Biochemistry

World of Revision

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Contents

Biochemistry

ENZYMES

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Basics of Enzymes

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Definition :

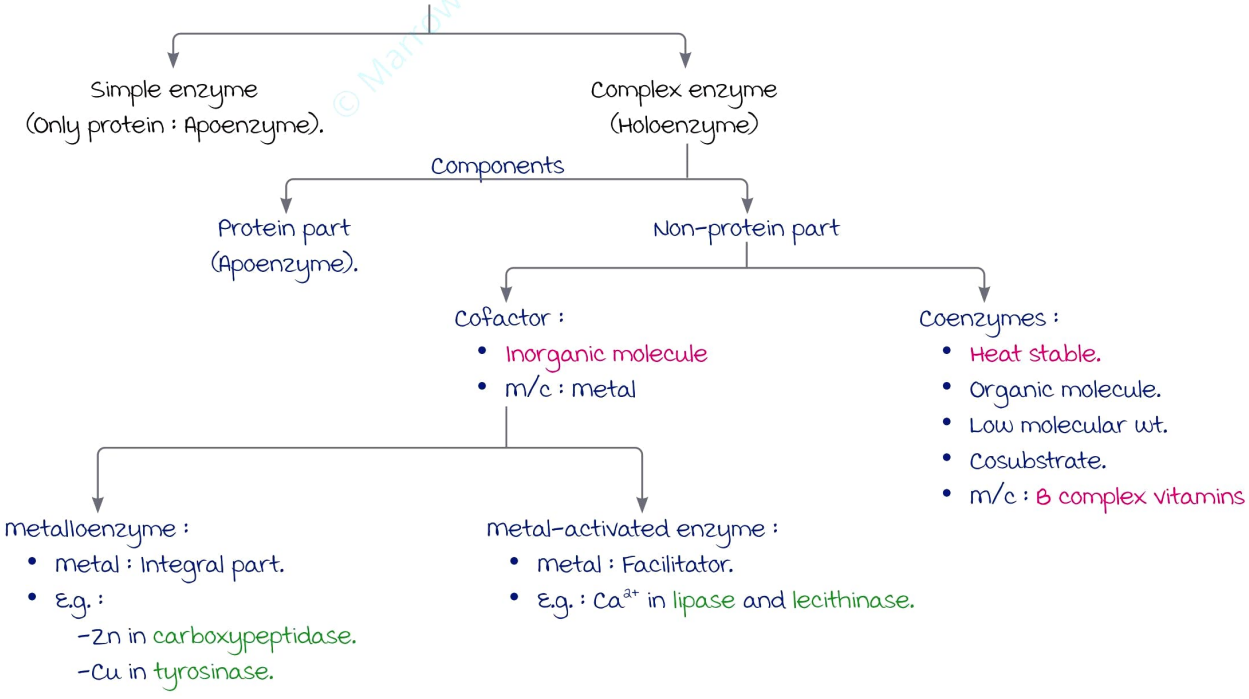
- Specialized proteins that act as biological catalyst.
- Exception : Ribozymes (RNA).

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) } Amino acid metabolism • Decarboxylation • ALA synthase : Heme synthesis • Glycogen phosphorylase : Carbohydrate metabolism
Folic acid	THFA	All 1 Carbon reactions
Cobalamin	• Methyl B_{12} • Adenosyl B_{12}	• Methionine synthase • Methyl malonyl CoA mutase
Lipoate	Lipoamide	Oxidative decarboxylation
Ascorbic acid	-	Hydroxylation (Prolyl & lysyl hydroxylase) : Collagen synthesis

Cofactors :

metal	Reaction catalysed
Zinc	• Carbonic anhydrase • Carboxypeptidase A & B • Alcohol dehydrogenase • Cytosolic SOD (Free radical scavenger)
Magnesium	ATP/PO_4 group involved : • Kinase • Mutase • Phosphatase • Enolase
Iron	Heme iron : • Hemoglobin, myoglobin • Peroxidase • Complex III & IV of ETC (Cytochrome) • Catalase • Nitric oxide synthase • Tryptophan pyrrolase
	Non-heme iron : Complex I, II and III of ETC (Fe-S complex)

Zn deficiency features

↓Retinol dehydrogenase

↓

Visual disturbances

Mo deficiency

- ↓Xanthine oxidase
- Hypouricemia

Cu deficiency

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

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metal	Reaction catalysed
Manganese	• Kinase • Phosphatase • Mitochondrial SOD • Arginase • Ribonucleotide reductase
Molybdenum	Xanthine oxidase
Potassium	• Na^+– 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

