

Enzymes and metabolism

Revision notes • IB Biology C1.1: enzymes as catalysts, metabolism, active sites and induced fit, factors affecting rate, activation energy and HL enzyme inhibition.

For IB Diploma Biology, Standard Level and Higher Level (first assessment 2025). **HL only** is additional higher level content, for HL students only.

Enzymes and metabolism Spec C1.1

Enzymes as catalysts and their role in metabolism Spec C1.1.1, C1.1.2, C1.1.3

An **enzyme** is a protein that acts as a **biological catalyst**: it increases the rate of a chemical reaction and is not changed or used up by the reaction, so one enzyme molecule can be used again and again.

Without enzymes, most reactions in cells would happen far too slowly at body temperature to keep the organism alive. Raising the temperature enough to speed them up would damage cell structures. Enzymes give fast rates at the moderate temperatures found in cells, and the cell can switch reactions on or off by making, activating or inhibiting particular enzymes.

Metabolism

Metabolism is the complex network of interdependent and interacting chemical reactions occurring in living organisms. The product of one reaction is often the substrate of the next, so reactions are linked into pathways, and pathways share molecules with each other.

Enzymes are **specific**: each one catalyses one reaction or one type of reaction. Living organisms therefore need many different enzymes, often thousands. Because every step depends on its own enzyme, control over metabolism can be exerted through these enzymes, for example by changing how much of an enzyme is made or how active it is.

Anabolic and catabolic reactions

The two types of metabolic reaction		
	Anabolism	Catabolism
What happens	Larger molecules built from smaller ones	Larger molecules broken down into smaller ones
Typical reaction	Condensation: monomers joined, water released	Hydrolysis (water used to split bonds) or oxidation
Energy	Needs an energy input (usually from ATP)	Often releases energy
Examples	Protein synthesis (amino acids joined by peptide bonds); glycogen formation from glucose; photosynthesis (carbon compounds made from CO ₂)	Hydrolysis of macromolecules into monomers in digestion; oxidation of substrates such as glucose in respiration

Anabolism	Reactions that build macromolecules from monomers, for example by condensation.
Catabolism	Reactions that break down macromolecules into monomers, for example by hydrolysis, or oxidise substrates as in respiration.

Common mistake: Photosynthesis is anabolic and respiration is catabolic. Do not describe digestion as anabolic just because it happens before new molecules are built.

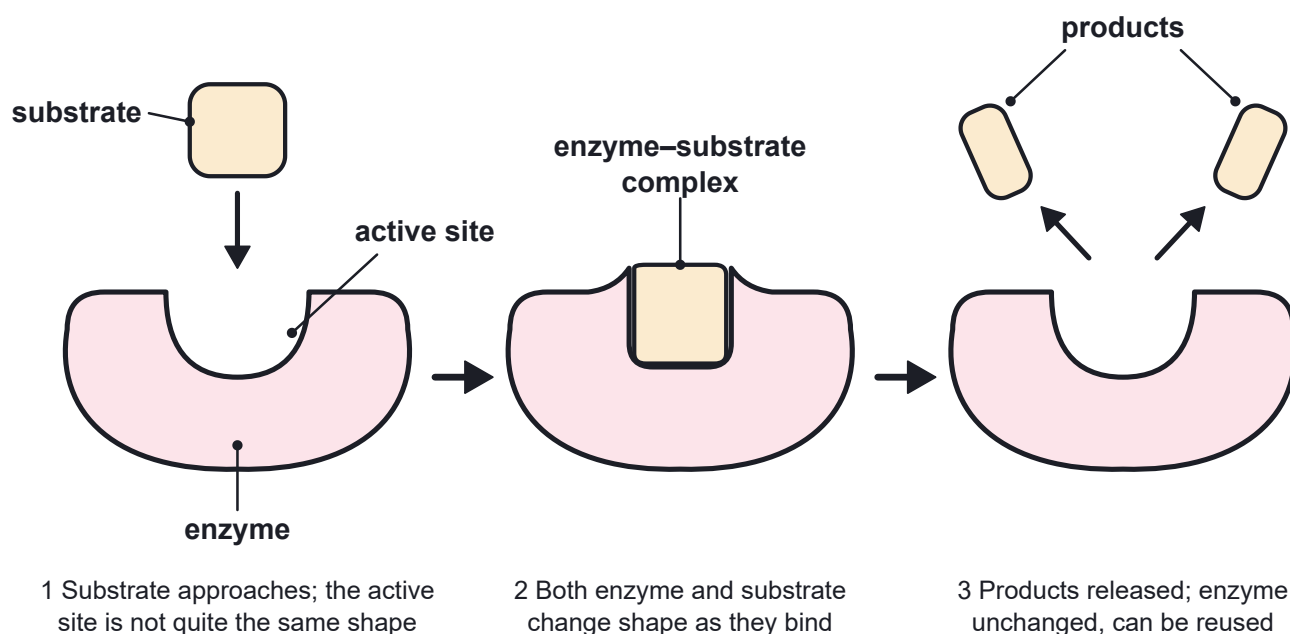
Active sites, induced fit, collisions and denaturation Spec C1.1.4, C1.1.5, C1.1.6, C1.1.7

