Course Companion

# A-Level Biology

Every topic handout in one volume

全部专题讲义合集

exercises.lol

## Contents 目录

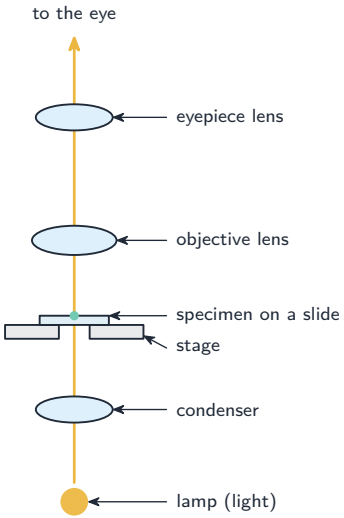

1. **Cell structure** ..... 3
2. **Biological molecules** ..... 14
3. **Enzymes** ..... 26
4. **Cell membranes and transport** ..... 38
5. **The mitotic cell cycle** ..... 51
6. **Nucleic acids and protein synthesis** ..... 59
7. **Transport in plants** ..... 71
8. **Transport in mammals** ..... 83
9. **Gas exchange** ..... 95
10. **Infectious diseases** ..... 103
11. **Immunity** ..... 111
12. **Energy and respiration** ..... 124
13. **Photosynthesis** ..... 136
14. **Homeostasis** ..... 146
15. **Control and coordination** ..... 161
16. **Inheritance** ..... 175
17. **Selection and evolution** ..... 187
18. **Classification, biodiversity and conservation** ..... 196
19. **Genetic technology** ..... 208

# Cell structure

A-Level Biology

## How we study cells

Cells 细胞 are very small, so you cannot see them with your eyes alone. You use a **microscope** 显微镜 to make a bigger picture of them. The first kind you meet is the **light microscope** 光学显微镜. It shines light through a thin **specimen** 标本 (the material you look at) and uses glass lenses to enlarge the view.

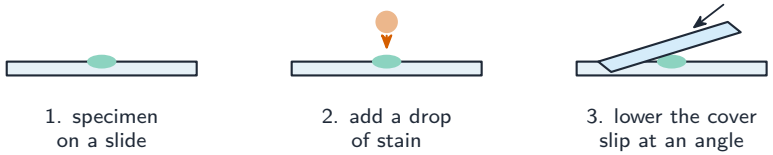



*A light microscope: light passes up through the specimen, then two lenses (the objective and the eyepiece) magnify it*

### Making a slide and drawing what you see

To look at living material, you make a **temporary preparation** 临时装片. You put a small, thin piece of material on a glass **slide** 载玻片, add a drop of **stain** 染色剂 (a coloured liquid that makes parts easier to see), then lower a thin **cover slip** 盖玻片 on top to flatten it and keep out air.






*Making a temporary wet mount – lower the cover slip at an angle so no air bubbles are trapped*

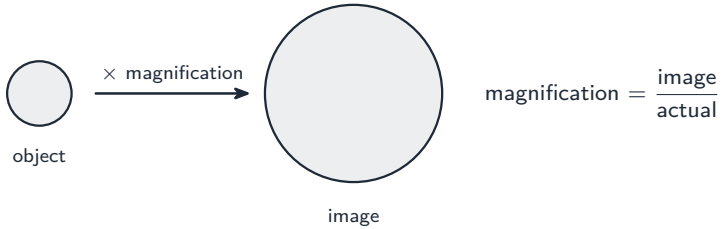
When you draw cells from a slide or a photograph, follow simple rules:

- use a sharp pencil and clear, single lines (no shading).
- draw only what you can really see, with the parts in the correct sizes.
- label the parts with straight lines that do not cross.

### Magnification and actual size

**Magnification** 放大倍数 tells you how many times bigger the image is than the real object. It has no unit. You find it with one equation:

$$\text{magnification} = \frac{\text{size of image}}{\text{actual size of object}}$$




*Magnification = image size ÷ actual size*

You can rearrange this to find any one value from the other two:

$$\text{actual size} = \frac{\text{size of image}}{\text{magnification}}$$

The top and the bottom of the fraction **must use the same unit**. Cells are tiny, so you work in small units:

- 1 mm = 1000 micrometre 微米 (µm)
- 1 µm = 1000 nanometre 纳米 (nm)
- so 1 mm = 1 000 000 nm.



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**Worked example.** In a photomicrograph at magnification 5000, a **chloroplast** 叶绿体 measures 25 mm across. Its actual size is

$$\frac{25\ \text{mm}}{5000} = 0.005\ \text{mm} = 5\ \mu\text{m}.$$

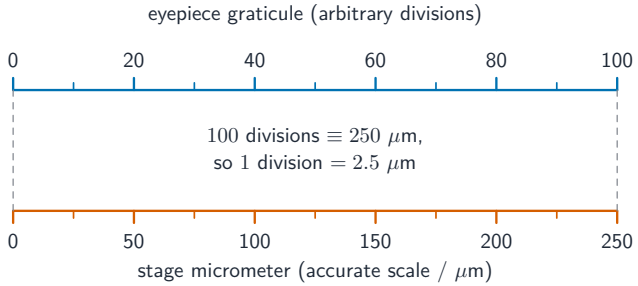
The same equation works for drawings, photomicrographs 显微照片 (photos taken through a light microscope) and **electron micrographs** 电子显微照片 (the most detailed photos, explained below). Always convert to the same unit first, then divide.

**Worked example (a scale bar).** An electron micrograph has a scale bar labelled 1 $\mu$m; the bar measures 20 mm with a ruler. Find the magnification, then the actual length of a mitochondrion that is 48 mm long in the image. Convert: 20 mm = 20 000 $\mu$m. Magnification = 20 000 ÷ 1 = ×20 000. Actual length = 48 000 $\mu$m ÷ 20 000 = 2.4 $\mu$m. Give a magnification to the same number of significant figures as the data, with a × sign and no unit.

## Eyepiece graticule and stage micrometer

To measure a real cell under the microscope, you use an **eyepiece graticule** 目镜测微尺 – a tiny scale inside the eyepiece. Its divisions have no fixed size, so first you must **calibrate** 校准 them (work out what one division is worth).

You calibrate using a **stage micrometer** 载物台测微尺 – a special slide with an accurate scale on it (often 1 mm split into 100 parts, so each part is 10 µm). You line up the two scales, count how many graticule divisions fit a known length, and divide. Once calibrated, you can swap in your specimen and measure it with the graticule.




*Calibrate the graticule by lining it up with the stage micrometer's known scale*



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**Worked example.** With the ×40 objective, 40 eyepiece units line up exactly with 10 divisions of a stage micrometer whose divisions are 10 $\mu$m each. (a) Find the value of one eyepiece unit. (b) A cell is 16 eyepiece units long. Find its actual length. (a) 10 divisions = 10 × 10 = 100 $\mu$m, so one eyepiece unit = 100 ÷ 40 = 2.5 $\mu$m. (b) 16 × 2.5 = 40 $\mu$m. With a different objective lens, the value of one eyepiece unit changes, so the graticule must be calibrated again. Measure several cells and find the mean.

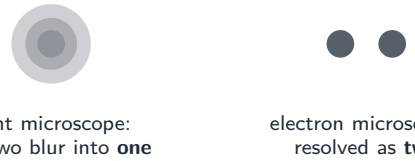
## Resolution and magnification

These two words are easy to mix up. The examiner gives marks for the difference.

- **Magnification** is how many times bigger the image is than the object.
- **Resolution** 分辨率 is the smallest distance between two points that still lets you see them as **two** separate points.

Making an image bigger does not always show more detail. Past a certain point you just get a bigger, blurry image. Resolution sets the real limit on detail.

A light microscope has lower resolution because light has a fairly long **wavelength** 波长. An **electron microscope** 电子显微镜 uses beams of **electrons** 电子 instead of light. Electrons have a much shorter wavelength, so the resolution is far higher and you can see very small structures inside the cell. There are two kinds: **scanning** 扫描 (shows the surface in 3D) and **transmission** 透射 (passes electrons through a thin slice to show inside detail).



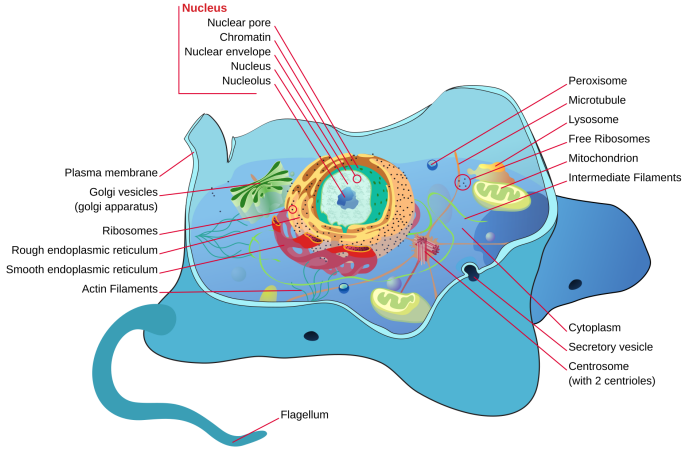

*Resolution: a light microscope blurs two very close points into one; an electron microscope, with its shorter wavelength, resolves them as two*

| | Light microscope | Transmission electron microscope (TEM) | Scanning electron microscope (SEM) |
|---|---|---|---|
| resolution | about 200 nm | about 0.5 nm | about 3–10 nm |
| useful magnification | up to about ×1500 | up to about ×500 000 | up to about ×100 000 |
| specimen | living or dead; thin and stained | dead; very thin slice, in a vacuum, stained with heavy metals | dead; whole surface coated with metal, in a vacuum |
| image | colour | black and white (false colour can be added) | 3D-looking image of the surface |

A light microscope can show the nucleus, chloroplasts and (just) mitochondria, but not ribosomes, the ER or the detail of membranes, which are smaller than 200 nm across. These **ultrastructure** 超微结构 details can be seen only with an electron microscope.

## Eukaryotic cells and their organelles

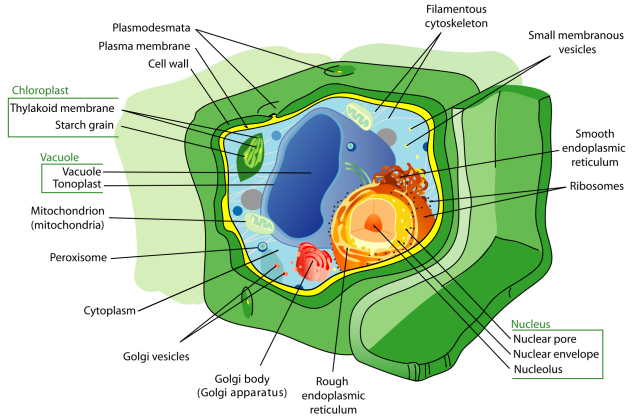
Plant and animal cells are **eukaryotic cells** 真核细胞: their DNA is kept inside a **nucleus** 细胞核. Inside the cell are many small parts called **organelles** 细胞器, each with its own job. The jelly-like fluid around them is the **cytoplasm** 细胞质.




*A generalised animal cell and its organelles*



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*A plant cell also has a cell wall, chloroplasts and a large vacuole*

In a photomicrograph or electron micrograph you identify organelles by their shape, size and position; in a drawing you show their outlines and label them.

| Organelle | Structure | Function |
|---|---|---|
| **cell surface membrane** 细胞膜 | thin layer around the cell | controls what enters and leaves the cell |
| nucleus | large, surrounded by a **nuclear envelope** 核膜 (a double membrane with holes); contains a **nucleolus** 核仁 | holds the DNA; controls the cell; the nucleolus makes ribosomes |
| **rough endoplasmic reticulum** 粗面内质网 (rough ER) | sheets of membrane with ribosomes on the surface | makes and transports **proteins** 蛋白质 (for example **antibodies** 抗体) |
| **smooth endoplasmic reticulum** 滑面内质网 (smooth ER) | sheets of membrane, no ribosomes | makes **lipids** 脂质 |

| Organelle | Structure | Function |
|---|---|---|
| **Golgi body** 高尔基体 | stack of flat membrane sacs | changes and packs proteins and lipids into **vesicles** 囊泡 for **secretion** 分泌 |
| **mitochondria** 线粒体 | oval, with a folded inner membrane; has small circular DNA | site of aerobic **respiration** 呼吸作用 – makes ATP, the cell's energy 能量 supply |
| **ribosomes** 核糖体 | very small; 80S in the cytoplasm, 70S in chloroplasts and mitochondria | join **amino acids** 氨基酸 to **synthesise** 合成 proteins |
| **lysosomes** 溶酶体 | small sacs of **enzymes** 酶 | break down old organelles and waste |
| **centrioles** 中心粒 and **microtubules** 微管 | small tubes made of protein | help move chromosomes and form the cell's "skeleton" |
| **cilia** 纤毛 | tiny hairs on the cell surface that beat | move fluid or move the cell |
| **microvilli** 微绒毛 | tiny folds of the cell surface membrane | increase surface area for **absorption** 吸收 |
| **chloroplasts** (plants) | green, with stacked membranes; has small circular DNA | site of **photosynthesis** 光合作用 |
| **cell wall** 细胞壁 (plants) | strong outer layer of **cellulose** 纤维素 | supports and protects the cell; stops it bursting |
| **plasmodesmata** 胞间连丝 (plants) | tiny channels through the cell walls | link the cytoplasm of neighbouring cells |
| large permanent **vacuole** 液泡 (plants) | big sac of watery fluid, with a membrane called the **tonoplast** 液泡膜 | stores water and keeps the cell firm |

Cells use **ATP** made in respiration as their energy supply for every job that needs energy, such as making proteins, moving things and dividing.

**How the organelles work together: making and secreting a protein.**

1. The gene for the protein is transcribed in the **nucleus**; the mRNA leaves through a nuclear pore.



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2. **Ribosomes** on the rough ER translate the mRNA, and the protein enters the space inside the **rough ER**, where it is folded.
3. The protein is carried in a **vesicle** that buds off the rough ER and fuses with the **Golgi body**.
4. In the Golgi body the protein is modified (for example, carbohydrate is added to make a glycoprotein) and packaged into new vesicles.
5. The vesicles move along **microtubules** to the cell surface membrane, fuse with it and release the protein outside the cell (**exocytosis**).
6. **Mitochondria** supply the ATP for protein synthesis and for moving the vesicles.

Cells that secrete a lot of protein, such as pancreas cells making digestive enzymes, have much rough ER, a large Golgi body and many mitochondria.

**Recognising organelles in an electron micrograph.** The nucleus is the largest structure, with a darker patch (the nucleolus) and a double membrane with pores. Mitochondria are oval, about 1–5 $\mu$m long, with folded inner membranes (cristae). Rough ER looks like parallel lines dotted with small black dots (ribosomes); smooth ER has no dots and is more tube-like. The Golgi body is a stack of curved, flattened sacs with small round vesicles at its edges. Chloroplasts are larger than mitochondria, with stacks of thylakoids (grana).

### ■ Comparing plant and animal cells

| Feature | Plant cell | Animal cell |
|---|---|---|
| cell wall | present (cellulose) | absent |
| chloroplasts | present | absent |
| large permanent vacuole | present | absent (only small, temporary ones) |
| centrioles | absent in most | present |
| shape | fixed and regular | rounder and more flexible |

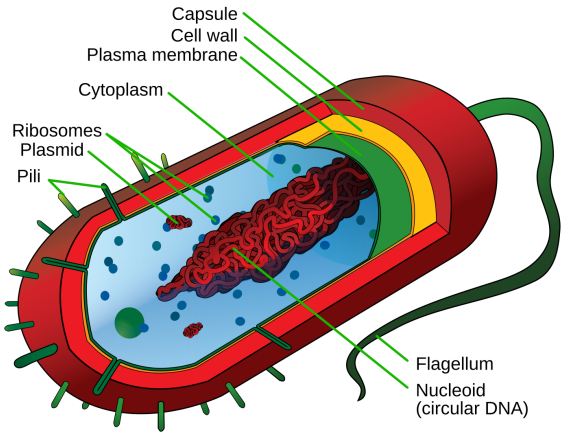
Both have a cell surface membrane, cytoplasm, a nucleus, mitochondria, ribosomes, ER and a Golgi body.

## Prokaryotic cells (bacteria)

A **prokaryotic cell** 原核细胞, such as a **bacterium** 细菌, is much smaller and simpler than a eukaryotic cell. Its key features are:

- **unicellular** 单细胞 – it is a single cell.
- generally 1–5 µm across.
- a cell wall made of **peptidoglycan** 肽聚糖 (not cellulose).
- circular DNA lying free in the cytoplasm – there is **no nucleus**.

- 70S ribosomes (smaller than the 80S ones in the cytoplasm of eukaryotes).
- **no organelles surrounded by a double membrane** – so no nucleus, no mitochondria and no chloroplasts.




*A prokaryotic cell: the circular DNA (nucleoid) lies free, with no nucleus and no double-membrane organelles*

### Comparing prokaryotic and eukaryotic cells

| Feature | Prokaryotic cell | Eukaryotic cell |
|---|---|---|
| size | about 1–5 µm | about 10–100 µm |
| DNA | circular, free in cytoplasm | linear, inside a nucleus |
| nucleus | none | present |
| double-membrane organelles | none | mitochondria (and chloroplasts in plants) |
| ribosomes | 70S | 80S (with 70S inside mitochondria and chloroplasts) |
| cell wall | peptidoglycan | cellulose (plants) or none (animals) |

## Viruses

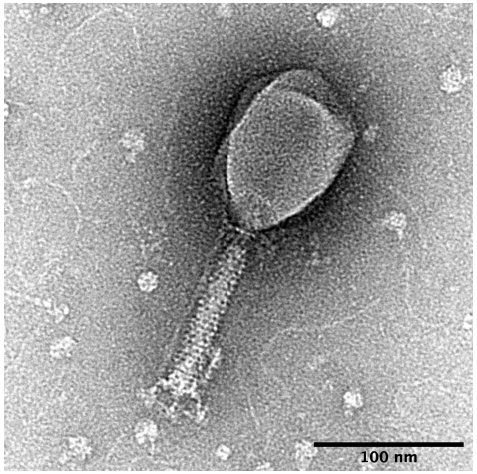
All **viruses** 病毒 are **non-cellular** 非细胞 – they are not made of cells at all. Each virus is built from just two or three parts:

- a core of **nucleic acid** 核酸, which is **either DNA or RNA** (never both).

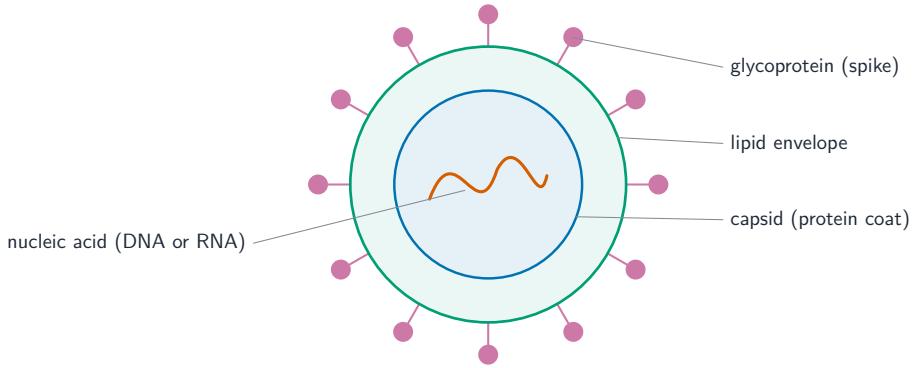


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- a protein coat around the core called a **capsid** 衣壳.
- in some viruses, an outer **envelope** 包膜 made of **phospholipids** 磷脂.




*A real virus, magnified hugely. The rounded head is the protein capsid wrapped around the nucleic acid core; the tail injects that nucleic acid into a bacterium. Note the scale bar – the whole virus is about 100 nm, far smaller than any cell*




*A generalised virus: nucleic acid inside a protein capsid, with a lipid envelope in some viruses*

A virus has no cytoplasm, no organelles and no ribosomes. It cannot respire or make its own proteins. It can only copy itself inside a living **host** 宿主 cell, so it sits at the edge of what we call "living".

**Common mistakes.**

- Saying a higher magnification always shows more detail. Detail is limited by **resolution**; magnifying past it gives a bigger, blurry image.
- Saying electron microscopes are better "because they magnify more". The key reason is that electrons have a **shorter wavelength**, so the **resolution** is higher.
- Measuring with an eyepiece graticule without calibrating it. Its divisions have no fixed size; calibrate against a **stage micrometer** at each objective lens, because the value changes with magnification.
- Saying ribosomes are organelles bounded by a membrane. Ribosomes have **no membrane**, which is why prokaryotes have them.
- Saying mitochondria "make energy". They release energy from respiration and use it to make **ATP**.
- Saying bacteria have a cellulose cell wall. A bacterial cell wall is made of **peptidoglycan**.
- Describing a virus with a cell membrane, cytoplasm or ribosomes. A virus is **not a cell**: only nucleic acid in a capsid, sometimes with an envelope.
- Giving a magnification with a unit. Magnification has **no unit**: write $\times 20\,000$.

## Exam tips

- Magnification = image size ÷ actual size – **convert units first** (mm ↔ $\mu$m ↔ nm), then rearrange for whichever is unknown.
- Distinguish **magnification** (how many times larger) from **resolution** (smallest distance still seen as two points); electron microscopes resolve more because electrons have a shorter wavelength.
- Give each organelle a **structure + function** pair (e.g. mitochondrion: folded inner membrane → aerobic respiration).
- State the **prokaryote vs eukaryote** differences exactly: no nucleus, smaller (70S) ribosomes, no membrane-bound organelles, circular DNA.
- Viruses are **not cells** (acellular) – describe them only by capsid, genetic material and (sometimes) an envelope.



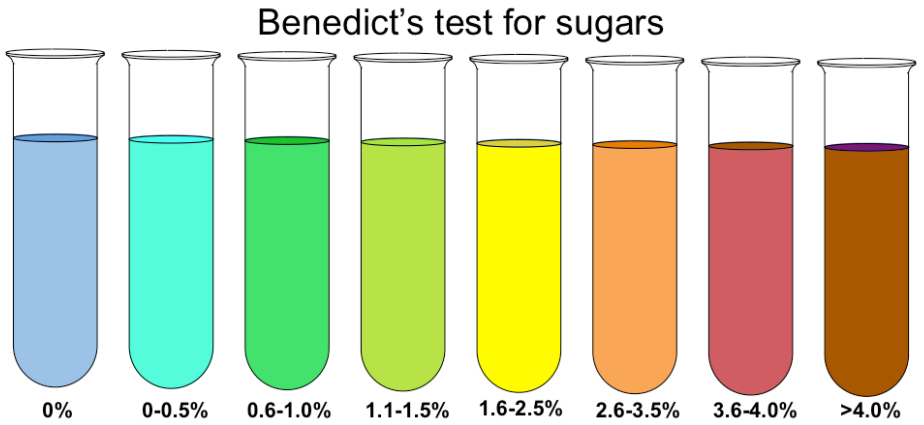
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# Biological molecules

A-Level Biology

## Testing for biological molecules

Living things are built from four main kinds of biological **molecule** 分子: **carbohydrates** 碳水化合物, **lipids** 脂质, **proteins** 蛋白质 and **nucleic acids** 核酸. You can use simple chemical tests to find out which kinds are present in a sample.

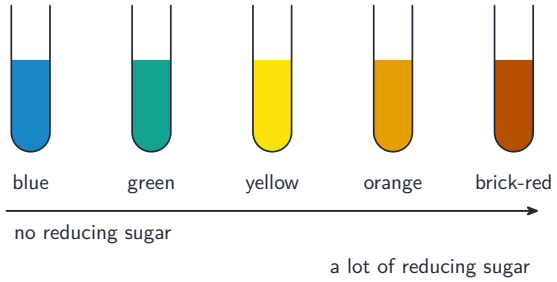



*Benedict's test: blue turns green, then orange, then brick-red as more reducing sugar is present*

| Test | What it finds | Method | Positive result |
|---|---|---|---|
| Benedict's test | **reducing sugar** 还原糖 | add Benedict's solution and heat in a water bath | a green, yellow, orange or brick-red **precipitate** 沉淀 |
| iodine test | **starch** 淀粉 | add orange-brown **iodine** 碘 solution | colour changes to blue-black |
| emulsion test | **lipid** | mix sample with ethanol, then pour into water | a white, cloudy **emulsion** 乳浊液 forms |
| **biuret** 双缩脲 test | **protein** | add biuret solution at room temperature | blue changes to purple |

### Semi-quantitative Benedict's test

The normal Benedict's test only tells you "yes or no". A **semi-quantitative** 半定量 test gives a rough amount. First you **standardise** 标准化 the test: you run it on solutions of known **concentration** 浓度 and record the result for each. Then you can estimate an unknown by either:




*After heating, the colour of Benedict's solution shows how much reducing sugar is present*

- the **time to the first colour change** (more sugar changes colour faster), or
- comparing the final colour to your set of colour standards.

Keep sample and reagent volumes, water-bath temperature and the colour-change endpoint the same for standards and the unknown. Use a water blank, repeat readings and use closer standards around the estimate; do not assume the time is proportional to concentration.

For example, a student heats 2 $cm^3$ of each glucose standard with 2 $cm^3$ of Benedict's solution in a water bath at 95 °C and times the first colour change.

| **Glucose concentration / %** | **0.0** | **0.25** | **0.5** | **1.0** | **2.0** |
|---|---|---|---|---|---|
| Time to first colour change / s | no change | 160 | 95 | 52 | 30 |

**Worked example.** An unknown solution, tested in exactly the same way as these standards, changes colour after 70 s. Estimate its concentration and say how to improve the estimate. 70 s lies between 95 s (0.5%) and 52 s (1.0%), so the unknown is **between 0.5% and 1.0%** glucose, roughly 0.75%. Plot time against concentration and read the unknown off the curve, rather than assuming a straight line. To improve it: make more standards between 0.5% and 1.0% (for example 0.6, 0.7, 0.8, 0.9%), repeat each test three times and use the mean, and judge the endpoint against a fixed colour card so the same change is timed each time.

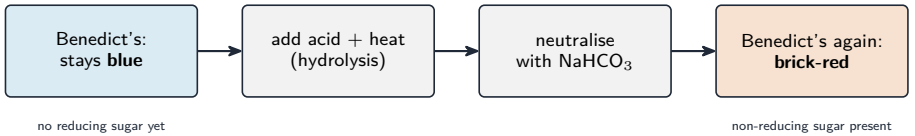


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### Testing for non-reducing sugars

Some sugars, such as sucrose, are **non-reducing sugar** 非还原糖: they give a negative Benedict's test. To detect them:

1. Do a normal Benedict's test first. It stays blue (reducing sugar is not detected under these conditions).
2. Take a fresh sample and add dilute **hydrochloric acid** 盐酸, then heat. This **acid hydrolysis** breaks the sugar into smaller reducing sugars.
3. Cool, then **neutralise** 中和 the acid with sodium hydrogencarbonate.
4. Add Benedict's solution and heat in a water bath. A coloured precipitate after an initially negative test supports a non-reducing sugar in a sample known to contain sugars; it does not identify sucrose specifically.




*Testing for a non-reducing sugar: hydrolyse it with acid first, then the second Benedict's test turns red*

**Worked example.** A solution is known to contain one dissolved sugar and no starch. One portion gives a negative Benedict's test. A fresh portion is heated with dilute hydrochloric acid, cooled, neutralised and re-tested with Benedict's in a water bath; it gives an orange precipitate. This supports a non-reducing sugar: hydrolysis releases reducing monosaccharides, and neutralisation restores the alkaline conditions needed for the test. The sugar is not identified as sucrose by this result alone. Without the sample context, other carbohydrates that release reducing sugars on hydrolysis must also be considered. A positive initial test followed by another positive test alone would not establish an additional non-reducing sugar.

## Carbohydrates

### Monomers, polymers and macromolecules

- a **monomer** 单体 is a small molecule that is a single unit.
- a **polymer** 聚合物 is a long molecule made of many monomers joined together.
- a **macromolecule** 大分子 is any very large molecule.

Sugars come in three sizes:

- a **monosaccharide** 单糖 is a single sugar unit, such as **glucose** 葡萄糖 and fructose.
- a **disaccharide** 二糖 is two units joined, such as maltose and sucrose.

- a **polysaccharide** 多糖 is many units joined into a polymer.

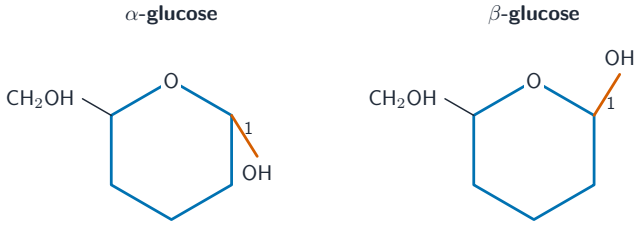
Glucose, **fructose** 果糖 and **maltose** 麦芽糖 are reducing sugars. **Sucrose** 蔗糖 is a non-reducing sugar.

## Two ring forms of glucose

Glucose has six carbon atoms and forms a ring. There are two ring forms. They differ only at carbon 1:

- in **α-glucose**, the –OH group on carbon 1 points **down**, below the ring.
- in **β-glucose**, the –OH group on carbon 1 points **up**, above the ring.

This small difference decides which polysaccharide the glucose can build.



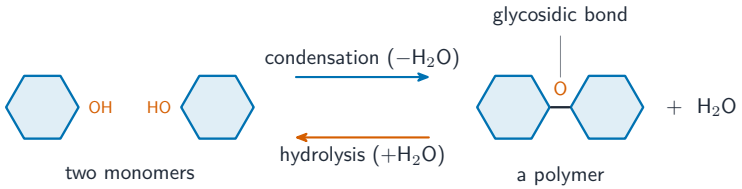

only carbon 1 differs: the OH points **down** in α, **up** in β

*The two ring forms differ only at carbon 1: the –OH points down in α, up in β*

## Joining and breaking sugars

Monomers are joined by strong **covalent bonds** 共价键. When two sugars join, a **glycosidic bond** 糖苷键 forms between them. This happens by **condensation** 缩合: a molecule of water is removed each time a bond forms.

The reverse is **hydrolysis** 水解: a water molecule is added to break a glycosidic bond. This is why the non-reducing sugar test needs acid and heat – they hydrolyse sucrose into glucose and fructose.




*Condensation removes water to join monomers; hydrolysis adds water to split them*



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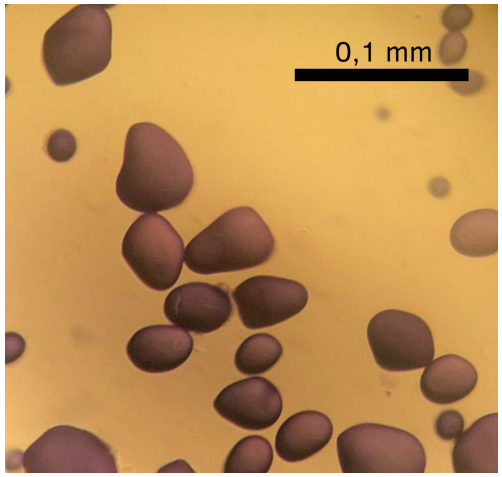
## Storage polysaccharides: starch and glycogen

**Starch** is the energy 能量 store in plants. It is made of two polymers of α-glucose:

- **amylose** 直链淀粉 – a long, unbranched chain that coils into a spiral.
- **amylopectin** 支链淀粉 – a chain with many side branches.

**Glycogen** 糖原 is the energy store in animals. It is like amylopectin but has even more branches, so it can be broken down quickly when energy is needed.

These stores suit their job well: they are compact, they are **insoluble** 不溶 (so they do not leave the cell), and they do not change the **water potential** 水势 of the cell (so they do not pull water in by **osmosis** 渗透). The many branches give many ends, so glucose can be added or removed fast.




*Real starch grains inside a potato, stained by iodine. Each grain is a dense, insoluble package of amylose and amylopectin – note the scale: the largest are only about 0.1 mm across*

## Cellulose

**Cellulose** 纤维素 is made of β-glucose. Because of the β form, every other glucose is flipped over, so the chains are long and straight. Many straight chains lie side by side and are held together by **hydrogen bonds** 氢键 into strong bundles called **microfibrils** 微纤丝. These give the plant **cell wall** 细胞壁 its strength and stop the cell bursting.

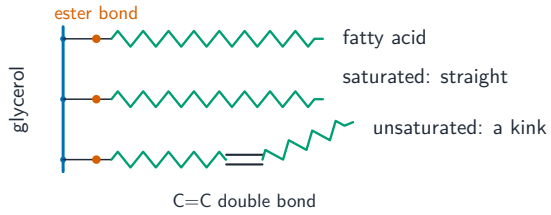



*The shape fits the job: amylose coils and amylopectin/glycogen branch (for compact stores), while straight cellulose chains pack into strong fibres*

## Lipids

### Triglycerides

A **triglyceride** 甘油三酯 is the main fat or oil. It is **non-polar** 非极性 and **hydrophobic** 疏水 (it does not mix with water). It is made from one **glycerol** 甘油 molecule joined to three **fatty acids** 脂肪酸 by **ester bonds** 酯键. Each ester bond forms by condensation, so three water molecules are removed.




3 ester bonds form → 3 $H_2O$ removed (condensation)

*One glycerol plus three fatty acid tails; a straight tail is saturated, a kinked one unsaturated*

Fatty acids are of two kinds:

- **saturated** 饱和 – no carbon–carbon **double bonds** 双键; these fats are usually solid.
- **unsaturated** 不饱和 – one or more double bonds; these oils are usually liquid.

Triglycerides make a good long-term energy store: they release about twice as much energy per gram as carbohydrates, they are insoluble, and they store little extra mass because they hold no water. Under the skin they also give **insulation** 隔热 and protect the organs.

Link each function to a feature of the structure:

- **energy store** – the long **hydrocarbon** 烃 tails hold many C–H bonds, which release a lot of energy when oxidised in respiration.



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- **compact store** – they are insoluble, so they do not change the water potential of the cell, and they do not need water stored with them.
- **metabolic water** 代谢水 – oxidising triglycerides releases a lot of water, which matters to desert animals such as camels and kangaroo rats.
- **buoyancy** 浮力 – fat is less dense than water, which helps aquatic mammals such as whales and seals to float.
- **insulation** – fat conducts heat slowly, and the **myelin** 髓鞘 sheath around many neurones is lipid, which insulates them electrically.

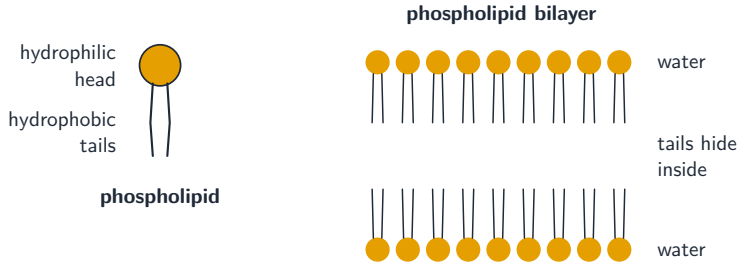
> **Worked example.** How many water molecules are needed to hydrolyse one triglyceride completely, and what are the products? There are **three** ester bonds, and hydrolysis of each bond uses one water molecule, so **three** water molecules are needed. The products are one glycerol and three fatty acids.

### Phospholipids

A **phospholipid** 磷脂 is like a triglyceride, but one fatty acid is replaced by a **phosphate** 磷酸 group. This gives the molecule two ends with different behaviour:

- a **hydrophilic** 亲水 ("water-loving") **polar** 极性 phosphate head.
- two hydrophobic ("water-fearing") fatty acid tails.

This split personality is why phospholipids form the membranes around cells.




*The hydrophilic heads face the water; the hydrophobic tails hide inside, forming a bilayer*

## Proteins

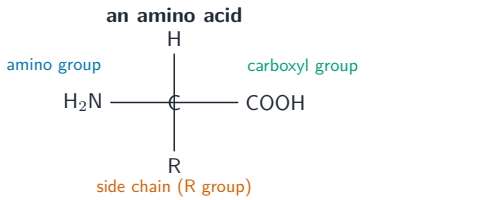
### Amino acids and the peptide bond

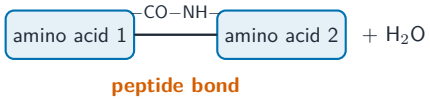
Proteins are polymers of **amino acids** 氨基酸. Every amino acid has the same general structure around a central carbon atom: an **amino group** 氨基 ($-NH_2$), a **carboxyl group** 羧基 (–COOH), a hydrogen atom, and a variable **side chain** 侧链 (the R group). The R group is different in each amino acid.

Two amino acids join by condensation. The bond formed between the amino group of

one and the carboxyl group of the next is a **peptide bond** 肽键, and a water molecule is removed. Many amino acids joined this way make a **polypeptide** 多肽. Adding water (hydrolysis) breaks a peptide bond.

> **Worked example.** A polypeptide has 120 amino acids. How many peptide bonds does it have, and how many water molecules were removed when it formed? Each peptide bond joins two neighbours in the chain, so a chain of $n$ amino acids has $n - 1$ bonds: **119 peptide bonds**, and **119 water molecules** were removed. Hydrolysing it completely would use 119 water molecules.



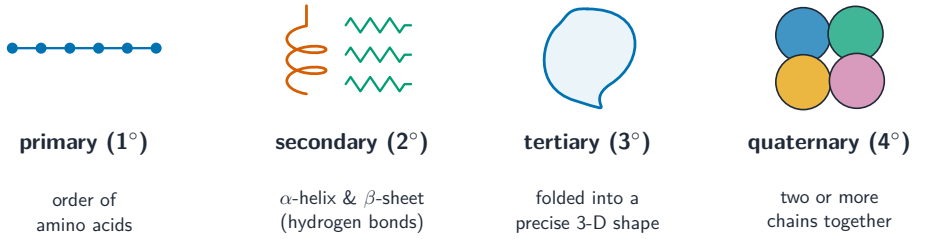

condensation removes one water for each peptide bond

*Every amino acid has an amino group, a carboxyl group and an R group; two join by a peptide bond*



## Four levels of protein structure

| Level | What it means |
|---|---|
| **primary structure** 一级结构 | the order of amino acids in the chain |
| **secondary structure** 二级结构 | local shapes – the **$\alpha$-helix** 螺旋 and the **$\beta$-pleated sheet** 折叠片 – held by hydrogen bonds between backbone groups |
| **tertiary structure** 三级结构 | the whole chain folded into a precise 3-D shape |
| **quaternary structure** 四级结构 | two or more polypeptide chains joined into one protein |




*The four levels: primary → secondary → tertiary → quaternary structure*

The tertiary folding is stabilised by several kinds of interaction involving R groups:

- **hydrophobic interactions** 疏水作用 (non-polar R groups cluster away from water).
- hydrogen bonding.
- **ionic bonds** 离子键 (between charged R groups).
- covalent bonding, including strong **disulfide bonds** 二硫键.

## Globular and fibrous proteins

- **globular proteins** 球状蛋白质 fold into a rounded shape, are usually **soluble** 可溶, and do jobs in the body (for example enzymes and haemoglobin).
- **fibrous proteins** 纤维状蛋白质 form long strands, are usually insoluble, and give structure and support (for example collagen).



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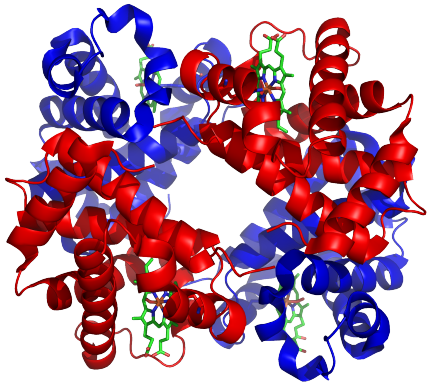
### Haemoglobin – a globular protein

**Haemoglobin** 血红蛋白 carries **oxygen** 氧气 in red blood cells. It has a quaternary structure made of four polypeptide chains: two alpha ($\alpha$-globin) chains and two beta ($\beta$-globin) chains. Each chain holds a **haem group** 血红素. At the centre of each haem group is an **iron** 铁 ion, and this is where one oxygen molecule binds. Four chains mean one haemoglobin molecule can carry four oxygen molecules.

Its structure fits its job:

- **hydrophilic** R groups lie on the **outside** of each chain, so haemoglobin is **soluble** in the watery cytoplasm of the red blood cell.
- **hydrophobic** R groups point **inwards**, folding the chain tightly round a pocket that holds the haem group in place.
- the four chains fit together precisely, so when one oxygen binds, the shape of the molecule changes slightly and the next oxygen binds more easily.

**Worked example (primary structure matters).** In **sickle cell anaemia** 镰状细胞贫血, one amino acid in each $\beta$ chain is changed: **glutamic acid**, which has a charged, hydrophilic R group, is replaced by **valine**, which has a non-polar, hydrophobic R group. Explain why this one change matters. The valine sits on the **outside** of the molecule. When oxygen levels are low, its hydrophobic R group sticks to a hydrophobic area on another haemoglobin molecule, so the molecules join into long fibres. These make the haemoglobin less soluble and pull the red blood cell into a sickle shape, which carries less oxygen and can block capillaries. A change in the primary structure changes the shape and the properties of the whole protein.



*A real haemoglobin molecule, worked out from X-ray data. Count them: two alpha chains (red), two beta chains (blue), and one green haem group held in each – so four oxygen molecules in total*



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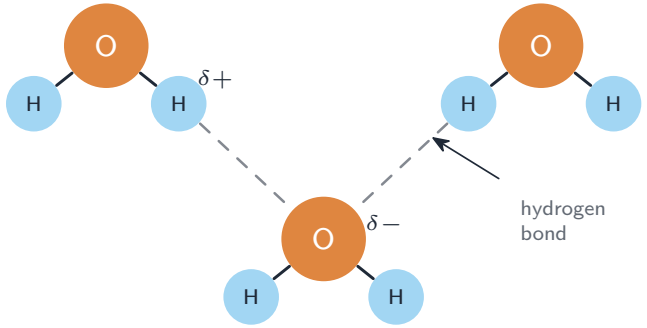
### Collagen – a fibrous protein

**Collagen** 胶原蛋白 gives strength to skin, **tendons** 肌腱, bone and blood vessel walls. One collagen molecule is three helical polypeptide chains wound tightly into a triple helix, stabilised by hydrogen bonds between chains. Glycine occurs at about every third position; its small side chain allows close packing. Many of these molecules lie side by side, slightly staggered, and have covalent cross-links between molecules, forming thick **fibres** 纤维. The staggered, cross-linked arrangement makes collagen very strong when pulled.

## Water

Water is a small molecule, but its two O–H bonds are **polar**: the oxygen end is slightly negative and the hydrogen ends are slightly positive. So one water molecule attracts its neighbours, forming weak hydrogen bonds between them. These hydrogen bonds explain water's useful properties:

- **solvent action** – water is a good **solvent** 溶剂, so many substances dissolve in it. This lets reactions happen and lets substances be carried around the body.
- **high specific heat capacity** 比热容 – water needs a lot of energy to warm up, so its temperature stays steady. This protects living things from quick temperature changes.
- **latent heat of vaporisation** 汽化潜热 – water needs a lot of energy to **evaporate** 蒸发. So when water evaporates (for example as sweat dries), it carries away a lot of heat and cools the body.




*Water is polar ($\delta-$ oxygen, $\delta+$ hydrogens), so its molecules attract each other by hydrogen bonds – the reason for all the properties above*

**Common mistakes.**

- Writing that condensation "adds water" or that hydrolysis "removes water". **Condensation** removes a water molecule as a bond forms; **hydrolysis** uses a water molecule to break one.
- Saying cellulose is made of $\alpha$-glucose, or that starch has hydrogen-bonded microfibrils. Cellulose is **$\beta$-glucose**: alternate units are flipped, so the chains are straight and lie side by side, held by hydrogen bonds.
- Saying glycogen is a good store "because it is soluble". It is **insoluble**, so it does not change the water potential of the cell; its many branches give many ends for fast release of glucose.
- Saying a triglyceride is a polymer. Three fatty acids on one glycerol is not a chain of repeating monomers, so lipids are **not polymers**.
- Saying the secondary structure is held by bonds between R groups. The $\alpha$-helix and $\beta$-pleated sheet are held by hydrogen bonds between **backbone** groups; the R groups hold the tertiary structure.
- Saying a disulfide bond forms between any two amino acids. It forms only between two **cysteine** 半胱氨酸 R groups, which contain sulfur.
- Calling hydrogen bonds strong. Each hydrogen bond is **weak**; there are so many of them that together they give strength (cellulose) or a high specific heat capacity (water).

## Exam tips

- Learn each **food test** as reagent + positive result + colour change (Benedict's → coloured precipitate, not necessarily brick-red; iodine → blue-black; biuret → purple; emulsion → white).
- Benedict's detects **reducing** sugars; for a non-reducing sugar you must heat a fresh portion with acid, cool and neutralise it, then re-test in a water bath.
- Name the bond precisely: **glycosidic** (carbohydrates), **ester** (lipids), **peptide** (proteins) – all made by **condensation** (water removed).
- Link structure to function: cellulose (straight chains, H-bonds → strong), glycogen/starch (branched/coiled → compact store).
- For proteins, name the bond at each level: primary (peptide), secondary (hydrogen), tertiary (R-group interactions), quaternary.
- A chain of $n$ monomers has $n - 1$ bonds, so $n - 1$ water molecules are removed when it forms; a triglyceride has 3 ester bonds.
- For haemoglobin, link the structure to the job: hydrophilic R groups outside make it soluble; four haem groups carry four $O_2$ molecules.



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# Enzymes

A-Level Biology

## What enzymes are

**Enzymes** 酶 are **globular proteins** 球状蛋白质 – a type of **protein** 蛋白质 with a rounded, soluble shape. They are biological catalysts: they **catalyse** 催化 (speed up) the chemical reactions in living things, and they are not used up, so each enzyme works again and again.

Enzymes work in two places:

- **intracellular** 细胞内 enzymes work inside the **cell** 细胞 that made them. An example is **catalase** 过氧化氢酶, which breaks down harmful hydrogen peroxide.
- **extracellular** 细胞外 enzymes are **secreted** 分泌 (sent out) to work outside the cell. An example is **amylase** 淀粉酶, which is released into the gut to **digest** 消化 **starch** 淀粉.



*Yeast enzymes ferment sugar, giving off bubbles of carbon dioxide*

## How enzymes work

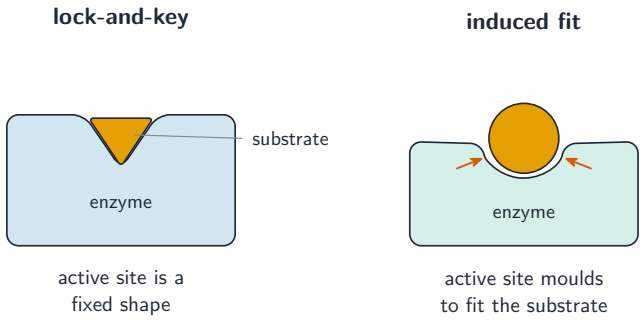
Each enzyme has a special pocket called the **active site** 活性位点. The molecule it acts on is its **substrate** 底物. The substrate fits into the active site to form an **enzyme–substrate complex** 酶底物复合物. The reaction then happens, and the **products** 产物 leave, freeing the active site for the next substrate.

## Specificity

An enzyme is **specific**: it usually works on only one substrate. This is because the shape of the active site is **complementary** 互补 to (fits) the shape of that substrate and no other. We call this **specificity** 专一性.

Two ideas explain how the substrate fits:

- the **lock-and-key hypothesis** 锁钥学说 – the active site is a fixed shape, and only a substrate with the matching shape fits, like a key in a lock.
- the **induced-fit hypothesis** 诱导契合学说 – the active site is not quite the right shape at first. When the substrate binds, the active site changes shape a little to wrap around it tightly. This idea fits the evidence better.

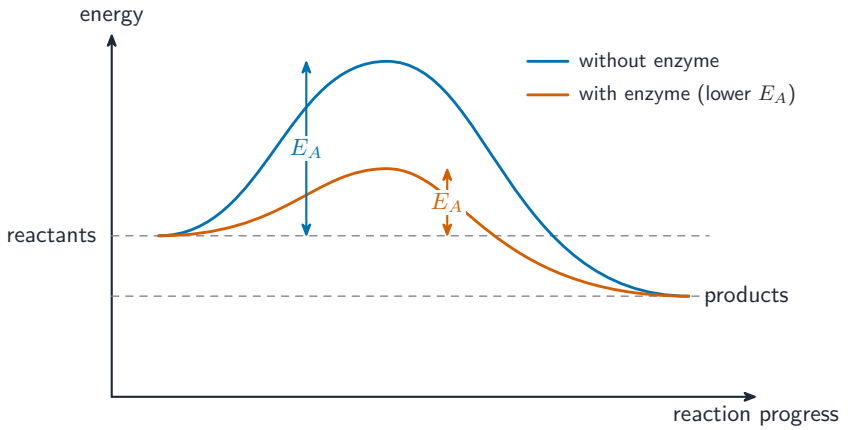



*Lock-and-key: a fixed active site. Induced fit: the active site changes shape to grip the substrate*

## Lowering activation energy

Every reaction needs a small "push" of energy to start, called the **activation energy** 活化能. An enzyme lowers the activation energy. This lets the reaction go quickly at the cell's normal **temperature** 温度, instead of needing high heat.






*The enzyme route has a lower activation energy ($E_A$), so more molecules can react*

## Measuring the rate of a reaction

You can follow an enzyme reaction in two ways:

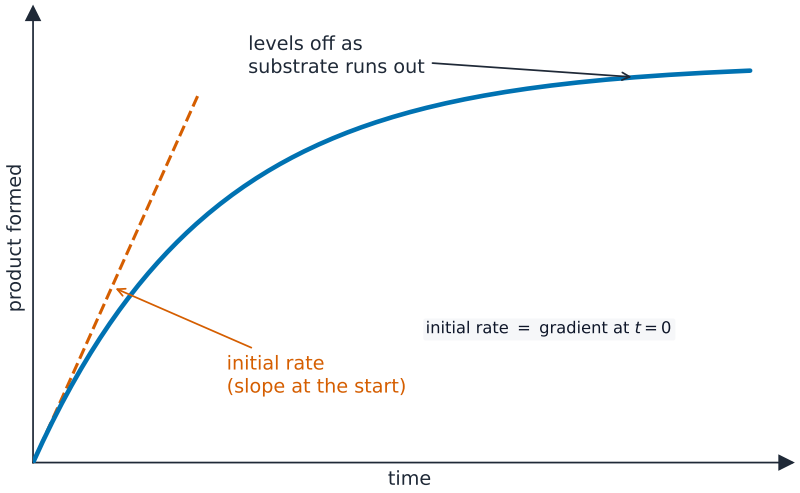
- measure how fast **product** is made. With catalase, oxygen gas is a product, so you collect the gas and measure its volume over time.
- measure how fast substrate disappears. With amylase, you remove samples and use the iodine test; the blue-black colour fades as the starch is used up.

A **colorimeter** 比色计 makes this exact. It shines light through the tube and measures how much light is absorbed, so a colour change becomes a number you can plot.

The **rate of reaction** 反应速率 is steepest at the start (most substrate present), so the **initial rate** (the slope at time zero) is the fairest value to compare.



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*Product builds fastest at the start; the initial rate is the slope of the tangent at time zero – the fairest value to compare*

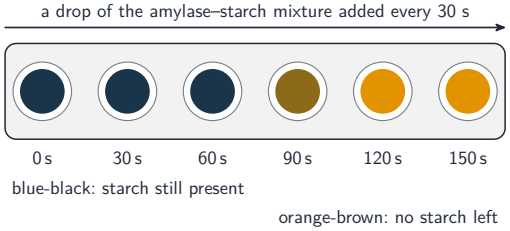
**Worked example.** In the first 20 seconds of a catalase reaction, 16 $cm^3$ of oxygen is collected. Estimate the rate of reaction.

$$\text{rate} = \frac{\text{volume of product}}{\text{time}} = \frac{16}{20} = 0.8 \text{ cm}^3\,\text{s}^{-1}.$$

Because the reaction is fastest at the start, measuring over this short early interval gives a value close to the initial rate; averaging over a longer time would include the slower later stages and underestimate it.

