ENZYMOLOGY – I

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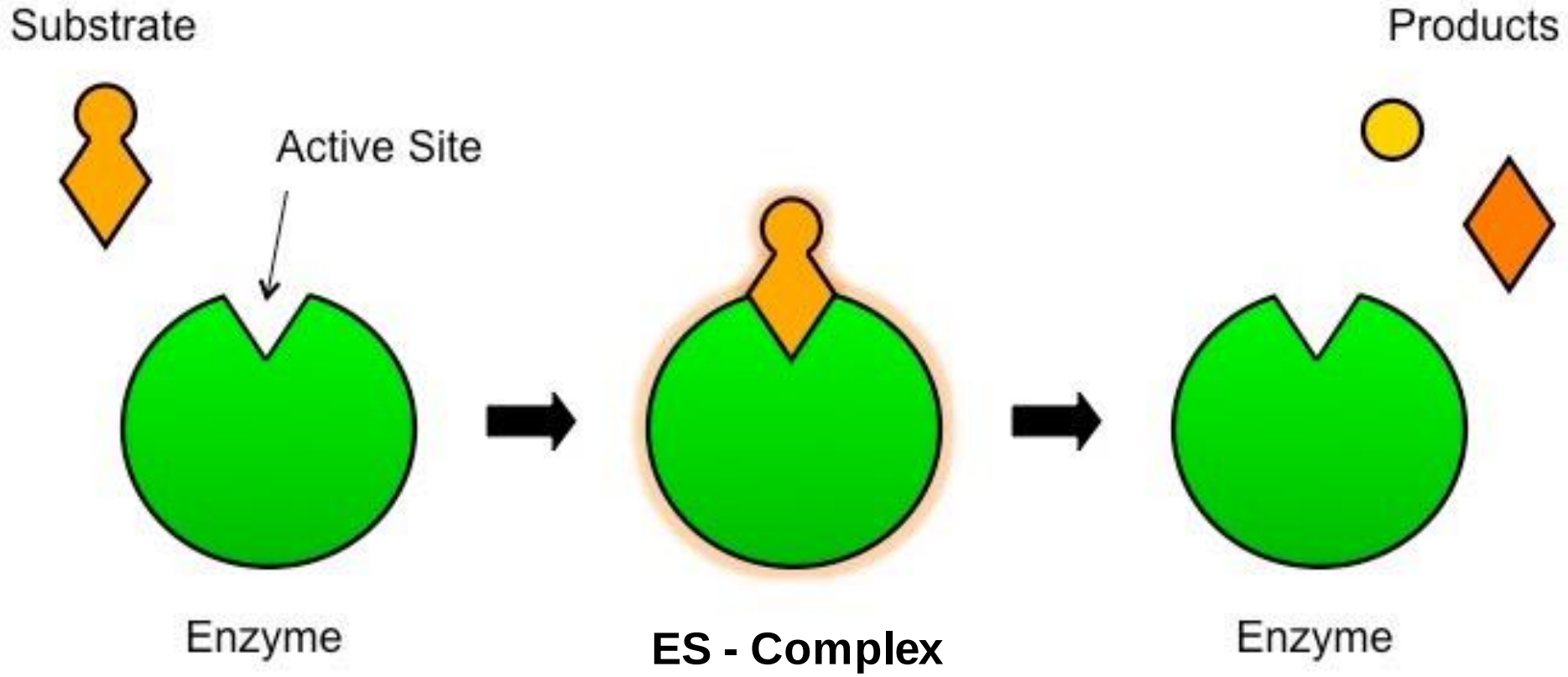

Substrate
Active Site
Products
Enzyme
ES - Complex
Enzyme

Enzymes- An introduction

- Biologic (organic catalysts) polymers that catalyze the chemical reactions.

- Enzymes are neither consumed nor permanently altered as a consequence of their participation in a reaction.

- With the exception of catalytic RNA molecules, or ribozymes, enzymes are proteins.

- In addition to being highly efficient, enzymes are also extremely selective catalysts.

