

Biochemistry

World of Revision

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ENZYMES

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Basics of Enzymes

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Definition :

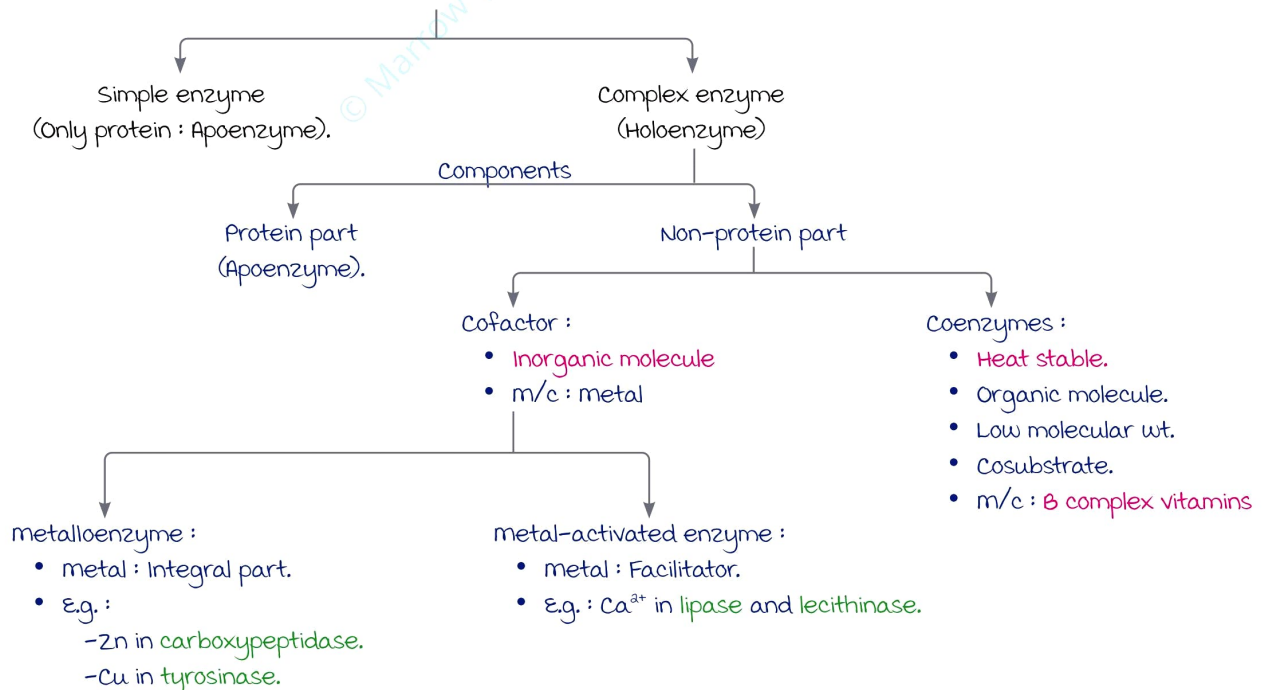
- Specialized proteins that act as **biological catalyst**.
- Exception : **Ribozymes** (RNA).

Ribozyme	Location	Function
Peptidyl transferase	28 Sr RNA	Peptide bond synthesis
Sn RNA	Spliceosome	RNA splicing
Group II introns (Self splicing)	-	
Ribonuclease P	-	Post-transcriptional modification of tRNA

Properties of Enzymes :

- 16% by weight : Nitrogen.
- Heat labile**.
- Precipitated by protein precipitating agents.

Types of Enzymes :



Prosthetic group : Co-enzyme/Co-factor tightly integrated into apoenzyme.

