Cellular and Molecular Biochemistry [FHS1104]

Enzymology

Section (A)

Lecture {8}

MBCHB/BDS
1ST YEAR SEM.-1
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Yasser Khater

{Lecture (8) Outline}

- Introduction to Enzymes
- Properties of Enzymes
- Classification of Enzymes
- Nomenclature of Enzymes

Introduction:

- **Enzymology:** study of Enzyme
- **Enzymes :**Are **biological** catalyst that enhance the rate of biochemical reactions.

E+S ⇨ **[ES]** ⇨ **[EP]** ⇨ **E+P**

- the enzymatic reaction rates are **millions** of times **faster** than **uncatalyzed(non enzymatic)** reactions.

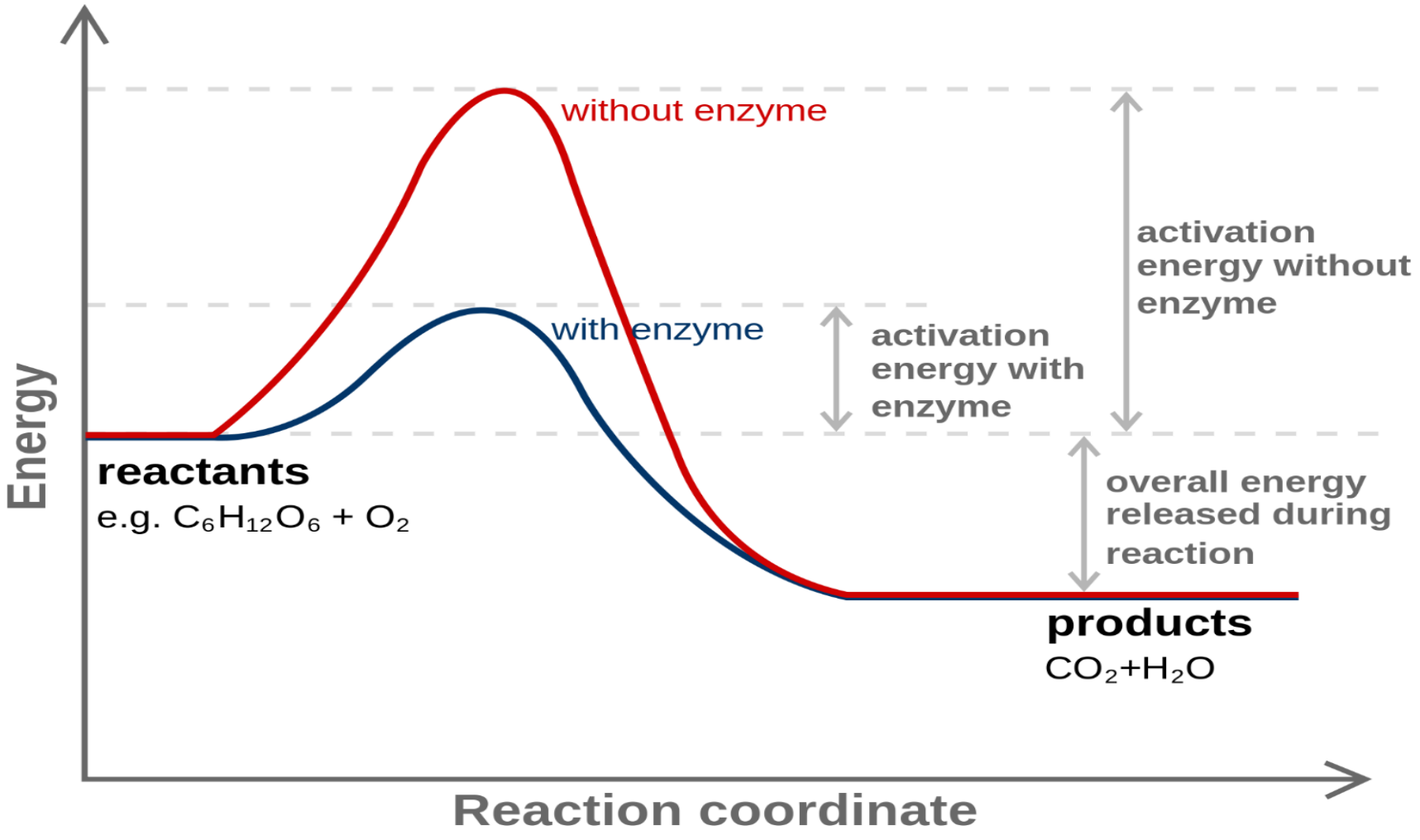
Why Enzymes Are Needed ?

In many chemical reactions the amount of energy needed to start the reaction called activation energy is high , enzyme lowers activation energy which is needed to cause molecules to join together.

Activation energy:

is the difference between the energy levels of the ground state and the transition state.

How Enzyme Decrease Energy of Activation Energy.



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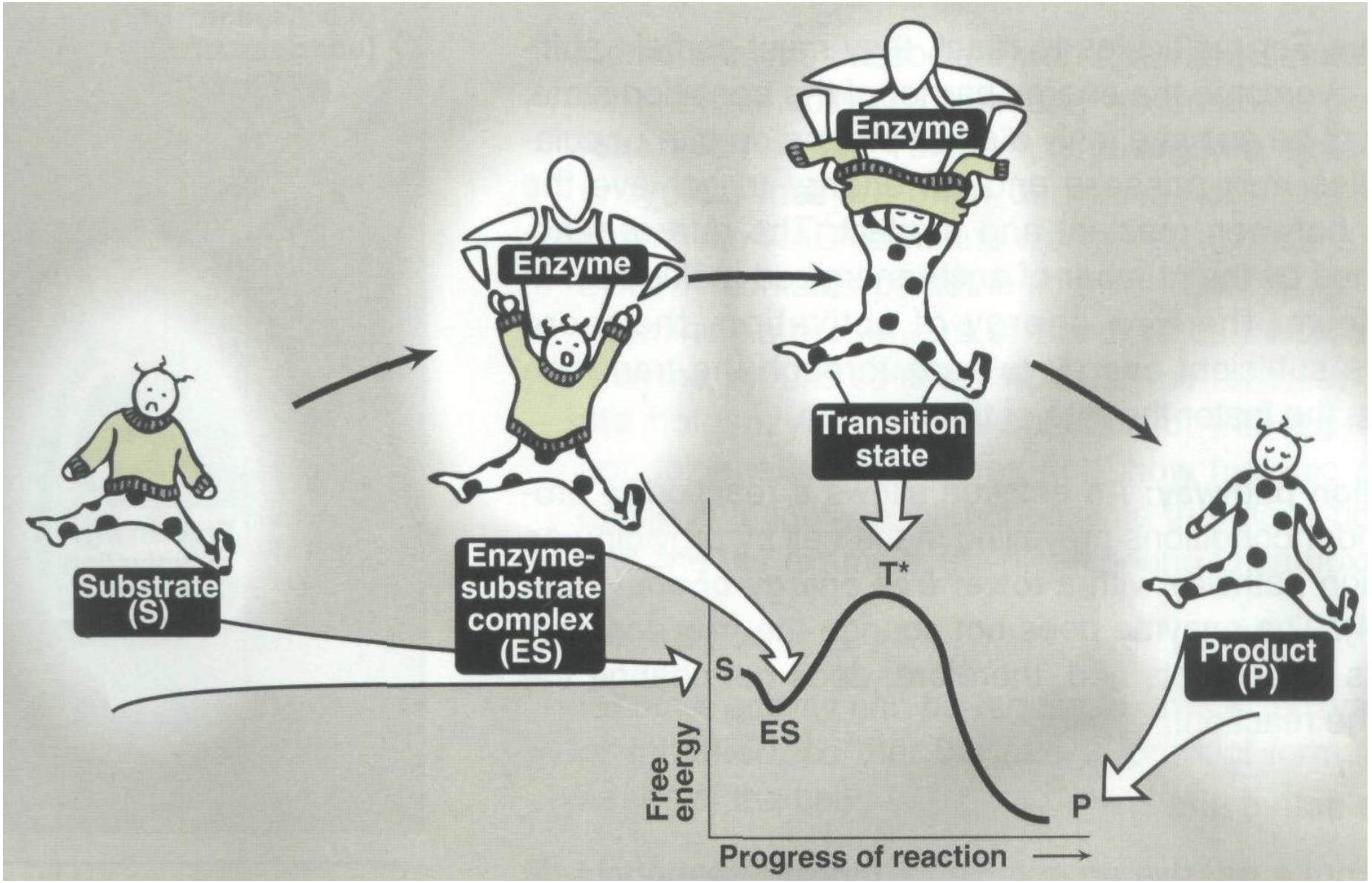


