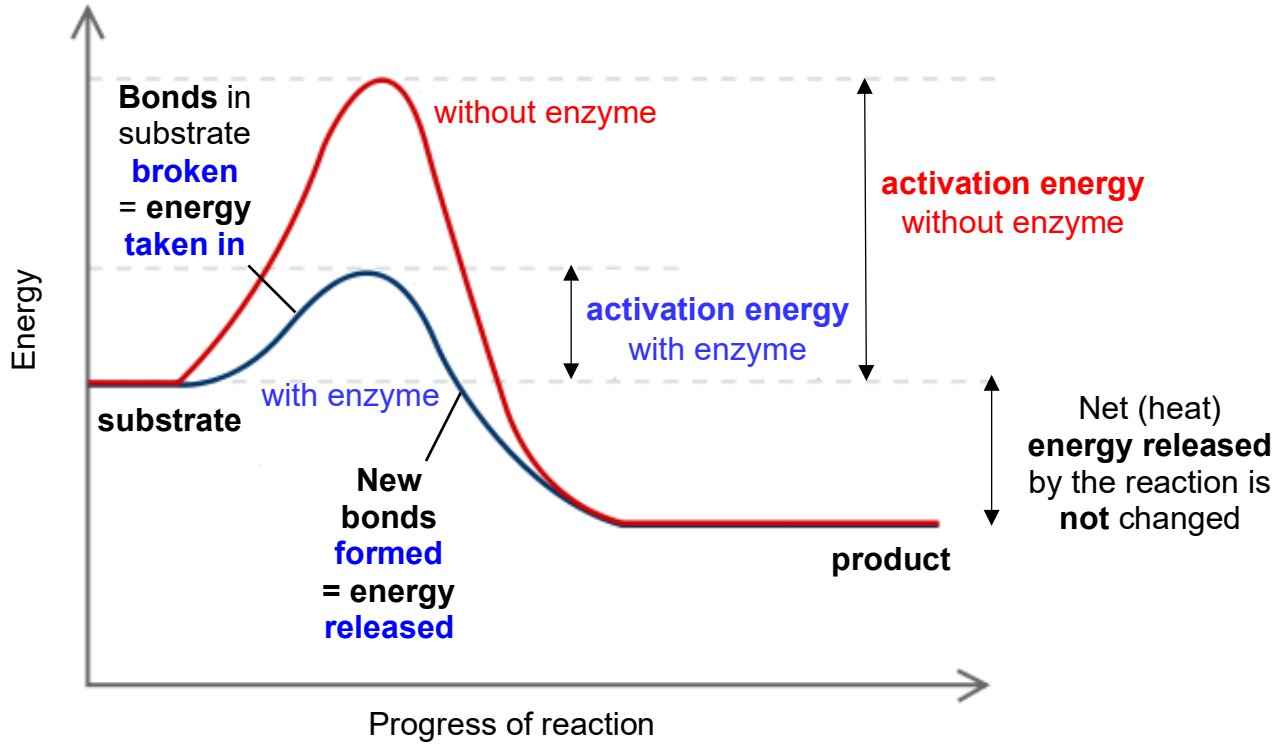
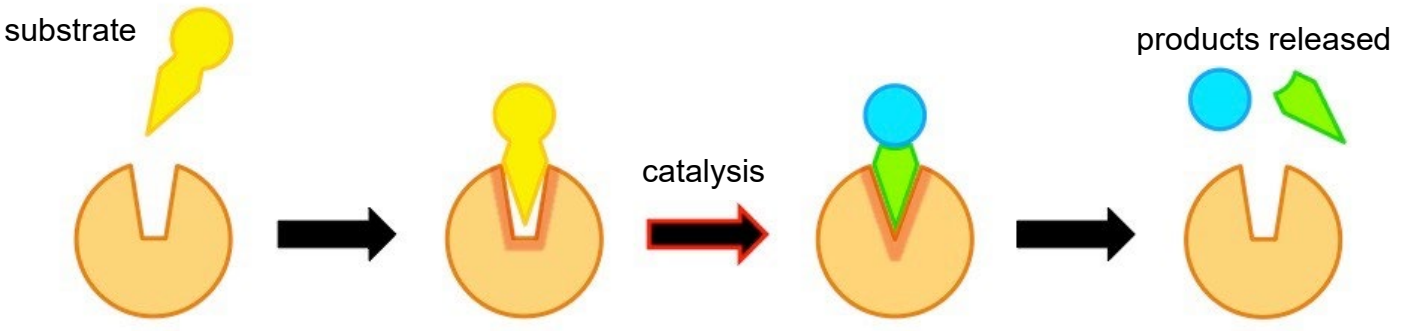
A. ACTIVATION ENERGY

