MEGA LECTURE

IB DP BIOLOGY

Theme C: Interaction and Interdependence

C1.1 Enzymes and Metabolism

Revision Notes · Standard and Higher Level

Fahad H. Ahmad

+92 323 509 4443 | Megalecture.com

Original notes prepared for the IB Diploma Programme Biology course (first assessment 2025)

What the syllabus requires

By the end of C1.1 you should be able to work confidently with each of the understandings below. Use this checklist for a final revision sweep. Items marked **(HL)** are examined only at Higher Level; everything else is common to SL and HL.

Understanding	You should be able to...
Enzymes as catalysts	Explain that enzymes are globular proteins that speed up reactions by lowering activation energy without being consumed.
Active site and specificity	Describe the enzyme-substrate complex and account for specificity using the lock-and-key and induced-fit models.
Factors affecting activity	Interpret and explain graphs of rate against temperature, pH, substrate concentration and enzyme concentration.
Denaturation	Relate the loss of tertiary structure to a change in active-site shape and loss of catalytic function.
Immobilised enzymes	Outline the advantages and give a named application such as lactase.
Metabolism	Distinguish anabolic (condensation) from catabolic (hydrolysis) reactions and describe metabolic pathways.
Enzyme inhibition (HL)	Compare competitive and non-competitive inhibition and explain end-product (feedback) inhibition.
Cofactors and Km (HL)	Describe the role of cofactors and coenzymes and interpret V_{max} and K_m.

> **Exam note:** SL and HL share the core of C1.1. HL candidates additionally study inhibition, feedback control, cofactors, and the Michaelis-Menten description of enzyme kinetics. HL-only material is flagged (HL) throughout.

1. Enzymes as biological catalysts

A **catalyst** is a substance that increases the rate of a chemical reaction without itself being permanently changed or used up. **Enzymes** are biological catalysts: they are almost all **globular proteins**, folded into a precise three-dimensional shape. Because an enzyme is not consumed, a single molecule can catalyse the same reaction thousands of times per second before it is eventually recycled or broken down.

Why reactions need help: activation energy

Even reactions that release energy overall do not happen spontaneously at a useful rate, because reactants must first pass through an unstable, high-energy **transition state**. The minimum energy the reactants must gain to reach this state is the **activation energy** (E_a). At body temperature few molecules possess this much energy, so the uncatalysed rate is very slow.

Enzymes work by providing an alternative reaction route with a **lower activation energy**. More of the reactant molecules now have enough energy to react on collision, so the rate rises dramatically — often by a factor of a million or more.

The energy profile

Picture a graph of potential energy (y-axis) against the progress of the reaction (x-axis). Reactants start at a certain energy on the left and products end at a lower energy on the right (for an energy-releasing reaction). Between them the curve rises to a peak — the transition state. The height of that peak above the reactants is the activation energy. Adding an enzyme **lowers the peak**: a second, lower curve reaches the same products. Crucially, the enzyme changes only the height of the barrier; the starting and finishing energy levels — and therefore the overall energy change (ΔG) — are unchanged.

> **Common misconception:** Enzymes lower the activation energy; they do **not** change the overall energy released or absorbed by a reaction (ΔG), and they do not make an energetically unfavourable reaction become favourable. They only make a possible reaction go faster.

2. The active site and the enzyme-substrate complex

The molecule an enzyme acts on is its **substrate**. Catalysis takes place in a small pocket or cleft on the enzyme surface called the **active site**, which is formed by only a few of the amino acids in the folded protein. The precise shape and chemistry of the active site are determined by the enzyme's tertiary structure.

The catalytic cycle

- The substrate collides with, and binds to, the active site, forming an **enzyme-substrate complex**. The fit is highly specific.
- Within the complex the substrate is held in the ideal orientation and its bonds are strained or brought close to reactive groups, lowering the activation energy of the reaction.
- The reaction proceeds, briefly giving an **enzyme-product complex** in which the newly formed product(s) still occupy the active site.
- The product no longer fits the active site as well as the substrate did, so it is released. The enzyme is unchanged and free to bind another substrate molecule.