Enzymes are **globular proteins**. The polypeptide is folded into a compact, roughly spherical shape that is usually soluble in water. Part of the surface forms the **active site**, the region where the substrate binds and the reaction is catalysed.

The active site is made of only a **few amino acids**. Their R groups give it a particular shape and chemical properties (charge, polarity, hydrophobic areas). But these few amino acids are held in exactly the right positions by interactions between amino acids throughout the rest of the protein (hydrogen bonds, ionic bonds, disulfide bonds and hydrophobic interactions). The whole three-dimensional structure is needed for the active site to work.

Induced-fit binding

The substrate binds to the active site by chemical attraction between them. In the **induced-fit** model, both the substrate and the enzyme change shape when binding occurs. The active site moulds more tightly around the substrate, which stresses bonds in the substrate and makes them easier to break or form. The products are then released and the active site returns to its original shape.



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Induced fit: **both the enzyme and the substrate change shape** as the substrate binds to the active site.

Molecular motion and collisions

For a reaction to be catalysed, a substrate molecule and an active site must **collide**, in a suitable orientation. Enzymes and substrates dissolved in water move randomly, and these collisions happen by chance. Sometimes only one of them moves: large substrate molecules (such as starch in a starch grain

or cellulose in a cell wall) may be immobilised while enzymes move to them, and some enzymes are immobilised by being embedded in membranes while their substrates move to them.

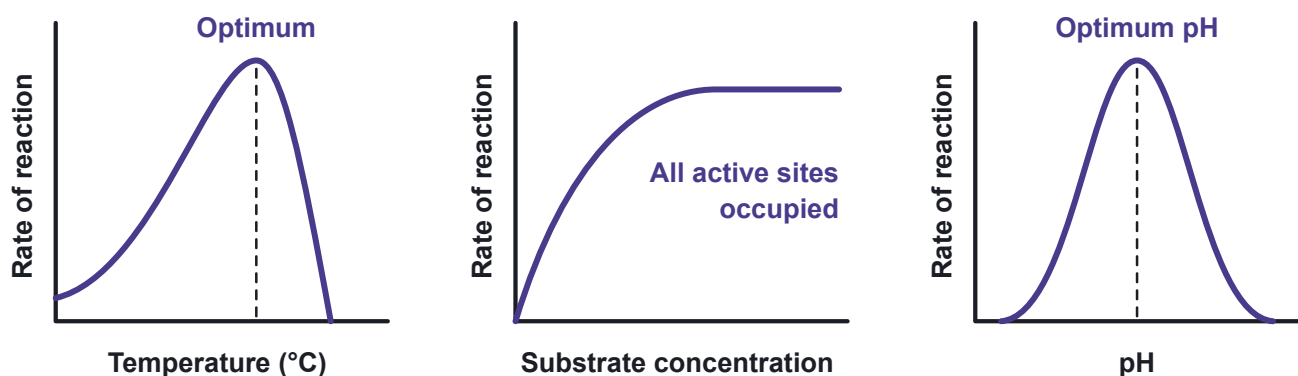
Specificity and denaturation

Enzyme-substrate **specificity** exists because only a substrate with a shape and chemical properties that match the active site can bind to it. Change the structure of the active site and binding fails.