## Planning an enzyme investigation

Exam questions often ask you to describe or improve a method. Three common set-ups:




*Iodine on a spotting tile stays blue-black while starch remains and turns orange-brown when the amylase has digested it all*



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- **Catalase and hydrogen peroxide.** Put a fixed volume of hydrogen peroxide in a conical flask connected to a **gas syringe** (or a delivery tube into an upturned measuring cylinder full of water). Add the catalase (a yeast suspension, or discs of potato or liver of the same size), close the flask at once, and record the volume of oxygen every 10 s. Or soak small filter-paper discs in catalase, drop them into hydrogen peroxide and time how long each takes to rise to the surface: the faster the oxygen is made, the sooner the disc floats.
- **Amylase and starch.** Put one drop of iodine solution in each well of a **spotting tile**. Mix the amylase and starch, start a stop clock, and every 30 s put a drop of the mixture into the next well. Record the time when the iodine **no longer turns blue-black** (stays orange-brown): the end point, when all the starch has been digested.
- **Colorimeter.** Measure the colour of the mixture at intervals, for example the fading blue-black of starch with iodine, or the brown product made by catechol oxidase. First set the colorimeter to zero with a **blank** (a tube of everything except the coloured substance), and use the same filter for every reading.

**Converting a time into a rate.** If you measure how long the reaction takes to reach an end point, the rate is the reciprocal of the time:

$$\text{rate} = \frac{1}{\text{time}} \quad (\text{s}^{-1})$$

For example, if the starch is all gone after 120 s at 30 °C and after 40 s at 40 °C, the rates are $1/120 = 0.0083$ $s^{-1}$ and $1/40 = 0.025$ $s^{-1}$: three times as fast.

**Making it a fair test.**

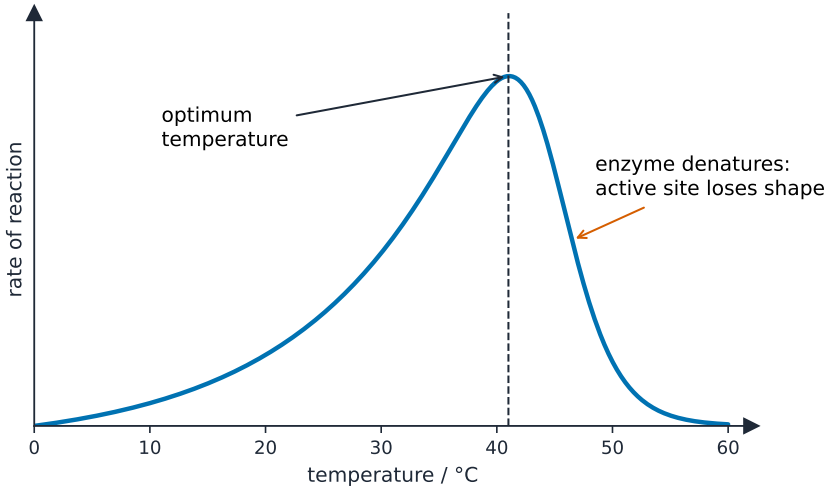
| What to do | Why |
|---|---|
| put enzyme and substrate in separate tubes in the **water bath** for 5 min before mixing | so both are at the set temperature when the reaction starts |
| add a **buffer** to every tube | to keep the pH constant (enzymes are sensitive to pH) |
| keep the volumes and concentrations of enzyme and substrate the same | only the independent variable may change |
| set up a **control**: the same tube with **boiled** (denatured) enzyme, or with water instead of enzyme | to show that the change is caused by the enzyme |
| repeat each condition at least three times and find a mean | to spot anomalous results and make the results more reliable |
| use at least five values of the independent variable over a wide range | to show the pattern and find an optimum |

To find the optimum more precisely, repeat the experiment with smaller steps of temperature (or pH) near the highest rate you found.

## Factors that affect enzyme activity

### Temperature

As temperature rises, molecules gain more **kinetic energy** 动能 and **collide** 碰撞 more often, so the rate rises. But above the **optimum temperature** 最适温度 the enzyme begins to **denature** 变性: the heat breaks the bonds holding its shape, so the active site changes and no longer fits the substrate. The rate then falls quickly.



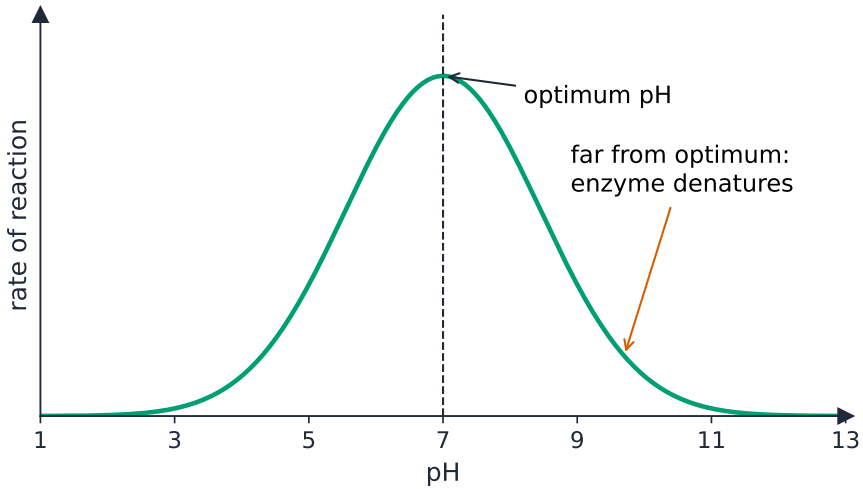

*Rate rises to the optimum, then falls fast as the enzyme denatures*

### pH

Each enzyme has an optimum pH. If the pH moves too far from it, the enzyme denatures and the rate drops. To study pH fairly, you keep it steady with a **buffer solution** 缓冲液.



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*The rate peaks at the optimum pH and falls away on either side*

### Enzyme concentration

With plenty of substrate, more enzyme means more active sites, so the rate goes up in proportion to enzyme concentration. If the substrate runs short, the line levels off: now the substrate limits the rate, because there are free active sites with nothing to bind.

### Substrate concentration

At first, adding more substrate speeds the reaction. But once every active site is busy, adding more makes no difference – the rate levels off at a maximum.

### Inhibitor concentration

An **inhibitor** 抑制剂 is a molecule that slows an enzyme. The more inhibitor present, the lower the rate.

For both temperature and pH, explain the fall in rate in terms of bonds: a high temperature makes the enzyme molecule **vibrate** so much that **hydrogen bonds** and **ionic bonds** in its tertiary structure break; a change in pH alters the charges on the R groups (by adding or removing hydrogen ions), so ionic and hydrogen bonds break. Either way the active site changes shape, so fewer enzyme–substrate complexes form.

## V_max and the Michaelis–Menten constant

The levelling-off rate, when all active sites are full, is the maximum rate, written $V_{max}$.

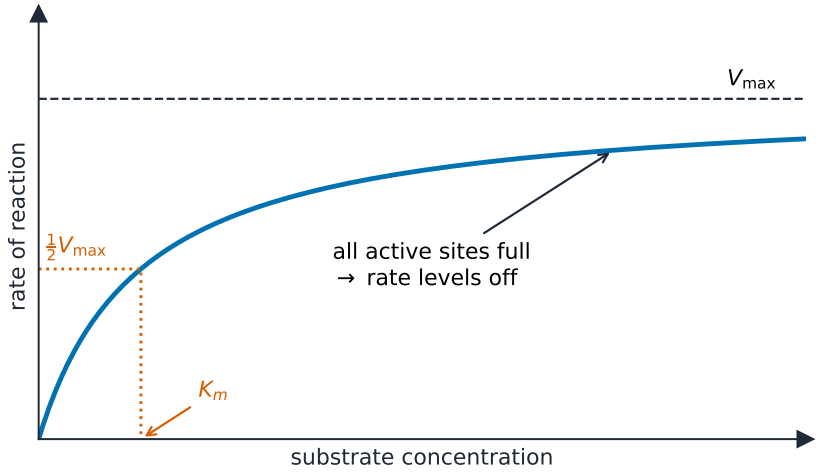
The **Michaelis–Menten constant** 米氏常数 ($K_m$) is the substrate concentration that gives **half** of $V_{max}$. It tells you about the enzyme's **affinity** 亲和力 (pulling power) for its substrate:

- a **low** $K_m$ means the enzyme reaches half-speed at a low substrate concentration, so it has a **high** affinity.
- a **high** $K_m$ means a **low** affinity.

So $K_m$ lets you compare how strongly different enzymes hold their substrates.

> **Worked example (finding $K_m$ from a graph).** A curve of rate against substrate concentration levels off at $V_{max} = 40$ $\mu$mol min$^{-1}$. Half of $V_{max}$ is 20 $\mu$mol min$^{-1}$. Draw a line across from 20 on the rate axis to the curve, then down to the concentration axis: it meets it at 2.5 mmol dm$^{-3}$, so $K_m = 2.5$ mmol dm$^{-3}$. A second enzyme with the same substrate has $K_m = 0.8$ mmol dm$^{-3}$, so it has the **higher** affinity: it binds the substrate well even when there is little of it. Always give $K_m$ as a **concentration**, with units, never as a rate.

To find $V_{max}$ and $K_m$, measure the **initial rate** at many substrate concentrations, keeping the enzyme concentration the same, and include high enough concentrations for the curve to level off.



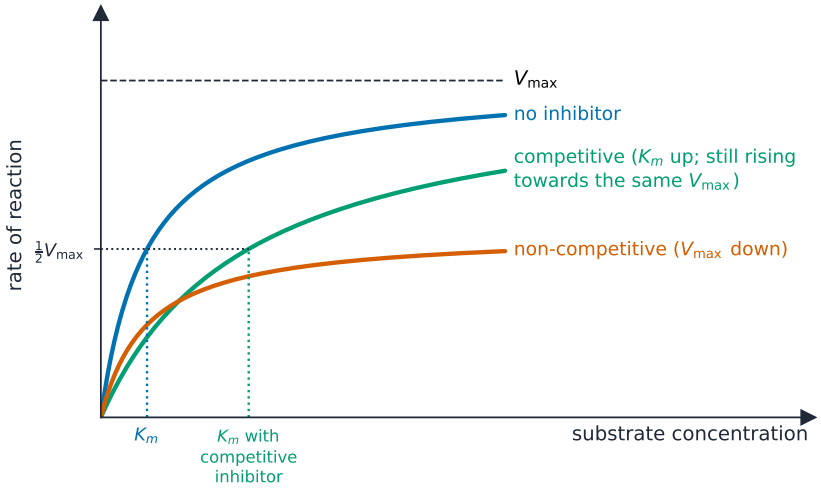

*Rate climbs to $V_{max}$ when all active sites are full; $K_m$ is the substrate concentration giving half $V_{max}$*



## Reversible inhibitors

Some inhibitors are **reversible** 可逆: they can leave the enzyme again. There are two types.

| Type | Where it binds | Effect of adding more substrate | Effect on $V_{max}$ and $K_m$ |
|---|---|---|---|
| **competitive inhibitor** 竞争性抑制剂 | in the active site (it has a similar shape to the substrate) | more substrate out-competes it, so its effect is reduced | $V_{max}$ unchanged; $K_m$ rises |
| **non-competitive inhibitor** 非竞争性抑制剂 | at another site, changing the active site's shape | adding more substrate does not help | $V_{max}$ falls; $K_m$ unchanged |




*A competitive inhibitor raises $K_m$ (more substrate overcomes it); a non-competitive one lowers $V_{max}$*

**Why the values change.** A competitive inhibitor takes some active sites at any one time, so more substrate is needed to reach half the maximum rate: $K_m$ rises. But at a very high substrate concentration, substrate molecules collide with the active sites far more often than inhibitor molecules, so the same $V_{max}$ is reached in the end. A non-competitive inhibitor changes the shape of the active site of every enzyme it binds to, so those enzymes cannot work at all, however much substrate is added: in effect there is less enzyme, so $V_{max}$ falls.

**Examples.** Malonate is a competitive inhibitor of the respiration enzyme succinate dehydrogenase, because its shape is close to that of the substrate, succinate. Many



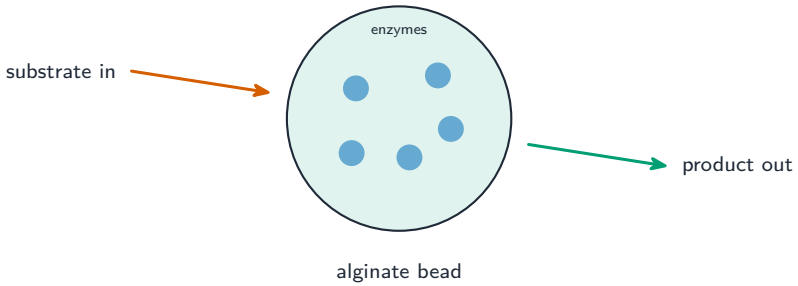
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drugs work as competitive inhibitors, for example the antibiotic sulfonamides. Heavy-metal ions such as lead and mercury, and cyanide (which binds to cytochrome oxidase), are non-competitive inhibitors.

**Telling them apart in an experiment.** Measure the rate at a range of substrate concentrations with and without the inhibitor. If adding a lot of substrate brings the rate back to the uninhibited maximum, the inhibitor is competitive; if the maximum stays lower, it is non-competitive.

## Immobilised enzymes

An **immobilised enzyme** 固定化酶 is fixed in place – for example, trapped inside small beads of **alginate** 海藻酸盐 – instead of floating free in solution. The substrate solution flows past the beads.




*The enzymes stay trapped in the bead while substrate flows in and product flows out – so the enzyme is never washed away*

A free enzyme usually works a little faster, because the substrate can reach it easily. But immobilised enzymes have big practical advantages:

- the enzyme is not washed away, so it can be used again and again.
- the product is pure – it is not mixed with enzyme.
- the enzyme is more stable, so it survives changes in temperature and pH better.
- the process can run continuously, with substrate flowing in and product flowing out.

**Making and comparing immobilised enzymes.** Mix the enzyme with sodium alginate solution and drip it from a syringe into calcium chloride solution: each drop sets at once into a jelly-like bead with enzyme trapped inside. Rinse the beads and pack them into a column (for example a syringe barrel with a tap or a gauze at the bottom). Pour the substrate solution through and test what comes out.

For example, with **lactase** immobilised in beads, milk poured through the column comes out containing glucose, which a glucose **test strip** shows. To compare immobilised and free enzyme, use the **same mass** of enzyme in each, and measure how fast



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the product appears; then do the same after heating both to a range of temperatures. The immobilised enzyme usually shows a slightly lower rate (the substrate must diffuse into the bead) but a **higher optimum temperature** and a wider working range, because the alginate holds the enzyme molecules in shape. A faster flow rate gives the substrate less time in contact with the enzyme, so less of it is converted.



*Biological washing powders contain enzymes that digest food and blood stains at low temperatures*

**Common mistakes.**

- Saying a cold enzyme is denatured. At a low temperature the enzyme is only **slow**: molecules move and collide less. Its shape is unchanged, so the rate rises again when it is warmed. Only high temperature or extreme pH denatures it.
- Saying the active site has the **same** shape as the substrate. It has a **complementary** shape, so the two fit together like a key in a lock.
- Saying denaturing breaks the peptide bonds. Heat and pH break the hydrogen bonds and ionic bonds that hold the **tertiary structure** 三级结构. The chain of amino acids stays whole, but the active site loses its shape.
- Explaining the plateau of a rate–substrate graph as "the enzyme is used up". The enzyme is not used up; every active site is busy, so enzyme concentration now limits the rate.
- Saying a competitive inhibitor lowers $V_{max}$. With enough substrate the substrate out-competes the inhibitor, so the same $V_{max}$ is reached; it is $K_m$ that rises.
- Reading $K_m$ at $V_{max}$. $K_m$ is the substrate concentration at **half** $V_{max}$.
- Assuming every enzyme has an optimum of 37 °C and pH 7. Pepsin in the stomach works best near pH 2, and enzymes from bacteria in hot springs work best near 70 °C.

## Exam tips

- Explain enzyme action with the **induced-fit** model (the active site moulds around the substrate) – now preferred to lock-and-key.
- Above the optimum the enzyme **denatures** (hydrogen bonds and tertiary structure break) – write "denatures", never "dies" or "is killed".
- Distinguish inhibitors: **competitive** binds the active site (overcome by more substrate, same $V_{max}$); **non-competitive** binds elsewhere (lower $V_{max}$).
- Compare rates using the **initial rate** (tangent at time zero) – the fairest measure, before substrate becomes limiting.
- In a method, name the control (boiled enzyme), the buffer, pre-incubation in the water bath and repeats; give rate = 1/time for an end-point method.
- $K_{\mathrm{m}}$ is a concentration read at half $V_{\max}$; a lower $K_{\mathrm{m}}$ means a higher affinity.
- Immobilised enzymes: alginate beads in calcium chloride; the enzyme is reused, the product is pure and the enzyme is more stable.



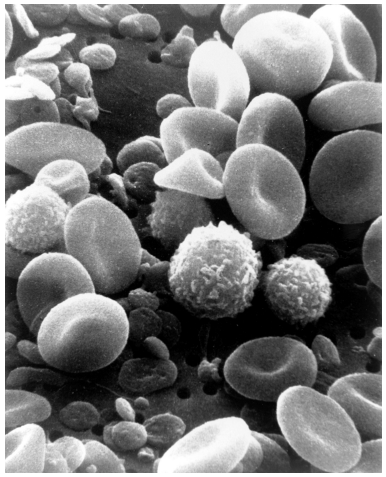
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# Cell membranes and transport

A-Level Biology

## The cell surface membrane

Every cell is wrapped in a **cell surface membrane** 细胞膜. We describe its structure with the **fluid mosaic model** 流动镶嵌模型.



*Red blood cells under a scanning electron microscope – each is wrapped in a cell surface membrane*

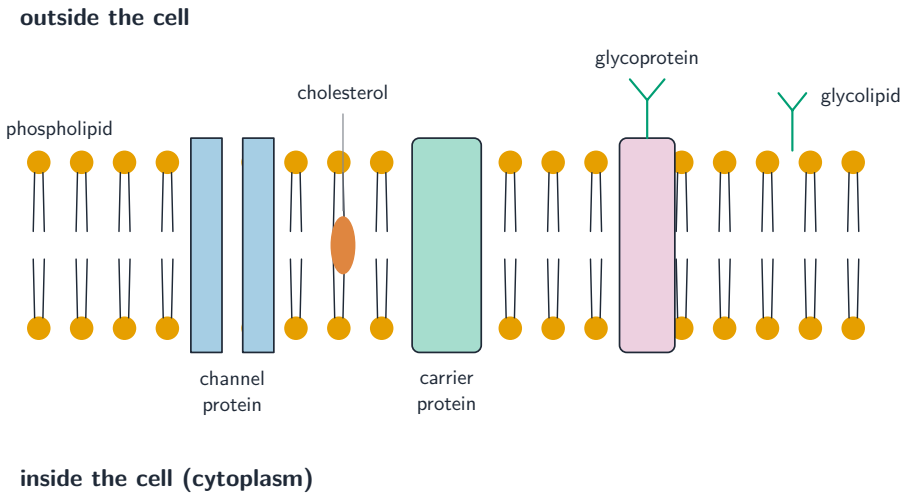
### The phospholipid bilayer

The membrane is built mainly from **phospholipids** 磷脂. Each phospholipid has a **hydrophilic** 亲水 ("water-loving") head and two **hydrophobic** 疏水 ("water-fearing") tails. There is water on both sides of the membrane, so the phospholipids line up in two layers – a **bilayer** 双层 – with the heads facing the water outside and inside, and the tails hidden in the middle, away from water. This arrangement forms by itself because of those hydrophilic and hydrophobic interactions.

The model is called "fluid" because the phospholipids are not fixed: they slide past each other, so the membrane can move and bend. It is called a "mosaic" because many **proteins** 蛋白质 are dotted through it, like tiles in a picture.

## What floats in the membrane

| Part | Where it sits | Main roles |
|---|---|---|
| phospholipids | the two layers | form the basic barrier |
| proteins | through the membrane or on its surface | transport, support and signalling |
| **carrier proteins** 载体蛋白 | span the membrane | carry specific molecules across |
| **channel proteins** 通道蛋白 | span the membrane | form water-filled pores for ions to pass |
| **cholesterol** 胆固醇 | between the phospholipid tails | controls **fluidity** 流动性 and adds strength |
| **glycolipids** 糖脂 and **glycoproteins** 糖蛋白 | carbohydrate chains on the outer surface | cell recognition; some act as **antigens** 抗原 |




*The fluid mosaic model: proteins, cholesterol and carbohydrate chains sit in a fluid phospholipid bilayer*

So the membrane molecules together give the membrane its **stability** 稳定性, its fluidity, its **permeability** 通透性 (control over what gets through), its transport jobs, its signalling jobs, and its cell recognition.

The membrane is **partially permeable** 半透膜: it lets some substances through easily but blocks others.



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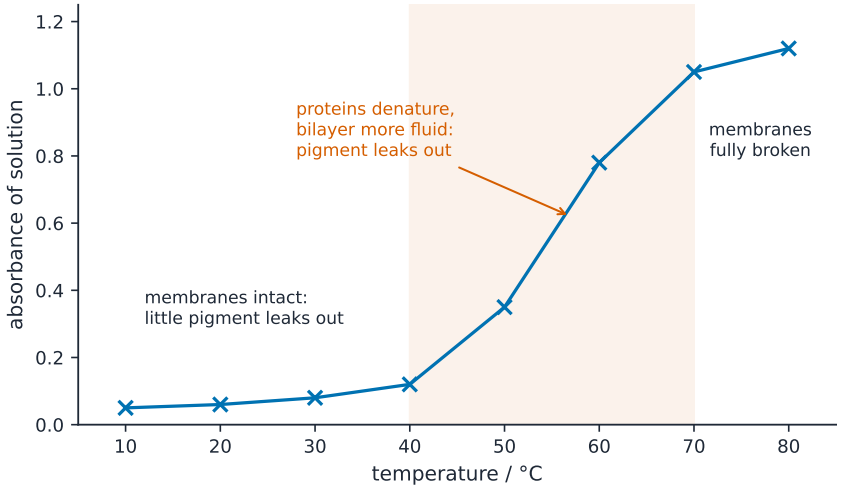
**More on each component.**

- The membrane is about **7 nm** thick. The hydrophobic core stops ions and polar molecules (such as glucose and amino acids) from passing straight through, so they need proteins.
- **Cholesterol** sits between the phospholipid tails. At body temperature it holds the tails together, making the membrane **less fluid** and less leaky to ions; at low temperatures it stops the tails packing too tightly, so the membrane does not become rigid. Animal cells have much more cholesterol than plant cells.
- **Glycoproteins** act as **receptors** for hormones and other signals, and both glycoproteins and glycolipids help cells recognise each other and stick together to form tissues. The carbohydrate chains also form hydrogen bonds with water, helping to keep the surface stable.
- Some proteins are **enzymes** (for example in the microvilli of the small intestine), and some hold the cytoskeleton in place.

## Investigating membrane permeability

Beetroot cells contain a red pigment (betalain) in their vacuoles. Normally the membranes stop it leaking out. Damaging the membranes lets it out, so the colour of the surrounding water shows how permeable the membranes are.

1. Cut equal-sized pieces of beetroot with a cork borer, and **wash** them well to remove pigment from the cells cut open.
2. Put the same number of pieces in the same volume of water in tubes held in water baths at different temperatures (for example 10 to 80 °C), for the same time (30 min).
3. Remove the pieces, shake the tubes, and measure the **absorbance** of each solution with a **colorimeter** 比色计 (using a blue-green filter), or compare the colours by eye against a set of standards.




*Beetroot pigment leaks out sharply above about 40 °C, as membrane proteins denature*

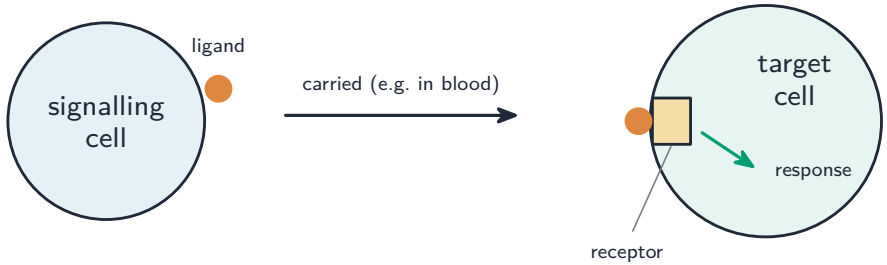
Above about 40 °C, the **proteins** in the membrane **denature**, leaving gaps, and the phospholipids move faster, so the bilayer becomes more fluid and leaky. The pigment escapes from the vacuole (through the tonoplast) and the cell surface membrane, so absorbance rises. Soaking pieces in **ethanol** solutions of increasing concentration has a similar effect: ethanol dissolves lipids in the membrane. Control variables: the size and surface area of the pieces, the volume of water, the time, and the same beetroot.

## Cell signalling

Cells talk to each other by **cell signalling** 细胞信号传递. The main stages are:

1. a cell **secretes** a signal chemical called a **ligand** 配体 (for example a **hormone** 激素).
2. the ligand is carried (often in the blood) to a **target cell** 靶细胞.
3. the ligand binds to a specific **receptor** 受体 on the target cell's surface membrane. The shape of the receptor matches that ligand only. Binding then triggers a particular response inside the target cell.






*The ligand fits one receptor shape only, so only cells with that receptor respond to the signal*

The receptor's binding site has a shape **complementary** to the ligand, so only target cells with that receptor respond. Binding changes the shape of the receptor protein, and this passes the signal across the membrane (**transduction**), often by making a **second messenger** such as cyclic AMP inside the cell, which starts a chain of reactions. Some receptors are channel proteins that open when the ligand binds. Small lipid-soluble signals, such as **steroid hormones**, can pass straight through the bilayer and bind to receptors **inside** the cell instead.

Signals can work over different distances: a hormone travels in the blood to cells all round the body, while a neurotransmitter crosses only the tiny gap between two neurones.

## Moving substances across the membrane

There are six processes. Some are **passive** 被动 (they need no energy 能量), and some are **active** (they use energy from ATP).

### ■ Simple diffusion

**Diffusion** 扩散 is the net movement of particles from where they are at a high **concentration** 浓度 to where they are at a low concentration, until they are spread evenly. **Simple diffusion** 简单扩散 is when particles pass straight through the bilayer, down the **concentration gradient** 浓度梯度. Only small or non-polar molecules can do this – such as **oxygen** 氧气 and **carbon dioxide** 二氧化碳. It is passive.

**What affects the rate of diffusion.**

- the **concentration gradient**: a steeper gradient gives faster diffusion;
- the **surface area** across which diffusion happens: a larger area, faster;
- the **distance** (thickness of the surface): a shorter distance, faster;
- **temperature**: particles have more kinetic energy and move faster;



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- the **size and nature** of the molecule: small, non-polar (lipid-soluble) molecules cross the bilayer fastest.

## Facilitated diffusion

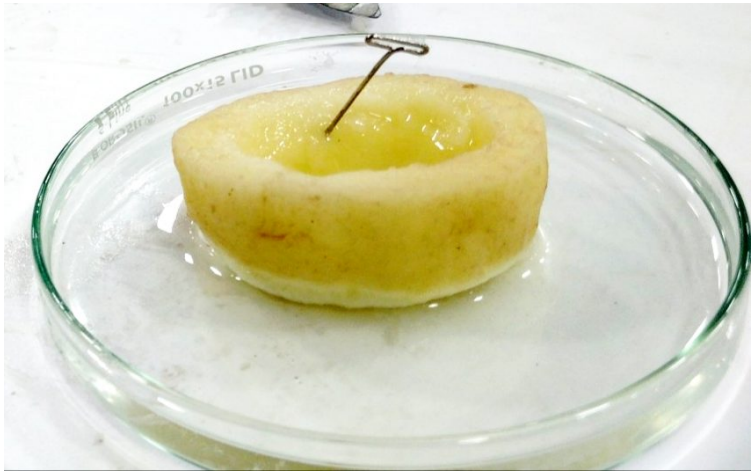
Charged **ions** 离子 and large polar molecules (such as **glucose** 葡萄糖) cannot cross the oily bilayer by themselves. In **facilitated diffusion** 易化扩散 they cross through channel proteins or carrier proteins, still moving down the concentration gradient. It is also passive.

- **Channel proteins** form water-filled pores. Each kind lets through only one kind of ion, and many are **gated**: they open or close in response to a signal (such as a change in voltage, or a ligand binding).
- **Carrier proteins** bind a specific molecule, change shape, and release it on the other side of the membrane.

Because there are only so many proteins, the rate of facilitated diffusion rises with the concentration gradient only until all the proteins are in use; then it levels off. Simple diffusion keeps rising in a straight line.

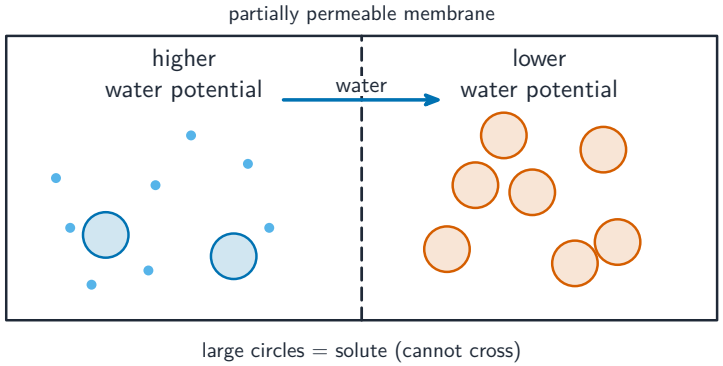
## Osmosis

**Osmosis** 渗透 is the diffusion of water across a partially permeable membrane, from a higher **water potential** 水势 to a lower water potential. It is passive.



*A potato osmometer: the sugar solution rises up the tube as water enters the potato by osmosis*



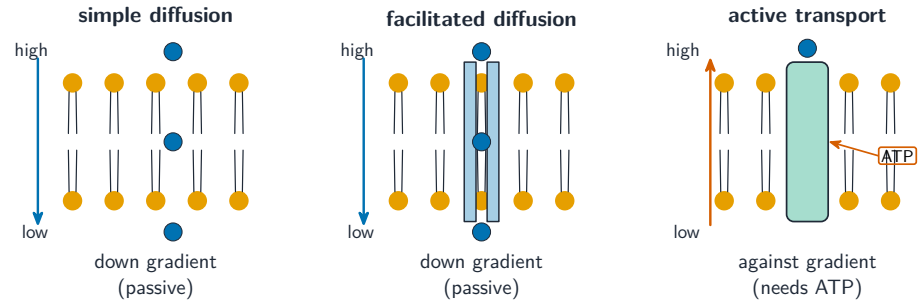



*Water crosses to the lower water potential; the solute is too big to cross the partially permeable membrane*

## Active transport

**Active transport** 主动运输 moves a substance **against** its concentration gradient – from low to high concentration. This needs carrier proteins and energy from ATP.

The best-known example is the **sodium–potassium pump** 钠钾泵, found in the cell surface membrane of almost all animal cells. Each time ATP is hydrolysed, the pump moves **3 sodium ions out** of the cell and **2 potassium ions in**, both against their gradients. The ATP phosphorylates the carrier protein, changing its shape. Active transport is used, for example, to take up mineral ions into root hair cells, to reabsorb glucose in the kidney, and to load sucrose into phloem. Anything that stops respiration (lack of oxygen, low temperature, or a respiratory poison such as cyanide) stops active transport, but does not stop diffusion.




*Diffusion and facilitated diffusion are passive (down the gradient); active transport goes against it and needs ATP*



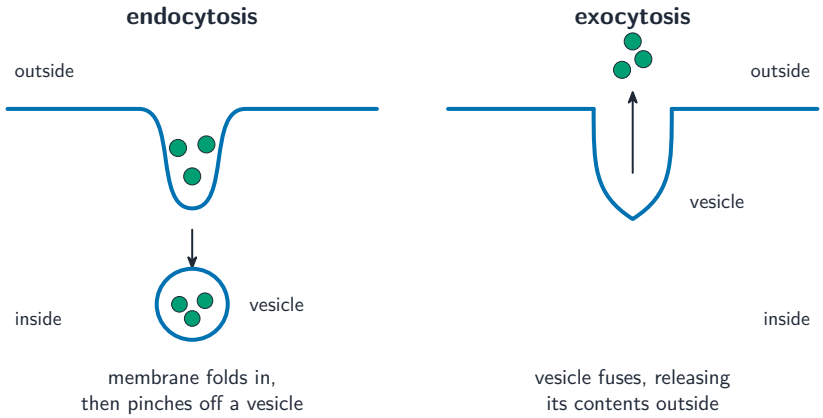
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### Endocytosis and exocytosis

These move large amounts of material in bulk, using ATP.

- in **endocytosis** 胞吞作用, the membrane folds inwards around material and pinches off a **vesicle** 囊泡 to bring it into the cell.
- in **exocytosis** 胞吐作用, a vesicle fuses with the membrane and releases its contents outside the cell.

Endocytosis of solid material (such as a bacterium taken in by a white blood cell) is called **phagocytosis** 吞噬作用; endocytosis of liquid is **pinocytosis** 胞饮作用. Exocytosis releases, for example, digestive enzymes from pancreas cells and mucus from goblet cells. ATP is needed to move the vesicles along the cytoskeleton and to change the shape of the membrane.




*Endocytosis brings material in by forming a vesicle; exocytosis fuses a vesicle to release its contents*

## Surface area to volume ratio

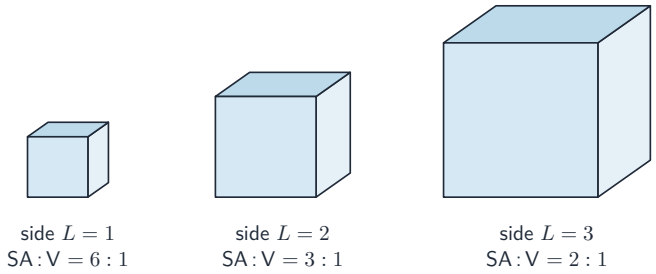
A cell takes in and removes substances across its surface. As an object gets bigger, its **volume** 体积 grows faster than its **surface area** 表面积. So the surface area to volume ratio gets **smaller** as size increases.

For a cube of side $L$:

$$\text{surface area} = 6L^2, \qquad \text{volume} = L^3, \qquad \text{ratio} = \frac{6}{L}.$$

A large $L$ gives a small ratio. This is why small cells (and thin, flat shapes) exchange materials quickly, while large cells cannot rely on diffusion alone.






a bigger cube (or cell) has a **smaller** surface area : volume ratio

*As a cube (or cell) grows, its surface area : volume ratio gets smaller*

**Worked example.** Compare the surface area : volume ratio of a cube-shaped cell of side 4 with one of side 10.

For side 4: surface area $= 6 \times 4^2 = 96$ and volume $= 4^3 = 64$, so the ratio is $96 : 64 = 1.5 : 1$. For side 10: surface area $= 6 \times 10^2 = 600$ and volume $= 10^3 = 1000$, so the ratio is $600 : 1000 = 0.6 : 1$. The larger cell has the smaller ratio, so it exchanges materials across its surface more slowly for its size – which is why large organisms need specialised exchange surfaces such as lungs and gills.

You can show this with **agar** 琼脂 blocks of different sizes soaked in dye or acid: the smallest block, with the largest surface area to volume ratio, changes colour all the way through fastest. Diffusion across non-living materials can also be studied with **dialysis tubing** 透析袋 (Visking tubing).

**The agar-block method.** Make agar containing an indicator (such as phenolphthalein, which is pink in alkali), and cut cubes of side 0.5, 1, 2 and 3 cm with a scalpel and ruler. Put each in the same volume of dilute hydrochloric acid at the same temperature, and time how long each takes to become **completely colourless**, or measure the depth of colourless agar after a fixed time. Acid diffuses in at the same rate per unit area in every block, so the depth reached in a given time is about the same; but in a large block that depth is a much smaller fraction of the whole, so the centre takes much longer to change. Keep the acid concentration, temperature and volume the same, and cut the cubes carefully, as errors in a small cube's side make a big difference to its surface area and volume.

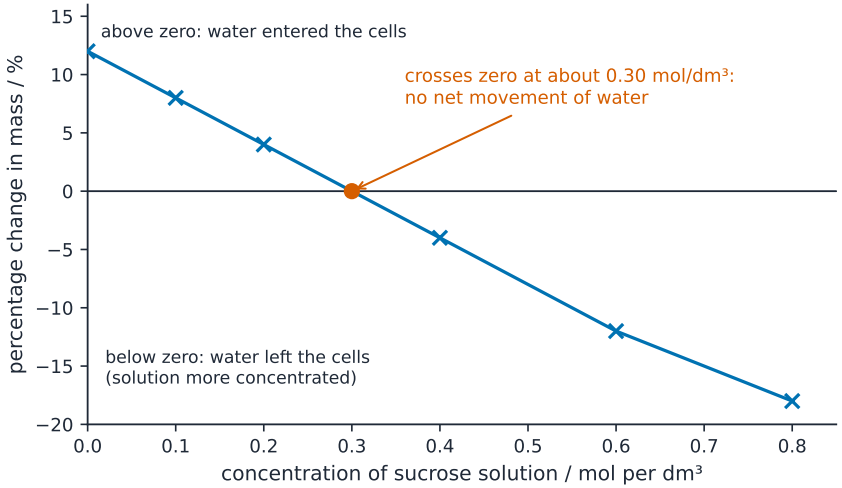
**Dialysis (Visking) tubing** is partially permeable: water and small molecules (glucose) pass through, but large ones (starch, sucrose in some tubing) do not. Fill a length with a solution, tie both ends, rinse it, and stand it in water; testing the water outside at intervals (for example with Benedict's solution or iodine) shows which molecules diffuse out. A tube of concentrated sucrose solution connected to a capillary tube makes the liquid rise, showing osmosis.



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## Water potential and living cells

**Water potential** measures how likely water is to leave a solution. Pure water has the highest water potential. Adding a **solute** 溶质 (a dissolved substance) lowers it. Water always moves by osmosis from a higher to a lower water potential.




*Where the line crosses zero, the solution matches the potato cells, so there is no net osmosis*

To estimate the water potential of plant tissue, you place pieces in sucrose solutions of different water potentials. The solution that causes **no change** in mass or length has about the same water potential as the tissue.

**Method.** Cut cylinders of potato of the same length and diameter with a cork borer, remove the skin, blot them dry and weigh each one. Put them in a series of sucrose solutions (for example 0.0, 0.2, 0.4, 0.6, 0.8 and 1.0 mol $dm^{-3}$) for at least 30 minutes, then blot and reweigh. Calculate the **percentage change in mass**, because the cylinders did not all start at the same mass:

$$\text{percentage change} = \frac{\text{final mass} - \text{initial mass}}{\text{initial mass}} \times 100$$



> **Worked example.** A cylinder of 2.50 g is 2.30 g after soaking in 0.6 mol $dm^{-3}$ sucrose. Percentage change $= (2.30 - 2.50)/2.50 \times 100 = -8.0\%$: it lost water, so the solution had a **lower** water potential than the potato cells. Plot percentage change against sucrose concentration, and draw a line of best fit. Where the line crosses **zero** (say at 0.32 mol $dm^{-3}$), there was no net osmosis, so the potato cells have the same water potential as a 0.32 mol $dm^{-3}$ sucrose solution. Read the water potential of that solution from a table. Repeat each concentration three times and find the mean; blot every cylinder in the same way, as left-over surface water adds mass.

**Water potential in numbers.** Water potential has the symbol $\Psi$ (psi) and is measured in kilopascals (kPa). Pure water has $\Psi = 0$; any solution has a **negative** value, and the more solute, the more negative. For example, a cell with $\Psi = -700$ kPa next to a cell with $\Psi = -400$ kPa will **gain** water from it, because $-400$ is higher (less negative) than $-700$.

### Effect on plant cells

- in a solution of **higher** water potential (for example **distilled water** 蒸馏水), water enters the cell. The cell swells and becomes **turgid** 膨胀, but the strong cell wall stops it bursting.
- in a solution of **lower** water potential, water leaves. The cell contents shrink and the membrane pulls away from the cell wall – this is **plasmolysis** 质壁分离.

### Effect on animal cells

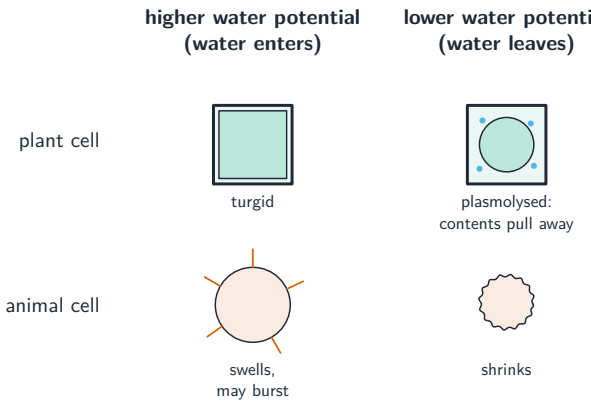
Animal cells have no cell wall to protect them.

- in a solution of higher water potential, water enters and the cell may burst. In a red blood cell this bursting is called **haemolysis** 溶血.
- in a solution of lower water potential, water leaves and the cell shrinks. A red blood cell shrinks and becomes wrinkled (it is **crenated**).

This is why solutions put into the blood in hospitals (such as saline drips) must have the same water potential as the blood plasma.



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*A plant cell becomes turgid or plasmolysed; an animal cell may burst (haemolysis) or shrink*

**Common mistakes.**

- Writing "water moves from a high concentration to a low concentration". This is unclear, because it could mean the concentration of water or of solute. Use water potential: water moves from a higher to a lower water potential.
- Saying the solute moves in osmosis. Osmosis is the movement of **water** only; the solute is usually too large to cross the membrane.
- Saying diffusion stops when the concentrations are equal. The particles keep moving both ways; only the **net** movement stops.
- Saying facilitated diffusion needs ATP because it uses proteins. Channel and carrier proteins only give a route; the substance still moves down its gradient, so no ATP is used.
- Saying a plant cell bursts in pure water. The cell wall pushes back, so the cell becomes turgid but does not burst.
- Saying the cell wall shrinks in plasmolysis. The wall keeps almost the same shape; the cytoplasm and membrane shrink and pull away from it.

## Exam tips

- Describe the membrane as a **fluid mosaic**: a phospholipid bilayer with proteins, cholesterol and glycoproteins.
- Sort each process: diffusion, facilitated diffusion and osmosis are **passive** (down a gradient); active transport and endo/exocytosis need **ATP** and can go against it.
- For osmosis always use **water potential** ($\Psi$): water moves from **high (less negative) to low (more negative)** $\Psi$; pure water is 0, the highest.



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- State the outcome by cell type: plant cell turgid/plasmolysed; animal cell lyses/crenates – link it to the water-potential gradient.
- Use **percentage** change in mass, and read the water potential where the line crosses zero.
- Beetroot: above about 40 °C membrane proteins denature and the bilayer becomes more fluid, so more pigment leaks out (higher absorbance).
- The $Na^+/K^+$ pump moves 3 $Na^+$ out and 2 $K^+$ in per ATP; anything that stops respiration stops active transport.

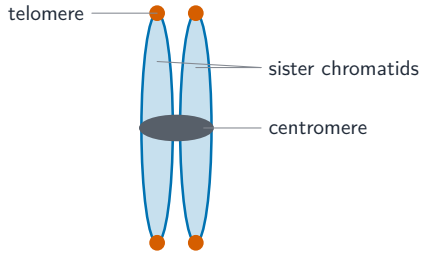
# The mitotic cell cycle

A-Level Biology

## The structure of a chromosome

A **chromosome** 染色体 is one very long molecule of DNA wound tightly around special **proteins** 蛋白质 called **histones** 组蛋白. Winding the DNA like this lets a huge length fit inside the nucleus and keeps it tidy.

Before a cell divides, its DNA is copied (this copying is called **replication** 复制). After copying, each chromosome is made of two identical copies joined together. These two copies are the **sister chromatids** 姐妹染色单体, and they are held together at a point called the **centromere** 着丝粒. The tips of each chromosome are capped by **telomeres** 端粒, which protect the ends.




one chromosome = two identical copies after DNA replication

*After replication a chromosome is two sister chromatids joined at the centromere, with telomeres at the tips*

## Why mitosis matters

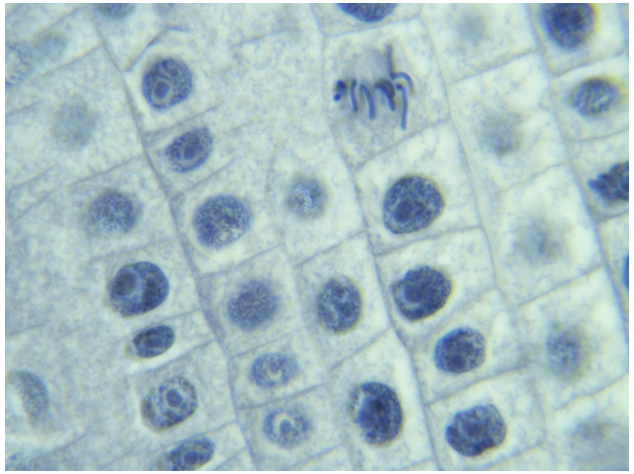
**Mitosis** 有丝分裂 is a type of nuclear division that makes two **daughter cells** 子细胞 that are **genetically identical** – they carry exactly the same **genes** 基因 as the parent cell and as each other.

This matters for:

- **growth** of **multicellular** 多细胞 **organisms** 生物体 (making more cells).
- **replacement** of damaged or dead cells.
- **repair** of **tissues** 组织 by making new cells.
- **asexual reproduction** 无性生殖 (one parent makes identical offspring).



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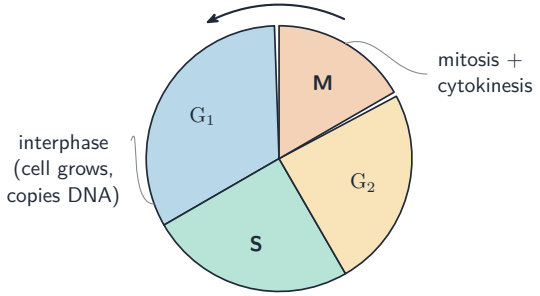


*Onion root tip at metaphase: mitosis produces identical body cells for growth and repair*

## The mitotic cell cycle

The **cell cycle** 细胞周期 is the full life of a cell from one division to the next. It has three parts:

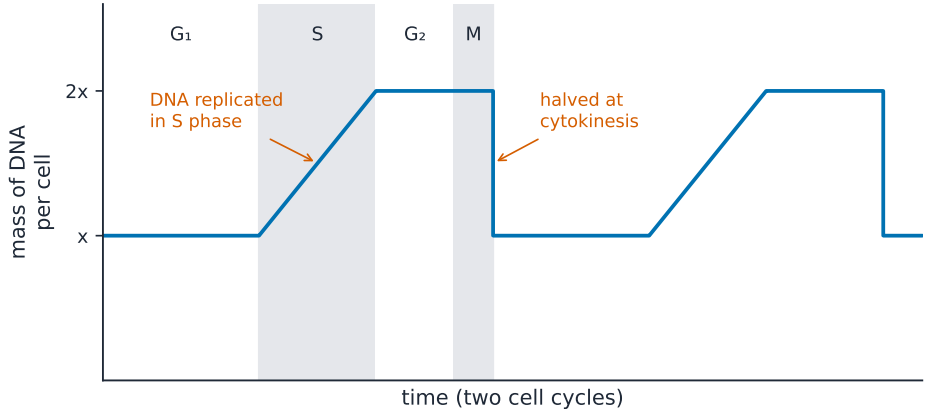
1. **interphase** 间期 – the longest part. The cell grows in the $\mathbf{G_1}$ phase, copies its DNA in the **S** phase (replication), and grows again and prepares to divide in the $\mathbf{G_2}$ phase.
2. **mitosis** – the nucleus divides into two identical nuclei.
3. **cytokinesis** 胞质分裂 – the rest of the cell splits, giving two separate daughter cells.




*Most of the cycle is interphase ($G_1$, $S$, $G_2$); mitosis ($M$) and cytokinesis are a short part*

What the cell does in each phase of interphase:

- **$G_1$**: the cell grows, makes proteins (including the enzymes needed for DNA replication) and new organelles such as mitochondria and ribosomes.
- **S**: every DNA molecule is **replicated**, and new histones are made, so each chromosome becomes two sister chromatids.
- **$G_2$**: the cell keeps growing, makes the proteins of the spindle (tubulin), and stores energy (ATP) for division. It checks the copied DNA for errors before mitosis begins.




*DNA per cell doubles during S phase and halves when the cell divides*

A graph of DNA per cell is a common exam question. The amount doubles gradually during **S** (not suddenly), stays at $2x$ through $G_2$ and mitosis, and halves when the cytoplasm divides at **cytokinesis**, so each daughter cell has the same amount ($x$) as the parent cell had in $G_1$.

### The mitotic index

The mitotic index is the fraction of cells in a sample that are in mitosis. You find it by counting cells under a microscope:

$$\text{mitotic index} = \frac{\text{number of cells in mitosis}}{\text{total number of cells}}.$$

**Worked example.** In a root-tip sample, 8 of the 50 cells seen are in mitosis. Find the mitotic index.

$$\text{mitotic index} = \frac{8}{50} = 0.16.$$

A high mitotic index means many cells are dividing quickly – normal in a growing root tip, but in adult animal tissue it can be a warning sign of uncontrolled growth.

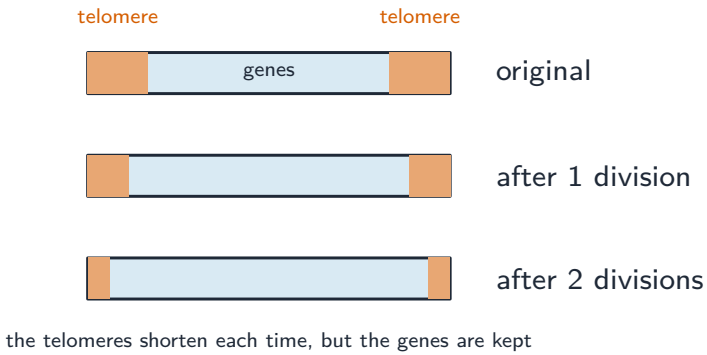


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**Worked example (timing the stages).** In a root tip the cell cycle takes 24 hours. Of 200 cells counted, 176 are in interphase, 14 in prophase, 4 in metaphase, 2 in anaphase and 4 in telophase. Estimate how long each stage lasts. A cell spends time in each stage in proportion to the number of cells found in it, so time = (cells in stage ÷ total) × cycle length. Interphase: $176/200 \times 24 = 21.1$ h. Prophase: $14/200 \times 24 = 1.7$ h. Metaphase: $4/200 \times 24 = 0.48$ h (about 29 min). Anaphase: $2/200 \times 24 = 0.24$ h (about 14 min), the shortest. Telophase: about 29 min. The mitotic index is $24/200 = 0.12$. To make the estimate reliable, count many cells in several fields of view, and only in the dividing zone just behind the root tip.

## Telomeres and the ends of chromosomes

When DNA is replicated, the copying cannot reach the very end of the molecule, so a little is lost each time. Telomeres are short, repeated lengths of DNA at the ends that carry **no genes**. Because the telomeres are shortened instead, no important genes are lost during replication.

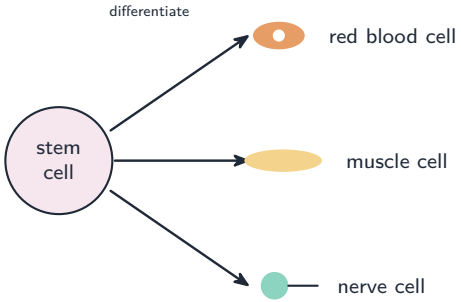



*The telomeres (which carry no genes) shorten a little at each division, so the genes in the middle are never lost*

Telomeres are made of a short base sequence (in humans TTAGGG) repeated thousands of times. After many divisions they become too short, and the cell stops dividing – one reason body cells can divide only a limited number of times. Stem cells, and most cancer cells, make an enzyme (**telomerase** 端粒酶) that adds the repeats back, so they can keep dividing.

## Stem cells

A **stem cell** 干细胞 is an unspecialised cell that can keep dividing by mitosis and can **differentiate** 分化 (change) into different specialised cell types. Stem cells are the source of new cells for replacing lost cells and repairing tissues.




