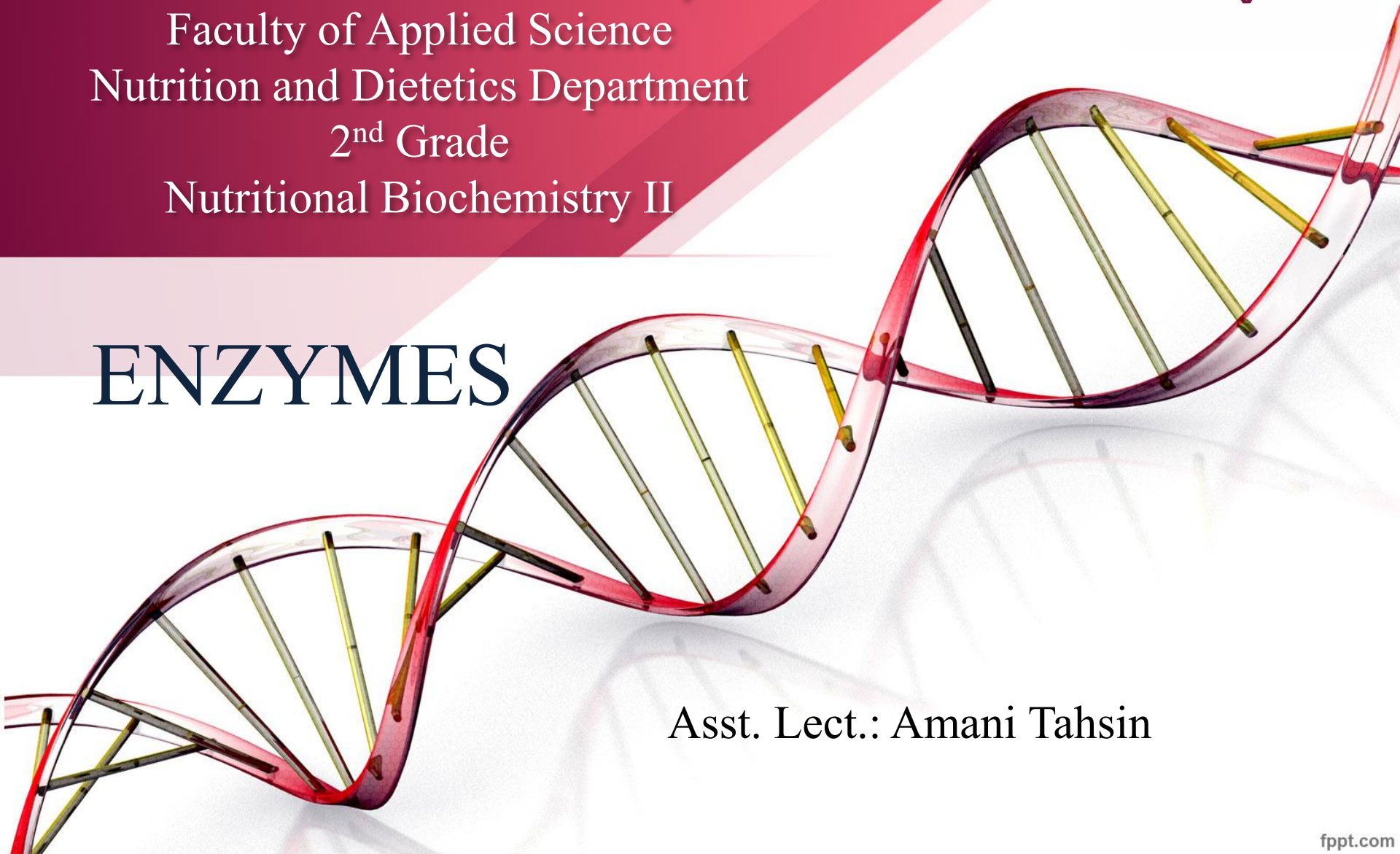
Tishk International University
Faculty of Applied Science
Nutrition and Dietetics Department
2nd Grade
Nutritional Biochemistry II

ENZYMES



Asst. Lect.: Amani Tahsin

Objectives

- Inhibition of Enzyme activity
- Regulation of Enzyme activity
- Enzymes in clinical diagnosis

Inhibitors

Any substance that can decrease the velocity of an enzyme-catalyzed reaction is called an *inhibitor*.