This whole sequence can be summarised as:

$$\mathbf{E + S \rightarrow ES \rightarrow EP \rightarrow E + P}$$

where E = enzyme, S = substrate, ES = enzyme-substrate complex, EP = enzyme-product complex and P = product. The enzyme (E) appears unchanged on both sides, confirming it is not used up.

> **Key term:** The formation of the **enzyme-substrate complex** is the central event of catalysis. Whenever you are asked how an enzyme works, naming this complex and linking it to lowering activation energy earns marks.

3. Specificity: lock-and-key and induced-fit

Each enzyme catalyses only one reaction or one narrow group of reactions. This **specificity** arises because the substrate must be **complementary in shape and chemistry** to the active site: only a molecule that fits can bind and react. Two models describe how this fit is achieved.

Lock-and-key model

The earliest model treats the active site as a rigid shape, like a lock, into which only one substrate — the matching key — fits exactly. It explains specificity simply, but it cannot account for the fact that many enzymes bind several related substrates, nor for the small shape changes seen when a substrate binds.

Induced-fit model

The modern model recognises that the active site is **flexible**. The substrate is only approximately complementary at first; as it binds, it **induces a change in the shape** of the active site so that the enzyme moulds more closely around it. This tighter grip strains the substrate's bonds and further lowers the activation energy. Induced fit explains catalysis better and accounts for the conformational changes that are actually observed.

Feature	Lock-and-key	Induced-fit
Active site	Rigid, fixed shape	Flexible, changes shape
Fit with substrate	Exact from the start	Becomes complementary as substrate binds
Explains specificity?	Yes	Yes
Explains shape change on binding?	No	Yes
Status	Simplified, older idea	Currently accepted model

> **Exam technique:** If asked to compare the models, give at least one similarity (both explain specificity through a complementary active site) and one clear difference (rigid versus flexible active site).

4. Factors affecting enzyme activity

The **rate** of an enzyme-controlled reaction is measured as the amount of substrate used, or product formed, per unit time. Four factors are examined; for each you should be able to sketch the graph and give the mechanism behind its shape.

(a) Temperature

Graph: rate rises with temperature to a peak at the **optimum** (around 37 °C for many human enzymes), then falls steeply to zero at higher temperatures — an asymmetric, skewed peak.

- **Rising part:** heating gives molecules more kinetic energy, so enzyme and substrate move faster and collide more often, and more collisions have enough energy to react. The frequency of successful collisions rises, so the rate rises.
- **Falling part:** above the optimum the extra vibration breaks the weak bonds (hydrogen bonds, ionic interactions) holding the tertiary structure together. The active site changes shape, the substrate no longer fits, and the enzyme is **denatured**. The fall is steep because denaturation is largely irreversible.

(b) pH

Graph: a bell-shaped curve, with maximum rate at the **optimum pH** and rate falling away on either side. Different enzymes have different optima — pepsin in the stomach works best near pH 2, while intestinal enzymes prefer around pH 8.

• At the optimum pH the charges on the amino acid side chains give the active site its correct shape and the correct charge to bind the substrate.

• Moving away from the optimum, excess H^+ or OH^- ions disrupt hydrogen bonds and ionic bonds and alter the charges on side chains. The active site changes shape and the enzyme is denatured, so the rate falls. Large pH changes cause permanent denaturation.