Denaturation is a change to the three-dimensional structure of the protein, caused by high temperature or extreme pH. Bonds holding the tertiary structure break, so the active site changes shape and its chemical properties change. The substrate can no longer bind, so the enzyme cannot catalyse the reaction. Denaturation is usually permanent.

Exam tip: When explaining denaturation, link the chain: bonds in the tertiary structure break, the active site changes shape, the substrate no longer fits or binds, so no enzyme-substrate complexes form.

Effects of temperature, pH and substrate concentration Spec C1.1.8, C1.1.9



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Generalised sketch graphs for the effects of temperature, substrate concentration and pH on the rate of an enzyme-catalysed reaction.

Temperature

As temperature rises, enzyme and substrate molecules have more kinetic energy and move faster. Collisions between substrate and active site become more frequent and more of them have enough energy to react, so the rate increases. Above the **optimum temperature**, the extra vibration breaks bonds holding the enzyme's structure; more and more enzyme molecules denature, so the rate falls steeply. The curve is not symmetrical: the fall is much steeper than the rise.

pH

Each enzyme has an **optimum pH**. A change in pH alters the concentration of hydrogen ions, which changes the charges on R groups in the active site and elsewhere. Ionic and hydrogen bonds are disrupted, so the substrate binds less well and the rate falls on either side of the optimum. Far from the optimum the enzyme is denatured. For example, pepsin in the stomach works best in acid conditions, while many enzymes in the small intestine work best near neutral pH.

Substrate concentration

At low substrate concentrations, raising the concentration increases the frequency of substrate-active site collisions, so the rate rises steeply. As the concentration increases further, more active sites are occupied at any moment, so the rise slows. Eventually **all active sites are occupied** nearly all the time and the rate levels off at a maximum. Enzyme concentration is then the limiting factor.

Exam tip: Sketch graphs like these are models. They can be evaluated by comparing them with real results from enzyme experiments. When describing a graph, give the trend, the optimum or the plateau, and quote values with units.

Measurements in enzyme-catalysed reactions

The rate of an enzyme-catalysed reaction is measured as the amount of **product formed** or **substrate used** per unit time. Common methods include measuring the volume of oxygen released when catalase breaks down hydrogen peroxide (gas syringe or displacement of water), and timing how long starch takes to disappear when amylase acts on it (samples tested with iodine). Rates can also be found from secondary data.

- Mean rate = change in amount $\div$ time taken.
- Initial rate: draw a tangent to the curve at time zero and find its gradient. This is the fairest comparison because the substrate concentration has not yet fallen.
- If only a time is measured (for example, time for starch to disappear), rate can be expressed as $1 \div$ time.

Calculating rates from enzyme data

Catalase was added to hydrogen peroxide. 18 cm³ of oxygen was collected in the first 30 s and 30 cm³ by 90 s. Calculate the mean rate over the first 30 s and over the whole 90 s.

1. First 30 s: rate = $18 \text{ cm}^3 \div 30 \text{ s} = 0.60 \text{ cm}^3 \text{ s}^{-1}$.
2. Whole 90 s: rate = $30 \text{ cm}^3 \div 90 \text{ s} = 0.33 \text{ cm}^3 \text{ s}^{-1}$.
3. The rate falls over time because substrate is used up, so there are fewer collisions with active sites.

