BHARATHIDASAN UNIVERSITY

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Programme: M.Sc., Biochemistry

Course Title : Enzymology
Course Code : BC102CR

Unit-I
Introduction of enzymes

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Definition

Biological macromolecules (mostly proteins) that catalyze chemical reactions by lowering activation energy.

Function

Accelerate metabolic reactions, regulate cellular processes, and maintain homeostasis.

Key Feature

Specificity and efficiency due to unique 3D structures; form enzyme-substrate complexes.

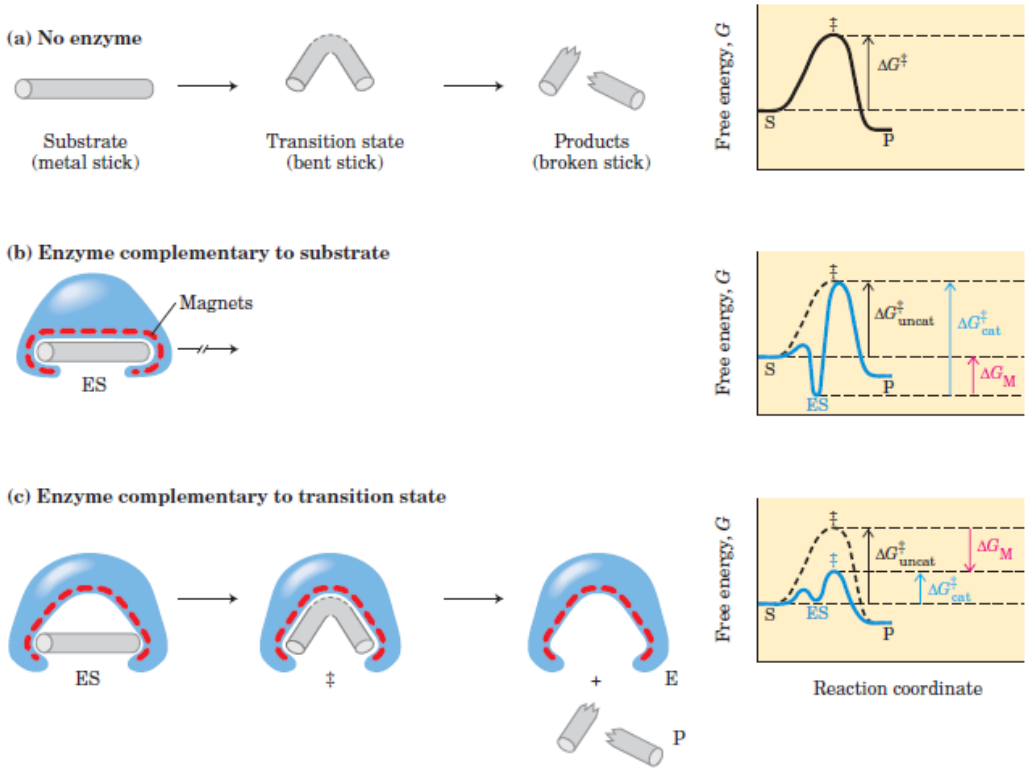


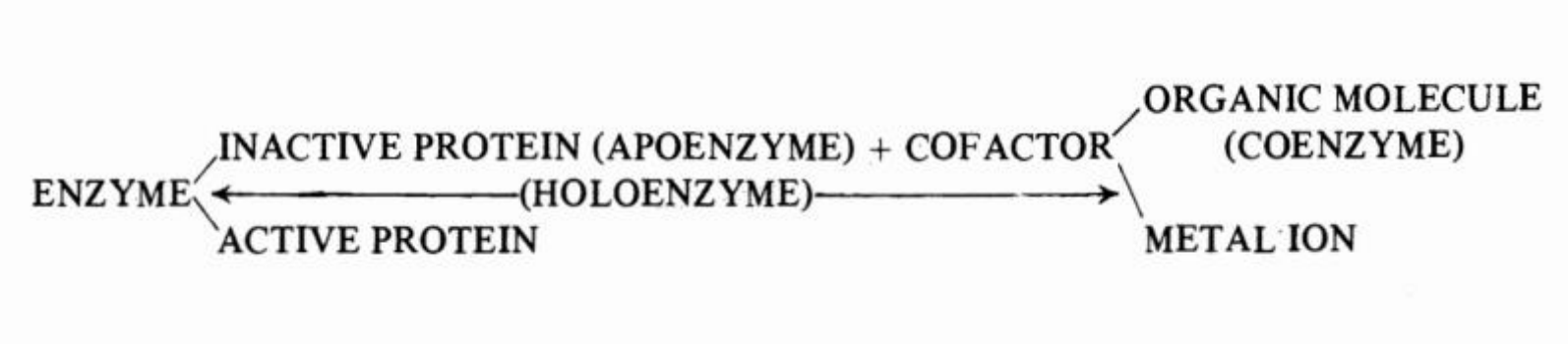
Fig. 1 An imaginary enzyme (stickase) designed to catalyze breakage of a metal stick.
Lehninger- Principles of Biochemistry