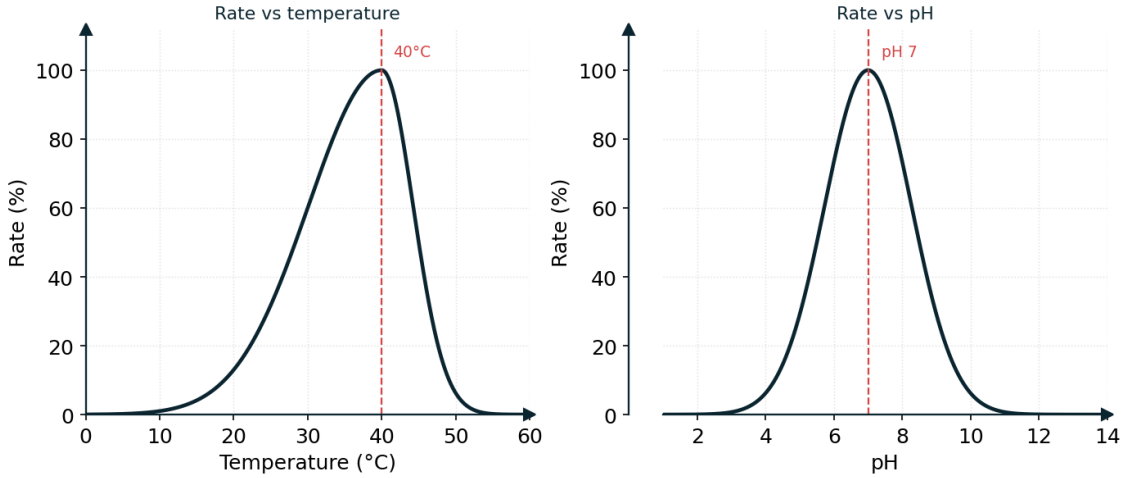

Figure 1. Computed rate against temperature (left) and against pH (right), each from an asymmetric/bell-shaped model. Audit: the curve peaks at 40°C (set optimum 40°C) and at pH 7.0 (set optimum pH 7), matching the values in the worked examples below.

(c) Substrate concentration

Graph: at low substrate concentration the rate rises steeply and almost linearly; as concentration increases the curve bends over and finally levels off at a **plateau** (the maximum rate, V_{max}).

• **Rising part:** when substrate is scarce, many active sites are empty. Adding substrate increases the frequency of enzyme-substrate collisions, so more complexes form per second and the rate rises.

• **Plateau:** at high substrate concentration virtually every active site is occupied at any instant — the enzyme is **saturated**. Adding more substrate cannot increase the rate because the enzymes are already working as fast as they can. Rate is now limited by enzyme concentration (or turnover rate), not by substrate.

(d) Enzyme concentration

Graph: provided substrate is in excess, rate is **directly proportional** to enzyme concentration — a straight line through the origin.

• More enzyme molecules means more active sites available, so more enzyme-substrate complexes form per second and the rate rises in proportion.

• The line only stays straight while substrate is plentiful. If substrate runs short, it becomes the limiting factor and the graph levels off despite more enzyme being present.

> **Limiting factors:** The rate is set by whichever factor is in shortest supply. Always state the factor you are varying and assume the others are held constant and non-limiting unless told otherwise.

5. Denaturation

Denaturation is a change in the three-dimensional shape of a protein caused by the breaking of the weak bonds — hydrogen bonds, ionic bonds and hydrophobic interactions — that maintain its **tertiary structure**. The sequence of amino acids (primary structure) is not broken; only the folding is lost.

For an enzyme the consequence is decisive: because the shape of the active site depends on the tertiary structure, denaturation **alters the active site**. The substrate can no longer bind, no enzyme-substrate complex forms, and the enzyme loses its catalytic function. High temperature and extremes of pH are the common causes; heavy-metal ions and some chemicals also denature enzymes.

> **Common misconception:** A denatured enzyme is not "killed" — enzymes are molecules, not living things, so they cannot die. Say the enzyme is **denatured** and has **lost its function** because its active site has changed shape. Also note denaturation is usually permanent, not a temporary slowing down.

6. Immobilised enzymes

An **immobilised enzyme** is one that is fixed or trapped onto an inert support — for example bound to beads, held in a gel capsule, or attached to a membrane — rather than being free in solution. Immobilised enzymes are widely used in industry and biotechnology.

