

UNIT-II :Chemical Kinetics-II :

SYLLABUS

Concept of activation energy and its calculation from Arrhenius equation. Theories of Reaction Rates: Collision theory and Activated Complex theory of bimolecular reactions. Comparison of the two theories (qualitative treatment only). Enzyme catalysis- Specificity, factors affecting enzyme catalysis, Inhibitors and Lock & key model. Michaelis- Menten equation- derivation, significance of Michaelis-Menten constant.

Activation Energy (E_a) is the **minimum amount of energy** that reactant molecules must possess for a chemical reaction to occur. It represents the **energy barrier** between reactants and products. Even exothermic reactions require an initial energy input to reach the **transition state** before forming products.

Without sufficient activation energy, molecules simply collide **elastically** and do not form products.

Activation energy ensures that only a certain **fraction of molecules** (those with enough energy) undergo the transformation.

Arrhenius Equation: $k = A e^{\frac{-E_a}{RT}}$

Where: k = rate constant A = frequency factor or pre-exponential factor T = absolute temperature (K)
E_a = activation energy (J/mol or kJ/mol) R = universal gas constant (8.314 J/mol ·K) e = base of natural logarithms

Taking natural logarithm on both sides:

$$\ln k = \ln A - \frac{E_a}{R} \frac{1}{T} \Rightarrow \ln k = \left(-\frac{E_a}{R}\right) \frac{1}{T} + \ln A$$

This is in the form of $y = mx + c$, a straight line where:

$$\text{slope (m)} = -\frac{E_a}{R}$$

So, if you **plot $\ln k$ vs $\frac{1}{T}$** , you get a straight line, and the **activation energy** can be calculated from the slope.

Collision Theory of Reaction Rates

Collision theory is a kinetic model that explains how and why chemical reactions occur at the molecular level. It emphasizes that for a reaction to occur, reactant particles must collide with one another.

Basic Assumptions of Collision Theory

1. Molecules must collide in order to react.
2. Only a fraction of collisions are effective in producing products.
3. An effective collision must have:
4. Sufficient energy to overcome the activation energy barrier (E_a).
5. Proper orientation to allow the breaking and formation of bonds.
6. Activation Energy (E_a): Minimum energy required for a collision to be successful.
7. Effective Collisions: Collisions that result in a chemical reaction.

8. Ineffective Collisions: Collisions that do not result in a reaction due to insufficient energy or incorrect orientation.

Derivation of the Rate Constant k for a Bimolecular Reaction Using Collision Theory

We consider a bimolecular reaction: $A+B \rightarrow \text{Products}$

According to **collision theory**, the rate of a reaction depends on:

1. **Collision frequency** between reactant molecules (how often A and B collide),
2. **Fraction of collisions with energy \geq activation energy**,
3. **Proper orientation (steric factor)**.

Derivation

Step 1: Collision Frequency Z_{AB}

In gases, the number of collisions per unit volume per second between molecules of A and B is given by:

$$Z_{AB} = N_A \cdot N_B \cdot \sigma_{AB} \sqrt{\frac{8KT}{\pi\mu}}$$

Where:

- N_A, N_B = number densities of A and B (mol/m^3),
- σ_{AB} = effective collision cross-sectional area (m^2),
- k = Boltzmann constant,
- T = absolute temperature (K),
- μ = reduced mass of A and B: $\mu = \frac{m_A m_B}{m_A + m_B}$

Step 2: Fraction of Effective Collisions

Only those collisions with kinetic energy **greater than or equal to the activation energy E_a** result in a reaction. This fraction is given by the **Boltzmann factor**:

$$f = e^{\frac{-E_a}{RT}}$$

Where: R = gas constant, T = temperature in Kelvin, E_a = activation energy

Step 3: Include the Steric Factor P

Not all collisions with sufficient energy lead to reaction unless molecules are **oriented correctly**. This is represented by a **steric factor P** (usually < 1):

P accounts for the **fraction of collisions** that have the **correct orientation**.

