Enzymes

CC-9
UNIT-3

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Enzymes

- Like a catalyst, they increase the rate of biological reactions (10^6 to 10^{12} times faster).
- But, they are not changed at the end of the reaction.
- They are made of proteins.
- Lower the activation energy for the reaction.
- Less energy is required to convert reactants to products.

Enzymes

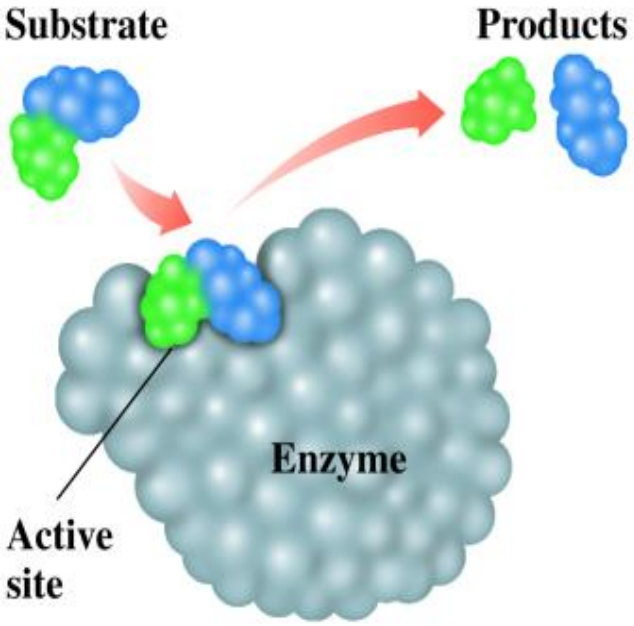
-**Most of enzymes are globular proteins** (water soluble).

<u>Enzymes are proteins</u>.

Proteins are polypeptides. They are long chains of amino acids.

The number, type, and sequence of amino acids determines a protein's shape.

So, what makes each enzyme different (i.e.: the active sites different) are the amino acids that make up each enzyme.



- **Most of enzymes are specific.**

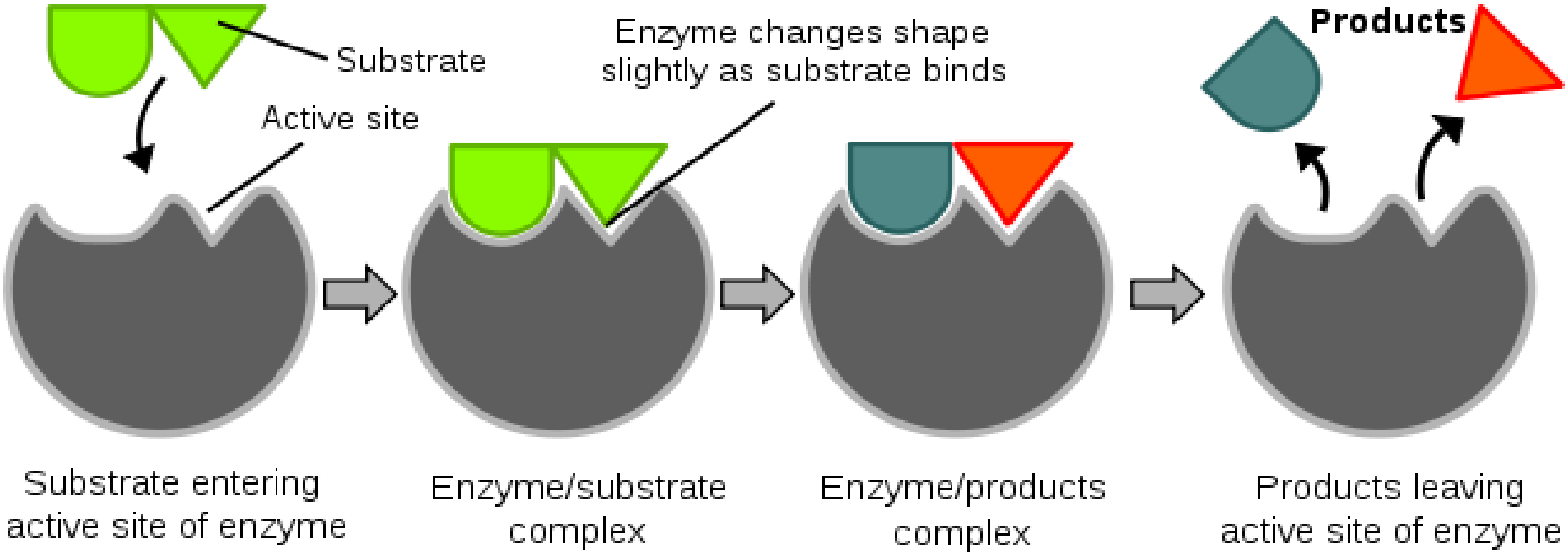
(Trypsin: cleaves the peptide bonds of proteins)

- **Some enzymes are localized according to need.**

(digestive enzymes: stomach)

Enzymes

- Used only temporarily
- Re-used again for the same reaction with other molecules
- Very little enzyme needed to help in many reactions

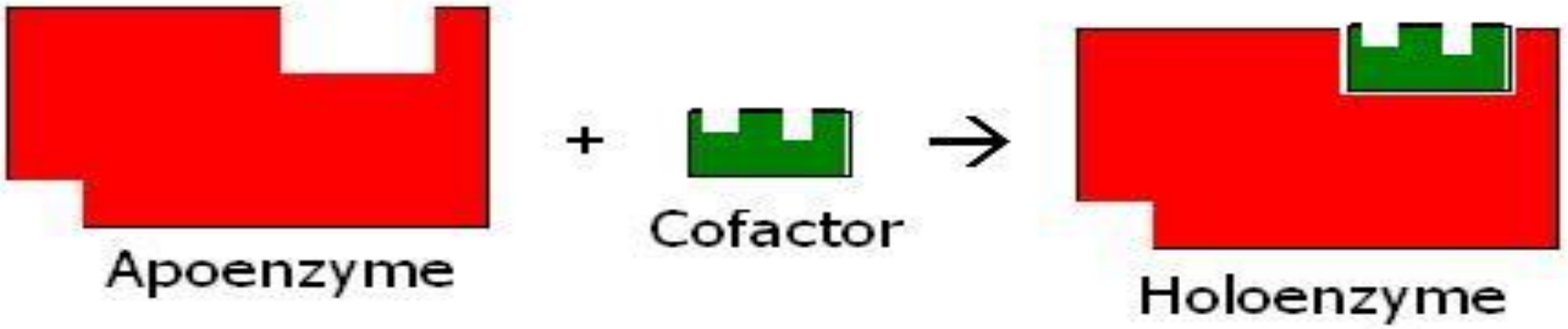


Parts of Enzyme complex

- **Many enzymes require the presence of small, nonprotein units or cofactors to carry out their particular reaction.**
- **Cofactors may be either one or more inorganic ions, such as Zn^{++} or Fe^{++} or a complex organic molecule called a coenzyme.**
- **A metal or coenzyme that is covalently attached to the enzyme is called a prosthetic group (e.g., heme in hemoglobin;).**