-Thermolabile, site specific, with a high turn over number compared to the inorganic catalysts.

IMPORTANT NOTES

- Catalysts ?Thier job is to accelerate the reaction (and the Enzyme act like this in the reaction.)

- Simple protien: consists only of amino acids
- Conjucated protein: a protein that has carbs of lipids attached to it.

- Glycoprotein: Carbohydrates + proteins.
- Lipoprotein: Lipids + Proteins.
- Nucleoproteins: Nucleic acid + protein.

- Organic catalysts: proteins in nature (except ribosome)
- Inorganic catalysts: metal ion .(hydrogination)

- Hydrogination reaction: turning the unsaturated to saturated protien .By adding H+ to the douple bond to remove it.

IMPORTANT NOTES

We have 2 types of catalysts:

1. Organic catalyst: Enzyme
2. Inorganic catalysts: Metal ion. [Hydrogenation]

Which is better between these two? Organic Catalysts.

- Turn Over Number:

Number of substrate molecules that would be converted into products per unit time per enzyme unit.

- Enzyme (Organic) can convert 10^{12}-10^{6} of the substrate molecule

- Metal ion can convert only (.stcudorp otni tcudorp etartsbus (10^{3}

IMPORTANT NOTES

- Characteristics of the Enzyme:

1. All Enzymes are proteins in nature EXCEPT Ribosomes.

2. The enzymes are never consumed , Nor altered as a consequence of thier participation in a reaction .They go and participate on another reaction as soon as the 1st reaction is done.

3. Enzymes are considered as (Globular protein) which means they have a dynamic (Constant change) function and do have a short life spawn.

ENZYMES ARE SELECTIVE AND SPECIFIC

- Lactate Dehydrogenase enzyme is catalyzing oxidation of lactate into pyruvate.

- Some enzymes may participate into multiple reactions like Isocitrate dehydrogense:

Exist in krebs cycle
Causing oxidation of isocitrate to be converted into Alpha-ketoglutarate.

- Enzymes are site specific:

The enzymes acting on the cell membrane And Not acting on any other site of the cell.

- Every part of the cell has it's own Enzymes.

- Thermolabile (unstable when heated): except some types that can catalyze a reaction in very high tempreture. (Taq DNA Polymerase)

CHARACTERISTICS OF THE ENZYMES

- Enzymes are organocatalysts
- Proteins in nature except ribosomes
- Globular protein, Have tertiary and quaternary structure.
- Have high turn over number (highly efficient)
- Extremly selective catalysts
- Never consumed and non-permenantly altered
- Thermolabile
- Site specific
- Any increase or decrease in the tempreture will effect the enzymatic activity .Because heat would cause protein denaturation (loss of quaternary of tertiary structure.)

Nomenclature of enzymes

-In most cases, enzyme names end in –ase

-The common name for a hydrolase is derived from the substrate

Urea: remove -a, replace with **-ase** = urease

Lactose: remove **- ose**, replace with **- ase** = lactase

- Other enzymes are named for the substrate and the reaction catalyzed

Lactate dehydrogenase

Pyruvate decarboxylase

Nomenclature of Enzymes (cont).

- Some names are historical - no direct relationship to substrate or reaction type:

1. Catalase
2. Pepsin :in the stomach, it's main function is to act on the proteins during digestion. Doesn't act on the starch
3. Chymotrypsin
4. Trypsin

Classification of Enzymes

- Enzyme Commission (EC) – according to **International Union of Biochemistry and Molecular Biology (IUBMB)**

- Each enzyme was given 4 digit numbes [1.2.3.4]