*One unspecialised stem cell can differentiate into many specialised cell types*

Stem cells differ in how many cell types they can produce:

| Type | Can become | Example |
|---|---|---|
| **totipotent** 全能的 | any cell type, including the placenta | the zygote and the first few cells of an embryo |
| **pluripotent** 多能的 | almost any cell type of the body | embryonic stem cells in the early embryo |
| **multipotent** 专能的 | a limited range of related cells | bone marrow stem cells (all the kinds of blood cell) |

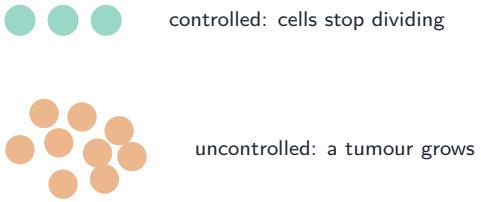
In an adult, stem cells replace cells that are lost all the time. Stem cells in the **bone marrow** divide by mitosis to make about 2.5 million new red blood cells every second, as well as white blood cells; stem cells at the base of the skin's epidermis and in the lining of the small intestine replace cells that are worn away. When a tissue is damaged, stem cells divide by mitosis to make new cells that then differentiate to repair it. Because the new cells are made by mitosis, they are genetically identical to the cells they replace.

## Uncontrolled division and tumours

The cell cycle is normally tightly controlled, so cells divide only when needed. If this control is lost, a cell may divide again and again without stopping. This uncontrolled division produces a lump of cells called a **tumour** 肿瘤.

**How control is lost.** The cell cycle is controlled by genes. Some genes code for proteins that **stimulate** division when it is needed; others code for proteins that **stop** the cycle at checkpoints (for example if the DNA is damaged) or that make a damaged cell destroy itself. A **mutation** 突变 in one of these genes can switch division permanently on, or remove the brake. Mutations build up over time, and are made more likely by **carcinogens** 致癌物 such as tobacco smoke, ultraviolet light and X-rays. A cell with enough mutations divides by mitosis again and again, ignoring the signals that would normally stop it, and all its daughter cells carry the same mutations.

A **benign** 良性的 tumour grows slowly and stays in one place, inside a capsule. A **malignant** 恶性的 tumour (a **cancer**) grows quickly and invades nearby tissue; cells can break away and travel in the blood or lymph to form new tumours elsewhere (**metastasis** 转移). A tumour can damage the organ it is in, press on nearby organs or blood vessels, and take nutrients and oxygen from normal tissue.




*Normally cells stop dividing when they should; if that control is lost, they keep dividing into a tumour*

## The stages of mitosis

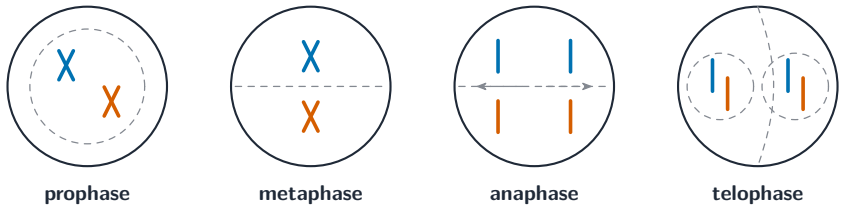
Mitosis runs through four stages. You should be able to recognise them in photomicrographs and slides.

| Stage | What happens |
|---|---|
| **prophase** 前期 | chromosomes coil up and become visible as two sister chromatids; the **nuclear envelope** 核膜 breaks down; a **spindle** 纺锤体 of fibres forms across the cell |
| **metaphase** 中期 | chromosomes line up along the middle (the **equator** 赤道); spindle fibres attach to each centromere |
| **anaphase** 后期 | the centromeres split; the sister chromatids are pulled to opposite ends (poles) of the cell |
| **telophase** 末期 | a set of chromosomes reaches each pole; a new nuclear envelope forms around each set, making two nuclei |

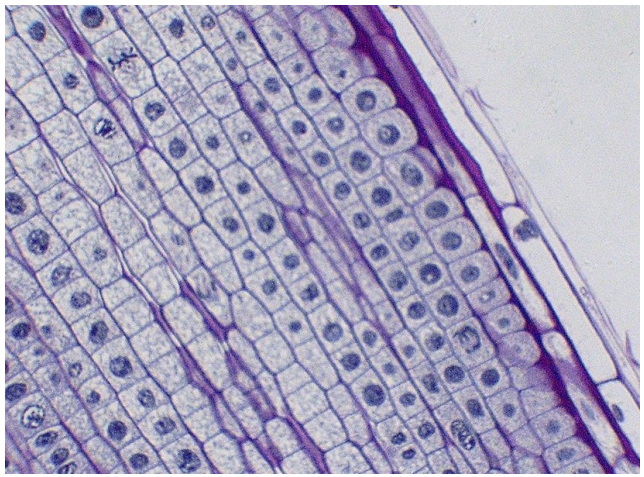




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*The four stages: prophase, metaphase, anaphase, telophase*



*A real onion root tip: in a growing tip many cells are caught dividing*

Cytokinesis then follows. In an animal cell the cell surface membrane pinches inwards to split the cell; in a plant cell a new wall forms across the middle. The result is two genetically identical daughter cells.

**Plant and animal cells compared.**

| | Animal cell | Plant cell |
|---|---|---|
| spindle forms from | two **centrioles** 中心粒, which move to opposite poles in prophase | the cytoplasm at each pole (no centrioles) |
| cytokinesis | the cell surface membrane pinches in from the outside (a cleavage furrow) | vesicles line up at the equator and fuse to form a **cell plate**, which grows outwards into a new cell wall |
| where in the body | in most tissues | only in **meristems** 分生组织, such as root and shoot tips |



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**Identifying the stages in a photomicrograph.** Look at the chromosomes, not the size of the cell. Visible threads still inside an intact nucleus, or a nucleus that has just gone: **prophase**. A neat line across the middle: **metaphase**. Two groups of V-shaped chromatids moving apart (the centromeres lead, the arms trail behind): **anaphase**. Two separate groups at the poles, perhaps with a new cell wall or a furrow starting between them: **telophase**. A round nucleus with a clear nucleolus and no visible chromosomes: **interphase**.

**Common mistakes.**

- Saying DNA is copied in prophase. It is copied earlier, in the **S phase** of interphase; by prophase each chromosome already has two chromatids.
- Calling interphase a "resting" phase. The cell is very active: it grows, makes proteins and organelles, and replicates its DNA.
- Saying the chromosome number doubles in the S phase. The amount of DNA doubles, but the number of chromosomes stays the same: each chromosome now has two chromatids joined at a centromere.
- Putting the splitting of the centromeres in metaphase. In metaphase the chromosomes only line up; the centromeres split at the start of **anaphase**.
- Counting a cell as "in mitosis" for the mitotic index just because its nucleus is visible. Count only cells whose chromosomes are visible as threads (prophase to telophase).

## Exam tips

- Learn the stages **in order** (prophase, metaphase, anaphase, telophase) with one key event each; interphase (G1, S, G2) is **not** part of mitosis.
- Mitosis gives **two genetically identical diploid** cells – for growth, repair and asexual reproduction.
- **Mitotic index** = cells in mitosis ÷ total cells; a high value means rapid division.
- Link **uncontrolled mitosis** to tumours and telomere shortening to the limit on the number of divisions.
- On a DNA-mass graph, the doubling slopes up through S phase; the halving is at cytokinesis.
- Time in a stage = (cells in that stage ÷ total cells counted) × length of the cycle.
- Tumour answers: mutation in a gene that controls the cell cycle → cells divide by mitosis without control → a mass of cells.

# Nucleic acids and protein synthesis

A-Level Biology

## Nucleotides – the building blocks

**Nucleic acids** 核酸 (DNA and RNA) are polymers of small units called **nucleotides** 核苷酸. Each nucleotide is made of three parts joined together:

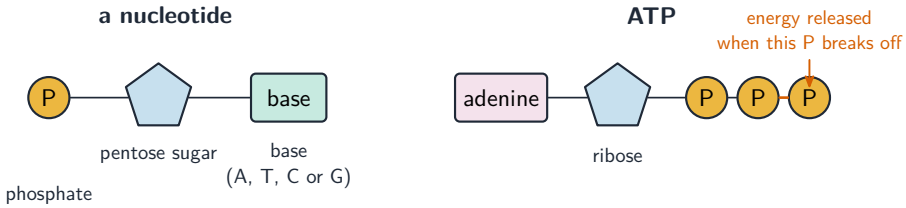
- a **phosphate** 磷酸 group,
- a sugar (a 5-carbon sugar),
- a nitrogen-containing **base** 碱基.

**ATP** is a special nucleotide. It has the base **adenine** 腺嘌呤, the sugar **ribose** 核糖, and **three** phosphate groups. Breaking off the last phosphate releases **energy** 能量 for the cell.

The reaction is a **hydrolysis**, catalysed by the enzyme ATPase:

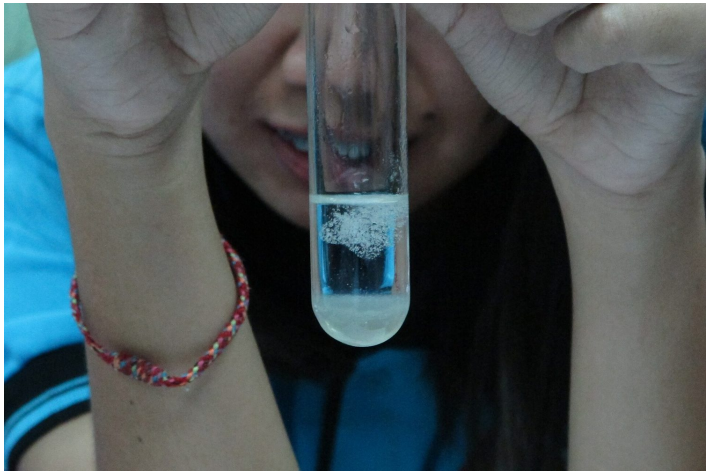
$$\mathrm{ATP} + \mathrm{H_2O} \rightarrow \mathrm{ADP} + \mathrm{P_i} \qquad \Delta G = -30.5 \text{ kJ mol}^{-1}$$

ATP suits its job as the cell's **energy currency**: it releases energy in small, usable amounts; it is soluble and moves easily around the cell; it is broken down in one quick step; and it is quickly remade from ADP and phosphate in respiration. It cannot be stored in large amounts, so it is made all the time, in the cell where it is needed.




*A nucleotide is a phosphate, a sugar and a base; ATP is a nucleotide with three phosphates*

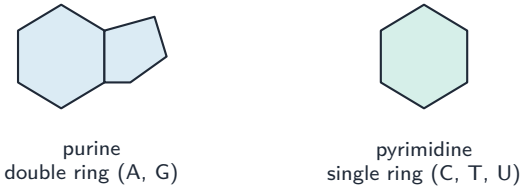




*DNA extracted from cells appears as pale, stringy strands of these nucleotide polymers*

There are five bases, in two groups:

- **purines** 嘌呤 have a **double ring** (two rings): adenine and **guanine** 鸟嘌呤.
- **pyrimidines** 嘧啶 have a **single ring** (one ring): **cytosine** 胞嘧啶, **thymine** 胸腺嘧啶 and **uracil** 尿嘧啶.




*The two groups differ in shape: a purine is a double ring, a pyrimidine a single ring – which is why a purine always pairs with a pyrimidine*

## The structure of DNA

A DNA molecule is two strands twisted together into a **double helix** 双螺旋.

Each **strand** 链 has a backbone of alternating sugar (here the sugar is **deoxyribose** 脱氧核糖) and phosphate. The sugar of one nucleotide is joined to the phosphate of the next by a **phosphodiester bond** 磷酸二酯键.

The two strands are held together by their bases, which meet in the middle. The pairing is exact – this is **complementary base pairing** 碱基互补配对:

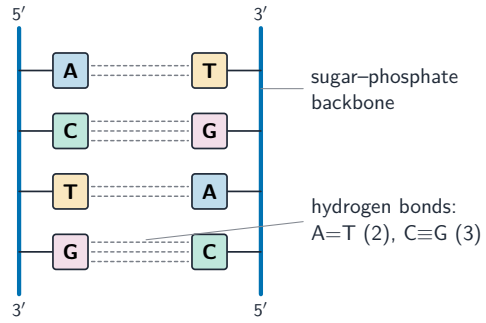
- A always pairs with T, held by **two hydrogen bonds** 氢键.



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- C always pairs with G, held by **three** hydrogen bonds (so a C–G **base pair** 碱基对 is harder to separate).

The two strands run in opposite directions: one goes 5′ to 3′ while the other goes 3′ to 5′. We say they are **antiparallel** 反平行.




the two strands run in opposite directions (antiparallel)

*Complementary base pairing: A pairs with T (2 hydrogen bonds), C with G (3); the strands are antiparallel*

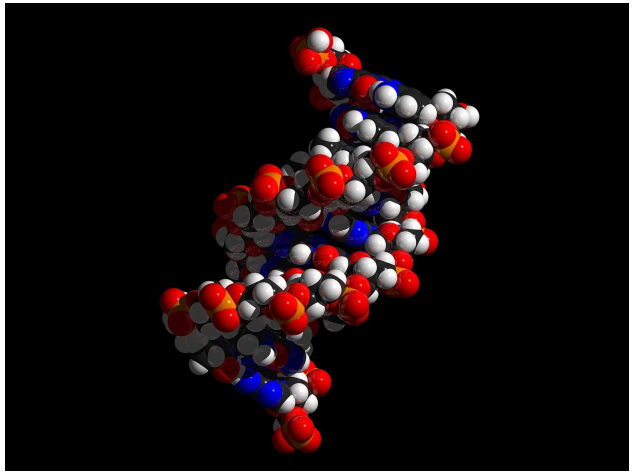
Base pairing is between a **purine** and a **pyrimidine**, so every base pair is the same width, and the two backbones stay a fixed distance apart. The bases are on the **inside** of the helix, protected by the backbone.

> **Worked example.** In a sample of DNA, 22% of the bases are adenine. What percentages are thymine, guanine and cytosine? A pairs with T, so thymine = 22%. Together A and T make 44%, leaving 56% for G and C. G pairs with C, so each is $56 \div 2 = 28\%$. This rule only works for **double-stranded** DNA; in single-stranded RNA, the amounts of A and U need not be equal.

The flat ladder above is twisted into a spiral. This space-filling model, where every atom is a ball, shows the real shape of the **double helix**:



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*A space-filling model of DNA: the two strands twist around each other into the **double helix** – the ladder of the diagram, coiled up*

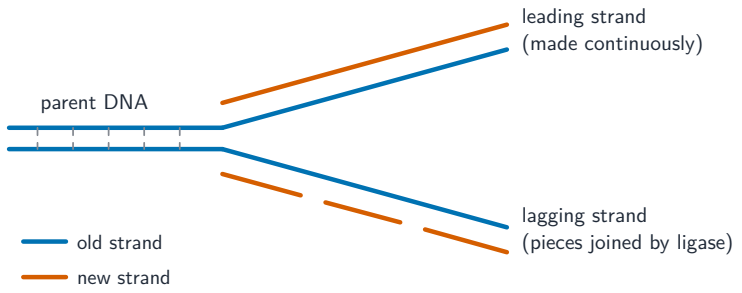
## DNA replication

DNA **replication** 复制 (copying) happens during the S phase of the cell cycle. It is **semi-conservative** 半保留复制: each new molecule keeps one old strand and one new strand. The steps are:

1. the double helix unwinds and the hydrogen bonds break, so the two strands separate.
2. each old strand acts as a template. Free nucleotides pair with the exposed bases by complementary base pairing.
3. the **enzyme** 酶 **DNA polymerase** 聚合酶 joins the new nucleotides into a strand. It can only add nucleotides in the 5′ to 3′ direction.

Because of that 5′ to 3′ rule, the two new strands are made differently:

- the **leading strand** 前导链 is built continuously, following the unwinding.
- the **lagging strand** 后随链 is built in short pieces, working away from the unwinding point. The enzyme **DNA ligase** 连接酶 then joins these pieces together.




each new molecule = one old strand + one new strand (semi-conservative)

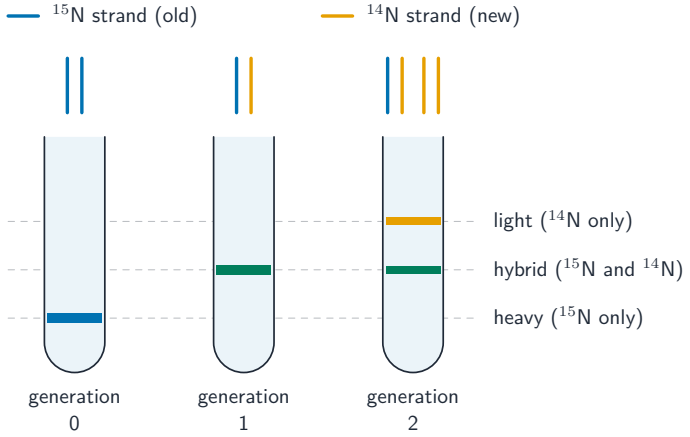
*Replication is semi-conservative: each new molecule keeps one old strand (blue) and one new strand (orange)*

The enzyme **helicase** 解旋酶 unwinds the helix and breaks the hydrogen bonds between the bases. Free nucleotides in the nucleus are **activated** (they carry extra phosphates), and the energy released when these are removed is used to form the phosphodiester bonds. Replication starts at many places along each chromosome at once, so a long molecule is copied quickly. Because the bases are copied by complementary base pairing, each new molecule is an almost exact copy of the old one.

### The evidence: Meselson and Stahl

1. Bacteria were grown for many generations in a medium whose only nitrogen was the **heavy** isotope $^{15}$N, so all their DNA contained $^{15}$N.
2. They were moved to a medium containing only the normal, **light** isotope $^{14}$N, and allowed to divide.
3. Samples were taken after each generation. The DNA was extracted and **centrifuged** in a solution of caesium chloride; DNA settles at the level that matches its density, so heavier DNA forms a band lower down the tube.






*Meselson and Stahl: one hybrid band after one generation, then hybrid and light bands, as semi-conservative replication predicts*

After **one** generation, all the DNA formed a single band at the **hybrid** density, halfway between heavy and light: each molecule had one $^{15}$N strand and one $^{14}$N strand. This ruled out **conservative** replication (which would give one heavy and one light band). After **two** generations, half the DNA was hybrid and half was light – exactly what semi-conservative replication predicts.

> **Worked example.** What would you expect after three generations? Each generation, every molecule separates into two strands, and each strand gets a new $^{14}$N partner. Of the 8 molecules from one original heavy molecule, the two original $^{15}$N strands are still each in one hybrid molecule; the other 6 are light. So $2/8 = 25\%$ hybrid and 75% light, with no heavy band.

## RNA

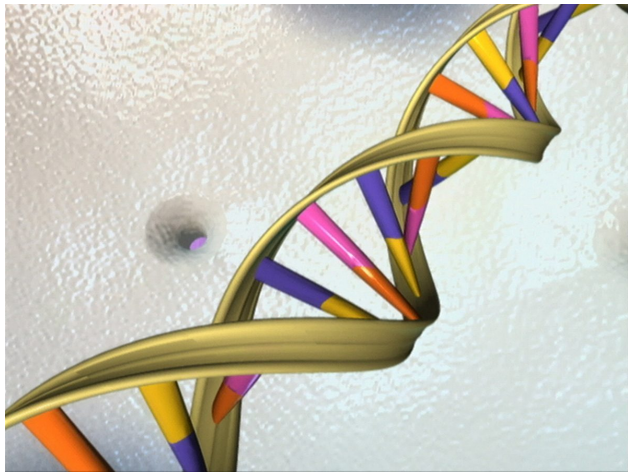
RNA is also made of nucleotides, but it is a single strand, its sugar is ribose, and it uses uracil in place of thymine. The most important type here is **messenger RNA (mRNA)**, which carries a copy of a gene's instructions out of the nucleus to be used.



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| Feature | DNA | RNA |
|---|---|---|
| sugar | deoxyribose | ribose |
| bases | A, T, C, G | A, U, C, G |
| strands | two, in a double helix | one (tRNA folds back on itself) |
| length | very long (millions of nucleotides) | short (hundreds to a few thousand) |
| where found | mostly in the nucleus | made in the nucleus, works mostly in the cytoplasm |
| job | stores the genetic information | mRNA carries a copy of a gene; tRNA brings amino acids; rRNA forms ribosomes |

**Transfer RNA (tRNA)** is a short strand, about 80 nucleotides long, folded into a clover-leaf shape held by hydrogen bonds between complementary bases. At one end is a site where a **specific amino acid** attaches; on a loop at the other end is the **anticodon**, a triplet of bases. **Ribosomal RNA (rRNA)**, together with proteins, makes up the ribosomes.



*DNA double helix: RNA is a related nucleic acid that carries genetic information into protein synthesis*



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## The genetic code

A **gene** 基因 is a sequence of DNA nucleotides that codes for one **polypeptide** 多肽.

The code is read in **triplets** 三联体 – groups of three bases. Each triplet either codes for one specific **amino acid** 氨基酸, or acts as a start or stop signal. The code is **universal**: nearly all living things use the same triplets for the same amino acids.

There are 64 possible triplets but only 20 common amino acids, so most amino acids are coded by more than one triplet.

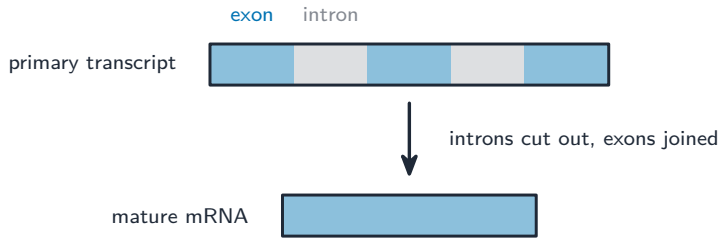
The code is also **non-overlapping**: each base is part of only one triplet, and the triplets are read one after another from a fixed starting point. The **start codon** (AUG on mRNA, which also codes for the amino acid methionine) marks where translation begins; three **stop codons** (UAA, UAG and UGA) code for no amino acid and end the polypeptide.

## Protein synthesis: transcription and translation

### Transcription (in the nucleus)

The DNA gene is copied into mRNA. This is **transcription** 转录.

- the strand of DNA that is copied is the **template strand** 模板链; the partner strand is the **non-transcribed strand** 非转录链.
- the enzyme **RNA polymerase** joins RNA nucleotides that pair with the template bases (with uracil pairing to adenine).
- in eukaryotes the first RNA made (the **primary transcript** 初级转录本) contains coding parts called **exons** 外显子 and non-coding parts called **introns** 内含子. The introns are cut out and the exons joined together to form the finished mRNA.




*Splicing: the non-coding introns are cut out and the coding exons joined to make the finished mRNA*

### Translation (at the ribosome)

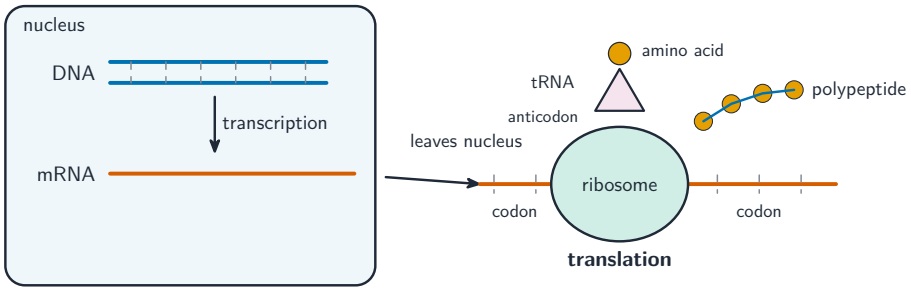
The mRNA leaves the nucleus and attaches to a **ribosome** 核糖体. Building the polypeptide from the mRNA code is **translation** 翻译.

- the mRNA is read in **codons** 密码子 (each codon is one triplet of mRNA bases).
- molecules of **transfer RNA (tRNA)** bring amino acids to the ribosome. Each tRNA has an **anticodon** 反密码子 that pairs with a matching codon.
- as the codons are read in order, the ribosome joins the amino acids with **peptide bonds** 肽键, building the polypeptide.

**Translation, step by step.**

1. In the cytoplasm, each tRNA is joined to its own amino acid by a specific enzyme, using energy from **ATP**.
2. The mRNA binds to the small subunit of a ribosome, at the start codon. The ribosome holds two codons at a time.
3. A tRNA whose anticodon is **complementary** to the first codon pairs with it by hydrogen bonds; a second tRNA pairs with the next codon.
4. A **peptide bond** forms between the two amino acids, catalysed by the ribosome. The first tRNA lets go of its amino acid and leaves, to collect another.
5. The ribosome moves along the mRNA by **one codon**, and the next tRNA arrives. This repeats, adding one amino acid at a time.
6. At a **stop codon**, no tRNA binds; the finished polypeptide is released. It may then be folded and modified in the rough ER and Golgi body.

Several ribosomes can translate the same mRNA at once, one behind another, so many copies of the polypeptide are made quickly.




*Transcription copies DNA into mRNA in the nucleus; translation at the ribosome builds the polypeptide*



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**Worked example.** A DNA template strand reads `TAC GGA CTT`. Give the mRNA codons, and say how many amino acids this part of the gene codes for. Transcribe by **complementary base pairing**, remembering that RNA uses **uracil** in place of thymine: `TAC` gives `AUG`, `GGA` gives `CCU`, `CTT` gives `GAA`. So the mRNA reads `AUG CCU GAA`. Each codon codes for one amino acid, so this part codes for **three**: methionine (`AUG`, which is also the **start** codon), proline (`CCU`) and glutamic acid (`GAA`). Two errors cost most of the marks here: pairing A with **T** instead of **U** when writing mRNA, and transcribing the **coding** strand instead of the **template** strand. The mRNA is complementary to the template, and identical to the coding strand apart from U replacing T.

## Gene mutations

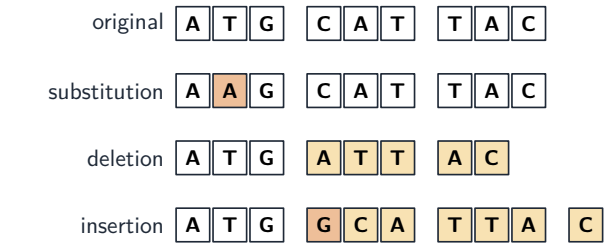
A gene **mutation** 突变 is a change in the base sequence of a DNA molecule. It may change the polypeptide made. There are three types:

- **substitution** 替换 – one base is swapped for a different base. This changes only one triplet: usually one amino acid changes, sometimes none (because most amino acids have more than one triplet), and if the new triplet is a stop codon the polypeptide is cut short.
- **deletion** 缺失 – a base is removed.
- **insertion** 插入 – an extra base is added.

A deletion or insertion shifts how every later triplet is read, so it usually changes many amino acids after that point and has a large effect on the polypeptide.

**Example: sickle cell anaemia.** In the gene for the $\beta$ chain of haemoglobin, a single **substitution** changes the triplet CTT to CAT on the template strand, so the mRNA codon GAA becomes GUA. The sixth amino acid of the $\beta$ chain becomes **valine** instead of **glutamic acid**. Valine is non-polar, while glutamic acid is charged, so at low oxygen concentration the haemoglobin molecules stick together into long fibres. These pull the red blood cells into a sickle shape; the cells carry less oxygen and block capillaries. One base change, one amino acid change – but a large effect, because that amino acid is on the surface of the molecule.

A mutation is more likely to have a big effect if it changes an amino acid in an enzyme's **active site**, or affects the bonds that hold the protein's shape, or makes an early stop codon. A deletion or insertion of **three** bases removes or adds one amino acid without a frameshift.




*A substitution changes one triplet; a deletion or insertion shifts every later triplet (a frameshift)*

**Common mistakes.**

- Saying DNA polymerase forms the hydrogen bonds between bases. The bases pair by themselves (complementary base pairing); DNA polymerase forms the **phosphodiester bonds** along the new strand.
- Saying DNA ligase joins base pairs. It joins the **pieces of the lagging strand**, along the sugar-phosphate backbone.
- Pairing A with T when writing **mRNA**. In RNA, A pairs with **U**.
- Saying the tRNA anticodon "codes for" the amino acid. The **codon** on the mRNA codes; the anticodon only makes sure the right tRNA binds.
- Saying every substitution changes the protein. Because the code is **degenerate** 简并 (most amino acids have more than one triplet), some substitutions change no amino acid at all.

## Exam tips

- DNA is **antiparallel**, held by hydrogen bonds (A=T two, C≡G three); replication is **semi-conservative** (each product keeps one old strand).
- State **where** and **what**: transcription (nucleus → mRNA), translation (ribosome, mRNA + tRNA → polypeptide).
- Describe the code with all four terms: **triplet, non-overlapping, degenerate, universal**.
- For a **gene mutation** (substitution, insertion, deletion) explain the effect on the protein – and why a substitution can be silent (degeneracy).
- Meselson and Stahl: one hybrid band after one generation rules out conservative replication; hybrid and light bands after two confirm semi-conservative.
- Base percentages: %A = %T and %C = %G in double-stranded DNA.



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- In translation, name the codon–anticodon pairing, the peptide bond, the ribosome moving one codon, and the stop codon.

# Transport in plants

A-Level Biology

## The two transport tissues

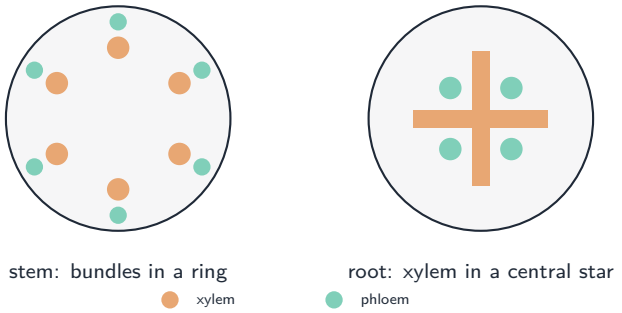
Plants move substances through two transport **tissues** 组织:

- **xylem** 木质部 carries water and dissolved **mineral ions** 矿物离子 up from the roots.
- **phloem** 韧皮部 carries dissolved foods (called **assimilates** 同化物, mainly sugars) to wherever they are needed.

In a **transverse section** 横切面 (a cut straight across) of a **dicotyledonous plant** 双子叶植物:

- in the **stem**, xylem and phloem sit together in bundles near the outside, with xylem on the inside of each bundle.
- in the **root**, the xylem is in the centre, often in a star shape, with phloem between the arms.
- in the **leaf**, both are found in the veins.

When you draw a plan diagram, you draw only the outlines of the tissues, not the single cells.




*Where the tissues sit: stem bundles form a ring near the edge (xylem inside); in the root the xylem makes a central star*



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*The wood of a tree trunk is xylem; each ring is one year of growth*

### Xylem vessels

Xylem water-carrying tubes are called **vessels** 导管. They are made of dead, empty cells joined end to end, with the end walls gone, so they form one long open pipe. Their walls are thickened and waterproofed with **lignin** 木质素. So the structure suits the job: the hollow, open tube with no contents lets water flow fast, and the lignin gives strength and support.

More features of xylem vessels:

- the lignin is laid down in rings, spirals or as a solid layer. It stops the vessel **collapsing** inwards under the tension of the water column, and makes the wall waterproof.
- small gaps in the lignin, called **pits** 纹孔, let water move sideways between neighbouring vessels and out to other cells, so water can go round a blocked or air-filled vessel.
- the vessels are narrow (about 0.01–0.2 mm across), so adhesion to the walls helps hold the water column up, and the column is less likely to break.
- xylem tissue also contains **tracheids** (narrow, tapering lignified cells), **fibres** (for support) and living **parenchyma** cells.

### Phloem sieve tubes and companion cells

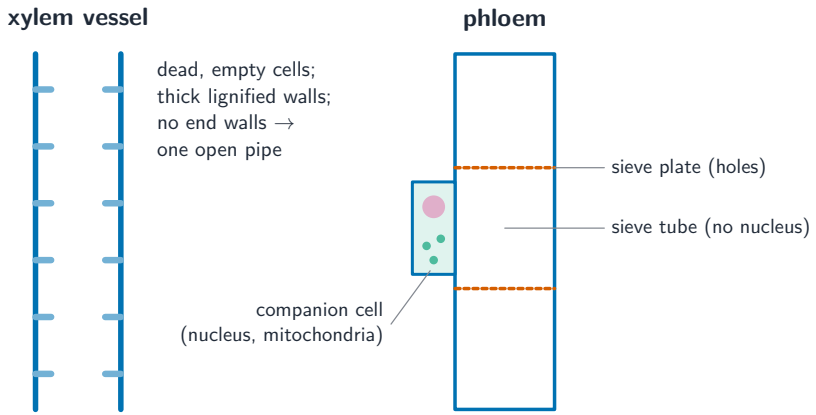
Phloem food-carrying tubes are called **sieve tubes** 筛管. They are living cells joined end to end, but their end walls are not gone – they become **sieve plates** 筛板 with many holes that sap flows through. To leave room for flow, a sieve tube cell loses most of its contents and has no nucleus.

Beside each sieve tube is a **companion cell** 伴胞. It keeps its **nucleus** 细胞核 and has many **mitochondria** 线粒体. It does the living work for the sieve tube and loads

sugars into it.

Many **plasmodesmata** link the companion cell to its sieve tube element, so the companion cell's nucleus and ribosomes can make the proteins the sieve tube needs. Its cell surface membrane is often folded inwards, giving a large area for the proton pumps and cotransporters that load sucrose.

| Feature | Xylem vessel | Phloem sieve tube |
|---|---|---|
| living or dead | dead | living (but no nucleus) |
| end walls | absent: a continuous tube | **sieve plates** with pores |
| walls | thick, lignified | thin, cellulose only |
| contents | none: water and mineral ions only | a thin layer of cytoplasm; phloem sap of sucrose and amino acids |
| direction of flow | up from roots to leaves only | from source to sink: up or down |
| how the flow is driven | tension from transpiration (passive) | pressure difference made by active loading of sucrose |

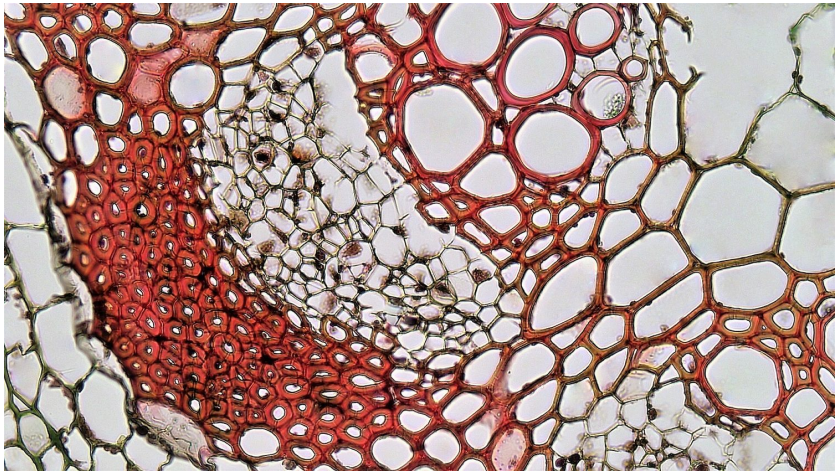



*Xylem is a dead, open pipe; phloem is living sieve tubes with sieve plates and companion cells*

This is what a real **vascular bundle** 维管束 looks like under the microscope, in a stained section of a young sunflower stem:



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*A real **vascular bundle** in section: the big red cells are xylem vessels (thick lignified walls); the smaller cells above are phloem*

## Water from the soil to the xylem

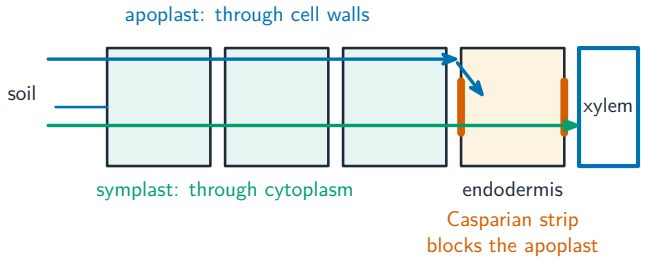
Water enters a **root hair cell** 根毛细胞 by **osmosis** 渗透, because the root hair has a lower water potential than the soil water. Water then crosses the root to the xylem by two pathways:

- the **apoplast pathway** 质外体途径 – water moves through the **cell walls** 细胞壁 (made of **cellulose** 纤维素) and the spaces between cells, without entering the cytoplasm. This is fast.
- the **symplast pathway** 共质体途径 – water moves through the cytoplasm of cells, passing from cell to cell through the **plasmodesmata** 胞间连丝.

At a ring of cells called the **endodermis** 内皮层, the apoplast pathway is blocked by the **Casparian strip** 凯氏带, a waterproof band of **suberin** 木栓质. This forces all the water through the cell membranes, which lets the plant control what enters the xylem.

**Mineral ions** are taken up into root hair cells mostly by **active transport**, because their concentration inside the cells is usually higher than in the soil. Their uptake needs ATP from respiration, so it stops if the roots are short of oxygen (as in waterlogged soil).

**Root pressure.** Endodermis cells actively pump mineral ions into the xylem. This lowers the water potential in the xylem, so water follows by osmosis, pushing the water up a short way. Root pressure is small and is not the main force in tall plants; it is shown by drops of sap oozing from a cut stem, and by drops of water at the leaf edges of some plants early in the morning. Because it depends on active transport, root pressure falls if a respiratory poison such as cyanide is added.




*The apoplast goes through the walls, the symplast through the cytoplasm; the Casparian strip blocks the apoplast at the endodermis*

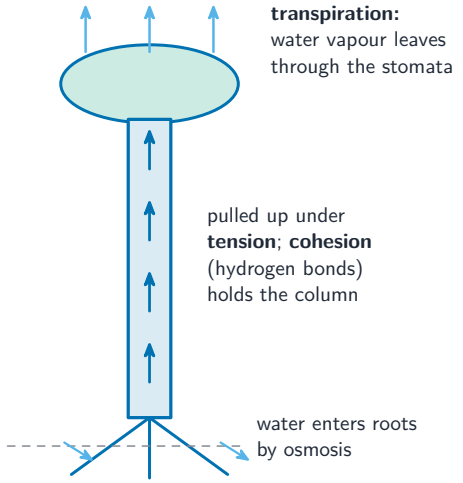
## Transpiration and the movement of water up the xylem

**Transpiration** 蒸腾作用 is the loss of water vapour from a plant. Water **evaporates** (turns to vapour) from the wet cell surfaces inside the leaf – this is **evaporation** 蒸发. The **water vapour** 水蒸气 then **diffuses** 扩散 out through the **stomata** 气孔 into the **atmosphere** 大气.

This loss at the top pulls water up the xylem in a continuous column. It works because of hydrogen bonding between water molecules:

- water molecules attract each other through **hydrogen bonds** 氢键, so they stick together. This sticking is **cohesion** 内聚力, and it lets the whole column be pulled up under **tension** 张力 (the cohesion–tension idea).
- water molecules also stick to the cellulose of the cell walls. This is **adhesion** 附着力, which helps hold the column in place.






*Transpiration at the leaf pulls the whole water column up the xylem; cohesion (hydrogen bonds) keeps it together*

**From the xylem to the air.** In the leaf, water leaves the xylem in the veins and moves to the **mesophyll** cells by the apoplast and symplast pathways. It evaporates from the wet walls of the spongy mesophyll cells into the **air spaces**, which are kept nearly saturated with water vapour. The vapour then diffuses out through the stomata, down a **water vapour potential gradient** to the drier air outside. As water evaporates from a mesophyll cell wall, more water is drawn into the wall from the cell next to it, and so on back to the xylem.

**Evidence for cohesion–tension.** The diameter of a tree trunk shrinks slightly in the middle of the day, when transpiration is fastest, because the tension in the xylem pulls the walls of the vessels inwards. If a xylem vessel is cut, air is drawn **in** rather than water leaking out, and the water column breaks, so the vessel can no longer carry water.



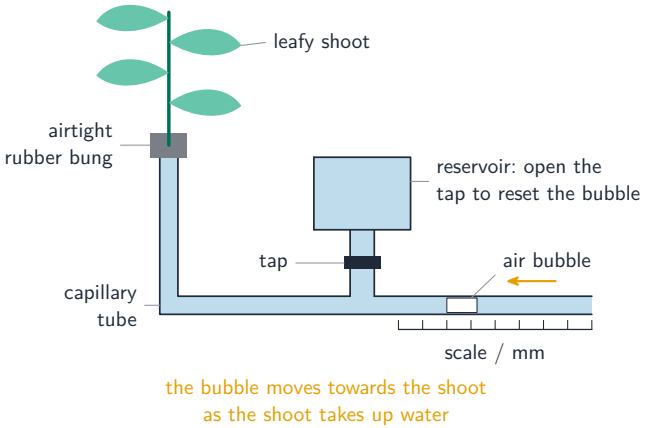
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## Factors that affect the rate of transpiration

| Factor | Effect | Why |
|---|---|---|
| light intensity | higher in light | stomata open in light, to let in $CO_2$ for photosynthesis |
| temperature | higher when warmer | water molecules have more kinetic energy, so they evaporate and diffuse faster; warm air also holds more water vapour, so the gradient is steeper |
| humidity | lower in humid air | less difference in water vapour concentration between the air spaces and the air outside |
| wind (air movement) | higher in wind | moist air near the stomata is blown away, keeping the gradient steep |
| water supply | lower when the soil is dry | the stomata close to save water |

## Measuring water uptake with a potometer

A **potometer** 蒸腾计 measures how fast a shoot **takes up** water, which is nearly the same as how fast it loses water by transpiration (a little is used in photosynthesis and to keep cells turgid).




*A potometer: as the shoot takes up water, the air bubble moves along the capillary tube*

1. Cut the shoot **under water**, at a slant, so that no air enters the xylem and breaks the water column.
2. Fit the shoot into the potometer under water, and make every joint **airtight** (with petroleum jelly), so that the only way water leaves is through the shoot. Dry the leaves.
3. Let the shoot settle for a few minutes in the conditions to be tested, then introduce an air bubble by lifting the end of the capillary out of the water for a moment.
4. Measure how far the bubble moves in a measured time. Reset it with water from the reservoir, and repeat three times.
5. Change one factor at a time (for example, a fan at different distances for wind, or a lamp at different distances for light, with a heat filter), keeping the others constant.

**Worked example.** In 5 minutes, the bubble moves 32 mm along a capillary tube of radius 0.5 mm. Calculate the rate of water uptake in $mm^3$ per minute. Volume of a cylinder $= \pi r^2 l = 3.14 \times 0.5^2 \times 32 = 25.1\ mm^3$. Rate $= 25.1 \div 5 = 5.0\ mm^3\ min^{-1}$. To compare shoots of different size, divide by the total **leaf area** (found by drawing round the leaves on graph paper), giving the rate per unit area.

**Worked example.** A plant cell with a water potential of −800 kPa is placed in a solution of water potential −400 kPa. Which way does water move, and what happens to the cell? Water always moves **down** a water potential gradient - from the **less negative** (higher) value to the **more negative** (lower) one. The solution at −400 is **higher** than the cell at −800, so water moves **into** the cell. The cell swells, the protoplast presses on the cell wall, the **pressure potential** rises, and the cell becomes **turgid**. Two traps: −400 is **greater** than −800, which is the sign error that reverses half of all answers; and pure water is the maximum at **0**, so every solution is negative and a water potential can never rise above zero.

## Xerophytes

A **xerophyte** 旱生植物 is a plant **adapted** 适应 to live where water is scarce. Its leaves reduce water loss by transpiration in several ways: a thick waxy **cuticle** 角质层, **stomata** sunk in pits, hairs that trap moist air, and leaves that can roll up. You should be able to draw a labelled leaf section showing these features.

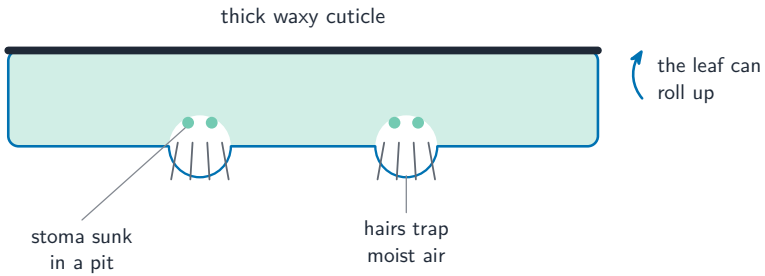
| Adaptation | How it reduces water loss | Example |
|---|---|---|
| thick waxy cuticle | waterproof barrier to evaporation from the epidermis | holly, cacti |
| sunken stomata in pits | moist air is trapped in the pit, so the water vapour gradient is less steep | marram grass, pine |



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| Adaptation | How it reduces water loss | Example |
|---|---|---|
| hairs on the leaf surface | trap a layer of still, moist air next to the stomata | marram grass (inside the rolled leaf) |
| rolled leaves | the stomata face into an enclosed space of humid air | marram grass |
| fewer stomata, or stomata only on the lower surface | less surface through which water vapour can escape | many desert plants |
| small leaves, needles or spines | smaller surface area for transpiration | pine needles, cactus spines |
| stomata that open at night | less water evaporates in the cool night; $CO_2$ is stored as an acid until day | cacti, pineapple |
| deep or widespread roots, water-storing stems | gain more water and store it | cacti |

**Marram grass** grows on sand dunes, where water drains away fast and there is often wind. Its leaves roll up in dry conditions, with the stomata on the inner surface, sunk in pits between ridges covered in hairs; the outer surface has a thick cuticle and no stomata.




*Xerophyte leaves cut water loss: a thick cuticle, sunken stomata, trapped moist air and rolling up*



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## Translocation: moving assimilates in the phloem

Assimilates such as **sucrose** 蔗糖 and **amino acids** 氨基酸 are carried in the phloem from a **source** 源 to a **sink** 库.

- a **source** is where the assimilate is made or released (for example a photosynthesising leaf).
- a **sink** is where it is used or stored (for example a growing root).

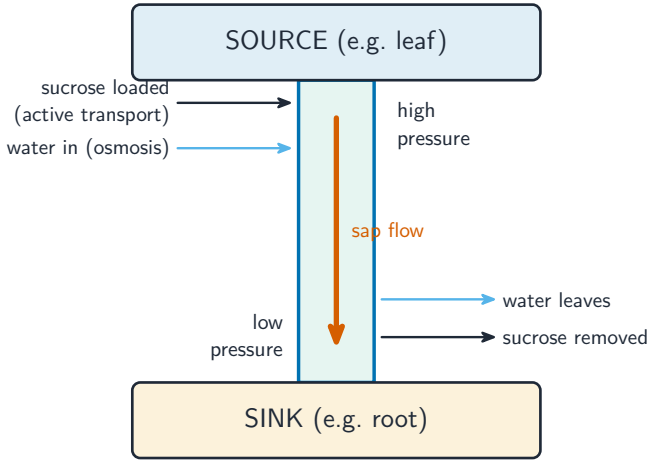
### Loading at the source

Companion cells load sucrose into the sieve tubes against its concentration gradient. They use **proton pumps** 质子泵 to pump hydrogen ions out, then **cotransporter proteins** 协同运输蛋白 bring sucrose back in together with those ions. This is a form of **active transport** 主动运输.

Loading sucrose lowers the **water potential** 水势 inside the sieve tube, so water follows by osmosis. This raises the **hydrostatic pressure** 静水压 there.

### Mass flow

At the sink, sucrose is removed, so the water potential rises, water leaves, and the pressure falls. The result is a pressure difference between source (high) and sink (low). Sap flows from high to low pressure down this gradient. This pressure-driven flow is called **mass flow** 集流.




*Loading sucrose at the source raises the pressure; sap then flows by mass flow to the sink*

**Loading in more detail.** Companion cells use ATP to pump hydrogen ions **out** into the cell walls around them. This makes a high concentration of hydrogen ions outside.

The hydrogen ions then diffuse back **into** the companion cell through cotransporter proteins, and each carries a sucrose molecule with it, against the sucrose concentration gradient. Sucrose then passes from the companion cell into the sieve tube through the plasmodesmata. At the sink, sucrose leaves the sieve tube (by diffusion or active transport) and is used in respiration or turned into starch for storage, which keeps its concentration low at the sink.

**Evidence for mass flow.**

- When an **aphid** feeds, its mouthparts pierce a single sieve tube. If the aphid is cut off, sap keeps flowing out of the mouthparts under pressure, and the sap contains sucrose – so the contents of sieve tubes are under pressure.
- The flow is faster than diffusion could ever be (up to about 1 m per hour).
- **Ringing**: if a ring of bark (containing the phloem) is removed from a tree trunk, the bark just above the ring swells, because sugars collect there.
- Phloem tissue uses a lot of ATP, and a respiratory poison stops translocation, which shows that loading is active.

Some observations do not fit the model perfectly: sucrose can move in different directions in neighbouring sieve tubes, and the sieve plates would seem to slow the flow a great deal.

**Common mistakes.**

- Saying water evaporates through the stomata. Water evaporates from the wet cell walls **inside** the leaf; the water vapour then **diffuses** out through the stomata.
- Saying the roots push or suck water up the stem. The main force is the **pull** from transpiration at the top, passed down the column by cohesion.
- Saying sucrose diffuses along the phloem. It is carried by **mass flow** of the whole sap, from high hydrostatic pressure at the source to low pressure at the sink.
- Saying phloem carries sugar only downwards. It carries assimilates from source to sink, which can be up (to a growing shoot tip) or down (to a root).
- Saying the Casparian strip stops water entering the root. It blocks only the **apoplast** route at the endodermis, so water must cross a cell membrane there.

## Exam tips

- State the tissue for each direction: **xylem** carries water up (dead, lignified), **phloem** carries assimilates both ways (living sieve tubes + companion cells).
- Explain water movement by **cohesion-tension**: transpiration pulls a continuous water column held by cohesion (H-bonds) and adhesion.
- List the factors affecting **transpiration rate** (light, temperature, humidity, air movement) and how a potometer measures uptake.
- For **xerophytes**, link each adaptation (thick cuticle, sunken stomata, rolled leaves, hairs) to reduced water loss.



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- Potometer: cut the shoot under water, seal every joint, change one factor at a time; volume $= \pi r^2 \times$ distance moved.
- A potometer measures water **uptake**, which is not quite the same as water loss.
- Explain a factor through the **water vapour gradient** between the air spaces and the air outside.
- Phloem loading: $H^+$ pumped out by companion cells, then $H^+$ and sucrose back in by **cotransport**; evidence for mass flow comes from aphid mouthparts and ringing.

# Transport in mammals

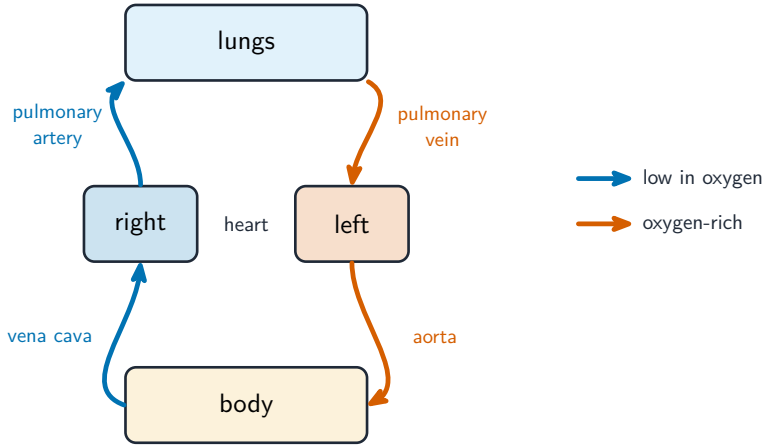
A-Level Biology

## The circulatory system

Mammals have a **closed double circulation**. "Closed" means the blood stays inside **blood vessels** 血管 the whole time. "Double" means the blood passes through the **heart** 心脏 twice for each full trip around the body. This gives two linked loops, so we call it a **double circulation** 双循环 and the whole thing a **circulatory system** 循环系统:

- the **pulmonary circulation** 肺循环 carries blood from the heart to the lungs and back.
- the **systemic circulation** 体循环 carries blood from the heart to the rest of the body and back.

Blood travels in this order: **arteries** 动脉 → **arterioles** 小动脉 → **capillaries** 毛细血管 → **venules** 小静脉 → **veins** 静脉.




*Double circulation: the pulmonary loop goes to the lungs, the systemic loop to the body; blood passes through the heart twice*

The main vessels are:

- the **pulmonary artery** 肺动脉 – carries blood low in **oxygen** 氧气 from the heart to the lungs.
- the **pulmonary vein** 肺静脉 – carries oxygen-rich blood from the lungs back to the heart.