Parts of Enzyme complex

- **A complete catalytically-active enzyme together with its coenzyme or metal ion is called a holoenzyme.**
- **The protein part of the enzyme on its own without its cofactor is termed an apoenzyme.**
- **Many coenzymes are derived from vitamin precursors which are often essential components of the organism's diet, thus giving rise to deficiency diseases when in inadequate supply.**

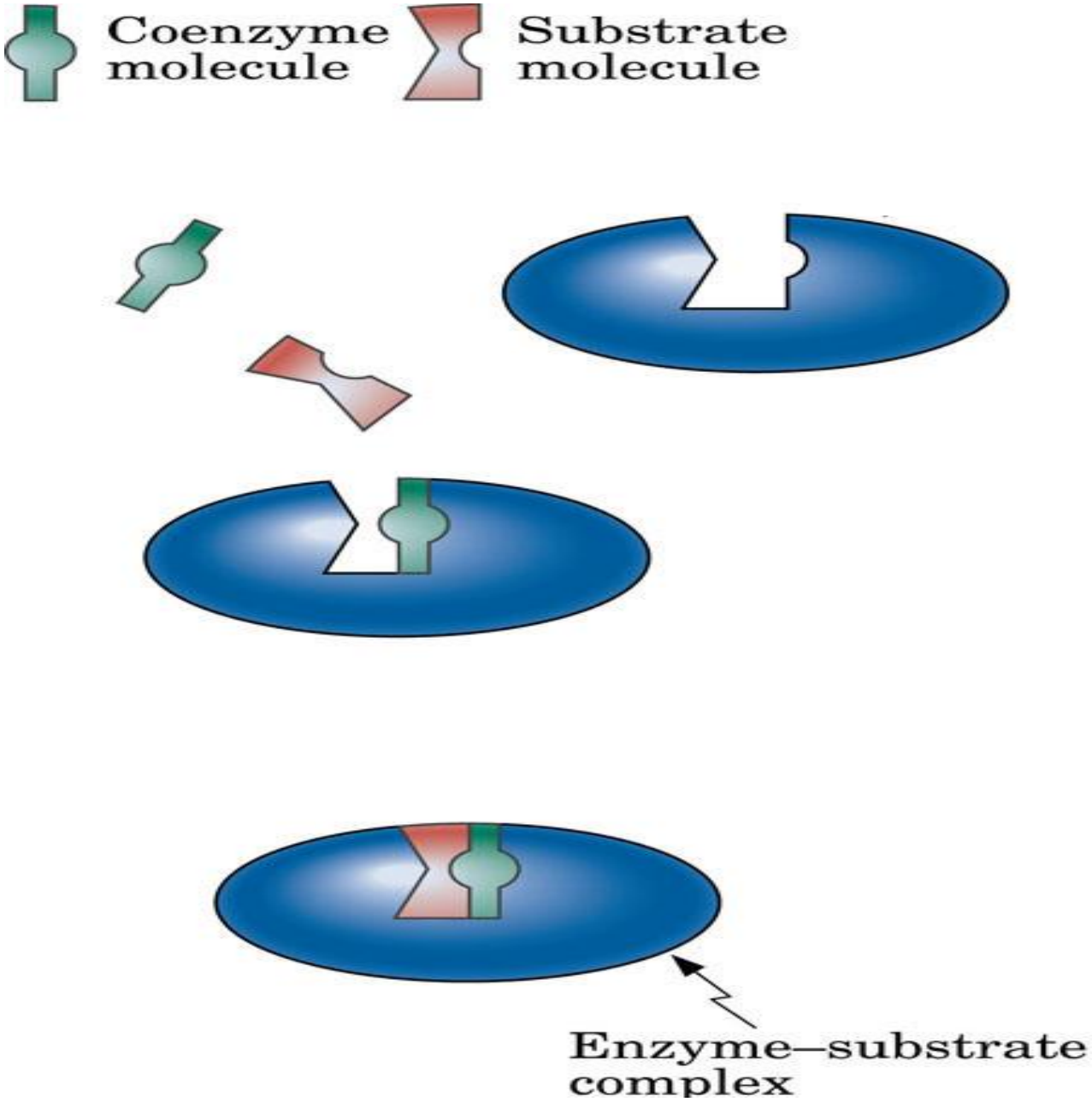


Active site

It is part of an enzyme where substrates bind and undergo a chemical reaction.

The active site of an enzyme is usually found in a cleft or pocket that is lined by amino acid residues (or nucleotides in ribozymes) that participates in recognition of the substrate.

Residues that directly participate in the catalytic reaction mechanism are called active site residues.

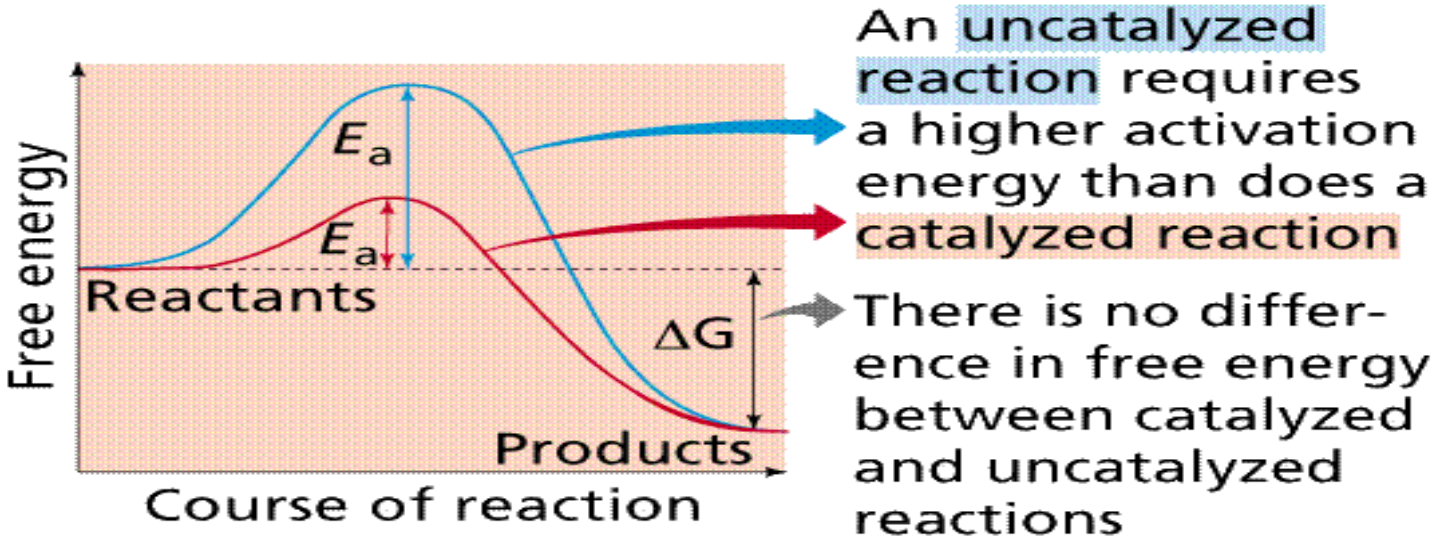

Coenzyme molecule
Substrate molecule
Enzyme–substrate complex

Mode of Action(Activation energy)