1st one of the 6 major classes of enzyme activity

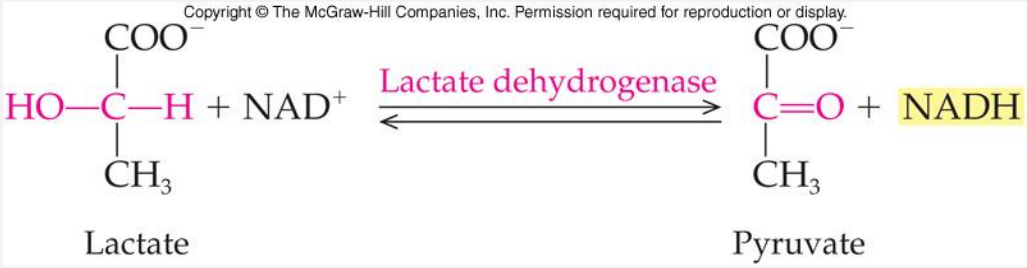
2nd the subclass (type of substrate or bond cleaved)

3rd the sub-subclass (group acted upon, cofactor required, etc...)

4th a serial number… (order in which enzyme was added to list)

1- Oxidoreductases (**EC.1**) catalyze redox reactions, such as (Alcohol dehydrogenase [EC 1.1.1.1])

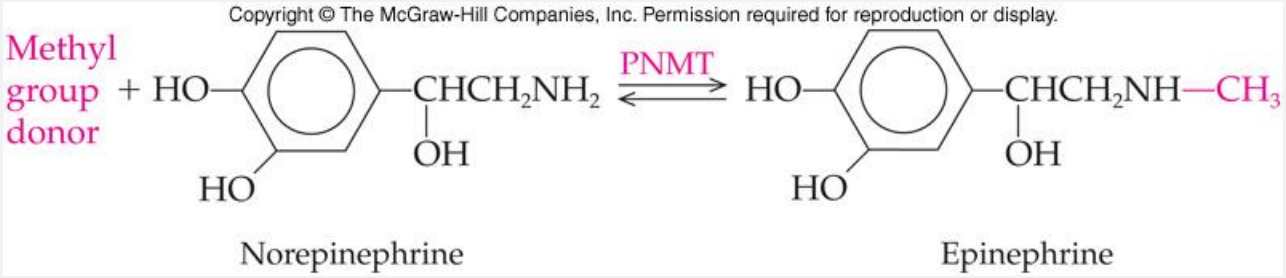
- Reductases
- Oxidases



2- Transferases (**EC.2**) transfer a group from one molecule to another, such as (Hexokinase [EC 2.7.1.2]) **Methyltransferase Enzyme**

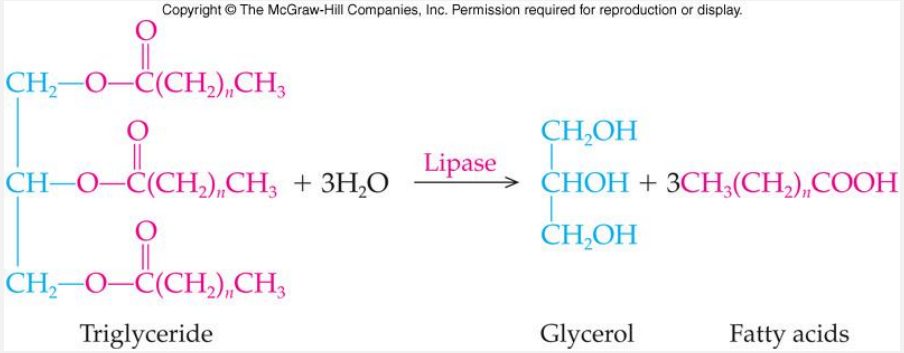
-Transaminases catalyze transfer of an amino group

- Kinases transfer a phosphate group



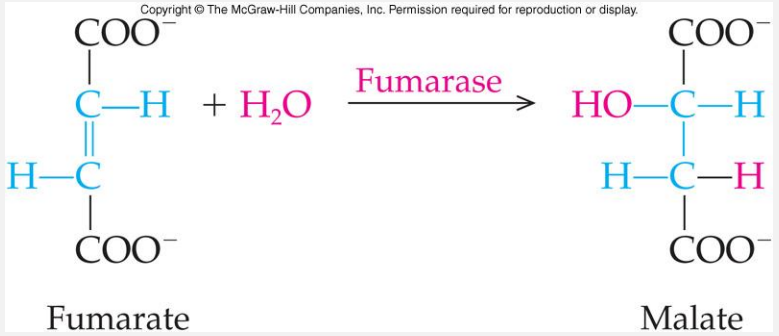
3- Hydrolases (**EC.3**) cleave bonds by adding water, such as
(Alkaline phosphatase [EC 3.1.3.1])