- Enzymes **lower** the **activation energy** for a reaction.
- This means it takes **less energy** to **break the bonds** within a **substrate**.
- This means that the **reaction** will happen **faster**.



Most biological reactions are exothermic – the energy released is greater than the activation energy

B. THE INDUCED FIT MODEL



Active site and substrate are **not complementary shapes** initially

Upon **binding**, the **active site changes shape** to **become complementary** to the **substrate**, accommodating a much **better fit**

Brings **substrate(s)** **closer together** in **active site** and **weakens bonds** in the **substrate** = **lowers activation energy**

Products leave the **active site** and the enzyme **returns** to its **original shape**

Advantages of the induced model over the lock and key model

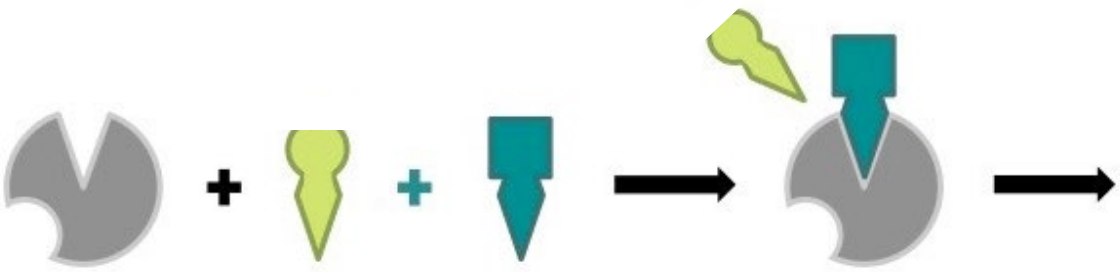
It explains how:

- **enzymes** may exhibit **broad specificity**
  - e.g. **lipase** can bind to a **variety** of **lipids**)
- **catalysis** may occur
  - the **active site shape change stresses bonds** in the **substrate**, increasing the rate of reaction

C. ENZYME INHIBITORS

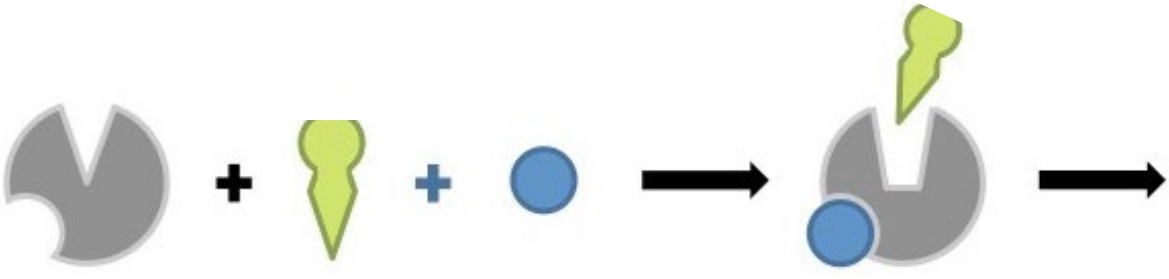
- These are molecules that **reduce the activity** of enzymes or even **prevent it completely**.
- There are **competitive** inhibitors and **non-competitive** inhibitors.