- A chemical reaction such as A → P takes place because a certain fraction of the substrate possesses enough energy to attain an activated condition called the transition state.
- The minimum energy required by the substrate to cross the energy barrier and there by form products is called as

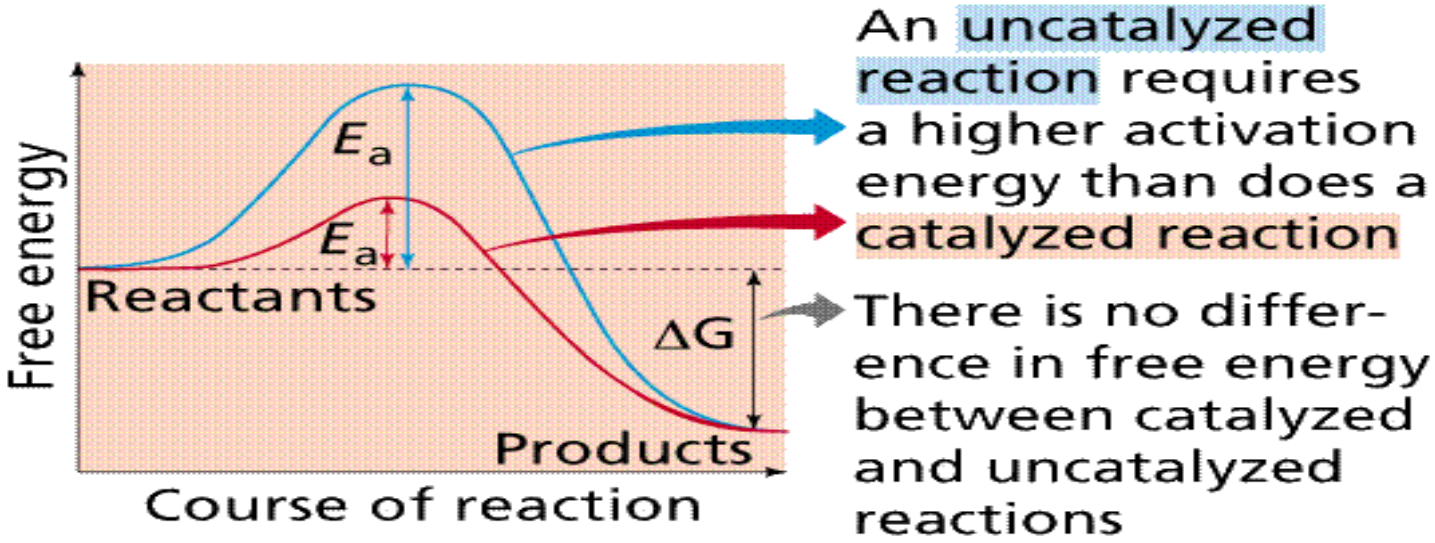
activation energy.

- Every reactant has the required amount of energy but during the course of time some energy is lost when the reactants undergo collisions in the form of heat.
- Hence, enzymes decrease the activation energy so that more number of reactants cross the energy barrier and products are formed.

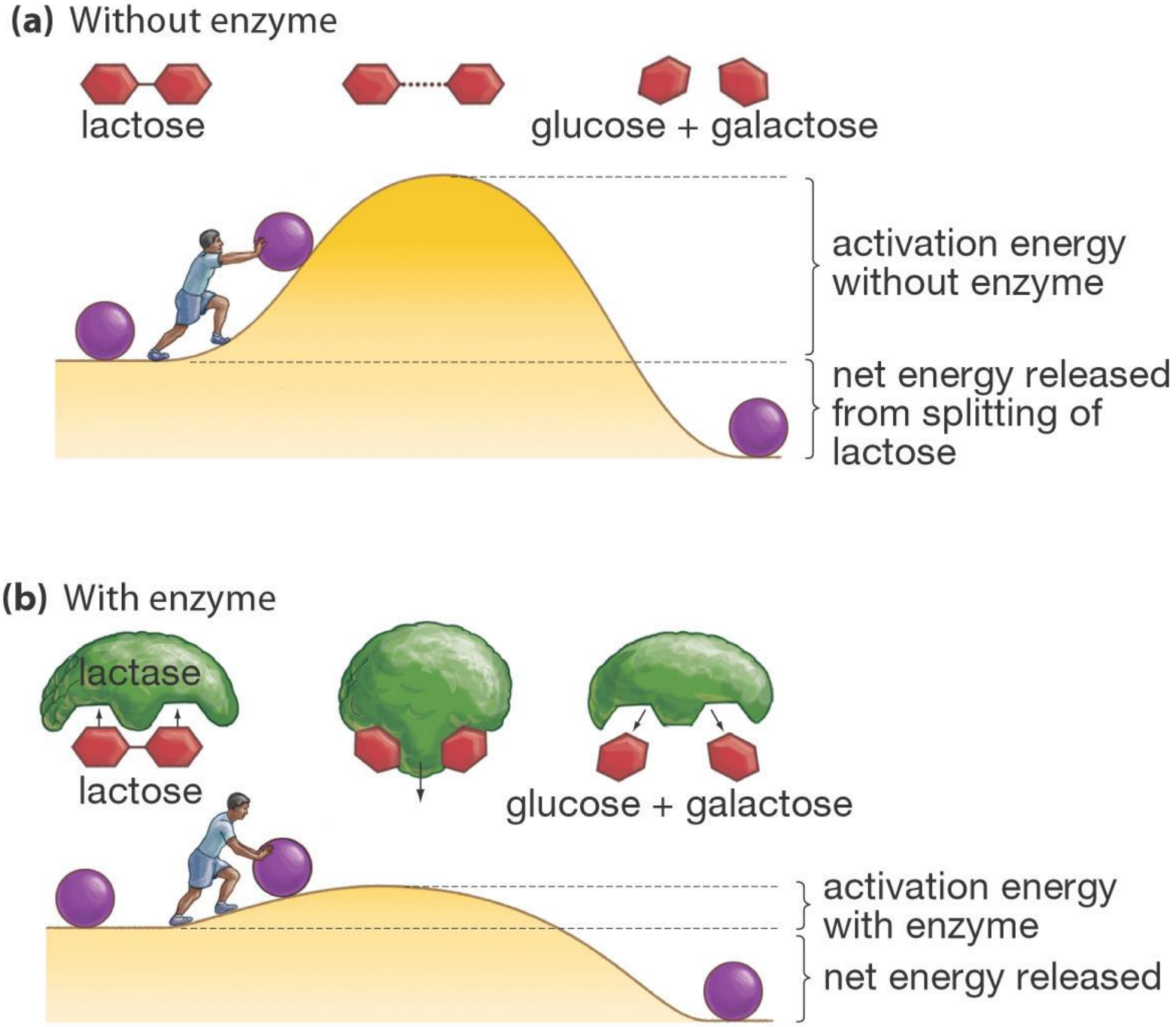


Mode of Action(Activation energy)

