

ALLOSTERIC ENZYMES

for

M.Sc (Biotech) IInd Semester Students

by

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- **Allosteric Enzyme** are those enzymes possess additional sites, known as **allosteric sites** besides the **active site**. The allosteric sites are unique places on the enzyme molecules; allosteric enzymes have one or more allosteric site.
- The term allosteric has been introduced by the two Noble laureates, **MONOD AND JACOB**, to denote an enzyme site, different from the active site ,which non competitively binds molecule other than the substrate and may influence the enzyme activity.

PROPERTIES OF ALLOSTERIC ENZYME

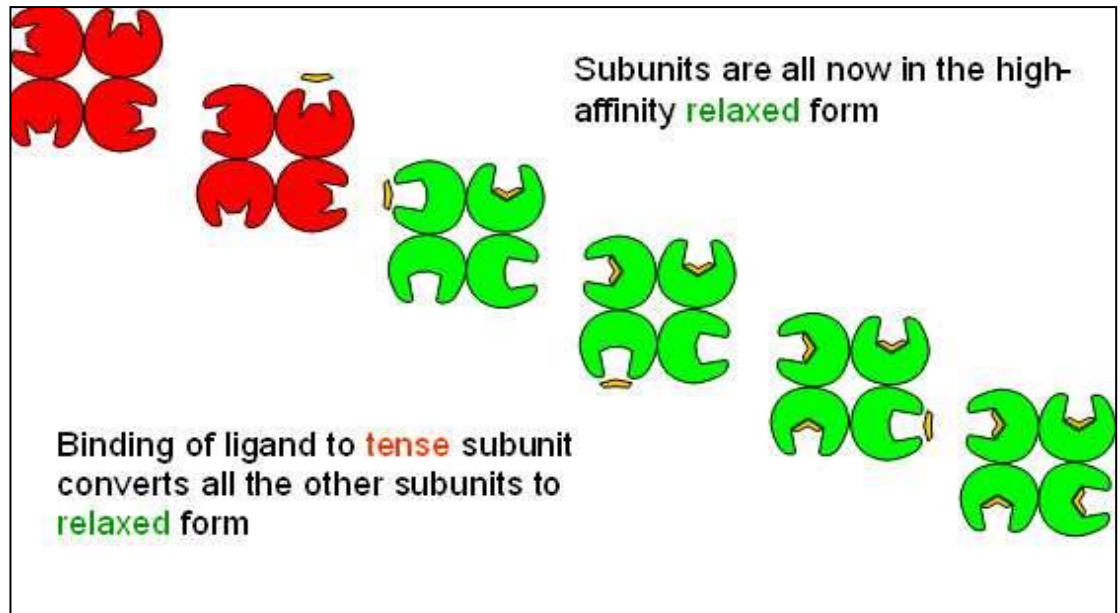
- Allosteric enzyme have one or more allosteric sites
- Allosteric sites are binding sites distinct from an enzyme active site or substrate binding site
- Molecule that bind to allosteric sites are called effector or modulator
- Effector may be positive or negative, this effector regulate the enzyme activity. The enzyme activity is increased when a positive allosteric effector binds at the allosteric site known as activator site. On the other hand, negative allosteric effector bind at the allosteric site called inhibitor site and inhibit the enzyme activity.
- Binding to allosteric sites alter the activity of the enzyme, this is called cooperative binding. Allosteric enzymes display sigmoidal plot of V_o vs $[S]$.