- Usually specific and work at low concentrations.
- Block the enzyme but they do not usually destroy it.
- Many drugs and poisons are inhibitors of enzymes in the nervous system.

➢ Inhibitors can be reversible or irreversible.

Irreversible Inhibitors

- Irreversible inhibitors bind to enzymes through covalent bonds.

(Combine with the functional groups of the amino acids in the active site, irreversibly)

e.g: Lead, forms covalent bonds with the sulfhydryl side chain of cysteine in proteins.

Ferrochelatase, an enzyme involved in heme synthesis, is irreversibly inhibited by lead.

Reversible Inhibitors

- Reversible inhibitors bind to enzymes through non-covalent bonds.

- Thus, dilution of the enzyme-inhibitor complex results in dissociation of the reversibly bound inhibitor and recovery of the enzyme activity.

The effect of enzyme inhibition

Commonly encountered types of inhibition:

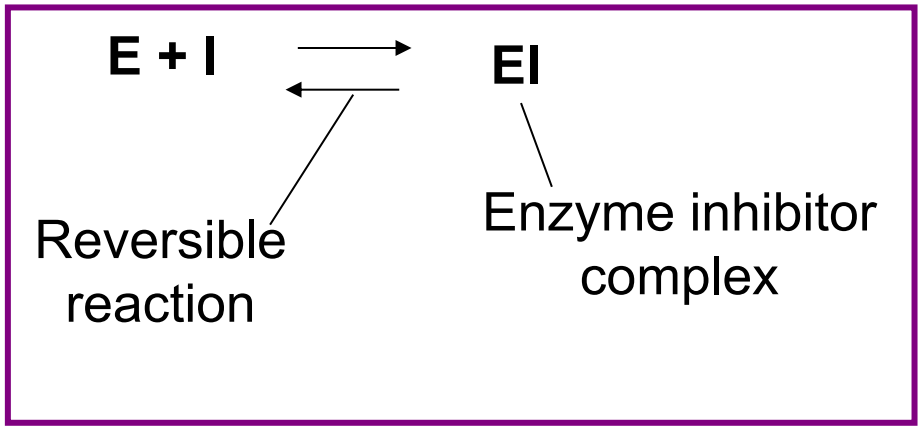
1) Competitive Inhibition
2) Non-competitive Inhibition