- The transition state of substrate is at the top of the energy barrier separating the reactants and products.
- The rate of a given chemical reaction is proportional to the concentration of this transition state species.
- The energy of activation is the amount of energy required to bring all the molecules in 1 mole of a substance at a given temperature to the transition state.
- Enzymes combine transiently with the substrate to produce a transition state intermediate having a lower energy of activation than the uncatalysed reaction. Thus they accelerate chemical reactions by lowering the energy of activation



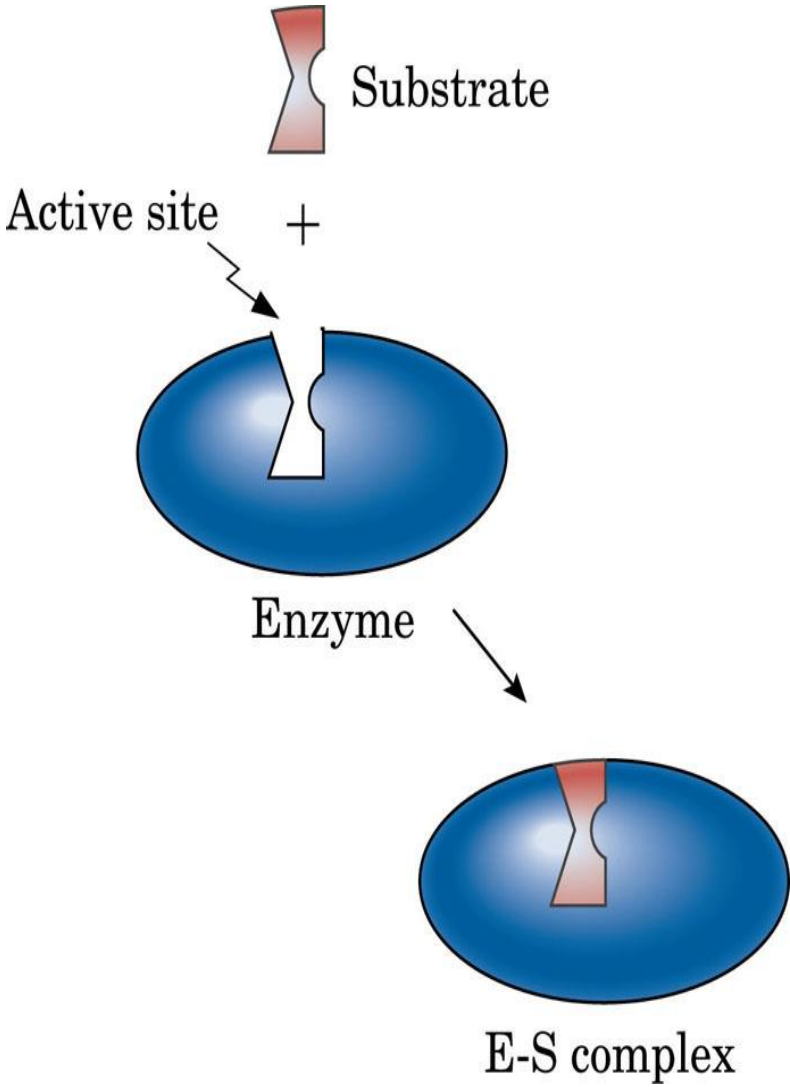
Enzymes Lower a Reaction's Activation Energy