Final Rate Expression

Multiplying all three components:

$$k = P \cdot Z_{AB} \cdot e^{\frac{-E_a}{RT}}$$

Substitute Z_{AB} into the expression:

$$k = P \cdot N_A \cdot N_B \cdot \sigma_{AB} \sqrt{\frac{8KT}{\Pi\mu}} e^{\frac{-E_a}{RT}}$$

This gives the **rate constant k** for a **bimolecular reaction** according to **collision theory**.

$$k = P \cdot Z_{AB} \cdot e^{\frac{-E_a}{RT}}$$

P: steric/orientation factor, Z_{AB} : collision frequency, $e^{-E_a/RT}$: energy factor (fraction of collisions with sufficient energy).

Activated Complex Theory (Transition State Theory)

This theory was developed by **Eyring** and **Polanyi** in the 1930s and explains the mechanism of chemical reactions based on the formation of an intermediate high-energy complex called the **activated complex** or **transition state**.

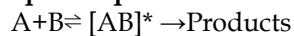
Postulates of Activated Complex Theory

1. Formation of Activated Complex:

Reactants first form an unstable high-energy intermediate species called the **activated complex** or **transition state** before forming products.

2. Equilibrium Between Reactants and Activated Complex:

There is a **quasi-equilibrium** between the reactants and the activated complex.



3. Decomposition of Activated Complex:

The activated complex then decomposes to form the products. The rate of reaction depends on how fast this decomposition occurs.

4. Rate Proportional to Concentration of Activated Complex:

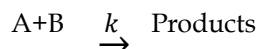
The rate of the reaction is proportional to the concentration of the activated complex and the frequency with which it crosses the energy barrier.

5. Boltzmann Distribution:

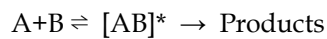
Only those molecules that have energy **equal to or greater than activation energy** can form the activated complex.

Derivation of the Rate Constant

Consider the bimolecular reaction:



This proceeds via the transition state $[AB]^*$:



Step 1: Equilibrium Concentration of Activated Complex

Let the equilibrium constant for the formation of the activated complex be:

$$K^* = \frac{[AB]^*}{[A][B]}$$

So, $[AB]^* = K^* [A][B]$

Step 2: Rate of Reaction

The activated complex decomposes into products with a characteristic frequency ν (vibration along reaction coordinate), then the rate of reaction is:

$$\text{Rate} = \nu \cdot [AB]^* = \nu K^* [A][B]$$

Hence, the **rate constant** k is: νK^* i.e., $k = \nu K^*$

Step 3: Expression for ν : According to statistical mechanics, ν is approximated as:

$$\nu = \frac{k_B T}{h}$$

Where: k_B : Boltzmann constant h : Planck's constant T : Temperature in Kelvin

Step 4: Expression for K^*

From thermodynamics:

$$K^* = e^{\frac{-\Delta G^*}{RT}}$$

Where: ΔG^* Gibbs free energy of activation

By substituting the values in the relation $k = \nu K^*$, the **rate constant** becomes:

$$k = \frac{k_B T}{h} e^{\frac{-\Delta G^*}{RT}}$$

Using: $\Delta G^* = \Delta H^* - T\Delta S^*$ Then,

$$k = \frac{k_B T}{h} e^{\frac{-(\Delta H^* - T\Delta S^*)}{RT}} \Rightarrow \frac{k_B T}{h} e^{\frac{(T\Delta S^* - \Delta H^*)}{RT}} \Rightarrow \frac{k_B T}{h} e^{\frac{\Delta S^*}{R}} e^{\frac{-\Delta H^*}{RT}}$$

Final Expression for Rate Constant (Activated Complex Theory) is

$$k = \frac{k_B T}{h} \cdot e^{\frac{\Delta S^*}{R}} \cdot e^{\frac{-\Delta H^*}{RT}}$$

Comparison of Collision Theory and Activated Complex Theory (qualitative treatment only)

