

Biomedical
Science

Molecular
Genetics



BMS 23110c | Fall 2026-2027

Enzymology

The Structure of Enzymes



Free Session

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What Is an Enzyme?

DEFINITION

Enzymes are **biological catalysts**. They speed up the rates of chemical reactions without themselves undergoing **any permanent change**.

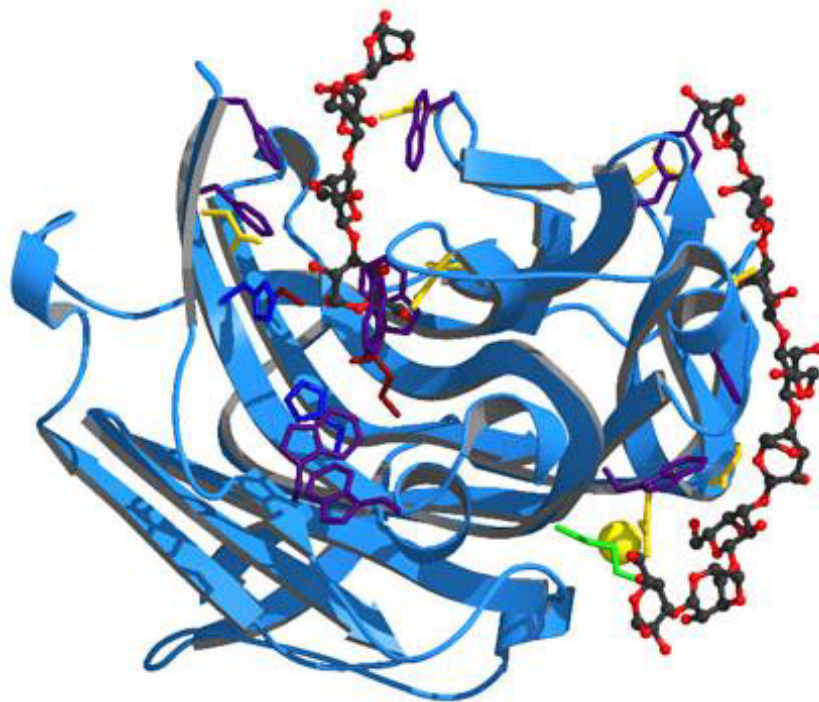
The study of enzymes is called **enzymology**.

Chemical nature

- The majority of enzymes are **proteins**
- Some consist of **RNA**, or a complex of protein and RNA (**ribozymes**)

Conditions & turnover

- Increase rates of reactions under **physiological conditions** (temperature and pH)
- Without themselves **being used up** in the reaction



Ribozymes — catalytic RNA and protein–RNA complexes



Historical Aspects

- 1 The term '**enzyme**' was coined in **1878** by Friedrich Wilhelm Kuhne
- 2 The name literally means '**in yeast**'
- 3 Because of the most recognizable reaction, popularly known as **alcohol fermentation** by zymase enzyme in yeast

en (G) = in

+

zyme (G) = yeast

→

enzyme = 'in yeast'



Friedrich Wilhelm Kuhne
coined the term in 1878



Critical for Every Aspect of Cellular Life

01

Cell structure,
function, shape
and motility

02

Cell cycle

03

Metabolism

04

Transcription

05

Protein synthesis

06

Hormone release

07

Surface receptor

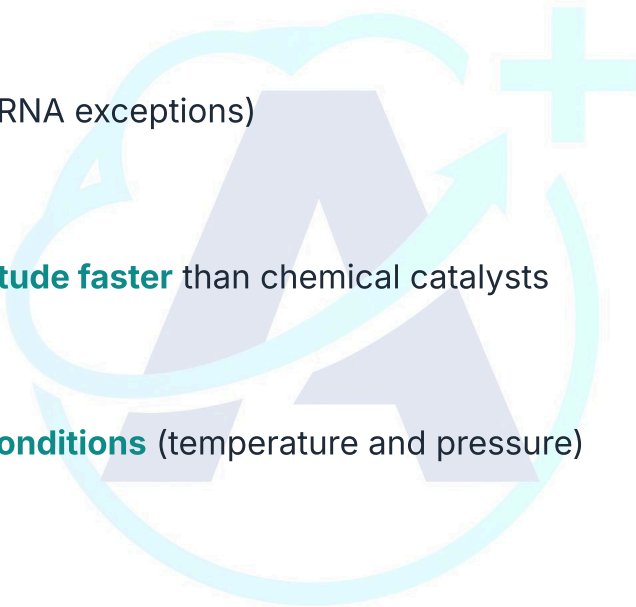
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Muscle
contraction