Competitive Inhibition

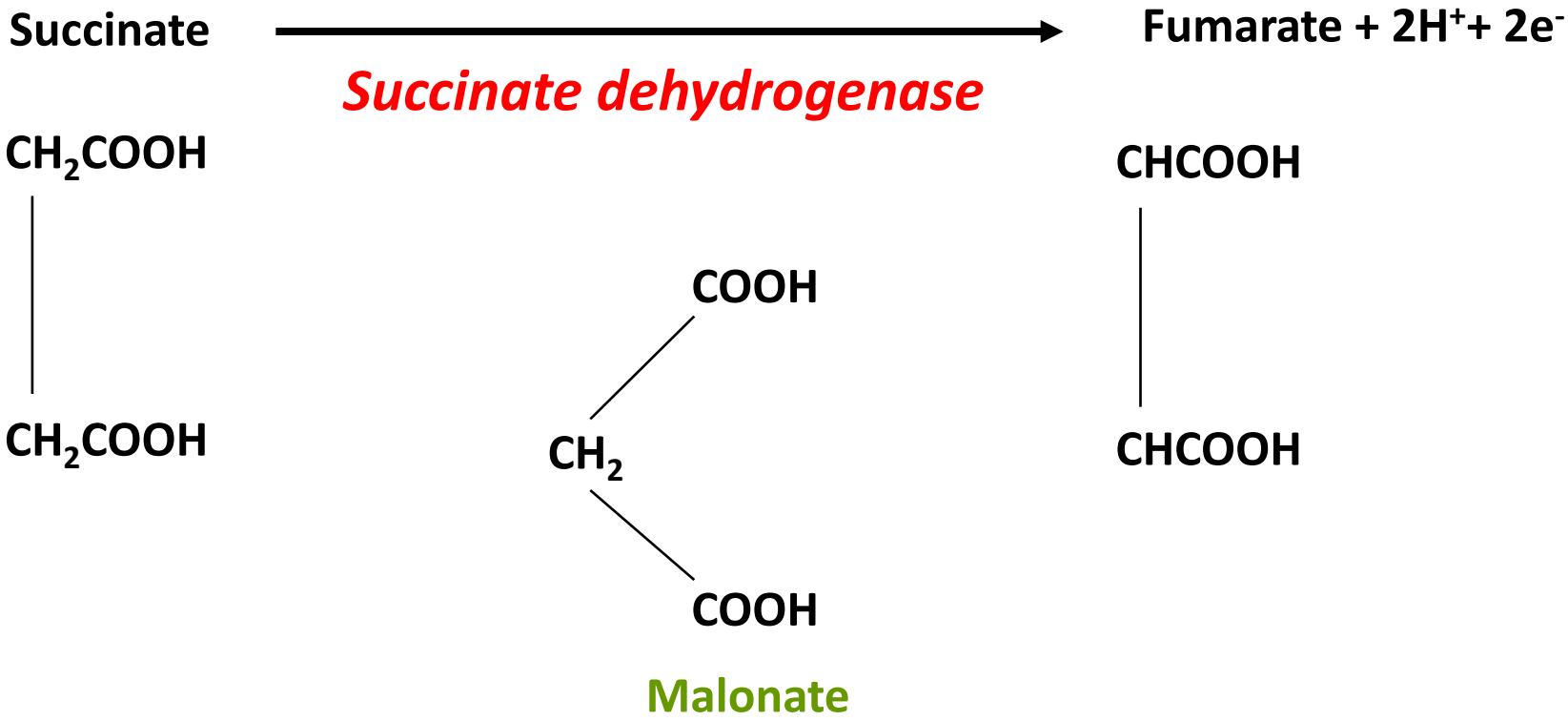
1) *Competitive:* These compete with the substrate molecules for the active site.

The inhibitor's action is proportional to its concentration

Resembles the substrate's structure closely.



The effect of enzyme inhibition



Competitive Inhibition

2) Non-competitive: Not influenced by the concentration of the substrate.

Inhibits by binding irreversibly to the enzyme but **not at the active site.**

Examples

- **Cyanide** combines with the iron in the enzyme's cytochrome oxidase
- Heavy metals, **Ag** or **Hg**, combine with **–SH** groups.

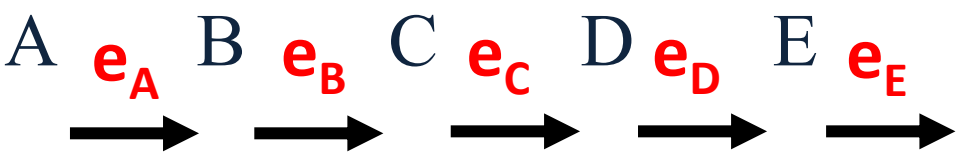
These can be removed by using a chelating agent such as EDTA.

Applications of inhibitors

- **Negative feedback**: end point or end product inhibition
- **Poisons** snake bite, plant alkaloids and nerve gases
- **Medicine** antibiotics, sulphonamides, sedatives and stimulants.

Enzyme pathways

Cell processes (e.g. respiration or photosynthesis) consist of series of pathways controlled by enzymes

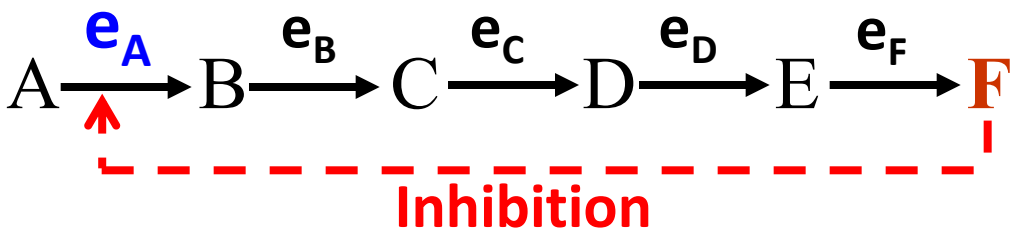


Each step is controlled by a different enzyme ($\mathbf{e_A}$, $\mathbf{e_B}$, $\mathbf{e_C}$ etc)

Possible because of enzyme specificity.