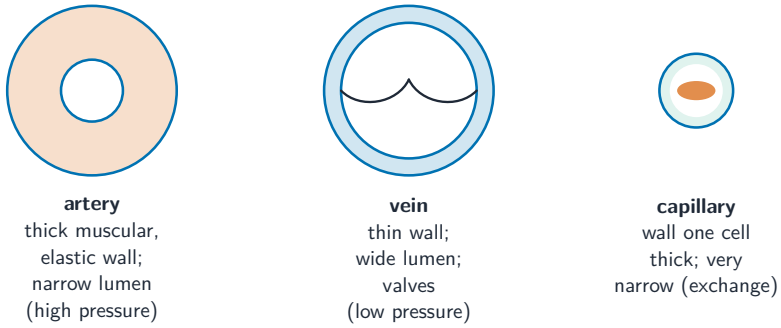


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- the **aorta** 主动脉 – the big artery that carries oxygen-rich blood from the heart to the body.
- the **vena cava** 腔静脉 – the big vein that returns oxygen-poor blood from the body to the heart.

### How the vessels suit their jobs

| Vessel | Structure | Function |
|---|---|---|
| artery | thick wall of **muscle** 肌肉 and **elastic** 弹性 fibres; narrow **lumen** 管腔 (the space inside) | carries blood at high pressure away from the heart; elastic walls stretch and **recoil** 回弹 to smooth the flow; muscle controls the flow |
| capillary | wall just one cell thick; very narrow | short distance for exchange of substances between blood and cells |
| vein | thin wall; wide lumen; has **valves** 瓣膜 | returns blood at low pressure to the heart; valves stop blood flowing backwards |




*An artery has a thick wall and narrow lumen; a vein a thin wall, wide lumen and valves; a capillary is one cell thick*

**The layers of the wall.** Arteries and veins have the same three layers, in different amounts:

- the inner **tunica intima**: a single layer of flat **endothelium** 内皮 cells, very smooth to reduce friction, on a thin layer of elastic fibres;
- the middle **tunica media**: **smooth muscle** and **elastic fibres**. It is very thick in arteries (elastic fibres dominate in the aorta and large arteries; muscle in smaller ones) and thin in veins;
- the outer **tunica externa**: mostly **collagen** 胶原蛋白 fibres, which are strong and stop the vessel over-stretching or bursting. It is the thickest layer in a vein.

A capillary wall is only the endothelium, often with small gaps between its cells, which let plasma out to form tissue fluid. Capillaries are about 7 µm across, just wide enough for one red blood cell at a time. **Arterioles** have much smooth muscle in proportion to their size: it contracts to narrow them (**vasoconstriction**) and relaxes to widen them (**vasodilation**), controlling how much blood reaches each organ.

**Recognising vessels in sections.** In a transverse section, an artery is round with a thick wall (wall thickness is a large share of its diameter), a narrow lumen, and a folded, wavy endothelium (because the elastic fibres recoil when the artery is cut). A vein is often flattened or irregular, with a thin wall and a wide lumen that may contain blood cells; a valve may be seen. A capillary is a ring of one or two flattened cells around a red blood cell. In an electron micrograph, the endothelium of a capillary is seen as a very thin layer with an occasional nucleus bulging into the lumen.

In a **plan diagram** of an artery or vein, draw the outlines of the three layers as concentric lines, keeping their relative thickness correct, and label tunica intima, media and externa and the lumen; do not draw cells.

## Blood cells

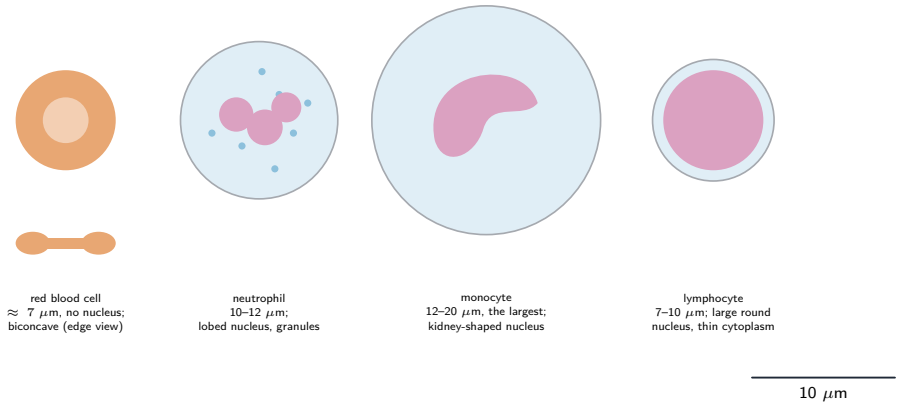
You should recognise: **red blood cells** 红细胞 (which carry oxygen), and three white blood cells – **monocytes** 单核细胞, **neutrophils** 中性粒细胞 and **lymphocytes** 淋巴细胞.

| Cell | Size | Nucleus | Other features |
|---|---|---|---|
| red blood cell | about 7 µm | none | biconcave disc, giving a large surface area; full of haemoglobin; flexible, so it squeezes through capillaries |
| neutrophil | 10–12 µm | one nucleus with 2–5 **lobes** | granular cytoplasm (lysosomes); phagocytosis of bacteria |
| monocyte | 12–20 µm, the largest | large, **kidney-shaped** | leaves the blood and becomes a macrophage |
| lymphocyte | 7–10 µm | large and round, filling almost the whole cell | a thin ring of cytoplasm; B cells make antibodies, T cells kill infected cells |

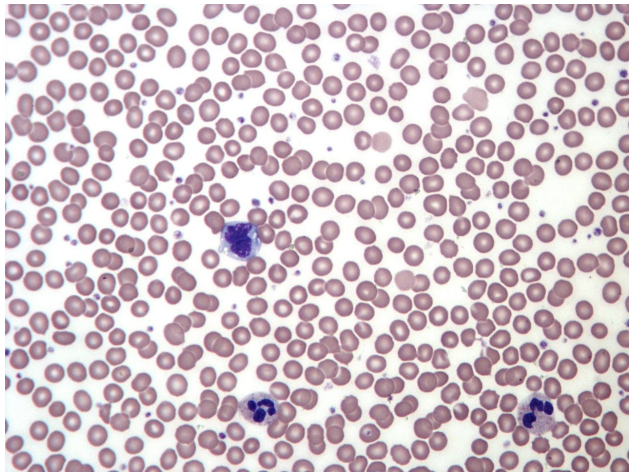
Red blood cells have no nucleus and no mitochondria, which leaves more room for haemoglobin; they respire anaerobically, so they use none of the oxygen they carry.



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*The four cells to recognise, roughly to scale*



*A stained **blood smear**: many small red cells, plus a lymphocyte (centre) and neutrophils (lobed nucleus) – the white cells are larger and have a nucleus*

## Water, plasma and tissue fluid

Water is the main part of blood. It is a good **solvent** 溶剂, so it carries dissolved substances, and it has a high **specific heat capacity** 比热容, so the blood's temperature stays steady.

At the start of a capillary, the high blood pressure pushes liquid (but not the cells or large proteins) out of the **plasma** 血浆 and through the capillary wall. This liquid around the cells is **tissue fluid** 组织液. It supplies the cells with oxygen and glucose and carries waste away. Most of it returns to the capillary at the far end, where the

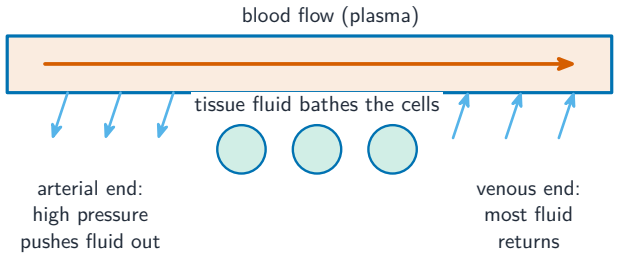
pressure is lower.

**Two forces.** Fluid movement across the capillary wall depends on two opposing forces:

- the **hydrostatic pressure** 静水压 of the blood, which pushes fluid **out**. It is high at the arterial end (about 4.3 kPa) and falls along the capillary as fluid leaves and friction slows the blood (to about 1.6 kPa).
- the **water potential** of the blood, which draws water back **in**. The plasma proteins (such as albumin) stay in the blood, so the plasma has a lower water potential than the tissue fluid; this effect stays about the same all along the capillary.

At the arterial end, hydrostatic pressure wins, so fluid is pushed out. At the venous end, the hydrostatic pressure has fallen below the pull of the water potential, so water returns by osmosis, carrying carbon dioxide and other wastes. About 10% of the tissue fluid does not return to the capillaries: it drains into blind-ended **lymph** 淋巴 vessels and is returned to the blood near the heart. If the blood pressure is too high, or the plasma has too little protein (for example in severe malnutrition), tissue fluid builds up and the tissues swell (**oedema** 水肿).

The functions of tissue fluid: it carries oxygen, glucose, amino acids, ions and hormones from the blood to the cells; it carries carbon dioxide, urea and other wastes from the cells back to the blood; and it gives the cells a steady surrounding liquid. Tissue fluid has the same make-up as plasma, except that it has almost no proteins and no red blood cells or platelets.

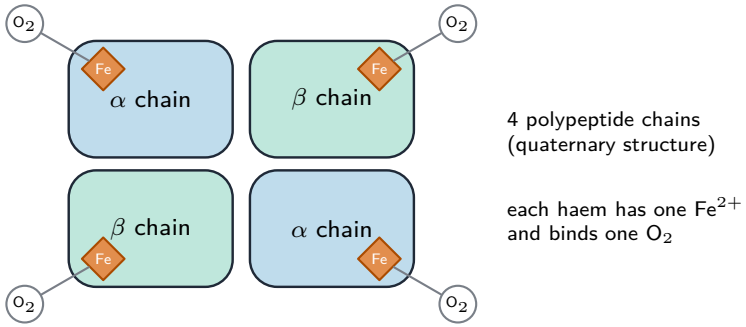



*High pressure at the arterial end pushes fluid out to form tissue fluid; most returns at the venous end*

## Transport of oxygen and carbon dioxide

### Carrying oxygen

Oxygen is carried by **haemoglobin** 血红蛋白 in the red blood cells. Haemoglobin is a **globular** protein with a **quaternary structure**: four polypeptide chains (two $\alpha$ chains and two $\beta$ chains), each holding a **haem** group with an iron ion ($Fe^{2+}$) at its centre. Each haem binds one oxygen molecule, so one haemoglobin molecule carries up to **four** oxygen molecules, forming oxyhaemoglobin. We show how well haemoglobin holds oxygen with the **oxygen dissociation curve** 氧解离曲线. This S-shaped graph plots the **saturation** 饱和度 (how full of oxygen the haemoglobin is) against the **partial pressure** 分压 of oxygen:




*Haemoglobin: four chains, four haem groups, up to four oxygen molecules*

- where the partial pressure of oxygen is **high** (in the lungs), haemoglobin loads up and becomes almost fully saturated.
- where it is **low** (in respiring tissues), haemoglobin unloads its oxygen for the cells to use.

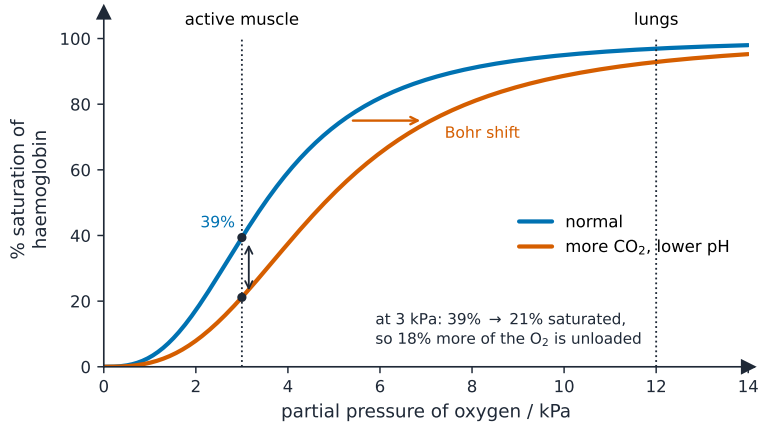
### The Bohr shift

When tissues are very active, they release more **carbon dioxide** 二氧化碳, which lowers the pH. This makes haemoglobin release oxygen more easily, so the curve moves to the right. This helpful change is the **Bohr shift** 波尔位移: oxygen is given up exactly where it is most needed.

**Why.** In an active tissue, carbon dioxide enters red blood cells and carbonic anhydrase turns it into carbonic acid, which releases **hydrogen ions**. The hydrogen ions bind to haemoglobin and change its shape, which **lowers its affinity** for oxygen, so it releases more oxygen at the same partial pressure. In the lungs the opposite happens: carbon dioxide leaves, the hydrogen ions leave haemoglobin, and its affinity rises again, so it loads oxygen well.

The effect is largest at the partial pressures found in tissues (2–5 kPa), on the steep part of the curve. At the high partial pressure in the lungs (about 12 kPa), both curves are near the top, so loading is hardly affected.


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Bohr shift (right): ↑ $CO_2$/ ↓ pH → lower $O_2$ affinity → unload at tissues

*Haemoglobin loads oxygen in the lungs and unloads it in the tissues; the Bohr shift moves the curve right so more is released*

### Carrying carbon dioxide

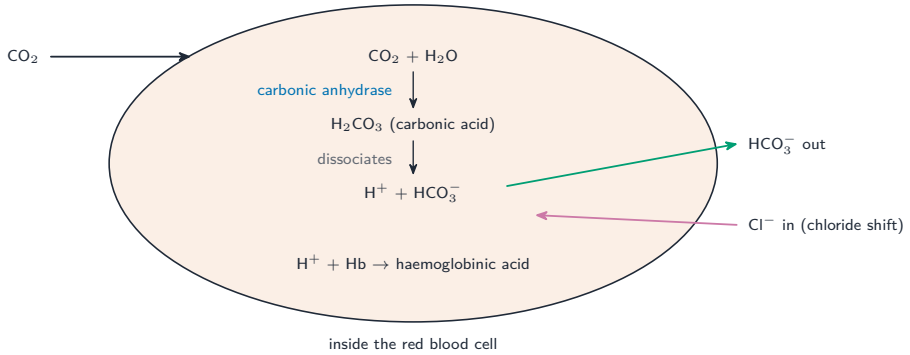
A little carbon dioxide dissolves straight into the plasma, but most is carried after a reaction inside the red blood cells:

1. the **enzyme** 酶 **carbonic anhydrase** 碳酸酐酶 speeds up the reaction of carbon dioxide with water to make carbonic acid.
2. the carbonic acid splits into hydrogen ions and **hydrogencarbonate ions** 碳酸氢根离子.
3. the hydrogencarbonate ions move out into the plasma. This is the main way carbon dioxide is carried.
4. to keep the charge balanced, **chloride ions** 氯离子 move into the red blood cells. This movement is the **chloride shift** 氯转移.
5. the hydrogen ions join haemoglobin to form **haemoglobinic acid** 血红蛋白酸; this mops up the hydrogen ions and keeps the pH steady.

Some carbon dioxide also joins haemoglobin directly to form **carbamino-haemoglobin** 氨甲酰血红蛋白.



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*Most $CO_2$ travels as hydrogencarbonate ions; the chloride shift keeps the charge balanced and haemoglobin mops up the $H^+$*

> **Worked example.** At the lungs the partial pressure of oxygen is about 12 kPa and haemoglobin is about 97% saturated; in an exercising muscle it is about 3 kPa and saturation falls to about 39%. How much oxygen is unloaded, and why is the curve S-shaped? Subtract the saturations: $97 - 39 = \mathbf{58\%}$ of the haemoglobin's oxygen is released in the muscle. The **S shape** comes from **cooperative binding** - the first oxygen to bind changes haemoglobin's shape so the next ones bind more easily, which is why the middle of the curve is so steep. That steepness is the point: a **small** fall in partial pressure in a respiring tissue causes a **large** release of oxygen. The extra carbon dioxide in an exercising muscle lowers the pH and shifts the curve **right**, so even more is unloaded at the same partial pressure. On the graph the shifted curve gives about 21% at 3 kPa, so the haemoglobin now gives up $97 - 21 = 76\%$ of its oxygen instead of 58%. (In the lungs carbon dioxide is low again, so the blood is back on the normal curve and loads to about 97%.) That is the **Bohr shift** doing its job.

## The heart

### Structure

The heart has four chambers. The two upper chambers are the **atria** 心房 (singular: atrium); they have thin walls because they only push blood down into the chambers below. The two lower chambers are the **ventricles** 心室; they have thick muscular walls because they pump blood out of the heart.

The left ventricle wall is thicker than the right ventricle wall, because the left side must pump blood all the way round the body, while the right side only pumps to the nearby lungs.

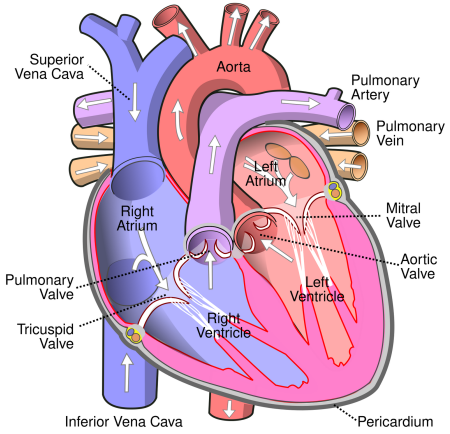
**External structure.** The heart is made of **cardiac muscle** 心肌, which contracts

without tiring. On its outer surface run the **coronary arteries** 冠状动脉, which branch from the base of the aorta and carry oxygenated blood to the heart muscle itself; a blockage in one starves part of the muscle of oxygen and causes a heart attack. The atria sit at the top (the **base**), with the aorta, pulmonary artery, venae cavae and pulmonary veins joined to them.

**Internal structure.**

- A wall of muscle, the **septum** 中隔, separates the left and right sides, so oxygenated and deoxygenated blood never mix.
- Between each atrium and ventricle is an **atrioventricular (AV) valve**: the **tricuspid** valve (three flaps) on the right, and the **bicuspid** (mitral) valve (two flaps) on the left. The flaps are held by tough **tendons** (chordae tendineae) attached to small **papillary muscles** in the ventricle wall; these stop the valves turning inside out when the ventricles contract.
- At the base of the aorta and the pulmonary artery are **semilunar valves** 半月瓣 – three half-moon-shaped pockets that fill with blood and close when the ventricle relaxes.
- The **SAN** sits in the wall of the right atrium, near the entry of the vena cava.

Follow the blood through the heart: vena cava → right atrium → tricuspid valve → right ventricle → semilunar valve → pulmonary artery → lungs → pulmonary vein → left atrium → bicuspid valve → left ventricle → semilunar valve → aorta.



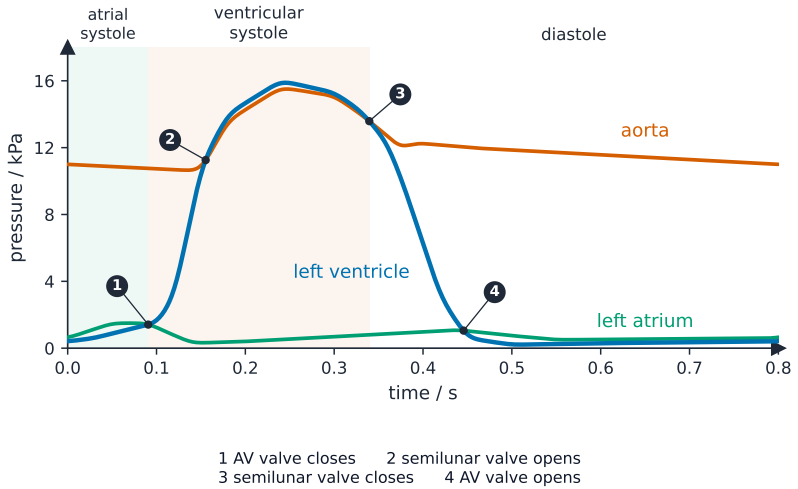

*The four chambers, the valves and the main vessels; the left ventricle wall is the thickest*



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## The cardiac cycle

One heartbeat is the **cardiac cycle** 心动周期. It has two parts: **systole** 收缩期 (when heart muscle contracts) and **diastole** 舒张期 (when it relaxes and fills). When a chamber contracts, the pressure inside rises; this pressure change opens and closes the valves so that blood flows one way only.




*Every valve event is a crossing: the ventricle rising past the atrium (1) and the aorta (2), then falling past the aorta (3) and the atrium (4)*

A valve opens when the pressure behind it is higher than the pressure in front of it, and shuts when the pressure in front becomes higher. So read the graph at the four places where the ventricle curve crosses another curve:

1. The **AV valve** 房室瓣 **closes**: the ventricle starts to contract and its pressure rises above the atrium's. This stops blood flowing back into the atrium.
2. The **semilunar valve opens**: the ventricle pressure rises above the aorta's. Blood is pushed into the aorta, so the two pressures now rise and fall together.
3. The **semilunar valve closes**: the ventricle relaxes and its pressure falls below the aorta's. The small notch in the aorta curve is the blood bouncing back against the closed valve.
4. The **AV valve opens**: the ventricle pressure falls below the atrium's, and the ventricle starts to fill again.

Between 1 and 2, and between 3 and 4, **both** valves are shut. The volume of blood in the ventricle cannot change, so the pressure changes very fast.

**Worked example.** Use the graph. (a) For how long is blood leaving the left ventricle? (b) What is the heart rate? (c) Why does the aorta pressure never fall to zero?

- (a) Blood leaves only while the semilunar valve is open, from point 2 (about 0.16 s) to point 3 (about 0.34 s): $0.34 - 0.16 = 0.18$ s.
- (b) One cycle takes 0.8 s, so the heart rate is $60 \div 0.8 = 75$ beats per minute.
- (c) The elastic wall of the aorta stretches when blood is pushed in, then **recoils** in diastole, keeping the blood under pressure and moving.

**Common mistakes.**

- Saying a valve is opened or closed by muscles. Valves move only because of the pressure difference across them.
- Saying the ventricle pressure rises far above the aorta's. Once the semilunar valve is open, the two are almost the same.
- Mixing up the sides. On a graph for the **left** side, the peak is about 16 kPa; the right ventricle reaches only about a fifth of that, because the lungs are close.
- Reading the AV valve events off the aorta curve. The AV valve is between the atrium and the ventricle, so use those two curves.

### Controlling the heartbeat

The heart sets its own rhythm:

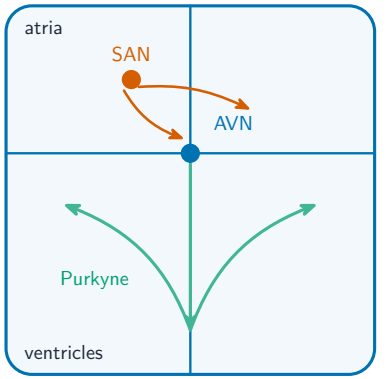
- the **sinoatrial node** 窦房结 in the right atrium is the pacemaker. It sends out a wave of electrical excitation that spreads across the atria and makes them contract.
- the **atrioventricular node** 房室结 picks up the wave, holds it back for a moment (so the atria empty first), then passes it on.
- the **Purkyne tissue** 浦肯野组织 carries the wave down and through the ventricle walls, so the ventricles contract from the bottom upwards and push blood out.

**Why the delay matters.** Between the atria and the ventricles there is a band of **non-conducting** fibrous tissue, so the wave cannot pass straight from the atria to the ventricles: it can cross only at the AVN. The AVN delays it by about 0.1 s, which gives the atria time to finish contracting and the ventricles time to fill before they contract. The wave then travels down the **bundle of His** in the septum to the **apex** (the bottom) of the heart, and up the ventricle walls in the Purkyne tissue. So the ventricles contract from the apex upwards, squeezing blood up and out through the arteries at the top, like toothpaste from a tube.

Cardiac muscle is **myogenic** 肌源性: it starts its own contractions, without any nerve impulse. Nerves from the brain only speed up or slow down the rate set by the SAN.



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SAN fires → atria contract → AVN delays → Purkyne → ventricles contract from the bottom up

*The SAN sets the rhythm; the wave passes to the AVN, then the Purkyne tissue makes the ventricles contract bottom-up*

## Exam tips

- Trace the **double circulation** and name the chambers, valves and vessels; the left ventricle wall is thicker (pumps further at higher pressure).
- Read the **cardiac-cycle** pressure graph: a valve opens/closes when the pressures across it cross over.
- Explain the **oxygen dissociation curve** (S-shaped) and the **Bohr shift** (more CO2 shifts it right, unloading more O2 to active tissue).
- Most CO2 is carried as **hydrogencarbonate** (via the chloride shift).
- Tissue fluid: hydrostatic pressure pushes fluid out at the arterial end; the water potential of the plasma (proteins stay in) draws water back at the venous end; the rest drains as lymph.
- Haemoglobin: four polypeptides, four haem groups, so four $O_2$; $H^+$ from carbonic acid changes its shape and lowers its affinity (Bohr shift).
- Heart: the band of non-conducting tissue forces the wave through the AVN, giving a delay so the ventricles fill first; the Purkyne tissue makes them contract from the apex upwards.

# Gas exchange

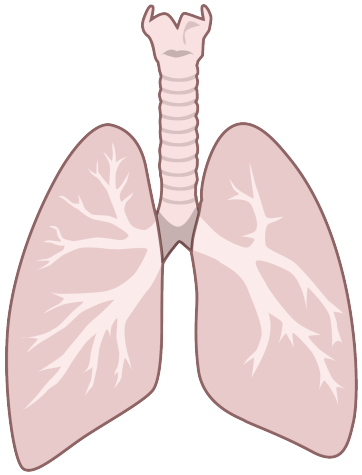
A-Level Biology

## The gas exchange system

Your body needs to take in oxygen and get rid of carbon dioxide. This swap happens in the **gas exchange** 气体交换 system. Air follows this path into the body:

- down the **trachea** 气管 (the windpipe),
- into two **bronchi** 支气管 (one to each lung),
- into many smaller **bronchioles** 细支气管,
- and finally into tiny air sacs called **alveoli** 肺泡, deep in the **lungs** 肺.

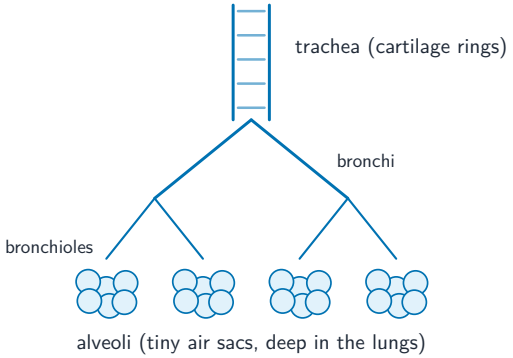
Each alveolus is wrapped in a network of **capillaries** 毛细血管, so air and blood are brought very close together.



*The human lungs, where gas exchange takes place across millions of alveoli*



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*Air passes down the trachea, into the bronchi and bronchioles, to the alveoli*

## The tissues of the airways and what they do

| Tissue | Where it is | Function |
|---|---|---|
| **cartilage** 软骨 | C-shaped rings in the trachea and bronchi | holds the airway open so it cannot collapse when you breathe in |
| **ciliated epithelium** 纤毛上皮 | lining the trachea and bronchi | tiny hairs called **cilia** 纤毛 beat to sweep **mucus** 黏液 up towards the throat, away from the lungs |
| **goblet cells** 杯状细胞 and **mucous glands** 黏液腺 | in the lining of the airways | make the mucus, which traps dust and **microbes** 微生物 that you breathe in |
| **smooth muscle** 平滑肌 | in the walls of bronchi and bronchioles | contracts to make the airway narrower |
| **elastic fibres** 弹性纤维 | in the airway and alveolus walls | stretch when you breathe in, then spring back to help push air out |
| **squamous epithelium** 扁平上皮 | the very thin, flat lining of the alveoli | gives a very short distance for gases to cross |

The cilia, goblet cells and mucous glands work together to keep the lungs clean and healthy: the mucus traps dirt and microbes, and the cilia carry it away to be swallowed.

## Where each tissue is found

The tissues change along the airway. As the tubes get narrower, cartilage disappears, the epithelium gets thinner, and smooth muscle and elastic fibres take over:

| Tissue | Trachea | Bronchus | Bronchiole | Alveolus |
|---|---|---|---|---|
| cartilage | C-shaped rings | irregular plates | none | none |
| ciliated epithelium | yes | yes | yes (thinner, cells shorter) | none |
| goblet cells | yes | yes | few or none in the smallest | none |
| mucous glands | yes | yes | none | none |
| smooth muscle | yes (behind the gap in each C-ring) | yes | yes, a large part of the wall | none |
| elastic fibres | yes | yes | yes | yes |
| squamous epithelium | none | none | none | yes, forms the wall |
| capillaries | in the wall | in the wall | in the wall | a dense network around each one |

**More on the functions.**

- **Cartilage** is strong but flexible. It stops the trachea and bronchi collapsing when the air pressure inside falls as you breathe in. The rings in the trachea are C-shaped, open at the back, so the oesophagus behind it can bulge forward when you swallow food.
- **Smooth muscle** contracts to narrow the bronchioles (constriction) and relaxes to widen them (dilation), controlling how much air reaches the alveoli. In an asthma attack it contracts strongly and the airways become very narrow.
- **Elastic fibres** in the alveolar walls stretch as the alveoli fill with air, then **recoil**, helping to push air out and stopping the alveoli from bursting.
- **Mucous glands** lie in the submucosa beneath the epithelium of the trachea and bronchi; they make extra mucus, which flows out through ducts onto the surface.



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- **Squamous epithelium** cells are very thin and flat, giving a diffusion distance of only about 0.1–0.5 $\mu$m between air and blood.

## Recognising the tissues and airways in micrographs

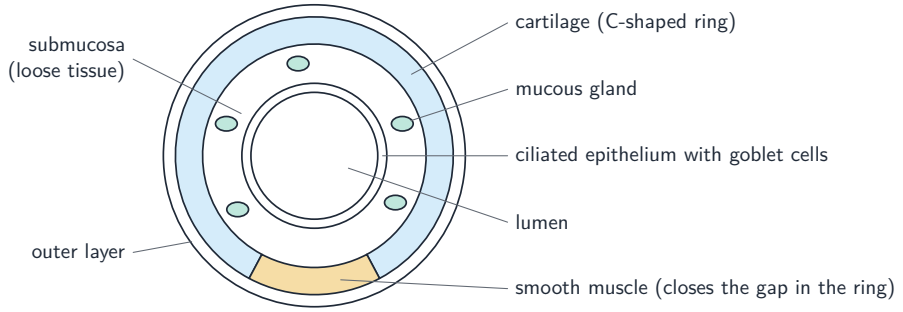
- **Trachea**: a wide lumen, a thick C-shaped ring of cartilage (stains blue or purple, smooth and glassy), ciliated epithelium lining the lumen with goblet cells (pale, cup-shaped cells among the ciliated ones).
- **Bronchus**: smaller, with separate **plates** of cartilage rather than a ring.
- **Bronchiole**: no cartilage; a ring of smooth muscle around a small, often folded lumen; a thin ciliated epithelium.
- **Alveoli**: a lace-like network of thin walls enclosing empty spaces, with capillaries (some containing red blood cells) in the walls.

On an **electron micrograph**, cilia appear as many fine projections on the surface of the epithelial cells, each with a regular arrangement of microtubules in cross-section; goblet cells contain many vesicles of mucus.

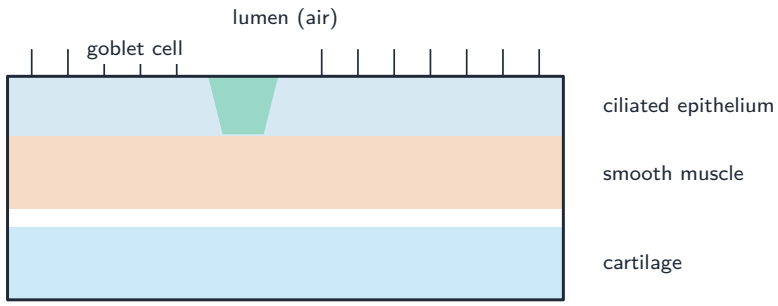
## Drawing a plan diagram

A **plan diagram** 平面图 shows the outlines of the **tissues**, not individual cells. To draw one of a transverse section of the trachea or bronchus:

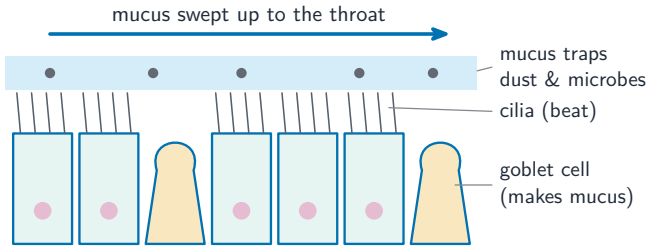
1. Use a sharp pencil and draw clear, continuous lines – no shading and no sketchy lines.
2. Draw only the **boundaries** between tissue layers, keeping their relative thicknesses correct.
3. Do not draw any cells (not even goblet cells): show the epithelium as a thin band.
4. Label with ruled lines that touch the tissue, with no arrowheads.
5. Make it large enough to fill the space given.




*A plan diagram of the trachea wall: tissue layers as outlines, no individual cells*




*A section through the airway wall: cilia and goblet cells line the lumen, with smooth muscle and supporting cartilage behind*




*Goblet cells make mucus that traps dust and microbes; the cilia sweep it up to the throat*

## Gas exchange in the alveoli

The alveoli are excellent surfaces for exchanging gases, because they have:

- a very large total surface area (millions of tiny sacs),
- very thin walls – the squamous epithelium of the alveolus and the capillary wall are each only one cell thick, so the distance to cross is tiny,
- a rich blood supply from the capillary network,
- a moist lining, so gases dissolve before crossing.

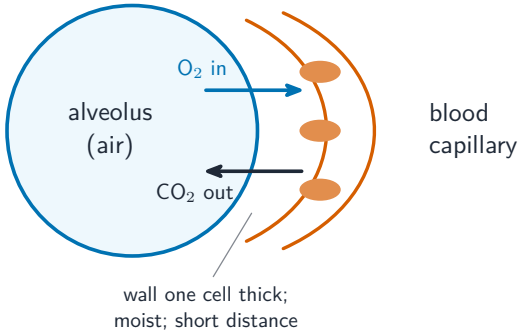
Gases move by **diffusion** 扩散 down their **concentration gradients** 浓度梯度:

- **oxygen** 氧气 is at a high concentration in the alveolar air and a low concentration in the blood, so it diffuses from the air into the blood.



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- **carbon dioxide** 二氧化碳 is at a high concentration in the blood and a low concentration in the alveolar air, so it diffuses from the blood into the air to be breathed out.




*Across the thin, moist wall, oxygen diffuses into the blood and carbon dioxide diffuses out*

Under the microscope, real lung tissue looks like a fine pink lace. The many open spaces are the alveoli, and the thin pink lines between them are the walls where gas exchange happens:



*Real lung tissue stained for the microscope: the open spaces are alveoli and the thin pink walls are where gases cross; a small airway sits in the centre*

Breathing keeps fresh air in the alveoli, and the flowing blood keeps carrying gases away. Both of these keep the concentration gradients steep, so gas exchange stays fast.

**Describing the exchange step by step.** Oxygen in the alveolar air dissolves in the thin layer of moisture lining the alveolus. It then diffuses across the squamous

epithelium of the alveolus and the **endothelium** 内皮 of the capillary (two very thin cells), into the plasma, and into a red blood cell, where it combines with haemoglobin. Carbon dioxide travels the opposite way, from the plasma (mostly carried as hydrogencarbonate ions), across the same two cells into the alveolar air. The capillaries are so narrow that red blood cells are squeezed against the wall, which shortens the diffusion distance further and slows the cells down, giving more time for exchange.

> **Worked example.** Use Fick's law to explain why the alveoli allow such rapid gas exchange. Fick's law makes the rate of diffusion proportional to
>
> $$\frac{\text{surface area} \times \text{concentration difference}}{\text{diffusion distance}}$$
>
> so a fast rate needs all three terms working for it. **Surface area**: millions of alveoli give a huge total area, roughly 70 $m^2$. **Diffusion distance**: the alveolar epithelium and the capillary endothelium are each one flattened cell thick, so oxygen crosses in under 1 $\mu$m. **Concentration difference**: ventilation constantly refreshes the air while the circulation constantly carries oxygenated blood away, so a **steep gradient is maintained**. Tie each adaptation to the **term of the equation** it serves - listing "big surface area, thin walls, good blood supply" without linking them to Fick's law is the weaker answer.

**Common mistakes.**

- Writing "the alveoli have thin cell walls". Animal cells have **no** cell walls; write that the alveolar wall is one cell thick, or that the epithelium is thin.
- Saying elastic fibres contract to push air out. Only muscle contracts. Elastic fibres are **stretched** when you breathe in and **recoil** when you breathe out.
- Saying cilia kill or filter bacteria. The cilia beat to **move** the mucus, with the trapped dust and bacteria, up to the throat.
- Putting cartilage in the small bronchioles. Cartilage is in the trachea and bronchi; the bronchioles have smooth muscle and elastic fibres but no cartilage.
- Saying gas exchange happens in the bronchioles. It happens across the walls of the **alveoli** and their capillaries.

## Exam tips

- Link each **alveolar** feature to fast diffusion: large surface area, thin (one-cell) walls, moist surface, good blood supply – a "surface area, short distance, steep gradient" answer.
- Match airway tissue to function: cartilage (holds airways open), ciliated + goblet cells (trap and sweep mucus), smooth muscle and elastic fibres.
- Frame answers with **Fick's law** ideas: rate $\propto$ surface area $\times$ concentration difference $\div$ distance.



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- Learn the distribution table: cartilage only in the trachea (C-rings) and bronchi (plates); bronchioles have smooth muscle but no cartilage; alveoli have squamous epithelium and elastic fibres only.
- In a plan diagram draw tissue outlines only, never cells, with no shading.
- Explain the C-shape of the tracheal rings: it holds the airway open while letting the oesophagus expand when food is swallowed.

# Infectious diseases

A-Level Biology

## What causes infectious disease

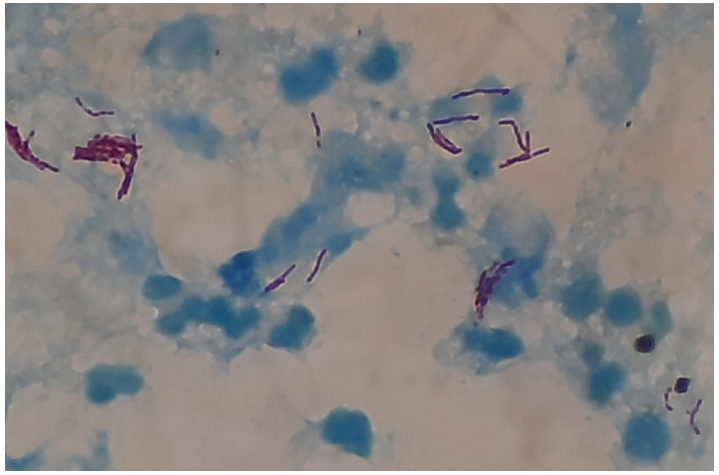
An **infectious disease** 传染病 is caused by a **pathogen** 病原体 – an organism that lives in or on a host and causes harm. Infectious diseases are **transmissible**: the pathogen can be **transmitted** 传播 (passed) from one person to another.

You need to know four diseases, the pathogen that causes each, and how each spreads.

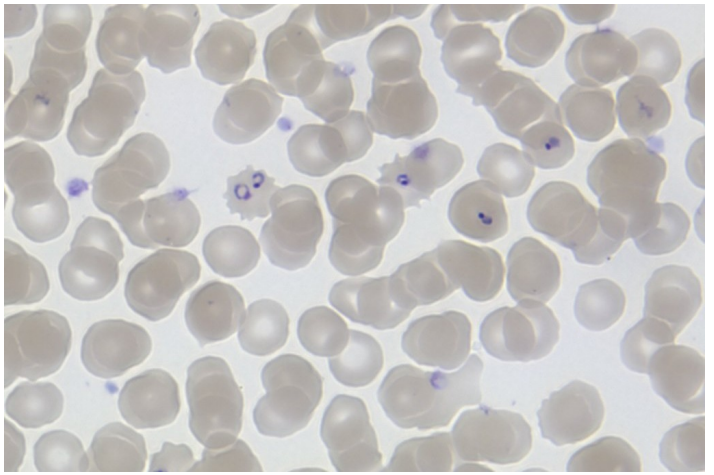
| Disease | Pathogen and type | How it spreads |
|---|---|---|
| **cholera** 霍乱 | the **bacterium** 细菌 *Vibrio cholerae* | drinking water or food **contaminated** 污染 with **faeces** 粪便 (human waste) |
| **malaria** 疟疾 | the **protoctist** 原生生物 *Plasmodium* | the bite of an infected **mosquito** 蚊子, which acts as a **vector** 媒介 (a carrier of the pathogen); also through infected blood |
| **tuberculosis (TB)** 结核病 | the bacteria *Mycobacterium tuberculosis* and *Mycobacterium bovis* | tiny airborne **droplets** 飞沫 from coughs and sneezes, which spread fast where people are crowded; *M. bovis* also spreads in unpasteurised milk or undercooked meat from infected cattle |
| **HIV/AIDS** | the **virus** 病毒 HIV (which leads to **AIDS** 艾滋病) | unprotected sex, infected blood (for example shared needles), and from mother to baby |

HIV infects and destroys certain white blood cells, so it slowly weakens the body's **immune system** 免疫系统.





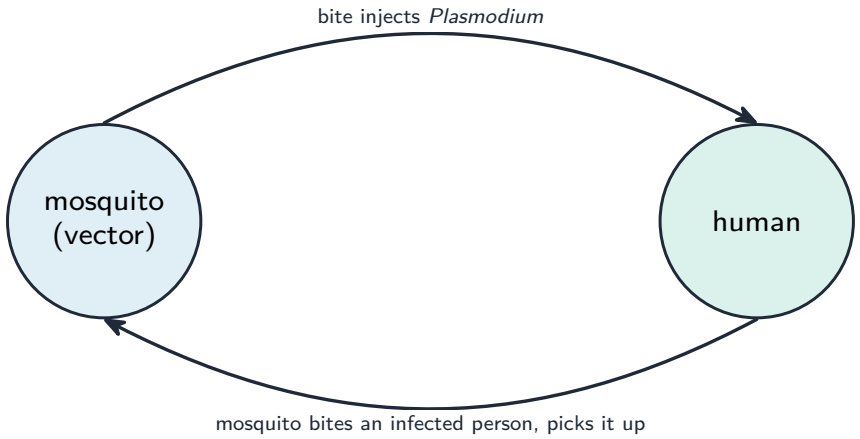
*The bacterium Mycobacterium (red rods) that causes tuberculosis, stained in a sputum sample*



*The protoctist Plasmodium (small dark rings) that causes malaria, living inside red blood cells*



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*Malaria needs a mosquito vector: the parasite passes from human to mosquito to human with each bite – which is why control targets the mosquito*

## Preventing and controlling these diseases

Control has **biological**, **social** and **economic** sides – the science of the pathogen, people's behaviour and education, and the money and resources available. Examples:

- **cholera**: provide clean water and proper sewage treatment; good hygiene; **vaccines** 疫苗 in some areas.
- **malaria**: sleep under nets; remove pools of still water where mosquitoes breed; spray **insecticides** 杀虫剂; take anti-malarial drugs.
- **TB**: find and treat infected people with a long course of antibiotics; give the BCG vaccine; reduce overcrowding; trace contacts of patients.
- **HIV**: use condoms; use clean needles; test donated blood; educate people. There is no cure and no vaccine yet, but drugs can slow the virus down.

In every case, cost (economic), people's willingness to change behaviour (social) and the supply of drugs or vaccines (biological) all affect how well a disease can be controlled.

### ■ Why each disease is hard to control

A "discuss" question wants the **difficulties** as well as the measures, sorted into biological, social and economic factors:



| Disease | Biological | Social | Economic |
|---|---|---|---|
| cholera | many people carry the bacterium without symptoms; the vaccine gives only short protection | outbreaks spread fast in refugee camps and after floods or earthquakes, when sewage mixes with drinking water | clean water supplies and sewage works are very expensive to build in poor or remote areas |
| malaria | *Plasmodium* has become resistant to several drugs, and mosquitoes to insecticides; the parasite hides inside liver and red blood cells; it changes its surface antigens, so no fully effective vaccine exists yet | nets must be used every night; people move between regions | the poorest countries carry most cases and cannot afford drugs, nets and spraying for everyone |
| TB | treatment needs several antibiotics for at least 6 months; strains resistant to many drugs (MDR-TB) have appeared; people with HIV are far more likely to develop TB; the BCG vaccine works poorly in adults | crowded housing and poor ventilation; patients stop taking drugs when they feel better; stigma stops people being tested | long courses of drugs and contact tracing are costly; testing cattle and pasteurising milk cost money |
| HIV | the virus mutates fast and its antigens keep changing, so no vaccine; it hides inside the DNA of host cells, so drugs cannot cure it | people may not know they are infected for years and pass it on; stigma; sexual behaviour is hard to change | antiretroviral drugs must be taken for life and are expensive; testing and education programmes need funding |



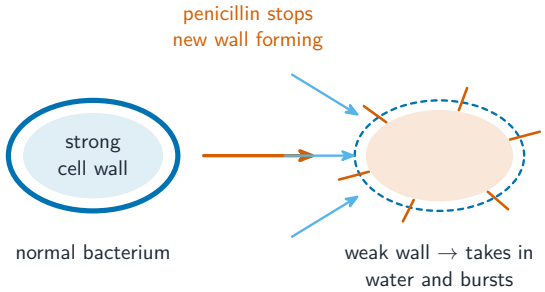
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**Worked example.** Suggest why malaria has not been eradicated, although smallpox has. Smallpox had no animal or insect host, so vaccinating everyone around each case stopped it. Malaria has a **vector**, the mosquito, which breeds wherever there is still water and has become resistant to insecticides. There is no fully effective vaccine, because *Plasmodium* spends much of its life inside human cells and changes its antigens. Drug resistance in *Plasmodium* means the drugs that once worked no longer do. And control is most needed in the poorest regions, where nets, drugs and spraying are hardest to pay for and deliver.

## Antibiotics

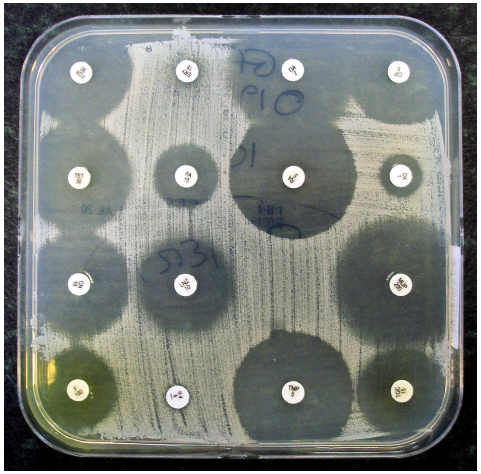
An **antibiotic** 抗生素 is a drug that kills bacteria or stops them growing. For example, **penicillin** 青霉素 stops bacteria from building their **cell walls** 细胞壁. As the bacterium grows, its weak wall cannot hold it, so the cell takes in water and bursts.

In more detail: a bacterial cell wall is made of **peptidoglycan** 肽聚糖 – long sugar chains joined by short peptide **cross-links** that make the wall strong. When a bacterium grows, enzymes in the wall make small gaps so that new material can be added, and other enzymes (**transpeptidases**) build the cross-links. Penicillin **inhibits** the cross-linking enzymes. The gaps are still made but are not repaired, so the wall becomes weak. Water enters the cell by osmosis, and the weakened wall cannot resist the pressure, so the cell bursts (**osmotic lysis**). Penicillin therefore works only on bacteria that are **growing**, and it does not harm human cells, which have no cell wall.




*Penicillin stops new cell wall forming, so the bacterium takes in water and bursts*





*How we test which antibiotic works. Each paper disc holds a different antibiotic. A clear ring means that antibiotic killed the bacteria around it – the bigger the ring, the more effective the drug. Discs with no ring are ones the bacteria resist*

Antibiotics do **not** work against **viruses**. A virus has no cell wall and no chemical reactions of its own to attack – it simply uses the machinery of the host cell. So there is no antibiotic target in a virus.

## Antibiotic resistance

Sometimes a **mutation** 突变 makes a bacterium **resistant** to an antibiotic, which means the antibiotic no longer kills it. This **resistance** 耐药性 is a serious problem:

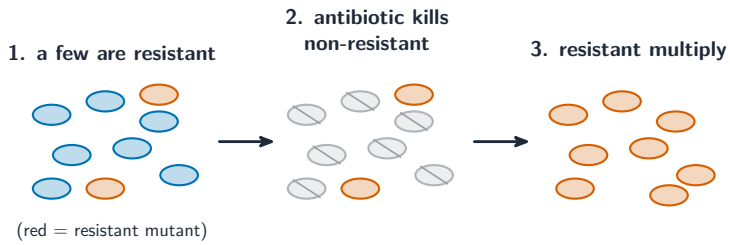
- when an antibiotic is used, the non-resistant bacteria die, but any resistant ones survive and multiply. Over time, more and more bacteria carry the resistance.
- some infections then become very hard, or impossible, to treat.

**How resistance genes spread.** One common resistance gene codes for an enzyme, **penicillinase** (a $\beta$-lactamase), which breaks down penicillin before it can act. Resistance genes are often carried on **plasmids**. When a resistant bacterium divides, every daughter cell receives the plasmid (vertical transmission). Bacteria can also pass a copy of a plasmid to another bacterium, even one of a different species, through a thin tube between them (**conjugation**, horizontal transmission). So resistance can spread through a population much faster than by mutation alone.

**Consequences.** Infections such as MRSA (methicillin-resistant *Staphylococcus aureus*) in hospitals and multidrug-resistant TB are hard to treat. Patients stay ill or in hospital for longer, more expensive drugs with more side effects are needed, and some operations and cancer treatments become riskier because infections afterwards may not be treatable. Developing new antibiotics is slow and costly.



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*Antibiotic resistance spreads by natural selection: the antibiotic kills the rest, so the resistant survivors take over*

Steps to slow resistance down:

- only use antibiotics when they are really needed (not for viral illnesses such as colds).
- always finish the full course, so no bacteria are left alive.
- use the correct antibiotic for the infection.
- reduce the heavy use of antibiotics in farming.
- in hospitals, wash hands between patients, isolate patients with resistant infections, and screen new patients.
- use a **narrow-spectrum** antibiotic (one that targets few kinds of bacteria) where possible, and change which antibiotics are used, so no single one is used all the time.
- develop new antibiotics, and test the infection to find which antibiotic it is sensitive to before prescribing.

> **Worked example.** A patient with influenza is prescribed an antibiotic. Explain why it will not help, and why it is actively harmful. Antibiotics work by attacking structures or processes that **bacteria** have and human cells do not - penicillin, for instance, blocks **cell wall** synthesis, so the growing bacterium bursts under osmotic pressure. A **virus** has no cell wall, no ribosomes of its own and no metabolism: it replicates **inside** the host's cells using the host's machinery, so there is simply no bacterial target for the drug to attack. Taking it anyway exposes the patient's harmless resident bacteria to the antibiotic, killing the susceptible ones and **selecting for resistant** ones - which is how resistance spreads through a population. Name the **target that is missing**: "viruses are not alive" is not the reason and earns nothing.

**Common mistakes.**

- Calling the mosquito the pathogen of malaria. The pathogen is the protoctist ***Plasmodium***; the mosquito is only the **vector** that carries it.



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- Saying the bacteria **become** resistant because they meet the antibiotic. A resistant allele arises by chance **mutation** first; the antibiotic then selects it by killing the non-resistant bacteria.
- Saying people or the body become resistant to an antibiotic. It is the **bacteria** that are resistant.
- Saying HIV is the same as AIDS. HIV is the **virus**; AIDS is the disease that develops later, when so many white blood cells are destroyed that other infections take hold.
- Writing that penicillin "attacks the cell wall". It stops the bacterium **building** its cell wall as it grows, so the weakened cell takes in water by osmosis and bursts.
- Giving only biological control measures when a question asks about social or economic factors. Name the people side (education, crowded housing, behaviour) and the money side (cost of drugs, vaccines, clean water) as well.