Historical Period	Milestone/Contributions
Ancient Observations	Use of fermentation in brewing and bread-making, though enzymes were unknown.
17th-18th Centuries	Early digestive studies by Spallanzani; observations of biological processes by Malpighi and van Leeuwenhoek.
19th Century	-Term "enzyme" coined by Wilhelm Kühne (1878). -Eduard Buchner proved enzymes work outside cells (1897, Nobel Prize 1907). -Louis Pasteur linked fermentation to "ferments" in yeast cells.
20th Century	- Emil Fischer's "lock-and-key model" (1894); later refined to "induced fit" by Daniel Koshland. - James Sumner crystallized urease (1926), proving enzymes are proteins (Nobel Prize 1946).
Modern Enzymology	Advances in structural biology (e.g., X-ray crystallography); applications in medicine, biotechnology, and industry.

- **Catalytic Power**
- The ability of enzymes to significantly accelerate reaction rates by lowering the activation energy compared to uncatalyzed reactions.
- **Reactivity**
- The capacity of enzymes to selectively bind substrates and facilitate chemical transformations through specific interactions at their active sites.
- **Regulation**
- Enzymatic activity is modulated through mechanisms such as allosteric control, covalent modification, feedback inhibition, or changes in enzyme expression to meet cellular needs.
- **Different Forms of Energy Transformation**
- Enzymes enable the conversion of energy from one form to another, such as chemical to mechanical (muscle contraction), chemical to electrical (nerve impulses), or chemical to heat (metabolism).

- **Holoenzyme**
- A complete, catalytically active enzyme, consisting of an apoenzyme (protein part) and its non-protein cofactors or coenzymes.
- **Apoenzyme**
- The inactive protein portion of an enzyme, requiring a cofactor or coenzyme to become catalytically active.
- **Coenzyme**
- Organic, non-protein molecules (e.g., NAD+, FAD) that assist enzymes by transporting chemical groups or electrons during reactions.
- **Cofactors**

Non-protein substances, which can be metal ions (e.g., Mg^{2+}, Zn^{2+}) or organic molecules, that enhance enzyme activity or are essential for its function



IUB System of Enzyme Classification

The IUB system classifies enzymes into **six major classes** based on the type of reaction they catalyze. Each enzyme is assigned a unique **EC number** comprising four numbers separated by periods (e.g., EC 1.1.1.1):

1.First Number: Main enzyme class.

2.Second Number: Subclass, detailing the type of substrate or reaction mechanism.

3.Third Number: Sub-subclass, specifying the substrate or reaction type in more detail.

4.Fourth Number: Serial number of the enzyme in its sub-subclass.

Class	Reaction Catalyzed	Example
1. Oxidoreductases	Catalyze oxidation-reduction (redox) reactions, transferring electrons or hydrogen.	Alcohol dehydrogenase (EC 1.1.1.1)
2. Transferases	Transfer functional groups (e.g., methyl, phosphate) between molecules.	Hexokinase (EC 2.7.1.1)
3. Hydrolases	Catalyze hydrolysis reactions, breaking bonds using water.	Amylase (EC 3.2.1.1)
4. Lyases	Add or remove groups to form double bonds or ring structures without hydrolysis.	Fumarase (EC 4.2.1.2)
5. Isomerases	Catalyze isomerization (rearrangement of atoms within a molecule).	Phosphoglucose isomerase (EC 5.3.1.9)
6. Ligases	Join two molecules by forming new bonds, usually coupled with ATP hydrolysis.	DNA ligase (EC 6.5.1.1)

Enzymes are biological catalysts that significantly speed up biochemical reactions. To do this, they form a temporary complex with the substrate molecule, called the enzyme-substrate complex. This complex facilitates the chemical reaction, converting the substrate into a product.