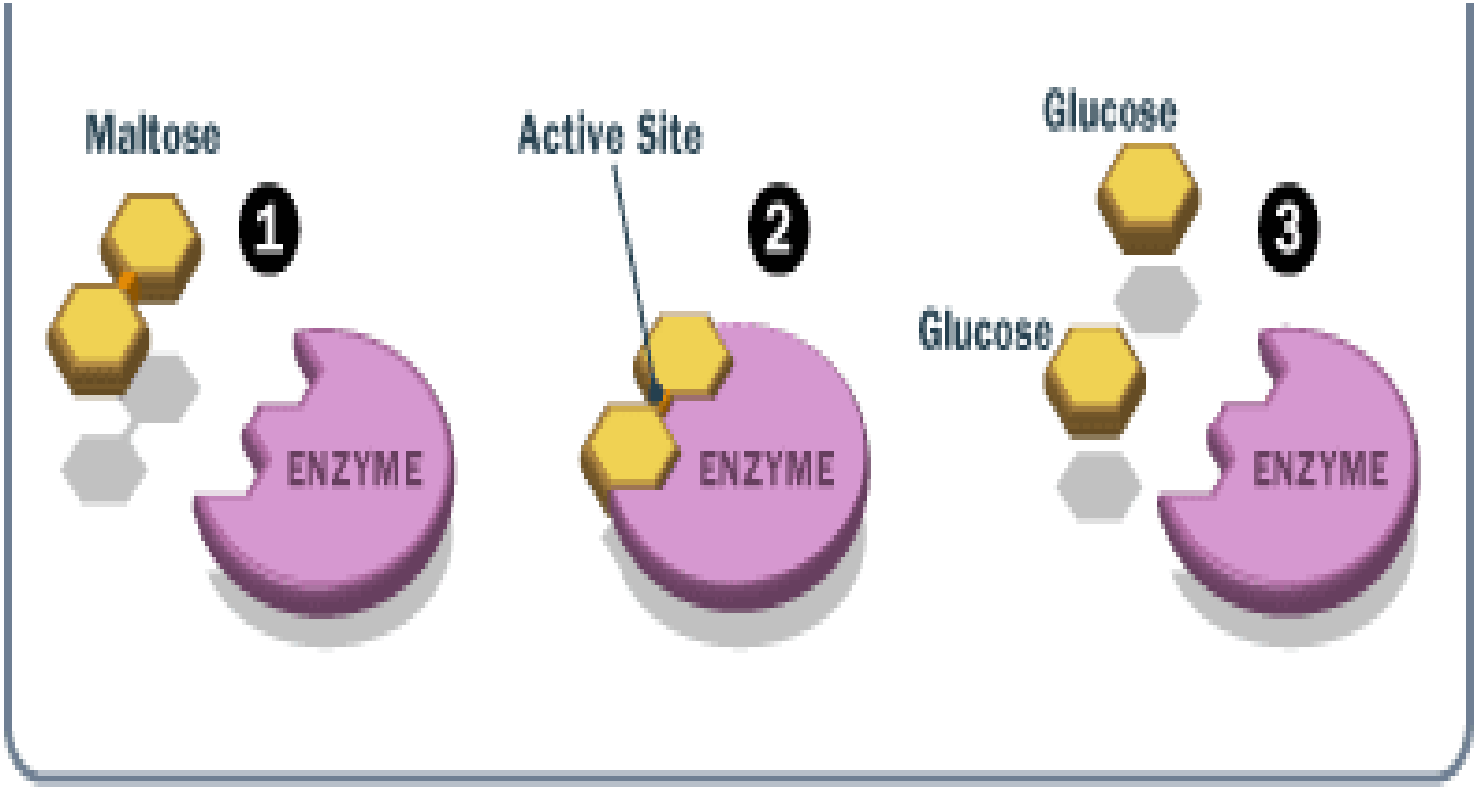
Mode of Action

lock-and-key model

- Proposed by Emil Fischer in 1894
- The shape of the substrate and the active site of the enzyme are thought to fit together like a key into its lock .
- The two shapes are considered as rigid and fixed, and perfectly complement each other when brought together in the right alignment.



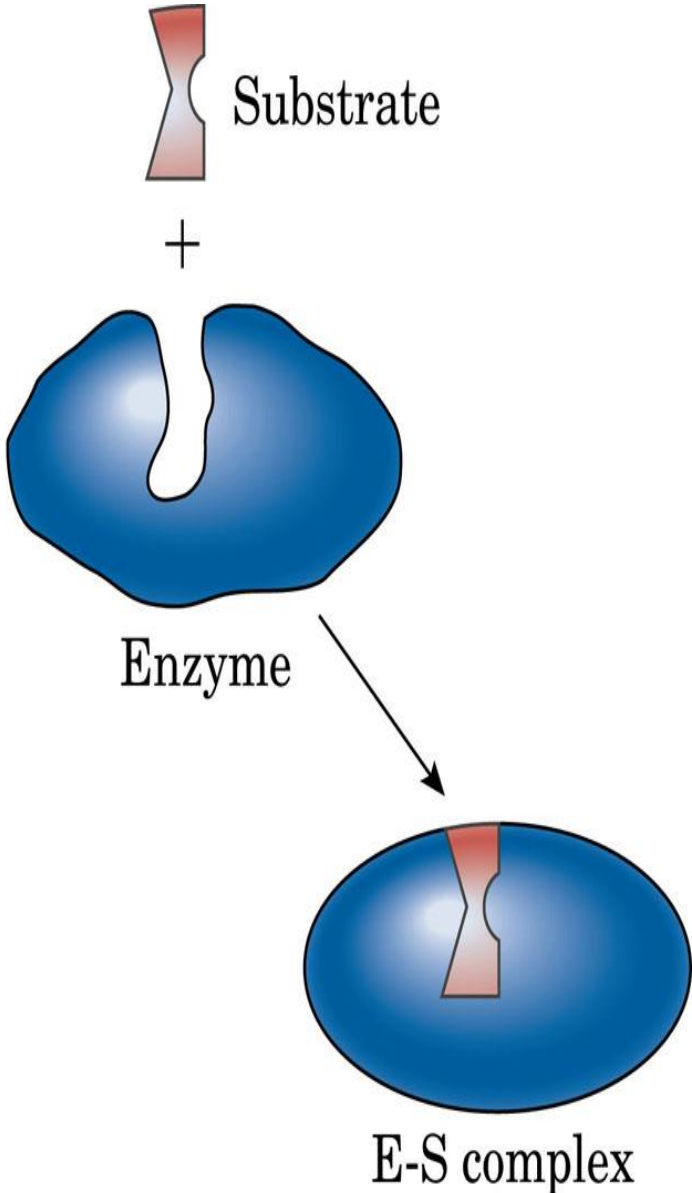
Example of lock-and-key model



Mode of Action

Induced-fit model

- Proposed in 1958 by Daniel E.Koshland, Jr.,
- The binding of substrate induces a conformational change in the active site of the enzyme.
- In addition, the enzyme may distort the substrate, forcing it into a conformation similar to that of the transition state.
- For example, the binding of glucose to hexokinase induces a conformational change in the structure of the enzyme such that the active site assumes a shape that is complementary to the substrate (glucose) only after it has bound to the enzyme.



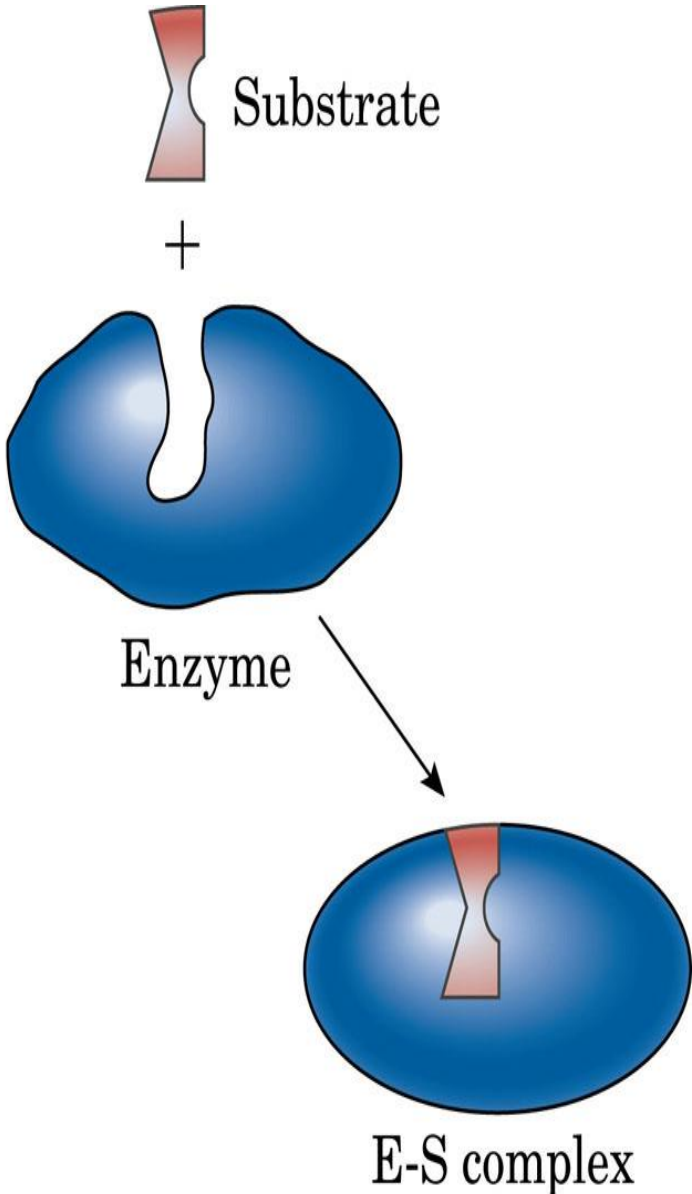
Induced-fit model

Enzyme structure is flexible, not rigid.