Properties of Enzymes

Properties of Enzymes:

1-Nature; Enzymes are protein in nature (*except* Ribozymes).

2-All enzymes contain functional site , called the active site , where reactant (substrate) are converted to product.

3-Specificity; Each enzyme has specific substrate.

Properties of Enzymes:

4-Some enzymes need cofactor

5- Activity of enzyme should be regulated, that is, increased or decreased, so that the rate of product formation responds to cellular need.

6.Enzymes don't change during the reaction; (Don't used up in the reaction).

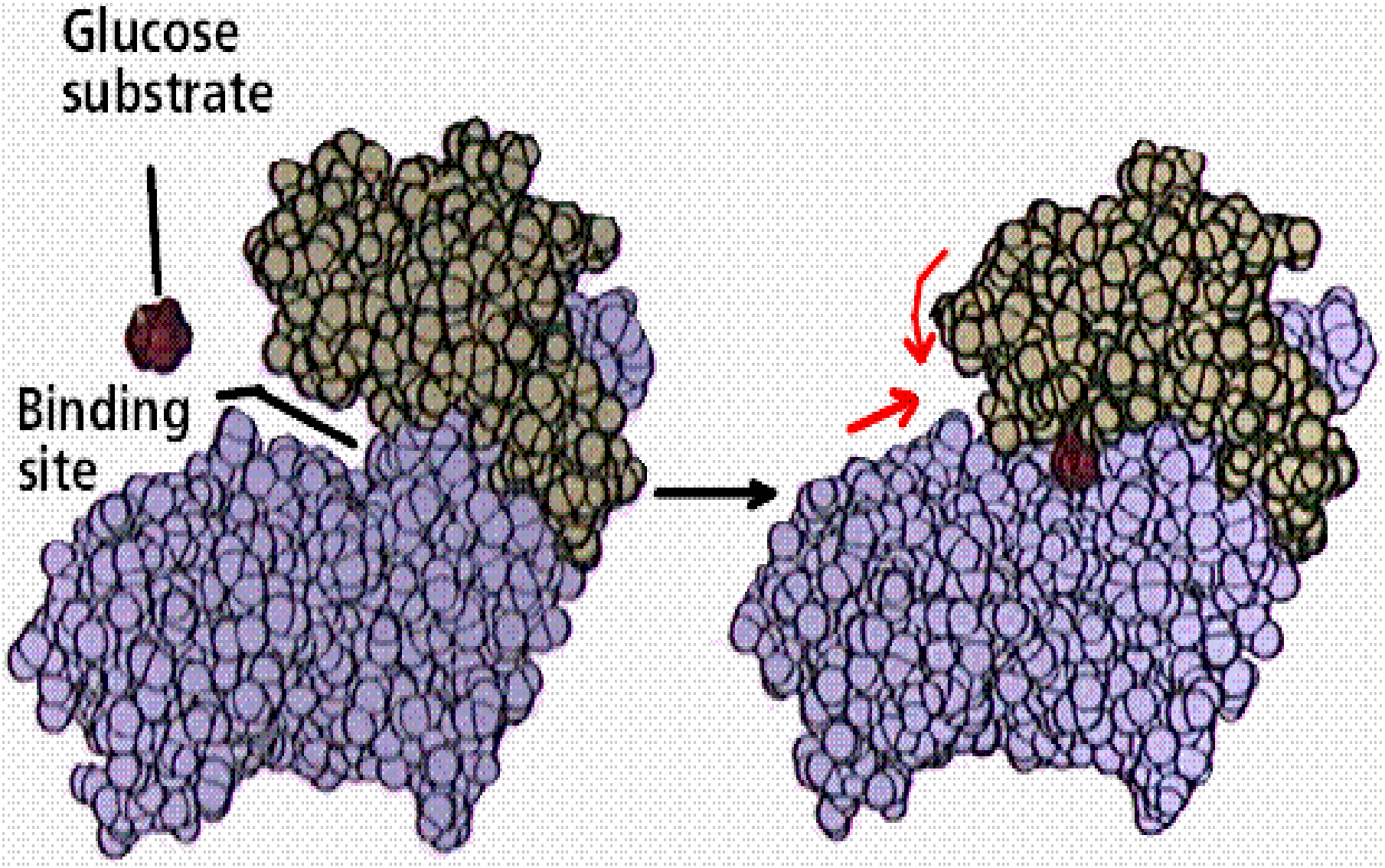
7. Sensitivity; each enzyme has optimal Temperature and pH.

1. Enzymes are protein and contain functional site

- Enzyme molecules contain a special pocket or cleft called the active site.
- The active site contains amino acid side chains that create a three-dimensional surface complementary to the substrate.
- The active site binds the substrate, forming an enzyme–substrate (ES) complex. ES is converted to an enzyme–product (EP) complex that dissociates to enzyme and product.
- E+S → [ES] → [EP] → E+P

1. Enzymes are protein and contain functional site

Substrate binding site



2. Each enzyme is specific to its substrate

- Enzymes are highly **specific**, interacting with one or a few substrates and catalyzing only one type of chemical reaction.
- a – **Absolute specificity** {enzymes attacks only one substrate e.g. urease attacks only urea }.
- b – **Relative specificity** { enzymes attack group of compound e.g. L amino acid oxidase attack **all L amino acids** not D amino acids .
- c – **Bond specificity** {Enzymes that are specific for a **bond or linkage** such as ester, peptide or glycosidic belong to this group}
- Liver esterase attack all ester bond.