- Phosphatases
- Peptidases
- Lipases



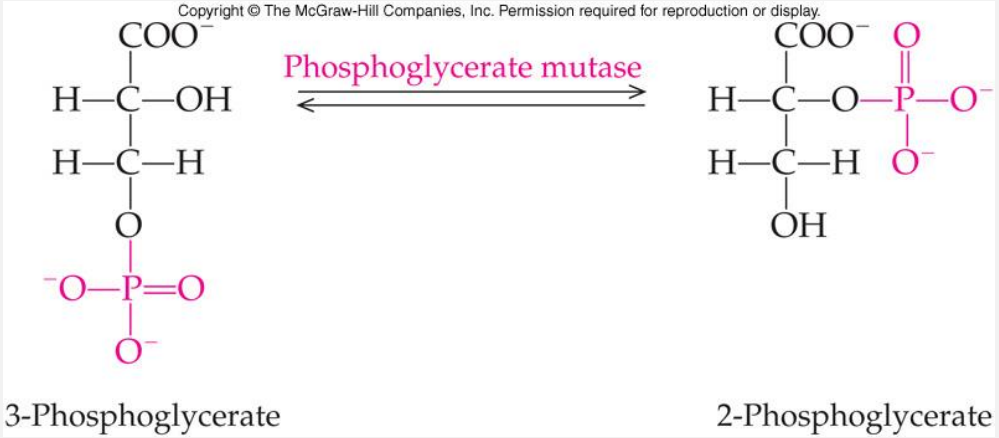
4- Lyases (**EC.4**) catalyze removal of groups to form double bonds or the reverse break double bonds, such as
(Pyruvate decarboxylase [EC 4.1.1.1])

- Decarboxylases
- Synthases

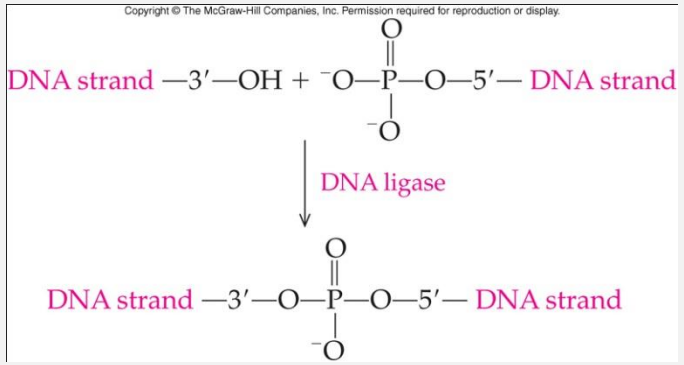


5- Isomerases (**EC.5**) catalyze intramolecular rearrangements, such as (Alanine racemase [EC 5.1.1.1])

- Epimerases
- Mutases



6- Ligases (**EC.6**) catalyze a reaction in which a C-C, C-S, C-O, or C-N bond is made or broken, such as (Isoleucine-tRNA ligase [EC 6.1.1.5])



Redox Reactions:

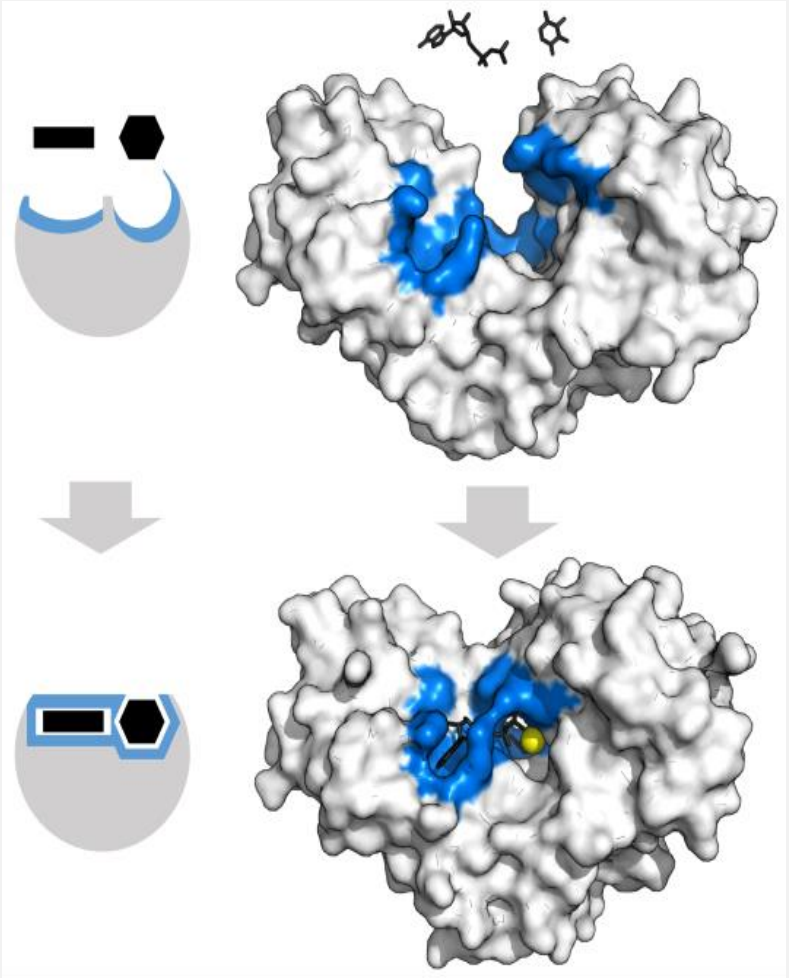
- It occurs in all the biological systems
- Oxidation never happen without reduction (and visa versa)
- Q (why Hydrogen isn’t allowed to be free intracellulary or extracellulary?
- Answer :PH intracellulary would be less than the PH in the blood , so it will be more acidic .And therefore it would affect the activity of the enzymes.

Active site

- Takes the form of a cleft or pocket
- Takes up a relatively small part of the total volume of an enzyme
- Substrates are bound to enzymes by multiple weak attractions
-The specificity of binding depends on the precisely defined arrangement of atoms in an active site

-The active sites of multimeric enzymes are located at the interface between subunits and recruit residues from more than one monomer

-Substrate: The substance which Enzyme works on to be converted Into products.



Active site:

- What are the character of the Active site?
- **Answer:** it allows the binding of the substrate to the enzyme.

- There should be specific reactive groups in the active site of the enzyme. Why ? To cause a reaction and to stabilize the substrate.

- Ionizaton of different groups to facilitate the interaction between the enzyme and the binding site of the substrate.

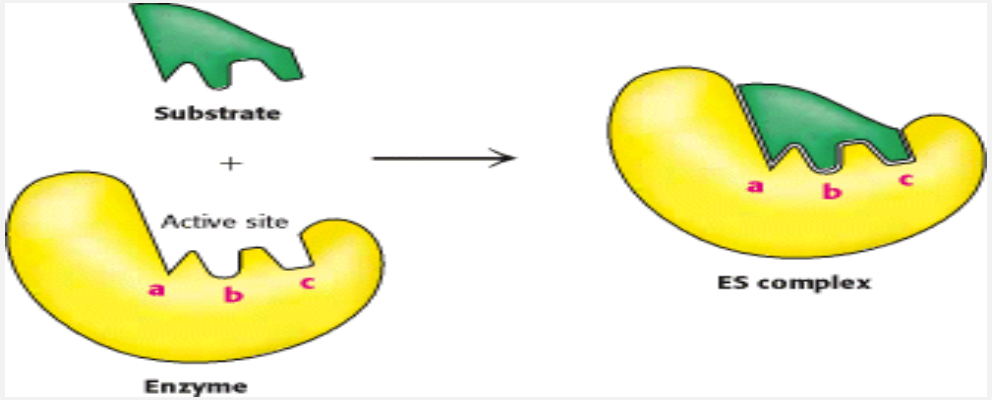
- Reactive groups in the active site:
  - Acidic A.A: Glutamate and Asparatate, they both give negative charge.
  - Basic A.A: Lysin, Histidine, Arginine.
  - Sulpha-hydric Containing A.A: Cystein.
  - Hydroxy containing A.A