Advantages

- The enzyme can be **recovered and reused**, which lowers cost, because it is not lost with the product.
- The **product is not contaminated** with enzyme, so less downstream purification is needed.
- Immobilised enzymes are generally **more stable** to changes in temperature and pH, because the support holds their shape.
- They allow **continuous flow** processing: substrate solution is passed over a column of immobilised enzyme and product flows out.

Example: lactase

Lactase immobilised on beads is used to produce **lactose-free milk**. Milk is passed through a column packed with lactase-coated beads; the enzyme hydrolyses lactose into glucose and galactose, which people with lactose intolerance can digest. Because the lactase stays on the beads, it never enters the milk and can be used continuously. Other examples include immobilised glucose isomerase (making fructose syrup) and enzymes in biosensors such as glucose test strips.

7. Metabolism

Metabolism is the sum of all the enzyme-controlled chemical reactions that occur within an organism (or a cell). These reactions do not happen in isolation: they are organised into **metabolic pathways** — ordered sequences in which the product of one enzyme-catalysed step becomes the substrate of the next.

Anabolism and catabolism

	Anabolic reactions	Catabolic reactions
What happens	Small molecules are built into larger ones	Large molecules are broken into smaller ones
Typical reaction	Condensation (removes water, forms bonds)	Hydrolysis (adds water, breaks bonds)

	Anabolic reactions	Catabolic reactions
Energy	Require energy (ATP is used)	Release energy
Example	Amino acids → protein; glucose → glycogen	Starch → glucose; respiration of glucose

Pathways: chains and cycles

A metabolic pathway may be a **chain**, in which a starting substrate is converted step by step into a final product (for example glycolysis converts glucose to pyruvate through a linear series of steps). Others are **cycles**, in which the starting molecule is regenerated each turn while intermediates are processed (for example the Krebs cycle). Every step is controlled by its own specific enzyme, so the cell can regulate the whole pathway precisely by controlling individual enzymes.

> **Why pathways matter:** Breaking a large reaction into small enzyme-catalysed steps lets the cell release or invest energy in manageable amounts and control each step independently — the basis of feedback inhibition (HL) below.

8. Enzyme inhibition (HL)

Inhibitors are molecules that reduce or stop enzyme activity. They are central to how cells regulate metabolism, and many drugs and poisons are enzyme inhibitors. Two main reversible types are compared here.

Competitive inhibition

A **competitive inhibitor** has a shape similar to the substrate, so it binds to the **active site** itself. While the inhibitor is bound, the substrate cannot enter, so no product forms at that enzyme. Inhibitor and substrate **compete** for the active site.

- The effect can be **overcome by increasing the substrate concentration**: with more substrate molecules present, they out-compete the inhibitor and are increasingly likely to reach the active site first.
- On a rate-against-substrate-concentration graph, the inhibited curve rises more slowly but eventually reaches the **same V_{max}** as the uninhibited enzyme (just at a higher substrate concentration).

Non-competitive (allosteric) inhibition

A **non-competitive inhibitor** binds to a site **other than the active site**, called an **allosteric site**. Its binding changes the enzyme's overall shape, which in turn **alters the shape of the active site** so the substrate can no longer bind (or cannot react effectively).

- The effect **cannot be overcome by adding more substrate**, because the inhibitor is not competing for the active site — the substrate simply cannot use the distorted active site.
- On the graph, the inhibited curve levels off at a **lower V_{max}** than the uninhibited enzyme, no matter how much substrate is added.

Feature	Competitive	Non-competitive
Binding site	Active site	Allosteric site (elsewhere)
Resembles substrate?	Yes	No

Feature	Competitive	Non-competitive
Effect on active site	Blocks it directly	Changes its shape indirectly
Overcome by more substrate?	Yes	No
Effect on V_{max}	Unchanged (reached later)	Reduced

Distinguishing the two from data: Give the enzyme lots of substrate. If the rate recovers to the normal maximum, the inhibitor is competitive; if the maximum stays depressed, it is non-competitive.