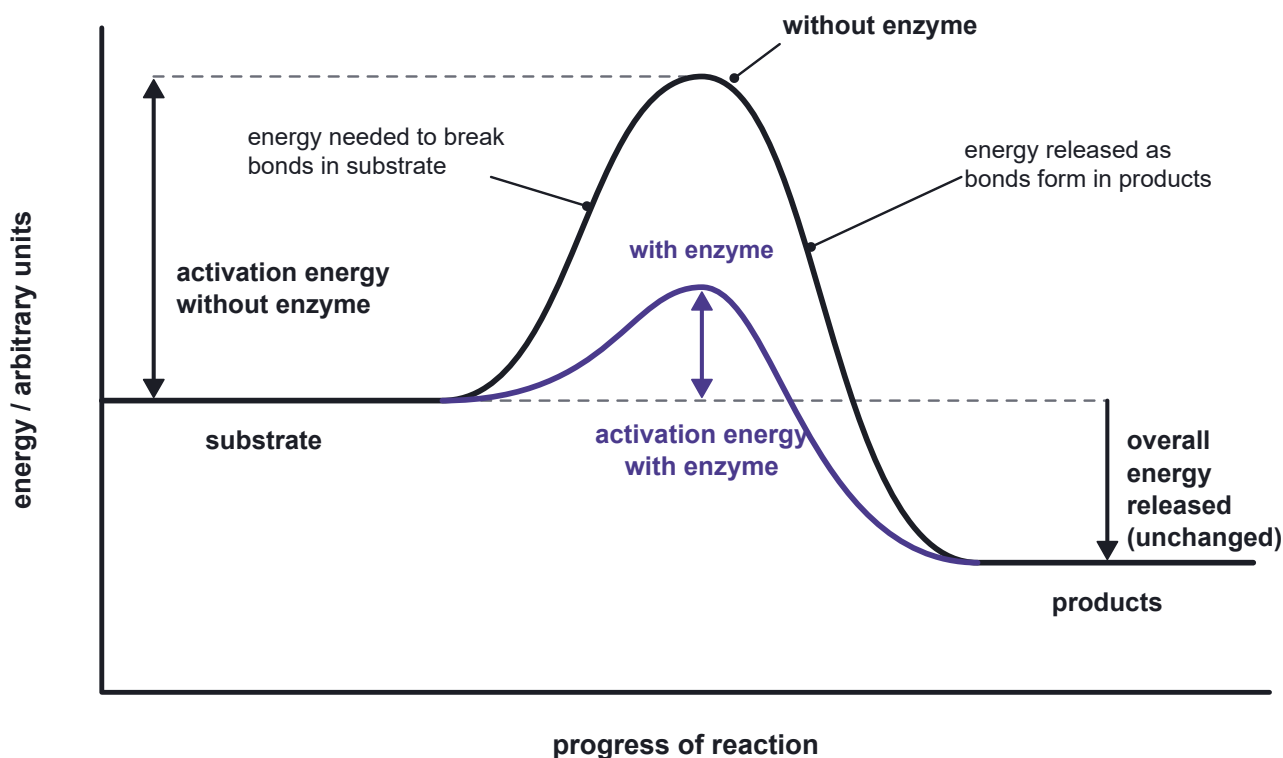
Answer: $0.60 \text{ cm}^3 \text{ s}^{-1}$ over the first 30 s; $0.33 \text{ cm}^3 \text{ s}^{-1}$ over 90 s.

Practical skill: Control temperature with a thermostatically controlled water bath, pH with buffer solutions, and keep enzyme concentration and volumes constant. Repeat each condition at least three times and calculate a mean.

Effect of enzymes on activation energy Spec C1.1.10

Before a reaction can happen, bonds within the substrate must be broken or weakened. This needs an input of energy called the **activation energy**. When new bonds form to make the products, energy is released (the energy yield). In many metabolic reactions the products have less energy than the substrates, so there is an overall release of energy.

Enzymes **lower the activation energy**. Binding to the active site stresses and weakens bonds in the substrate, so less energy is needed to reach the transition state. A larger proportion of substrate molecules then have enough energy to react, and the reaction is faster at the same temperature. The enzyme does **not** change the energy of the substrates or the products, so the overall energy change is unchanged.



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Enzymes **lower the activation energy**, measured from the substrate level to the peak; the overall energy change is unchanged.

Exam tip: On an energy graph, the activation energy is measured from the substrate level to the peak, not from the products or from zero.