## Exam tips

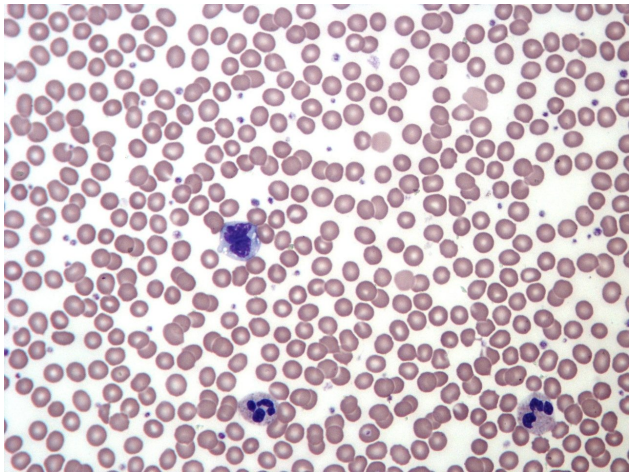
- For each named disease give the **pathogen and route** (cholera – bacterium, water; malaria – Plasmodium, mosquito vector; also TB, HIV/AIDS).
- Explain why **antibiotics** work on bacteria only (they target cell walls/enzymes, not viruses).
- Explain **antibiotic resistance** as natural selection: a resistant mutant survives and reproduces; reduce it by finishing courses and avoiding overuse.
- Penicillin inhibits the enzymes that build peptidoglycan cross-links in **growing** bacteria → weak wall → osmotic lysis.
- Resistance genes on plasmids spread vertically (division) and horizontally (conjugation).
- In a "discuss" answer, give biological, social **and** economic factors, and difficulties as well as measures.

# Immunity

A-Level Biology

## Phagocytes – the first defence

Your **immune system** 免疫系统 is the set of cells that defends the body against **pathogens** 病原体. The first cells to act are **phagocytes** 吞噬细胞, a group of white blood cells that includes **macrophages** 巨噬细胞 and **neutrophils** 中性粒细胞.



*A blood smear: the large stained cells are white blood cells, scattered among the many red cells*

A phagocyte destroys a pathogen by **phagocytosis** 吞噬作用: it surrounds the pathogen, takes it inside in a vesicle, and digests it with enzymes. After this, a macrophage displays parts of the pathogen on its own surface, ready to alert other immune cells.

The two kinds of phagocyte do different jobs:



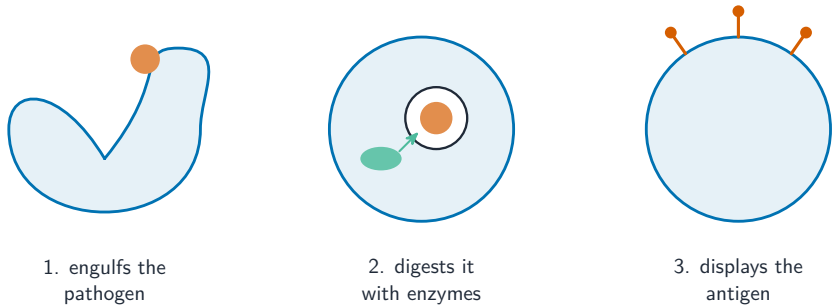
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| | Neutrophils | Macrophages |
|---|---|---|
| where | many in the blood; leave capillaries to reach an infected tissue | in organs such as the lungs, liver, lymph nodes and spleen |
| timing | the first to arrive, in large numbers | larger; arrive later and live for months |
| fate | short-lived: die after digesting a few pathogens (dead neutrophils make pus) | long-lived |
| extra role | – | **antigen presentation** 抗原呈递: they display the pathogen's antigens to T-lymphocytes |

Phagocytosis happens in a fixed order. Learn it as a sequence, because the marks are given step by step:

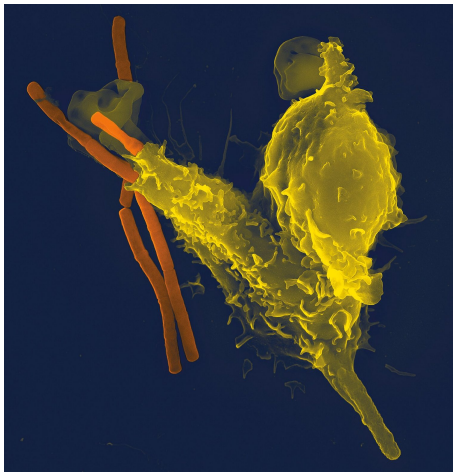
1. Damaged cells and pathogens release chemicals that **attract** the phagocyte (it moves towards them, up the concentration gradient).
2. **Receptors** 受体 on the phagocyte's membrane bind to the pathogen. Antibodies stuck to a pathogen make this easier.
3. The membrane flows round the pathogen and engulfs it by **endocytosis** 胞吞作用, forming a **phagocytic vacuole** 吞噬泡.
4. **Lysosomes** 溶酶体 fuse with the vacuole and release **hydrolytic enzymes** 水解酶, which digest the pathogen.
5. The soluble products are absorbed into the cytoplasm; a macrophage keeps the antigens and displays them on its surface.

The same steps let a phagocyte remove old or damaged body cells, such as worn-out red blood cells in the liver and spleen.




*Phagocytosis: the phagocyte engulfs the pathogen, digests it, then displays its antigen*

This false-coloured electron micrograph captures the moment in real life: a phagocyte reaching out to grab and engulf rod-shaped bacteria.



*A real **neutrophil** (yellow), one kind of phagocyte, reaching out to engulf rod-shaped bacteria (orange) by phagocytosis*

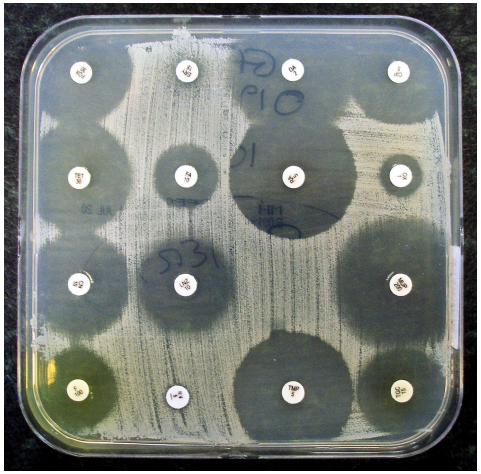
## Antigens: self and non-self

An **antigen** 抗原 is a molecule (usually a protein) on a cell surface that the immune system can recognise.

- **self antigens** 自身抗原 are the body's own markers. The immune system learns to ignore them.
- **non-self antigens** 非自身抗原 are foreign, for example the antigens on a pathogen. These trigger an immune response.



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*Clear zones on a culture plate: the immune system recognises non-self antigens and attacks foreign cells*

## The primary immune response

The first time a new pathogen enters, the body makes a slow **immune response** 免疫反应. The main steps are:

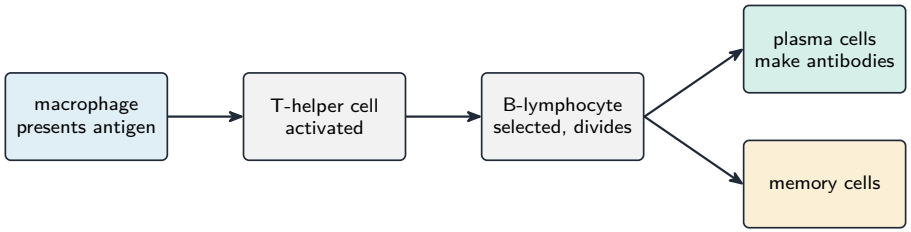
1. a macrophage engulfs the pathogen and displays its antigen.
2. **T-helper cells** 辅助性 T 细胞 recognise that antigen and become active. They release chemicals that switch on other cells.
3. **B-lymphocytes** 淋巴细胞 with a matching shape are selected. They divide to form **plasma cells** 浆细胞, which pour out **antibodies** 抗体, and **memory cells** 记忆细胞.
4. **T-killer cells** 杀伤性 T 细胞 destroy the body's own cells that have been infected.

In more detail:

- **Lymphocytes** are made in the bone marrow. B-lymphocytes mature there; T-lymphocytes mature in the **thymus** 胸腺. Each lymphocyte has receptors of **one** shape, so it can bind only one antigen. Millions of different lymphocytes exist before any infection.
- **Clonal selection** 克隆选择: only the lymphocytes whose receptors are **complementary** 互补 to the antigen are activated.
- **Clonal expansion** 克隆扩增: the selected lymphocyte divides many times by **mitosis**, making a clone of identical cells.
- **T-helper cells** release **cytokines** 细胞因子, chemical signals that stimulate the matching B-lymphocytes to divide and become plasma cells, and stimulate macrophages to engulf more pathogens.

- **Plasma cells** have a lot of rough endoplasmic reticulum and Golgi, because they make and secrete antibodies, about 2000 per second each. They live only a few days.
- **T-killer cells** attach to body cells that display the antigen (for example, a cell infected by a virus) and release toxic chemicals that make holes in the membrane, killing the cell.

These steps take several days, because the few B-lymphocytes that match the antigen must first be found and then divide many times. This delay is the **lag** at the start of the primary response, and it is why you feel ill during a first infection.



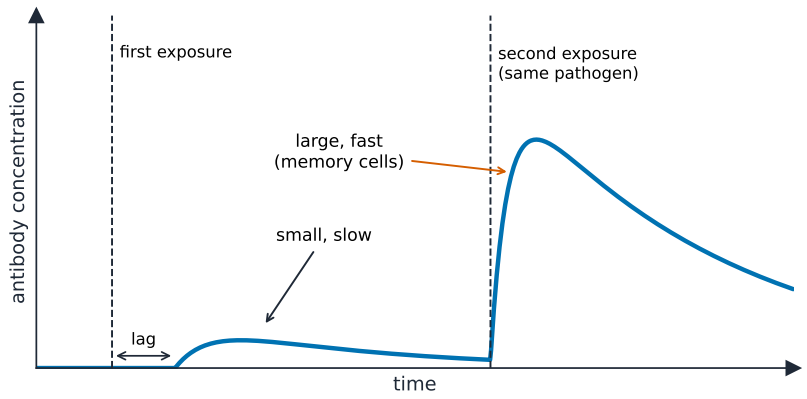

*Only the B-lymphocyte whose shape matches the antigen is selected and cloned – into antibody-making plasma cells and long-lived memory cells*

## Memory cells and long-term immunity

Memory cells stay in the body for years after the infection is over. If the **same** pathogen enters again, the memory cells start a **secondary** immune response that is much faster and larger than the first. The pathogen is destroyed before it can make you ill. This is what we mean by long-term immunity.



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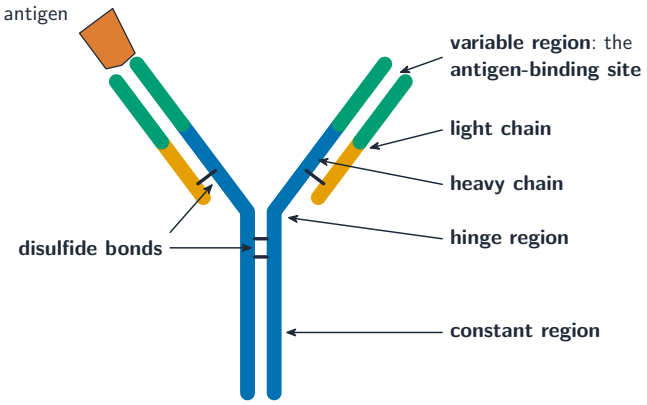

*The secondary response is faster and larger, because memory cells are ready*

## Antibodies

An antibody is a Y-shaped protein made by plasma cells. The two tips of the Y are **antigen-binding sites** 抗原结合位点. Each site has a special shape, called the **variable region** 可变区, that fits one antigen only, like a lock and key.

The syllabus asks you to **relate the molecular structure to the function**. Each part of the molecule has a job:

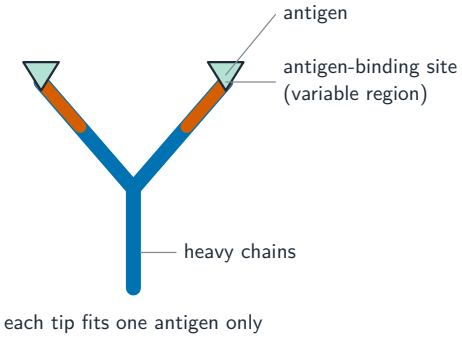
| Structure | Why it matters |
|---|---|
| four **polypeptide** 多肽 chains: two long **heavy chains** 重链 and two short **light chains** 轻链 (a quaternary structure) | together they fold into the Y shape |
| **disulfide bonds** 二硫键 between the chains | hold the four chains together, so the molecule is stable in blood and tissue fluid |
| **variable region** at the end of each arm, on both a heavy and a light chain | its amino acid sequence differs between antibodies, so each binding site has a shape **complementary** to one antigen: this gives **specificity** |
| **two** antigen-binding sites | one antibody can bind two antigens, so it can link pathogens together |
| **hinge region** 铰链区 | lets the arms move apart or together, so the antibody can bind antigens at different distances |
| **constant region** 恒定区 (the stem) | the same in all antibodies of one class; it binds to **receptors on phagocytes**, so it marks the pathogen for engulfing |




*An antibody is four polypeptide chains held by disulfide bonds; the variable regions at the tips make two antigen-binding sites*



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*An antibody is Y-shaped; the two tips are the variable regions that bind one specific antigen*

Antibodies help in several ways. Notice that each function uses one part of the structure:

- **agglutination** 凝集: the two binding sites attach to antigens on two different pathogens, so pathogens clump together. They cannot spread and phagocytes can engulf many at once.
- **neutralisation** 中和: antibodies (antitoxins) bind to toxins, or to the parts of a virus that attach to host cells, so the toxin or virus cannot act.
- **opsonisation** 调理作用: antibodies coat a pathogen and their constant regions bind to receptors on phagocytes, so phagocytosis is faster.
- **lysis**: some antibodies attach to bacteria and trigger proteins in the blood that punch holes in the bacterial wall.

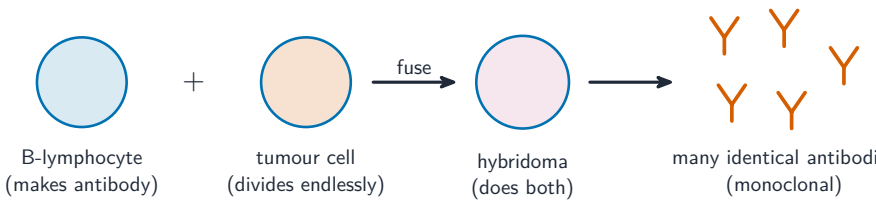
> **Worked example (3 marks).** *A drug is made from a monoclonal antibody. Explain why it binds only to its target protein.* "The variable region has a specific sequence of amino acids (1), so the antigen-binding site has a specific shape (1) that is complementary to the shape of the target antigen only, and they bind (1)." Use the words *variable region*, *specific shape* and *complementary*.

## Monoclonal antibodies

A **monoclonal antibody** 单克隆抗体 is a single type of antibody, all identical. They are made by the **hybridoma** 杂交瘤 method:

1. A mouse is injected with the antigen. Over several weeks it makes an immune response, so it has B-lymphocytes (plasma cells) that produce the wanted antibody.
2. The B-lymphocytes are removed from the mouse's **spleen** 脾.
3. They are fused with **myeloma** 骨髓瘤 cells (cancer cells, which divide endlessly), using a chemical such as polyethylene glycol. The fused cell is a **hybridoma**.

4. The hybridoma cells are separated into single wells and **screened**: only cells that make the wanted antibody are kept.
5. Each selected hybridoma is **cloned** and grown in culture. It both makes the antibody **and** divides without stopping, producing large amounts of one identical antibody.




*Fusing a B-lymphocyte with a tumour cell makes a hybridoma that pours out one identical (monoclonal) antibody*

Monoclonal antibodies are used in the **diagnosis** 诊断 of disease (to detect a specific molecule, as in a pregnancy test) and in treatment (to carry drugs to specific target cells, such as cancer cells).

**Diagnosis: the dipstick test.** Many rapid tests (for pregnancy, cholera or COVID-19) use two kinds of monoclonal antibody on a strip:

- **Mobile** 可移动的 antibodies near the bottom are attached to a coloured marker (often tiny gold particles). They bind the antigen in the sample and are carried up the strip with the liquid.
- **Immobilised** 固定的 antibodies are fixed in a line further up. They bind a **different** part of the same antigen, so they catch the antigen–antibody–marker complex. The marker collects and a coloured line appears: a positive result.
- A **control line** has immobilised antibodies that bind the mobile antibodies themselves. It turns coloured every time, which shows the liquid has flowed and the test has worked.

Because each antibody binds one antigen only, a strip with two different mobile antibodies and two test lines can tell two strains of a pathogen apart.

**Treatment.** A monoclonal antibody can be the drug itself, or carry one:

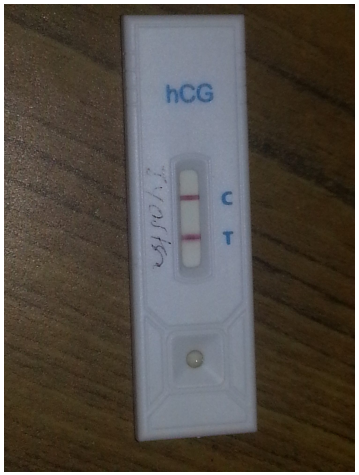
- it can **block** a molecule: for example, trastuzumab binds to a receptor protein found in large numbers on some breast cancer cells, so the receptor cannot signal the cell to divide; abciximab binds to a protein on platelets, so they cannot stick together and form a clot.
- it can mark cancer cells so the immune system destroys them, or **carry** a toxic drug or radioactive substance straight to the target cells.

Because the antibody binds only cells with the target antigen, healthy cells are mostly



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spared and there are fewer side effects. Mouse antibodies are non-self to humans, so they are **humanised** 人源化 (most of the molecule is changed to the human sequence) to stop the patient's immune system attacking them.

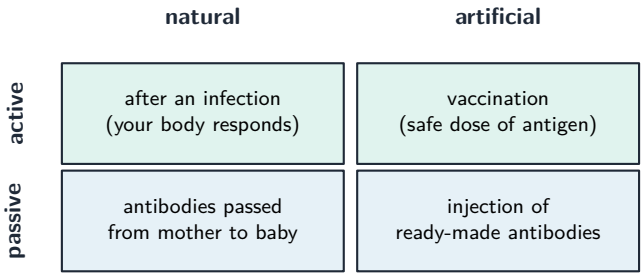



*A pregnancy test is monoclonal antibodies at work. The antibodies are fixed at the T line and grab only one molecule – the pregnancy hormone hCG. The T line turns red only if hCG is in the urine; the C line always appears, to show the test ran properly*

## Types of immunity

Immunity can be active or passive, and natural or artificial.

- **active immunity** 主动免疫 – your own body meets an antigen and makes its own antibodies and memory cells. It is slow to start but long-lasting.
- **passive immunity** 被动免疫 – ready-made antibodies are given to you from outside. It works at once but does not last, because there are no memory cells.
- **natural immunity** 天然免疫 – gained in a natural way (active: after an infection; passive: antibodies passed from mother to baby).
- **artificial immunity** 人工免疫 – gained on purpose (active: your body is made to respond to a safe dose of antigen; passive: you are injected with ready-made antibodies).




**active** = your body makes its own antibodies (slow, long-lasting);
**passive** = ready-made antibodies given (fast, short-lived)

*Active immunity (your body responds) lasts; passive immunity (ready-made antibodies) is fast but short*

## Vaccination

A **vaccine** 疫苗 contains antigens – often a dead or weakened pathogen, or part of one. The antigens trigger a primary immune response and make memory cells, so you gain long-term immunity **without** becoming ill.

**Vaccination** 疫苗接种 programmes can control the spread of a disease across a population. If enough people are vaccinated, the pathogen cannot pass easily from person to person. This protects even the people who are not vaccinated, an effect called **herd immunity** 群体免疫. The more easily a disease spreads, the higher the share of people that must be vaccinated: about 95% for measles.

A vaccination programme works best when it:

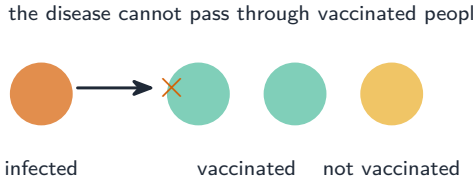
- vaccinates a **high proportion** of the population, starting with young children, and gives **boosters** 加强针 where one dose does not give lasting immunity;
- makes the vaccine free or cheap and reaches rural as well as urban areas, with enough supply, trained staff and a **cold chain** 冷链 (keeping vaccines cool so they still work);
- keeps records, uses **surveillance** 监测 to find every new case, and practises **ring vaccination** 环形接种: vaccinating everyone around a new case so the pathogen has nowhere to go;
- educates people about the disease and the vaccine.

**Smallpox** 天花 was eradicated in 1980 because its virus was stable (its antigens did not change, so one vaccine worked everywhere), it infected only humans, every case had a visible rash and could be isolated quickly, and a live vaccine gave lasting immunity from one dose. Some diseases are harder to control by vaccination:



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- **antigenic variation** 抗原变异: the antigens change often (influenza), so memory cells made last year no longer match and a new vaccine is needed;
- many strains exist, so one vaccine cannot cover them all;
- the pathogen hides **inside** body cells (the malaria parasite in liver and red blood cells, *M. tuberculosis* in macrophages), away from antibodies;
- the vaccine needs several doses or refrigeration, which is hard in remote areas; and some people refuse vaccination.




*Herd immunity: when enough people are vaccinated, the pathogen cannot reach the few who are not*

**Worked example.** Classify each as active or passive, natural or artificial: (a) a baby receives antibodies in breast milk; (b) a child is vaccinated against measles; (c) someone recovers from chickenpox; (d) a patient bitten by a snake is given antivenom. Ask two questions each time. **Did the person make the antibodies themselves?** If yes it is **active**; if they were handed ready-made ones, it is **passive**. **Did it happen by chance or deliberately?** Naturally, or artificially. So (a) is **natural passive** - ready-made antibodies by a natural route; (b) is **artificial active** - the vaccine's antigens make the child produce their own; (c) is **natural active** - the infection made them produce their own; (d) is **artificial passive** - ready-made antibodies given deliberately. Only **active** immunity makes **memory cells**, which is exactly why passive immunity acts immediately but is **short-lived**.

**Common mistakes.**

- Saying the body makes antibodies "for" a pathogen after it arrives. The B-lymphocyte with the matching receptor already exists; the antigen **selects** it and it is then cloned.
- Saying memory cells make antibodies. Memory cells divide fast into plasma cells when the antigen returns; the **plasma cells** make the antibodies.
- Saying antibodies kill pathogens. Antibodies bind antigens: they clump pathogens together, block toxins and mark pathogens for phagocytes, which do the killing.

- Saying a vaccine contains antibodies. A vaccine contains **antigens**; your own cells then make the antibodies and memory cells. Ready-made antibodies give passive immunity.
- Saying the secondary response is faster "because the body remembers". Name the cells: there are many more memory cells than the first matching B-lymphocytes, so there is almost no lag and far more antibody is made.
- Calling a monoclonal antibody "a mixture of antibodies". Every molecule is identical, made by one clone of hybridoma cells, so it binds one antigen only.

## Exam tips

- Distinguish **phagocytes** (engulf, non-specific) from lymphocytes: B cells → antibodies (humoral), T cells (helper/killer, cell-mediated).
- Label an **antibody** (heavy and light chains, disulfide bonds, variable region and antigen-binding site, hinge, constant region) and tie each part to a function: variable region → specificity; two sites → agglutination; constant region → binds phagocytes.
- In a dipstick question, the **mobile** antibodies carry the marker, the **immobilised** antibodies at the test line catch the complex, and the **control** line catches mobile antibodies to show the test worked.
- Describe phagocytosis in order: attracted → receptors bind → engulf (endocytosis) → lysosomes fuse → hydrolytic enzymes digest.
- Compare the **primary and secondary response** on a graph – memory cells make the secondary faster and larger.
- Distinguish **active vs passive** and **natural vs artificial** immunity with an example of each; explain vaccination and herd immunity.



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# Energy and respiration

A-Level Biology

## Why living things need energy

Cells need a steady supply of **energy** 能量, which they get from **respiration** 呼吸作用. Energy is needed for:

- **active transport** 主动运输 (moving substances against a gradient),
- movement (for example muscle contraction),
- **anabolic** 合成代谢 reactions – the building of large molecules, such as in DNA replication and protein synthesis.

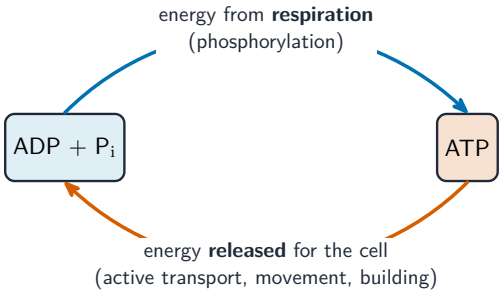



*During exercise, muscles need a constant supply of energy released by respiration*

## ATP – the energy currency

ATP is the molecule that carries energy to where it is needed. It is made from ADP and a phosphate group; when it loses that phosphate again, it releases a small, usable burst of energy. ATP suits this job well, so we call it the **universal energy currency**:

- it releases energy quickly, in small amounts that match a cell's needs.
- it is easily made and re-made, again and again.
- it is small and soluble, so it moves easily around the cell.




*Respiration adds a phosphate to make ATP; the cell breaks it off again to release energy*

ATP is made in two ways: by direct transfer of a phosphate group in **phosphorylation** 磷酸化 reactions, and by **chemiosmosis** 化学渗透 across the membranes of **mitochondria** 线粒体 and chloroplasts.

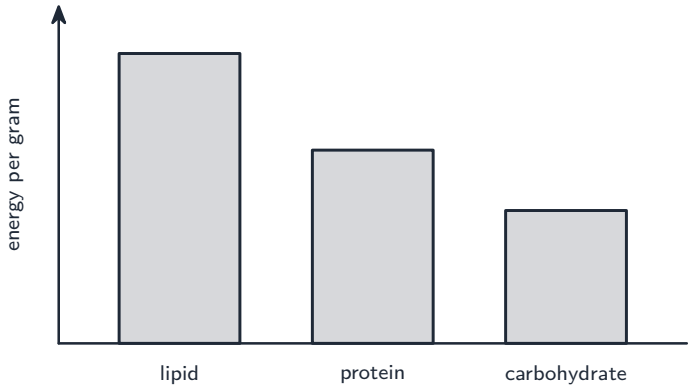
## Respiratory substrates and RQ

A **respiratory substrate** 呼吸底物 is a molecule that is broken down to release energy. Per gram, **lipids** release the most energy (they have the most hydrogen), proteins are next, and carbohydrates the least.

| Substrate | Energy density / kJ $g^{-1}$ |
|---|---|
| carbohydrate | 15.8 |
| lipid | 39.4 |
| protein | 17.0 |

**Why lipids release the most.** Most of the energy of respiration comes from oxidative phosphorylation, which uses the **hydrogen** atoms carried by reduced NAD and FAD. Fatty acids are long chains of $CH_2$ groups, so a lipid molecule has far more hydrogen atoms per gram than a carbohydrate (which already contains much oxygen). More hydrogen means more reduced NAD, more electrons passing along the chain, and more ATP; and more oxygen is needed to accept them, forming more water.






*Lipids release the most energy per gram, then proteins, then carbohydrates*

The **respiratory quotient** 呼吸商 (RQ) compares the gases exchanged:

$$\text{RQ} = \frac{\text{molecules of carbon dioxide produced}}{\text{molecules of oxygen taken in}}$$

You can work out the RQ from a respiration equation. Carbohydrates give an RQ of about 1.0, lipids about 0.7 and proteins about 0.9.

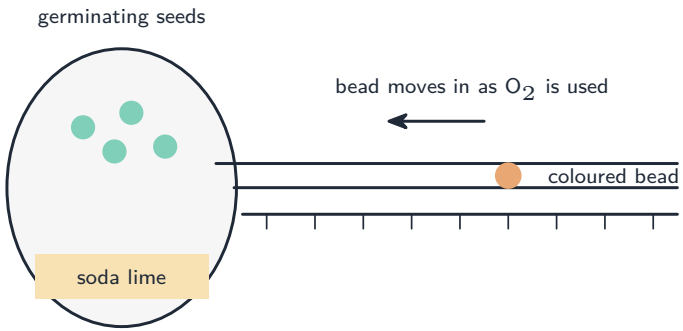
> **Worked example.** Find the RQ for the aerobic respiration of glucose: $C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O$.
>
> $$\text{RQ} = \frac{CO_2 \text{ produced}}{O_2 \text{ taken in}} = \frac{6}{6} = 1.0.$$
>
> This is why an RQ near 1.0 suggests the organism is respiring carbohydrate; a lower RQ (about 0.7) suggests it is using lipid, which needs more oxygen per molecule of $CO_2$.

> **Worked example (a lipid).** Triolein is respired: $C_{57}H_{104}O_6 + 80O_2 \rightarrow 57CO_2 + 52H_2O$. RQ $= 57/80 = 0.71$. An RQ above 1 means some respiration is **anaerobic** (carbon dioxide is given off by yeast or plant cells without oxygen being used), or that carbohydrate is being turned into fat. A mixture of substrates gives a value in between: an RQ of 0.85 suggests a mixture of carbohydrate and lipid.

A **respirometer** 呼吸计 measures the **oxygen** 氧气 taken in by living things, such as **germinating** 萌发 seeds or small **invertebrates** 无脊椎动物, and is used to find their RQ.



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*The soda lime absorbs the $CO_2$ given off, so the gas volume falls only by the oxygen used – and the bead moves in by that amount*

**Using a respirometer.**

1. Put the organisms (for example 10 g of germinating peas) in one tube, on a gauze above **soda lime** (or potassium hydroxide solution), which absorbs carbon dioxide.
2. Set up a **control** tube with the same volume of glass beads instead of living organisms. Connecting it to the other side of a U-tube manometer cancels out any change in volume caused by changes in temperature or pressure.
3. Stand both tubes in a **water bath** at a constant temperature for 10 minutes, with the tap open, so the apparatus reaches the temperature.
4. Close the tap and measure how far the liquid moves along the capillary in a set time. Since the carbon dioxide is absorbed, the movement shows the volume of **oxygen** used. Volume $= \pi r^2 \times$ distance.
5. To find the carbon dioxide produced, repeat **without** soda lime (replace it with water). The movement now shows oxygen used **minus** carbon dioxide given out.

> **Worked example (finding the RQ).** With soda lime, the liquid moved 40 mm in 10 min; without soda lime, it moved 6 mm in the same direction. Oxygen used $\propto 40$; oxygen used minus carbon dioxide produced $\propto 6$, so carbon dioxide produced $\propto 40-6=34$. RQ $= 34/40 = 0.85$: the seeds are respiring a mixture of carbohydrate and lipid. (If the liquid had not moved at all without soda lime, the RQ would be exactly 1.)

The same apparatus can be used to find the effect of temperature on the rate of respiration, by repeating with the water bath at different temperatures and dividing the volume of oxygen used by the time and the mass of organisms.

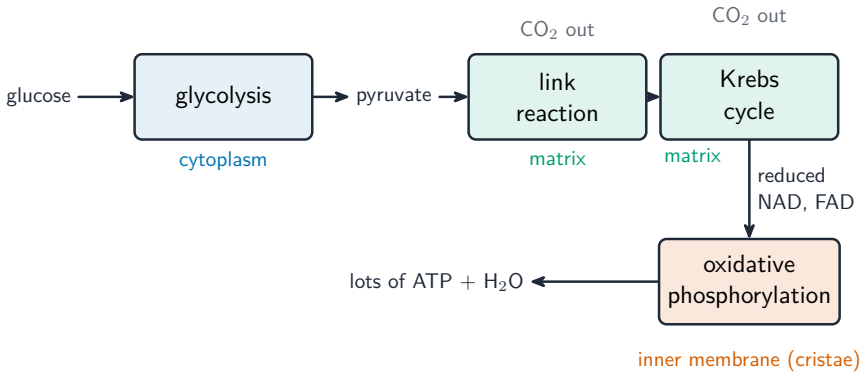


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## Aerobic respiration: the four stages

**Aerobic** 有氧 respiration (with oxygen) has four stages, each in a set place in the cell:

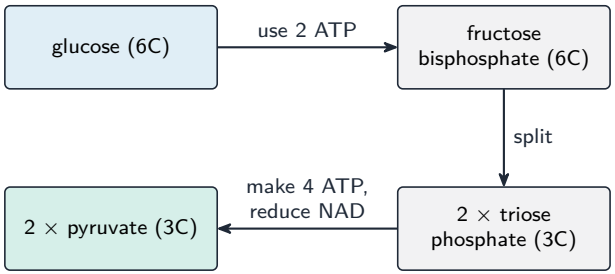
| Stage | Where it happens |
|---|---|
| **glycolysis** 糖酵解 | the **cytoplasm** 细胞质 |
| **link reaction** 连接反应 | the **matrix** 基质 of the mitochondria |
| **Krebs cycle** 克雷布斯循环 | the matrix of the mitochondria |
| **oxidative phosphorylation** 氧化磷酸化 | the inner membrane of the mitochondria |




*The four stages and where each happens; reduced NAD and FAD carry hydrogen to the inner membrane where most ATP is made*

### Glycolysis

**Glucose** 葡萄糖 (6 carbons) is first phosphorylated, using 2 ATP, to form fructose bisphosphate (6C). This 6C molecule is split into two triose phosphate molecules (3C each). These are then **oxidised** 氧化 to **pyruvate** 丙酮酸 (3C). Glycolysis makes a net gain of 2 ATP and some **reduced** 还原 NAD (NAD is a **coenzyme** 辅酶, a helper molecule).




*Glycolysis spends 2 ATP to start but makes 4, so the net gain is 2 ATP (plus reduced NAD) – and it needs no oxygen*

## The link reaction

When oxygen is available, pyruvate enters the mitochondria. There each pyruvate loses a **carbon dioxide** 二氧化碳 and is turned into a 2-carbon **acetyl** 乙酰基 group. This group is carried by **coenzyme A** 辅酶 A to form acetyl coenzyme A. Some carbon dioxide is released and NAD is reduced. Coenzyme A only carries the acetyl group: it hands it to the Krebs cycle and is then free to collect another one.

## The Krebs cycle

The 2C acetyl group joins a 4-carbon molecule, **oxaloacetate** 草酰乙酸, to make a 6-carbon molecule, **citrate** 柠檬酸. Citrate is then changed back to oxaloacetate in a series of small steps, ready to accept the next acetyl group. During these steps:

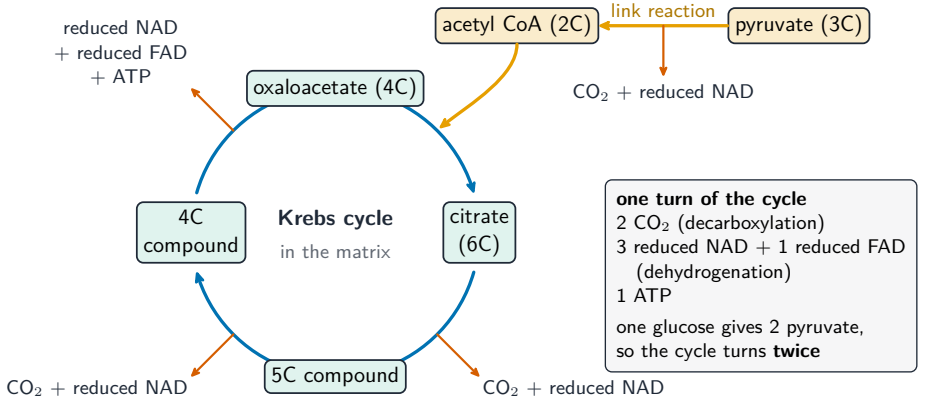
- **decarboxylation** 脱羧 removes carbon as carbon dioxide.
- **dehydrogenation** 脱氢 removes hydrogen, which **reduces** the coenzymes NAD and FAD.

The reduced NAD and FAD then carry the hydrogen to the carriers in the inner mitochondrial membrane.

Each turn of the cycle releases 2 $CO_2$, 3 reduced NAD, 1 reduced FAD and 1 ATP. One glucose gives two pyruvates, so the link reaction and the cycle each run **twice** per glucose. Notice how little ATP the cycle makes directly. Its main job is to load NAD and FAD with hydrogen; that hydrogen is what makes most of the ATP in the next stage.



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*The link reaction feeds acetyl CoA into the cycle. Each turn releases 2 $CO_2$ (decarboxylation), 3 reduced NAD and 1 reduced FAD (dehydrogenation), and 1 ATP*

## Oxidative phosphorylation

This stage makes most of the ATP:

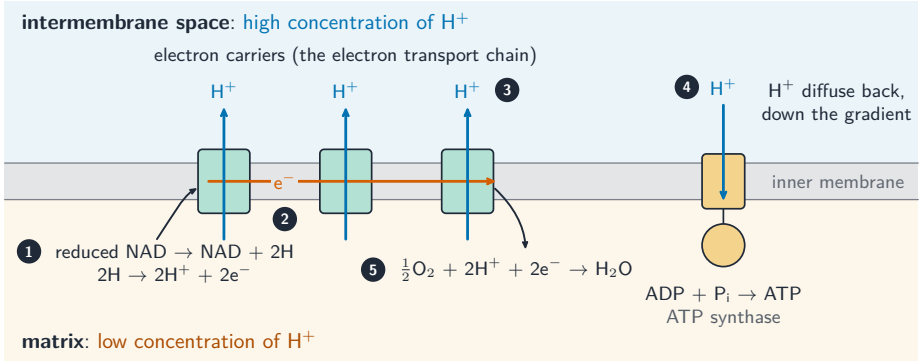
1. the hydrogen atoms split into **protons** 质子 and energetic **electrons** 电子.
2. the electrons pass along the **electron transport chain** 电子传递链, releasing energy as they go.
3. this energy is used to pump protons across the inner membrane.
4. the protons flow back into the matrix through a channel called **ATP synthase** ATP 合酶. This flow provides the energy to make ATP (this is chemiosmosis).
5. **oxygen** is the final electron acceptor: it joins with electrons and protons to form water.

**The ATP count.** Each reduced NAD gives enough energy for about **2.5 ATP**, and each reduced FAD (which passes its electrons in later along the chain) for about **1.5 ATP**. Per molecule of glucose:

| Stage | ATP made directly | Reduced NAD | Reduced FAD |
|---|---|---|---|
| glycolysis | 2 (net) | 2 | 0 |
| link reaction (×2) | 0 | 2 | 0 |
| Krebs cycle (×2) | 2 | 6 | 2 |
| total | 4 | 10 | 2 |

Oxidative phosphorylation: $10 \times 2.5 + 2 \times 1.5 = 28$ ATP, so the total is about **32 ATP** per glucose. The real figure is usually a little lower, because some protons leak back across the membrane and some ATP is used to move pyruvate and ADP into the mitochondrion. Anaerobic respiration makes only 2 ATP per glucose.

The **inner** membrane is impermeable to protons except through ATP synthase, so the proton gradient is kept; the outer membrane holds the intermembrane space close to the inner membrane, so a high proton concentration builds up quickly.




*Electrons pump protons ($H^+$) into the intermembrane space; they flow back through ATP synthase to make ATP (chemiosmosis)*

**Common mistakes.**

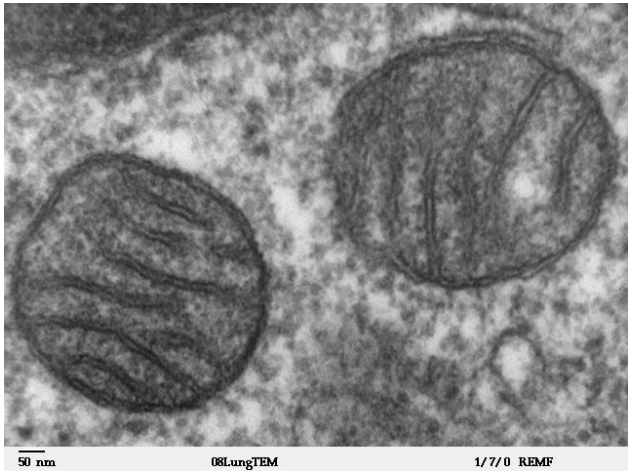
- Saying oxygen is needed to make carbon dioxide. The $CO_2$ comes from decarboxylation in the link reaction and the Krebs cycle. Oxygen is used only at the **end** of the chain, where it accepts electrons and forms water.
- Saying ATP synthase **pumps** protons. The carriers pump protons **out** of the matrix using the electrons' energy. Protons then flow **back** through ATP synthase by facilitated diffusion, down their concentration gradient.
- Saying the Krebs cycle makes "lots of ATP". It makes only one ATP per turn; most ATP is made by oxidative phosphorylation.
- Forgetting why no oxygen stops everything. Without oxygen to accept electrons, the chain backs up, so reduced NAD cannot be turned back into NAD, and the link reaction and Krebs cycle stop too.

### The structure of mitochondria

The inner membrane is folded into **cristae** 嵴, giving a large surface for the electron transport chain and ATP synthase. The matrix inside holds the substances and helpers for the link reaction and the Krebs cycle.



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*Two real mitochondria, photographed with an electron microscope. The dark stripes crossing the inside are the cristae – all that folding is what makes the surface for the electron transport chain so large*

## Anaerobic respiration

When there is no oxygen, only glycolysis can run. To keep glycolysis going, the cell must use up the reduced NAD. This happens by **fermentation** 发酵:

- in mammals, pyruvate is turned into **lactate** 乳酸 (lactate fermentation). The lactate is later broken down when oxygen returns.
- in **yeast** 酵母, pyruvate is turned into **ethanol** 乙醇 and carbon dioxide (ethanol fermentation).

$$\text{pyruvate} + \text{reduced NAD} \xrightarrow{\text{lactate dehydrogenase}} \text{lactate} + \text{NAD}$$

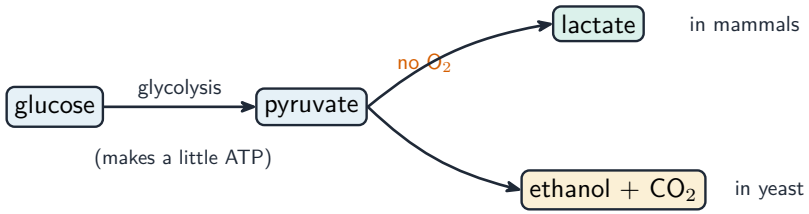
$$\text{pyruvate} \xrightarrow{\text{pyruvate decarboxylase}} \text{ethanal} + CO_2$$

$$\text{ethanal} + \text{reduced NAD} \xrightarrow{\text{alcohol dehydrogenase}} \text{ethanol} + \text{NAD}$$

Both routes make no extra ATP: their job is only to turn reduced NAD back into NAD, so that glycolysis can go on making its 2 ATP. Lactate fermentation can be **reversed**; ethanol fermentation cannot, because carbon dioxide is lost.

**What happens to the lactate.** Lactate passes from the muscles into the blood and is carried to the **liver**. When oxygen is available again, the liver turns it back into pyruvate, which is either oxidised in aerobic respiration or turned into glucose and stored as glycogen. The extra oxygen needed after exercise to do this is the **oxygen**

**debt**: it is why you keep breathing deeply after a sprint. Lactate also lowers the pH in muscle, which reduces enzyme activity and contributes to muscle fatigue.

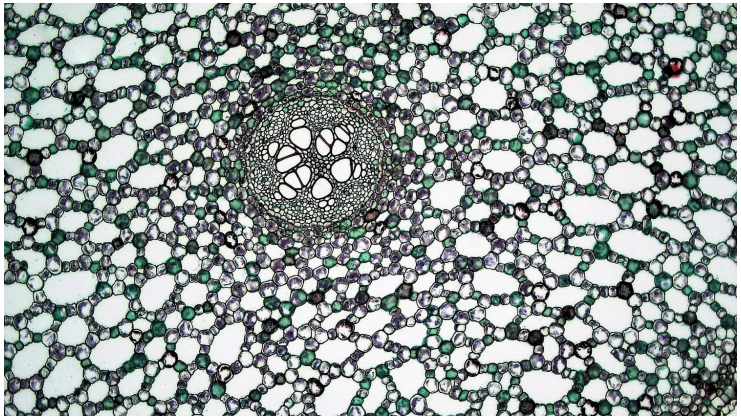



*Without oxygen, pyruvate becomes lactate (mammals) or ethanol (yeast); this regenerates NAD for glycolysis*

**Anaerobic** 无氧 respiration gives far less energy than aerobic respiration. Aerobic respiration also runs the Krebs cycle and oxidative phosphorylation, which release a lot more ATP, while anaerobic respiration gains only the small amount from glycolysis.

## Rice and waterlogged roots

Rice can grow with its roots under water, where there is little oxygen. It is adapted in three ways: it develops **aerenchyma** 通气组织 (air-filled spaces) in the roots to carry air down; the roots use ethanol fermentation to keep making some ATP; and the stems grow faster to reach the air above the water.



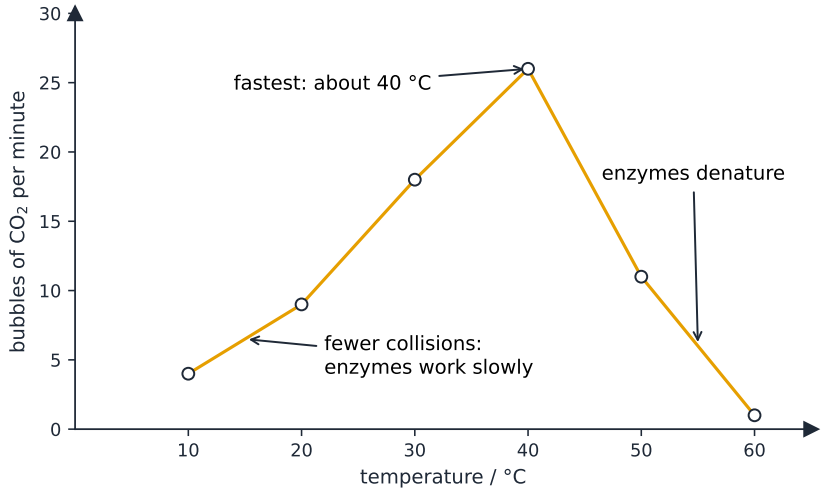
*A root of a plant that grows in water, seen in cross-section. The big white gaps are the aerenchyma – connected air channels that let oxygen diffuse all the way down to roots sitting in oxygen-poor mud*



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## Investigating the rate of respiration

A redox **indicator** 指示剂 such as DCPIP or methylene blue loses its colour when it gains hydrogen from respiring cells. The faster the colour is lost, the faster the yeast is respiring, so you can test the effect of temperature or substrate concentration. A respirometer can also be used to measure how temperature changes the rate of oxygen uptake.




*The rate rises to a peak near 40 °C, then falls as the enzymes are denatured*

**Method with yeast and methylene blue.** Put the same volume of yeast suspension and glucose solution in a set of tubes, each in a water bath at a different temperature, and leave them for 5 minutes to reach the temperature. Add the same volume of methylene blue to each, mix, and time how long each takes to turn colourless (compare with a tube of yeast without dye as a colour standard). Rate = 1/time. Dehydrogenase enzymes remove hydrogen from substrates in glycolysis and the Krebs cycle, and the dye takes it up. Do not shake the tubes once the dye is added, because oxygen from the air would re-oxidise it and turn it blue again. A control tube of **boiled** yeast stays blue.

## Exam tips

- State **where** each stage happens and its ATP yield: glycolysis (cytoplasm), link reaction + Krebs (matrix), oxidative phosphorylation (inner membrane, most ATP).
- Explain the roles of **NAD/FAD** (carry hydrogen to the electron transport chain) and of oxygen (the final electron acceptor).
- **RQ** = CO2 produced ÷ O2 used (≈ 1.0 carbohydrate, 0.7 lipid); know how a respirometer measures it.

- Anaerobic respiration gives lactate (animals) or ethanol + CO2 (yeast/plants) and far less ATP (glycolysis only).
- RQ from a respirometer: with soda lime → $O_2$ used; without → $O_2$ used minus $CO_2$ given out; $CO_2$ = the difference.
- About 2.5 ATP per reduced NAD and 1.5 per reduced FAD; about 32 ATP per glucose aerobically, 2 anaerobically.
- Lipids release more energy per gram because they have more hydrogen atoms, which feed the electron transport chain.
- The lactate is taken to the liver and turned back into pyruvate or glucose when oxygen returns (oxygen debt).



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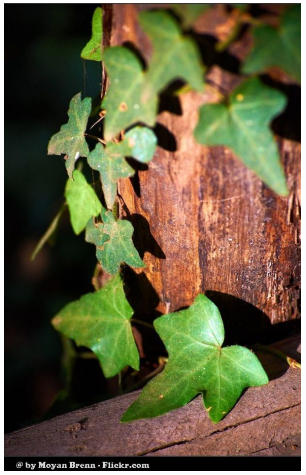
# Photosynthesis

A-Level Biology

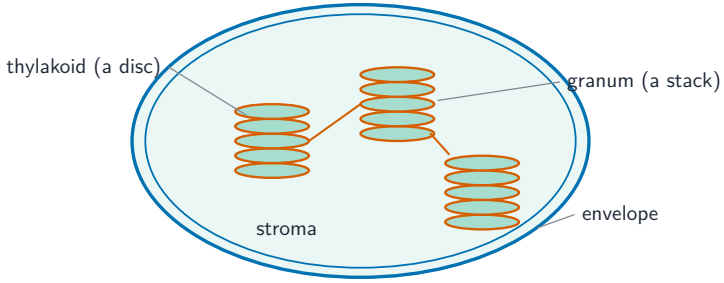
## The chloroplast

**Photosynthesis** 光合作用 happens inside the **chloroplast** 叶绿体. Its structure suits its two stages:

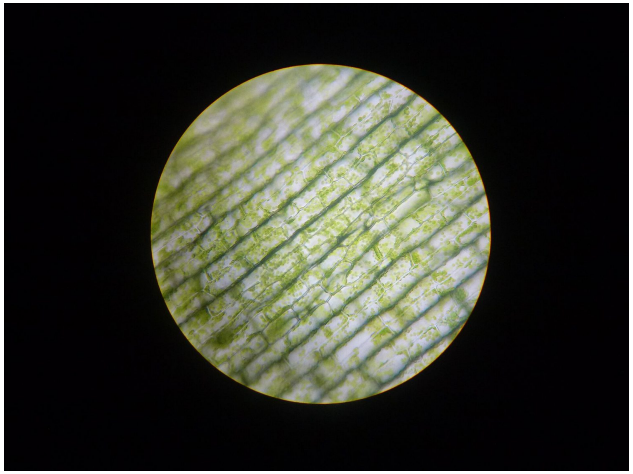
- inside are stacks of flat sacs called **thylakoids** 类囊体. A stack of thylakoids is a **granum** (plural **grana** 基粒). The thylakoid membranes hold the light-trapping pigments and are the site of the first stage.
- the fluid around the thylakoids is the **stroma** 基质, the site of the second stage.




*Leaves are green because their chloroplasts are full of the pigment chlorophyll*




*Thylakoids stack into grana (the first stage happens here); the stroma around them is where the second stage happens*



*Chloroplasts (the small green discs) inside the cells of an Elodea (pondweed) leaf, seen under a microscope*

The overall equation is

$$6CO_2 + 6H_2O \xrightarrow{\text{light, chlorophyll}} C_6H_{12}O_6 + 6O_2$$

**How the chloroplast suits its job.**

- The many thylakoid membranes give a very **large surface area** for the pigments, electron carriers and ATP synthase.
- The pigments are arranged in **photosystems** in the membranes, so light energy is passed efficiently to the reaction centres.
- The thylakoid space is small, so pumping protons into it quickly builds a steep **proton gradient**.
- The stroma contains the enzymes of the Calvin cycle (including rubisco), close to the thylakoids that supply ATP and reduced NADP.
- The chloroplast has its own circular **DNA** and 70S **ribosomes**, so it can make some of its own proteins. Starch grains and lipid droplets store the products.

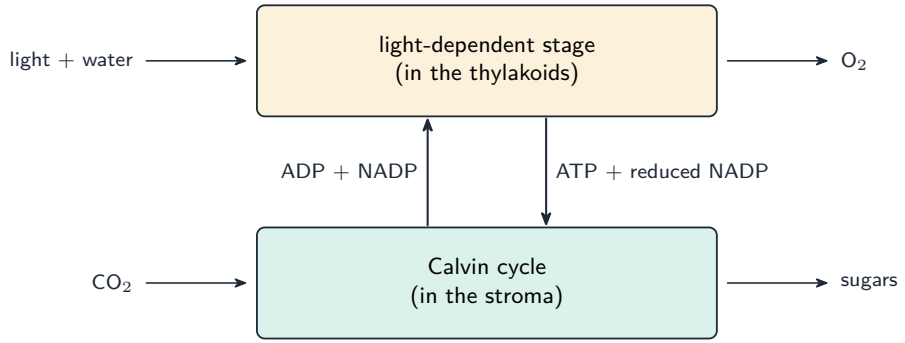
## The two stages of photosynthesis

Photosynthesis has two linked stages:

1. the **light-dependent stage** 光反应阶段 happens in the thylakoids. It uses light energy to make ATP and **reduced** 还原 NADP.
2. the **light-independent stage** 暗反应阶段, also called the **Calvin cycle** 卡尔文循环, happens in the stroma. It uses the ATP and reduced NADP from the first stage to build complex organic molecules from **carbon dioxide** 二氧化碳.