End point inhibition

- The first step (controlled by e_A) is often controlled by the end product (**F**)
- Therefore, **negative feedback** is possible



- The end products are controlling their own rate of production
- There is no build up of intermediates (B, C, D and E).

Example: Phosphofructokinase and ATP

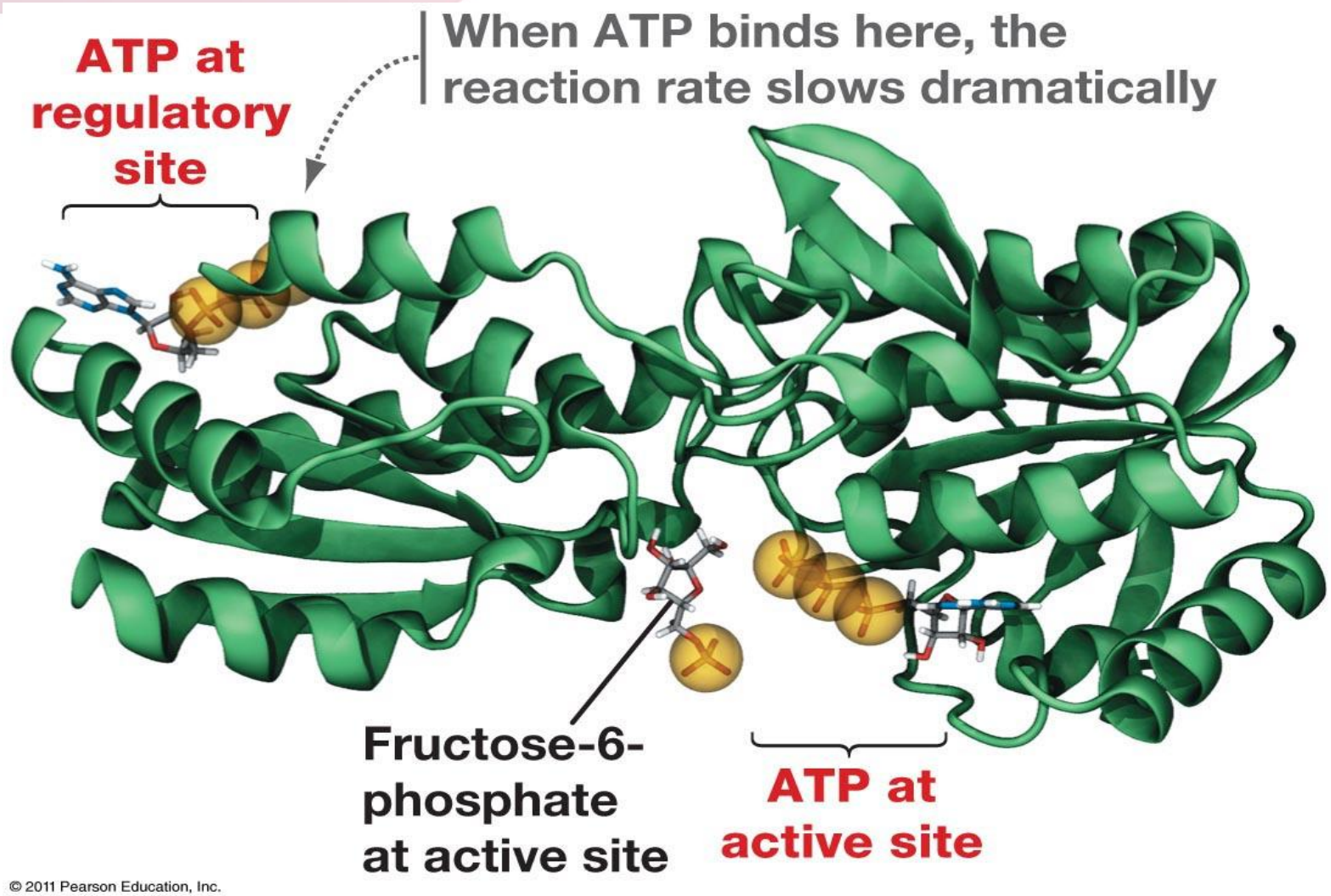
Substrate: Fructose-6-phosphate

Reaction

fructose-6-phosphate + ATP → fructose-1,6-bisphosphate + ADP