Exam tip: Linking question: enzymes are a clear structure–function relationship in a macromolecule. The folded polypeptide creates an active site that lowers activation energy for one specific reaction.

Intracellular and extracellular reactions, heat and metabolic pathways

Spec C1.1.11, C1.1.12, C1.1.13

HL only

Intracellular and extracellular enzymes

Where enzyme-catalysed reactions happen		
	Intracellular	Extracellular
Where the enzyme acts	Inside the cell that made it	Outside the cell that made it, after secretion by exocytosis
Examples	Glycolysis (cytoplasm); Krebs cycle (mitochondrial matrix)	Chemical digestion in the gut lumen, e.g. amylase, proteases and lipase
Why	Products are used within the cell	Food macromolecules are too large to enter cells, so they must be hydrolysed first

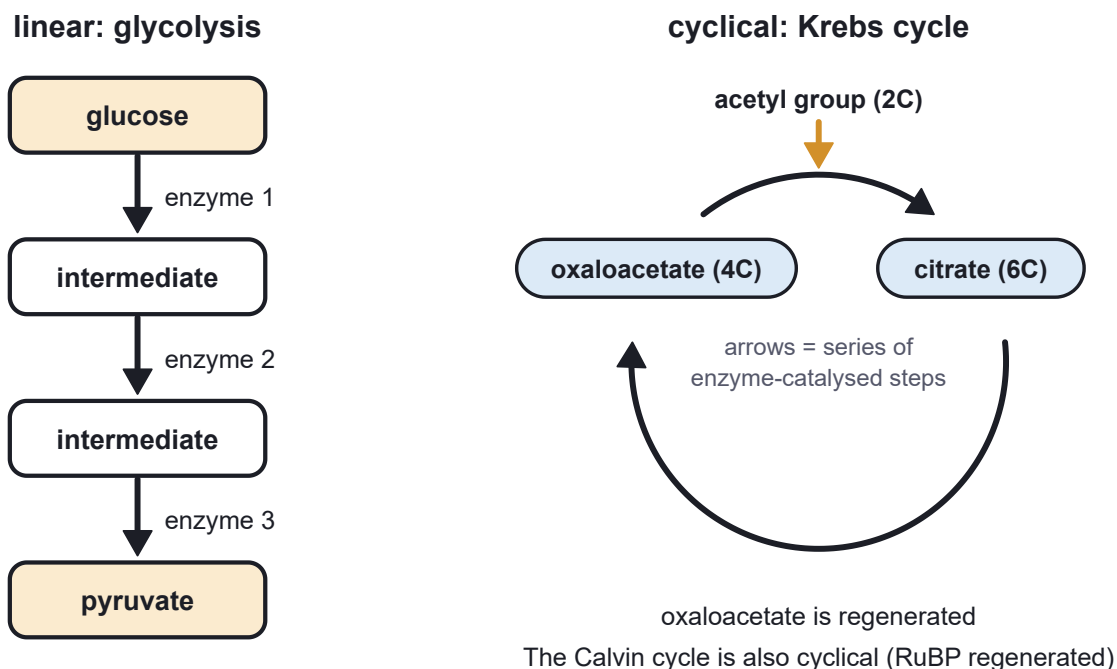
Heat from metabolism

No metabolic reaction is 100% efficient in energy transfer. Some energy is always transferred to the surroundings as **heat**, so heat generation is inevitable. Mammals and birds (and some other animals, such as some large fish and insects) depend on this heat to maintain a constant body temperature. They can increase heat output by increasing the rate of metabolic reactions, for example by shivering.

Linear and cyclical pathways

In a **linear** pathway, the substrate is converted through a chain of intermediates to an end product, each step catalysed by a different enzyme. **Glycolysis** is linear: glucose is converted step by step to pyruvate.

In a **cyclical** pathway, the last step regenerates the molecule that started the cycle, so intermediates are not used up. In the **Krebs cycle** an acetyl group joins oxaloacetate and oxaloacetate is regenerated. In the **Calvin cycle** CO_2 is fixed by RuBP and RuBP is regenerated.