Enzyme and substrate adjust the shape of the active site to bind substrate.

The range of substrate specificity increases.

A different substrate could not induce these structural changes and no catalysis would occur.



Enzyme Inhibition

Introduction

- **Inhibitors are chemicals that reduce the rate of enzymatic reactions.**
- **The are usually specific and they work at low concentrations.**
- **They block the enzyme but they do not usually destroy it.**
- **Since blocking an enzyme's activity can kill a pathogen or correct a metabolic imbalance, *many drugs are enzyme inhibitors*.**

Types of Enzyme Inhibition

Types of Inhibition:

Competitive

Non-competitive

Un-competitive

Product (Feedback) Inhibition

Irreversible inhibition

Allosteric inhibition

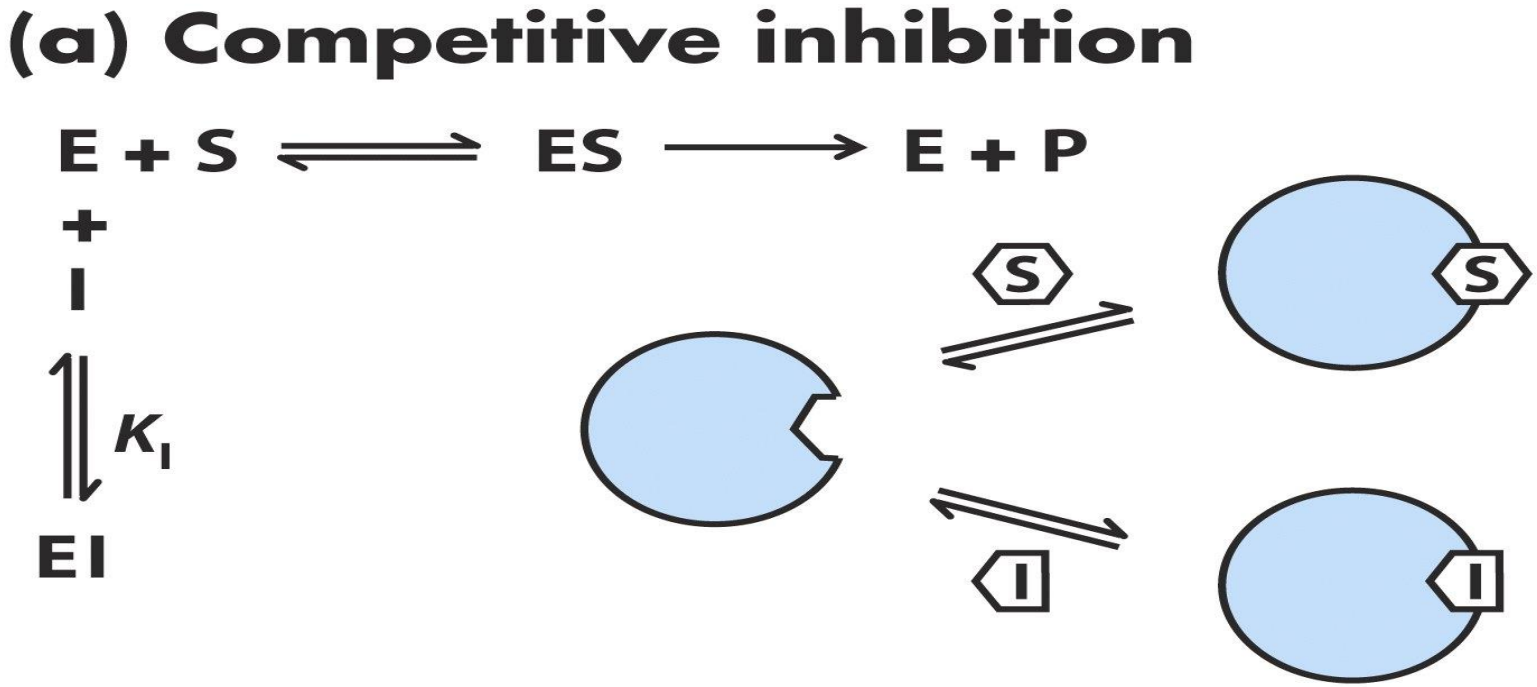
Competitive Inhibition

-Ic structrually resembles S, but is not an S

-Ic binds to free E at active site where S binds

-Ic competes with S for free E

-High S overcomes inhibition because all E is bound in ES complex; since rate [ES] and [ES] is max, rate is max; no EIc is present.