phosphofructokinase

Phosphofructokinase

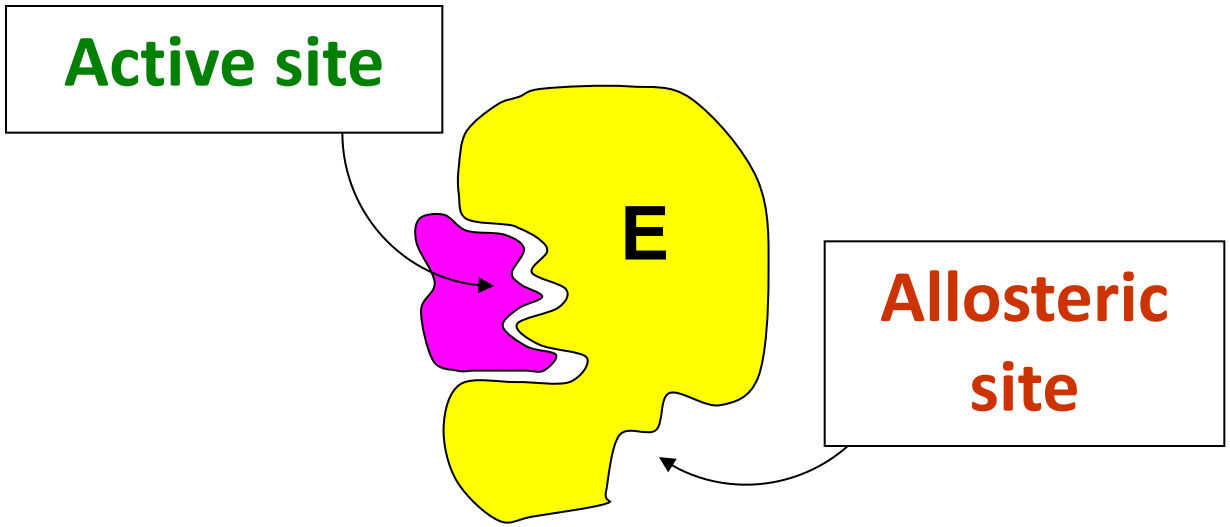


ATP is the end point

- This reaction near the beginning of the respiration pathway in cells
- The **end product** of respiration is **ATP**
- **If there is a lot of ATP** in the cell this enzyme is inhibited
- Respiration slows down and less ATP is produced
- As ATP is used up the inhibition stops and the reaction speeds up again.