Enzymes as Biological Catalysts

Enzymes speed up the rates of chemical reactions **without themselves undergoing any permanent change.**

- 1 **Accelerate** the rate of chemical reactions
 - 2 Capable of performing **multiple reactions** (recycled)
 - 3 **Proteins**, (a few RNA exceptions)
 - 4 **Orders of magnitude faster** than chemical catalysts
 - 5 Act under **mild conditions** (temperature and pressure)
 - 6 Highly **Specific**
 - 7 Tightly **Regulated**
- 

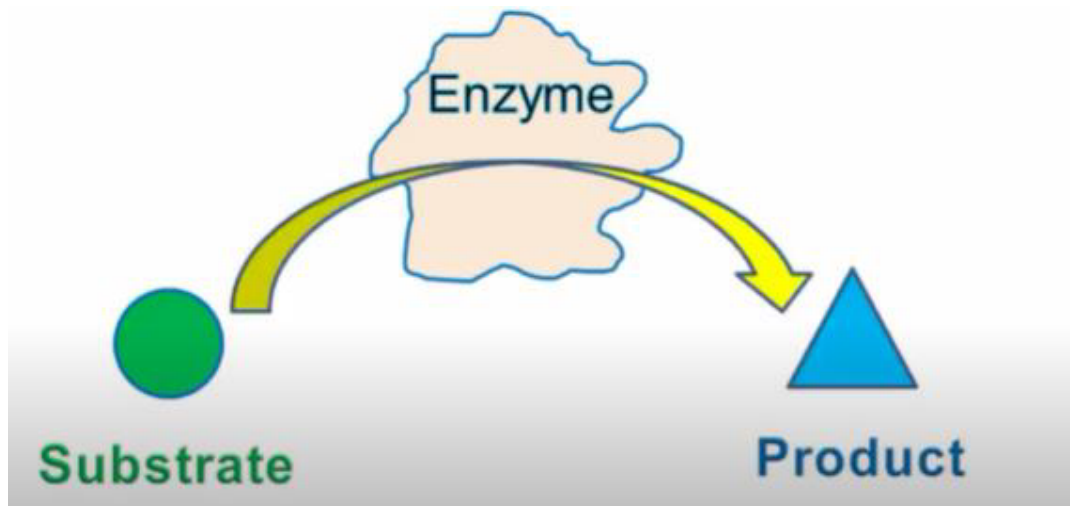
IN SUMMARY

They increase rates of reactions under **physiological conditions** (temperature and pH) without themselves being used up in the reaction.