Competitive inhibitors



enzyme | substrate | inhibitor | inhibitor has a **similar shape** to the **substrate** so it **binds** to the **active site** | substrate **cannot bind to the active site** so rate of reaction decreases

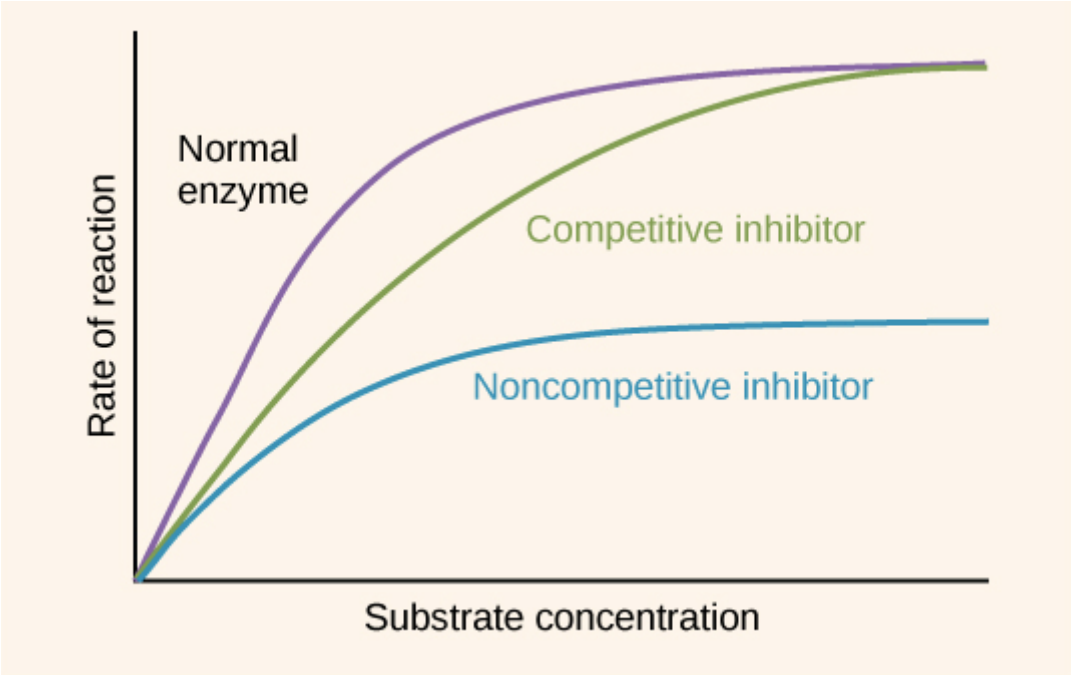
Non-competitive inhibitors



enzyme | substrate | inhibitor | inhibitor has a **different shape** to the **substrate** so it binds to an **allosteric site**. This **binding causes** the **active site** to **change shape**. | substrate **cannot bind to the active site** so rate of reaction decreases

Effect of increasing the substrate concentration on the degree of inhibition

- This is with a **fixed amount** of **enzyme** and **inhibitor** present.



Competitive Inhibitor

- Increasing the substrate concentration **decreases** the inhibition.
- (As) substrate **outcompetes** inhibitor
- (For) **active site**
- **More** active sites contain the **substrate**
- (So) **more product** formed

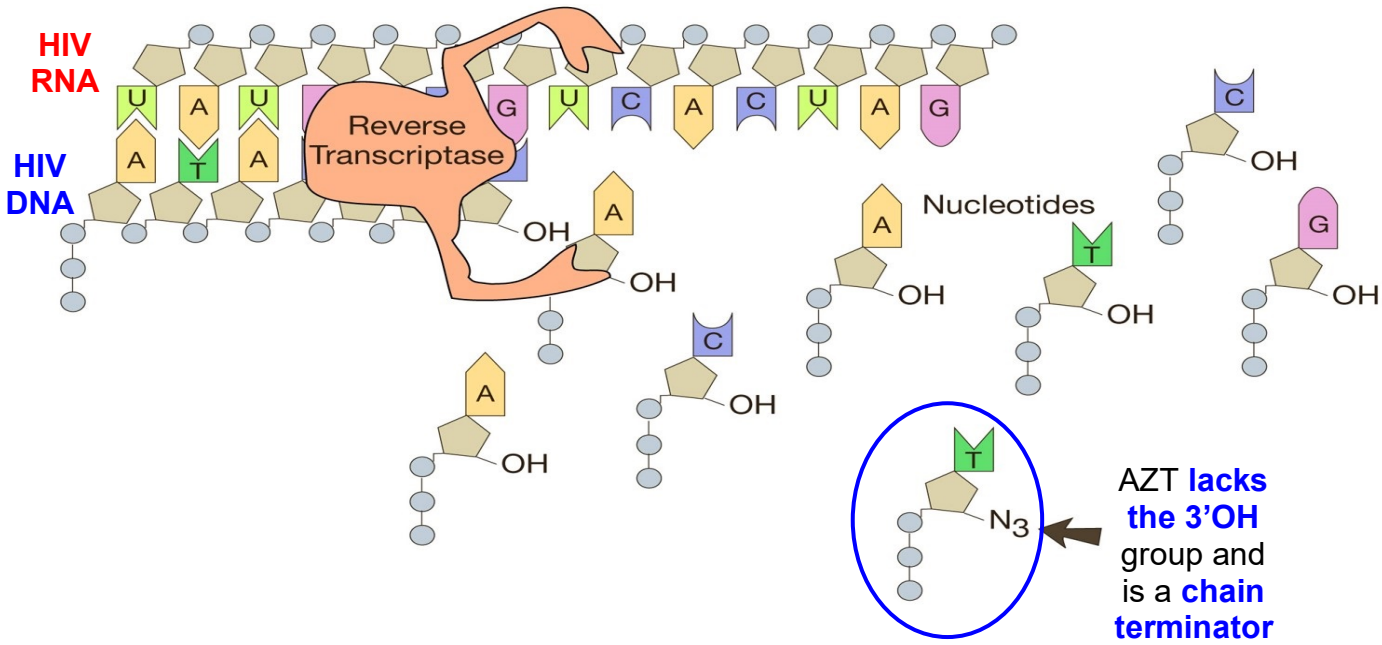
Non-competitive Inhibitor

- Increasing the substrate concentration has **no effect** on the inhibition.
- (As) inhibitor **binds** to **allosteric site** / does **not bind** to **active site**
- (So) **active site changes shape**
- (So) substrate **cannot fit** active site
- even at **high concentrations** of **substrate**

Comparing competitive and non-competitive inhibitors

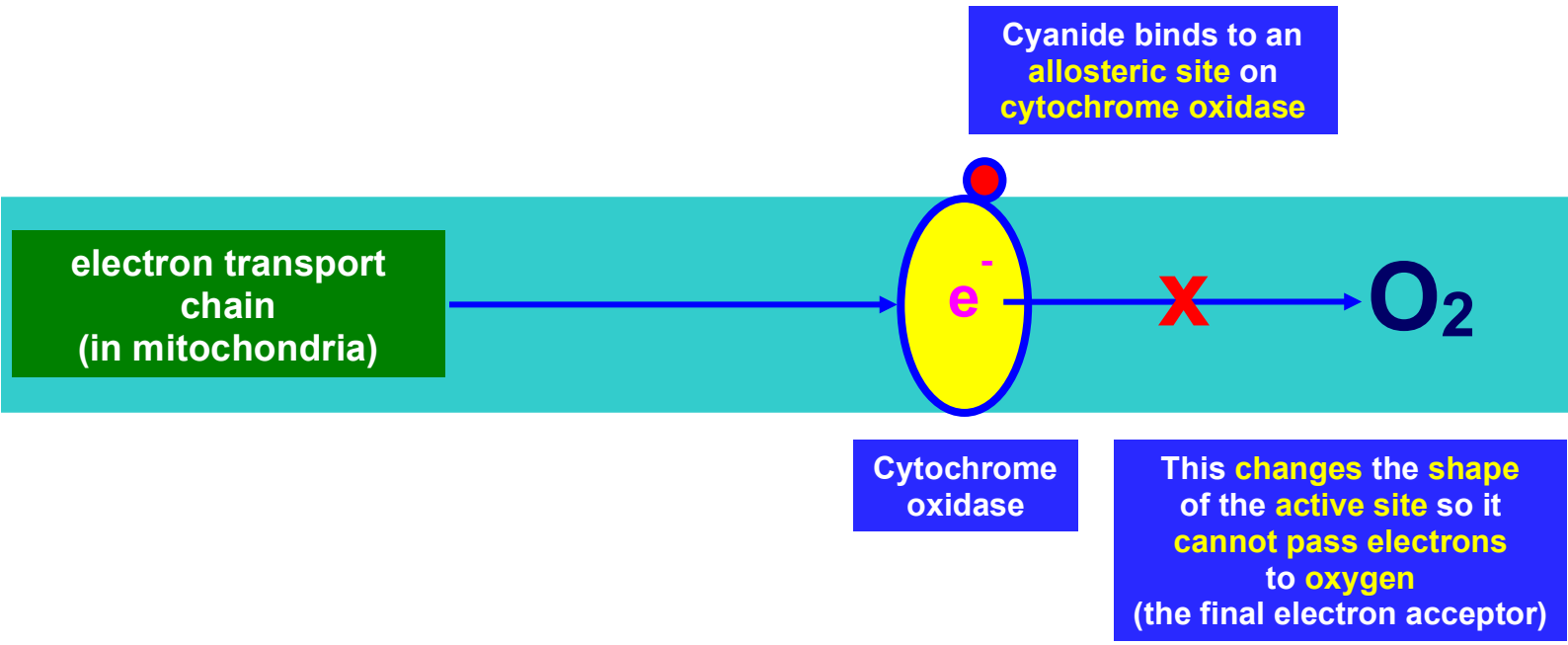
	Competitive inhibitor	Non-competitive inhibitor
Structure or shape	**Similar** to the substrate	**Different** to the substrate
Binds to	**Active** site	**Allosteric** site
Active site changes shape	**No**	**Yes**
Effect of increasing the substrate concentration	**Less** inhibition	**No effect** on inhibition
Example of inhibitor	**AZT**	**Cyanide**
Prevents the substrate from binding to the active site	**Yes**	