Enzyme substrate binding

-Two models have been proposed to explain how an enzyme binds its substrate: the lock-and –key model and the induced-fit model.

- Lock-and-Key Model of Enzyme-Substrate Binding, in this model, the active site of the unbound enzyme is complementary in shape to the substrate.

-"lock and key model" **accounted for the exquisite specificity of enzyme-substrate interactions**, the implied rigidity of the enzyme's active site failed to account for the dynamic changes that accompany catalysis.

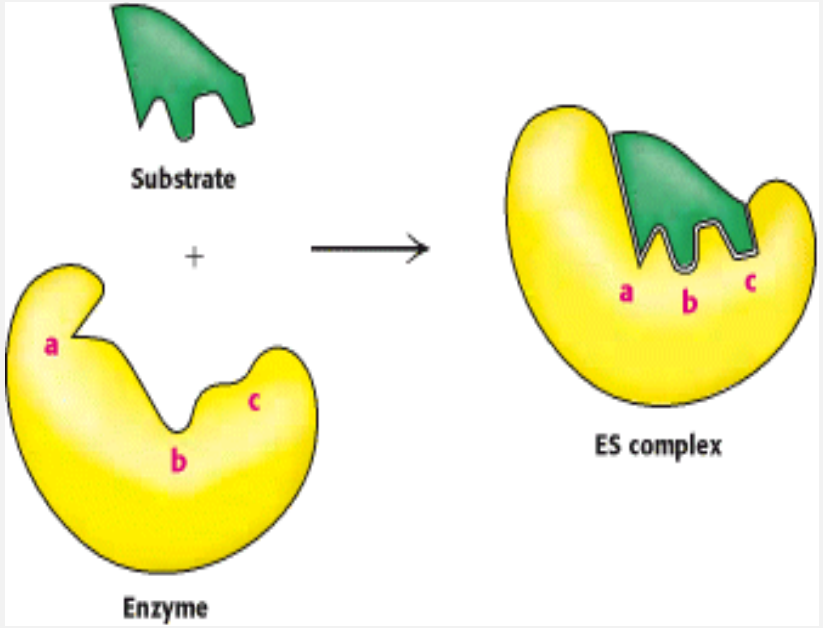


Induced-Fit Model of Enzyme-Substrate Binding

- In this model, the enzyme changes shape on substrate binding.

-The active site forms a shape complementary to the substrate only after the substrate has been bound.

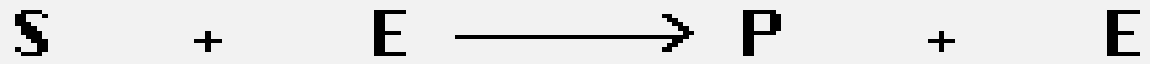
- When a substrate approaches and binds to an enzyme they induce a conformational change, a change analogous to placing a hand (substrate) into a glove (enzyme).