Feature	Collision Theory	Activated Complex Theory (Transition State Theory)
Basis	Kinetic theory of gases	Thermodynamics and statistical mechanics
Key Concept	Molecules must collide with proper orientation and sufficient energy	Formation of an activated complex (transition state) before product formation
Energy Requirement	Molecules must have energy \geq activation energy during collision	Free energy difference between reactants and transition state determines reaction rate
Rate Constant Expression	$k = P \cdot N_A \cdot N_B \cdot \sigma_{AB} \sqrt{\frac{8KT}{\pi\mu}} e^{\frac{-E_a}{RT}}$	$k = \frac{k_B T}{h} \cdot e^{\frac{\Delta S^\ddagger}{R}} \cdot e^{\frac{-\Delta H^\ddagger}{RT}}$
Orientation Role	Explicitly included via steric factor P	Implicit in entropy of activation ΔS^\ddagger
Reaction Pathway	Direct transformation upon effective collision	Formation and decomposition of an unstable intermediate (activated complex)
Applicability	Best suited for simple gas-phase bimolecular reactions	Applicable to gas, liquid, and complex reactions
Limitations	Oversimplified for many reactions, doesn't explain entropy effects	More detailed and universally applicable
Important Parameters	Collision frequency Z, steric factor P, activation energy E_a	ΔH^\ddagger , ΔS^\ddagger , ΔG^\ddagger , temperature T

Advantage	Simple and intuitive	Accurate and comprehensive, connects kinetics with thermodynamics
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Introduction to Enzyme Catalysis

Enzyme catalysis refers to the increase in the rate of a biochemical reaction caused by the participation of enzymes, which are biological macromolecules (mostly proteins) that act as catalysts.

Enzymes accelerate reactions by providing an alternative reaction pathway with a lower activation energy, without being consumed in the reaction. They are highly specific to their substrates and operate under mild conditions of temperature and pH, typical of living systems.

Features of Enzyme Catalysis

- **Specificity:** Enzymes are highly selective; they typically catalyze only one specific reaction or a group of closely related reactions.
- **Active Site:** The region of the enzyme where the substrate binds and the reaction takes place is called the **active site**.
- **Lock and Key Model:** The enzyme and substrate fit together like a key into a lock.
- **Induced Fit Model:** The enzyme changes shape slightly to accommodate the substrate more effectively.
- **Catalytic Efficiency:** Enzymes can increase reaction rates by factors of 10^6 to 10^{12} times.
- **Turnover Number:** The number of substrate molecules converted into product per enzyme molecule per unit time.

General Equation Enzyme Catalysis



Specificity of Enzyme Catalysis

Enzyme specificity refers to the ability of an enzyme to select and act on a particular substrate or a group of related substrates. This property is one of the most distinguishing features of enzymes compared to non-biological catalysts.

Types of Enzyme Specificity:

1. Absolute Specificity
 - The enzyme acts only on one specific substrate.
 - Example: *Urease* catalyzes only the hydrolysis of urea to ammonia and carbon dioxide.

2. Group Specificity

- The enzyme acts on substrates with a specific functional group.
- Example: *Alcohol dehydrogenase* acts on alcohols regardless of the carbon chain length.

3. Linkage Specificity

- The enzyme acts on a particular type of bond, regardless of the rest of the molecular structure.
- Example: *Proteases* cleave peptide bonds in proteins.

4. Stereochemical Specificity

- The enzyme acts only on a specific isomer (usually one enantiomer).
- Example: *Lactate dehydrogenase* acts only on L-lactate, not D-lactate.

Mechanism of Specificity:

- **Lock and Key Model:** The enzyme's active site has a shape that exactly matches the shape of the substrate.
- **Induced Fit Model:** The enzyme undergoes conformational changes upon substrate binding to achieve a tighter fit.

Importance of Specificity:

- Ensures precise regulation of biochemical pathways.
- Prevents unwanted side reactions.
- Increases efficiency and selectivity in metabolic processes.