How enzyme binds to substrate

There are two models to explain the specificity of the enzyme to its substrate:

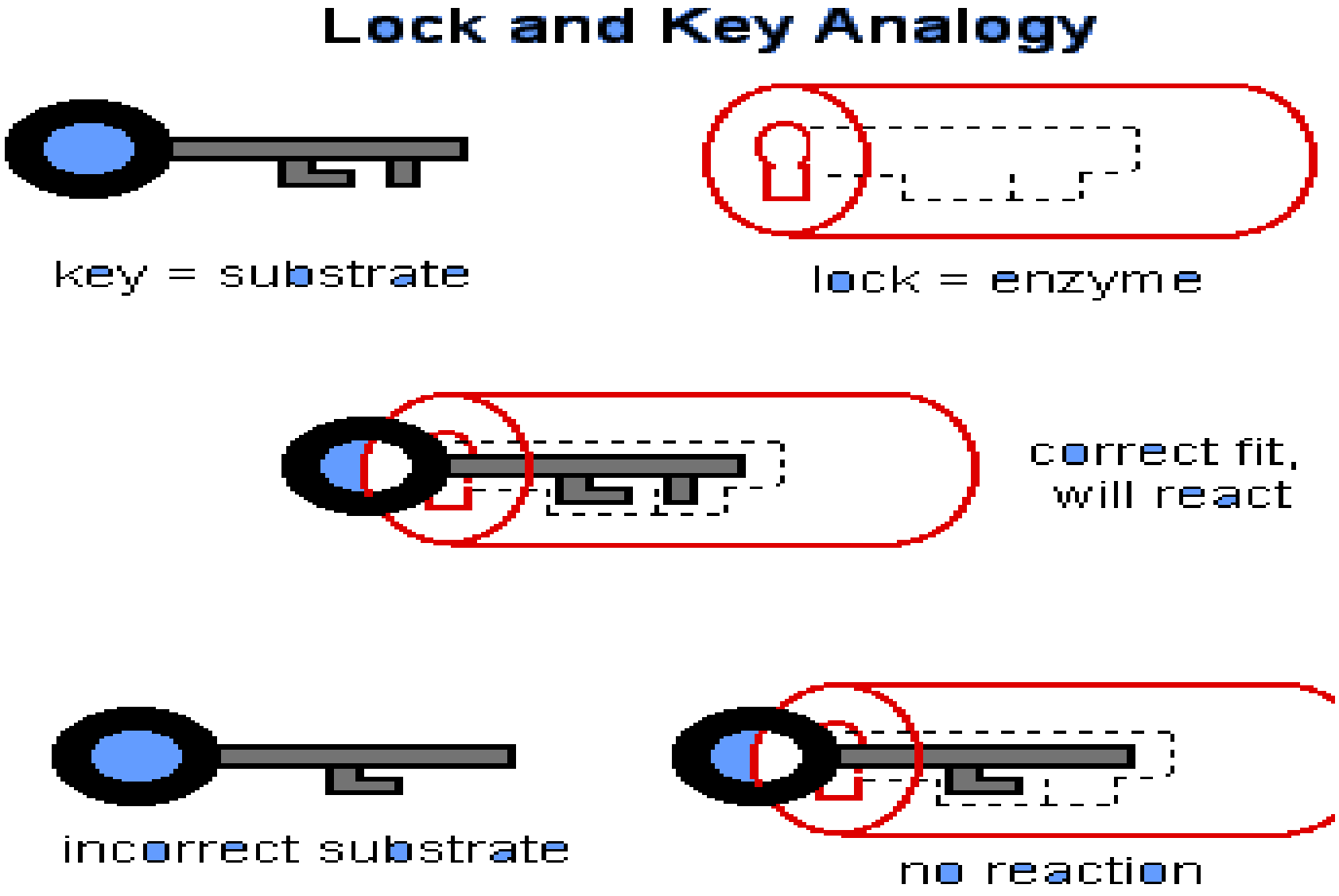
A. Lock and key model:

B. Induced-fit model:

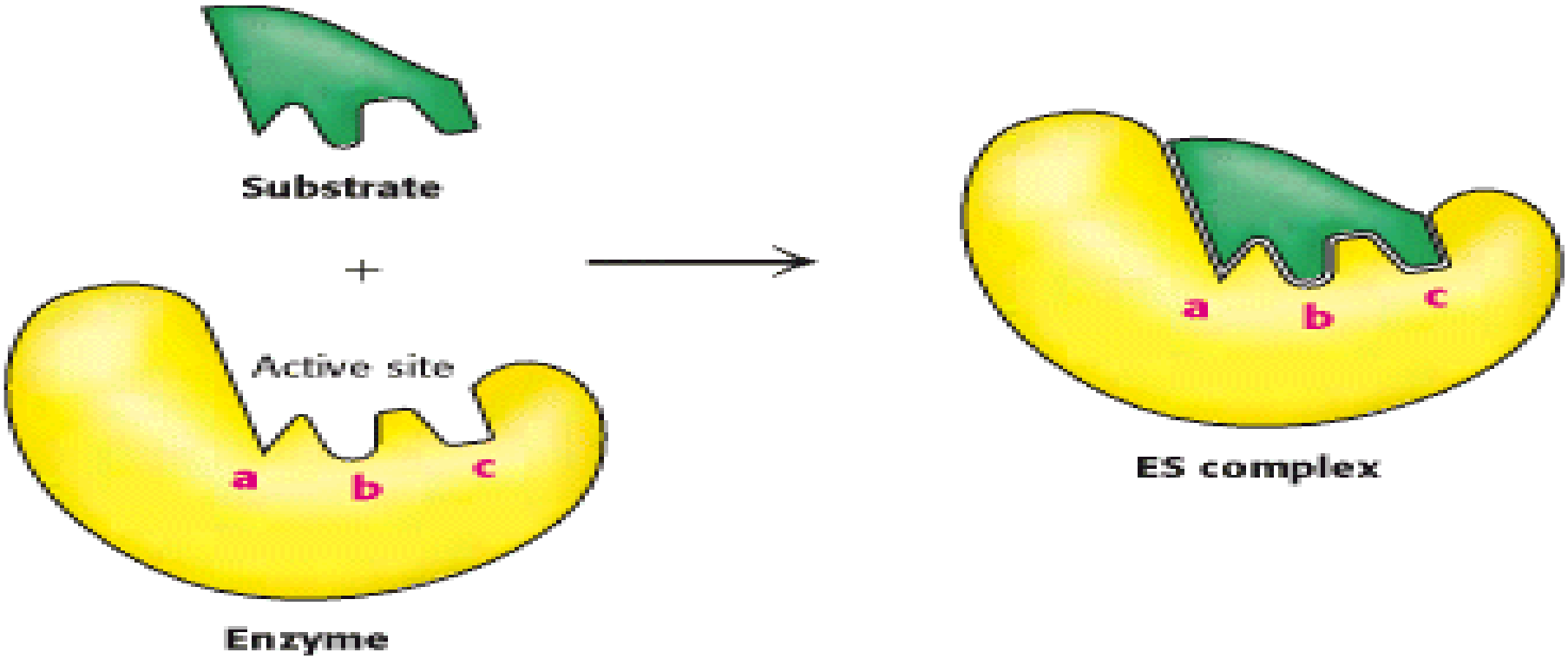
A. Lock and key model:

- Enzymes are very specific, because both the enzyme and the substrate possess specific complementary shapes that fit exactly into one another. This is often referred to as "the lock and key" model.
- The active site is rigid not flexible , and the substrate is complementary to the active site .

Lock and key model of enzyme-substrate binding



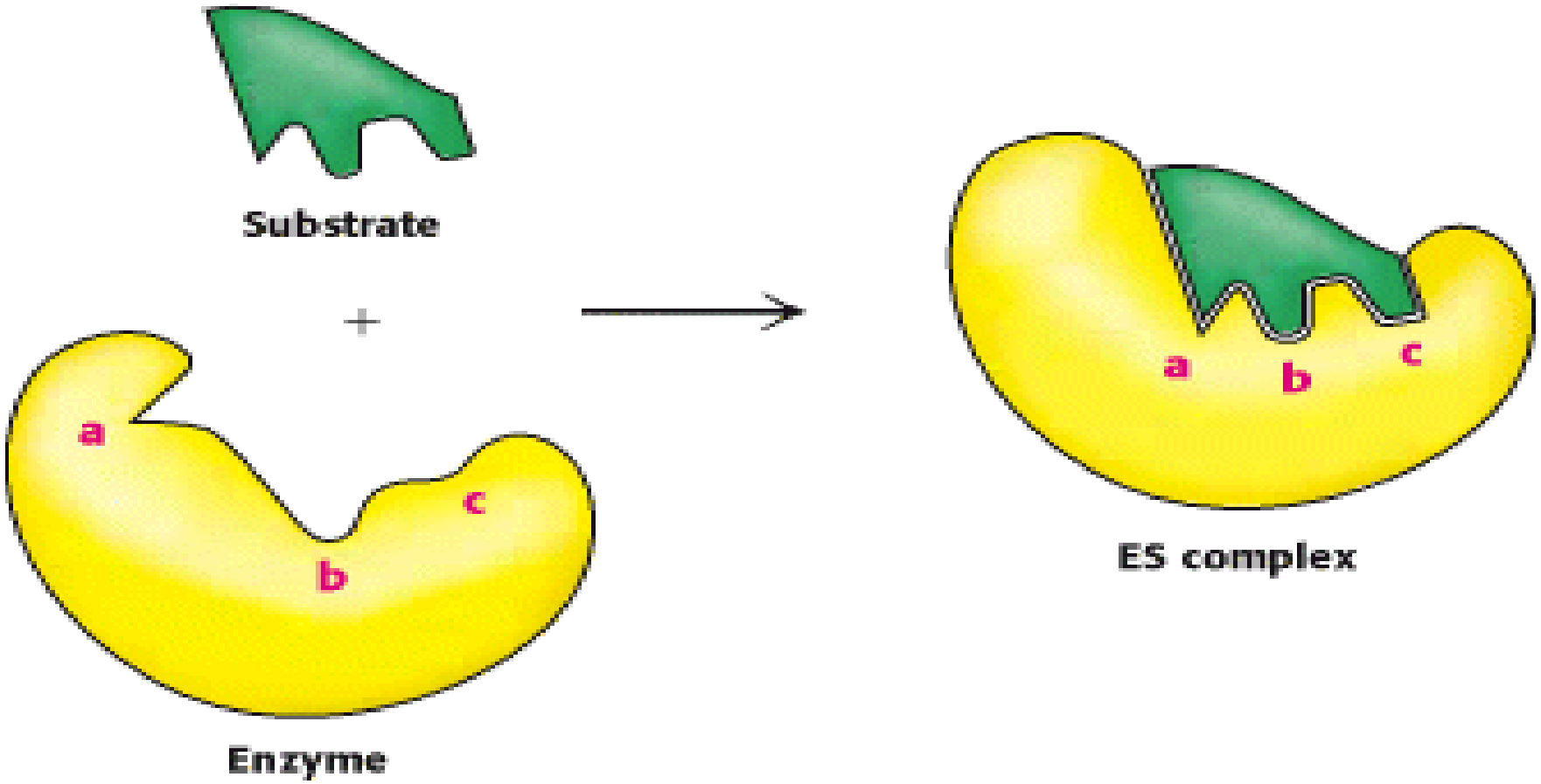
Lock and Key Model



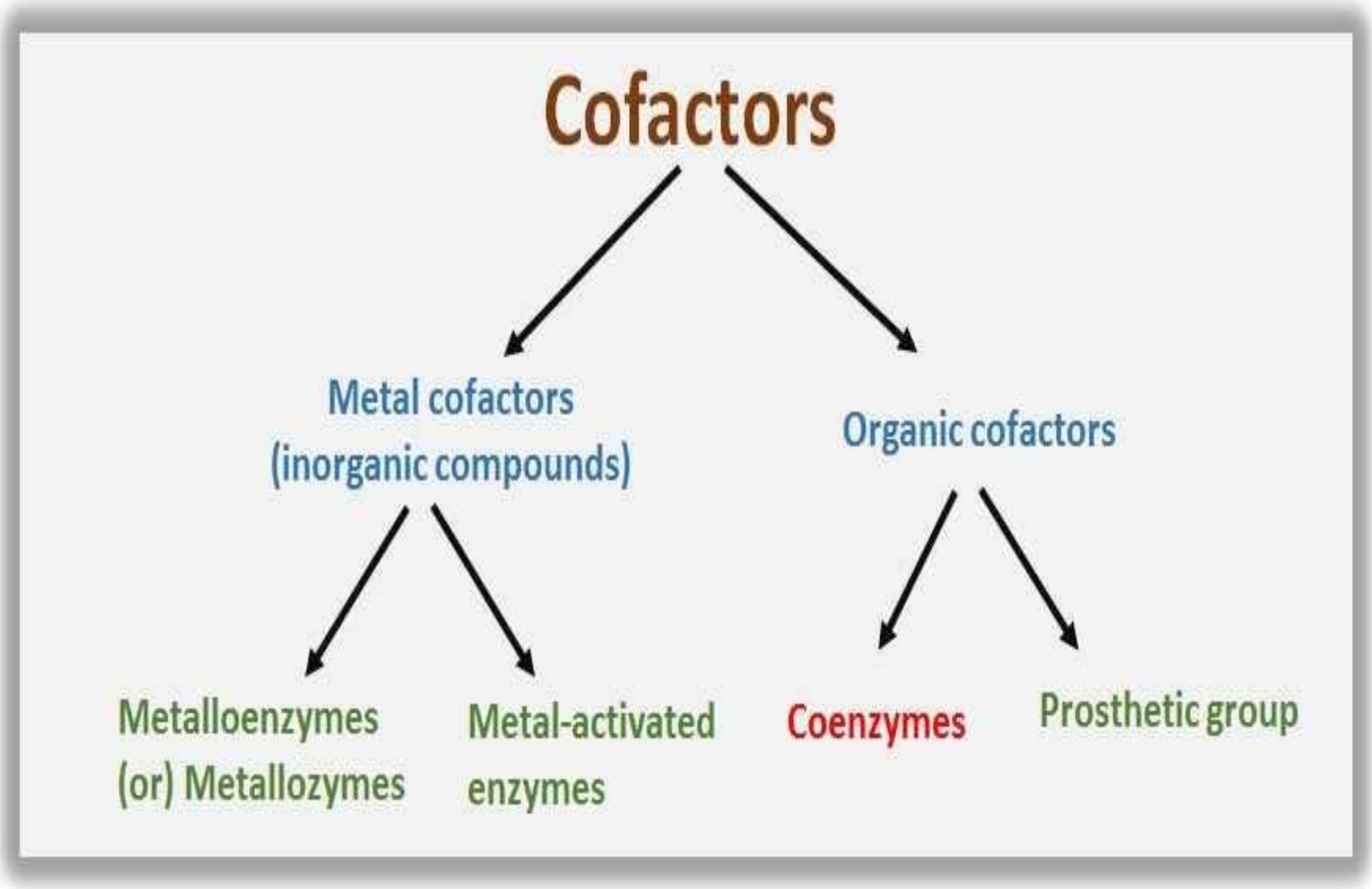
B. Induced-fit model:

- Active sites are flexible to fit their substrate structure , so they are not always active ,they are activated only when their substrate is present.
- Interaction of the substrate and the enzyme induces a conformational change in the enzyme resulting in the formation of stronger binding site . (This is the recommended model).