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 : • $NAD^+ \rightarrow NADH$ • $NADP^+ \rightarrow NADPH$: – G6PD – 6-Phosphogluconate DH } HMP shunt • FAD → $FADH_2$: – SDH – Acyl CoA DH – Cytoplasmic ICDH
	Oxygenase	Monooxygenase : Phenylalanine/tyrosine/ tryptophan hydroxylase (Require BH_4), cytochromes
	Oxidase	Forms H_2O or H_2O_2 → Source of ROS
	Peroxidase	• Glutathione peroxidase ($H_2O_2 \rightarrow H_2O$) • Free radical scavenger
	Catalase	• $H_2O_2 \rightarrow H_2O$ • Free radical scavenger • Enzyme marker of peroxisome
	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_2 – NAD^+ : Vit B_3	• Chronic alcoholism : Vit. B_1 def. → ↓PDH, α-KDH → ↓ATP (Fatigue) • Beri-beri : Vit. B_1 def. (D/t polished rice consumption) → Peripheral edema, Ptosis, Confabulation • Enzyme assay : Erythrocyte transketolase
B_7 dependent carboxylation	Requires : • ATP • Biotin • CO_2	Avidin (Raw egg) ⊖ Biotin dependent carboxylases
B_7 independent carboxylation	• AIR carboxylase • Gamma carboxylase : Needs vit. K • CPS : I and II	–

Enzyme Mechanism of Action

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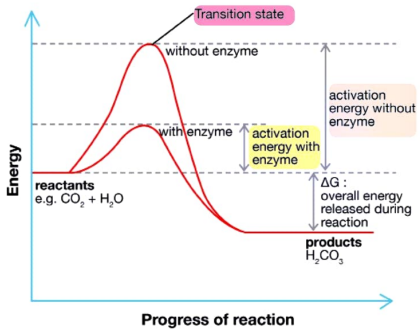
- Substrate binding : Active site.
- Site for regulator/modifier : Allosteric site.

Free energy change (ΔG) :

- Free energy change =
  ΔG = Energy of product − Energy of substrate.
- Enzyme → ↓Activation energy.
  (ε_{act} catalysed < ε_{act} uncatalysed)
  → No change in ΔG.



ΔG interpretation
• +ve : Unfavourable/endergonic reaction
• −ve : Favourable/exergonic reaction

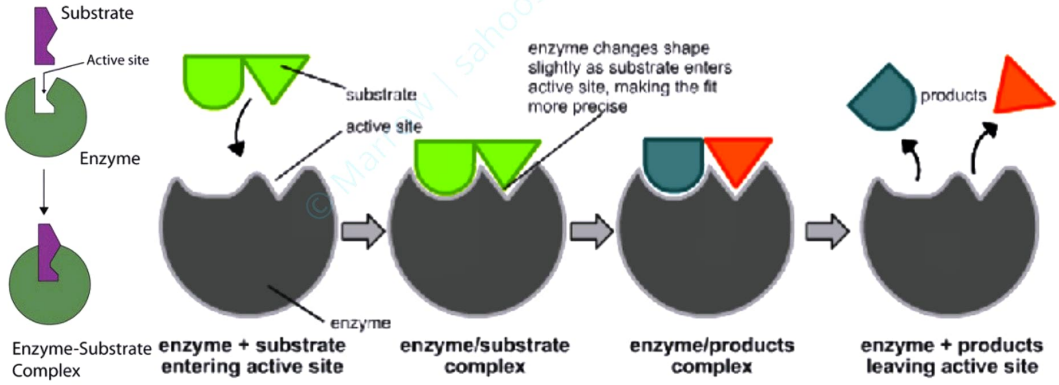
Enzyme-Substrate Complex :

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 → Lyase / Hydrolase

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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 :

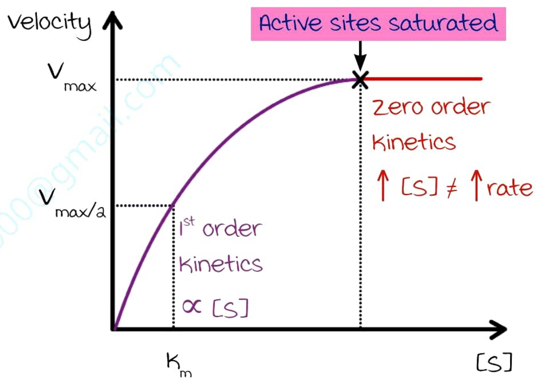
- Hyperbolic curve :

  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.

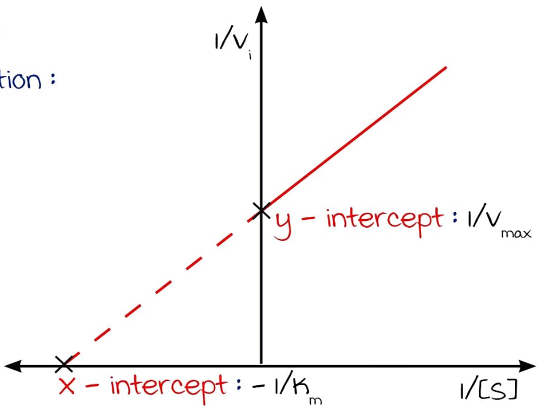


- Lineweaver-Burk plot (Straight line) :

  Reciprocal of Michaelis-Menten equation :

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

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



2. Enzyme concentration :