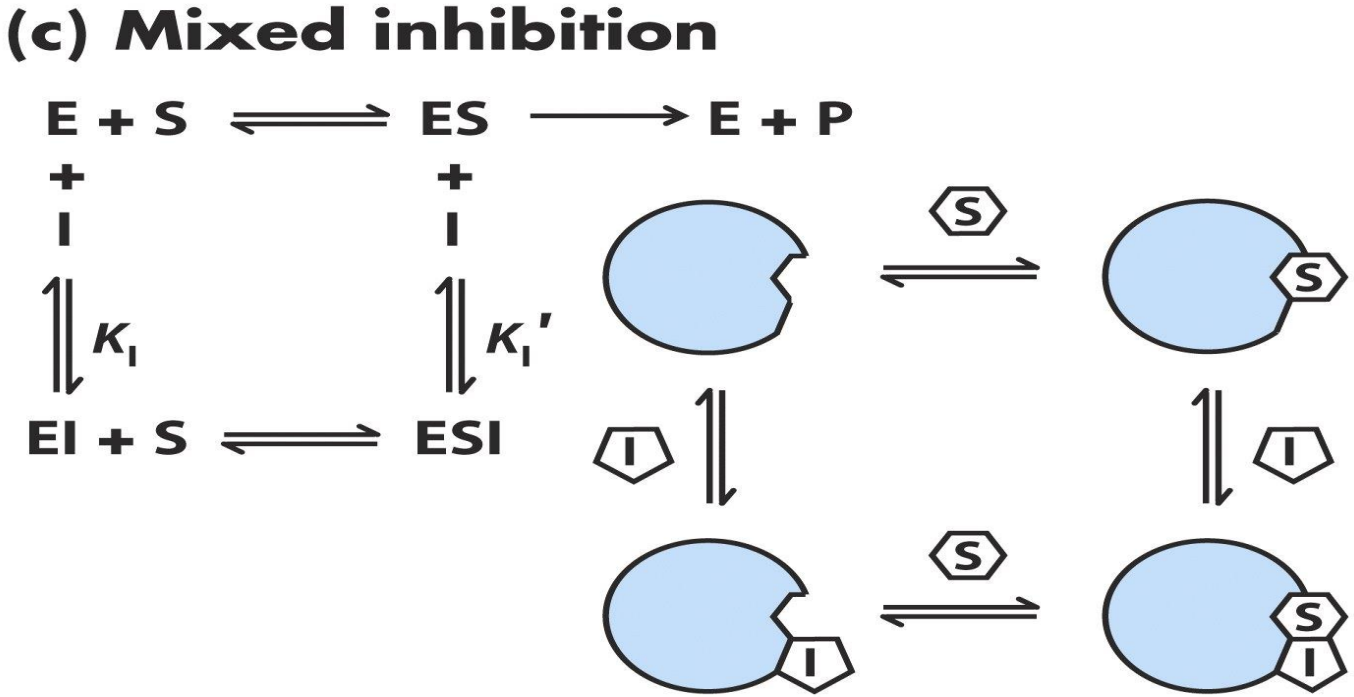
Non-competitive Inhibition

-Inc is not structurally similar to S; is not an S

-Inc binds to free E or ES at a site where S does not bind

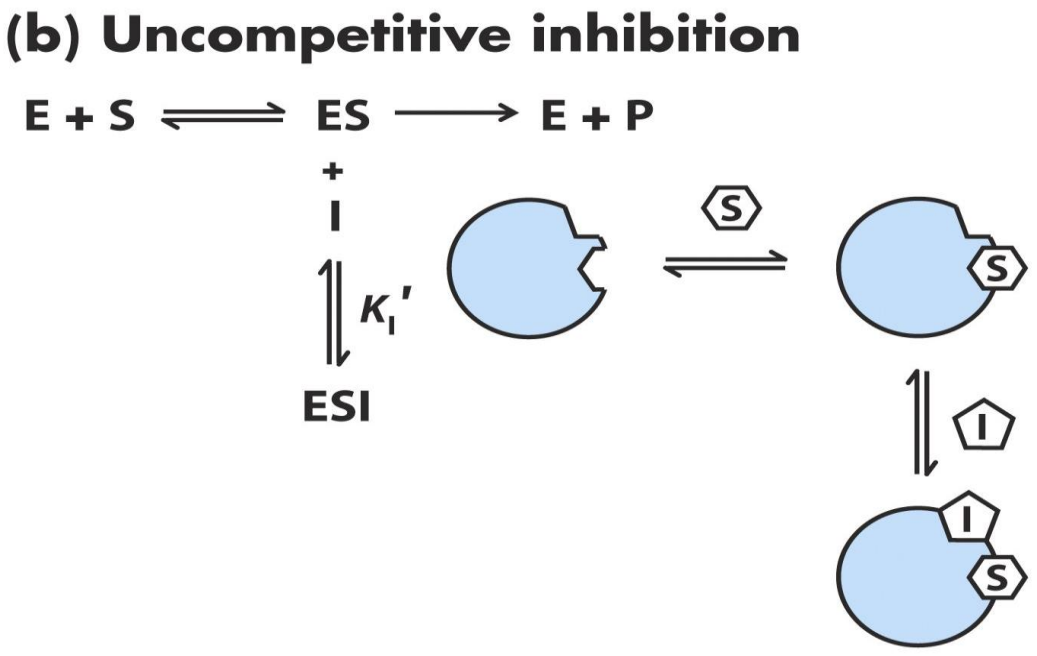
-Inc does NOT compete with S for free E

-High S cannot overcome inhibition because Inc binds to ES complex, inactivating it.



Un-competitive Inhibition

- This type of inhibition requires that one or more substrates bind to E before the inhibitor can bind
- Iu is not structurally similar to S; is not an S
- Iu binds to ES only; S opens up a site for I
- Iu binding site may be in active site but binding of I requires prior binding of S
- High S cannot overcome inhibition because presence of S is required to provide a site for binding of I



Product(Feedback) Inhibition

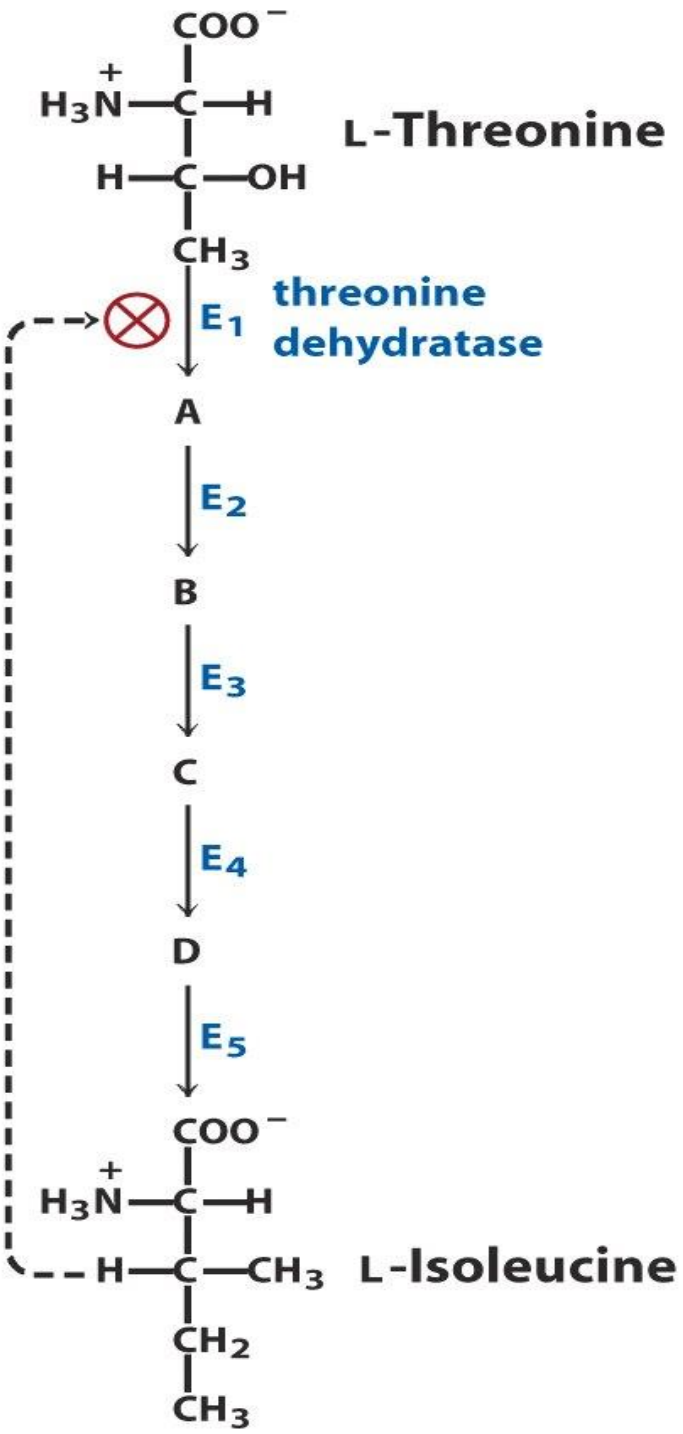
- Ip is structurally similar to S
- Ip binds to free E at active site where S binds
- Ip competes with S for free E
- At low S, resembles competitive inhibition
- However, at high S, the inhibition is not overcome
- because higher levels of P are generated which
- inhibit the enzyme
- **Example:** Phosphofructokinase and ATP
- **fructose-6-phosphate + ATP → fructose-1,6-bisphosphate + ADP**

Feedback Inhibition

An enzyme, early in the metabolic pathway, is inhibited by an end product.