B. Induced-fit model:



3. Some enzymes need coenzyme or cofactor



3. Some enzymes need coenzyme or cofactor

- Some enzymes require molecules other than proteins for enzymatic activity.
- **Holoenzyme** refers to the **active enzyme** with its **non**protein component.
- the enzyme without its **nonprotein** moiety is termed an **apoenzyme** and is inactive.

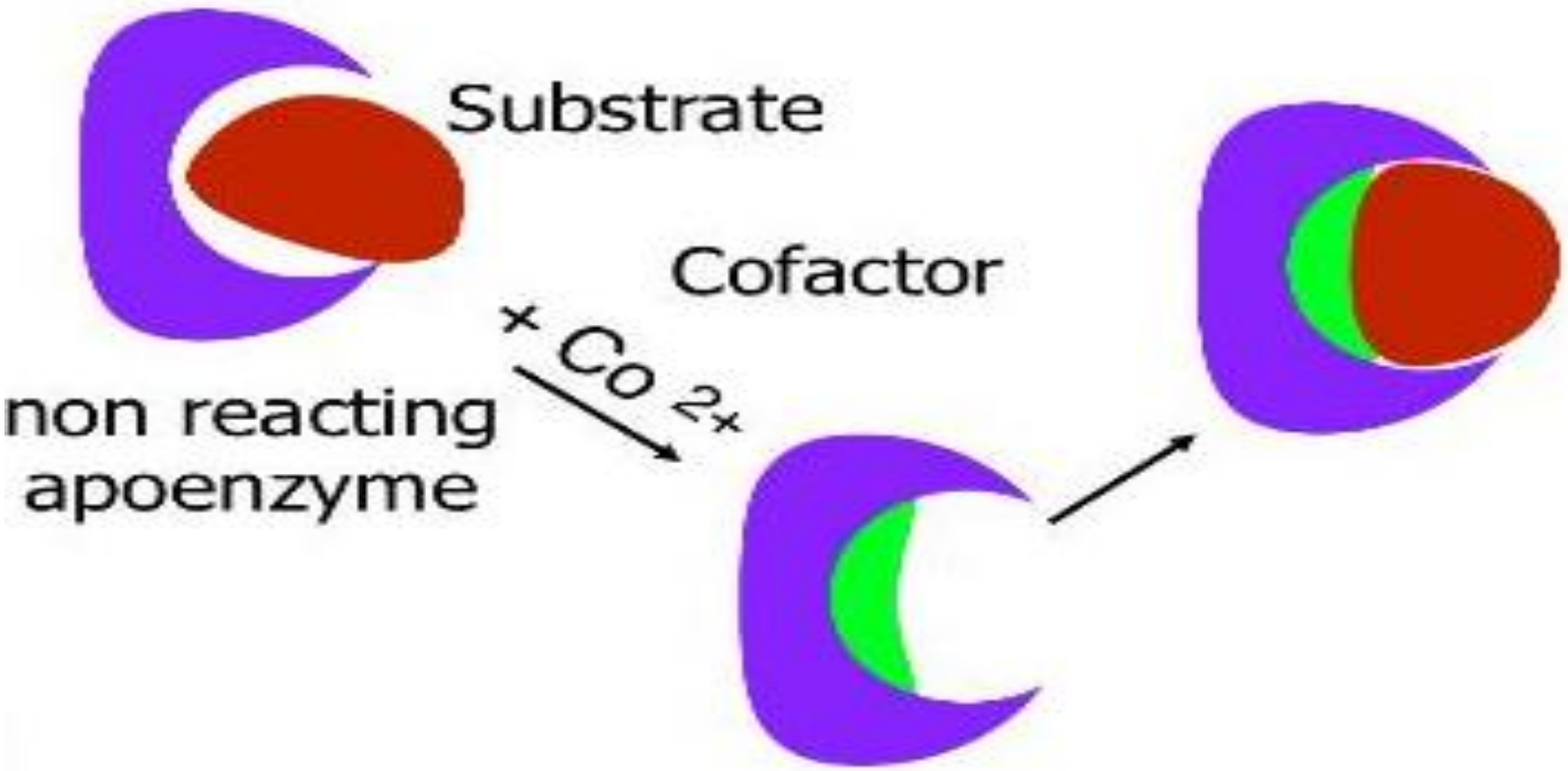
Cofactor + apoenzyme → holoenzyme

Non-protein protein

(inactive) (inactive) (active)

- If the non-protein part is a metal ion such as Zn^{2+} or Fe^{2+}, it is called a cofactor.
- If it is a small organic molecule, it is termed a coenzyme.
- Coenzymes frequently are derived from vitamins B For example, NAD+ contains niacin, coenzyme A contains pantothenic acid, and FAD contains riboflavin.