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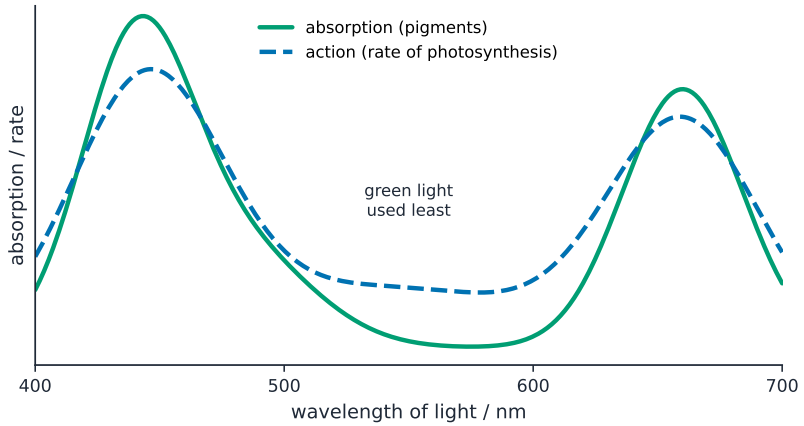

*The two stages are linked: the first makes the ATP and reduced NADP that the second spends to turn $CO_2$ into sugars*

## Chloroplast pigments

A **pigment** 色素 is a coloured substance that absorbs light. The thylakoids hold several pigments that work together to trap as much light as possible:

- **chlorophyll** 叶绿素 a and chlorophyll b (which absorb mainly red and blue light),
- **carotene** 胡萝卜素 and **xanthophyll** 叶黄素 (accessory pigments that absorb mainly blue and blue-green light, widening the range of wavelengths used, and pass the energy on to chlorophyll a).

We study them with two graphs. An **absorption spectrum** 吸收光谱 shows how much light each pigment absorbs at each wavelength. An **action spectrum** 作用光谱 shows how fast photosynthesis goes at each wavelength. The two graphs match closely, which shows the pigments drive photosynthesis.




action tracks absorption · green light used least

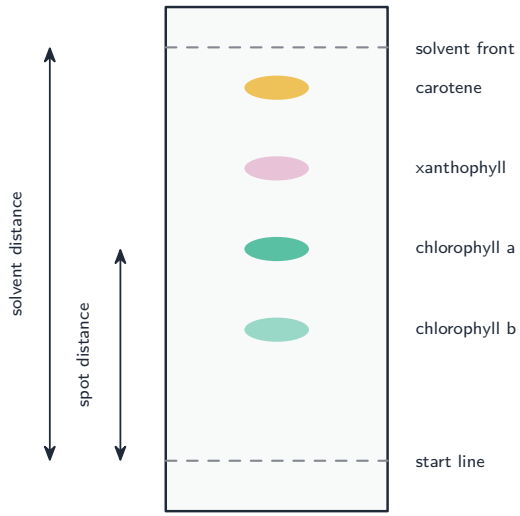
*The absorption spectrum and action spectrum match: blue and red light are used most, green light least*

You can separate the pigments by **chromatography** 色谱法: the pigments travel different distances up the paper. Each pigment is identified by its **Rf value** 比移值 (the distance the pigment moved divided by the distance the solvent moved).

**Method.** Grind leaves with a little sand and propanone (or ethanol) to break the cells and dissolve the pigments. Draw a pencil line (the **origin**) about 2 cm from the bottom of a strip of chromatography paper (pencil, because ink would dissolve and run). Use a fine capillary tube to put a small spot of the extract on the line; let it dry and repeat many times, to make a small, concentrated spot. Stand the paper in a little solvent in a closed tube, with the solvent **below** the origin (so the pigments do not dissolve straight into it). When the solvent has nearly reached the top, remove the paper, mark the **solvent front** at once, and let it dry. Work in a fume cupboard or a well-ventilated room, as the solvents are flammable and harmful. Pigments that are more soluble in the solvent, and less attracted to the paper, travel further.

> **Worked example.** The solvent moved 8.0 cm. A yellow-orange spot moved 7.6 cm and a blue-green spot 3.6 cm. Rf of the first $= 7.6/8.0 = 0.95$: **carotene**. Rf of the second $= 3.6/8.0 = 0.45$: **chlorophyll a**. An Rf value is always less than 1 and has no units. Comparing Rf values with those in a table (measured with the same solvent) identifies each pigment. **Thin-layer chromatography** (TLC), on a plate coated with silica, gives sharper, faster separations.






*Each pigment travels its own distance up the paper; its Rf is the spot distance divided by the solvent distance*

## The light-dependent stage

In the thylakoids, light is used to make ATP. This is **photophosphorylation** 光合磷酸化, and it comes in two forms.

**Photosystems.** In the thylakoid membrane, hundreds of pigment molecules are grouped into a **light-harvesting complex** (an antenna), arranged around a **reaction centre** that holds two molecules of chlorophyll a. Light absorbed by any pigment in the antenna is passed from molecule to molecule to the reaction centre. There, the energy **excites** an electron so much that it leaves the chlorophyll and is taken up by an **electron acceptor**: the chlorophyll is oxidised and the acceptor is reduced. The reaction centre of PSI absorbs best at 700 nm and that of PSII at 680 nm.

In **cyclic photophosphorylation** 循环光合磷酸化:

- only **photosystem** 光系统 I (PSI) is used.
- **photoactivation** 光激活 of chlorophyll occurs (light boosts its **electrons** 电子 to a higher energy).
- only ATP is made.

In **non-cyclic photophosphorylation** 非循环光合磷酸化:

- both photosystem I (PSI) and photosystem II (PSII) are used.
- photoactivation of chlorophyll occurs.



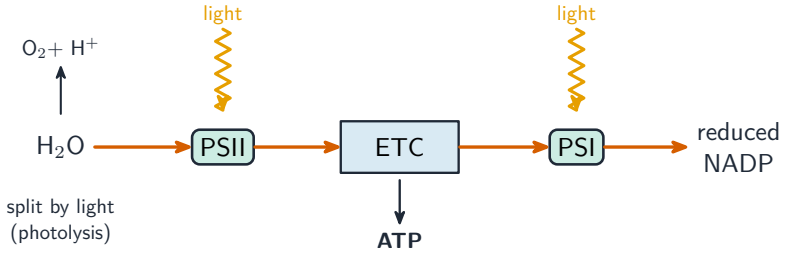
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- the **oxygen-evolving complex** 放氧复合体 carries out the **photolysis** 光解 (splitting by light) of water, which releases **oxygen** 氧气.
- both ATP and reduced NADP are made.

**Photolysis.** The chlorophyll in PSII has lost electrons, so it must get them back. An enzyme complex on the inner side of PSII splits water:

$$2H_2O \rightarrow 4H^+ + 4e^- + O_2$$

The electrons replace those lost from PSII; the hydrogen ions stay inside the thylakoid (adding to the proton gradient) and are later used to reduce NADP; the oxygen is a waste product that diffuses out of the leaf, or is used in respiration. In **non-cyclic** photophosphorylation, the electrons from PSII pass along the electron transport chain to PSI, and electrons from PSI are passed to **NADP**, which takes up a hydrogen ion from the stroma to become **reduced NADP**. In **cyclic** photophosphorylation, electrons from PSI pass back to the electron transport chain and return to PSI, making ATP but no reduced NADP and no oxygen. Cyclic photophosphorylation tops up the ATP, because the Calvin cycle needs three ATP for every two reduced NADP.




*In non-cyclic photophosphorylation, photolysis splits water; electrons flow PSII → PSI, making ATP and reduced NADP*

In both forms, energy is released in the same way:

1. energetic electrons pass along an **electron transport chain** 电子传递链, releasing energy as they go.
2. this energy is used to pump **protons** 质子 across the thylakoid membrane.
3. the protons flow back into the stroma through **ATP synthase** ATP 合酶, and this flow provides the energy to make ATP.

This way of making ATP, using the energy of a proton gradient, is called **chemiosmosis** 化学渗透. The protons are pumped **into** the thylakoid space, so it becomes more acidic than the stroma; ATP is made on the **stroma** side of the membrane, where it is needed for the Calvin cycle.

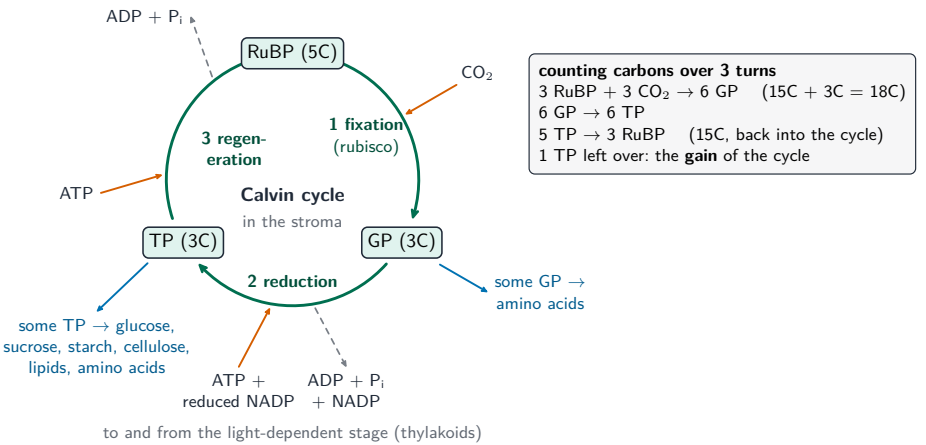


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## The Calvin cycle

The light-independent stage builds sugars in three main steps:

1. **fixation** 固定 – the **enzyme** 酶 rubisco joins carbon dioxide to a 5-carbon molecule, RuBP (ribulose bisphosphate). This makes two molecules of a 3-carbon compound, GP (glycerate 3-phosphate).
2. **reduction** – GP is reduced to TP (triose phosphate) using reduced NADP and ATP from the light-dependent stage.
3. **regeneration** – most of the TP is used to **regenerate** 再生 the RuBP (using more ATP), so the cycle can keep running.




*Fixation adds $CO_2$ to RuBP; reduction uses ATP and reduced NADP to make TP; regeneration uses ATP to remake RuBP. Only 1 TP in every 6 leaves the cycle*

Some TP leaves the cycle to make useful molecules. GP can be used to make some **amino acids** 氨基酸, and TP can be used to make **carbohydrates** 碳水化合物, **lipids** 脂质 and amino acids.

**Why so little TP leaves.** Count the carbons over three turns. Three RuBP (15 C) fix three $CO_2$ (3 C), giving six GP (18 C) and then six TP. Five of the TP (15 C) are needed to remake the three RuBP, so only **one** TP (3 C) is a gain. Six turns give two spare TP, enough to make one glucose (6 C).

**How the cycle was worked out.** Algae were given radioactive $^{14}CO_2$ for a few seconds at a time and then killed quickly; chromatography showed that GP was the first compound to become radioactive, then TP, then sugars. Following how GP and RuBP change when the light or the carbon dioxide is cut off (see the worked example below) showed the order of the steps.

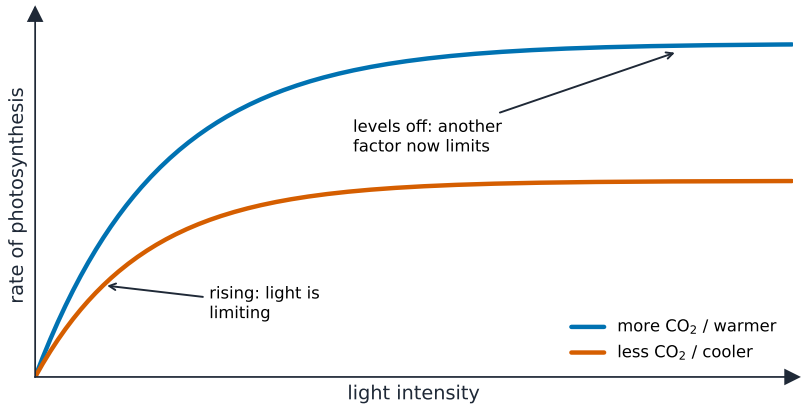
**Common mistakes.**

- Calling the Calvin cycle "the dark reaction" and saying it happens at night. It needs a steady supply of ATP and reduced NADP, so it stops soon after the light goes off.
- Saying rubisco makes TP. Rubisco only catalyses fixation, which makes GP. GP becomes TP in the reduction step.
- Forgetting that regeneration also uses ATP. Reduction uses ATP **and** reduced NADP; regeneration uses ATP only.
- Saying "one GP" is made. Fixation makes **two** GP from each RuBP and $CO_2$, since 5 C + 1 C = 2 × 3 C.

## Limiting factors

A **limiting factor** 限制因素 is the one in shortest supply that holds back the rate of photosynthesis. The three main ones are **light intensity** 光照强度, **carbon dioxide concentration** 浓度, and **temperature** 温度.

- raising light intensity speeds up photosynthesis, until some other factor becomes limiting.
- raising carbon dioxide concentration speeds it up, until some other factor becomes limiting.
- raising temperature speeds it up, but only to an optimum; too high and the enzymes denature.




the scarcest factor limits the rate · higher plateau: $CO_2$ or temperature was limiting

*While the rate rises, light is the limiting factor; where it levels off, another factor ($CO_2$ or temperature) limits it*

**Why each factor limits.** Light intensity limits the light-dependent stage: less ATP and reduced NADP are made. Carbon dioxide concentration limits fixation by rubisco. Temperature affects the **enzymes** of the Calvin cycle most (the light-dependent stage depends mainly on light, not temperature); above about 30–35 °C in many plants the rate falls, as enzymes begin to denature and stomata close.

**In glasshouses.** Growers raise the yield of crops such as tomatoes and lettuce by controlling all three factors: artificial lighting at night or in winter; burning paraffin or natural gas to raise the carbon dioxide concentration to about 0.1% (and to warm the air); and heaters set to the best temperature. Each costs money, so a grower raises a factor only while it is the one limiting the rate: adding more carbon dioxide when light is limiting gains nothing.

You can measure the rate of the light-dependent stage with a redox **indicator** 指示剂 such as DCPIP or methylene blue and a suspension of chloroplasts: the dye loses its colour as the chloroplasts work, and you can test different light intensities or light **wavelengths** 波长. DCPIP is blue when oxidised; it takes the electrons that would normally reduce NADP, and turns **colourless** when reduced. Grind leaves in an ice-cold, buffered solution of the same water potential as the chloroplasts (so they neither burst nor shrink), filter and centrifuge to get a chloroplast suspension, and keep it on ice. Add DCPIP to tubes of suspension at different distances from a lamp, and time how long each takes to lose its blue colour, or follow it in a colorimeter. Controls: a tube kept in the **dark** (stays blue) and a tube with no chloroplasts. With a whole **aquatic plant** 水生植物 you can count the bubbles of oxygen given off to compare rates under different conditions.

> **Worked example.** A plant photosynthesising steadily is suddenly deprived of carbon dioxide. What happens to the levels of GP and RuBP? Follow the cycle one step at a time. Carbon dioxide is fixed when **RuBP** combines with it, catalysed by rubisco, to make **GP**. Remove the carbon dioxide and that reaction stops, so GP is **no longer being made** - yet GP continues to be **used up**, reduced to TP using ATP and reduced NADP. So **GP falls**. Meanwhile RuBP is still being **regenerated** from TP but is no longer being **consumed**, so **RuBP rises**. The method never changes: find the reaction that stops, then ask of each substance whether it is still being **made** and still being **used**. Removing the **light** instead gives the mirror image: with no ATP or reduced NADP, GP cannot be reduced, so **GP rises and RuBP falls**.

**Pondweed and light intensity.** Put a piece of pondweed (*Elodea* or *Cabomba*) in dilute sodium hydrogencarbonate solution (to supply carbon dioxide), with a lamp at a measured distance $d$. Leave it for 5 minutes to adjust, then count the bubbles, or better, collect the gas in a capillary tube for a fixed time and measure the length of the gas column. Light intensity is proportional to $1/d^2$, so moving the lamp from 10 cm to 20 cm cuts the light intensity to one quarter. Keep the temperature constant by putting a beaker of water (a heat filter) between the lamp and the plant, and keep other lights off. Counting bubbles is not accurate, because bubbles vary in size; and the gas is not all oxygen, while some oxygen is used in respiration, so the method



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measures the **net** rate.

> **Worked example.** At 10 cm from the lamp, a plant produces 40 bubbles per minute. Calculate the relative light intensity at 10 cm and at 20 cm, and suggest the rate at 20 cm if light is the limiting factor. Relative intensity $= 1/d^2$: $1/10^2 = 0.01$ and $1/20^2 = 0.0025$, a quarter. If light limits the rate and the rate is proportional to light intensity, it would fall to about $40 \div 4 = 10$ bubbles per minute.

## Exam tips

- Separate the two stages: **light-dependent** (thylakoid – photolysis, ATP, reduced NADP, O2) and the **Calvin cycle** (stroma – CO2 fixed by rubisco, GP → TP).
- Read **limiting-factor** graphs: the plateau is where a different factor (light, CO2 or temperature) limits the rate.
- Interpret **chromatography** with the $R_f$ value to identify pigments.
- Link chloroplast structure to function (thylakoid stacks for the light reactions; stroma for the Calvin cycle).
- Photolysis: $2H_2O \rightarrow 4H^+ + 4e^- + O_2$; the electrons replace those lost from PSII.
- Cyclic: PSI only, ATP only. Non-cyclic: PSII and PSI, ATP, reduced NADP and oxygen.
- Light off: GP rises, RuBP falls. $CO_2$ removed: RuBP rises, GP falls.
- DCPIP turns from blue to colourless when it is reduced by electrons from the chloroplasts.
- Light intensity $\propto 1/d^2$; use a heat filter so that temperature is not a second variable.



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# Homeostasis

A-Level Biology

## What homeostasis is

**Homeostasis** 稳态 means keeping the conditions inside the body steady, even when the outside changes. Keeping things like temperature, water and blood glucose steady lets enzymes and cells work properly all the time.

**Why it matters in mammals.**

- **Temperature**: enzymes work fastest near 37 °C. Too cold, and reactions such as respiration slow down; too hot, and enzymes **denature**, because hydrogen bonds in their tertiary structure break and the active site changes shape.
- **Water potential of the blood**: if the blood becomes too dilute, water enters cells by osmosis and they swell and may burst; if it becomes too concentrated, cells lose water and shrink, and their metabolism fails.
- **Blood glucose**: cells, above all brain cells, need a steady supply of glucose for respiration. Too little, and cells run short of ATP (the person may faint or go into a coma); too much, and the blood's water potential falls, drawing water out of cells.
- **pH**: changes in pH alter the charges on amino acid R groups, so enzymes and other proteins lose their shape.

Keeping these steady also gives mammals **independence** from the outside: they can stay active in a cold night or a hot desert.




*A blood glucose meter: homeostasis keeps blood glucose within narrow limits*

### The principles of homeostasis

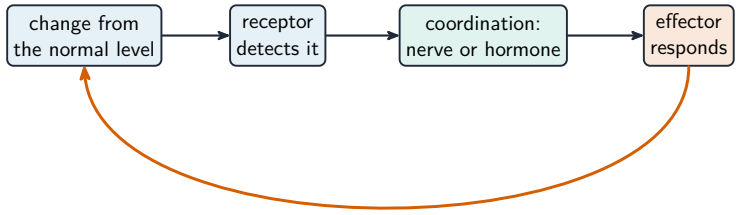
Most homeostasis follows the same plan:

- a change (an internal or external **stimulus** 刺激) is detected by a **receptor** 受体.
- a coordination system carries the message – either the **nervous system** 神经系统 (using nerve signals) or the **endocrine system** 内分泌系统 (using **hormones** 激素).
- an **effector** 效应器 (a muscle or a **gland** 腺体) makes a response that corrects the change.



*Sweating cools the body – part of temperature homeostasis, with the skin as the effector*

This works by **negative feedback** 负反馈: a change away from the normal level triggers a response that pushes it back towards normal.




*Negative feedback: a receptor detects a change and an effector corrects it, returning to normal*



## The liver and urea

The body cannot store extra amino acids. In the **liver** 肝脏, the process of **deamination** 脱氨基作用 removes the amino group from excess **amino acids** 氨基酸, and this is turned into **urea** 尿素. The urea is carried in the blood to the kidneys to be removed.

The amino group is removed as **ammonia** ($NH_3$), which is very soluble and very toxic. The rest of the amino acid becomes a keto acid, which can be respired or turned into glucose or fat. The ammonia is combined at once with carbon dioxide to make urea, which is much less toxic:

$$2NH_3 + CO_2 \rightarrow CO(NH_2)_2 + H_2O$$

Removing waste products of metabolism such as urea and carbon dioxide from the body is called **excretion** 排泄. Other nitrogen-containing wastes in urine are **creatinine** (from creatine in muscle) and uric acid.

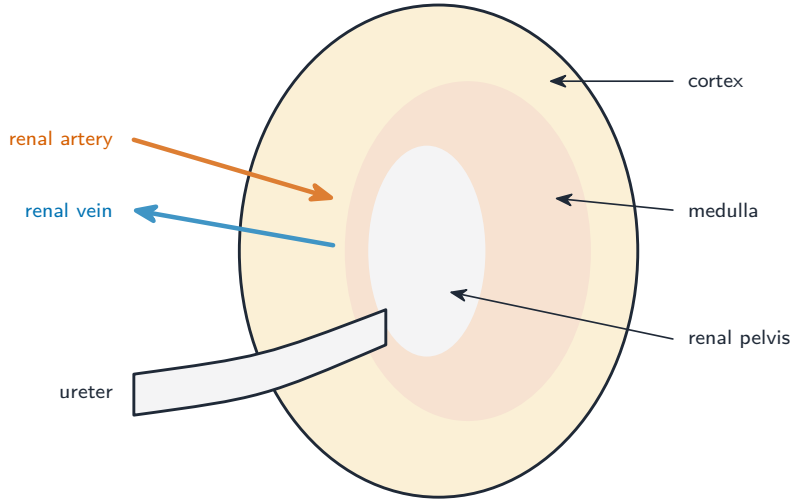
## The kidney

The **kidney** 肾脏 cleans the blood and controls its water content. Its parts are:

- an outer **fibrous capsule**,
- an outer region, the **cortex** 皮质,
- an inner region, the **medulla** 髓质,
- a central space, the **renal pelvis** 肾盂, which collects urine,
- the **ureter** 输尿管, which carries urine to the bladder,
- branches of the renal artery (bringing blood in) and renal vein (taking blood out).



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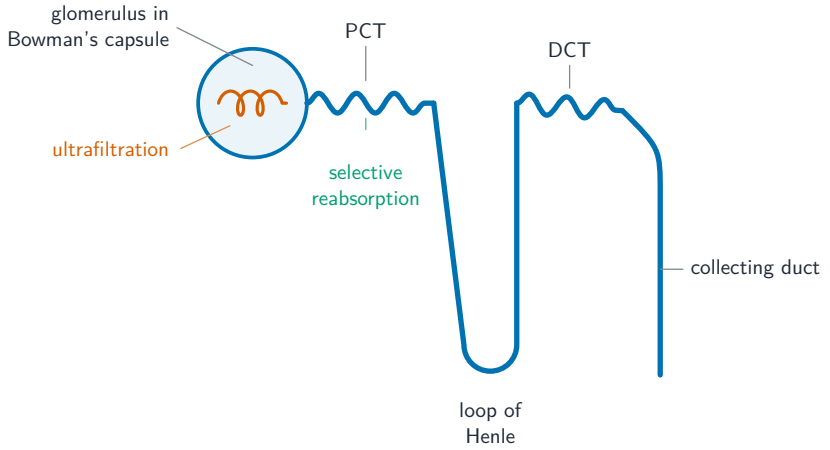

*A section through the kidney: blood is cleaned in the cortex and medulla, and urine collects in the renal pelvis before leaving down the ureter*

## The nephron

Each kidney holds about a million tiny tubes called **nephrons** 肾单位. Along a nephron are: the **glomerulus** 肾小球 (a knot of capillaries), the **Bowman's capsule** 鲍曼囊 around it, the **proximal convoluted tubule** 近曲小管, the **loop of Henle** 亨利环, the **distal convoluted tubule** 远曲小管, and the **collecting duct** 集合管.



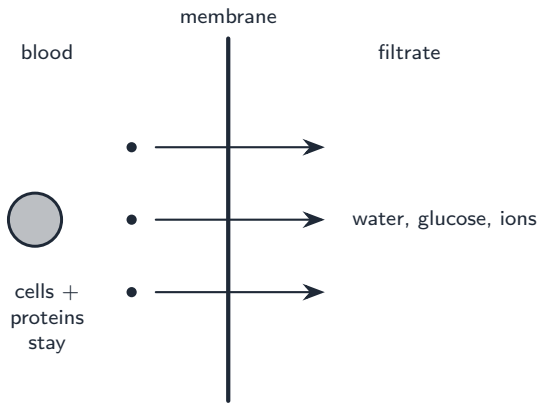
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*Ultrafiltration happens in the Bowman's capsule; selective reabsorption happens in the proximal convoluted tubule*

## Making urine

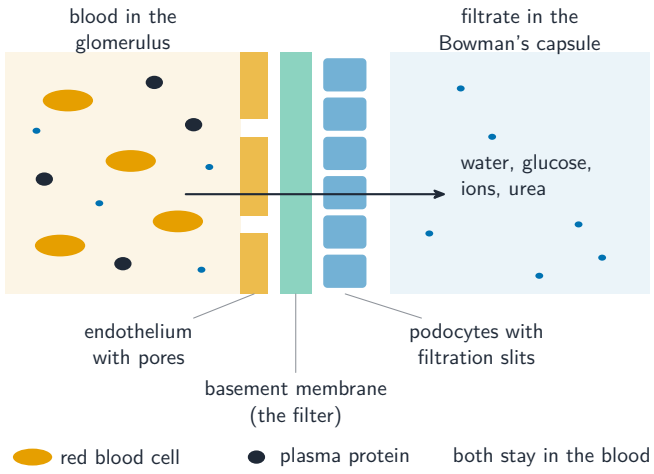
1. **Ultrafiltration** 超滤 happens in the Bowman's capsule. The blood in the glomerulus is under high pressure, so water and small molecules (**glucose** 葡萄糖, **ions** 离子, urea) are pushed out into the capsule, forming the **filtrate** 滤液. Blood cells and large proteins are too big to pass, so they stay in the blood.
2. **Selective reabsorption** 选择性重吸收 happens in the proximal convoluted tubule. Useful substances are taken back into the blood. All the glucose and much of the water and ions are reabsorbed here. The tubule wall is well suited to this: its cells have **microvilli** 微绒毛 to give a large surface area, and many **mitochondria** 线粒体 to power **active transport** 主动运输.




*Ultrafiltration keeps blood cells and proteins in the blood*

## How the Bowman's capsule and proximal tubule are built for their jobs

**The filter.** Between the blood in a glomerular capillary and the space inside the Bowman's capsule there are three layers:




*Three layers lie between the glomerular blood and the filtrate; the basement membrane holds back proteins and cells*

- the **endothelium** 内皮 of the capillary, which has many gaps (**pores**) between and through its cells, so it holds back only blood cells;



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- the **basement membrane** 基底膜, a fine mesh of collagen and glycoproteins. This is the real filter: it lets through molecules with a relative molecular mass below about 69 000, so plasma proteins such as albumin stay in the blood;
- the inner wall of the capsule, made of cells called **podocytes** 足细胞 with many foot-like branches. The gaps between the branches (**filtration slits**) let the filtrate pass into the capsule easily.

**The pressure.** The vessel bringing blood to the glomerulus (the **afferent arteriole**) is wider than the one taking it away (the **efferent arteriole**), so blood is squeezed into the glomerulus and its **hydrostatic pressure** is high. This pressure is greater than the pressure of the filtrate in the capsule, and greater than the pull of the water potential of the blood (which is lowered by the plasma proteins left behind), so fluid is forced out.

Typical concentrations, in g $dm^{-3}$:

| Substance | Blood plasma | Filtrate | Urine |
|---|---|---|---|
| protein | 80 | about 0.05 | 0 |
| glucose | 1.0 | 1.0 | 0 |
| urea | 0.3 | 0.3 | 20 |
| sodium ions | 3.3 | 3.3 | 3.5 |

Glucose and urea have the **same** concentration in plasma and filtrate, because they are small enough to pass freely; protein is almost absent from the filtrate. Glucose is absent from urine because all of it is reabsorbed. Urea is about 60 times more concentrated in urine than in filtrate, because most of the **water** has been reabsorbed while the urea stays behind.

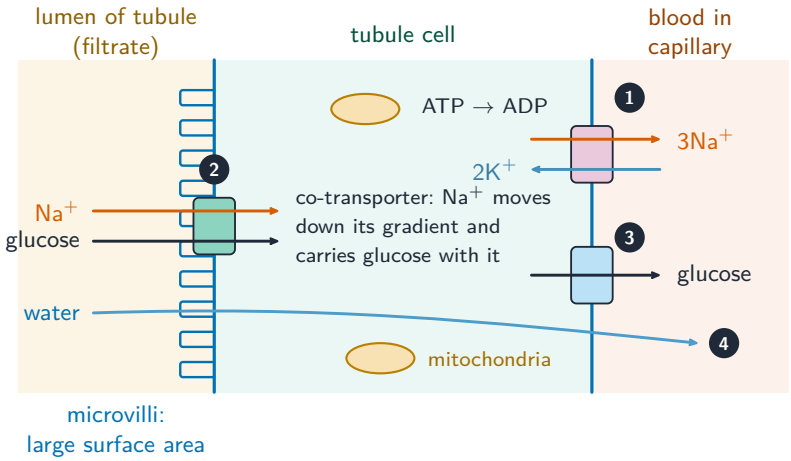
**The proximal convoluted tubule.** About 65% of the water and sodium ions, and all the glucose and amino acids, are reabsorbed here. Its cells have:

- **microvilli** on the side facing the lumen, giving a very large surface area for reabsorption;
- many **mitochondria**, making ATP for the sodium–potassium pumps;
- many **co-transporter proteins** in the membrane facing the lumen;
- a folded membrane on the side facing the blood (more space for pumps and carriers);
- **tight junctions** joining neighbouring cells near the lumen, so substances cannot leak back between the cells;
- a position very close to blood capillaries, giving a short diffusion distance.

**How glucose is reabsorbed.** Glucose is taken back even though the cell may already contain more glucose than the filtrate. The cell does this by **co-transport** 协同运输 (follow the numbers):

1. sodium–potassium pumps on the side of the cell facing the blood use ATP to pump sodium ions out of the cell. This keeps the sodium ion concentration inside the cell low.

2. sodium ions diffuse into the cell from the filtrate, down their concentration gradient, through a **co-transporter protein** 协同转运蛋白. Each one carries a glucose molecule in with it, even against the glucose concentration gradient.
3. glucose diffuses out of the other side of the cell into the blood, by facilitated diffusion.
4. as solutes leave the filtrate, its water potential rises, so water follows by **osmosis** 渗透.




*The pump keeps $[Na^+]$ low inside the cell, so $Na^+$ flows in from the filtrate and drags glucose with it*

So glucose reabsorption is **indirectly** active: the energy from ATP is used by the pump, not by the co-transporter. This is why the cells need many mitochondria. If the blood glucose concentration is very high (as in untreated diabetes), the co-transporters are all in use and some glucose stays in the urine.

### The rest of the nephron

- **Loop of Henle.** The descending limb is permeable to water; the ascending limb is **impermeable** to water but actively pumps sodium and chloride ions out into the tissue fluid of the medulla. This builds up a very low (very negative) water potential deep in the medulla. Because the two limbs run side by side with the fluid flowing in opposite directions, the effect is multiplied along the loop (a **countercurrent multiplier** 逆流倍增). Mammals that live in deserts, such as kangaroo rats, have very long loops and make very concentrated urine.
- **Distal convoluted tubule.** Its cells adjust the ion content of the blood, reabsorbing more sodium ions (and secreting potassium and hydrogen ions) as needed. It has many mitochondria.



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- **Collecting duct.** It runs down through the medulla, where the water potential of the tissue fluid is low, so water leaves the duct by osmosis – as long as the walls are permeable to water. ADH controls that permeability (see below).

> **Worked example.** The concentration of urea in the filtrate rises from 0.3 g $dm^{-3}$ in the Bowman's capsule to 20 g $dm^{-3}$ in the urine. Explain why. Urea is filtered but very little is reabsorbed, while about 99% of the water in the filtrate is reabsorbed – mostly in the proximal tubule, and then in the loop of Henle and collecting duct. The same mass of urea is left in a much smaller volume of water, so its concentration rises.

**Common mistakes.**

- Saying glucose is "actively transported" by the co-transporter. The co-transporter uses the sodium gradient; ATP is used by the sodium–potassium **pump**.
- Saying ultrafiltration is selective. It sorts only by **size**; selection happens afterwards, in the proximal convoluted tubule.
- Saying ADH "makes the kidney produce more water". ADH makes the collecting duct **more permeable** to water, so more water is **reabsorbed** into the blood.

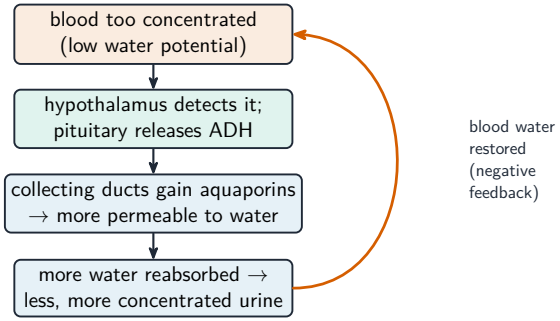
## Osmoregulation

**Osmoregulation** 渗透调节 controls the water content of the blood. It is run by the brain:

- the **hypothalamus** 下丘脑 detects the **water potential** 水势 of the blood.
- when the blood is too concentrated, the **pituitary gland** 垂体 releases **antidiuretic hormone** 抗利尿激素 (ADH).
- ADH makes the collecting ducts more permeable to water by adding water channels called **aquaporins** 水通道蛋白.

In more detail: the water potential of the blood is detected by **osmoreceptors** in the hypothalamus. These cells lose water and shrink when the blood is too concentrated. ADH is made in the hypothalamus and released into the blood from the **posterior** pituitary. In the collecting duct cells, ADH binds to receptors on the cell surface membrane, which starts a cAMP pathway inside the cell. This causes **vesicles** whose membranes contain aquaporins to move to the membrane facing the lumen and **fuse** with it, so many more water channels are in place. Water moves out of the duct by osmosis, through the aquaporins, into the tissue fluid of the medulla and then into the blood. When ADH falls, the aquaporins are taken back into vesicles by endocytosis, and the duct becomes less permeable again.

- more water is then reabsorbed back into the blood, so less, more concentrated urine is made. This is negative feedback.




*ADH makes the collecting ducts reabsorb more water, restoring the blood's water content by negative feedback*

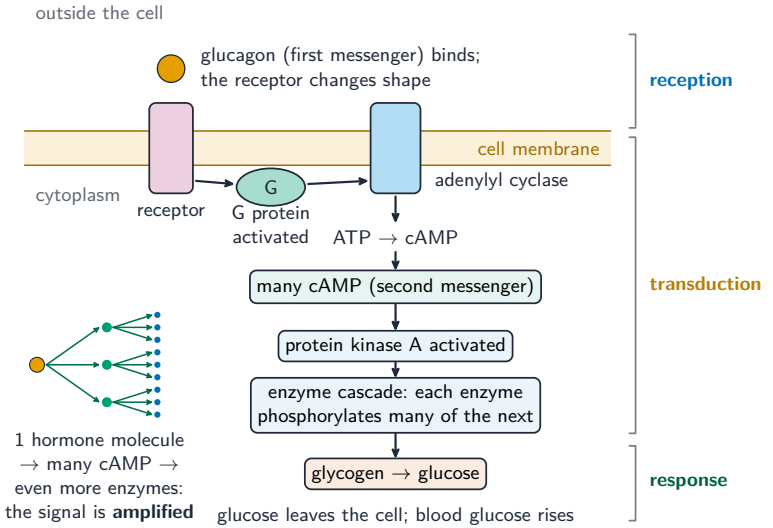
## Controlling blood glucose by cell signalling

When blood glucose falls, the hormone **glucagon** 胰高血糖素 is released. It shows how a hormone passes its message into a cell – **cell signalling** 细胞信号传递:

1. glucagon binds to a receptor on the liver cell surface, causing a **conformational change** 构象变化 (a change in the receptor's shape).
2. this activates a **G-protein** G 蛋白, which switches on the enzyme **adenylyl cyclase** 腺苷酸环化酶.
3. adenylyl cyclase makes a **second messenger** 第二信使 inside the cell, called **cyclic AMP** 环腺苷酸 (cAMP).
4. cAMP activates **protein kinase A** 蛋白激酶 A, which starts an **enzyme cascade** 酶级联反应 – one **enzyme** 酶 switches on the next, by **phosphorylation** 磷酸化.
5. because each enzyme switches on many of the next, the signal is greatly **amplified** 放大.
6. the final enzyme breaks down **glycogen** 糖原 into glucose, which raises the blood glucose level.



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*Glucagon never enters the cell: the receptor passes the message to a G protein, adenylyl cyclase and cAMP inside. Each step activates many of the next, so the signal is amplified*

**Common mistakes.**

- Saying glucagon enters the liver cell. Glucagon is a protein and cannot cross the membrane; only the **message** gets in, through the receptor and the second messenger.
- Saying glucagon "turns into" glucose, or that cAMP breaks down glycogen. cAMP only activates protein kinase A; the enzymes at the end of the cascade break down glycogen.
- Mixing up glucagon and glycogen. Glucagon is the hormone; glycogen is the stored carbohydrate it causes to be broken down.

### ■ Negative feedback and blood glucose

Blood glucose is held steady by two hormones working against each other:

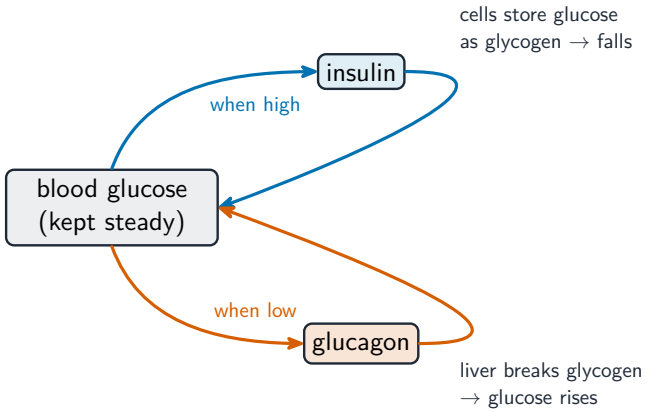
- when glucose is **high**, **insulin** 胰岛素 makes muscle and liver cells take in glucose and store it as glycogen, lowering the level.
- when glucose is **low**, glucagon makes liver cells break glycogen back into glucose, raising the level.

Both hormones are made in the **islets of Langerhans** 胰岛 in the pancreas: $\beta$ **cells** detect a rise in blood glucose and secrete insulin; $\alpha$ **cells** detect a fall and secrete glucagon. The pancreas is both the receptor and the gland.

**How insulin works.** Insulin is a protein, so, like glucagon, it acts through receptors on the cell surface. When it binds to its receptor on a muscle or fat cell:

1. the receptor (a kinase) phosphorylates proteins inside the cell, starting a signalling cascade;
2. vesicles carrying the glucose transporter **GLUT4** move to the cell surface membrane and fuse with it, so more glucose can enter the cell by facilitated diffusion;
3. inside, glucose is phosphorylated, which keeps the glucose concentration in the cell low so more diffuses in;
4. enzymes that turn glucose into glycogen (**glycogenesis** 糖原合成) are activated, and the cell respires more glucose.

In liver cells, insulin also switches on glycogen synthesis and stops glycogen breakdown. Glucagon does the opposite: it activates glycogen breakdown (**glycogenolysis** 糖原分解) and the making of glucose from amino acids and glycerol (**gluconeogenesis** 糖异生).




*Insulin and glucagon work against each other to keep blood glucose steady*

### Measuring glucose

**Test strips** 试纸 and **biosensors** 生物传感器 measure glucose in blood or urine. They use the enzymes **glucose oxidase** 葡萄糖氧化酶 and **peroxidase** 过氧化物酶, which react with glucose to give a colour change (or an electric signal in a biosensor) that shows how much glucose is present.

The two reactions on a test strip, in order:

$$\text{glucose} + O_2 \xrightarrow{\text{glucose oxidase}} \text{gluconolactone} + H_2O_2$$

$$H_2O_2 + \text{colourless dye} \xrightarrow{\text{peroxidase}} \text{coloured dye} + H_2O$$

The more glucose, the more hydrogen peroxide and the darker the colour, which is compared with a **colour chart**. A biosensor uses glucose oxidase fixed on an electrode: the reaction produces a small electric current proportional to the glucose concentration, shown as a number on the meter. It gives a precise reading from one drop of blood. Testing **urine** shows only that blood glucose has been high at some time since the bladder was last emptied (glucose appears in urine only when it is above about 10 mmol $dm^{-3}$), so it cannot show the present blood level.

> **Worked example.** A person drinks a large volume of water. Trace the homeostatic response. The blood's water potential **rises** (becomes less negative). **Osmoreceptors** in the hypothalamus detect this, so the posterior pituitary releases **less ADH**. With less ADH, fewer **aquaporins** are inserted into the collecting duct's membranes, so the duct becomes **less permeable** to water. Less water is reabsorbed, so a **large volume of dilute urine** is produced and the blood's water potential falls back towards normal. That return to the set point is what makes it **negative feedback** - the response reverses the original change. Name the **receptor**, the **hormone**, the **effector** and the **correction**: an answer that jumps from "drinks water" straight to "more urine" skips every marking point in between.

## Homeostasis in plants: the stomata

**Stomata** 气孔 are pores in a leaf. The plant opens and closes them to balance two needs: letting in **carbon dioxide** 二氧化碳 for **photosynthesis** 光合作用, and limiting water loss by **transpiration** 蒸腾作用. Stomata usually open by day and close at night, following a daily rhythm.

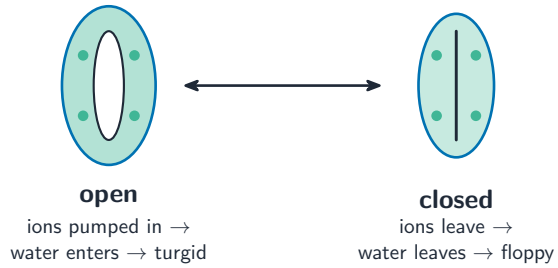
Each stoma is opened and closed by two **guard cells** 保卫细胞 around it:

- to **open**: the guard cells pump in ions, so their water potential falls and water enters by **osmosis**. They swell and bend apart, opening the pore.
- to **close**: ions leave, water follows out, the guard cells go floppy, and the pore closes.





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*Guard cells open the stoma by taking in water and turgid; they close it by losing water and going floppy*

**Opening in detail.** In the light, proton pumps in the guard cell membrane use ATP to pump hydrogen ions **out** of the cell. This makes the inside more negative, so **potassium ions** flow **in** through channels. Malate is also made inside the cell. The water potential of the guard cell falls, water enters by osmosis from neighbouring cells, and the guard cells become **turgid**. Their inner walls (next to the pore) are thicker and less stretchy than the outer walls, and cellulose fibres run around them in rings, so as they swell they curve apart and the pore opens.

Stomata respond to their surroundings: they open in **light** (for photosynthesis) and when the carbon dioxide concentration inside the leaf is **low**; they close in the dark, when carbon dioxide is high, and when the plant is short of water – even in the light, saving water matters more than gaining carbon dioxide.

When the plant is short of water (**water stress** 水分胁迫), the hormone **abscisic acid** 脱落酸 is released. It makes the guard cells lose ions and water so the stomata close, saving water. In this signalling, **calcium ions** 钙离子 act as a second messenger inside the guard cells.

**How abscisic acid closes the stomata, step by step.**

1. Roots in dry soil make abscisic acid (ABA), which travels to the leaves in the xylem; leaf cells also make it.
2. ABA binds to receptors on the guard cell surface membrane.
3. The proton pumps are inhibited, and calcium ions enter the cytoplasm (from outside and from the vacuole). Calcium is the **second messenger**.
4. Calcium ions open channels that let negative ions out, and potassium ions then leave the guard cells.
5. The water potential of the guard cells rises, so water leaves by osmosis. The guard cells become **flaccid** and the stoma closes.

**Investigating stomata.** Paint clear nail varnish on the lower surface of a leaf, let it dry, peel it off with clear sticky tape and stick it to a slide; or peel off a strip of lower epidermis directly. Count the stomata in a field of view of known area to find the **stomatal density**, and measure the width of the pore with an eyepiece graticule calibrated with a stage micrometer. Peels taken at different times of day, or from leaves floated on abscisic acid solutions of different concentrations, show how the aperture changes.



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## Exam tips

- Frame every answer as **negative feedback**: receptor → coordinator → effector → correction; name each part.
- **Blood glucose**: insulin lowers it (uptake, glycogenesis), glucagon raises it (glycogenolysis) – explain through cell signalling.
- **Kidney**: know ultrafiltration (Bowman's capsule), selective reabsorption (proximal tubule) and the role of **ADH** in osmoregulation.
- **Stomata** open when guard cells become turgid (K+ enters, water follows).
- Filtration barrier: endothelium with pores, **basement membrane** (the filter), podocytes; high pressure from a wide afferent and narrow efferent arteriole.
- Glucose and urea have equal concentrations in plasma and filtrate; the rise in urea in urine comes from **water** reabsorption.
- Insulin: receptor → GLUT4 vesicles fuse with the membrane → more glucose uptake → glycogenesis.
- ABA: receptors on guard cells → $Ca^{2+}$ second messenger → $K^{+}$ out → water out → flaccid → stoma closes.

# Control and coordination

A-Level Biology

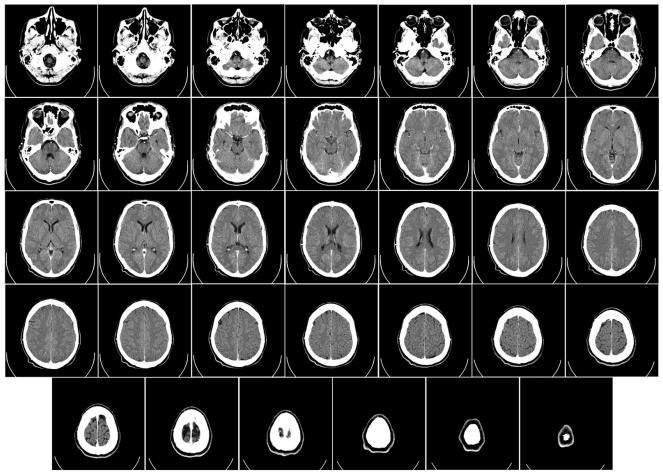
## Two systems for control

The body has two coordination systems. The **endocrine system** 内分泌系统 sends chemical **hormones** 激素 (such as ADH, glucagon and insulin) in the blood. The **nervous system** 神经系统 sends fast electrical signals along nerve cells.

**nervous system**
electrical impulses
along nerves — fast, short

**endocrine system**
chemical hormones
in the blood — slow, lasting

*Nervous control is fast and electrical; hormonal control is slow and chemical*



*A scan of the human brain, the control centre of the nervous system*



| Feature | Nervous system | Endocrine system |
|---|---|---|
| signal | electrical **impulse** 冲动 | chemical hormone |
| transport | along nerve cells | in the blood |
| speed | very fast | slower |
| how long it lasts | short | longer |
| where it acts | only the cells the neurone reaches (one muscle or gland) | any cell in the body with the right receptor, often many organs |

The endocrine system is made of **endocrine glands** 内分泌腺, such as the pituitary gland, the adrenal glands, the islets of Langerhans in the pancreas, and the ovaries and testes. They have **no ducts**: they secrete their hormones straight into the blood flowing through them. Most hormones are proteins or peptides (insulin, glucagon, ADH), which bind to receptors on the cell surface membrane; **steroid** hormones (such as oestrogen and testosterone) are lipid-soluble, so they pass through the membrane and bind to receptors inside the cell.

## Neurones

A **neurone** 神经元 is a nerve cell. There are three kinds:

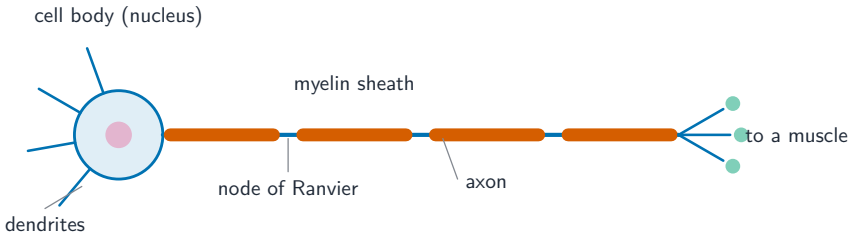
- a **sensory neurone** 感觉神经元 carries impulses from a receptor towards the brain or spinal cord.
- a **motor neurone** 运动神经元 carries impulses out to an effector, such as a **muscle** 肌肉.
- **intermediate neurones** 中间神经元 connect sensory neurones to motor neurones.

A neurone has a long fibre (the axon) along which the impulse travels.

**The parts of a motor neurone.** The **cell body** holds the nucleus and many ribosomes and much rough ER (making proteins such as the enzymes for neurotransmitter synthesis), and many mitochondria. Short branches called **dendrites** carry impulses **towards** the cell body from other neurones. A single long **axon** carries impulses **away** from it, and may be more than a metre long. The axon ends in many branches, each with a swelling called a **synaptic knob**. A **sensory** neurone has a long dendron bringing impulses from the receptor to a cell body that sits in a swelling just outside the spinal cord; an **intermediate** (relay) neurone is short and lies wholly inside the brain or spinal cord.

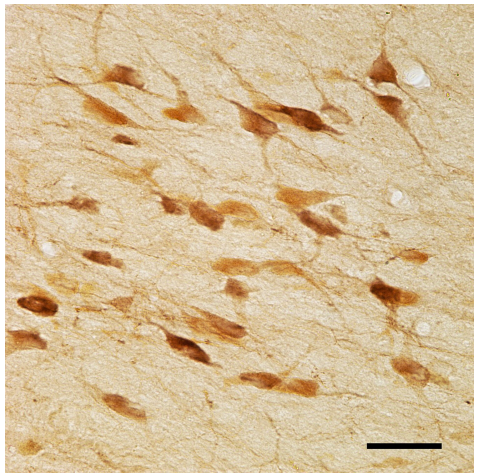


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*A motor neurone: the impulse travels along the axon, jumping between the gaps (nodes of Ranvier) in the myelin sheath*

This is what real neurones look like in a stained slice of brain tissue:



*Real **neurones** stained brown: you can see the cell bodies and the thin processes that carry signals to and from each cell*

## Detecting a stimulus

A **sensory receptor** 感受器 cell detects a **stimulus** 刺激 and starts an impulse in a sensory neurone. For example, a **chemoreceptor** 化学感受器 cell in a **taste bud** 味蕾 detects chemicals in food, and this triggers an **action potential** 动作电位 in the sensory neurone.

Receptors act as **transducers**: they change the energy of the stimulus (chemical, light, pressure, heat) into the electrical energy of an impulse. In a taste bud:

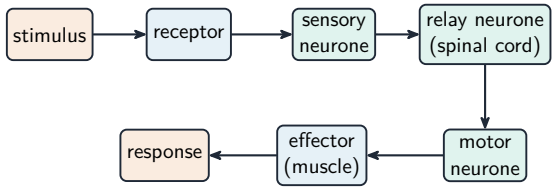
1. sodium ions from salty food diffuse into the chemoreceptor cell through sodium ion channels in its membrane (other tastes act through receptor proteins);



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2. this **depolarises** the receptor cell. The size of this change, the **receptor potential** 感受器电位 (or generator potential), depends on the strength of the stimulus: it is **not** all-or-nothing;
3. the depolarisation opens voltage-gated calcium ion channels, calcium ions enter, and the receptor cell releases neurotransmitter onto the sensory neurone;
4. if the sensory neurone is depolarised past its **threshold** 阈值 (about −55 mV), an action potential starts.