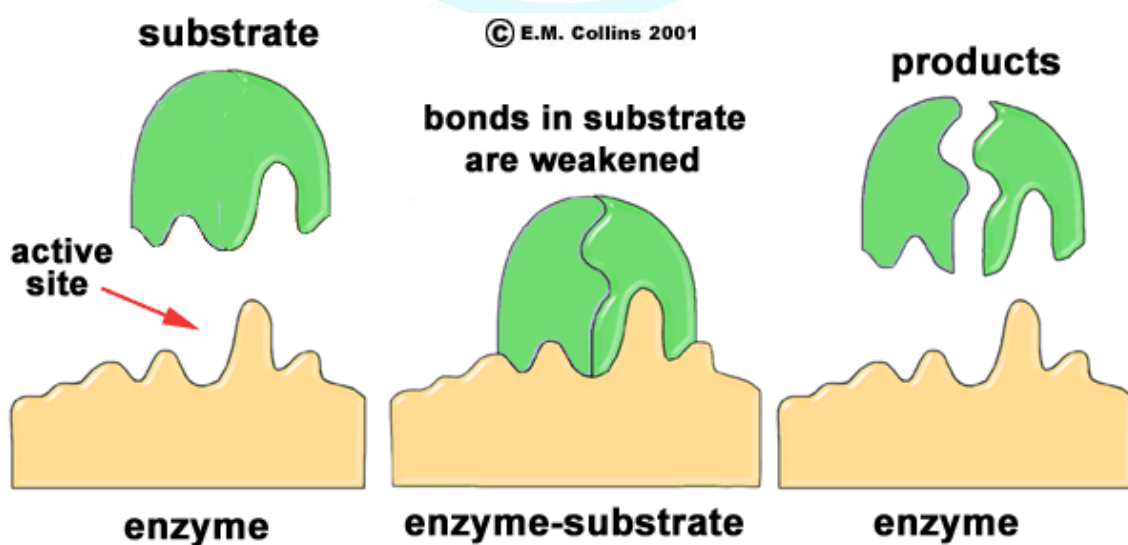


How Do Enzymes Work?

Nearly all (**thousands**) reactions in the body are catalyzed by enzymes converting a **substrate to a product**.



- 1 Enzymes are **specific**, act on one or few types of molecules (enzyme substrates) to give some type of molecular product
- 2 This binding of the substrate forces the enzyme to **change conformation** (oxygen binding to Hb)
- 3 This **decreases the energy of activation** needed to change the substrate to a transition state (unstable) and that allows the reaction to proceed to form a product and **regenerate the enzyme**



Active site → enzyme–substrate complex → products, with the enzyme regenerated



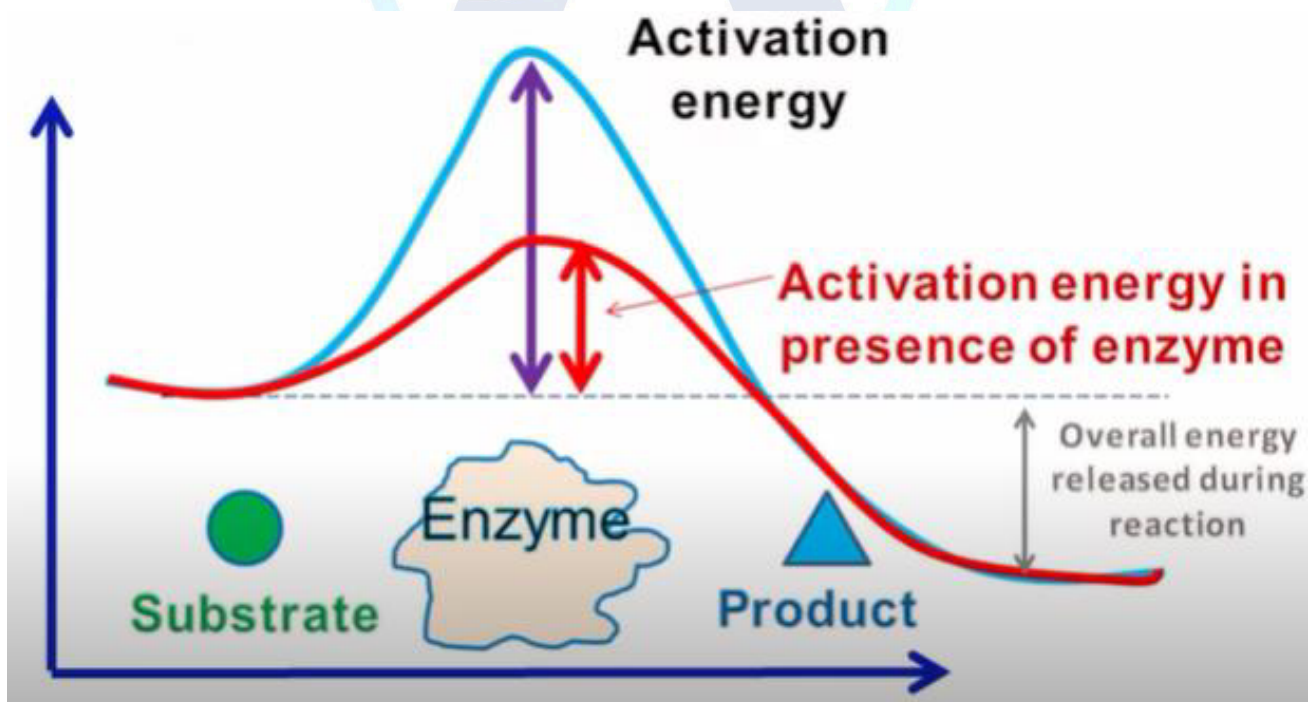
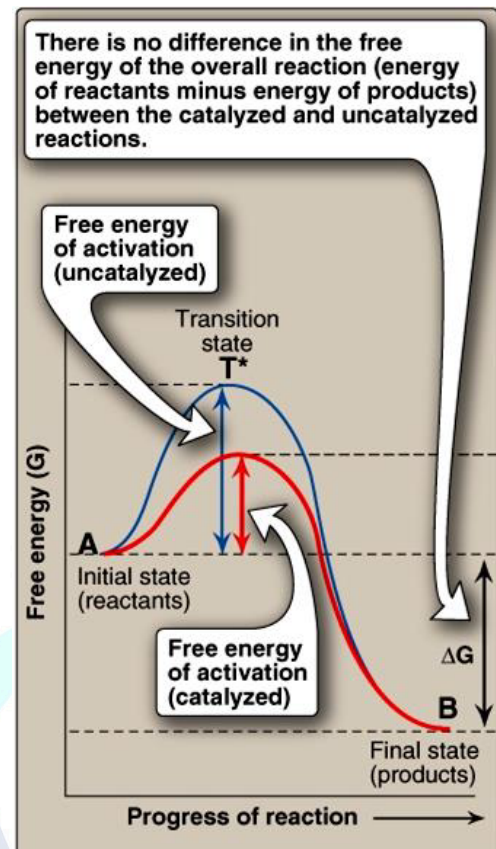
Activation Energy & the Transition State