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Linear pathways end in a product; in a **cyclical** pathway the starting molecule is **regenerated**.

Exam tip: To classify a pathway, ask whether the starting molecule is regenerated. If it is, the pathway is cyclical; if the substrate is used up to form an end product, it is linear.

Non-competitive and competitive inhibition Spec C1.1.14, C1.1.15 HL only

Allosteric sites and non-competitive inhibition

An **allosteric site** is a binding site on an enzyme other than the active site. Only specific substances can bind to it. When an inhibitor binds there, it causes interactions within the enzyme that lead to a **conformational change**: the shape of the protein changes, altering the active site enough to prevent catalysis. The substrate may still bind, but the reaction does not happen. Binding is reversible.

This is **non-competitive inhibition**: the inhibitor does not compete with the substrate for the active site. Adding more substrate does not remove the inhibitor, so the maximum rate is lowered at every substrate concentration.

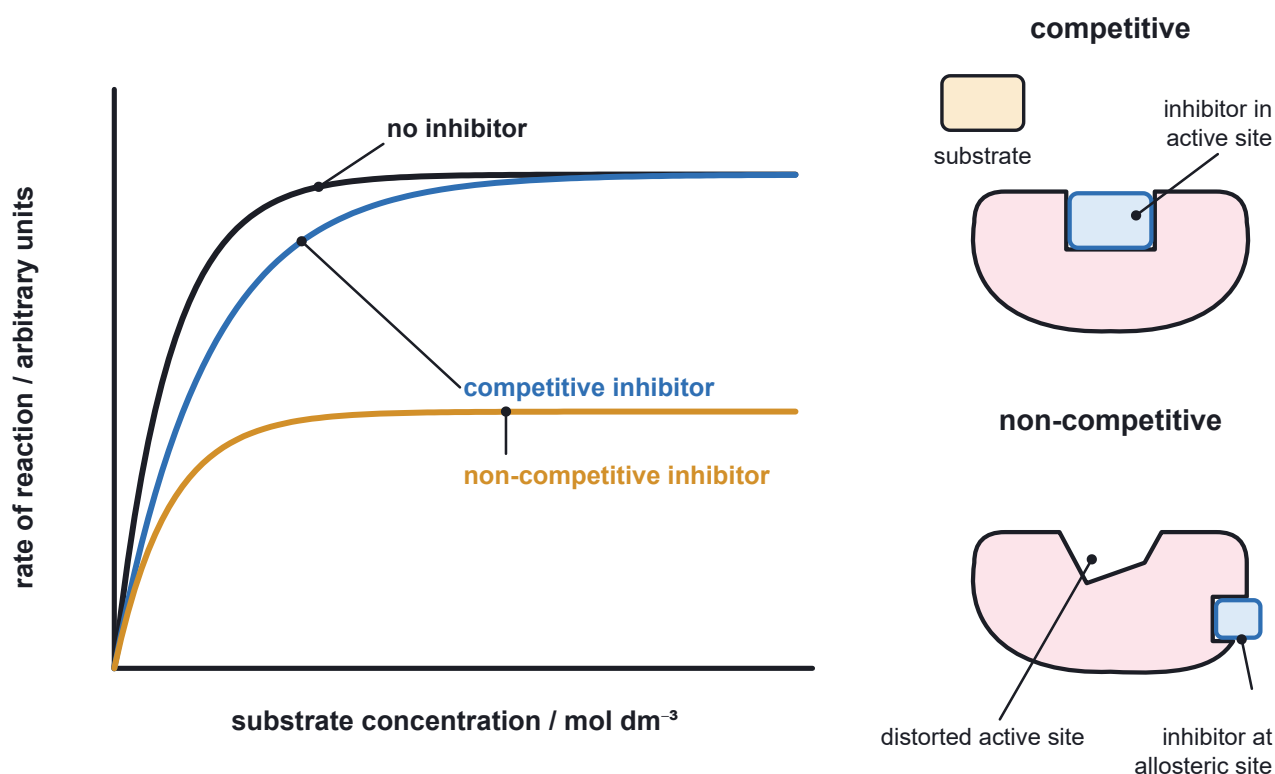
Competitive inhibition

A **competitive inhibitor** has a shape and chemistry similar to the substrate. It binds reversibly to the active site, blocking it, but is not converted into products. Substrate and inhibitor compete for the same site, so the proportion of active sites occupied by substrate depends on their relative concentrations. At high substrate concentrations the substrate wins most collisions, so the rate approaches the same maximum as without inhibitor.