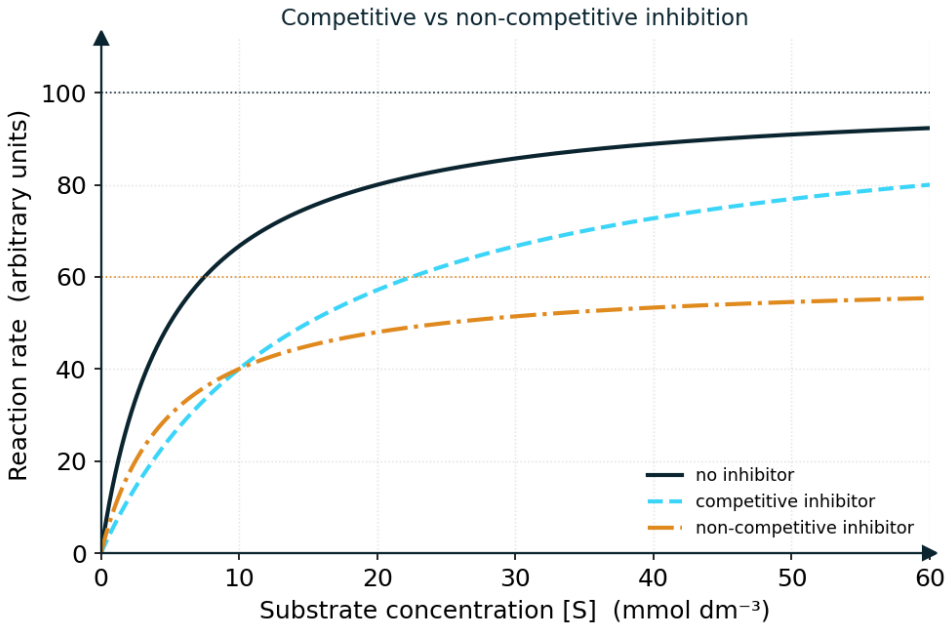

Figure 2. Michaelis-Menten curves with no inhibitor, a competitive inhibitor (apparent K_m raised to 15, V_{max} unchanged) and a non-competitive inhibitor (V_{max} reduced to 60, K_m unchanged). Audit-computed plateau rates at high [S] confirm this pattern.

End-product (feedback) inhibition

Cells regulate metabolic pathways using **end-product inhibition**, a form of negative feedback. The **final product** of a pathway acts as an **allosteric (non-competitive) inhibitor of an enzyme early in the same pathway** — usually the first, committed step.

- When the end product accumulates, it binds the early enzyme and switches the pathway off, preventing wasteful over-production.
- As the end product is used up, it detaches, the early enzyme becomes active again, and the pathway resumes. This keeps the product at a steady level.

A classic example is the amino acid isoleucine inhibiting the first enzyme of its own synthesis pathway.

Cofactors and coenzymes

Many enzymes need a non-protein helper molecule to function:

- **Cofactors** are non-protein components required for activity. Some are inorganic ions (for example Zn^{2+}, Mg^{2+}, Fe^{2+}).

- **Coenzymes** are organic (carbon-based) cofactors that bind temporarily and often carry chemical groups or electrons between reactions. Many are derived from **vitamins** — for example NAD^+ (from niacin) and FAD (from riboflavin) carry hydrogen/electrons in respiration.
- A tightly and permanently bound cofactor is called a **prosthetic group** (for example the haem group in some enzymes).

9. Michaelis-Menten kinetics (HL)

The rise-then-plateau shape of the rate-against-substrate-concentration curve is described quantitatively by the **Michaelis-Menten model**. Two constants summarise the curve.