Key and Lock model	Induced fit model
Rigid	Flexible
Unchangable	Changable
Binding only if there are complemantary	Partial binding to be suitable for the binding of the substrate

Mechanism of Action of Enzymes

- Enzymes are catalysts and increase the speed of a chemical reaction without themselves undergoing any permanent chemical change. They are neither used up in the reaction nor do they appear as reaction products.
- The basic enzymatic reaction can be represented as follows:



- Where E represents the enzyme catalyzing the reaction, S the substrate, the substance being changed, and P the product of the reaction.
- The mechanism of action of enzymes can be explained by two perspectives:

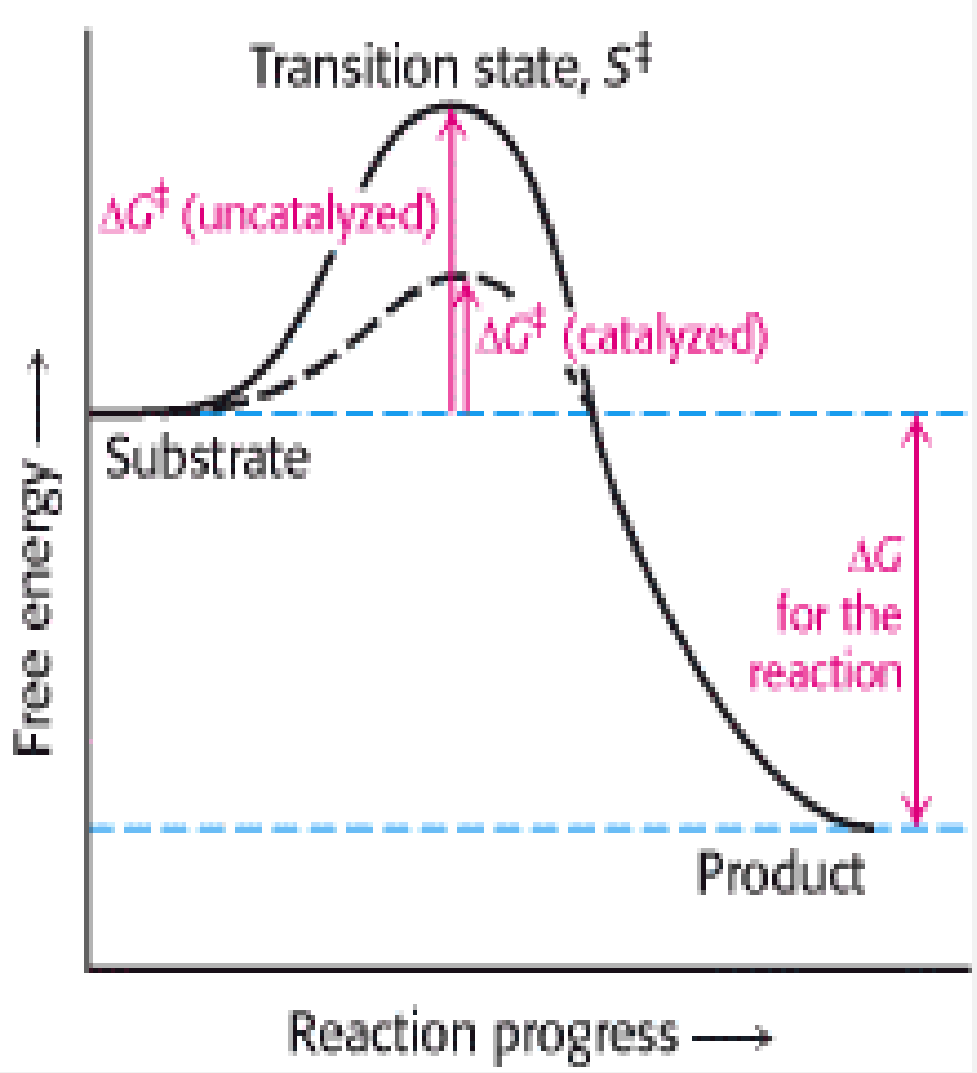
1- Thermodynamic changes

2- Processes at the active site

Thermodynamic changes

- All enzymes accelerate reaction rates by providing transition states with a lowered ΔG F for formation of the transition states.

-The lower activation energy means that more molecules have the required energy to reach the transition state.



Thermodynamic changes Cont:

- The main target of the enzyme is to shorten the time required to reach the transition state.
- And therefore decreasing the energy required for the activation.

- The molecules of the substrate will have enough energy to be in the transition state and to allow the converion of the substrate into products.

THANK YOU