TRANSITION STATE

Intermediate formed between the **initial chemical reactant and the product.**

Enzymes **reduce the free energy of activation** of the reactions they catalyze.

For substrate (reactant) to become product — catalyzed or not — the substrate **must pass through the transition state.**



Activation energy in the presence of enzyme — the overall energy released during the reaction is unchanged



Remarkable Properties as Catalysts

THE THREE MOST IMPORTANT PROPERTIES

1

Catalytic Power

Rate acceleration up to 10^{17} fold

2

Specificity

Distinguishes closely related species

3

Regulation

Activity tuned by ions and covalent change



Catalytic Power

- Ability to catalyze biochemical reaction
- Enzymes may increase the rate of a reaction by as much as **10^{17} fold**

Enzyme	Nonenzymatic rate k_{non} (s ⁻¹)	Enzymatic rate k_{cat} (s ⁻¹)	Rate acceleration $k_{\text{cat}}/k_{\text{non}}$
cyclophilin ^a	2.8×10^{-2}	1.3×10^4	4.6×10^5
carbonic anhydrase ^a	1.3×10^{-1}	10^6	7.7×10^6
chorismate mutase ^a	2.6×10^{-5}	50	1.9×10^6
chymotrypsin ^b	4×10^{-9}	4×10^{-2}	10^7
triosephosphate isomerase ^b	6×10^{-7}	2×10^3	3×10^9
fumarase ^b	2×10^{-8}	2×10^3	10^{11}
ketosteroid isomerase ^a	1.7×10^{-7}	6.6×10^4	3.9×10^{11}
carboxypeptidase A ^a	3×10^{-9}	578	1.9×10^{11}
adenosine deaminase ^a	1.8×10^{10}	370	2.1×10^{12}
urease ^b	3×10^{-10}	3×10^4	10^{14}
alkaline phosphatase ^b	10^{-15}	10^2	10^{17}
orotidine 5'-phosphate decarboxylase ^a	2.8×10^{-16}	39	1.4×10^{17}

Examples of the catalytic power of enzymes



Specificity

Ability to distinguish between **closely related chemical species** in the enzyme's active site.