- **V_{max}** is the maximum rate, reached when the enzyme is fully saturated with substrate. It depends on the amount of enzyme and how fast each enzyme turns substrate into product.
- **K_m** (the Michaelis constant) is the substrate concentration at which the reaction runs at **half of V_{max}**. It is an **indicator of the affinity** of the enzyme for its substrate.

Interpreting K_m

A **low K_m** means the enzyme reaches half its maximum rate at a low substrate concentration, so it binds substrate effectively even when substrate is scarce: this indicates **high affinity**. A **high K_m** means a lot of substrate is needed to reach half V_{max}, indicating **low affinity**. K_m is read from the graph as the substrate concentration on the x-axis corresponding to a rate of $V_{max}/2$.

Constant	What it measures	Read from graph as
V_{max}	Maximum rate at saturation	The plateau height (the asymptote)
K_m	Substrate concentration giving $V_{max}/2$; inverse indicator of affinity	x-value where rate = $V_{max}/2$

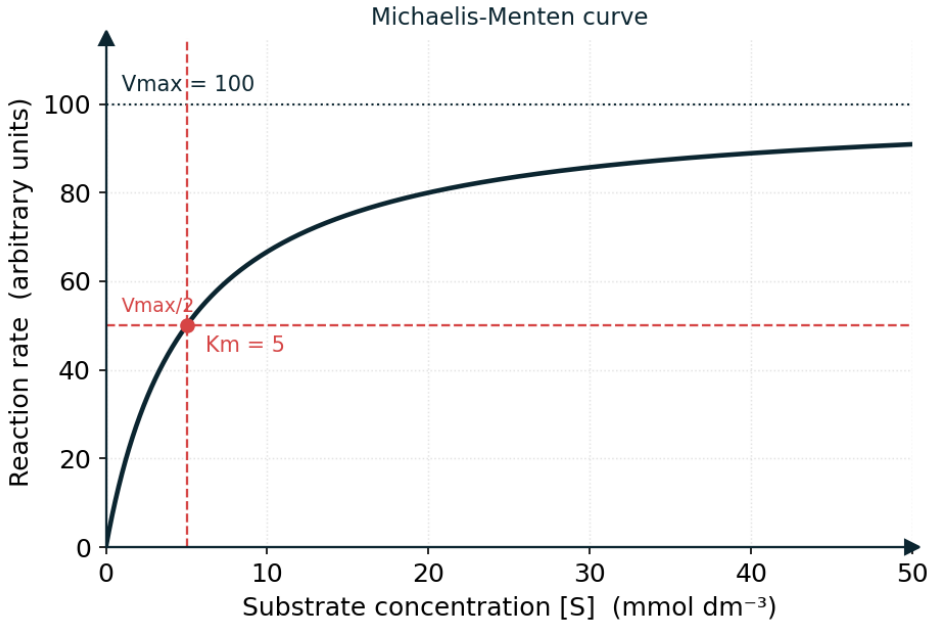

Figure 3. Michaelis-Menten curve computed from V_{max} = 100 and K_m = 5 mmol dm^{-3}. Audit: the rate at [S] = K_m is computed as 50.0, exactly $V_{max}/2$ = 50.0, confirming the defining property of K_m.

Affinity shortcut: Low K_m → high affinity; high K_m → low affinity. A competitive inhibitor **raises** the apparent K_m (V_{max} unchanged); a non-competitive inhibitor **lowers V_{max}**.

10. Worked examples and exam skills

Worked example 1 - reading a temperature graph

A student measures the rate of an enzyme reaction from 0 to 60 °C. The rate rises to a peak at 40 °C then falls sharply to zero by 55 °C. Explain the shape.

0-40 °C: heating increases kinetic energy, so enzyme and substrate collide more often and more collisions are successful; the number of enzyme-substrate complexes formed per second rises, so the rate increases.

Above 40 °C: increased vibration breaks hydrogen and ionic bonds in the tertiary structure; the active site changes shape (the enzyme denatures), substrate can no longer bind, and the rate falls to zero.

