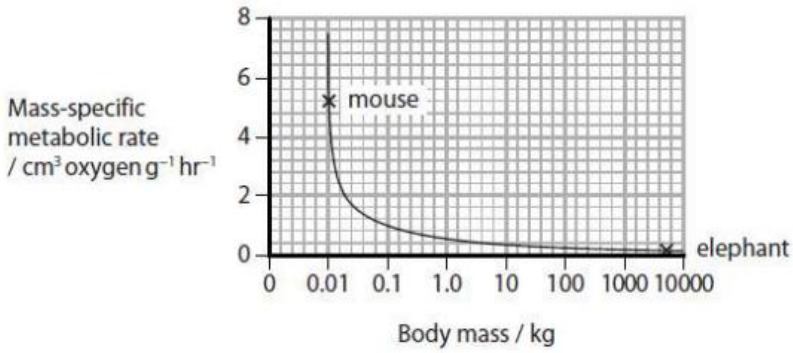
Graph 1



Graph 2 shows the mass-specific metabolic rate for a mouse and for an elephant.

Mass-specific metabolic rate is a measure of how much oxygen is needed for chemical reactions per gram of body tissue.

Graph 2



Explain the difference in the oxygen dissociation curves of haemoglobin for a mouse and for an elephant.

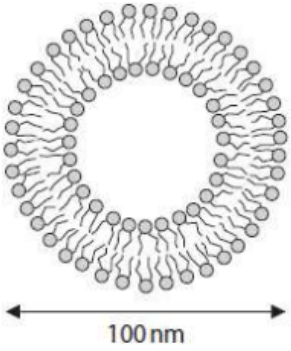
Use the information in both graphs to support your answer.

Q3.

Liposomes are spherical structures composed of phospholipids. They can be made by adding phospholipids to water.

Liposomes can be used to study membrane permeability.

(a) The diagram shows a liposome.



(i) Calculate the volume of this liposome, using the formula

$$V = \frac{4}{3}\pi r^3$$

(ii) Explain the arrangement of phospholipids in liposomes.

(b) The presence of cholesterol in the membrane affects membrane permeability.

A student investigated the effect of cholesterol on the permeability of liposomes to glycerol at different temperatures.

Liposomes were made by replacing 20% and 50% of the phospholipid with cholesterol.

Liposomes without cholesterol were also made.

The graph shows the results of this investigation.

(i) How does glycerol pass through the liposome membrane?

(1)

- ☐ **A** active transport
- ☐ **B** diffusion
- ☐ **C** endocytosis
- ☐ **D** osmosis

(ii) Describe the effects of cholesterol and temperature on membrane permeability, as shown in the graph.

(iii) Explain why cholesterol and temperature affect membrane permeability.

Q4.

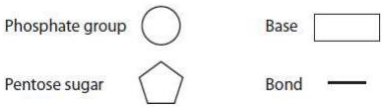
Nucleic acids include DNA and RNA.

(a) Each single strand of a DNA molecule is synthesised from mononucleotides.

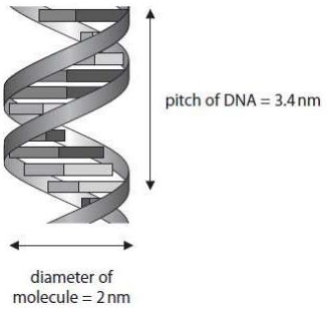
Draw a diagram to show two mononucleotides joined together in a single strand of DNA.

Use the symbols shown for each component in your diagram.

(3)



(b) The diagram represents part of a DNA molecule.



The pitch is the length of one complete turn in the double helix.
There are 10 base pairs in one pitch.

(i) Calculate the distance between one base and the next base on one strand of DNA.

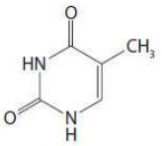
Give your answer to an appropriate number of significant figures.

(1)

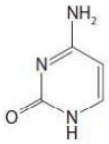
Answer ..... nm

(ii) The diagram shows the structure of thymine and four other bases, **P**, **Q**, **R** and **S**.

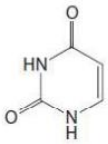
Bases **P** and **S** can form three hydrogen bonds each and bases **Q** and **R** can form two hydrogen bonds each.



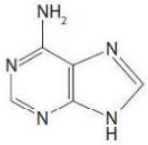
thymine



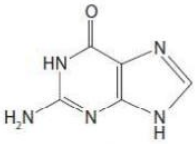
base **P**



base **Q**



base **R**



base **S**

Explain which of the four bases **P**, **Q**, **R** or **S** is adenine.

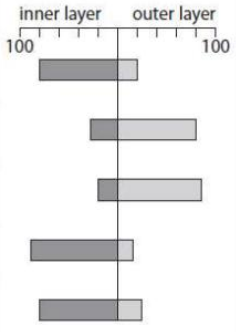
(2)

(c) Compare and contrast the structure of messenger RNA (mRNA) with the structure of transfer RNA (tRNA).

Q5.

Platelets are involved in the blood clotting process.

(a) The table shows the phospholipid content of the membranes of platelets.

Phospholipid	Percentage of total membrane phospholipids (%)	Percentage distribution of phospholipids in the membrane (%)
phosphatidylethanolamine	30	
phosphatidylcholine	27	
sphingomyelin	23	
phosphatidylserine	15	
other types	5	

When platelets trigger the blood clotting process, more phosphatidylserine molecules move into the outer layer of the membrane.

(i) Estimate the ratio of phosphatidylserine in the inner layer to that in the outer layer before the blood clotting process is triggered.

(1)

Answer .....

(ii) Describe the effect that the movement of phosphatidylserine into the outer layer will have on the content of phospholipids in the membranes of platelets.

Q7.

Red-green colour blindness is a common trait in humans.

(a) The gene for red-green colour blindness is located on the X chromosome.

State what is meant by the term **gene.**

(b) Describe how the two strands of DNA forming the double helix in a gene are held together.

(c) Explain why each codon for the DNA genetic code must contain at least three bases.

(d) A red-green colour blind father and an unaffected heterozygous mother had a child.

Determine the probability of this child being red-green colour blind.

Use a genetic diagram to support your answer.