Cofactors e.g. $Zn2^{+}$, $Fe2^{+}$

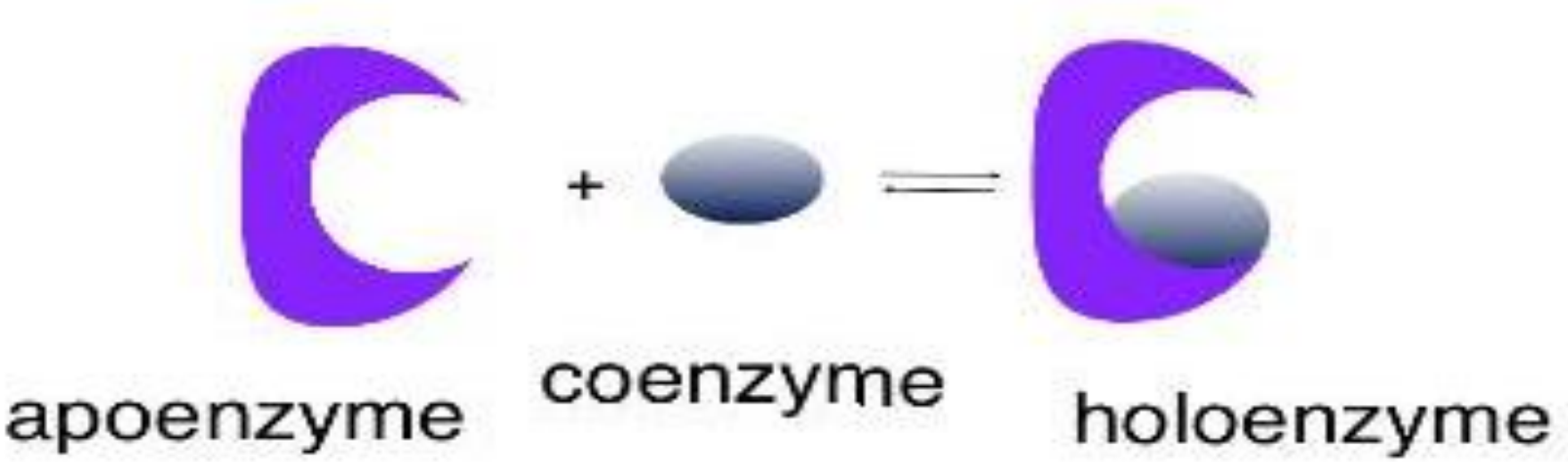


Example of coenzymes:

TPP	(Vit B1)
FAD^+,FMN^+	(Vit B2)
$NAD(P)^+$	(Vit B3)
$NAD(P)^+$	(Vit B3)
Coenzyme A	(Vit B5)
PLP	(Vit B6)

Coenzymes e.g. NAD+, FAD+

A second unit that temporarily binds to an apoenzyme in order for it to work.



4.Regulation of enzyme activity :

- **Enzyme activity can be regulated, that is, enzymes can be activated or inhibited, so that the rate of product formation responds to the needs of the cell.**
- **Enzyme activity can be regulated by:**

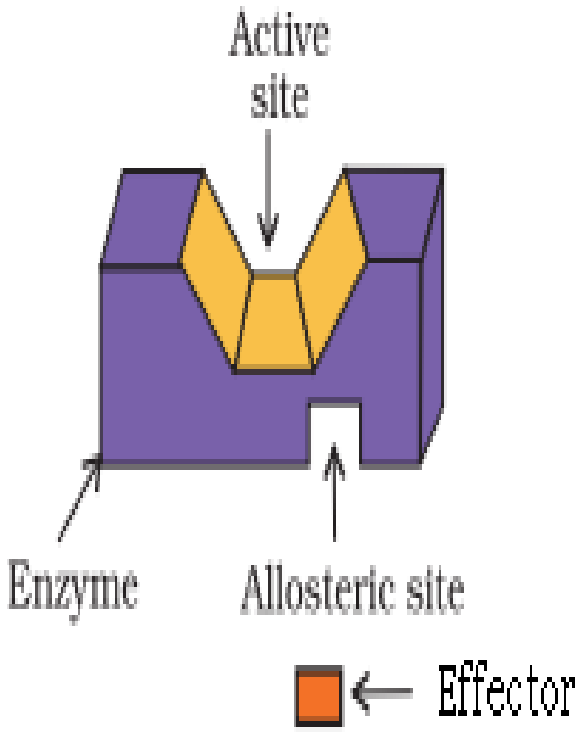
1. Allosteric binding sites.

2. Regulation of enzymes by covalent modification.

3. Enzyme Synthesis Level(Transcriptional Control).

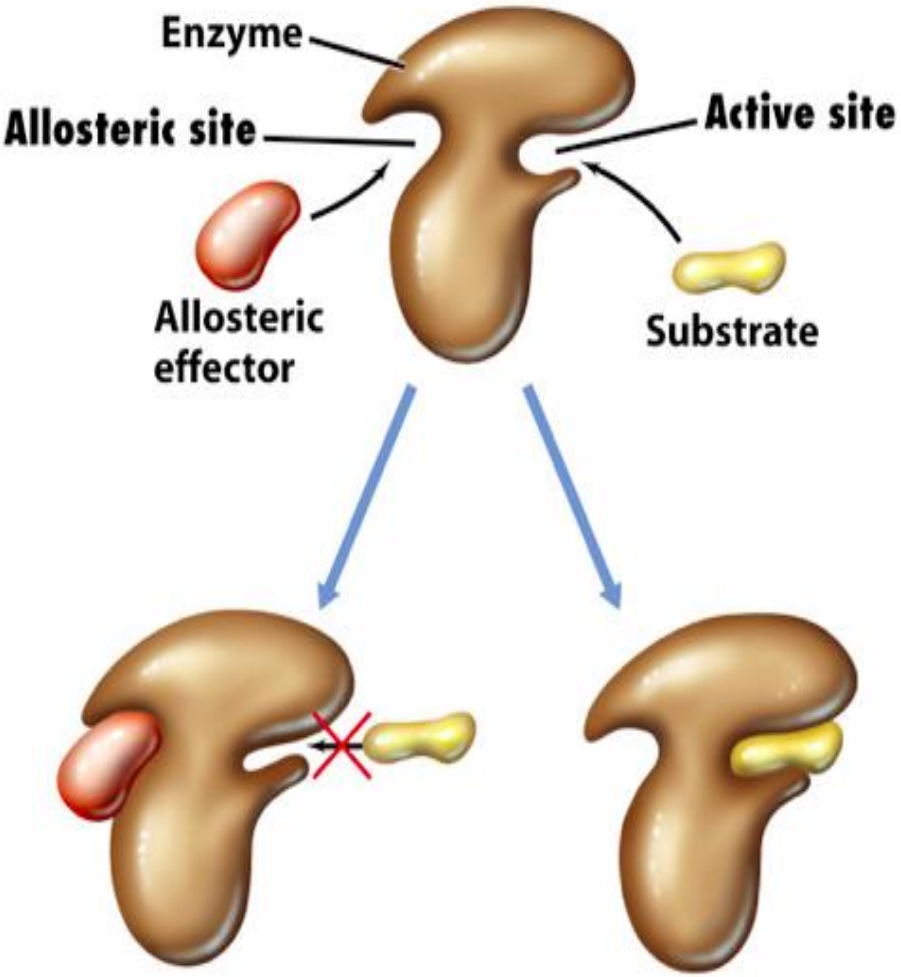
(1) Allosteric Regulation:

- Many Enzymes contain another site called regulatory site or (Allosteric Site).
- Effector (or Modifier) binds non-covalently to the allosteric site and cause conformational change to the enzyme and hence affect its activity.



(1) Allosteric Regulation:

Effectors that inhibit enzyme activity are termed negative effectors, whereas those that increase enzyme activity are called positive effectors.



(1) Allosteric Regulation:

The effector can:

Alter the affinity of the enzyme to substrate,

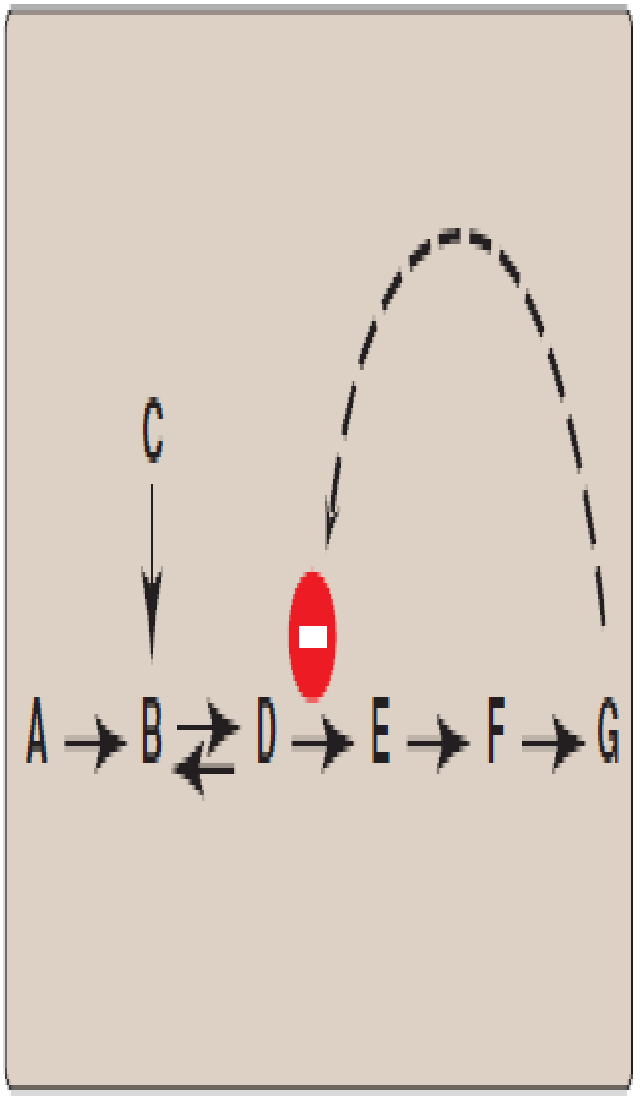
Alter the catalytic activity of the enzyme, or both.

The effector (Ligand) could be substrate, immediate product, end product, coenzyme, metabolites from different metabolic pathway or any other effectors.

(1) Allosteric Regulation:

When the **substrate** itself acts as effector, it called **Homotropic effector,** and mostly **positive** effector, i.e., increase the catalytic properties of the enzyme.

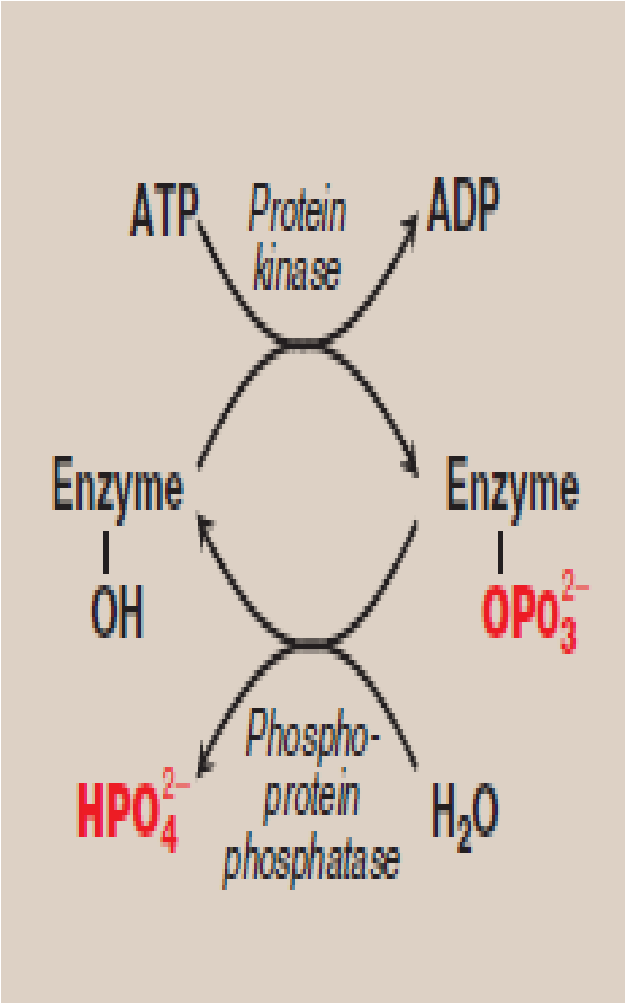
When the effector is not the substrate, it called **Heterotrophic effector,** such as **feedback inhibition** by the **end product.**