Optimum = 40 °C, the temperature of maximum rate.

Worked example 2 - distinguishing inhibitors from data

Without inhibitor an enzyme reaches V_{max} = 50 −mol s^{-1}. With inhibitor X the rate still reaches 50 −mol s^{-1} but only at much higher substrate concentration. With inhibitor Y the rate never exceeds 30 −mol s^{-1} however much substrate is added. Classify X and Y.

X is competitive: V_{max} is unchanged, so extra substrate out-competes the inhibitor for the active site and full rate is restored.

Y is non-competitive: V_{max} is reduced and cannot be recovered with more substrate, because Y binds an allosteric site and distorts the active site.

(Read "-mol" as micromoles; the unit symbol is written in full in exams.)

Worked example 3 - explaining denaturation by pH

Salivary amylase has an optimum of pH 7 and stops working when it reaches the stomach (pH 2). Explain, in terms of structure.

The high H^+ concentration at pH 2 disrupts the ionic bonds and hydrogen bonds that hold amylase in its folded (tertiary) shape and alters the charges on its side chains.

The active site therefore changes shape; starch can no longer bind to form an enzyme-substrate complex, so the enzyme is denatured and activity stops. The change is permanent.

Worked example 4 - calculating a rate from data

In an experiment, 12 cm^3 of oxygen is released by catalase acting on hydrogen peroxide in 30 s. Calculate the mean rate of reaction, and predict the effect of doubling the enzyme concentration (substrate in excess).

Mean rate = volume / time = 12 / 30 = **0.40 cm^3 s^{-1}**.

With substrate in excess, rate is proportional to enzyme concentration, so doubling the catalase roughly **doubles** the rate to about 0.80 cm^3 s^{-1} (until substrate begins to run low).

Worked example 5 - explaining feedback inhibition (HL)

In a three-enzyme pathway P → Q → R → S, the end product S inhibits enzyme 1. Explain how this regulates the pathway.

When S accumulates, it binds to an allosteric site on enzyme 1 (the first, committed step), changing that enzyme's active site so P can no longer be converted. This is non-competitive, end-product inhibition, which switches the pathway off and prevents over-production of S.

As S is used up its concentration falls, it detaches from enzyme 1, the active site is restored, and the pathway restarts. This negative feedback keeps S at a steady level.

Worked example 6 - interpreting K■ (HL)

Enzyme A has K_m = 2 mmol dm^{-3}; enzyme B (catalysing the same reaction) has K_m = 20 mmol dm^{-3}. Which has the higher affinity for the substrate, and why?

Enzyme A. A lower K_m means half the maximum rate is reached at a lower substrate concentration, so A binds substrate effectively even when it is scarce - indicating higher affinity. Enzyme B needs ten times more substrate to reach $V_{max}/2$, so it has lower affinity.

11. Common pitfalls

- Saying enzymes change the energy released by a reaction. They lower the **activation energy** only; the overall energy change (ΔG) is unchanged.
- Writing that a denatured enzyme is "killed" or "dead". Enzymes are molecules; say the active site has **changed shape** so the enzyme has lost function.
- Confusing the two inhibitor types at high substrate concentration. Only **competitive** inhibition is overcome by adding substrate; non-competitive is not.
- Claiming enzymes are "used up" in the reaction. They are regenerated unchanged and reused many times.
- Treating temperature and pH graphs as the same shape. The temperature curve is a skewed peak with a steep denaturation drop; the pH curve is a fairly symmetrical bell.
- Forgetting to state that other factors are held constant when describing the effect of the one you are varying.

- Confusing anabolism with catabolism: anabolism **builds** (condensation, uses energy); catabolism **breaks down** (hydrolysis, releases energy).