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Coenzymes :

Vitamin	Active form	Reaction involved
Thiamine	Thiamine di/pyrophosphate (TDP/TPP)	- Oxidative decarboxylation : BCKD, α-KGDH, PDH - Transketolase
Riboflavin	FAD, FMN	Dehydrogenase (Succinate, acyl CoA)
Niacin	NAD ⁺ , NADP ⁺	most dehydrogenases
Pantothenic acid	CoA, Acyl carrier protein	All reactions with acetyl CoA, succinyl CoA & fatty acid synthase complex
Pyridoxine	Pyridoxal phosphate	- Transamination - Transulfuration (Cystathionine-β synthase & cystathionase) - Decarboxylation - ALA synthase : Heme synthesis - Glycogen phosphorylase : Carbohydrate metabolism Amino acid metabolism
Folic acid	THFA	All 1 Carbon reactions
Cobalamin	- methy B₁₂ - Adenosyl B₁₂	- methionine synthase - methy malonyl CoA mutase
Lipoate	Lipoamide	Oxidative decarboxylation
Ascorbic acid	-	Hydroxylation (Prolyl & lysyl hydroxylase) : Collagen synthesis

Co-factors :

metal	Reaction catalysed
Zinc	- Carbonic anhydrase - Carboxypeptidase A & B - Alcohol dehydrogenase - Cytosolic SOD (Free radical scavenger)
magnesium	ATP/PO ₄ group involved : - Kinase - Phosphatase - mutase - Enolase
Iron	Heme iron : - Hemoglobin, myoglobin - Complex III & IV of ETC (Cytochrome) - Nitric oxide synthase - Peroxidase - Catalase - Tryptophan pyrrolase Non-heme iron : Complex I, II and III of ETC (Fe-S complex)

Zn deficiency features

↓ Retinol dehydrogenase
↓
Visual disturbances

no deficiency

- ↓ xanthine oxidase
- Hypouricemia

Cu deficiency

- Depigmentation/hypopigmentation
- X-ray : Similar to scurvy
- Menke's disease :
Lysyl oxidase defect (ATP 7A gene)

metal	Reaction catalysed
manganese	- Kinase - Phosphatase - mitochondrial SOD - Arginase - Ribonucleotide reductase
molybdenum	Xanthine oxidase
Potassium	$\text{Na}^+ - \text{K}^+$ ATPase - Pyruvate kinase
Copper	- Tyrosinase (melanin production) - Complex IV of ETC (Cytochrome c oxidase) - Lysyl oxidase : - Covalent cross linking of collagen (Quarter staggered arrangement) - Oxidative deamination of lysyl and hydroxylysyl residues.
Nickel	Urease
Calcium	- Lecithinase - Lipase

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Note :

vit. C deficiency leads to defective collagen D/t ↓ lysyl hydroxylase and prolyl hydroxylase.

Classification of Enzymes

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Class	Class name	Details & examples
I : Oxidoreductases	Dehydrogenase	Transfer hydrogen elements to an acceptor : $\text{NAD}^+ \rightarrow \text{NADH}$ $\text{FAD} \rightarrow \text{FADH}_2$ - Acyl CoA DH $\text{NADP}^+ \rightarrow \text{NADPH}$ - Gl6PD 6-Phosphogluconate DH - Cytoplasmic ICDH } HMP shunt
	Oxygenase	monooxygenase : Phenylalanine/tyrosine/tryptophan hydroxylase (Require BH_4), cytochromes
	Oxidase	Forms H_2O or $\text{H}_2\text{O}_2 \rightarrow$ Source of ROS
	Peroxidase	- Glutathione peroxidase ($\text{H}_2\text{O}_2 \rightarrow \text{H}_2\text{O}$) - Free radical scavenger
	Catalase	$\text{H}_2\text{O}_2 \rightarrow \text{H}_2\text{O}$ - Enzyme marker of peroxisome - Free radical scavenger
	Reductase	Reductive biosynthesis : - NADPH utilizer (generated by HMP shunt) - Fatty acid, cholesterol & steroid synthesis
II	Transferase	- Transfers functional group - E.g. : - Kinases (Hexo/glucokinase) - Phosphorylases (Glycogen phosphorylase)
III	Hydrolase	- Breaks covalent bonds by adding H_2O - E.g. : - All digestive enzymes - Phosphatase - Arginase