A stronger stimulus gives a larger receptor potential, which makes the sensory neurone fire action potentials **more often**. A stimulus too weak to reach the threshold gives no impulse at all.

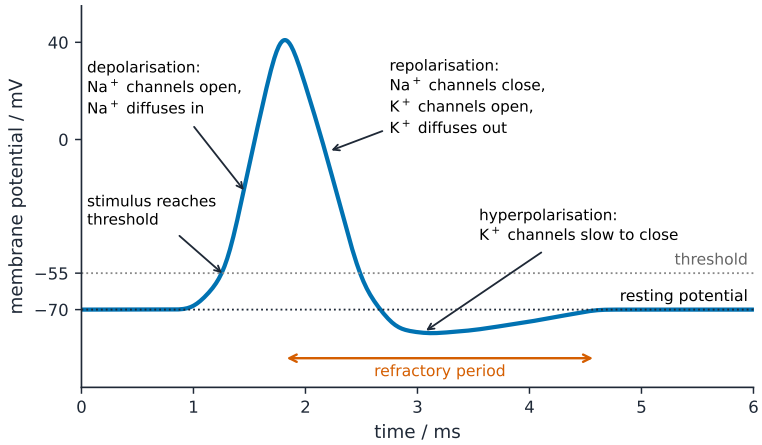



*A reflex arc: stimulus → receptor → sensory neurone → relay → motor neurone → effector → response*

## The nerve impulse

The impulse is a change in the voltage across the neurone's membrane.

- **resting potential** 静息电位 – when no impulse passes, the inside is negative compared to the outside. This is maintained by a pump that moves sodium ions out and potassium ions in, and by the membrane being more permeable to potassium.
- **action potential** – a stimulus makes sodium channels open, so sodium ions rush in and the inside briefly becomes positive (depolarisation). Then the sodium channels close and potassium channels open, potassium ions leave, and the **membrane potential** 膜电位 returns to negative (repolarisation). The potassium channels are slow to close, so for a moment the inside becomes even more negative than at rest: this is **hyperpolarisation** 超极化.
- **refractory period** 不应期 – just after an action potential, the sodium channels cannot open again for a short time while the membrane returns to its resting potential. So each impulse is separate (discrete), travels in one direction only, and there is a limit on how often impulses can be sent (their frequency).




all-or-nothing: once threshold is reached, a full spike fires (no partial APs)

*An action potential: $Na^+$ in (depolarisation), $K^+$ out (repolarisation), an overshoot below rest (hyperpolarisation); the refractory period lasts until rest is restored*

## How the impulse travels along the axon

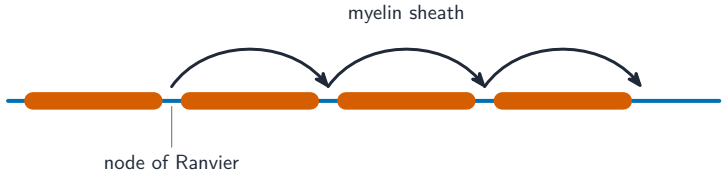
When one part of the axon is depolarised, its inside is positive while the next part is still negative at rest. Sodium ions that have entered diffuse sideways inside the axon towards the negative region, forming **local circuits** 局部电流. This raises the potential of the next part to the threshold, so its voltage-gated sodium channels open and an action potential starts there. The part behind is in its refractory period, so the impulse can only move **forwards**. In this way the action potential is passed along like a wave, with the same size all the way.

## Faster impulses: myelin

Some neurones are wrapped in a fatty **myelin sheath** 髓鞘. The impulse cannot cross the sheath, so it jumps from one gap to the next. This jumping, called **saltatory conduction** 跳跃式传导, makes the impulse travel much faster.



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the impulse jumps from node to node (saltatory conduction) → faster

*The impulse jumps node to node – saltatory conduction – so a myelinated neurone conducts much faster*

Myelin is made by **Schwann cells** 施万细胞, which wrap themselves many times around the axon, so the sheath is many layers of cell membrane, rich in lipid. Ions cannot pass through it, so action potentials happen only at the **nodes of Ranvier**, the short gaps (about every 1 mm) between Schwann cells. The local circuits stretch from one node to the next, so the impulse jumps over the myelinated parts.

| Factor | Effect on speed | Example |
|---|---|---|
| myelin | much faster: up to about 100 m $s^{-1}$, compared with 0.5–10 m $s^{-1}$ in a non-myelinated axon | motor neurones to the leg |
| axon diameter | a wider axon is faster: less resistance to the flow of ions inside it | the giant axons of squid (non-myelinated, about 25 m $s^{-1}$) |
| temperature | warmer is faster (up to about 40 °C): ions diffuse faster | impulses are faster in mammals and birds than in cold-blooded animals |

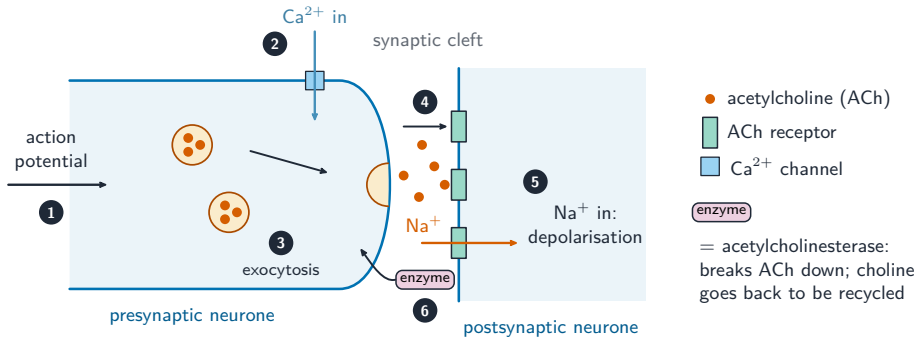
**Common mistakes.**

- Saying the sodium–potassium pump causes depolarisation. The pump keeps up the resting potential; depolarisation is caused by sodium ions diffusing in through **voltage-gated channels** 电压门控通道.
- Saying the ions are "pumped" during an action potential. $Na^+$ and $K^+$ move by **facilitated diffusion** 易化扩散 through channels, down their concentration gradients.
- Saying a stronger stimulus gives a bigger action potential. Every action potential has the same size (all-or-nothing); a stronger stimulus gives **more frequent** impulses.
- Saying the impulse "jumps along the myelin". It jumps **between nodes of Ranvier**, where there is no myelin and ions can cross the membrane.

## The synapse

A **synapse** 突触 is a tiny gap between two neurones. A **cholinergic synapse** 胆碱能突触 passes the signal like this (the numbers match the figure):

1. an action potential arrives at the end of the first (presynaptic) neurone.
2. the depolarisation opens voltage-gated **calcium ion** 钙离子 channels, and calcium ions diffuse in.
3. this makes vesicles move to the membrane and fuse with it, releasing the **neurotransmitter** 神经递质 **acetylcholine** 乙酰胆碱 (ACh) into the gap by **exocytosis** 胞吐作用.
4. ACh diffuses across the gap and binds to receptors on the next (postsynaptic) neurone.
5. the receptors open sodium ion channels. Sodium ions diffuse in and depolarise the membrane; if the threshold is reached, a new action potential starts.
6. the enzyme **acetylcholinesterase** 乙酰胆碱酯酶 breaks ACh down, so it stops stimulating the receptors. The choline is taken back into the first neurone and used to make more ACh.




*$Ca^{2+}$ in, ACh released and bound, $Na^+$ in on the far side; then the enzyme clears the cleft and the choline is recycled*

Because only the presynaptic side has vesicles and only the postsynaptic side has receptors, a synapse passes impulses in **one direction** only.

**What synapses do.**

- They make impulses travel in **one direction** only.
- They allow **integration**: one neurone may receive synapses from many others, and it fires only if enough transmitter arrives at the same time to reach the threshold. In this way weak or chance signals are filtered out, and signals from several neurones can be combined.



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- Impulses from one neurone can be passed to many others, spreading the signal (for example to many muscle fibres).
- Repeated use of a synapse can strengthen it, which is part of **learning** and memory.

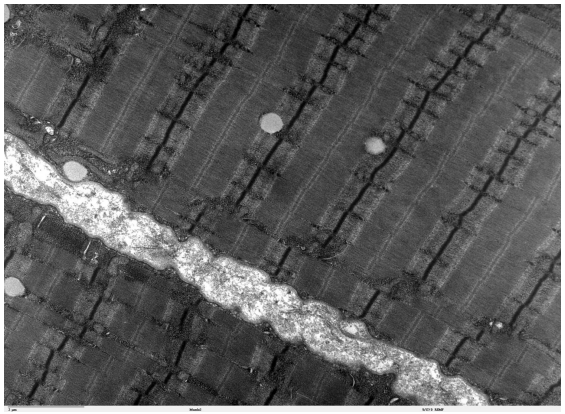
The presynaptic knob has many **mitochondria** (to make ATP for re-making acetylcholine and for pumping calcium ions back out) and much smooth ER. A synapse delays the impulse by about 0.5 ms. Drugs and poisons often act at synapses: for example, some insecticides inhibit acetylcholinesterase, so ACh is not broken down and the postsynaptic membrane stays depolarised, causing continuous muscle contraction.

## Muscles and how they contract

A **neuromuscular junction** 神经肌肉接头 is like a synapse, but between a motor neurone and a muscle.

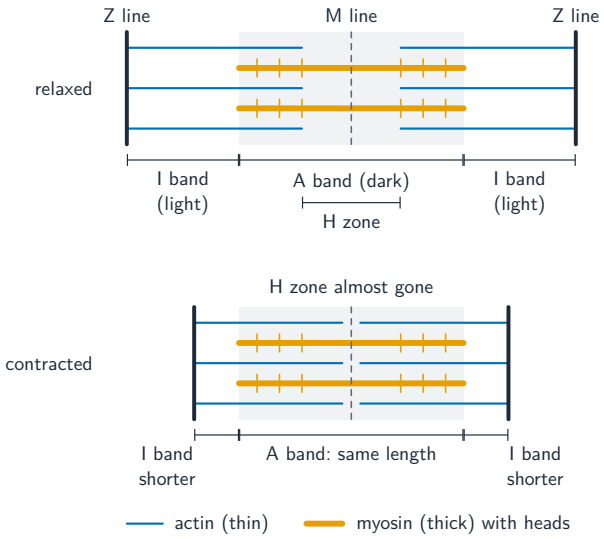
At a neuromuscular junction, ACh is released from the motor neurone and binds to receptors on the muscle fibre's cell surface membrane (the **sarcolemma** 肌膜). Sodium ions enter, and the depolarisation (the **end-plate potential**) starts an action potential that spreads over the sarcolemma and down the T-tubules. Unlike a synapse between neurones, one impulse at a neuromuscular junction is always enough to make the muscle fibre contract; and the postsynaptic membrane is folded, giving room for many receptors.

**Striated muscle** 横纹肌 is made of long fibres. Each fibre is divided into repeating units called **sarcomeres** 肌节. Inside are two kinds of **filament** 肌丝: thick ones (myosin) and thin ones (actin). The **T-tubule** T 小管 system carries the impulse deep into the fibre, and the **sarcoplasmic reticulum** 肌质网 stores and releases calcium ions.



*This is where the name "striated" comes from. Each repeating dark-light block is one sarcomere; the bands are the thick and thin filaments overlapping by different amounts. When the muscle contracts, the filaments slide past each other and each sarcomere gets shorter*

**The bands of a sarcomere.** On an electron micrograph each sarcomere runs from one **Z line** to the next. The **A band** is dark: it is the length of the thick myosin filaments (with actin overlapping them at each end). The **I band** is light: it contains only thin actin filaments, and the Z line runs through its middle. The **H zone**, in the centre of the A band, contains only myosin. The **M line** in the middle holds the myosin filaments together.



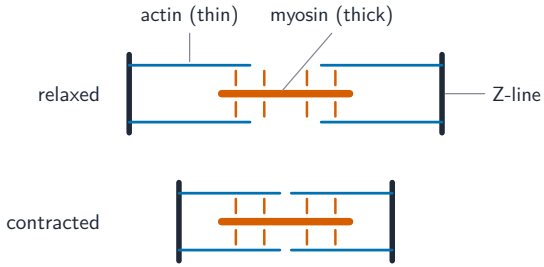

*In contraction the A band keeps its length; the I band and H zone shorten as actin slides over myosin*

The **sliding filament model** 肌丝滑动模型 explains contraction:

1. an impulse causes the sarcoplasmic reticulum to release calcium ions.
2. the calcium ions bind to **troponin** 肌钙蛋白, which makes **tropomyosin** 原肌球蛋白 move and uncover the binding sites on the actin.
3. the myosin heads attach to the actin and pull it inwards, using energy from ATP.
4. the thin filaments slide over the thick ones, so each sarcomere gets shorter and the muscle contracts.



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the filaments slide over each other, so the sarcomere shortens

*Sliding filament model: thin actin slides over thick myosin, so the sarcomere shortens*

When the muscle contracts, the filaments themselves do **not** get shorter: they slide over each other. So the **A band** stays the same length (myosin is the same length), while the **I band** and the **H zone** get shorter, and the Z lines move closer together. This is the evidence for the sliding filament model.

**The cross-bridge cycle in more detail.**

1. With calcium ions bound to troponin and the binding sites uncovered, a myosin head (carrying ADP and phosphate from an earlier ATP) binds to actin, forming a **cross-bridge**.
2. The head releases the ADP and phosphate and tilts, pulling the actin filament towards the M line: the **power stroke**.
3. A new ATP molecule binds to the head, which makes it **detach** from the actin.
4. The myosin head (an ATPase) hydrolyses the ATP, and the energy released moves the head back to its upright position, ready to bind again further along the actin.

Each myosin head repeats this cycle many times a second while calcium ions are present. When impulses stop, calcium ions are pumped back into the sarcoplasmic reticulum by **active transport** (using ATP), tropomyosin covers the binding sites again, and the muscle relaxes. ATP is therefore needed both to detach myosin from actin and to pump calcium back; muscle fibres have many mitochondria. Muscles also store energy as **creatine phosphate**, which quickly gives its phosphate to ADP to make more ATP during short bursts of activity.

## Control and coordination in plants

### The Venus fly trap

The **Venus fly trap** 捕蝇草 has tiny hairs on its trap-like leaves. When an insect touches the hairs, a fast electrical signal spreads, the cells quickly lose water and change shape, and the trap snaps shut to catch the insect.

**How the trap closes, step by step.** The trap is a leaf modified into two **lobes**, each with three stiff **sensory hairs** on its inner surface.

1. When a hair is bent, ion channels in the cells at its base open. Calcium ions enter, depolarising the cells, and an **action potential** spreads across the lobes.
2. One touch is not enough: the trap closes only if a hair is touched **twice within about 20 seconds** (or two hairs are touched). This stops the trap closing for a raindrop or a piece of dirt, which would waste a lot of energy.
3. The action potential makes cells in the lobes move ions quickly. Hydrogen ions are pumped into the cell walls of the outer layers, loosening them (as in acid growth), and water moves rapidly by osmosis between the cell layers.
4. The lobes are curved outwards (convex) when open, held under tension. The sudden change in turgor and wall stiffness makes each lobe **flip** to curve inwards (concave), and the trap shuts in about 0.1 s.
5. The spikes along the edges interlock, caging the insect. If the insect keeps moving, it triggers more action potentials, and the trap seals tightly and secretes enzymes to digest it.

Re-opening needs cell growth, so it is slow (hours), and each trap can close only a few times. The plant lives in soil poor in nitrogen, so the insects are a source of nitrogen compounds.



*An open trap. The long spikes around the edge only cage the insect – it is the few short, stiff trigger hairs standing on the red surface that must be touched to fire the signal*

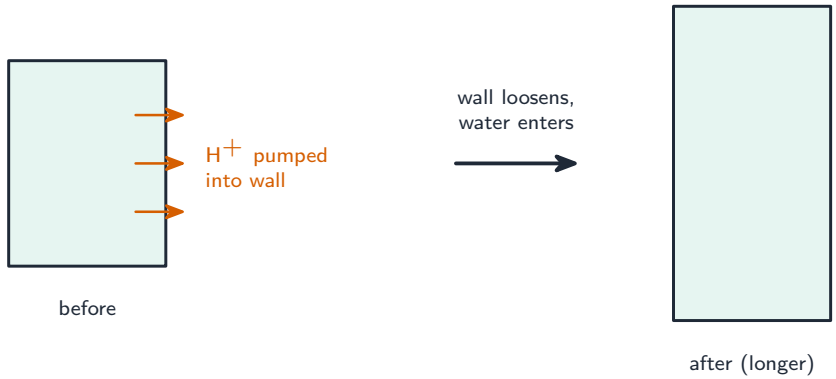


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## Auxin and growth

**Auxin** 生长素 is a plant hormone that makes cells grow longer (**elongation** 伸长 growth). It does this by making the cell pump **protons** 质子 (hydrogen ions) into the **cell wall** 细胞壁. This **acidifies** 酸化 the wall, which loosens it, so the cell can stretch as water enters.

In more detail: auxin is made in the tips of shoots and roots and moves back from the tip. It binds to a receptor protein in the cell, which activates **proton pumps** in the cell surface membrane. These use ATP to pump hydrogen ions into the cell wall. The low pH activates proteins called **expansins**, which break the hydrogen bonds between cellulose microfibrils, so the microfibrils can slide apart. The cell's turgor pressure then stretches the loosened wall, and the cell takes in water by osmosis and grows longer. The low pH also keeps potassium ions entering the cell, which helps to keep its water potential low. Only cells just behind the tip, in the **zone of elongation**, respond in this way.




*Auxin's "acid growth": $H^+$ pumped into the wall loosens it, so the cell stretches longer as water enters*

## Gibberellin and germination

**Gibberellin** 赤霉素 controls the **germination** 萌发 of **barley** 大麦 seeds. It switches on the genes that make amylase, which then breaks down stored starch into sugars to feed the growing seedling.

**Step by step.**

1. The seed absorbs water, which activates the **embryo**.
2. The embryo makes gibberellin, which diffuses to the **aleurone layer** 糊粉层, a protein-rich layer of cells around the starch store (the **endosperm** 胚乳).

3. In the aleurone cells, gibberellin causes the breakdown of **DELLA proteins**. DELLA proteins normally bind to a **transcription factor** and stop it working.
4. Freed from DELLA, the transcription factor binds to the promoter of the **amylase gene**, so the gene is transcribed and amylase is made.
5. Amylase is secreted into the endosperm, where it hydrolyses starch to maltose. Maltose is turned into glucose and carried to the embryo, which uses it for respiration and to build new cells as it grows.

Gibberellin also makes stems grow taller (by causing cell elongation and division between the nodes). The dwarf form of many plants (for example dwarf pea plants with short stems) has a mutation in a gene for an enzyme that makes active gibberellin: the dominant allele **Le** gives tall plants, and the recessive **le** gives short plants with little active gibberellin.

> **Worked example.** Explain why a nerve impulse crosses a synapse in **one direction only**, and why myelination speeds it up along an axon. At a synapse the **vesicles** of neurotransmitter are found only in the **presynaptic** neurone, and the **receptors** only on the **postsynaptic** membrane - so transmitter can only ever cross one way, which makes the synapse a one-way valve. Along a **myelinated** axon the myelin sheath **insulates** the membrane, so ions can only cross at the **nodes of Ranvier**; the impulse therefore jumps from node to node (**saltatory conduction**) instead of depolarising every part of the membrane in turn, which is far faster and uses less ATP. Locate the **structure** responsible for each effect: vesicles and receptors give the direction, insulation and nodes give the speed.

## Exam tips

- Explain the **resting potential** (Na+/K+ pump; more negative inside) then the **action potential** (depolarisation → repolarisation) as all-or-nothing.
- **Saltatory conduction** (myelin, nodes of Ranvier) speeds the impulse; the refractory period makes it one-way and discrete.
- **Synapse** order: Ca2+ in → vesicles fuse → neurotransmitter → receptors → new impulse.
- Muscle contraction: the **sliding-filament** model (actin, myosin, ATP, Ca2+).
- On a sarcomere in contraction, the **A band stays the same**; the I band and H zone shorten.
- ATP is needed to **detach** the myosin head and to pump calcium back into the sarcoplasmic reticulum.
- Receptor potentials are graded; action potentials are all-or-nothing. A stronger stimulus raises the **frequency** of impulses.
- Venus fly trap: two touches within about 20 s → action potential → rapid water movement and wall loosening → lobes flip from convex to concave.



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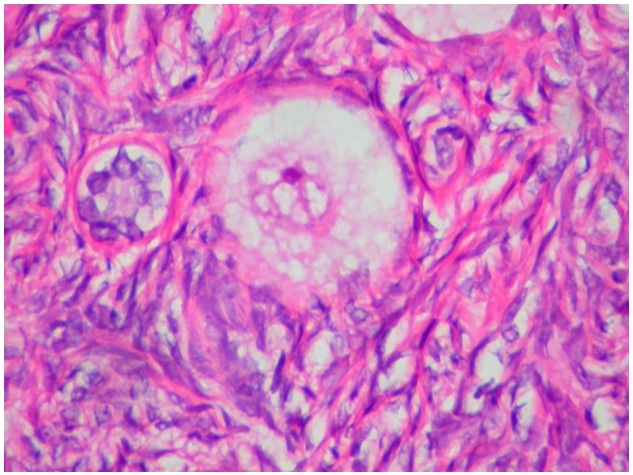
- Gibberellin → DELLA proteins broken down → transcription factor free → amylase gene transcribed in the aleurone layer → starch hydrolysed.

# Inheritance

A-Level Biology

## Meiosis and how it creates variation

A **diploid** 二倍体 cell (2n) has two full sets of **chromosomes** 染色体 – one set from each parent. A **haploid** 单倍体 cell (n) has just one set.

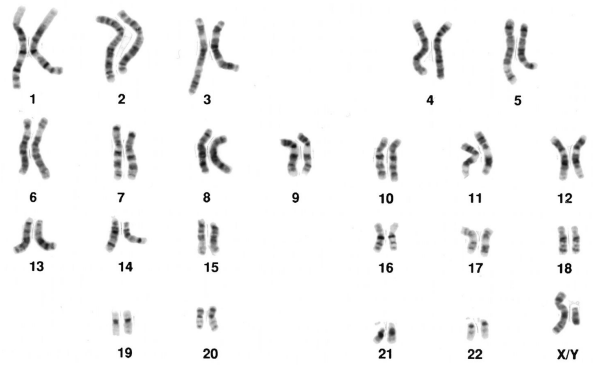


*A human egg cell (ovum) – a haploid gamete produced by meiosis*

Chromosomes come in **homologous chromosomes** 同源染色体 pairs: the two chromosomes in a pair are the same length and carry the same **genes** 基因 (though they may carry different versions of them).

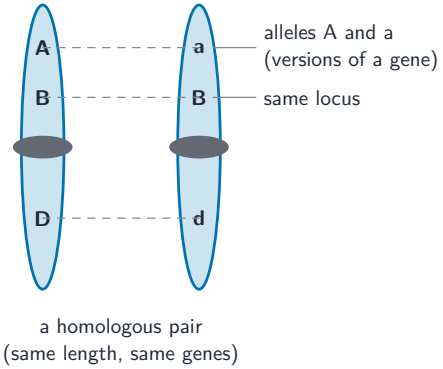


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**Normal Karyotype**

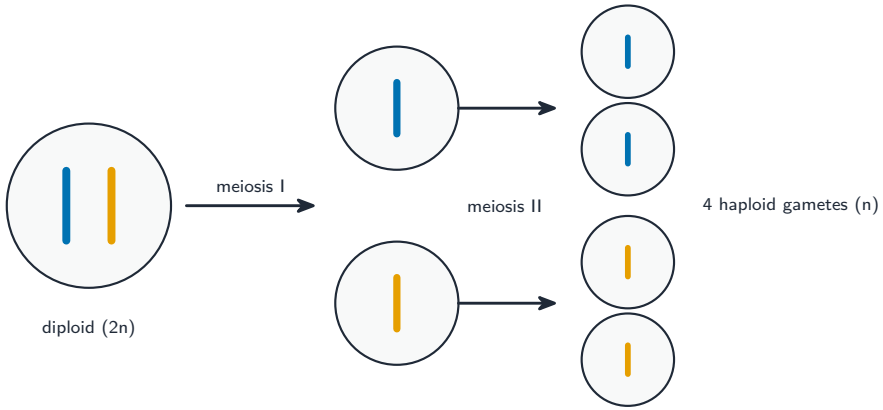
*A human **karyotype**: the 46 chromosomes sorted into 23 homologous pairs (the last pair, X and Y, shows this is a male)*




*A homologous pair carries the same genes at the same loci, but the alleles (versions) may differ*

**Gametes** 配子 (sex cells) must be haploid. If they were diploid, the chromosome number would double at every generation. So gametes are made by a special division, **meiosis** 减数分裂, which halves the chromosome number.

Meiosis has two divisions, one after the other, so there are eight named stages: prophase I, metaphase I, anaphase I and telophase I, then prophase II, metaphase II, anaphase II and telophase II. As in mitosis, the **nuclear envelope** 核膜 breaks down, a **spindle** 纺锤体 forms, and the chromosomes are moved by the spindle.




*Two divisions halve the chromosome number: meiosis I separates the homologous pair, meiosis II separates the chromatids – giving four haploid gametes*

## The stages of meiosis, step by step

Before meiosis starts, every chromosome is copied in interphase, so it is made of two identical **sister chromatids** 姐妹染色单体 joined at the **centromere** 着丝粒.

| Stage | What happens to the chromosomes |
|---|---|
| prophase I | chromosomes condense; each homologous pair comes together to form a **bivalent** 二价体; crossing over happens at points called **chiasmata** 交叉 (one is a chiasma); the nuclear envelope breaks down and the spindle forms |
| metaphase I | the bivalents line up on the **equator** 赤道 of the spindle; each pair faces the poles in a random way (independent assortment) |
| anaphase I | the two chromosomes of each **pair** are pulled to opposite poles; the centromeres do **not** divide, so each chromosome still has two chromatids |
| telophase I | two nuclei form, each **haploid** (one chromosome from every pair) |
| prophase II | chromosomes condense again and new spindles form |
| metaphase II | single chromosomes line up on the equator |
| anaphase II | the centromeres divide and the **sister chromatids** are pulled to opposite poles |
| telophase II | four haploid nuclei form; the cytoplasm divides to give four cells |



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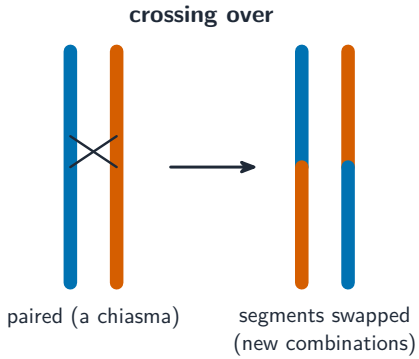
So meiosis I separates the **homologous chromosomes** (this is where the number halves), and meiosis II separates the **chromatids**, as in mitosis.

> **Worked example.** A cell has a diploid number of 8 ($2n = 8$). How many chromosomes and chromatids are there in each cell at (a) metaphase I, (b) metaphase II, (c) the end of telophase II?

(a) Metaphase I: nothing has separated yet, so there are **8 chromosomes**, each of two chromatids: **16 chromatids**. (b) Metaphase II: meiosis I has sent one chromosome of each pair to each cell, so **4 chromosomes**, still with two chromatids each: **8 chromatids**. (c) After telophase II the chromatids have separated, so each cell has **4 chromosomes** of one chromatid each.

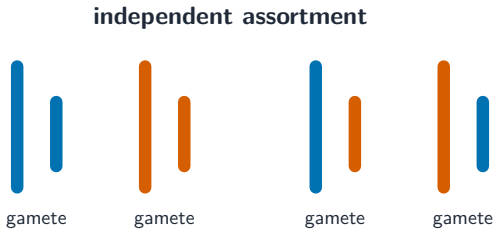
Meiosis makes the gametes **genetically different** from each other in two ways:

- **crossing over** 交叉互换 – homologous chromosomes swap matching pieces, mixing the alleles.




*Crossing over: paired chromosomes swap matching segments at a chiasma, making new allele combinations*

- **independent assortment** 自由组合 – the pairs line up in a random order, so each gamete gets a random mix of the parent's chromosomes.




*Independent assortment: chromosome pairs line up in a random order, so gametes get many different mixes*

Then at **fertilisation** 受精, any gamete can fuse with any other. This random fusion makes every new individual genetically different.

**How many combinations?** With $n$ pairs of homologous chromosomes, independent assortment alone can give $2^n$ different combinations in the gametes. A human has 23 pairs, so one person can make $2^{23}$ (about 8 million) kinds of gamete, before crossing over adds even more. Two parents can then make $2^{23} \times 2^{23}$ (about 70 million million) different combinations of chromosomes in their children.

## The language of genetics

You must know these terms exactly:

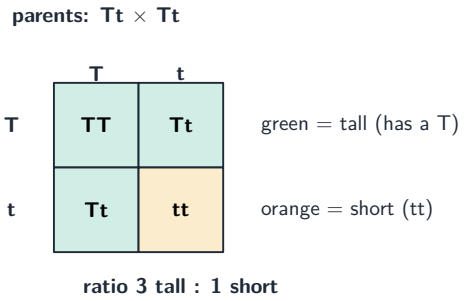
- a **gene** is a length of DNA that codes for a **protein** 蛋白质. Its position on a chromosome is its **locus** 基因座.
- an **allele** 等位基因 is one version of a gene.
- a **dominant** 显性 allele shows its effect even when only one copy is present; a **recessive** 隐性 allele only shows when two copies are present.
- **codominant** 共显性 alleles both show their effect together.
- the **genotype** 基因型 is the alleles an organism has; the **phenotype** 表现型 is the features you can see.
- **homozygous** 纯合 means the two alleles are the same; **heterozygous** 杂合 means they are different.
- a **test cross** 测交 crosses an organism with the recessive homozygote to find its unknown genotype.



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## Genetic diagrams and crosses

You show a cross with a genetic diagram, often using a **Punnett square** 庞纳特方格 – a grid that shows all the ways the gametes can combine.




*A Punnett square for Tt × Tt: the offspring are 3 tall : 1 short (T is dominant)*

- a **monohybrid cross** 单基因杂交 follows one gene; a **dihybrid cross** 双基因杂交 follows two genes at once.
- some genes have **multiple alleles** 复等位基因 (more than two versions in the population), such as the alleles for human blood groups.
- in **sex linkage** 伴性遗传, the gene is on the X chromosome, so the result is different for males and females.
- in **linkage** 连锁, genes on the same **autosome** 常染色体 (a non-sex chromosome) tend to be inherited together.
- in **epistasis** 上位性, one gene affects how another gene is shown.

### Worked crosses

**Codominance.** In a plant, the alleles $C^R$ (red) and $C^W$ (white) are codominant: the heterozygote $C^RC^W$ is pink. Cross two pink plants. Gametes: $C^R$ or $C^W$ from each. Offspring: $C^RC^R$ (red) : $C^RC^W$ (pink) : $C^WC^W$ (white) = 1 : 2 : 1. With codominance, each genotype has its own phenotype, so the ratio is not 3:1. Codominant alleles are written as the gene letter with **superscripts**, never as capital and small letters.

**Multiple alleles.** The ABO blood group gene has three alleles: $I^A$ and $I^B$ are codominant, and $I^o$ is recessive to both. A man of group A ($I^AI^o$) and a woman of group B ($I^BI^o$) can have children of **all four** groups: $I^AI^B$ (AB), $I^AI^o$ (A), $I^BI^o$ (B) and $I^oI^o$ (O), each with a probability of 1/4.

**Sex linkage.** Haemophilia is caused by a recessive allele $X^h$ on the X chromosome; the Y chromosome carries no copy of the gene. A carrier woman ($X^HX^h$) and a man without haemophilia ($X^HY$):

| Gametes | $X^H$ (father) | Y (father) |
|---|---|---|
| $X^H$ (mother) | $X^HX^H$ girl, unaffected | $X^HY$ boy, unaffected |
| $X^h$ (mother) | $X^HX^h$ girl, carrier | $X^hY$ boy, **haemophilia** |

Each son has a 1/2 chance of haemophilia; no daughter has it, but half are carriers. Males need only **one** recessive allele to show the condition, because they have only one X chromosome; so sex-linked recessive conditions are far more common in males. A father passes his X chromosome to all his daughters and none of his sons.

**Dihybrid cross.** In peas, round seed (R) is dominant to wrinkled (r), and yellow (Y) is dominant to green (y), and the two genes are on different chromosomes. Cross two plants heterozygous for both, RrYy × RrYy. Each parent makes four kinds of gamete in equal numbers, because the genes assort independently: RY, Ry, rY and ry. A 4 × 4 Punnett square gives 16 combinations:

| Phenotype | Genotypes | Number of the 16 |
|---|---|---|
| round, yellow | R_Y_ | 9 |
| round, green | R_yy | 3 |
| wrinkled, yellow | rrY_ | 3 |
| wrinkled, green | rryy | 1 |

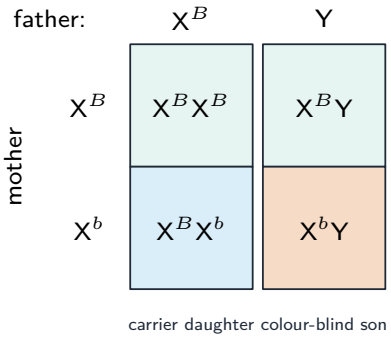
So the ratio is **9:3:3:1**. A dihybrid **test cross** (RrYy × rryy) gives 1:1:1:1.

**Autosomal linkage.** If the two genes are close together on the **same** chromosome, they do not assort independently: the alleles on one chromosome tend to go into the same gamete. A cross that would give 9:3:3:1 then gives mostly the two **parental** combinations, and only a few **recombinant** offspring – those made when crossing over happens between the two loci. A test cross that gives far more than 25% of each parental type, and far fewer of the new combinations, shows that the genes are linked.

**Epistasis.** In mice, gene A controls whether pigment is made: A (pigment made) is dominant to a (no pigment, white). Gene B controls the colour of the pigment: B (agouti, grey-brown hair) is dominant to b (black). Mice that are **aa** are white whatever their alleles of gene B: gene A is epistatic to gene B. AaBb × AaBb gives 9 A_B_ (agouti), 3 A_bb (black) and 4 aa (white, whatever their B alleles), so the ratio is **9:3:4** instead of 9:3:3:1. Other forms of epistasis give 9:7, 12:3:1 or 15:1. A dihybrid ratio of 16 parts that is not 9:3:3:1 suggests epistasis.



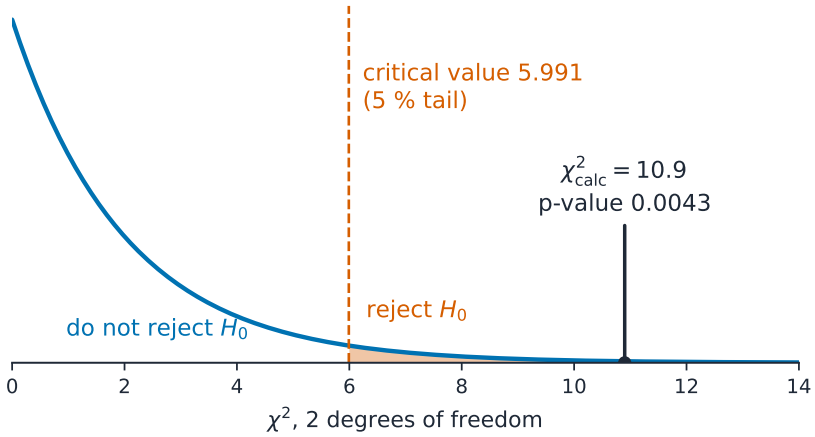
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*Because the gene is on the X chromosome, a carrier mother's sons may be colour-blind while her daughters are only carriers – a different result by sex*

## The chi-squared test

The **chi-squared test** 卡方检验 compares the results you actually counted (the *observed* numbers, $O$) with the results you expected from the genetic diagram (the *expected* numbers, $E$). It tells you whether the difference is small enough to be due to chance, or large enough to mean something else is going on.




*Reject $H_0$ when the statistic falls in the 5 % tail*

You add up, for every group, the squared difference between observed and expected, divided by the expected:

$$\chi^2 = \sum \frac{(O-E)^2}{E}$$

Then you compare this $\chi^2$ value with a **critical value** from a table. The row you use is set by the *degrees of freedom* (the number of groups minus 1). If $\chi^2$ is **less than** the critical value, the difference is not significant – the results fit the expected ratio, and any difference is just chance. If $\chi^2$ is **greater than** the critical value, the difference is significant, so some other factor is involved.

> **Worked example.** A Tt × Tt cross gives 160 offspring: 114 tall and 46 short. Test whether this fits the expected 3 : 1 ratio.

The expected numbers are $\frac{3}{4} \times 160 = 120$ tall and $\frac{1}{4} \times 160 = 40$ short. Then:

$$\chi^2 = \frac{(114-120)^2}{120} + \frac{(46-40)^2}{40} = \frac{36}{120} + \frac{36}{40} = 0.30 + 0.90 = 1.20.$$

There are 2 groups, so degrees of freedom $= 2 - 1 = 1$. The critical value at $p = 0.05$ is 3.84. Because $1.20 < 3.84$, the difference is **not significant**: the results fit a 3 : 1 ratio, and the small difference is due to chance.

> **Worked example (a dihybrid cross).** A dihybrid cross is expected to give 9:3:3:1. Of 320 offspring, the counts are 196, 52, 58 and 14. Is the result a good fit?

| | **Class 1** | **Class 2** | **Class 3** | **Class 4** |
|---|---|---|---|---|
| $O$ | 196 | 52 | 58 | 14 |
| $E$ | $\frac{9}{16} \times 320 = 180$ | 60 | 60 | 20 |
| $(O-E)^2/E$ | 1.42 | 1.07 | 0.07 | 1.80 |

$\chi^2 = 1.42 + 1.07 + 0.07 + 1.80 = 4.36$. There are 4 classes, so 3 degrees of freedom; the critical value at $p = 0.05$ is **7.82**. As $4.36 < 7.82$, the difference is not significant: the results fit 9:3:3:1, so the genes are probably assorting independently. If $\chi^2$ had been larger than 7.82, the difference would be significant, suggesting that the genes are **linked**, or that epistasis is involved.

## From genes to proteins to phenotype

A gene codes for a protein, and that protein affects the phenotype. If the gene is faulty, the protein is faulty, and the phenotype changes:

| **Gene** | **Protein** | **Effect of a faulty allele** |
|---|---|---|
| TYR | the **enzyme** 酶 tyrosinase | **albinism** 白化病 (no pigment made) |
| HBB | **haemoglobin** 血红蛋白 | **sickle cell anaemia** 镰状细胞贫血 |
| F8 | factor VIII (helps blood clot) | **haemophilia** 血友病 |
| HTT | huntingtin | **Huntington's disease** 亨廷顿病 |



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### Gibberellin and stem height

In pea plants, the dominant allele *Le* codes for a working enzyme that makes **gibberellin** 赤霉素, so the plant grows tall by stem **elongation** 伸长. The recessive allele *le* codes for a broken enzyme, so little gibberellin is made and the plant is short.

## Gene control

Not all genes are switched on all the time. Cells control which proteins they make.

- **structural genes** 结构基因 code for useful proteins such as enzymes; **regulatory genes** 调节基因 control whether other genes are switched on.
- an **inducible enzyme** 可诱导酶 is made only when it is needed; a **repressible enzyme** 可抑制酶 is normally made but can be switched off.

### The lac operon

In a **prokaryote** 原核生物 such as a bacterium, a group of genes called the **lac operon** 乳糖操纵子 controls the digestion of lactose:

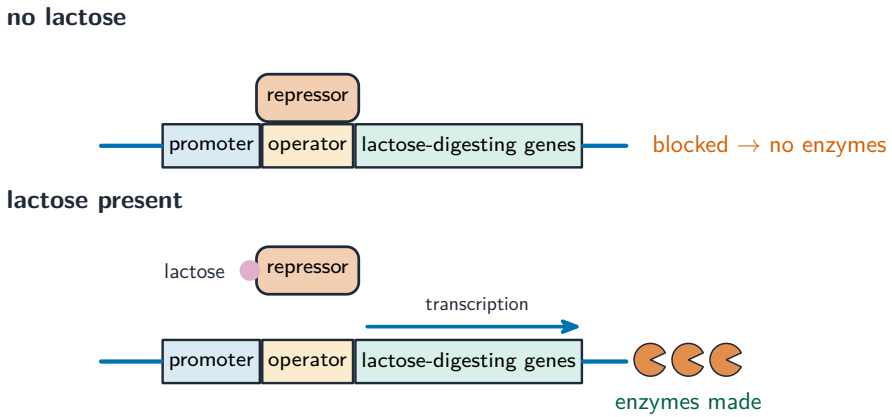
- when there is **no** lactose, a **repressor** 阻遏物 protein binds to the **operator** (a short control sequence within the operon) and blocks **transcription** 转录, so the lactose-digesting enzymes are not made.
- when lactose **is** present, it binds to the repressor and pulls it off. Transcription can now happen, and the enzymes are made. The enzymes are therefore inducible.

**In more detail.** The operon is a length of DNA with a **promoter** (where RNA polymerase binds), the **operator**, and three **structural genes** that are transcribed together as one mRNA:

- *lacZ* codes for **$\beta$-galactosidase**, which hydrolyses lactose to glucose and galactose;
- *lacY* codes for **lactose permease**, a carrier protein that takes lactose into the cell;
- *lacA* codes for transacetylase.

A separate **regulatory gene**, *lacI*, outside the operon, codes for the repressor protein. The repressor has two binding sites: one fits the operator, and one fits lactose. When lactose binds, the repressor changes **shape** and can no longer bind to the operator, so RNA polymerase can move along the structural genes. The bacterium therefore makes the enzymes only when lactose is there to be used, and does not waste energy and amino acids making them at other times. When the lactose has all been used, the repressor binds to the operator again.

A mutation in the **operator** that stops the repressor binding, or in *lacI* that makes a repressor that cannot bind to the operator, means the enzymes are made all the time, with or without lactose.




*The lac operon: a repressor blocks the genes until lactose pulls it off, so the enzymes are inducible*

### Control in eukaryotes

In eukaryotes, **transcription factors** 转录因子 are proteins that bind to DNA and control **gene expression** 基因表达, by increasing or decreasing the rate of transcription.

Gibberellin switches genes on in this way: it causes the breakdown of **DELLA** protein repressors. These DELLA proteins normally block the factors that turn on transcription, so removing them lets those genes be expressed.

A transcription factor works by binding to the **promoter** region of a gene. Some help RNA polymerase to bind (switching the gene on); others block it. Hormones often act through transcription factors: a steroid hormone such as oestrogen passes through the cell surface membrane and binds to a receptor protein in the cytoplasm, and the hormone–receptor complex enters the nucleus and acts as a transcription factor. This is how one cell type can express a different set of genes from another, although they have the same DNA.

**Common mistakes.**

- Saying the chromosome number halves in meiosis II. It halves in **meiosis I**, when the homologous pairs separate; meiosis II separates sister chromatids.
- Mixing up homologous chromosomes and sister chromatids. Homologous chromosomes come from **different** parents and may carry different alleles; sister chromatids are identical copies joined at a centromere.
- Saying crossing over happens between sister chromatids. It happens between chromatids of the two **homologous** chromosomes in a bivalent; swapping identical pieces would change nothing.



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- Writing a gene and an allele as the same thing. The gene is for a feature (eye colour); the alleles are its versions (blue, brown).
- In a chi-squared test, using percentages or ratios instead of the **numbers** of offspring, or comparing with 3.84 when there is more than one degree of freedom.

## Exam tips

- Set out a cross fully: **parental genotypes → gametes (in circles) → Punnett square → offspring ratio and phenotypes**.
- Use the **chi-squared** test to compare observed with expected; degrees of freedom = classes $-1$, compare with 3.84 at $p = 0.05$.
- Recognise codominance, multiple alleles, sex linkage, epistasis and linkage – each alters the expected ratio.
- **Meiosis** creates variation by crossing over and independent assortment – state both.
- Write codominant and sex-linked alleles with superscripts ($C^RC^W$, $X^HX^h$), and show the Y chromosome with no allele.
- Learn the expected ratios: 3:1, 1:2:1 (codominance), 1:1 (test cross), 9:3:3:1 and 1:1:1:1 (dihybrid), 9:3:4 (epistasis).
- Many parental types and few recombinants in a dihybrid test cross means the genes are **linked**.
- Lac operon: regulatory gene → repressor; lactose binds the repressor, changing its shape so that it leaves the operator.

# Selection and evolution

A-Level Biology

## Variation

**Variation** 变异 means the differences between individuals. It has three possible causes:

- **genetic** factors only – set by the **alleles** 等位基因 you inherit (for example human blood group).
- **environmental factors** 环境因素 only – set by your surroundings (for example a scar, or the language you speak).
- a **combination** of both – most features, such as height and body mass, depend on genes **and** on diet and lifestyle.



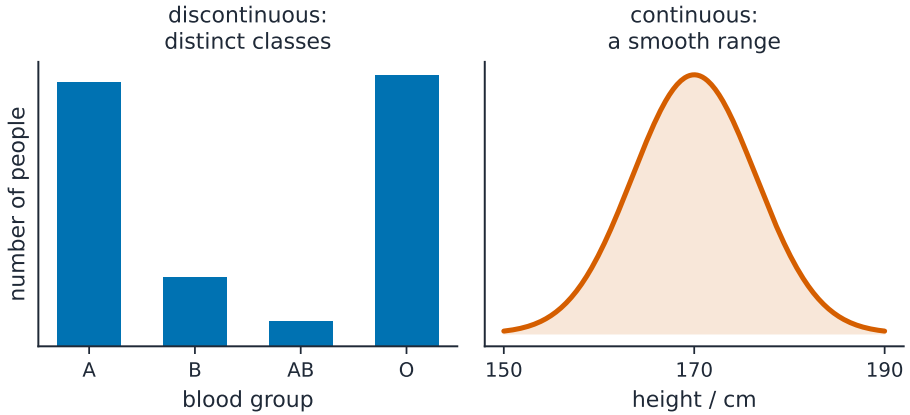
*Banded snails (Cepaea nemoralis) show striking variation in shell colour and banding*

There are two patterns of variation:

- **discontinuous variation** 不连续变异 – clear, separate groups with nothing in between (for example blood group A, B, AB or O). It is usually controlled by one or a few **genes** 基因, with little effect from the environment.
- **continuous variation** 连续变异 – a smooth range from one extreme to the other (for example height). It is controlled by many genes together, plus the environment.



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*Discontinuous variation falls into separate groups; continuous variation is a smooth range*

**The genetic basis.** In discontinuous variation, one gene has a few alleles, and each genotype gives a clearly different phenotype (with dominance, or codominance as in the $I^A$ and $I^B$ blood-group alleles). In continuous variation, many genes (**polygenes** 多基因), often on different chromosomes, each have a small **additive** effect: every "tall" allele adds a little height. With many genes, there are very many possible combinations, giving a smooth range; the environment (diet, light, water) then blurs the steps between them still further.

To compare the means of two samples (for example the heights of plants in sun and in shade), you use the **t-test**, which tells you whether the difference is large enough to be real, or just due to chance.

### ■ Using the t-test

The formula is given in the exam:

$$t = \frac{|\bar{x}_1 - \bar{x}_2|}{\sqrt{\frac{s_1^2}{n_1} + \frac{s_2^2}{n_2}}}, \qquad \text{degrees of freedom} = n_1 + n_2 - 2$$

where $\bar{x}$ is a mean, $s$ a standard deviation and $n$ the number in the sample. The steps are:

1. State the **null hypothesis** 零假设: there is no significant difference between the two means.
2. Calculate $t$ and the degrees of freedom.
3. Look up the **critical value** in the table at $p = 0.05$ (a 5% probability that the difference is due to chance).

4. If $t$ is **greater** than the critical value, reject the null hypothesis: the difference is **significant**. If it is smaller, accept the null hypothesis: the difference could be due to chance.

> **Worked example.** The lengths of 10 leaves from a plant in the shade have mean 52 mm and $s = 4.0$ mm; 10 leaves from the sun have mean 46 mm and $s = 3.5$ mm. Is the difference significant? (Critical value for 18 degrees of freedom at $p = 0.05$ is 2.10.)

$$t = \frac{52 - 46}{\sqrt{\frac{4.0^2}{10} + \frac{3.5^2}{10}}} = \frac{6}{\sqrt{1.6 + 1.225}} = \frac{6}{1.68} = 3.57$$

Degrees of freedom $= 10 + 10 - 2 = 18$. As $3.57 > 2.10$, reject the null hypothesis: the probability that this difference is due to chance is less than 5%, so shade leaves are significantly longer. The test only works for data that are roughly **normally distributed** (continuous variation), with samples of fewer than about 30.

## Natural selection

A **population** 种群 produces far more **offspring** 后代 than can survive, so the offspring must **compete** 竞争 for resources such as food and space. This is the "struggle for existence". The individuals that are best **adapted** 适应 are most likely to survive, **reproduce** 繁殖, and pass on their alleles to the next generation. Over many generations, the helpful alleles become more common in the population. This is **natural selection** 自然选择.



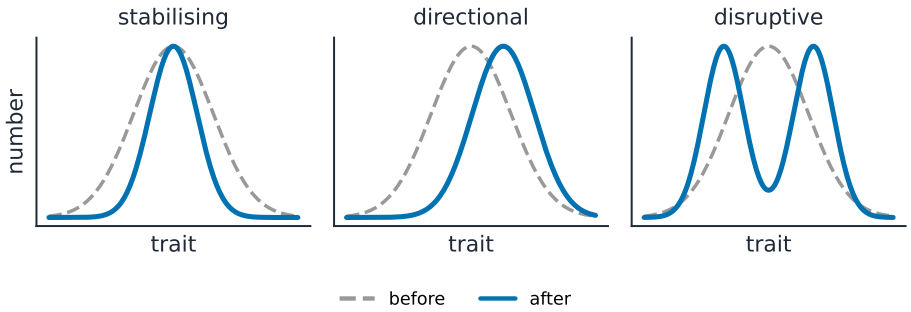
*The **peppered moth** shows natural selection: the dark form hides on dark, sooty bark, while the pale speckled form hides on pale **lichen** – birds eat whichever stands out*



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Environmental conditions can push selection in three ways:

- **stabilising selection** 稳定选择 favours the average and removes the extremes, so the mean stays the same and the range of variation narrows.
- **directional selection** 定向选择 favours one extreme, so the mean shifts that way.
- **disruptive selection** 分裂选择 favours both extremes and removes the average.




stabilising: favours the mean · directional: one extreme · disruptive: both extremes

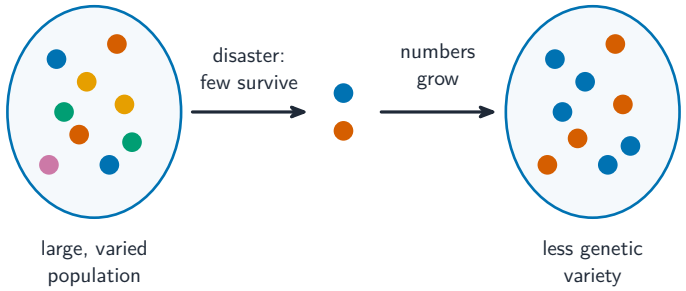
*Stabilising narrows the range, directional shifts the mean, disruptive splits it in two*

| Type | Example |
|---|---|
| stabilising | human birth mass: very small and very large babies have lower survival, so the mean stays near 3.5 kg |
| directional | bacteria exposed to an antibiotic; the dark peppered moth when soot darkened tree trunks in industrial areas |
| disruptive | a habitat with two kinds of background (light sand and dark rock) favours both pale and dark animals, while intermediate ones are seen by predators |

Each answer needs the chain: **variation** exists → a **selection pressure** acts → individuals with an advantageous phenotype **survive and reproduce** more → they pass on their **alleles** → the **allele frequency** changes over generations.

Allele frequencies can also change in other ways:

- the **founder effect** 奠基者效应 – a few individuals start a new population, so they carry only some of the alleles of the original group.
- **genetic drift** 遗传漂变 – in a small population, allele frequencies change by chance from generation to generation.
- the **bottleneck effect** 瓶颈效应 – a sudden fall in population size leaves few survivors, reducing the variety of alleles.




