DP Biology – C1.1 (HL extension)

Controlling metabolism

- How do enzymes work with other molecules?
- Which parts of metabolism depend on one another?

HL statements C1.1.11–17. Textbook pp. 396–404.

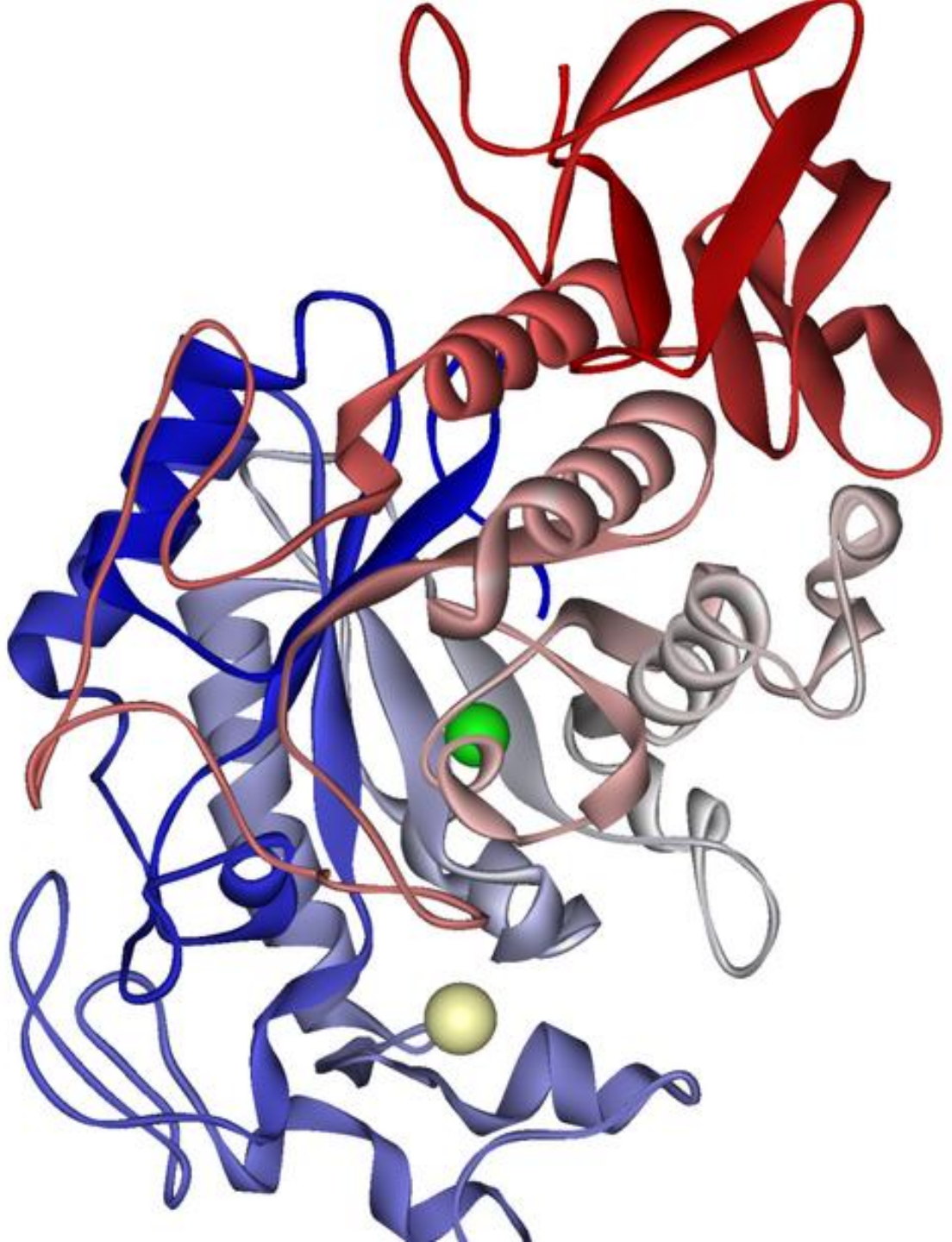


Image: salivary amylase, an extracellular enzyme. Public domain.