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Class	Class name	Details & examples
IV	Lyase	- Breaks covalent bond without H_2O addition - Form double bonds by atom elimination or adding groups - E.g.: - Aldolase - Fumarase - Aconitase - Enolase - Simple decarboxylase (require PLP)
V	Isomerase	E.g.: - Isomerase (Produces isomers) - Racemase (D & L isomers) - Mutase (Intramolecular PO_4 transfer)
VI	Ligase	- Coupling of molecules with breakdown of ATP - E.g.: - Synthetase - Carboxylase (Requires biotin)
VII	Translocase	- Transfer of ions/molecules across membrane - E.g.: H^+ pump/Ca^{2+} channel

Carboxylation & decarboxylation reactions :

Types	Reactions & cofactors	Applied biochemistry
Simple decarboxylation : Class IV	Synthesis of : - GABA - Serotonin - Epinephrine - Norepinephrine Requires PLP (vit B_6)	vit B_6 deficiency : Resistant seizures in neonate
Oxidative decarboxylation : Class I	- multienzyme complexes : - E1 : PDH/α-KGDH/BCKD - E2 : Dihydrolipoyl transacylase - E3 : Dihydrolipoamide DH 5 coenzymes : - TPP : vit B_1 - CoA : vit B_5 - Lipoamide - FAD : vit B_a NAD^+ : vit B_3	- Chronic alcoholism : vit. B_1 def. $\rightarrow$ $\downarrow$ PDH, α-KDH $\rightarrow$ $\downarrow$ ATP (Fatigue) - Beri-beri : vit. B_1 def. $\rightarrow$ - Peripheral edema - Ptois - Confabulation - Enzyme assay : Erythrocyte transketolase
B_7 dependent carboxylation	Requires : - ATP - Biotin CO_2	Avidin (Raw egg) $\xrightarrow{\ominus}$ Biotin dependent carboxylases
B_7 independent carboxylation	- AKR carboxylase - Gamma carboxylase : Needs vit. K - CPS : I and II	-

Enzyme Mechanism of Action

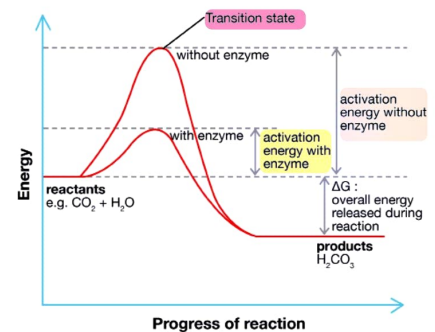
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- Substrate binding : **Active site**.
- Site for regulator/modifier : **Allosteric site**.

Free energy change (ΔG) :

- Free energy change =
 $\Delta G = \text{Energy of product} - \text{Energy of substrate}$.
- Enzyme $\rightarrow$ $\downarrow$ Activation energy.
 $(\epsilon_{\text{act}}^{\text{catalysed}} < \epsilon_{\text{act}}^{\text{uncatalysed}})$
 $\rightarrow$ No change in ΔG .



ΔG interpretation

- +ve : Unfavourable/endergonic reaction
- -ve : Favourable/exergonic reaction

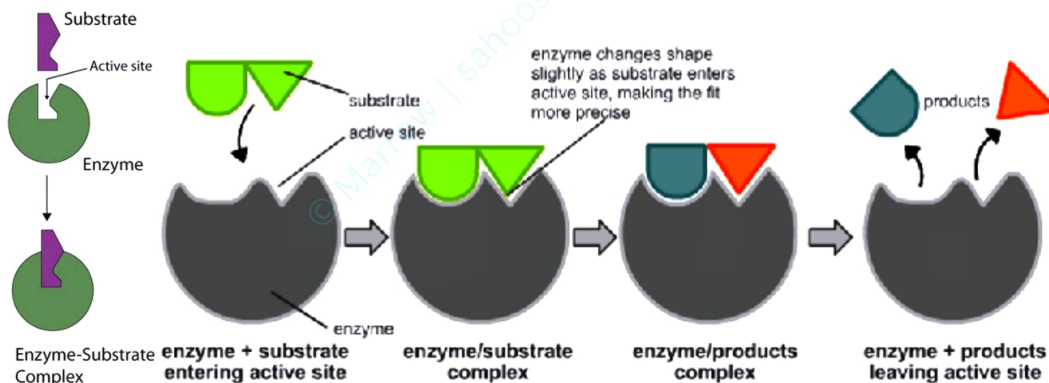
Enzyme-Substrate Complex :