*A bottleneck: only a few survive a disaster, so the recovered population has less genetic variety*

Examples: the northern elephant seal was hunted down to perhaps 20 animals in the 1890s; today there are over 100 000, but they have very little genetic variation, which is a bottleneck. In some small, isolated human communities founded by a few families, a rare allele (for example one causing extra fingers) is far more common than elsewhere: the founder effect. Small populations with little variation are more at risk if the environment changes or a new disease appears, because few individuals may have alleles that let them survive.

### Antibiotic resistance as natural selection

A chance **mutation** 突变 makes a few bacteria **resistant** to an **antibiotic** 抗生素. When the antibiotic is used, the non-resistant bacteria die, but the resistant ones survive and reproduce. Over time the **resistance** 耐药性 spreads through the population. This is natural selection in action.

## The Hardy–Weinberg principle

The **Hardy–Weinberg principle** 哈迪-温伯格原理 lets you calculate the **allele frequencies** 等位基因频率 and **genotype** 基因型 frequencies in a population. It only holds true when there is a large population, mating is random, and there is no mutation, no migration and no natural selection.

Call the frequency of the dominant allele $p$ and the frequency of the recessive allele $q$. There are only two alleles, so:

$$p + q = 1.$$

The genotype frequencies then add up to 1, where $p^2$ is homozygous dominant, $2pq$ is heterozygous (the carriers), and $q^2$ is homozygous recessive:

$$p^2 + 2pq + q^2 = 1.$$



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> **Worked example.** A recessive condition affects 1 in every 100 people. Find the frequency of carriers.

Only the homozygous recessive genotype ($q^2$) shows the condition, so $q^2 = \frac{1}{100} = 0.01$, giving $q = \sqrt{0.01} = 0.1$. Then $p = 1 - q = 0.9$. The carriers are the heterozygotes:

$$2pq = 2 \times 0.9 \times 0.1 = 0.18.$$

So about 18% of the population are carriers – far more than the 1% who show the condition.

> **Worked example (from the dominant phenotype).** In a population of moths, 84% have dark wings (dominant allele D) and 16% pale wings (dd). Find the frequency of each genotype. Start from the recessive phenotype: $q^2 = 0.16$, so $q = 0.4$ and $p = 0.6$. Then DD $= p^2 = 0.36$ and Dd $= 2pq = 0.48$ (check: $0.36 + 0.48 = 0.84$, the dark moths). If later generations no longer fit these values, one of the conditions is broken – most often, selection is acting.

$$p + q = 1$$
$$p^2 + 2pq + q^2 = 1$$

| | |
|---|---|
| $p$ | frequency of allele *A* |
| $q$ | frequency of allele *a* |
| $p^2$ | frequency of genotype *AA* |
| $2pq$ | frequency of genotype *Aa* |
| $q^2$ | frequency of genotype *aa* |

*H–W equilibrium: no selection, mutation, migration, drift, or non-random mating*

*Hardy–Weinberg: allele frequencies $p$ and $q$ give genotype frequencies $p^2$, $2pq$, $q^2$*

## Selective breeding (artificial selection)

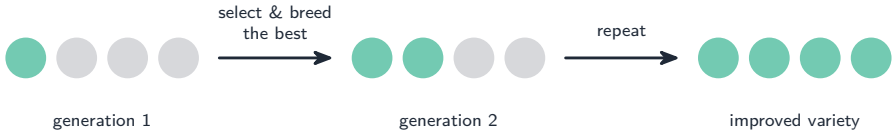
In **selective breeding** 选择育种, also called **artificial selection** 人工选择, humans (not nature) choose which organisms breed, so that useful features are passed on. Examples:

- breeding **disease resistance** 抗病性 into varieties of wheat and rice.
- using **inbreeding** 近交 and **hybridisation** 杂交 (crossing different lines) to make vigorous, uniform maize.

- breeding dairy cattle to improve their milk **yield** 产量.

**How each is done.**

- **Disease resistance in wheat and rice.** A variety with high yield but no resistance is crossed with a wild or old variety that resists a disease (such as stem rust in wheat, or blast in rice). The offspring that show resistance are selected and crossed back to the high-yielding variety again and again, until the new variety has both the resistance and the high yield.
- **Maize.** Repeated **inbreeding** (self-pollinating a line for several generations) makes the plants **homozygous** at most loci, so a line is uniform, but it also brings together harmful recessive alleles, so inbred plants are small and weak (**inbreeding depression** 近交衰退). Crossing two different inbred lines gives **$F_1$ hybrids** that are heterozygous at many loci: they are vigorous and high-yielding (**hybrid vigour** 杂种优势), and all genetically identical, so they grow evenly and can be harvested by machine at the same time. Farmers buy new hybrid seed every year, because the next generation is not uniform.
- **Dairy cattle.** Cows with the highest milk yield are chosen. A bull cannot be measured for milk, so bulls are chosen by **progeny testing**: the milk yields of a bull's daughters are recorded. The best bulls' semen is used to inseminate many cows (**artificial insemination**). Over many generations, milk yield has risen greatly, but at a cost: some high-yielding cows have more health problems, and the genetic variety of the breed has fallen.




*Selective breeding: choosing only the best to breed each generation makes the wanted feature more and more common*

## Evolution

**Evolution** 进化 is the slow formation of new **species** 物种 from earlier ones, as the **gene pool** 基因库 (all the alleles in a population) changes from generation to generation.

DNA **sequence** 序列 data can show how closely related two species are: the more similar their DNA sequences, the more recently they shared a common ancestor.

Mutations build up in DNA at a roughly steady rate over time. So two species that split from a common ancestor long ago have had time to collect many differences in a gene, while two that split recently have few. Scientists compare the base sequence



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of the same gene (for example the gene for cytochrome c, or mitochondrial DNA) in several species and count the differences; the numbers are used to build a family tree. Amino acid sequences of the same protein can be compared in the same way.

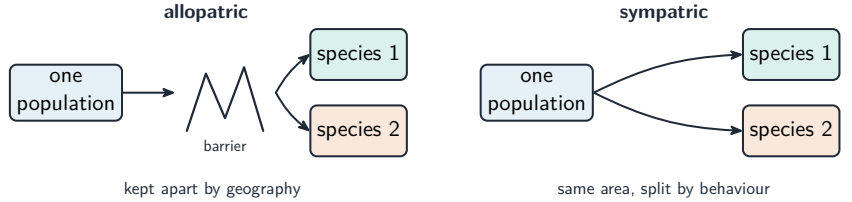
> **Worked example.** A stretch of the same gene differs from the human sequence by 1.2% in chimpanzees, 1.6% in gorillas and 3.1% in orangutans. Which species is most closely related to humans? Chimpanzees: their sequence has the **fewest** differences from the human one, so humans and chimpanzees shared a common ancestor most recently. Orangutans branched off earliest.

**Speciation** 物种形成 happens when two populations become genetically separated, so they can no longer breed together. This genetic **isolation** 隔离 can come about in two ways:

- **allopatric speciation** 异域物种形成 – the populations are kept apart by a **geographical separation** 地理隔离, such as a sea or a mountain range.
- **sympatric speciation** 同域物种形成 – the populations live in the same area but are separated by differences in behaviour or way of life.

**Allopatric speciation, step by step.** A population is split by a geographical barrier, so there is **no gene flow** between the two groups. The two areas have different conditions, so **different selection pressures** act on them, and different mutations arise in each; genetic drift may also act if a group is small. Over many generations the **gene pools** become more and more different. Eventually, even if the barrier is removed, the two groups can no longer interbreed to produce **fertile** offspring: they are two species. Darwin's finches on the Galápagos islands are a classic example.

**Sympatric speciation.** Without a barrier, other things can stop gene flow. **Ecological** separation: two groups use different habitats or foods in the same area (for example insects that feed and mate on different host plants). **Behavioural** separation: different courtship songs, displays or mating times mean the groups no longer choose each other as mates. In plants, a mistake in cell division can double the chromosome number (**polyploidy** 多倍体); the polyploid plant cannot breed with its parent species to give fertile offspring, so it is a new species at once.




*Allopatric speciation needs a physical barrier; sympatric speciation happens in the same area*

**Common mistakes.**

- Using the frequency of the dominant **phenotype** as $p^2$. People with the dominant phenotype are $p^2 + 2pq$; only the recessive phenotype gives one genotype directly, so always start from $q^2$.
- Forgetting the square root. If $q^2 = 0.01$ then $q = 0.1$, not 0.01, and the carrier frequency is $2pq$, not $pq$.
- Saying a mutation happens **because** an organism needs it. Mutations are random; the selection pressure only decides which existing alleles become more common.
- Saying individuals evolve. A single organism cannot change its alleles; it is the **allele frequency in the population** that changes over generations.
- Mixing up genetic drift and natural selection. Drift is change by **chance**, strongest in small populations; selection is change because some alleles give a better chance of survival.
- Saying speciation has happened just because two groups look different. A new species forms only when the populations are **reproductively isolated** and can no longer breed to give fertile offspring.

## Exam tips

- Explain **natural selection** as a sequence: variation → selection pressure → the better-adapted survive and reproduce → allele frequency changes.
- Use the **Hardy–Weinberg** equations ($p + q = 1$, $p^2 + 2pq + q^2 = 1$); $q^2$ is the recessive-phenotype frequency – a common calculation.
- Distinguish **stabilising, directional and disruptive** selection with an example of each.
- Distinguish **allopatric vs sympatric** speciation: both need reproductive isolation, caused by geographical separation (allopatric) or by ecological or behavioural differences within one area (sympatric).



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# Classification, biodiversity and conservation

A-Level Biology

## Classifying living things

A **species** 物种 can be defined in more than one way:

- the **biological** species concept – a group whose members can breed together to produce fertile offspring.
- the **morphological** species concept – a group whose members look alike.
- the **ecological** species concept – a group that fills the same role in its surroundings.



*A museum insect collection: classification groups organisms by their shared features*

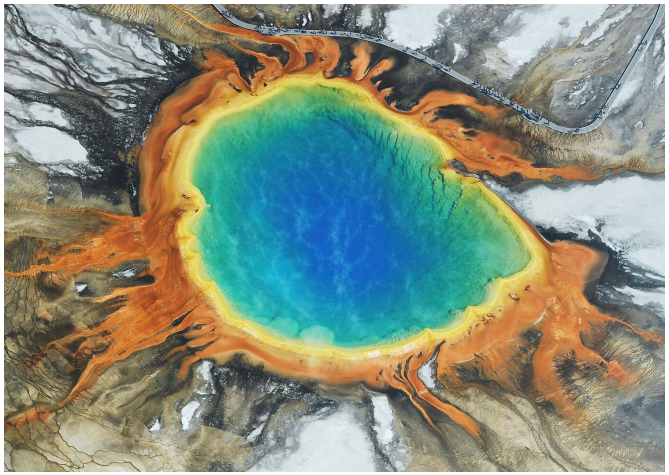
Each concept has a weakness. The biological concept cannot be used for organisms that reproduce **asexually** (such as bacteria), for fossils, or for populations that never meet; the morphological concept can be fooled when males and females look very different, or when unrelated species look alike. Scientists now also compare **DNA sequences** to decide whether two groups are one species.

### The three domains

The largest groups in **classification** 分类 are three **domains** 域:

- **Archaea** 古菌 and **Bacteria** 细菌 – both are **prokaryotes** 原核生物 (no nucleus). They look similar but differ in their membrane lipids, their ribosomal RNA, and the make-up of their **cell walls** 细胞壁.
- **Eukarya** 真核生物 – all organisms whose cells have a nucleus.

| Feature | Bacteria | Archaea | Eukarya |
|---|---|---|---|
| nucleus | none | none | present |
| membrane-bound organelles | none | none | present (mitochondria, ER, Golgi) |
| ribosomes | 70S | 70S, but rRNA and proteins more like those of eukaryotes | 80S in the cytoplasm |
| cell wall | contains peptidoglycan | no peptidoglycan | cellulose (plants), chitin (fungi) or none (animals) |
| membrane lipids | glycerol joined to unbranched fatty acids by ester bonds | glycerol joined to branched chains by ether bonds | as in bacteria (ester bonds) |
| DNA | circular, no histones | circular, with histone-like proteins | linear, wound on histones |



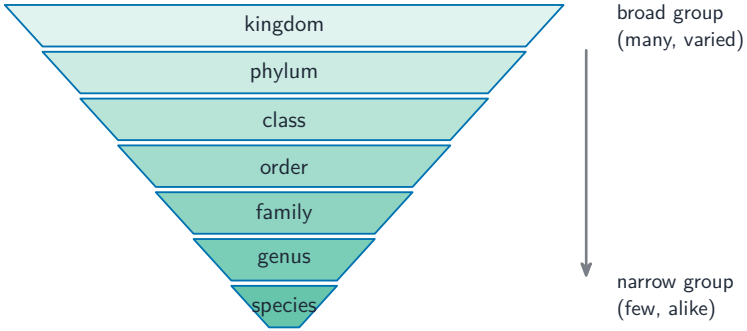
*Each coloured ring around this scalding spring is a different community of microbes living at a different temperature. Archaea like these – thriving where almost nothing else can – were the clue that they form a domain of their own, separate from ordinary bacteria*



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## The taxonomic hierarchy

Inside the Eukarya domain, organisms are sorted into a **taxonomic hierarchy** 分类层级 – a set of smaller and smaller groups: **kingdom** 界, **phylum** 门, **class** 纲, **order** 目, **family** 科, **genus** 属 and species.

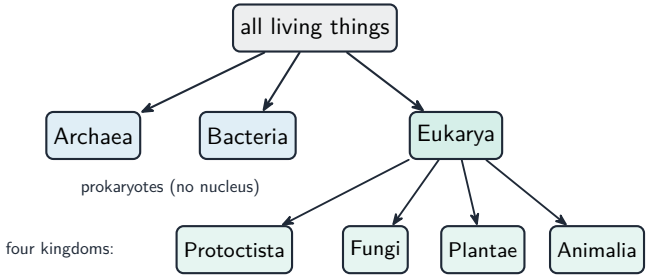



*Each level of the taxonomic hierarchy is a smaller, more closely related group, ending at a single species*

The Eukarya are split into four kingdoms:

- **Protoctista** 原生生物界 – mostly single-celled (such as *Amoeba*).
- **Fungi** 真菌界 – feed by absorbing food; have cell walls of chitin.
- **Plantae** 植物界 – make their own food by photosynthesis.
- **Animalia** 动物界 – feed on other organisms.

| Kingdom | Cells | Cell wall | Nutrition | Other features |
|---|---|---|---|---|
| Protoctista | eukaryotic; mostly single-celled, some multicellular (seaweeds) | some have one | varied: some photosynthesise, some feed on others | a mixed group of eukaryotes that do not fit the other kingdoms |
| Fungi | eukaryotic; mostly made of thread-like **hyphae**, some single-celled (yeast) | chitin | heterotrophic: secrete enzymes onto food and absorb the products | store glycogen; reproduce by spores |
| Plantae | eukaryotic, multicellular | cellulose | autotrophic: photosynthesis in chloroplasts | large vacuole; store starch |
| Animalia | eukaryotic, multicellular | none | heterotrophic: ingest food | nervous coordination; store glycogen; most can move |




*The three domains: Archaea and Bacteria are prokaryotes; the Eukarya split into four kingdoms*

Viruses are not placed in these groups. They are classified by the type of **nucleic acid** 核酸 they contain (DNA or RNA) and whether it is **single-stranded** 单链 or **double-stranded** 双链.

For example, the smallpox virus has double-stranded DNA; HIV, measles and influenza viruses have single-stranded RNA; the virus that causes rotavirus diarrhoea has double-stranded RNA. Viruses are left out of the domains because they are not cells: they have no cytoplasm or ribosomes and can reproduce only inside a host cell.



## Biodiversity

An **ecosystem** 生态系统 is all the living things in an area together with their non-living surroundings. A **niche** 生态位 is the particular role and place of a species within it.

A coral reef is a good picture of high biodiversity – many different corals, fish and other species living together:



*A **coral reef** is one of the most biodiverse habitats on Earth: many species of coral and fish share one small area*

**Biodiversity** 生物多样性 can be measured at three levels:

- the number and range of different ecosystems and **habitats** 栖息地.
- the number of species and their relative **abundance** 丰度 (how common each one is).
- the genetic variation within each species.



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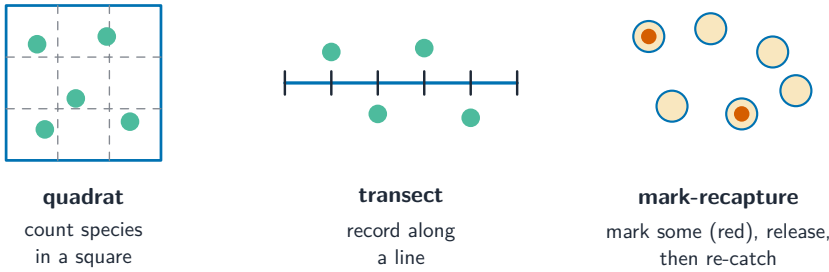



*Biodiversity is measured at three levels: the range of ecosystems, the number of species, and the genetic variation within a species*

## Sampling an area

You cannot count every organism, so you take samples. **Random sampling** 随机取样 (choosing positions by chance) avoids bias and gives a fair picture. Useful methods are:

- **quadrats** 样方 – square frames placed to count or estimate the species inside them.
- **transects** 样带 – counting along a line across the area (a line transect records what touches the line; a belt transect counts within a strip).
- **mark-release-recapture** 标志重捕法 – for moving animals: catch, mark and release some, then later see what fraction of a new catch is marked (the Lincoln index).




*Quadrats and transects sample fixed plants; mark-release-recapture estimates numbers of moving animals*

**Recording what is in a quadrat.** There are several ways, and an exam question may ask you to choose one:

- **species frequency**: the percentage of quadrats in which a species is found (it is in 12 of 20 quadrats, so its frequency is 60%).



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- **species density**: the number of individuals per square metre – for plants that can be counted one by one.
- **percentage cover**: the percentage of the quadrat's area covered by a species, used when single plants cannot be counted (grass, moss). A quadrat divided into 100 small squares makes it easier to estimate.
- an **abundance scale** such as ACFOR (abundant, common, frequent, occasional, rare): quick, but **subjective**, because different people judge differently.

To decide how many quadrats are enough, keep adding quadrats and plotting the running total of species found; stop when the curve levels off.

**Placing them at random.** Lay two tape measures at right angles along two sides of the area. Use a random-number generator to give two coordinates, and place the quadrat where they meet. Repeat for every quadrat. Along a **belt transect**, place quadrats at regular intervals (for example every 2 m) instead, because the aim is to see how the species change along the line; record an abiotic factor (light intensity, soil moisture, pH) at each point too.

To link the spread of a species to **biotic factors** 生物因素 (living) or **abiotic factors** 非生物因素 (non-living), you can use Spearman's rank or Pearson's **correlation** 相关性. To measure the diversity of an area as a single number, you use **Simpson's index of diversity** 辛普森多样性指数: a higher value means more diverse and usually more stable.

## Simpson's index of diversity

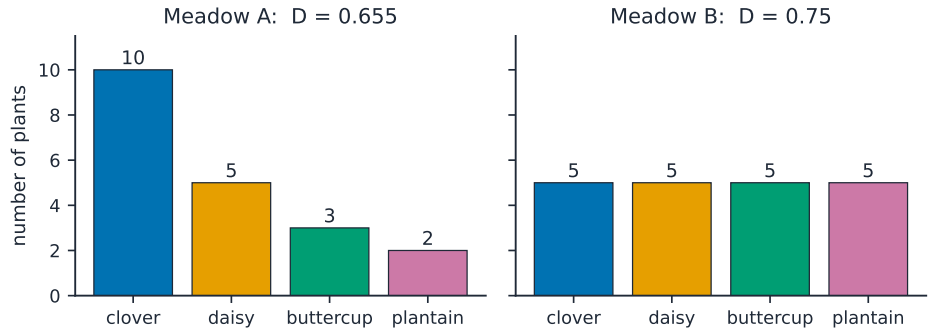
$$D = 1 - \sum \left(\frac{n}{N}\right)^2$$

where $n$ is the number of individuals of one species and $N$ the total number of individuals of all species. $D$ lies between 0 (one species only) and nearly 1 (many species, evenly spread).

**Worked example.** Two meadows each have 20 plants of four species.

| Species | Meadow A: $n$ | A: $(n/N)^2$ | Meadow B: $n$ | B: $(n/N)^2$ |
|---|---|---|---|---|
| clover | 10 | 0.2500 | 5 | 0.0625 |
| daisy | 5 | 0.0625 | 5 | 0.0625 |
| buttercup | 3 | 0.0225 | 5 | 0.0625 |
| plantain | 2 | 0.0100 | 5 | 0.0625 |
| sum | 20 | 0.3450 | 20 | 0.2500 |

Meadow A: $D = 1 - 0.345 = 0.655$. Meadow B: $D = 1 - 0.25 = 0.75$. Both have the same **species richness** (four species), but B is more diverse because its individuals are spread **evenly** among the species; in A, clover dominates. A more diverse community is usually more stable, because each species has more food sources and the loss of one species has less effect.




*Same richness, different evenness: meadow B is more diverse*

## Spearman's rank and Pearson's correlation

**Spearman's rank correlation** 斯皮尔曼等级相关 tests whether two variables are linked when the data are not normally distributed, or are ranks. The formula is given:

$$r_s = 1 - \frac{6\sum D^2}{n(n^2-1)}$$

where $D$ is the difference between the two ranks of each sample and $n$ the number of pairs.

> **Worked example.** A student measured light intensity and the percentage cover of a woodland plant in 8 quadrats. Rank each variable (1 = highest), find the differences and square them:

| Quadrat | Light / arbitrary units | Rank | Cover / % | Rank | $D$ | $D^2$ |
|---|---|---|---|---|---|---|
| 1 | 12 | 6 | 20 | 6 | 0 | 0 |
| 2 | 25 | 2 | 45 | 1 | 1 | 1 |
| 3 | 8 | 7 | 15 | 7 | 0 | 0 |
| 4 | 30 | 1 | 35 | 3 | −2 | 4 |
| 5 | 18 | 4 | 40 | 2 | 2 | 4 |
| 6 | 22 | 3 | 30 | 4 | −1 | 1 |
| 7 | 5 | 8 | 10 | 8 | 0 | 0 |
| 8 | 15 | 5 | 25 | 5 | 0 | 0 |

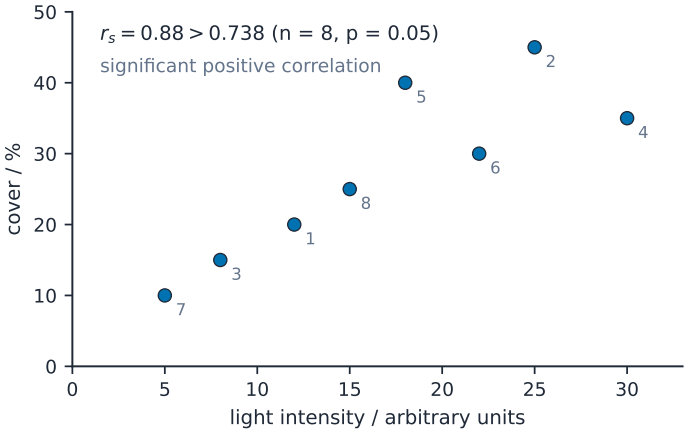


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$\sum D^2 = 10$, so

$$r_s = 1 - \frac{6 \times 10}{8 \times (64-1)} = 1 - \frac{60}{504} = 0.88$$

The null hypothesis is that there is no correlation between light intensity and cover. The critical value for $n = 8$ at $p = 0.05$ is 0.738. As $0.88 > 0.738$, reject the null hypothesis: there is a significant **positive** correlation. This does not prove that light **causes** the higher cover. (Two equal values share the mean of the ranks they would take: two values tied for 3rd and 4th are both ranked 3.5.)




*The eight quadrats: a significant positive correlation, not proof of cause*

**Pearson's correlation coefficient** $r$ is used instead when both variables are measured on a continuous scale and are roughly **normally distributed**, with a **linear** relationship (check with a scatter graph first). Like $r_s$, it runs from $-1$ (perfect negative) through 0 (none) to $+1$ (perfect positive).

> **Worked example.** 60 snails are caught, marked and released. Later, 80 snails are caught, of which 15 are marked. Estimate the population. The Lincoln index assumes the marked animals have **mixed back in evenly**, so the fraction marked in the second sample equals the fraction marked in the whole population:

$$N = \frac{\text{first sample} \times \text{second sample}}{\text{number marked in the second}} = \frac{60 \times 80}{15} = 320$$

So there are about **320** snails. The estimate is only as good as its assumptions, so state them: no births, deaths or migration between the two catches; the marks neither rub off nor make the animal easier for a predator to spot; and enough time is allowed for mixing. Break one and the estimate breaks with it - a mark that attracts predators lowers the recapture count and therefore **overestimates** the population.

## Conservation

A species can become **extinct** 灭绝 (die out completely) because of **climate change** 气候变化, competition (often from new species), hunting by humans, or the damage and loss of its habitats.

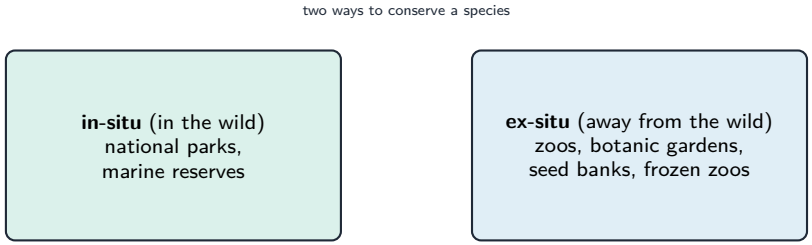
We try to protect biodiversity because other species give us food, medicines and materials, help keep ecosystems stable, and have value in themselves.

Reasons for conserving species and ecosystems, sorted as an exam answer expects:

- **moral and ethical**: every species has a right to exist, and we have a duty to pass a rich world on to future generations.
- **ecological**: species depend on each other in food webs; losing one (for example a pollinator or a top predator) can affect many others. Ecosystems provide **services** such as pollination, clean water, soil formation and the recycling of nutrients.
- **economic**: food crops and their wild relatives (a source of alleles for disease resistance), timber, fibres, medicines (many drugs, such as aspirin and some cancer drugs, came from plants), and income from tourism.
- **aesthetic and social**: people value wild places and wildlife for recreation and well-being.

### Ways to conserve species

- **zoos** 动物园 and **botanic gardens** 植物园 keep and breed **endangered species** 濒危物种.
- protected **conservation** 保护 areas, such as national parks and marine parks, keep habitats safe.
- 'frozen zoos' store frozen cells, eggs and sperm, and **seed banks** 种子库 store seeds for the future.




*Conservation is either in-situ (protecting species in their own habitat) or ex-situ (keeping and breeding them away from the wild)*

**Advantages and drawbacks.** Protected areas (**in situ**) keep species in their natural habitat with all the other species they depend on, and protect many species at once, but they are hard to police against poaching and cannot protect against climate change.



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Zoos, botanic gardens and seed banks (**ex situ**) protect a species from threats in the wild and allow captive breeding, but a small captive population has little genetic diversity, animals may not breed or may behave unnaturally, and releasing them back to the wild often fails if the habitat is not restored. A **seed bank** stores seeds dried to a low water content at about −20 °C, where they stay alive for decades; samples are tested for **germination** regularly, and fresh seed is grown when the viability falls.

For rare mammals, **assisted reproduction** can boost numbers: **in vitro fertilisation** 体外受精 (IVF), **embryo transfer** 胚胎移植, and **surrogacy** 代孕 (another female carries the young).

In IVF, a female is given hormones so that she releases several eggs, which are collected and fertilised with sperm in a dish. The early embryos can be placed in the uterus of the same female, or in a **surrogate** mother of a closely related, more common species (embryo transfer), so one rare female can produce many more young than she could carry herself. Eggs, sperm and embryos can be frozen in liquid nitrogen (a **frozen zoo**) and sent between zoos, so animals far apart can breed without the stress of moving them, which keeps the genetic diversity of the captive population high.

Conservationists also control **invasive species** 入侵物种, which are brought in from elsewhere and out-compete native species.

An invasive species often has no natural predators or diseases in its new home, so its population grows quickly. It may compete with native species for food or space, eat them, or bring in a disease. For example, cane toads taken to Australia to control beetles poison the native predators that eat them; rats introduced to islands eat the eggs of ground-nesting birds. Control methods include trapping, shooting or poisoning, removing invasive plants by hand, and checking imports at borders so that new species are not brought in.

Two organisations help worldwide: the IUCN, which lists how threatened each species is, and CITES, which controls the international trade in endangered animals and plants.

**Common mistakes.**

- Saying biodiversity is just the number of species. That is **species richness** 物种丰富度; biodiversity also counts how evenly the individuals are spread among the species, the variety of habitats, and the genetic variation within each species.
- Reading a high Simpson's index as low diversity. In the syllabus form $D = 1 - \sum(n/N)^2$, a value **near 1** means high diversity and a value near 0 means low diversity.
- Placing quadrats where the plants look interesting. Choose positions **at random**, for example from random-number coordinates, so the sample is not biased.
- Using a random quadrat to show how plants change across a shore or from a path. Where a factor changes along a line, use a **belt or line transect**.
- Saying a correlation proves that one factor causes the change. A significant correlation shows only a **link**; something else may cause both.

- Listing bacteria and archaea as one kingdom. They are two separate **domains**; both are prokaryotes but they differ in membrane lipids, ribosomal RNA and cell walls.
- Putting viruses in a kingdom. Viruses are not cells, so they sit outside the three domains and are classified by their nucleic acid.

## Exam tips

- Learn the **taxonomic hierarchy** (domain → kingdom → … → species) and the three domains; a species interbreeds to give **fertile** offspring.
- Measure biodiversity with **Simpson's index** (a higher value = more diverse) and explain why high biodiversity aids stability.
- Give **in-situ vs ex-situ** conservation methods with the advantage of each.
- Simpson's index: square each $n/N$, add them, subtract from 1; compare two sites by both richness and evenness.
- Spearman's rank: state the null hypothesis, rank both variables, compare $r_s$ with the critical value, and say "correlation", never "causes".
- Choose percentage cover for plants that cannot be counted, and a belt transect when a factor changes along a line.



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# Genetic technology

A-Level Biology

## Principles of genetic technology

**Recombinant** 重组 DNA is DNA that has been made by joining together DNA from two different sources. **Genetic engineering** 基因工程 is the deliberate changing of an organism's genetic material – often by transferring a **gene** 基因 into an organism so that the gene is **expressed** (switched on to make its **protein** 蛋白质).




*A thermal cycler (PCR machine) makes many copies of a DNA sample*

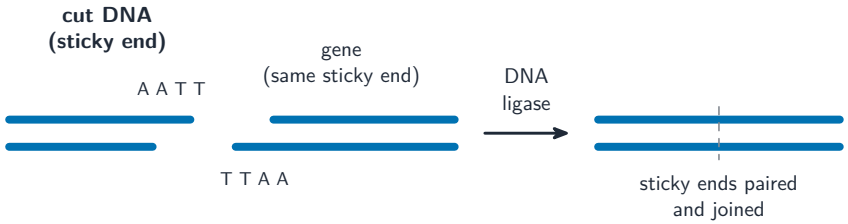
The gene to be transferred can be obtained in three ways:

- cut out of the DNA of a **donor** 供体 organism,
- made from the donor's mRNA, using the enzyme **reverse transcriptase** 逆转录酶,
- built chemically from **nucleotides** 核苷酸.

**Why use mRNA?** A human gene contains **introns** 内含子 (non-coding sequences), and bacteria cannot remove them, so a bacterium given the gene itself would make the wrong protein. Cells that make a lot of one protein (for example $\beta$ cells of the pancreas making insulin) contain many copies of its mRNA, which has already had its introns removed. Reverse transcriptase uses the mRNA as a template to make single-stranded **complementary DNA** 互补 DNA (cDNA); DNA polymerase then makes it double-stranded. The cDNA has no introns, so a bacterium can express it.

## The tools

| Tool | Role |
|---|---|
| **restriction endonuclease** 限制性内切酶 | cuts DNA at a specific base sequence, leaving "sticky ends" |
| DNA **ligase** 连接酶 | joins pieces of DNA together |
| **plasmid** 质粒 | a small ring of bacterial DNA used as a **cloning vector** 载体 to carry the gene into a cell |
| DNA **polymerase** 聚合酶 | copies DNA |
| reverse transcriptase | makes DNA from an mRNA template |




*A restriction endonuclease leaves matching sticky ends; DNA ligase joins a gene to the cut DNA*

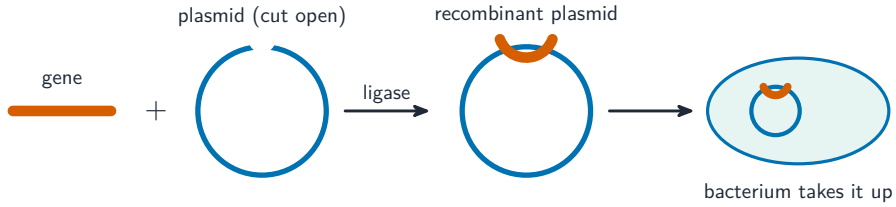
A **promoter** 启动子 often has to be transferred along with the gene. The promoter is the "switch" that lets the gene be transcribed in its new organism, so without it the gene would stay silent.

A promoter is the region of DNA just before a gene where **RNA polymerase** binds to start transcription. Bacterial RNA polymerase does not recognise most eukaryotic promoters, so a gene put into bacteria is usually joined to a **bacterial** promoter. The promoter can also choose where the gene is expressed: in Golden Rice, a promoter active only in the endosperm makes the new protein only in the grain.

To check the gene has gone in and is working, scientists add a **marker gene** 标记基因 next to it – for example one that codes for a **fluorescent** 荧光 (glowing) product. If the cells glow, the transfer worked.



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*A plasmid acts as a cloning vector: the gene is joined into it, and the recombinant plasmid is taken up by a bacterium*

**Making a recombinant bacterium, step by step.**

1. Cut the plasmid and the gene with the **same** restriction enzyme, so they have complementary sticky ends.
2. Mix them: the sticky ends pair by hydrogen bonds between complementary bases, and **DNA ligase** forms phosphodiester bonds to seal the sugar–phosphate backbone. Some plasmids close up again without the gene.
3. Get the plasmids into bacteria: mix them with the bacteria in ice-cold **calcium chloride** solution and then give a brief **heat shock** (about 42 °C), which makes the bacterial membranes more permeable; or use a short electric pulse (electroporation). Only a small fraction of the bacteria (often fewer than 1%) take up a plasmid, so the next step is essential.
4. **Identify** the bacteria that have taken up the recombinant plasmid, using the marker gene, and grow them in large numbers in a fermenter.

A useful plasmid has a **replication origin** (so it is copied in the bacterium), one or more **marker genes**, and a single site for each of several restriction enzymes, where the gene can be inserted.

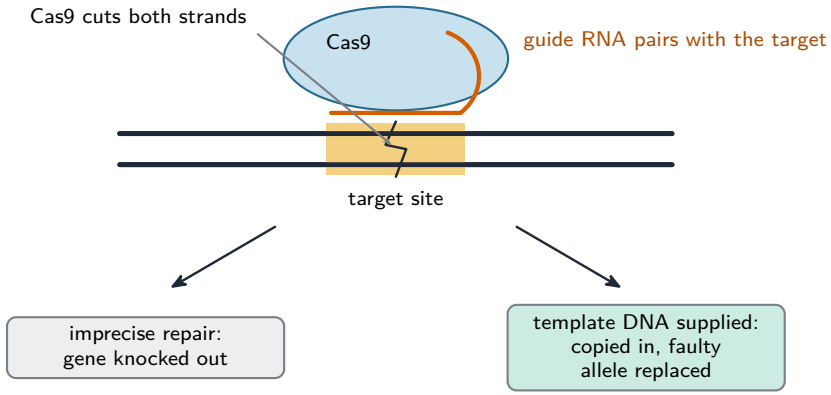
**Marker genes.** In the past, plasmids carried genes for **antibiotic resistance**: bacteria were grown on agar containing the antibiotic, and only those that had taken up a plasmid survived. This method has mostly been replaced, because it could help to spread antibiotic resistance. Today, markers whose product can simply be seen are used: the gene for **green fluorescent protein** (GFP, from a jellyfish), which glows green under ultraviolet light, or the gene for the enzyme **$\beta$-glucuronidase** (GUS), which turns a colourless substrate blue. If the gene to be transferred is inserted next to the marker, cells that show the marker are very likely to contain the gene too.

## Gene editing

**Gene editing** 基因编辑 is a precise form of genetic engineering. It inserts, deletes or replaces DNA at an exact site in the **genome** 基因组.

The best-known method is **CRISPR–Cas9**. A short **guide RNA** is made with a base sequence complementary to the target site in the DNA. The guide RNA is joined

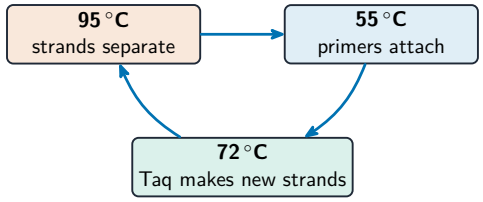
to the enzyme **Cas9**, an endonuclease. The guide RNA pairs with the target sequence, and Cas9 cuts both DNA strands at exactly that point. The cell then repairs the cut: its repair is often imprecise, which knocks the gene out; or, if a piece of DNA with the wanted sequence is supplied, the cell may copy it into the gap, replacing a faulty allele. Because the guide RNA can be designed for almost any sequence, almost any gene in almost any organism can be targeted.




*CRISPR–Cas9: the guide RNA finds the site, Cas9 cuts, the cell's repair does the editing*

## Copying and sorting DNA

- the **polymerase chain reaction** 聚合酶链式反应 (PCR) is used to **clone** 克隆 and **amplify** 扩增 DNA – to make millions of copies. It repeats cycles of heating and cooling, using a heat-stable enzyme called Taq polymerase.




*PCR repeats heat-and-cool cycles; each cycle doubles the DNA, making millions of copies*

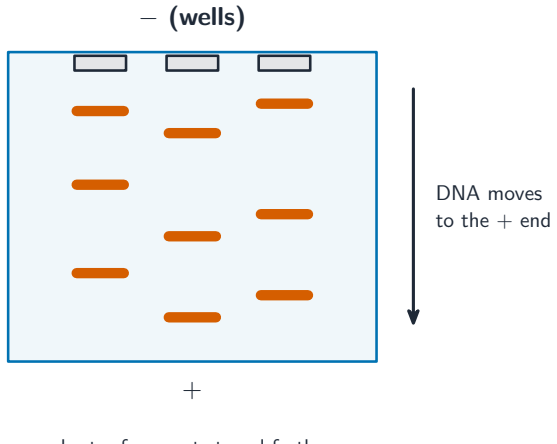
A PCR mixture contains the DNA sample, two kinds of **primer** (short single-stranded DNA, about 20 bases, each complementary to one end of the target sequence), free



**nucleotides**, **Taq polymerase** and a buffer. Taq polymerase comes from *Thermus aquaticus*, a bacterium of hot springs, so it is **not denatured** at 95 °C and need not be added again each cycle; its optimum is about 72 °C. Each cycle takes a few minutes, and the machine (a thermal cycler) changes temperature automatically.

> **Worked example.** Starting with one double-stranded DNA molecule, how many copies are there after 20 cycles? Each cycle doubles the number: $2^{20} = 1\,048\,576$, about a million. After 30 cycles, $2^{30}$ is about $10^9$. So PCR can amplify the DNA in a single hair root or a speck of blood until there is enough to analyse.

- **gel electrophoresis** 凝胶电泳 separates DNA **fragments** 片段 by length. The fragments move through a gel in an electric field, and shorter fragments move further, so the lengths spread out into bands.




*Gel electrophoresis: DNA moves towards the + end, and shorter fragments travel further, sorting them by length*

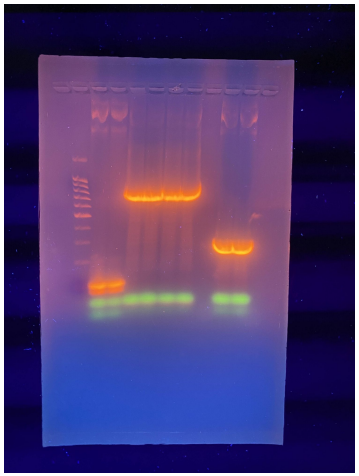
**Method.** Pour **agarose** gel with a comb in it to make **wells** at one end, and cover it with buffer solution. Load the DNA samples into the wells, with a **DNA ladder** (fragments of known lengths) in one well for comparison. Connect the electrodes so that the wells are at the **negative** end, and switch on. DNA is negatively charged because of its **phosphate groups**, so it moves towards the positive electrode; the gel acts as a mesh, so short fragments slip through faster. Switch off before the fastest fragments reach the end. The DNA is invisible, so stain it with a dye that glows under ultraviolet light, or use radioactive or fluorescent probes. The length of each fragment is found by comparing how far it has moved with the bands of the ladder. Proteins can be separated in a similar way, by their charge and size.

**Uses.** In **genetic fingerprinting** (DNA profiling), regions of DNA with short re-



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peated sequences, whose number of repeats varies between people, are amplified by PCR and run on a gel. Each person (except identical twins) has a different pattern of bands; a child has every band from one or other of its parents. This is used to identify suspects from crime-scene samples, to settle questions of who is the father of a child, and to identify species or study how closely related they are.



*A real gel under **UV light**: the left lane is a DNA ladder, and the glowing bands show how the fragments have separated by length*

- **microarrays** 微阵列 are used to study whole **genomes** and to detect which genes are switched on, by picking up their mRNA.

A microarray is a small glass slide carrying thousands of tiny spots, each with many copies of a different single-stranded DNA **probe** (one for each gene). To find which genes are expressed in a tissue, mRNA is extracted and turned into cDNA, which is labelled with a **fluorescent** dye. The cDNA is washed over the slide: it binds (hybridises) only to spots whose probes have a complementary sequence. After washing off unbound cDNA, a scanner measures the fluorescence of each spot; the brighter the spot, the more that gene was being transcribed. Comparing two samples labelled in different colours (for example cancer cells in red and normal cells in green) shows which genes are switched on or off in the disease. Microarrays can also compare the genomes of two species, by using their DNA instead of cDNA.

- **databases** 数据库 store the nucleotide sequences of genes and the **amino acid** 氨基酸 sequences of proteins, so scientists anywhere can compare them.

Storing and analysing this information with computers is called **bioinformatics** 生物信息学. A scientist with a newly sequenced gene can search a database to find similar genes in other species (suggesting what the gene does), and can predict the amino acid sequence of its protein. For example, comparing the genomes of many *Plasmodium* strains has helped in the search for drug targets and vaccines against malaria.



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# Genetic technology in medicine

## Recombinant human proteins

A human gene can be put into bacteria or other cells so that they make a **recombinant** human **protein** – an exact copy of the human one. This is safer and never in short supply, and it avoids using proteins taken from animals or donors. Examples are **insulin** 胰岛素 (for **diabetes** 糖尿病), factor VIII (for haemophilia) and adenosine deaminase (for a faulty immune system).

| Advantage of recombinant protein | Compared with the old source |
|---|---|
| identical to the human protein, so it works better and there are fewer allergic reactions or immune responses | insulin from pigs and cattle differs by one to three amino acids |
| no risk of passing on infections | factor VIII from donated blood once carried HIV and hepatitis viruses |
| can be made in large amounts, all the time, and more cheaply | animal pancreases and donated blood are limited |
| acceptable to people who avoid animal products for religious or ethical reasons | pig and cow insulin |

Proteins that need sugar groups added, or complex folding, are made in yeast or in cultured mammal cells instead of bacteria, because bacteria have no Golgi body or rough ER to modify them.



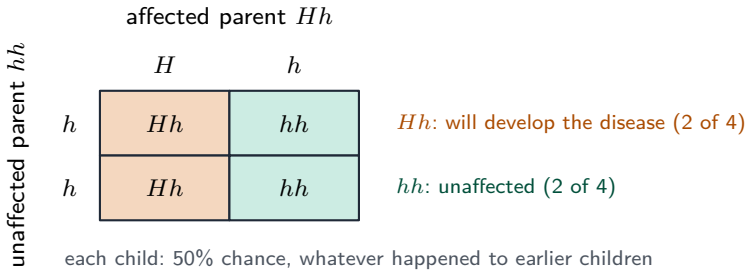

*The same tools make a human protein: the insulin gene goes into bacteria, which become living factories – so the insulin is an exact human copy and never in short supply*

## Genetic screening

**Genetic screening** 基因筛查 tests a person's DNA for disease alleles before symptoms appear. Examples are the BRCA1 and BRCA2 alleles (which raise the risk of **breast cancer** 乳腺癌), **Huntington's disease** 亨廷顿病, and **cystic fibrosis** 囊性纤维化. Knowing the result helps people make informed choices about treatment and family.

For example, a woman who tests positive for a harmful BRCA1 allele has a much higher lifetime risk of breast and ovarian cancer; she can choose more frequent screening,

preventive drugs, or surgery to remove the breasts or ovaries. Embryos produced by IVF can be screened before one is placed in the uterus (**pre-implantation genetic diagnosis**), so a couple who both carry the cystic fibrosis allele can choose an embryo without the disease. But screening for Huntington's disease, which has **no cure**, raises hard questions: a positive result tells a healthy young adult that they will develop the disease, and that each of their children has a 50% chance of inheriting it. Genetic counselling is offered before and after testing.




*Huntington's is dominant: an affected parent passes it to each child with a 50% chance*

## Gene therapy

**Gene therapy** 基因治疗 treats a genetic disease by putting a working copy of a gene into the patient's cells. It has been used for SCID (a disease in which the immune system fails) and for some inherited eye diseases.

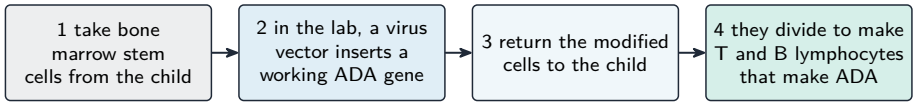
**Vectors.** The new allele must be carried into the cells:

- **viruses**, with their own disease-causing genes removed. **Retroviruses** and **lentiviruses** insert their DNA into the host's chromosomes, so the gene is passed on to every daughter cell, but it may be inserted in the middle of another gene and cause cancer. **Adenoviruses** and **adeno-associated viruses** (AAV) do not insert their DNA, so the effect may wear off and treatment must be repeated; adenoviruses can also cause an immune response.
- **liposomes** – tiny spheres of phospholipid that fuse with the cell surface membrane. They are safer, but less efficient.

**SCID.** Children with SCID lack a working gene for the enzyme **adenosine deaminase** (ADA), so their T and B lymphocytes die and they have almost no immune response. In gene therapy, bone marrow stem cells are taken from the child, a virus is used to insert a working ADA gene into them in the laboratory, and the cells are returned to the child. The stem cells divide to make lymphocytes that can make the enzyme.



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one working copy is enough for a recessive disease, so the faulty allele is left in place

*Gene therapy for SCID: the working ADA gene is added to stem cells outside the body*

The treatment works best for diseases caused by **one recessive allele** – the faulty allele does not need to be removed, because one working copy is enough. It has been much harder for **cystic fibrosis**: the new gene must reach the lining of the lungs, where the mucus is a barrier, and the lining cells are replaced every few weeks.

**Somatic and germ-line therapy.** Changing **body** (somatic) cells affects only the patient. Changing gametes or an early embryo (**germ-line** gene therapy) would also change all the patient's descendants; it is illegal in humans in most countries, because the long-term effects are unknown and the future children cannot consent.

## Social and ethical questions

Genetic screening and gene therapy raise concerns: who should see your genetic results, whether insurers or employers could misuse them, whether changes are safe and permanent, and who decides. These **ethical** 伦理 and social questions must be weighed against the benefits.

# Genetically modified organisms in agriculture

**Genetic engineering** can help feed a growing world by improving farmed animals and crops. Examples of **genetically modified organisms** 转基因生物 (GMOs) are:

- **GM salmon** 鲑鱼 that grow to size faster.
- **soybean** 大豆 made resistant to a **herbicide** 除草剂, so weeds can be sprayed without harming the crop.
- **cotton** 棉花 made resistant to insect **pests** 害虫, because it makes a protein that kills the insects.

**How each is made, and why.**

- **Bt cotton and maize** carry a gene from the soil bacterium *Bacillus thuringiensis* (Bt) for a protein toxin. The toxin kills only certain insect larvae (such as bollworms) that eat the plant; it is harmless to mammals. Farmers spray less insecticide, so fewer harmless insects are killed and costs fall. But pests resistant to the toxin can evolve, and farmers are told to plant some non-GM plants nearby (a "refuge") to slow this.
- **Herbicide-resistant soybean** carries a gene for a form of an enzyme that the herbicide **glyphosate** cannot inhibit. The farmer can spray the whole field once, killing the weeds that compete with the crop for light, water and ions, without

harming the soybean. A risk is that the gene could spread by pollen to wild relatives, or that weeds become resistant to glyphosate.

- **GM salmon** carry a growth-hormone gene from another salmon species, joined to a promoter from another fish that keeps it switched on all year. They reach market size in about half the time. The fish are female and sterile, and are farmed inland in tanks, so that they cannot breed with wild salmon.
- **Golden Rice** carries genes (from maize and a soil bacterium) for the enzymes that make **$\beta$-carotene**, which the body turns into vitamin A, in the rice grain. It is meant to reduce vitamin A deficiency, which causes blindness in many children in countries where rice is the main food.



*Both plants faced the same insects. The insect-resistant GM cotton on the left is barely touched; the ordinary cotton on the right has been stripped – because the GM plant makes a protein that kills the pests as they feed*

GMOs also raise ethical and social questions: whether they are safe to eat, what effect they have on the environment and wild species, whether the engineered genes might spread, and whether a few large companies should control the food supply.



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**Worked example.** A tiny DNA sample from a crime scene must be amplified and then compared with a suspect's. Outline the two techniques and what each achieves. **PCR** copies the DNA in repeated cycles: **denaturation** at about 95 °C separates the strands, **annealing** at about 55 °C lets **primers** 引物 bind at each end of the target, and **extension** at about 72 °C has **Taq polymerase** build the new strands. Each cycle **doubles** the amount, so $n$ cycles give $2^n$ copies - 30 cycles turn one molecule into roughly a billion. **Gel electrophoresis** then separates the fragments: DNA is **negatively charged** because of its phosphate groups, so it moves towards the **anode**, and **shorter fragments travel further** through the gel. Matching band patterns point to the same source. Taq polymerase is used because it is **thermostable** - an ordinary polymerase would denature at 95 °C in the very first cycle.

**Common mistakes.**

- Cutting the gene and the plasmid with different restriction enzymes. Use the **same** restriction enzyme, so both have complementary sticky ends that can pair before ligase seals them.
- Saying DNA ligase cuts DNA, or that restriction enzymes join it. Restriction enzymes **cut**; ligase **joins** the sugar–phosphate backbones.
- Saying larger fragments move further in gel electrophoresis. **Shorter** fragments move further, because they pass through the gel more easily.
- Saying DNA moves to the negative electrode. DNA is **negatively charged** (phosphate groups), so it moves towards the positive electrode (anode).
- Leaving the primers out of a PCR outline. Taq polymerase can only add nucleotides to an existing strand, so a **primer** must bind at each end of the target first.
- Forgetting the promoter. A gene moved into a new organism is not **transcribed** unless a suitable promoter is moved with it.
- Saying gene therapy changes the children of the patient. Gene therapy on **body cells** affects only the patient; the faulty allele can still be passed on in the gametes.

## Exam tips

- Outline the toolkit: **restriction enzymes** (cut at specific sequences, sticky ends), **ligase** (join), **plasmid vectors**, and **PCR** (amplify).
- Explain **gel electrophoresis**: DNA separates by size, smaller fragments travel further – used in genetic fingerprinting.
- Give a balanced **benefit vs concern** for GMOs and gene therapy.
- Explain why cDNA is made from mRNA: it has no introns, which bacteria cannot remove.
- Getting plasmids into bacteria: calcium chloride and heat shock; identify successful cells with a **marker gene** (GFP glows under UV).
- PCR copies: $2^n$ after $n$ cycles; Taq polymerase is not denatured at 95 °C.

- Microarrays: fluorescent cDNA hybridises to complementary probes; brightness shows how much a gene is expressed.
- Gene therapy vectors: viruses (efficient, but may cause cancer or an immune response) and liposomes (safer, less efficient).



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