Often takes place at the committed step of the pathway, the step which commits a metabolite to a pathway.

In most cases, the first enzyme of the multi-reaction pathway (catabolism, anabolism) is a regulatory enzyme to avoid unneeded accumulation of the intermediates.

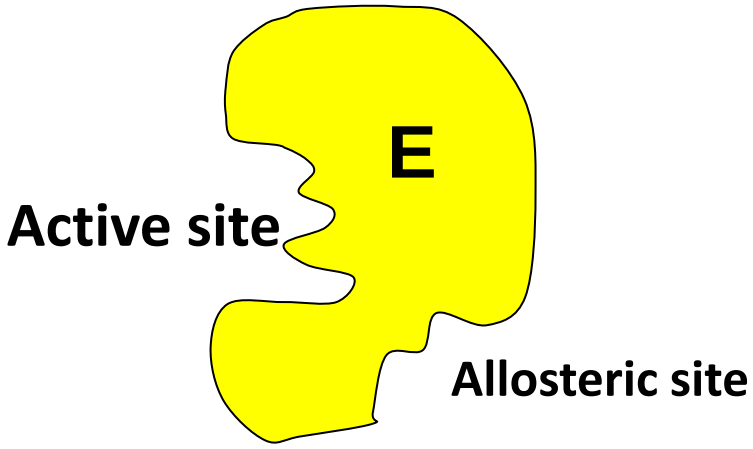


Irreversible inhibition

- **Inhibitors bind covalently with enzyme**
- **Cannot be removed by dialysis or other way**
- **Permanently modify the active site residues (functional group) which the enzyme become inactive.**

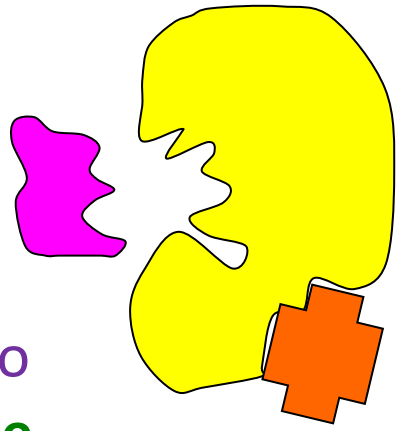
Allosteric inhibition

Allosteric means **“other site”**



Allosteric inhibition

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



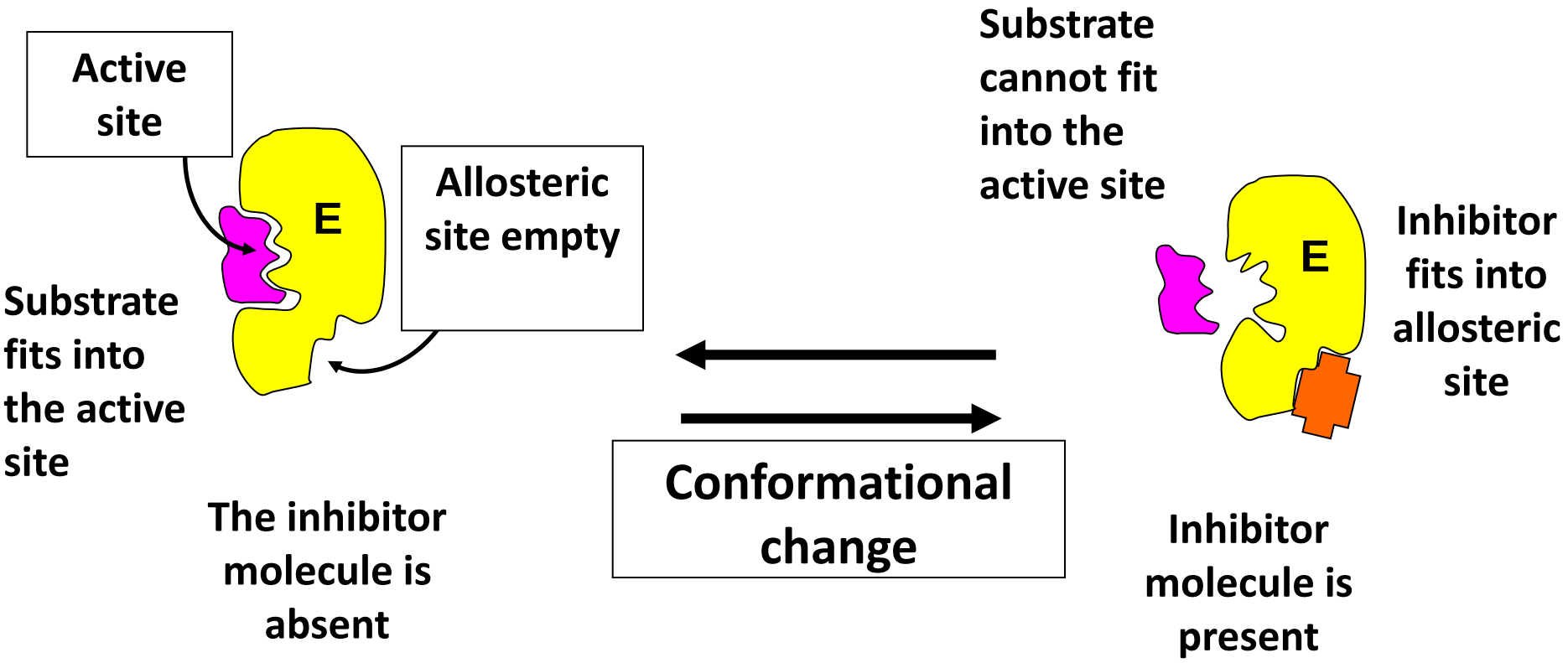
Inhibitor molecule

Substrate cannot fit into the **active site**

Inhibitor fits into **allosteric site**

Allosteric inhibition

This allosteric site switches the enzyme on and off



Allosteric inhibition

A change in shape

- Inhibitor, when 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.