Two primary models explain how this complex forms:

1. **Fisher's Lock-and-Key Model:**

•**Rigid Structure:** This model, proposed by Emil Fischer in 1894, suggests that the enzyme's active site has a rigid, pre-existing shape that perfectly complements the shape of the substrate.

•**Specific Fit:** The substrate fits into the active site like a key fitting into a lock.

•**Limitations:** While this model explains enzyme specificity, it doesn't account for the flexibility of enzymes and the induced fit mechanism

2. Koshland's Induced Fit Model:

•**Flexible Structure:** This model, proposed by Daniel Koshland in 1958, recognizes that enzymes are not rigid but flexible molecules.

•**Induced Conformational Change:** When the substrate binds to the active site, it induces a conformational change in the enzyme. This change optimizes the active site for catalysis.

•**Enhanced Binding:** The induced fit strengthens the binding between the enzyme and substrate, facilitating the reaction.

- · **Enzyme Specificity:** Enzymes are highly specific, meaning they only catalyze specific reactions with specific substrates.
- · **Active Site:** The active site is the region of the enzyme where the substrate binds and the reaction takes place.
- · **Enzyme-Substrate Complex:** This complex lowers the activation energy of the reaction, making it easier for the reaction to proceed.
- · **Product Formation:** After the reaction, the product is released from the enzyme, and the enzyme is free to bind to another substrate molecule.

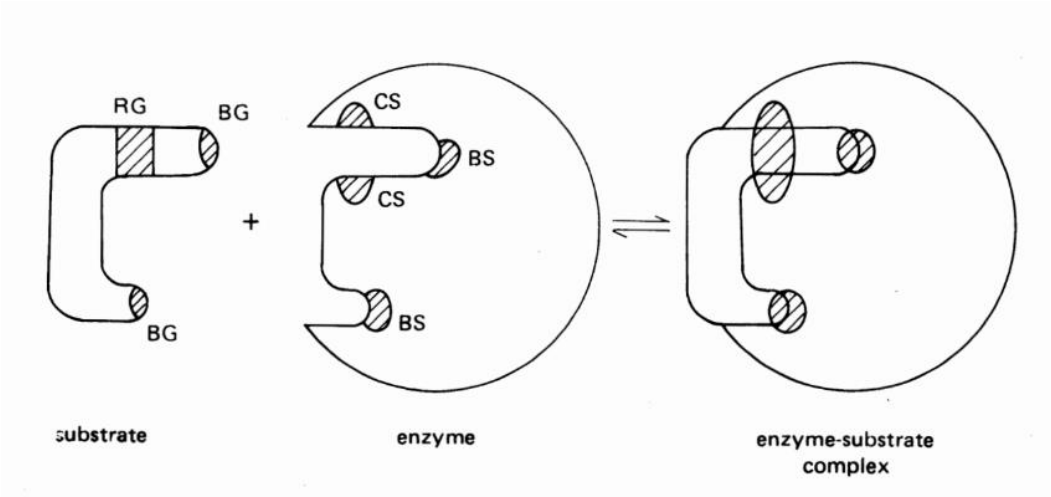


Fig. 2 Diagrammatic representation of the interaction between an enzyme and its substrate, according to the lock and key model.

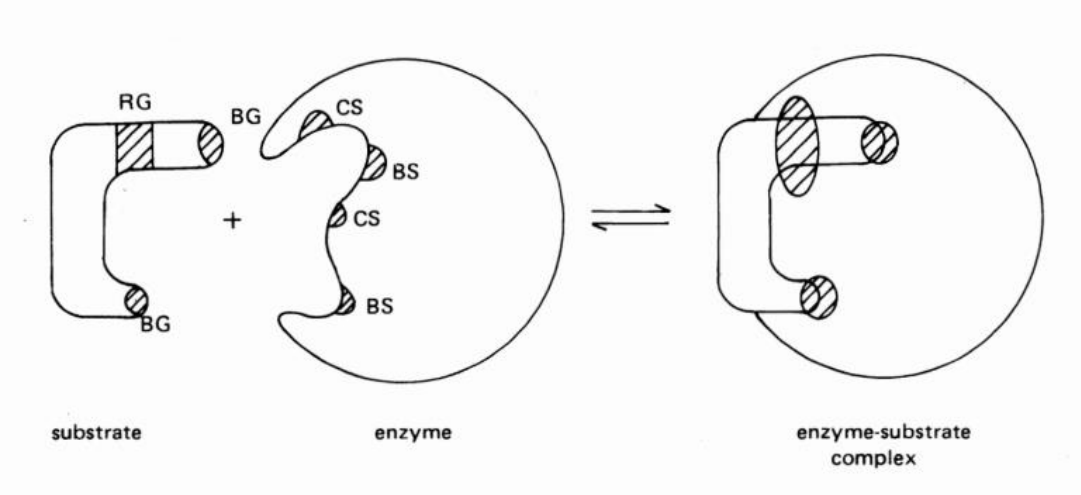


Fig. 3 Diagrammatic representation of the interaction between an enzyme and its substrate, according to the induced-fit model.

Enzymes- Trevor Palmer

Collision Theory, Activation Energy, and Transition State Theory

These theories help us understand the dynamics of chemical reactions.

Collision Theory

- **Basic Principle:** For a reaction to occur, reactant particles must collide with sufficient energy and proper orientation.
- **Energy Requirement:** The colliding particles must possess a minimum amount of energy, known as the **activation energy (Ea)**, to break existing bonds and form new ones.
- **Orientation Factor:** The molecules must collide in a specific orientation for the reaction to proceed.

Activation Energy (Ea)

- **Energy Barrier:** It's the minimum energy required to initiate a chemical reaction.
- **Role in Reaction Rate:** A higher activation energy leads to a slower reaction rate, as fewer particles possess the necessary energy to overcome the barrier.
- **Lowering Ea with Catalysts:** Catalysts work by providing an alternative reaction pathway with a lower activation energy, thereby increasing the reaction rate.

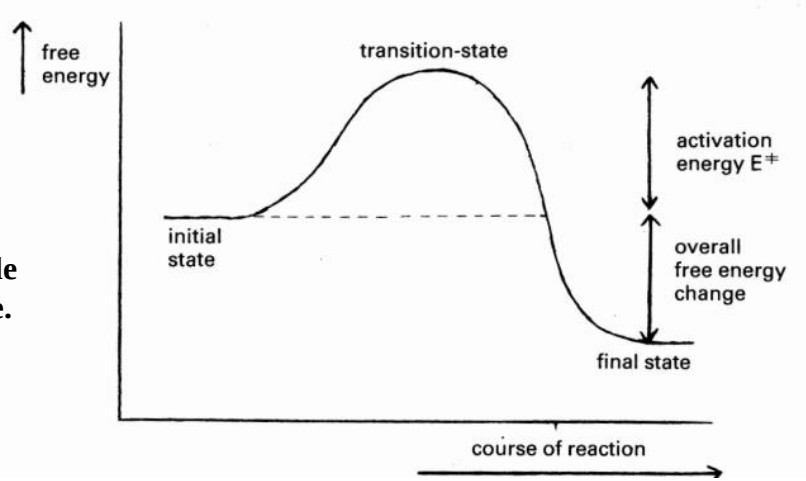


Fig. 4 - Free energy changes for an energetically favourable reaction proceeding via the formation of a transition- state. Enzymes – Trevor Palmer.

Transition State Theory

- **Transition State:** As reactant molecules collide with sufficient energy and orientation, they form a high-energy intermediate state called the **transition state** or **activated complex**.
- **Energy Peak:** The transition state represents the peak of the energy barrier.

Product Formation: The transition state can either revert to reactants or proceed to form products.

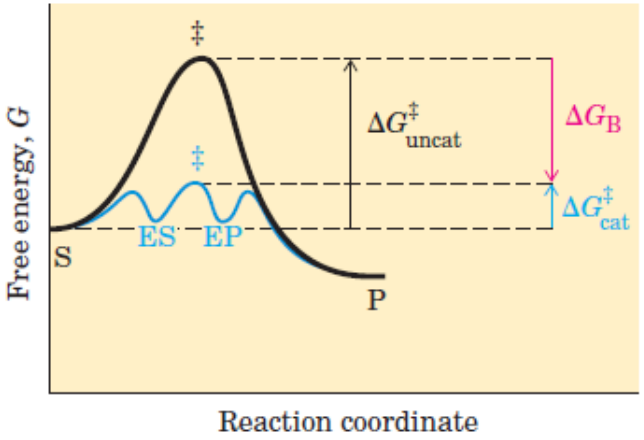


Fig. 5 Role of binding energy in catalysis. To lower the activation energy for a reaction, the system must acquire an amount of energy equivalent to the amount by which $\Delta G\#$ is lowered. Much of this energy comes from binding energy (ΔG_B) contributed by the formation of weak noncovalent interactions between substrate and enzyme in the transition state.

Lehninger- Principles of Biochemistry

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