Emil-Fischer's template theory :

- Lock and key mechanism.
- Could not explain dynamic changes.

Koshland's induced fit theory :

Conformational change in active site induced by substrate during binding.



mechanisms that Lower Activation Energy (ϵ_{act}) :

mechanism	Details	Examples
Catalysis by proximity	Reactants in bond-forming distance	-
Acid-base catalysis	Amino acid at catalytic site Proton donors Proton acceptors	Aspartate proteases (Pepsin)
Covalent catalysis	Transient covalent bond b/w : Enzyme + substrate	Serine proteases
metal-ion catalysis	metal ions facilitate reaction	Zn in Carboxy peptidase
Catalysis by strain	Enzyme strains & breaks substrate	Lytic reaction $\rightarrow$ Lyase Hydrolyase

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Enzyme Kinetics

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Equilibrium constant (K_{eq}):

- Independent of enzyme action.
- $K_{eq} = \frac{[Products]}{[Substrates]}$
- $K_{eq} = 1$: Reversible reaction at equilibrium.

Factors Affecting Rate of Reaction 🧬:

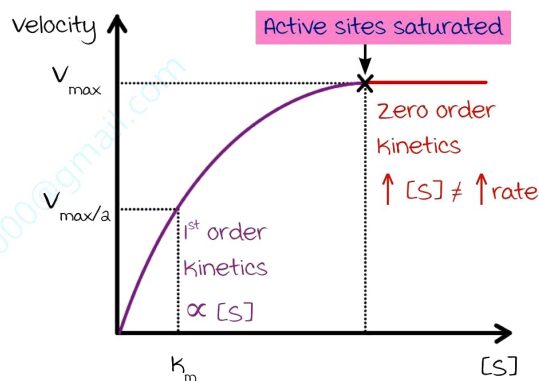
1. Substrate concentration:

- Hyperbolic curve:

Michaelis-Menten equation:

$$V_i = \frac{V_{max} \times [S]}{K_m + [S]}$$

K_m value (Michaelis constant)
$[S]$ at $V_{max}/2$. $\propto \frac{1}{\text{enzyme affinity to substrate}}$ - If $[S] = 1000 K_m$: Zero order kinetics - Signature of E-S complex - Ideal substrate: Lowest K_m

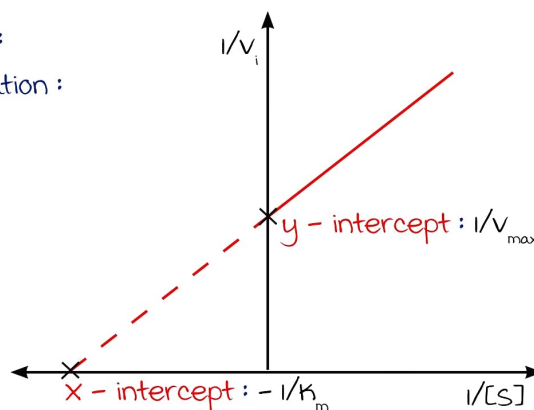


- Lineweaver-Burk plot (Straight line):

Reciprocal of Michaelis-Menten equation:

$$\frac{1}{V_i} = \frac{K_m}{V_{max}} \times \frac{1}{[S]} + \frac{1}{V_{max}}$$

$\uparrow$ $\uparrow$ $\uparrow$ $\uparrow$
 $y = a \times x + b$



2. Enzyme concentration:

