# Key Area 1.6

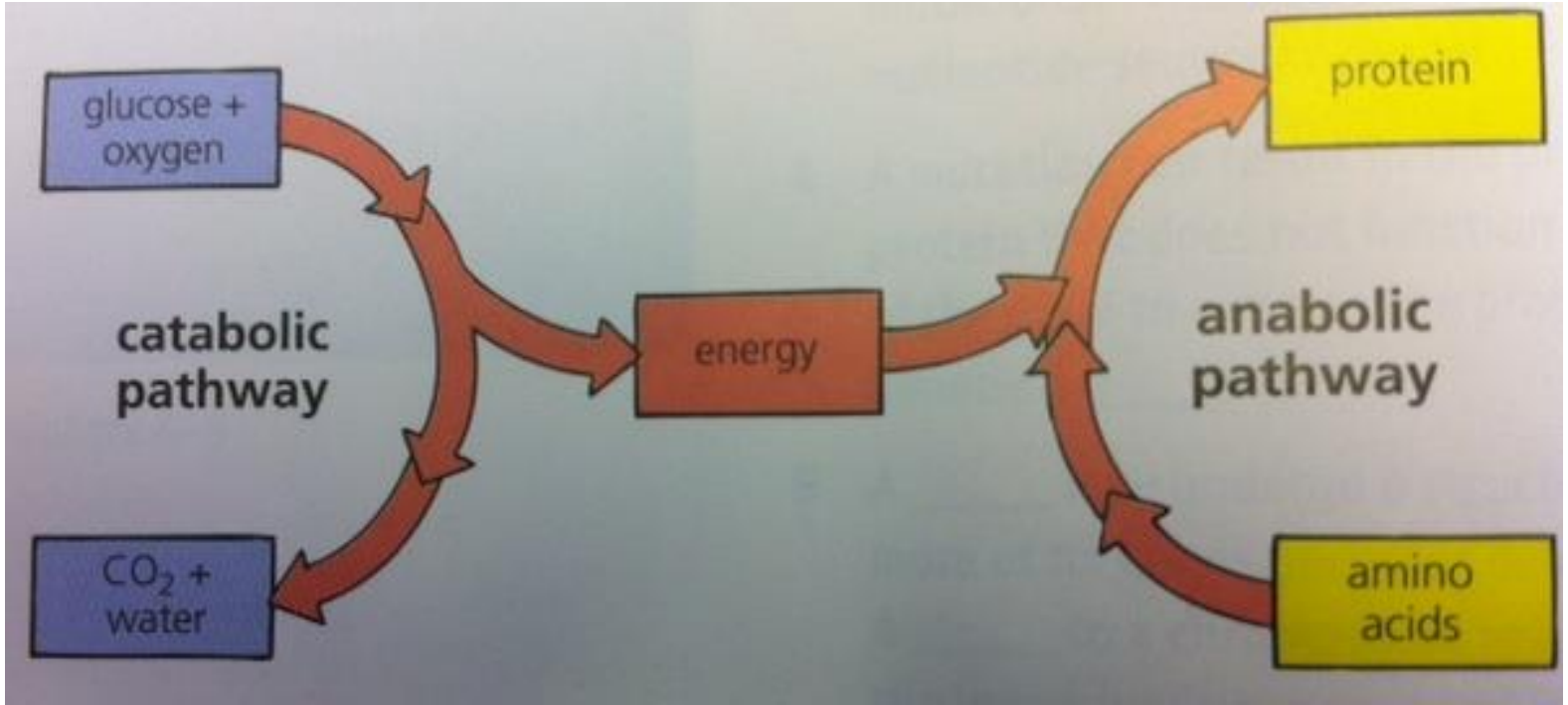
## Metabolic Pathways

# Learning Intentions

- Describe what metabolic pathways are.
- State that metabolic pathways can be reversible and irreversible, and have alternative routes.
- Describe the two different types of reaction that take place in a metabolic pathway: anabolic and catabolic.

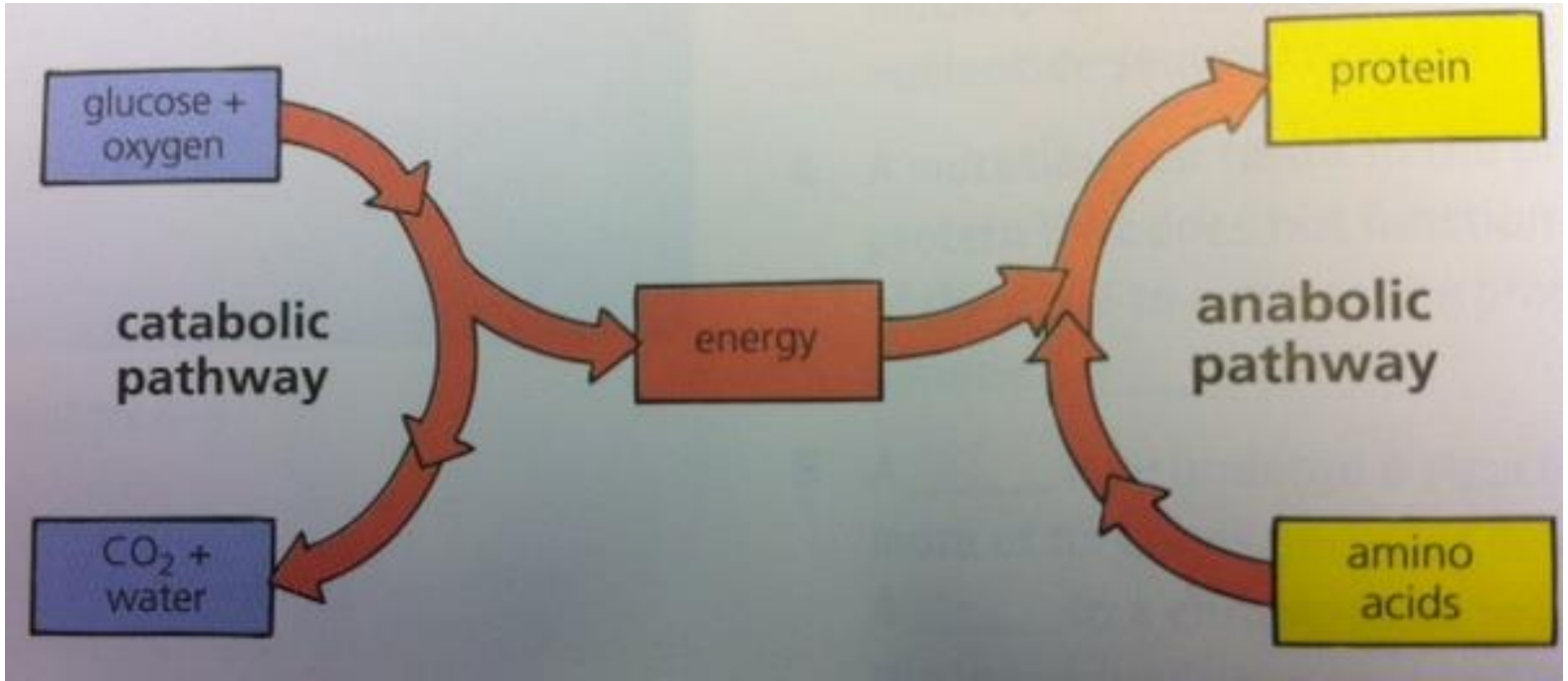
# Cell Metabolism

- Metabolic pathways are integrated and controlled pathways of enzyme-catalysed reactions within a cell.
- Metabolic pathways can have reversible steps, irreversible steps, and alternative routes.



# Cell Metabolism

- Reactions within metabolic pathways can be anabolic and catabolic.
- Anabolic reactions build up large molecules from small molecules. These **require energy**.
- Catabolic reactions break down **large** molecules into **smaller** molecules and **release energy**.



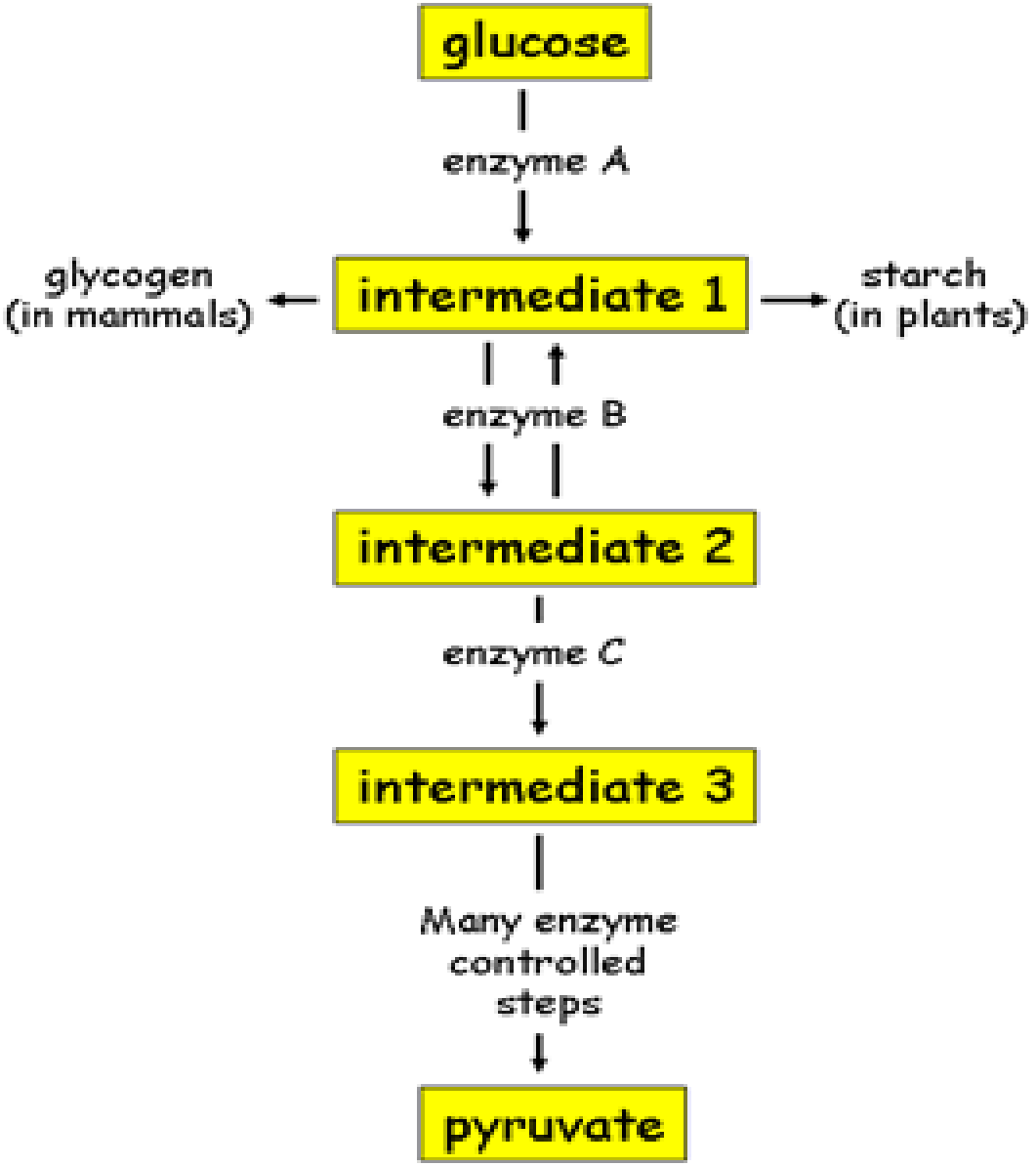
# Learning Intentions

- State that metabolic pathways are controlled by the presence or absence of particular enzymes.

- State that metabolic pathways rate of reaction are regulated by key enzymes within the pathway.

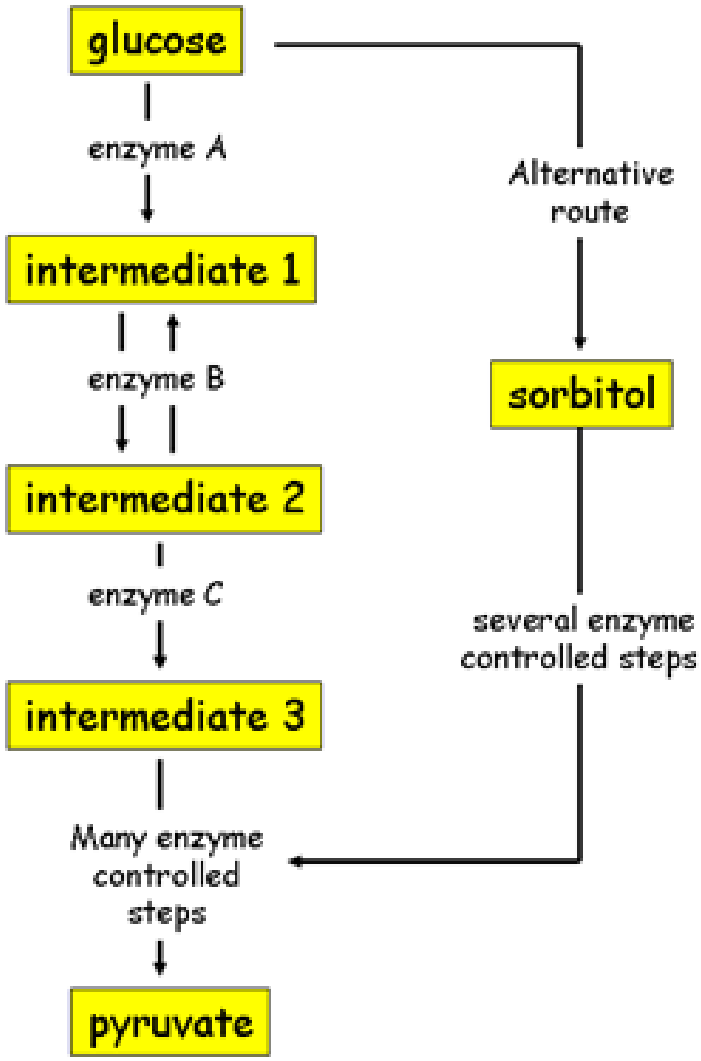
# Metabolic Pathways

- Metabolic pathways are regulated by the presence or absence of particular enzymes that catalyse specific reactions.
- A pathway often has reversible, irreversible & alternative steps that help with this control.



# Alternative Routes

- Metabolic pathways can also take alternative routes that allow steps to be bypassed.
- The example shown occurs when a cell has a plentiful supply of glucose.



# Summary

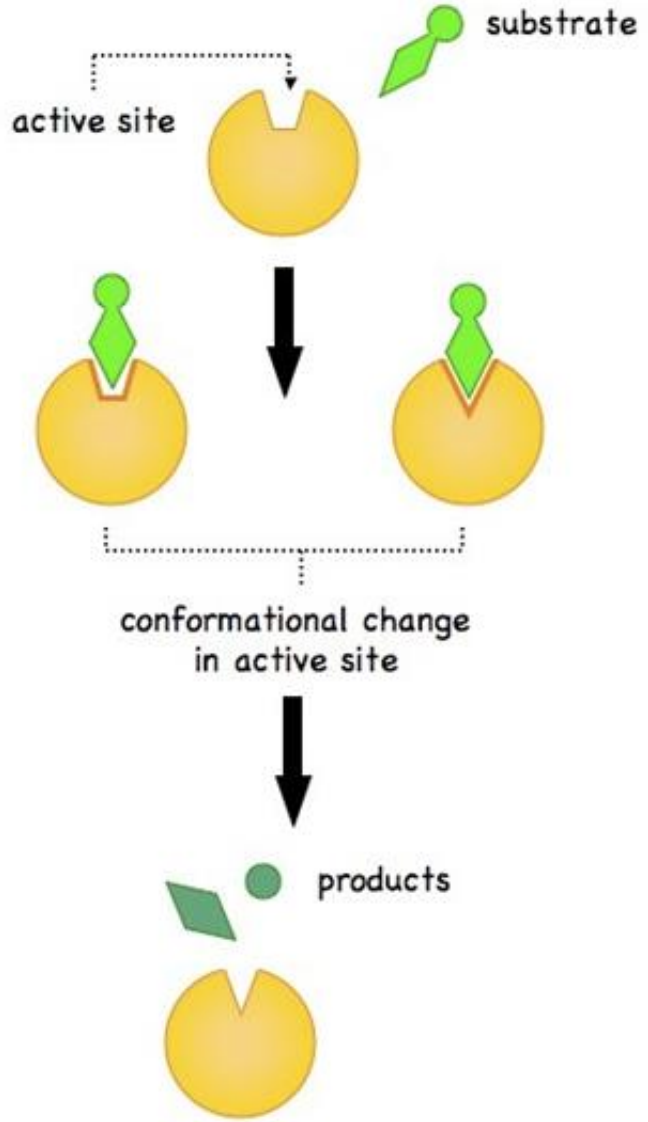
- Metabolism is the integrated and controlled pathways of enzyme catalysed reactions within a cell.
- Metabolic pathways involve biosynthetic pathways (anabolic, require the input of energy) and pathways that break down molecules (catabolic, usually release energy).
- Metabolic pathways can have reversible and irreversible steps. They can also have alternative routes that can bypass steps in a pathway.

# Learning Intentions

- Describe what “induced fit” means using the words active site, activation energy and affinity.

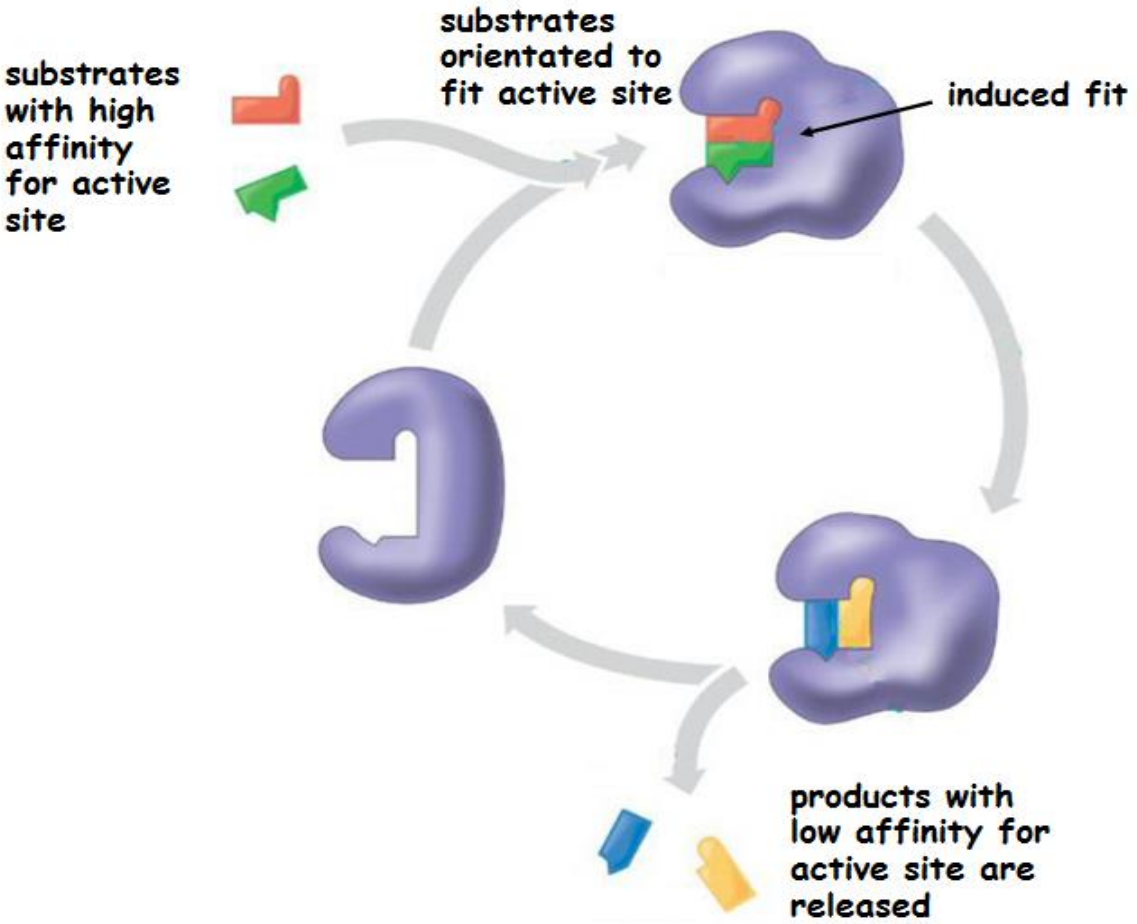
# Induced Fit

- The shape of an active site is specific to the shape of a substrate
- However, the active site is flexible. The shape of the active site can change slightly when it comes into contact with a substrate molecule so that the active site fits it better.
- The substrate molecule(s) have a high affinity for the active site and the subsequent products have a low affinity allowing them to leave the active site.



# Substrate Affinity

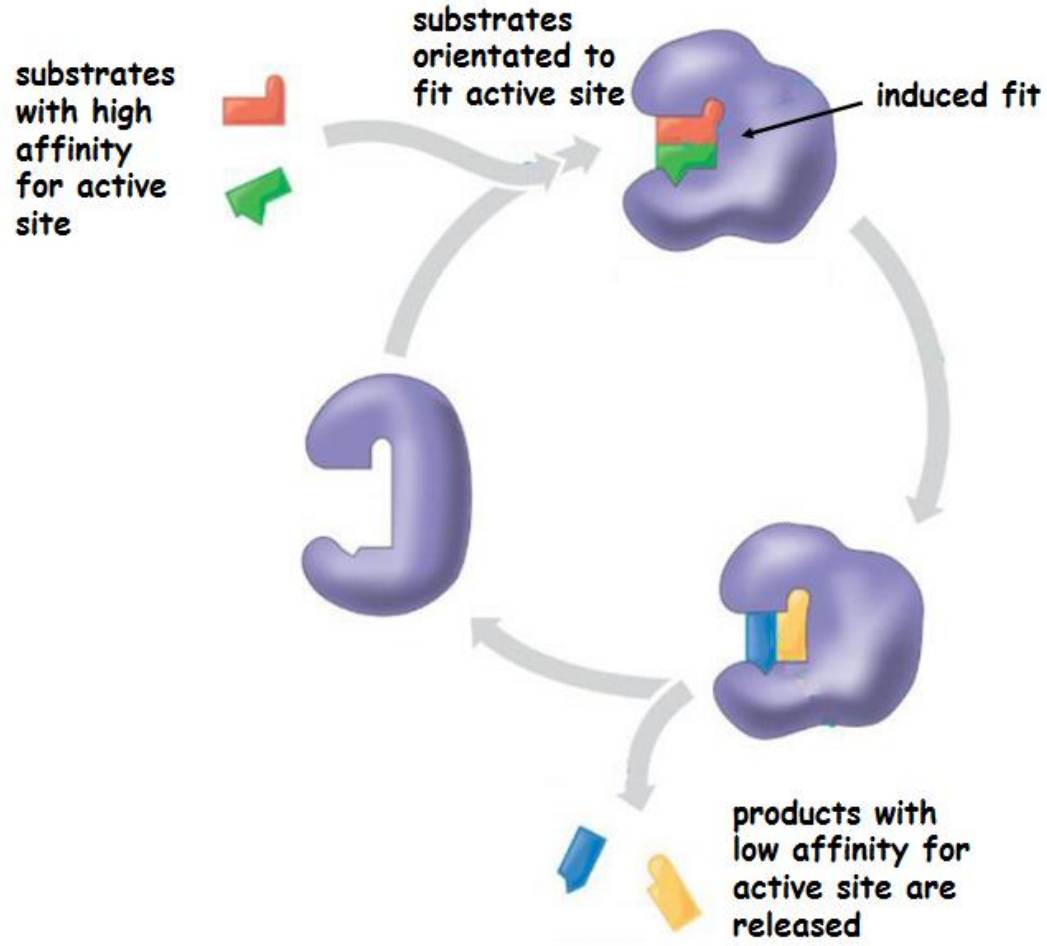
- When there are two or more reactants, the shape of the active site determines the **orientation** of the reactants (how they line up)
- This ensures that they are held together in such a way that the reaction between them can take place. **This lowers the activation energy required for the reaction to occur.**



# Product Affinity

- The active site holds the two reactants closely together in an induced fit.

- Once the reaction has taken place, the products have a **low affinity** for the active site and are released.

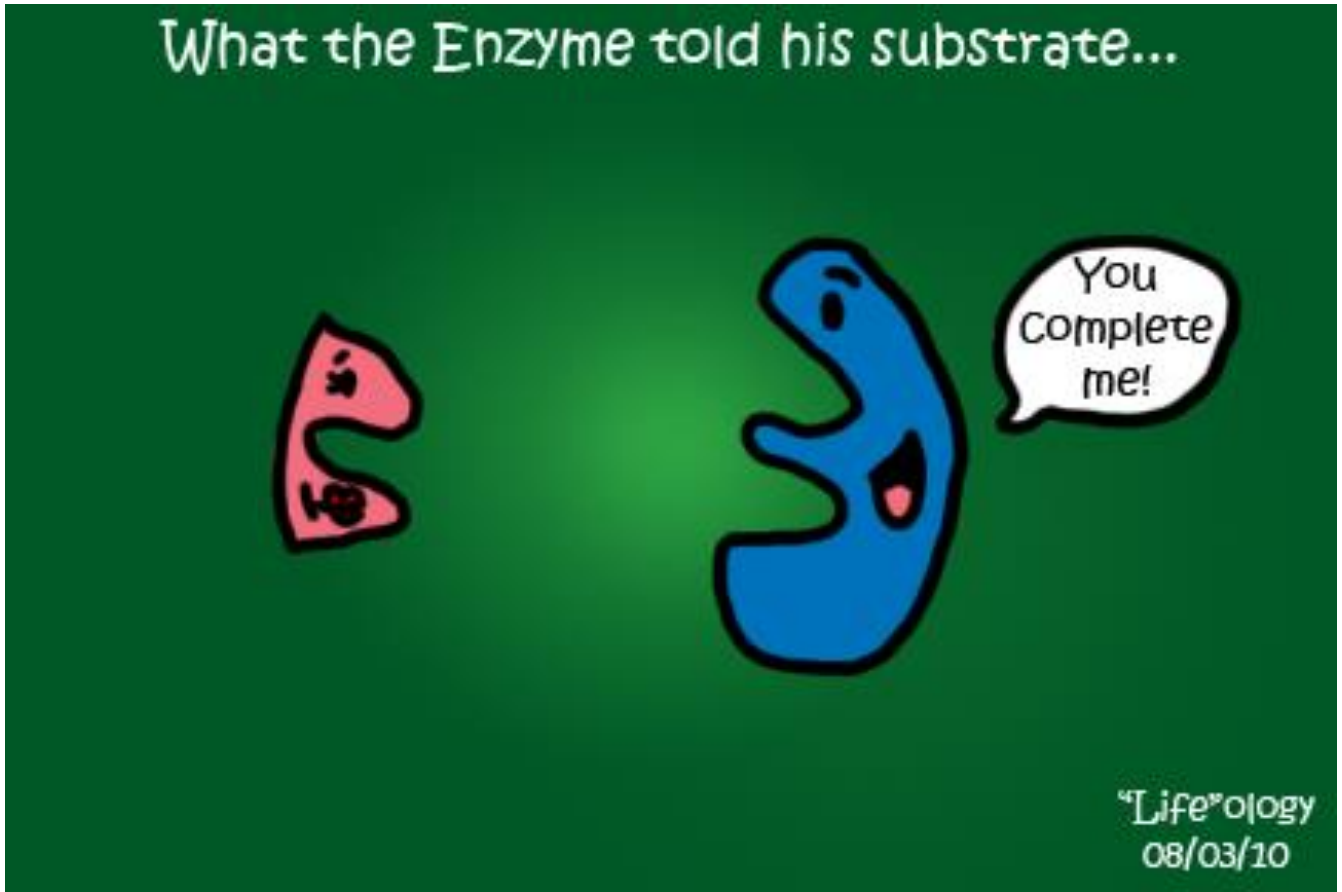


# Active Site Summary

- The substrate attaches to the active site on the enzyme.
- The active site orientates (lines up) the molecules.
- This causes an induced fit - the enzyme changes shape slightly so that the active site fits better
- This lowers the activation energy required for the reaction to occur
- Products are released as they have a low affinity for the active site.

# Task

Explain the role of the active site in enzyme-catalysed reactions (3 marks)



# Answer

1. The substrate attaches to the active site (on the enzyme).
2. The active site orientates/lines up the molecules.
3. This causes an induced fit/the enzyme to change shape slightly so that the active site fits better.
4. This lowers the activation energy (required for the reaction to occur).
5. Products are released as they have a low affinity for/attraction to the active site.

# Learning Intention

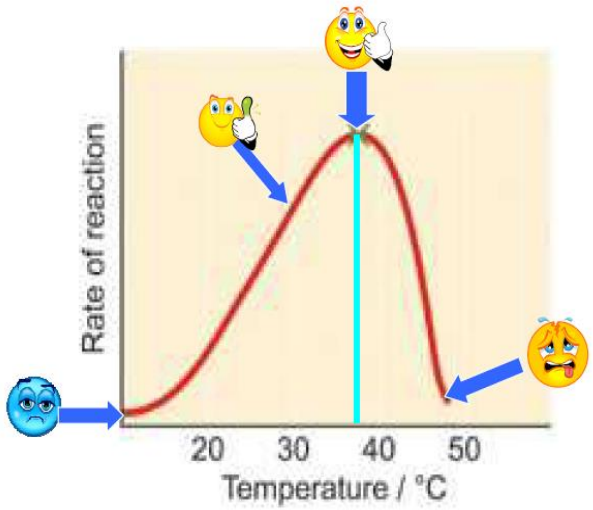
- State the effects of substrate concentration on the direction and rate of enzyme reactions

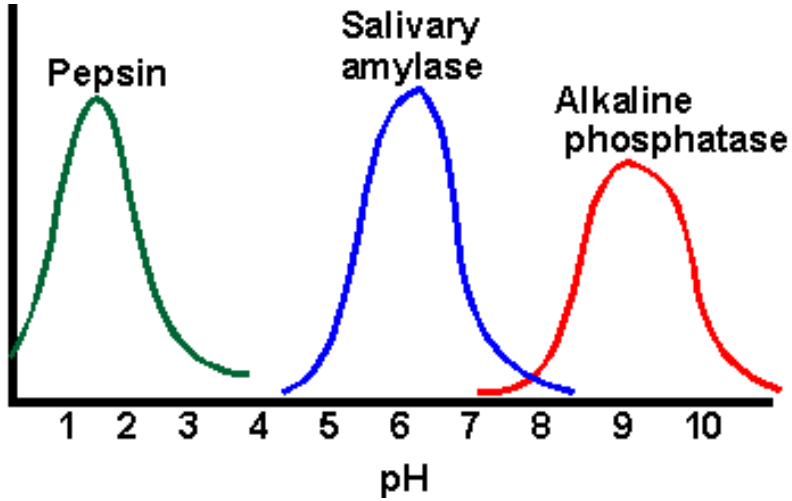
# Factors Affecting Enzyme Action

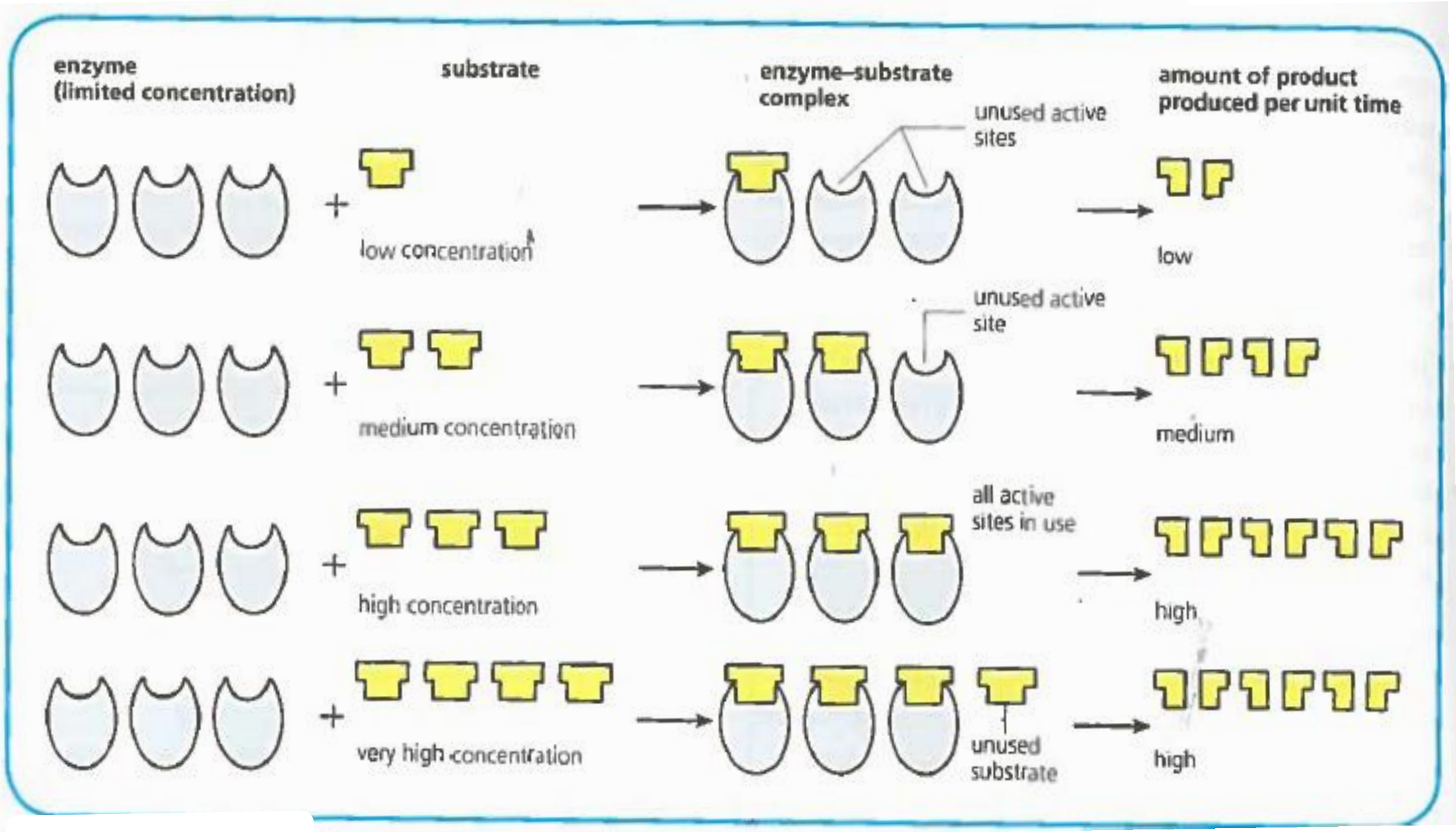
- The direction and rate of enzyme reactions can be affected by temperature, pH and:

➢ **substrate concentration**

➢ **end product concentration** ***(feedback inhibition – we'll come back to this!)***



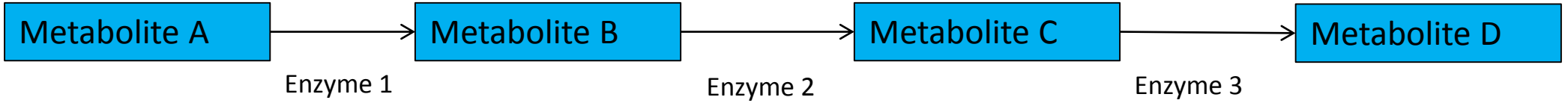

enzyme (limited concentration)
substrate
enzyme–substrate complex
amount of product produced per unit time
low concentration
unused active sites
low
medium concentration
unused active site
medium
high concentration
all active sites in use
high
very high concentration
unused substrate
high

# Learning Intention

- Some metabolic reactions are reversible and the presence of a substrate or the removal of a product will drive a sequence of reactions in a particular direction.

# Direction of enzyme action

- A metabolic pathway will generally involve a group of enzymes




- As A becomes available, enzyme 1 becomes active and converts A to B.
- When B is present, enzyme 2 becomes active and converts B to C ,etc.
- A constant supply of A entering the system ensures that the sequence of reactions is driven in the direction of A to D.
- The product of one reaction acts as the substrate of the next.

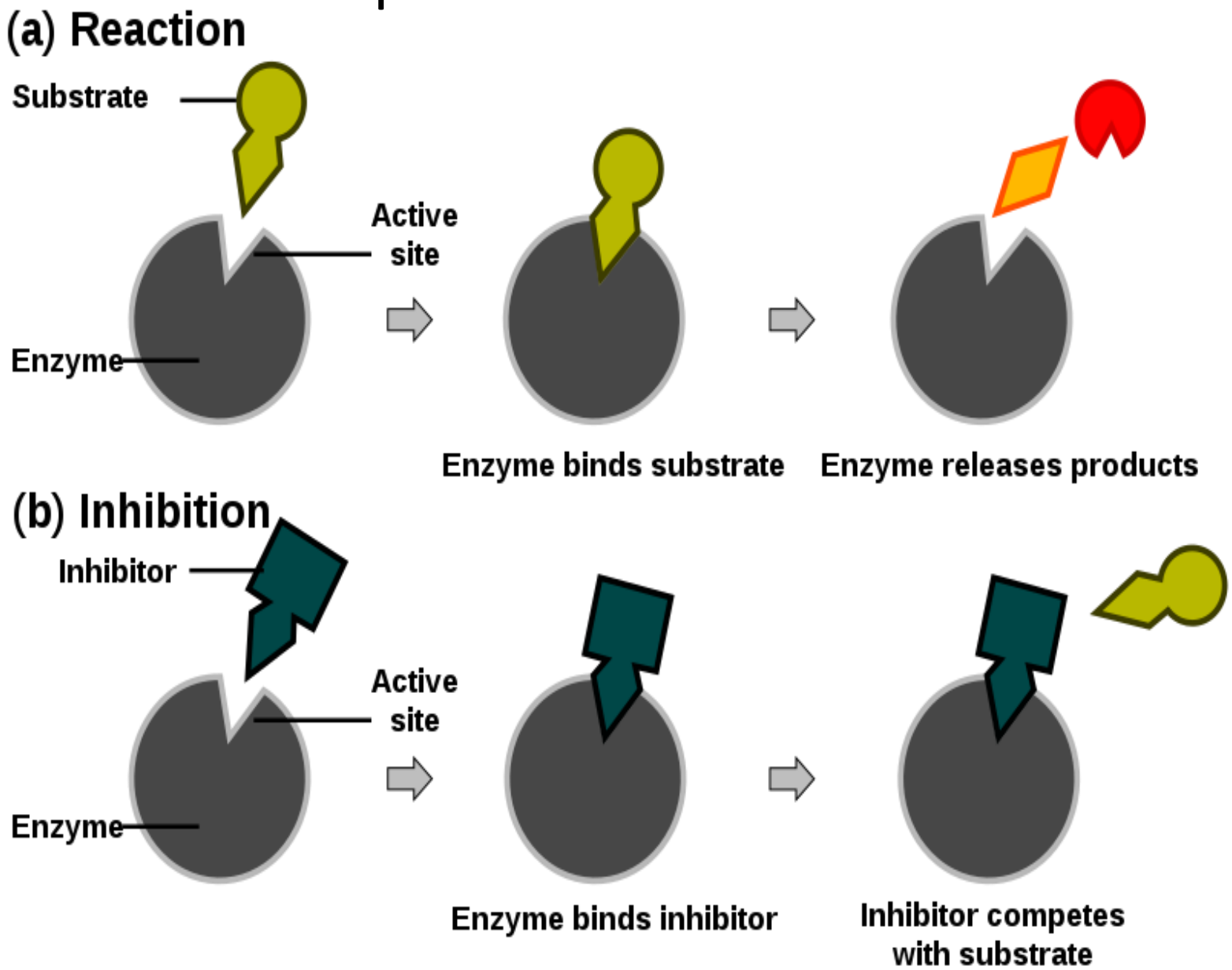
# Reversibility of enzyme action

- Most metabolic reactions are reversible.
- Frequently, an enzyme can catalyse  a reaction both ways.
- The actual direction of reaction depends on the relative concentrations of reactants and products.
- Metabolic pathways generally do not occur in isolation.
- Consider the previous pathway- if, due to a related biochemical reaction, the concentration of metabolite C  increased to an unusually high level, and B was to decrease , then enzyme 2 would reverse and convert some of C back to B until a balance (equilibrium) was established again.

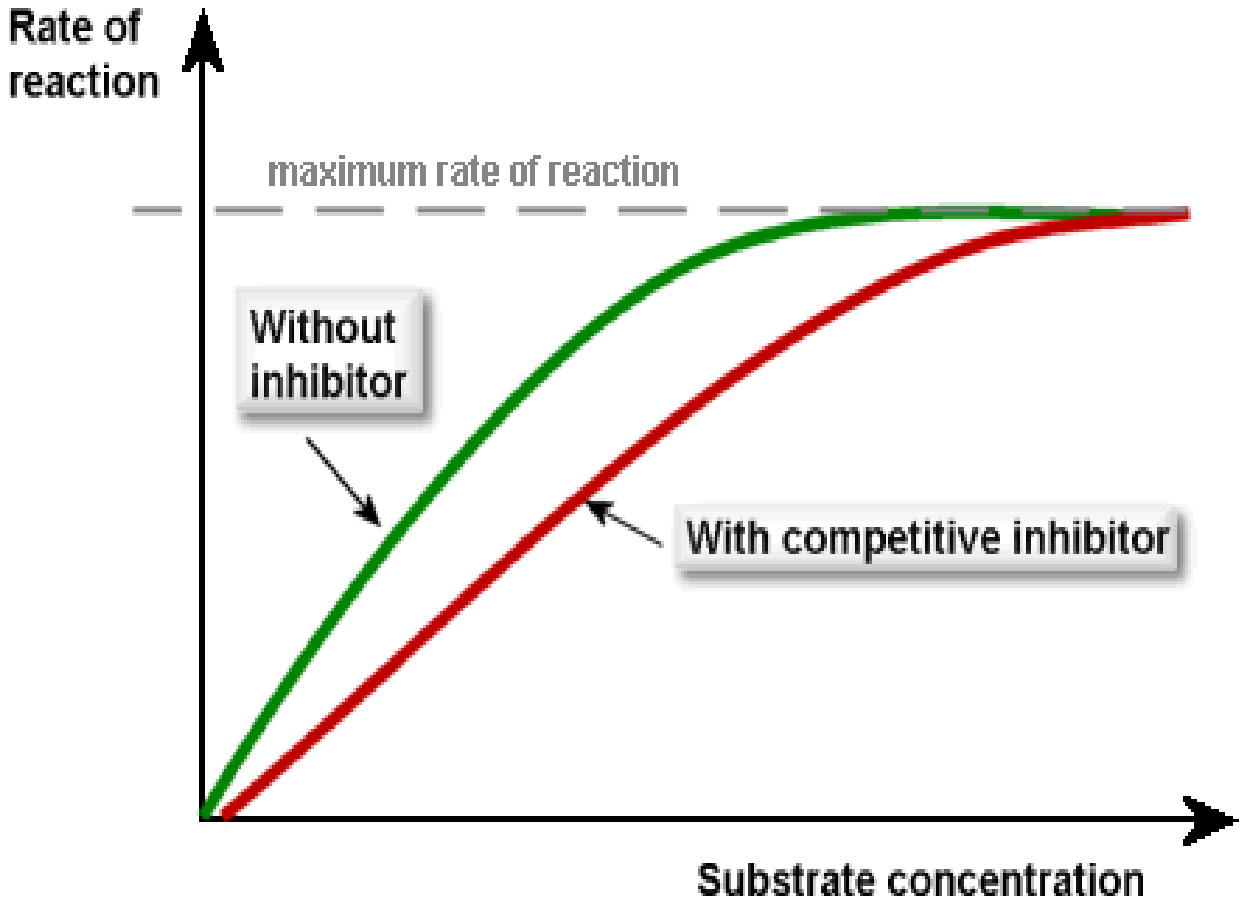
# Competitive Inhibitors

- Molecules of a **competitive inhibitor** compete with molecules of the substrate for the active sites on the enzyme.
- The inhibitor is able to do this because molecular structure is similar to that of the substrate and can attach itself to the enzymes active site.
- When the active site is blocked by the inhibitor, then the substrate cannot bind to it, and the rate of reaction is reduced.
- However, this (competitive inhibition) **can be reversed by increasing the substrate concentration.**

# Competitive Inhibition



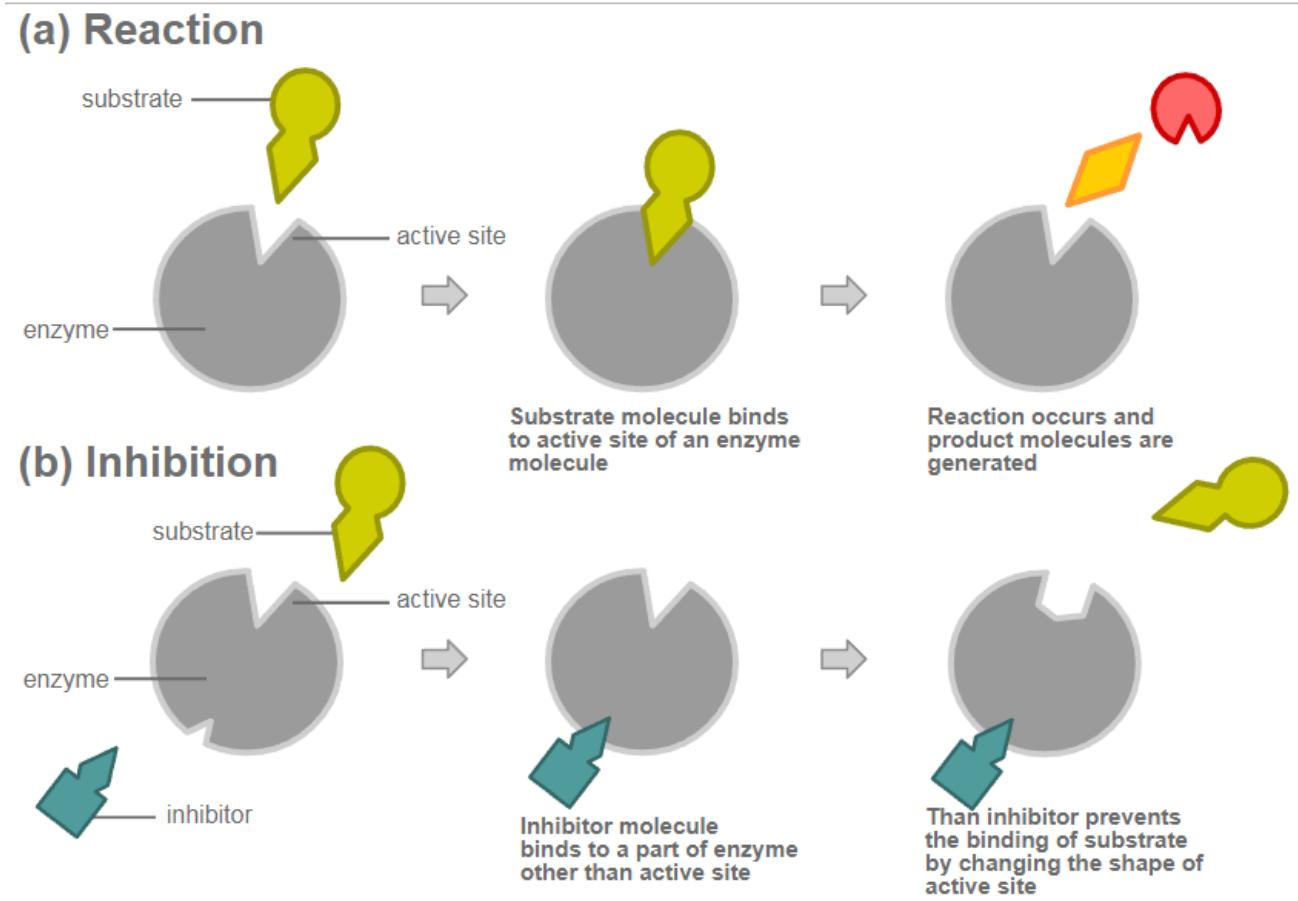
# Effect of increasing substrate concentration on competitive inhibition




- The graph shows the effect of increasing substrate concentration on rate of reaction for a limited mass of enzyme affected by a limited mass of inhibitor.
- On the next slide, there is a detailed description of what is occurring in this graph…….

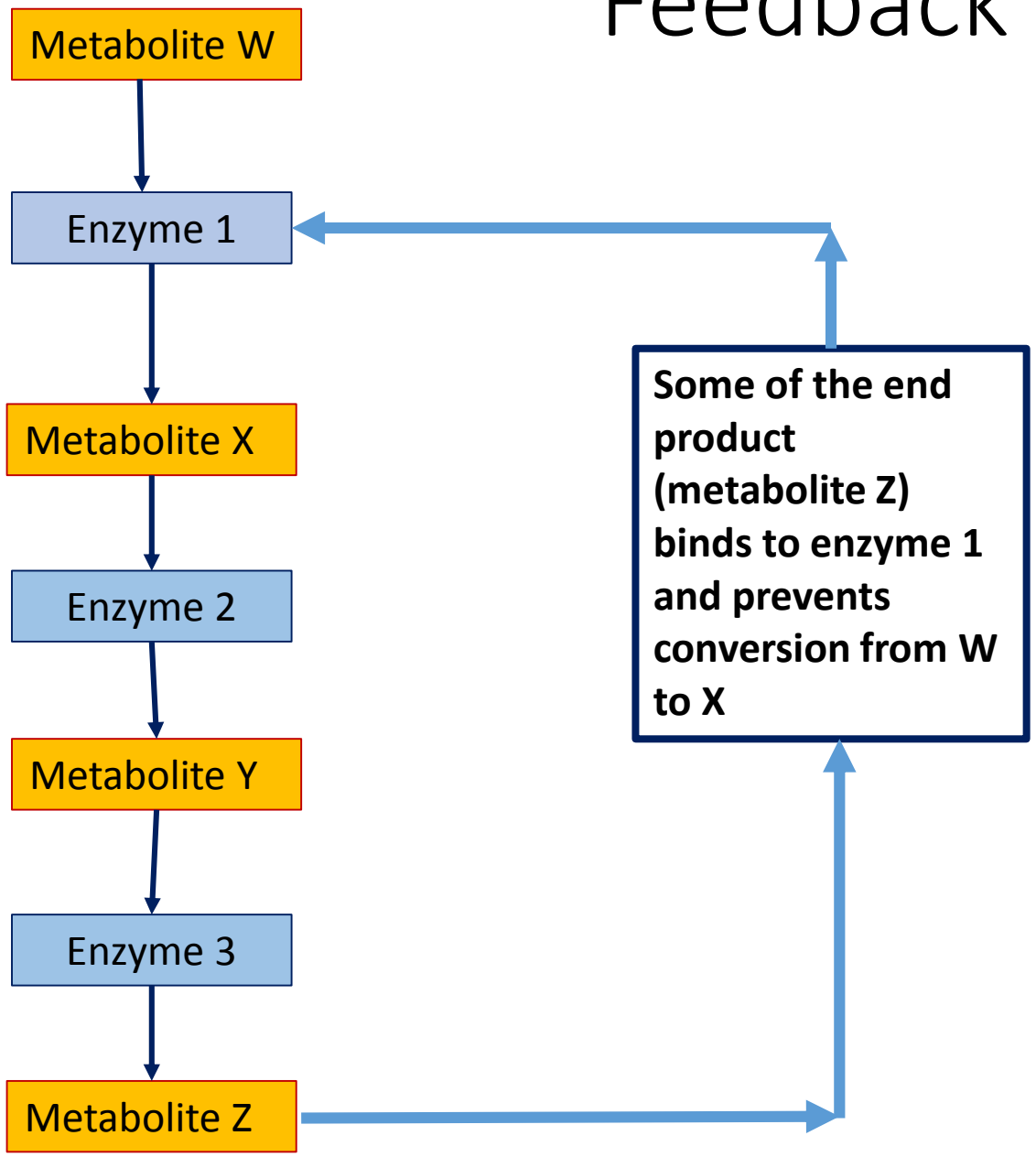
- The line in the graph labelled ‘without inhibitor’ shows that the increase in the substrate concentration brings about an increase in reaction rate, until a point is reached where all active sites on the enzyme molecules are occupied and then the graph levels off.
- The line in the graph labelled ‘competitive inhibitor’ shows an increase in the substrate concentration, which in turn brings about an increase in the reaction rate also. However, although the competitive inhibitor is competing for, and occupying some of the enzymes active sites, the true substrate is also occupying some of the sites.
- As the substrate molecules increase in concentration and outnumber those of the competitive inhibitor, more sites become occupied by the true substrates and not the inhibitor molecules.
- The reaction rate will continue to increase until all the active sites are occupied.
- Investigation: Page 93 – Inhibition of β-galactosidase by galactose.

# Non-competitive Inhibition




- Non-competitive inhibitors are molecules with a different structure from the substrate molecule.
- They do not fit into the active site of the enzyme but bind to another part of the enzyme molecule.
- This changes the shape of the active site, so that it can no longer combine with the substrate molecule.
- Non-competitive inhibition cannot be reversed by increasing substrate concentration. It has a permanent effect.

# Feedback Inhibition




- Feedback inhibition occurs when the end product in the metabolic pathway reaches a critical concentration.
- The end-product then inhibits an earlier enzyme, blocking the pathway, and so prevents further synthesis of the end-product.
- **Investigate on page 95: Phenolphthalein Phosphate & Phosphatase experiment.**

# Summary

1. Some metabolic reactions are reversible and the presence of a substrate or the removal of a product will drive a sequence of reactions in a particular direction.
2. Competitive inhibitors bind at the active site preventing the substrate from binding. Competitive inhibition can be reversed by increasing substrate concentration.
3. Non-competitive inhibitors bind away from the active site but change the shape of the active site preventing the substrate from binding. Non-competitive inhibition cannot be reversed by increasing substrate concentration.
4. Feedback inhibition occurs when the end product in the metabolic pathway reaches a critical concentration. The end-product then inhibits an earlier enzyme, blocking the pathway, and so prevents further synthesis of the end-product.