MODEL OF ALLOSTERIC REGULATION

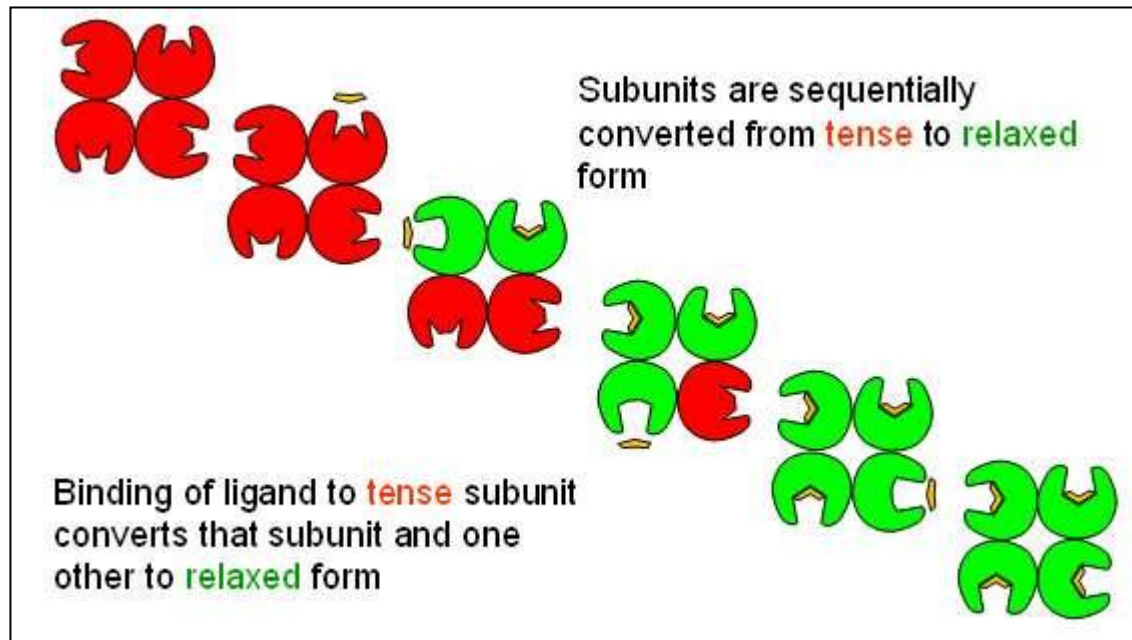
Two main model have been proposed to describe the mechnastic basis of enzyme allostery:

- ***Concerted model*** : Given by **MONOD, WYMAN AND CHANGEUX** (MWC)
- ***Sequential model***: Given by **KOSHLAND, NEMETHY AND FILMER** (KNF)

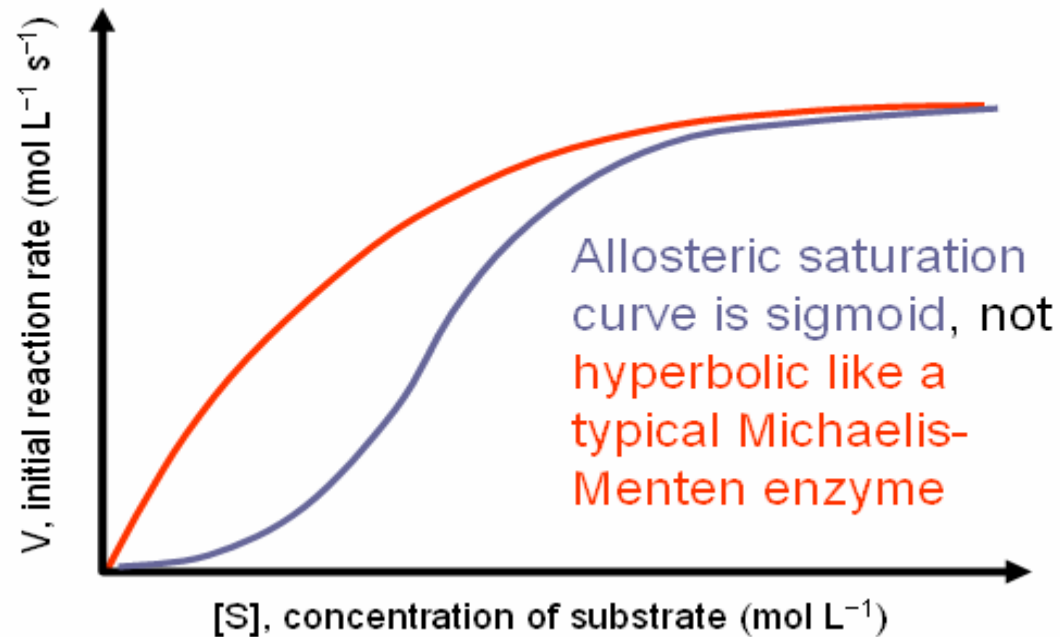
Concerted model of allosteric regulation:



Sequential model of allosteric regulation:



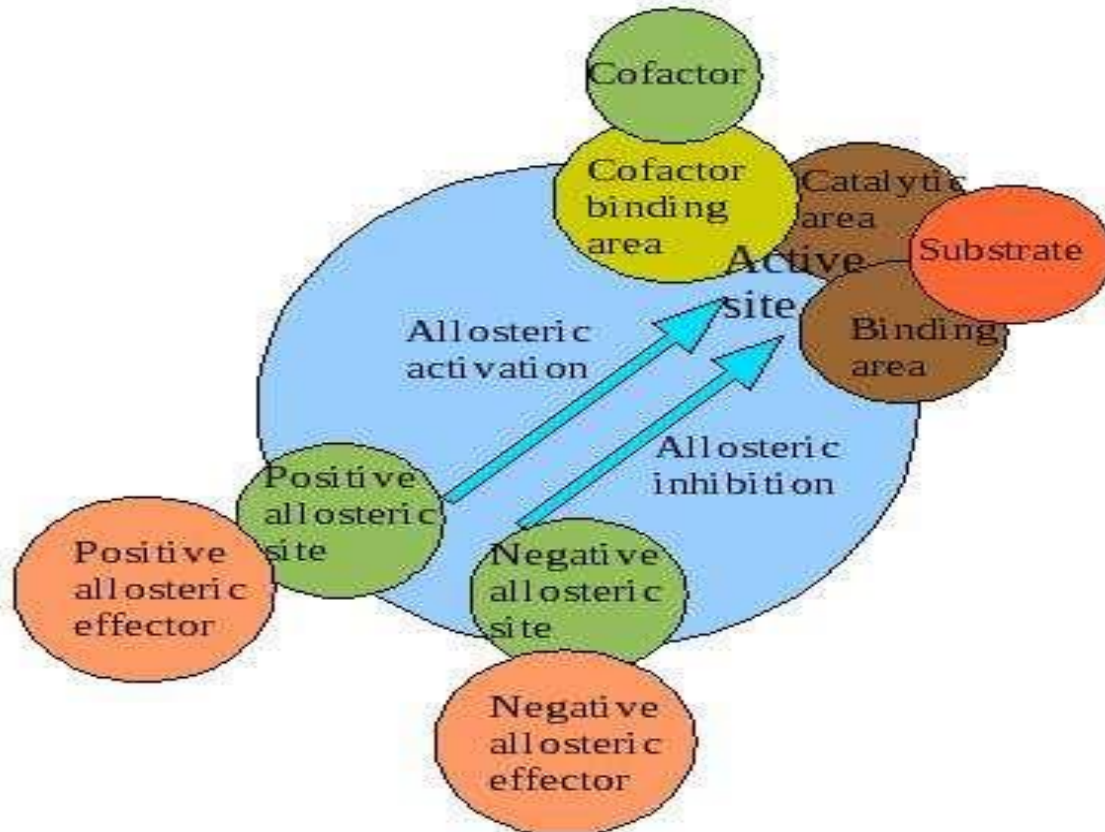
SIGMOID CURVE OF ALLOSTERIC ENZYME



ALLOSTERIC EFFECTOR

Allosteric effectors are of two types:

- ***Positive allosteric effector***
- ***Negative allosteric effector***

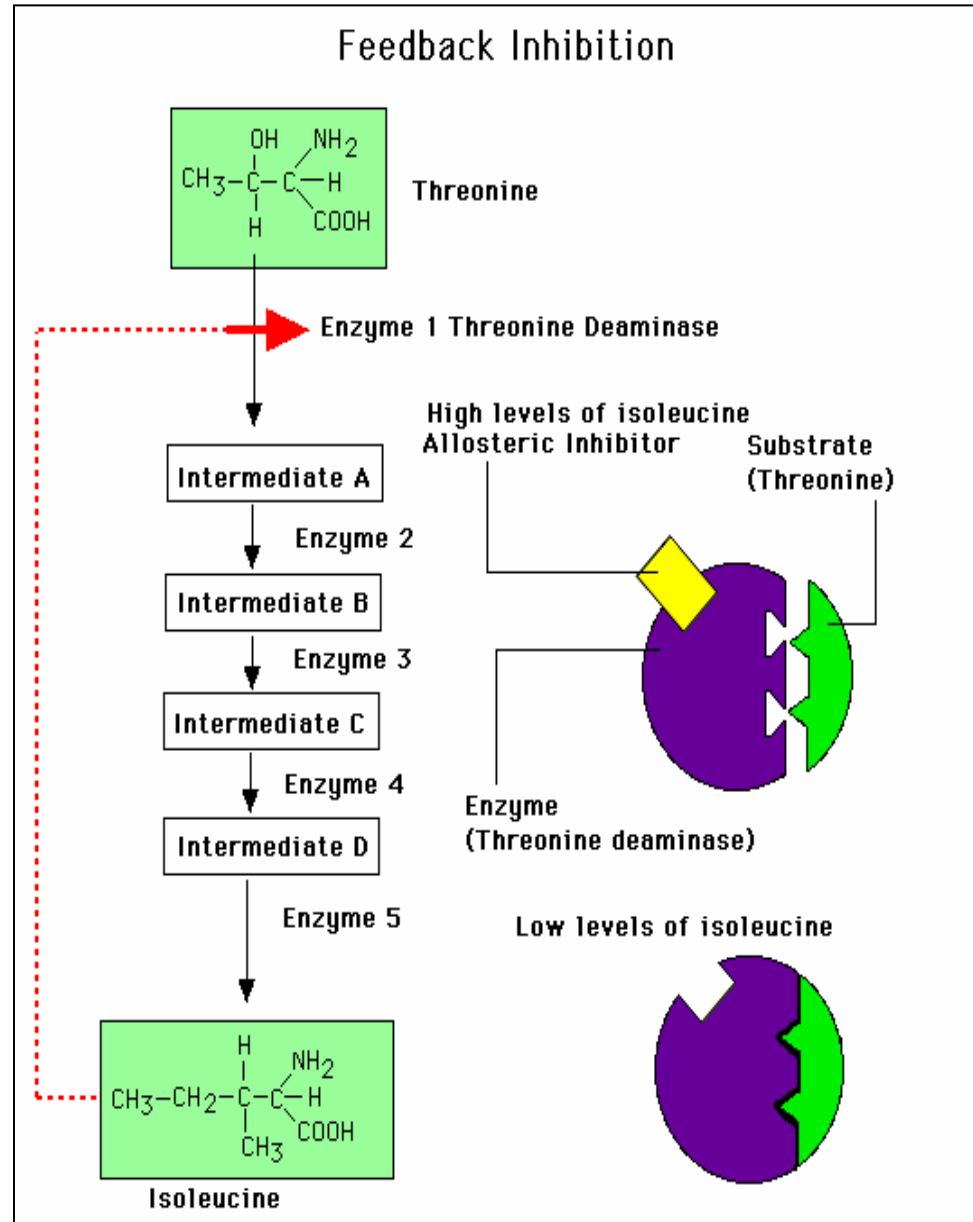
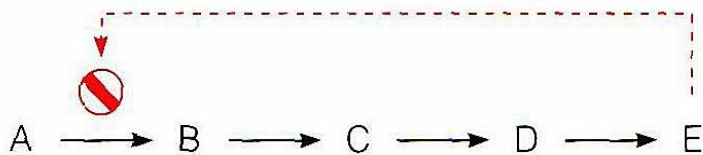


TYPES OF ALLOSTERIC REGULATION

- **Homotropic:** A homotropic allosteric modulator is a substrate for its target enzyme, as well as a regulatory molecule of the enzyme's activity. It is typically an activator of the enzyme. For example, O₂ is a homotropic allosteric modulator of hemoglobin.
- **Heterotropic:** A heterotropic allosteric modulator is a regulatory molecule that is not also the enzyme's substrate. It may be either an activator or an inhibitor of the enzyme. For example, H⁺, CO₂, and 2,3-bisphosphoglycerate are heterotropic allosteric modulators of hemoglobin.

Allosteric Inhibition: Feed-back inhibition

- **Heterotropic Inhibition:**
The effector may be different from the substrate, in this case effector is said to be heterotropic effector. For example the feedback mechanism.



APPLICATION

- The combined use of physical techniques (for example, x-ray crystallography and solution small angle x-ray scattering or SAXS) and genetic techniques (site-directed mutagenesis or SDM) has enabled researchers to investigate more deeply the molecular basis of allostery.
- The *Escherichia coli* enzyme aspartate carbamoyltransferase (ATCase) has established itself as one of the model system's for allosteric regulation. However, it is irrefutable that the canonical allosteric system that has shaped our current understanding of allostery is tetrameric vertebrate Hemoglobin.
- Long-range allostery is especially important in cell signaling.
- Pharmacology

Thank you