Objectives for each class

Class	Statements	By the end of the class, you can...
1	C1.1.11–13	Compare intracellular and extracellular reactions, explain why metabolism releases heat, and compare linear and cyclical pathways
2	C1.1.14–15	Compare non-competitive (allosteric) and competitive inhibition, using statins
3	C1.1.16	Explain feedback inhibition, using the pathway that makes isoleucine
4	C1.1.17	Explain mechanism-based inhibition by penicillin, and how bacteria resist it

Where enzymes work

C1.1.11

	Intracellular	Extracellular
Where	Inside the cell that made them: cytoplasm, organelles, membranes	Outside the cell that made them
Examples	Glycolysis (cytoplasm); Krebs cycle (mitochondrial matrix)	Digestion in the gut, for example amylase and protease
Made by	Mostly free ribosomes	Ribosomes on rough ER; secreted by exocytosis

Think about it

Fungi digest their food outside their bodies, and so do many bacteria. Suggest why secreting enzymes is useful for an organism that lives in its food.

Metabolism releases heat

C1.1.12



Emperor penguins. Ian Duffy, CC BY 2.0.

- No energy transfer in metabolism is 100% efficient: some energy is always lost as heat
- For example, aerobic respiration stores only about a third of the energy in glucose as ATP
- Mammals and birds use this heat to keep a constant body temperature (endotherms)
- Shivering raises heat output; brown fat releases heat directly from respiration



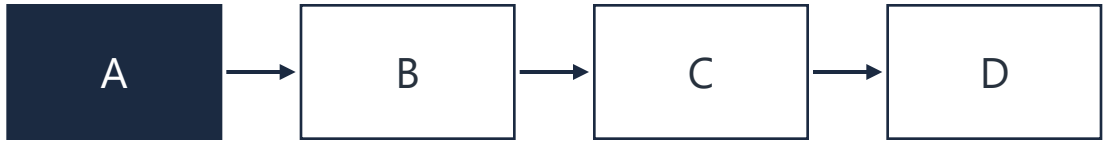
A steaming compost heap. Albarubescens, CC BY-SA 4.0.

Question

Compost heaps can reach 60 °C. Which organisms release this heat, and why does a large heap get hotter than a small one?

Linear and cyclical pathways

C1.1.13



Linear: glycolysis (glucose to pyruvate)

Key idea

Each step has its own enzyme, so each step can be controlled.

	Linear	Cyclical
Shape	Chain from a starting substrate to an end product	The last step regenerates the first substrate
Examples	Glycolysis	Krebs cycle; Calvin cycle
Feature	Each intermediate used once	A small amount of carrier (oxaloacetate, RuBP) handles many molecules

Inhibitors that bind elsewhere

C1.1.14

- An **allosteric site** is a binding site away from the active site
- Only specific molecules fit it
- Binding changes the shape of the enzyme, so the active site no longer catalyses the reaction
- Binding is reversible: when the inhibitor leaves, the enzyme works again
- Adding more substrate does not overcome the inhibition

Why "non-competitive"?

The inhibitor does not compete with the substrate for the active site. Both can be bound at once, but the enzyme cannot convert the substrate. So the maximum rate is lowered.

Competitive inhibition: statins

- A competitive inhibitor is similar in shape to the substrate
- It binds reversibly to the **active site**, blocking the substrate
- Increasing substrate concentration outcompetes it, so the maximum rate can still be reached
- **Statins** resemble HMG-CoA and inhibit HMG-CoA reductase, an enzyme in cholesterol synthesis in the liver

Statins in medicine

Less cholesterol is made, so LDL in the blood falls. This lowers the risk of atherosclerosis and coronary heart disease.

	Competitive	Non-competitive
Binds to	Active site	Allosteric site
Effect of more substrate	Overcomes inhibition	No effect on inhibition

Telling inhibitors apart

C1.1.14–15

Substrate / mmol dm^{-3}	No inhibitor	Inhibitor X	Inhibitor Y
2	40	15	20
5	70	35	35
10	88	62	44
20	96	86	48
40	100	97	50

Activity

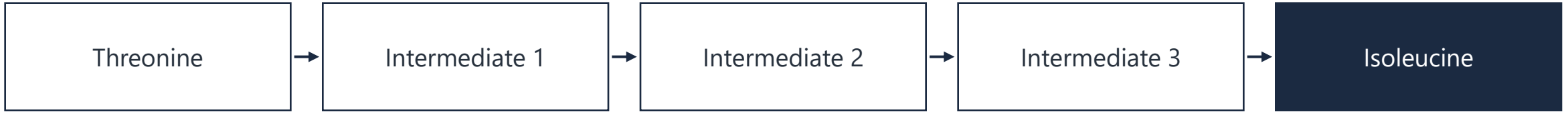
Invented data. Rates are % of the maximum without inhibitor. Plot all three curves on one graph. Which inhibitor is competitive? Which is non-competitive? Justify each with the data.