Factors Affecting Enzyme Catalysis

- A. **Effect of Temperature:** Enzyme activity increases with temperature up to an optimum level, usually around 37–40°C for enzymes in the human body. Beyond this point, enzymes begin to denature, losing their structure and function, leading to a sharp decrease in activity.
- B. **Effect of pH:** Each enzyme has a specific pH range in which it operates most effectively. Deviations from this optimal pH can alter the ionization state of the active site or the substrate, reducing binding efficiency and catalysis.
- C. **Effect of Substrate Concentration:** Increasing substrate concentration generally increases the rate of enzyme-catalyzed reactions, as more substrate molecules are available to occupy active sites. However, once all enzyme active sites are saturated (V_{max}), further increases in substrate concentration have no effect.
- D. **Effect of Enzyme Concentration:** If sufficient substrate is available, increasing enzyme concentration increases the reaction rate proportionally, since more active sites are available for catalysis.

- E. Effect of Presence of Inhibitors: Inhibitors reduce enzyme activity. Competitive inhibitors compete with the substrate for the active site, while non-competitive inhibitors bind elsewhere, altering enzyme structure. Uncompetitive inhibitors bind only to the enzyme-substrate complex.
- F. Effect of Presence of Activators or Coenzymes: Certain molecules such as metal ions (e.g., Zn^{2+} , Mg^{2+}) or coenzymes (e.g., NAD^+ , FAD) enhance enzymatic activity by stabilizing the active site or participating in the reaction.
- G. Effect of Time of Reaction: Over time, substrate is consumed and product accumulates. Eventually, equilibrium is reached, and the net reaction rate decreases.
- H. Effect of Product Concentration: Accumulation of the reaction product can lead to feedback inhibition, where the product inhibits the enzyme that produced it, thereby slowing or stopping the reaction.
- I. Effect of Ionic Strength of the Medium: High salt concentrations or changes in ionic strength can affect the structure of enzymes or the binding of substrates, altering the catalytic activity.
- J. Effect of Light and Radiation: For enzymes that are light-sensitive (e.g., those involved in photosynthesis), exposure to light can initiate or enhance catalytic activity. Conversely, strong radiation may damage enzymes.

Types of Enzyme Inhibitors:

1. Competitive Inhibitors:
 - Compete with the substrate for binding at the active site of the enzyme.
 - Structurally resemble the substrate.
 - Effect can be overcome by increasing substrate concentration.
 - Example: Malonate inhibits succinate dehydrogenase (similar to succinate).
2. Non-Competitive Inhibitors:
 - Bind to a site other than the active site (an allosteric site).
 - Change the enzyme's shape, making it less effective or inactive.
 - Cannot be reversed by increasing substrate concentration.
 - Example: Heavy metal ions like Hg^{2+} or Ag^+ can inhibit enzyme activity.
3. Uncompetitive Inhibitors:
 - Bind only to the enzyme-substrate complex.
 - Prevent the reaction from completing by locking the substrate in place.

- Rare and typically found in multi-substrate reactions.
4. Irreversible Inhibitors:
- Form covalent bonds with the enzyme.
 - Permanently inactivate the enzyme.
 - Example: Penicillin irreversibly inhibits bacterial transpeptidase.
5. Feedback Inhibitors:
- End products of a metabolic pathway inhibit an enzyme earlier in the pathway.
 - Used by cells to regulate the amount of product.
 - Example: ATP inhibits phosphofructokinase in glycolysis.

Enzyme Activity: Lock & Key Model

Definition:

The **Lock and Key model** is a classical explanation of how enzymes and substrates interact. Proposed by **Emil Fischer in 1894**, it suggests that the **enzyme's active site (lock)** has a specific geometric shape that exactly fits the **substrate (key)**.

Features:

Specificity: Just as only the right key fits into a specific lock, only a **substrate with the correct shape** fits into the **active site** of the enzyme.

No Structural Change: The enzyme does **not change its shape** to accommodate the substrate. Instead, **only the correctly shaped substrate** can bind.

Temporary Binding: The enzyme-substrate complex forms temporarily. Once the reaction is complete, the **products are released** and the **enzyme remains unchanged**, ready for another cycle.