12. Quick reference

Idea	Key statement
Enzyme action	Lowers activation energy by forming an enzyme-substrate complex; not used up
Specificity	Active site is complementary to substrate (lock-and-key / induced-fit)
Temperature	Rate rises to optimum, then falls as enzyme denatures
pH	Bell-shaped curve about an optimum pH; extremes denature
Substrate concentration	Rate rises then plateaus at V_{max} when enzyme is saturated
Enzyme concentration	Rate directly proportional (while substrate is in excess)
Denaturation	Loss of tertiary structure → altered active site → loss of function
Anabolism / catabolism	Build up by condensation (uses energy) / break down by hydrolysis (releases energy)
Competitive inhibitor (HL)	Binds active site; overcome by more substrate; V_{max} unchanged
Non-competitive (HL)	Binds allosteric site; not overcome by substrate; V_{max} reduced
Feedback inhibition (HL)	End product inhibits an early enzyme, regulating the pathway
K_m (HL)	Substrate concentration at $V_{max}/2$; low K_m = high affinity

13. Test yourself

Attempt these without notes; full answers follow.

1. Define *activation energy* and explain how an enzyme increases the rate of a reaction. (3 marks)

2. Compare the lock-and-key and induced-fit models of enzyme action. (3 marks)

3. Sketch and explain the effect of increasing substrate concentration on the rate of an enzyme-controlled reaction. (4 marks)

4. Explain why an enzyme heated to 80 °C loses its activity permanently. (3 marks)

5. State two advantages of using immobilised enzymes and give one named example. (3 marks)

6. Distinguish between anabolic and catabolic reactions, giving one example of each. (4 marks)

7. (HL) A drug binds to an enzyme's active site and its effect is reduced when substrate concentration is raised. Identify the type of inhibition and justify your answer. (3 marks)

8. (HL) Explain how end-product inhibition prevents a cell from over-producing a substance. (4 marks)

Answers

1. Activation energy is the minimum energy reactants must gain to reach the transition state and react (1). The enzyme provides an alternative route with a lower activation energy (1), so a greater proportion of collisions are successful and the rate increases; the enzyme is not used up (1).

2. Both explain specificity through an active site complementary to the substrate (1). In lock-and-key the active site is a rigid, fixed shape (1); in induced-fit it is flexible and changes shape as the substrate binds to fit more closely (1).

3. Curve rises steeply then levels off at a plateau (V_{max}) (1). At low concentration many active sites are empty, so adding substrate increases enzyme-substrate collisions and rate (1). At high concentration the active sites are saturated/all occupied (1), so adding more substrate cannot increase the rate; enzyme concentration is now limiting (1).

4. The heat energy breaks the hydrogen and ionic bonds holding the tertiary structure (1); the active site changes shape so substrate can no longer bind / no enzyme-substrate complex forms (1); this denaturation is irreversible, so activity is lost permanently (1).

5. Any two of: the enzyme can be recovered and reused; the product is not contaminated by enzyme; greater stability to temperature/pH; allows continuous flow (2). Example: lactase immobilised on beads to make lactose-free milk (1).

6. Anabolic reactions build larger molecules from smaller ones, usually by condensation and requiring energy (1); example: amino acids joined to form a protein (1). Catabolic reactions break larger molecules into smaller ones, usually by hydrolysis and releasing energy (1); example: starch hydrolysed to glucose / respiration of glucose (1).

7. (HL) Competitive inhibition (1). The drug resembles the substrate and binds the active site (1); raising the substrate concentration lets substrate out-compete the drug for the active site, restoring the rate, which is characteristic of competitive inhibitors (1).

8. (HL) The end product of the pathway binds to an allosteric site on an enzyme early in the pathway (1), changing that enzyme's active site so it can no longer bind its substrate (non-competitive) (1). This switches the pathway off when product is plentiful (1); as the product is used up it detaches and the pathway restarts, keeping the product at a steady level (negative feedback) (1).

End of C1.1 Enzymes and Metabolism revision notes. Prepared originally for Megalecture; all diagrams described in words for you to sketch and annotate as you revise.