Hint

Look at the rates at high substrate concentration. Which inhibitor stops mattering when there is plenty of substrate?

Feedback inhibition: isoleucine

C1.1.16



Enzyme 1, threonine deaminase, is inhibited by isoleucine binding to its allosteric site.

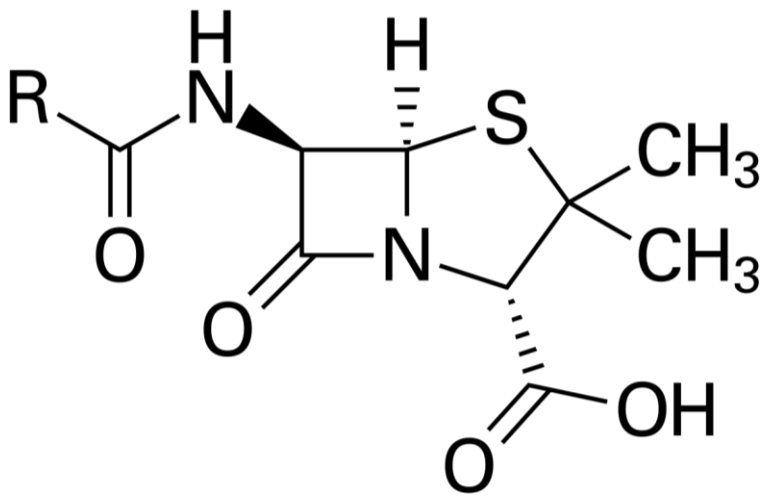
- When isoleucine builds up, it binds threonine deaminase and slows the whole pathway
- When isoleucine is used up (for protein synthesis), it leaves the allosteric site and the pathway restarts
- This is **negative feedback**: the end product controls its own production
- No energy or threonine is wasted making isoleucine the cell does not need

Why the first enzyme?

Inhibiting the first step stops all the intermediates building up. Inhibiting a later step would waste the earlier steps.

Mechanism-based inhibition: penicillin

C1.1.17



Core structure of penicillin. Public domain.

- Bacteria use **transpeptidases** to cross-link peptidoglycan in their cell walls
- Penicillin enters the active site, and the enzyme starts to react with it
- Its strained four-membered ring opens and forms a **covalent bond** with the active site
- The enzyme is permanently inactivated: irreversible inhibition
- Without cross-links, walls are weak and growing bacteria burst

Resistance

Some bacteria, such as MRSA, have a changed transpeptidase. Its active site has a different shape, so penicillin binds poorly, while the enzyme still cross-links the wall. Other bacteria make penicillinase, which breaks the penicillin ring before it reaches the enzyme.

Four ways to slow an enzyme

C1.1.14–17

Type	Binding site	Reversible?	Example
Competitive	Active site	Yes	Statins and HMG-CoA reductase
Non-competitive	Allosteric site	Yes	Many heavy metal ions
Feedback	Allosteric site	Yes	Isoleucine and threonine deaminase
Mechanism-based	Active site, covalent bond	No	Penicillin and transpeptidase

Think about it

Why must a cell replace an enzyme that has been mechanism-inhibited, but not one that was competitively inhibited?

Check that you can explain

1. Examples of intracellular and extracellular enzyme reactions
2. Why metabolism always releases heat, and how endotherms use it
3. Linear and cyclical pathways, with examples
4. How allosteric inhibitors work, and why extra substrate does not help
5. How statins act as competitive inhibitors
6. How isoleucine controls its own pathway
7. How penicillin inhibits transpeptidase, and how resistance arises

Exit activity: 5 minutes

On your own and without notes. Hand this in as you leave.

1. Give one example each of an intracellular and an extracellular enzyme reaction.
2. Explain why increasing substrate concentration reduces the effect of a statin.
3. State why penicillin is called a mechanism-based inhibitor.

Image credits

Salivary alpha-amylase 1SMD.png – Own work. – Public domain

Aptenodytes forsteri -Snow Hill Island, Antarctica -adults and juvenile-8.jpg – Ian Duffy from UK – CC BY 2.0

Steam from compost heaps.jpg – Albarubescens – CC BY-SA 4.0

Penicillin core.svg – Yikrazuul – Public domain

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