AZT: An example of a competitive inhibitor



- AZT is a **competitive inhibitor** of **reverse transcriptase** (an enzyme in HIV)
- AZT is a **similar shape** to the normal nucleotide that contains thymine
- But is a **chain terminator**.
- AZT **binds** to the **active site** of **reverse transcriptase**.
- This **prevents** HIV from converting **RNA → DNA**
- **Reverse transcriptase** has a **much higher affinity** for **AZT** than that of **DNA polymerase**
- So synthesis of **HIV DNA** is **prevented** more than that of human DNA

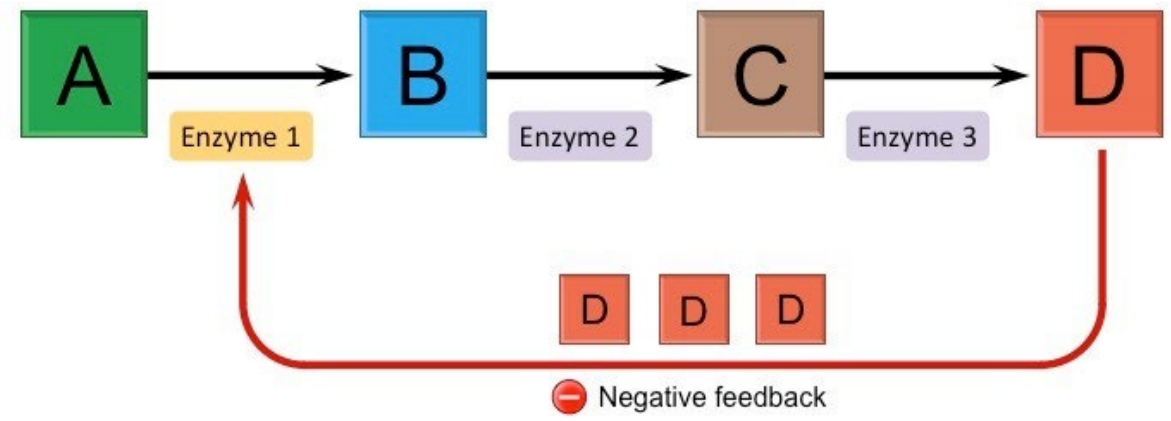
Cyanide: An example of a non-competitive inhibitor