Statins are competitive inhibitors used as drugs to lower blood cholesterol. They inhibit an enzyme in the liver (HMG-CoA reductase) that catalyses a step in the pathway that synthesises cholesterol.

Comparing the two types of reversible inhibition

	Competitive	Non-competitive
Where the inhibitor binds	Active site	Allosteric site
Shape of inhibitor	Similar to the substrate	Not similar to the substrate
Interaction with substrate	Inhibitor and substrate compete for the active site	No competition; both can bind at once
Effect of raising substrate concentration	Overcomes inhibition; maximum rate eventually reached	Does not overcome inhibition; maximum rate lowered
Example	Statins	End-product inhibitors acting at allosteric sites



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At high substrate concentration a **competitive** inhibitor is outcompeted; a **non-competitive** inhibitor lowers the maximum rate.

Exam tip: To tell the types apart from a graph, look at high substrate concentrations: if the inhibited curve reaches the uninhibited maximum, the inhibitor is competitive.

Feedback inhibition and mechanism-based inhibition Spec C1.1.16, C1.1.17 HL only

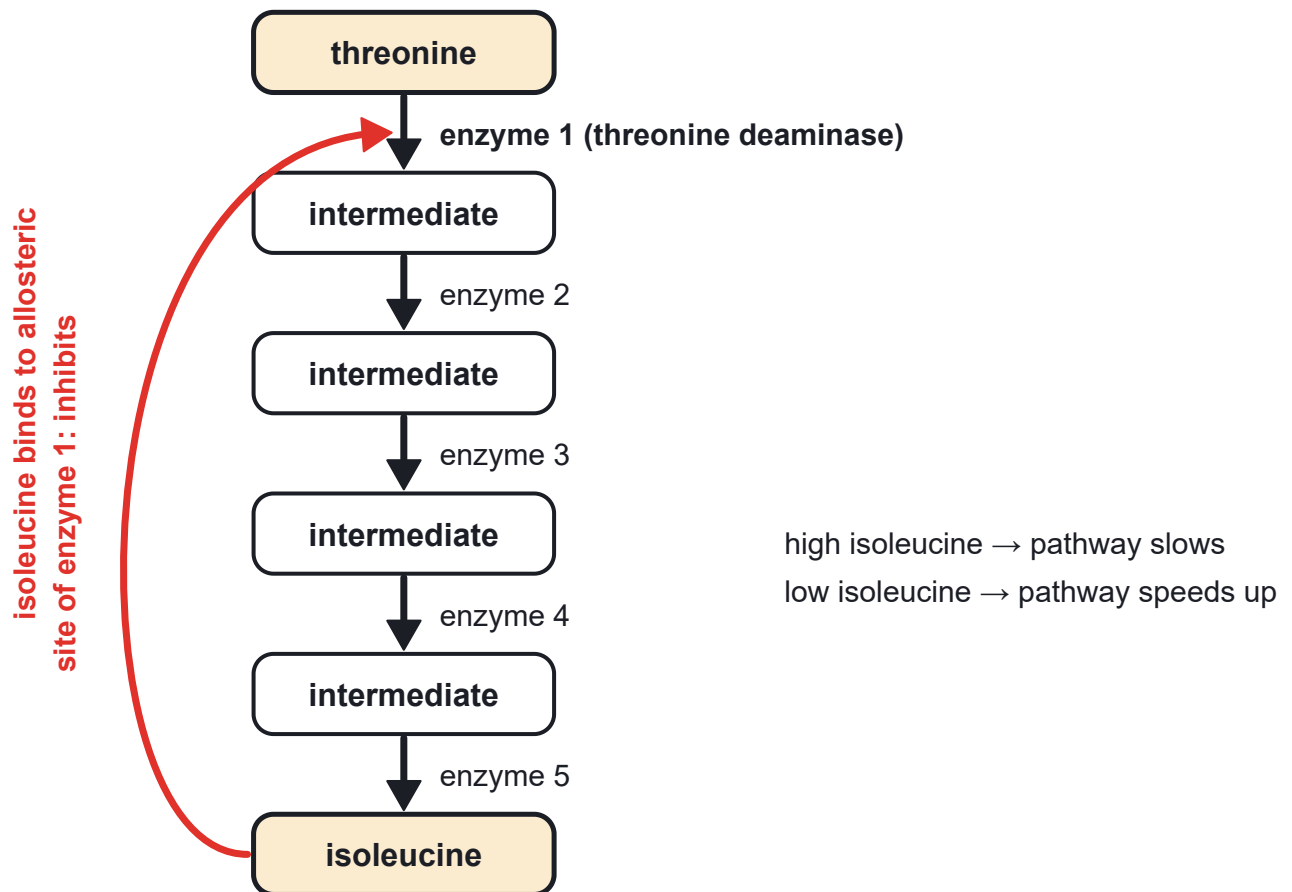
Feedback inhibition

In **feedback inhibition** the end product of a metabolic pathway inhibits an enzyme that catalyses an early step, usually the first. The end product binds to an allosteric site, so this is a form of non-competitive inhibition, and binding is reversible.

The pathway that produces the amino acid **isoleucine** from threonine has five steps, each catalysed by a different enzyme. Isoleucine binds to the allosteric site of the first enzyme, threonine deaminase (also called threonine dehydratase).

1. When isoleucine concentration is high, more isoleucine molecules bind to threonine deaminase.
2. The enzyme is inhibited, so the whole pathway slows and less isoleucine is made.
3. As isoleucine is used up (for example in protein synthesis), its concentration falls and it leaves the allosteric sites.
4. The enzyme becomes active again and production increases.

The concentration of the end product is therefore kept within a narrow range, and threonine and energy are not wasted making isoleucine that is not needed.