Steps in the Lock & Key Mechanism:

1. **Recognition:** The enzyme recognizes and binds to the substrate due to its specific shape.
2. **Formation of Enzyme-Substrate Complex (E-S):** This complex is stable enough for the reaction to proceed.
3. **Catalysis:** The substrate undergoes a chemical change to form the product.
4. **Product Release:** The product is released, and the enzyme remains unchanged.

Example: Enzyme: Sucrase **Substrate:** Sucrose **Reaction:** Sucrose is hydrolyzed into glucose and fructose. Sucrase has an active site shaped to fit sucrose only – not other disaccharides.

Limitations of the Lock & Key Model:

- It doesn't explain **flexibility** in enzymes or **induced fit**.
- Some enzymes **change shape** slightly to accommodate the substrate – this led to the **Induced Fit model**.

Michaelis-Menten Equation: Derivation and Significance of constant.(Km)

Michaelis and Menten (1913) developed a **mathematical model** describing the **rate of enzymatic reactions** by relating the reaction rate (v) to the **substrate concentration ([S])**.

Reaction Scheme:



Where, E = enzyme S = substrate ES = enzyme-substrate complex P = product k_1 , k_{-1} , and k_2 are rate constants

Assumptions: According to Michaelis-Menten

1. **Formation of ES is rapid and reversible.**
2. **Breakdown of ES into product is slow and rate-limiting.**
3. **[ES] reaches a steady-state:** its formation and breakdown rates are equal (steady-state approximation).

Derivation:

Step 1: Steady-state approximation

- The enzyme E and substrate S quickly combine to form an **enzyme-substrate complex (ES)**.
- The ES complex either **dissociates back** into E and S or proceeds **forward** to form **product (P)**.
- the **concentration of the intermediate complex [ES] becomes constant** after a very short time. That means $\frac{d[ES]}{dt} = 0$ This is called the **steady-state condition**

$$\text{If } \frac{d[ES]}{dt} = 0 \Rightarrow k_1[E][S] - (k_{-1}+k_2)[ES] = 0 \quad ([ES] \text{ consumption rate} = [ES] \text{ formation rate})$$

$$\text{Solve for [ES]: } [ES] = \frac{k_1[E][S]}{(k_{-1}+k_2)}$$

Step 2: Define Michaelis-Menten constant (Km)

$$K_m = \frac{(k_{-1}+k_2)}{(k_1)} \quad \text{So, } [ES] = \frac{[E][S]}{(K_m)} \quad \text{OR } [E] = \frac{[ES]K_m}{[S]}$$

Total enzyme concentration

$$[E]_T = [E] + [ES] \Rightarrow [E] = [E]_T - [ES]$$

$$\Rightarrow [ES] = [E]_T - [E] = [E]_T - \frac{[ES]k_m}{[S]}$$

Substitute [E] into : [ES]

$$\Rightarrow [ES] + \frac{[ES]k_m}{[S]} = [E]_T$$

$$\Rightarrow [ES] \left(1 + \frac{k_m}{[S]}\right) = [E]_T$$

$$\text{Solve for [ES]: } [ES] = \frac{[E]_T [S]}{[S] + k_m}$$

Step 4: Reaction rate

$$v = \frac{d[P]}{dt} = k_2[ES] \Rightarrow v = k_2[ES]$$

$$\text{Substitute [ES] value in the above equation : } v = k_2 \frac{[E]_T [S]}{[S] + k_m}$$

$$v = \frac{V_{max}[S]}{[S] + k_m} \quad \text{Where } V_{max} = k_2[E]_T$$

The equation $v = \frac{V_{max}[S]}{[S] + k_m}$ is called Michaelis-Menten Equation

Significance of K_m (Michaelis constant):

1. Affinity Indicator: K_m is inversely related to enzyme-substrate affinity. Lower $K_m \Rightarrow$ higher affinity.
2. Substrate Concentration at Half-Maximum Velocity: When $v = \frac{V_{max}}{2}$, then $[S] = K_m$
3. Helps Compare Enzymes: Enzymes with different K_m values have different substrate binding capabilities.
4. Physiological Relevance: In cells, many enzymes operate around $[S] = K_m$, making them sensitive to changes in $[S]$.