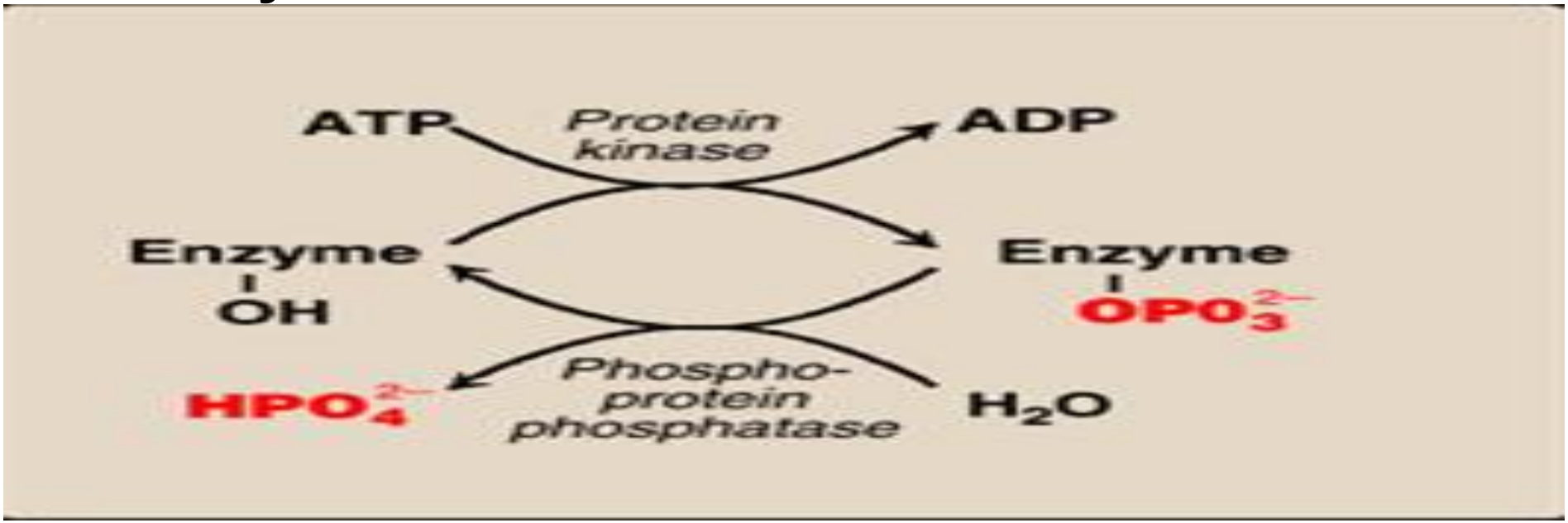
(2) Covalent Modification:

Mostly involve:

- **ATP-dependent phosphorylation of the enzyme protein by a protein kinase, or**
- **Dephosphorylation of the enzyme by a phosphoprotein phosphatase**
- **Depending on the enzyme, phosphorylation / dephosphorylation may activate or inactivate the enzyme.**

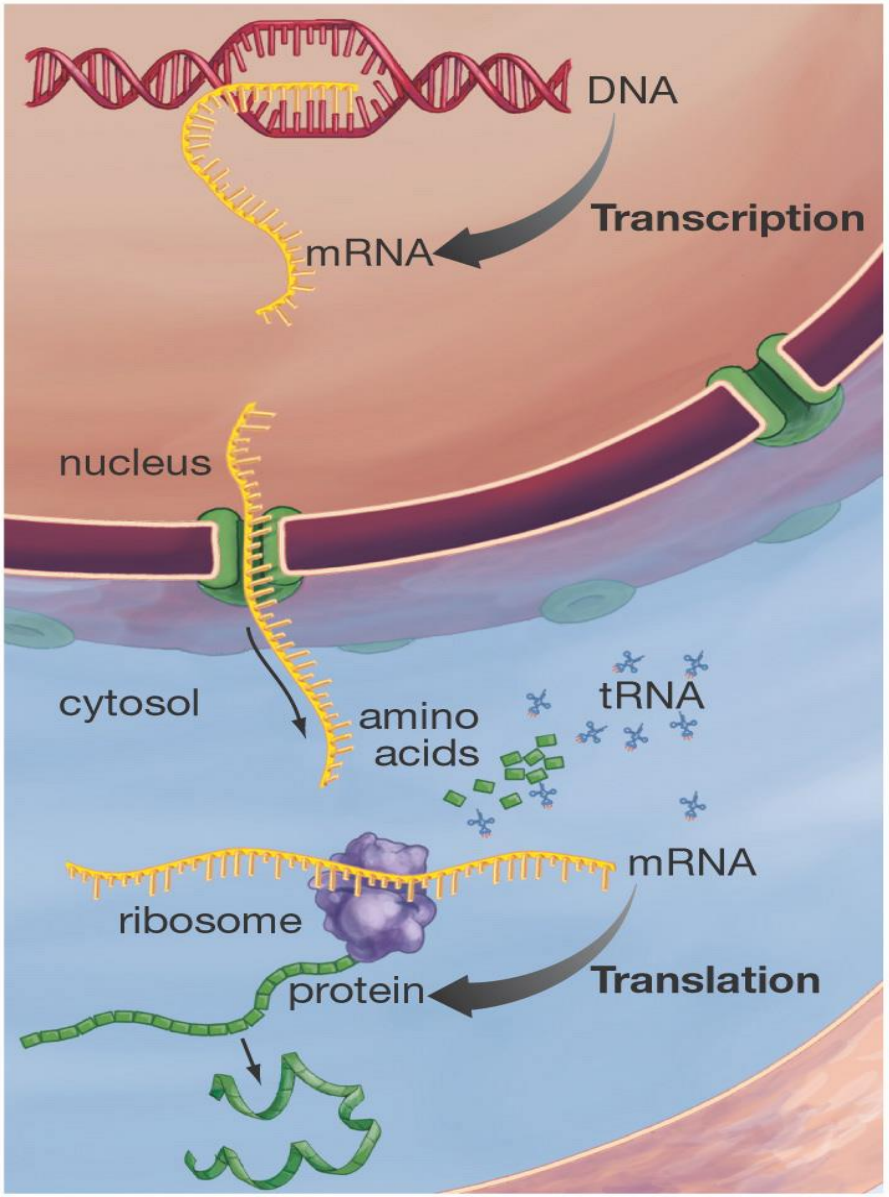


For example; phosphorylation of glycogen phosphorylase (an enzyme that degrades glycogen) increases its activity, whereas the addition of phosphate to glycogen synthase (an enzyme that synthesizes glycogen) decreases its activity.



(3) Transcriptional Control:

- Enzymes are proteins, and any protein has its own Genetic Information (code) at the level of DNA.
- This genetic code should be copied as mRNA (Transcription) and then Decoded (Translation) to form protein.



(3) Transcriptional Control:

- **Transcriptional control: Increase (Induction) or Decrease (Repression) of enzyme protein biosynthesis at the genetic level (mRNA Production).**
- **Post transcription modifications**
- **mRNA stability**
- **Post translation modifications**
- **Result: enzyme quantity increase or decrease.**

References:

1-lipincotts biochemistry 8th edition 2022

2. Harpers 25th , 27th and 32nd edition 2023

3- Lehninger principles biochemistry 8th edition 2021

4- Medical biochemistry 6th edition 2023

5- Mark Basic Medical biochemistry 6th edition 2023

6- Stryer biochemistry.


Thank You