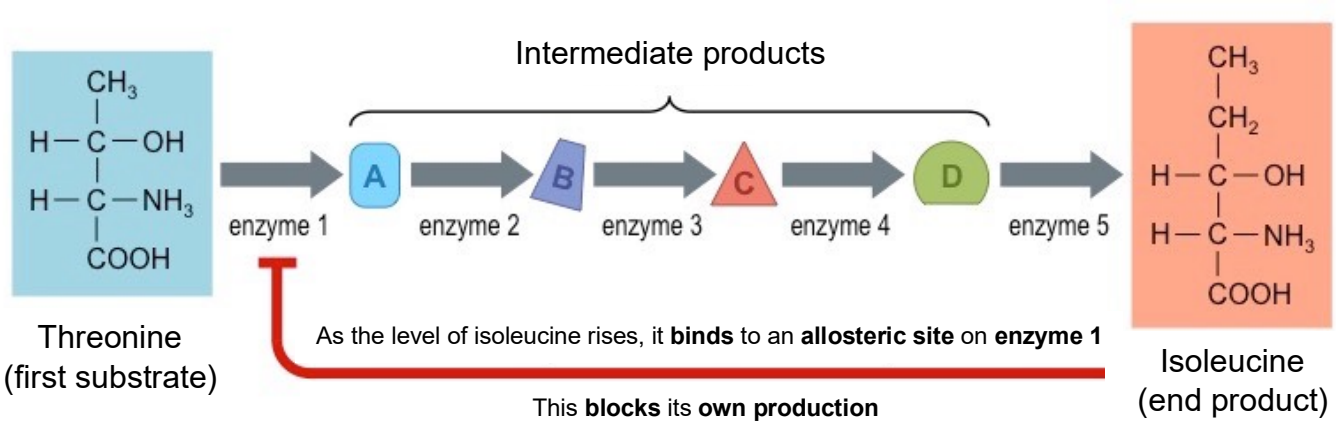
- The **electron transport chain** **stops**.
- **Aerobic respiration** **stops**.
- **ATP production** **stops**.
- **Death** happens **very quickly**.

D. END-PRODUCT INHIBITION

- The **final product** of a pathway acts as a **non-competitive** inhibitor to **inhibit its own production**.
- The **final product** binds to an **allosteric site** on the **first enzyme** of the pathway.
- This **changes the shape** of the **active site** and **prevents** a **build up** of **excess intermediates** or **product**.



Example: Threonine dehydratase and isoleucine



How isoleucine inhibits its own production

- As isoleucine level **rises**, it **binds** to an **allosteric site** on **enzyme 1**.
- It acts as a **non-competitive inhibitor**, **changing** the **active site shape**.
- (So) **intermediates** not made.
- (So) isoleucine level **falls**.
- It **stops** its **own** production.
- This is **negative feedback**.
- This ensures that isoleucine production does not **use up all available stocks** of **threonine**.

How isoleucine production starts again

- When isoleucine level **falls**, **less enzyme 1s** are **inhibited** so its level **rises again**.
- Also, **binding** of isoleucine is **reversible**.
- If isoleucine **detaches**, the **active site returns** to its **original shape**.
- (So) substrate **can** now **bind** to active site.
- (So) **intermediates** and **isoleucine** can be made again.

APPLICATION

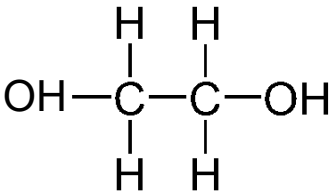
Ethylene glycol is a substance found in antifreeze. Drinking antifreeze can kill a person.

The liver contains an enzyme that breaks down ethylene glycol. However, the products of this reaction are even more toxic than the ethylene glycol.

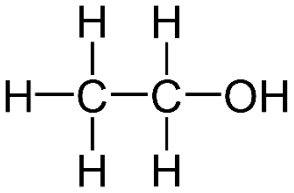
Ethylene glycol poisoning is treated by making a person drink ethanol (alcohol).

The diagram below shows the structures of ethylene glycol and ethanol.

Ethylene glycol



Ethanol (alcohol)



Explain why drinking ethanol prevents a person dying from ethylene glycol poisoning. [4]

Any **four** from:

- Ethylene glycol and ethanol have **similar structures/shapes**
- Ethanol is a **competitive inhibitor**
- (So) binds to **active site**
- (So) substrate/ethylene glycol **cannot bind** to **active site**
- (So) **toxic/poisonous products not produced** / less toxic/poisonous products produced