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Feedback inhibition: isoleucine binds to the **allosteric site of threonine deaminase**, so production slows when isoleucine is high.

Mechanism-based inhibition

In **mechanism-based inhibition** an inhibitor binds irreversibly to the active site and causes a chemical change to it, so the enzyme is permanently inactivated. Raising the substrate concentration has no effect.

Penicillin inhibits **transpeptidases**, bacterial enzymes that form the cross-links between peptidoglycan chains in the cell wall. Penicillin enters the active site and forms a permanent covalent bond with an amino acid there. Without cross-links, the walls of growing bacteria are weak and the cells burst due to osmotic pressure.

Some bacteria are **resistant to penicillin** because they have a changed transpeptidase. Its active site has a different structure, so penicillin binds poorly or not at all, but the enzyme can still make cross-links. The gene for the altered transpeptidase can spread through a population by natural selection when penicillin is used.

Common mistake: Mechanism-based inhibition is not competitive inhibition. Competitive inhibitors bind reversibly; penicillin binds irreversibly and changes the active site chemically.

Quick check

1. What is metabolism?
2. Give one example of an anabolic and one of a catabolic reaction.
3. In the induced-fit model, what changes shape when the substrate binds?
4. What happens to the activation energy and the overall energy change when an enzyme catalyses a reaction?
5. **HL only** Which enzyme does isoleucine inhibit in feedback inhibition?

Quick check answers

Enzymes and metabolism

1. The complex network of interdependent and interacting chemical reactions occurring in living organisms.
2. Anabolic: protein synthesis, glycogen formation or photosynthesis. Catabolic: hydrolysis in digestion or oxidation of glucose in respiration.
3. Both the substrate and the enzyme's active site.
4. The activation energy is lowered; the overall energy change is unchanged.
5. Threonine deaminase, the first enzyme of the pathway, at its allosteric site.