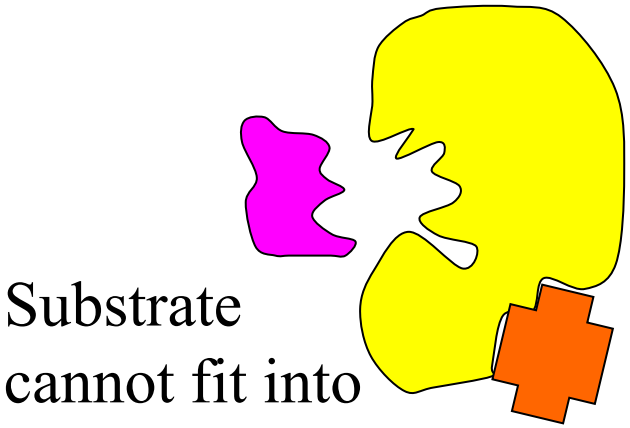
The switch: Allosteric inhibition

Allosteric means **“other site”**

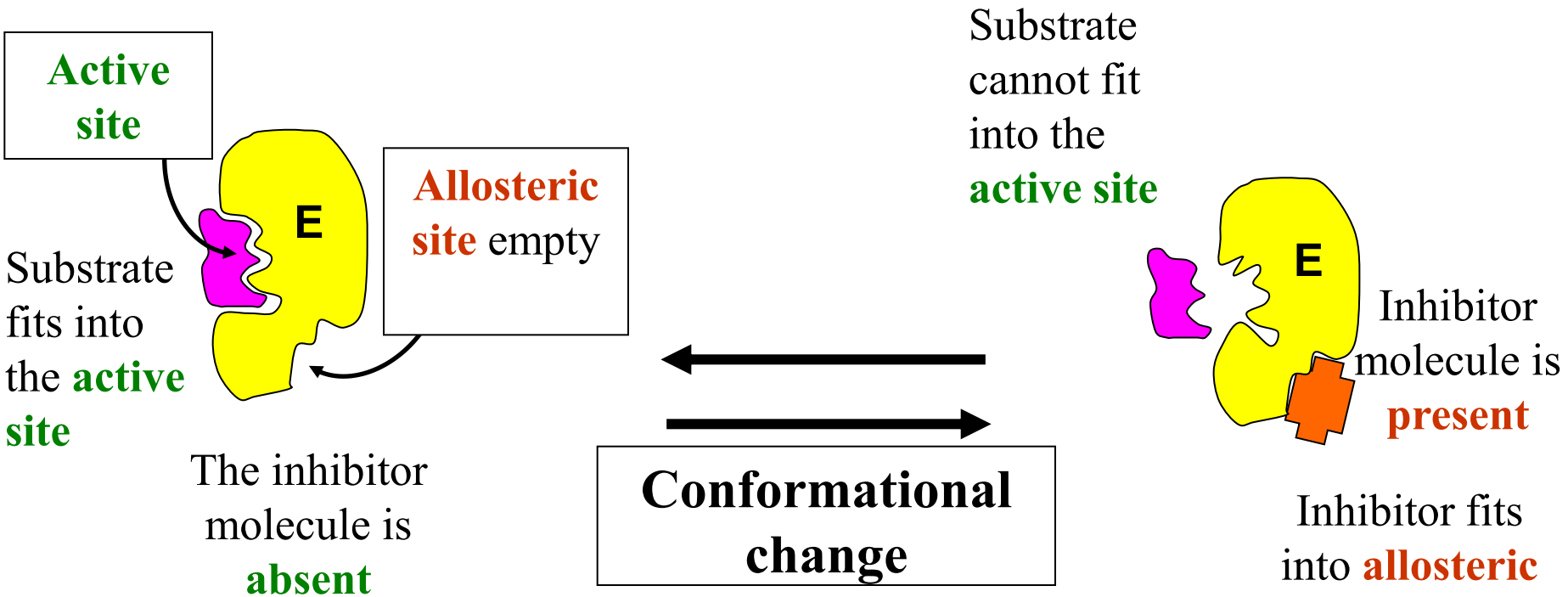


Switching off

- These enzymes have **two receptor sites**
- One site fits the substrate like other enzymes
- The other site fits an inhibitor molecule.



This allosteric site switches the enzyme on and off



A change in shape

- Inhibitor is present
  Fits into its site
  Conformational change in the enzyme molecule
- The enzyme's molecular shape changes
- The **active site** of the substrate changes
- The substrate cannot bind with the enzyme.

Negative feedback is achieved

- The reaction slows down
- **Not** competitive inhibition but it is reversible
- Inhibitor concentration diminishes
  Enzyme's conformation changes back to its active form
- The reaction speeds up again.

Summary

Competitive

- Inhibits the enzyme activity
- Increasing the inhibitor concentration increases the effect
- Inhibitor competes with the substrate at the active site (similar molecule)
- Active site stays the same

Non-competitive

- Inhibits the enzyme activity
- Changing the concentration of inhibitor does not influence the effect
- Inhibitor does not bind at the active site
- Active site may change shape (e.g. allosteric inhibition)