Most enzymes are highly specific in both

- The nature of the **substrates** they utilize
- The **reaction** they catalyze

Selectivity – worked example

A given enzyme is very selective, e.g. **urease** will only catalyze the reaction with **urea**.



Lock and Key Theory

EMIL FISCHER, 1984

Proposed the **'lock and key' hypothesis**.

key = substrate

+

lock = enzyme

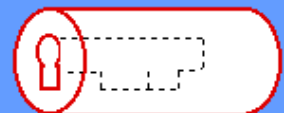
correct fit → will react

incorrect substrate → no reaction

Lock and Key Analogy



key = substrate



lock = enzyme



correct fit,
will react



incorrect substrate



no reaction

C. Ophardt, c. 2003

The lock and key analogy

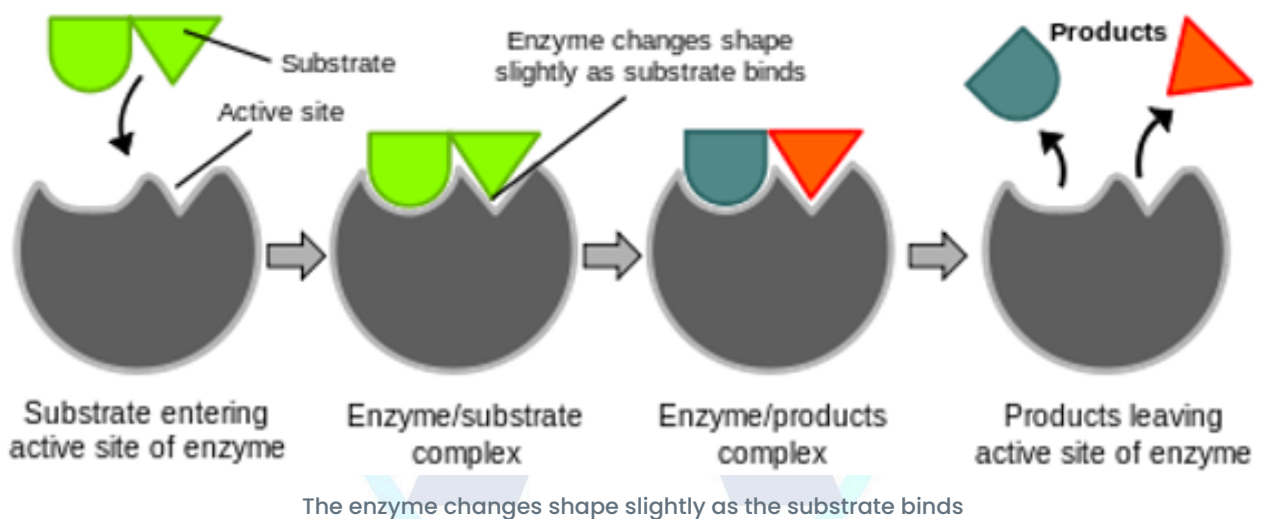


Induced Fit Theory

KOSHLAND, 1958

Proposed the **'induced fit' theory**.

Substrate plays a role in determining the **final shape of the enzyme**, and the enzyme is **partially flexible**.



Regulation

Catalytic activity is regulated by

- Small **ions** or other molecules
- Small changes in their **covalent structure**

Example — phosphorylase

Catalyzes the first step in the breakdown of **glycogen in skeletal muscle**. Its regulation by both Ca^{2+} and hormones such as adrenalin involves a complex sequence of events.



Cofactors — Metal Ions

COFACTOR

Many enzymes require a **non-protein component for activity**; this is termed a cofactor.

One group of cofactors comprises **metal ions**.

Carboxypeptidase

An enzyme catalyzing the hydrolysis of proteins from the C-terminal end — requires **zinc** for activity.

The kinases

Enzymes that catalyze the transfer of the γ-phosphoryl group of ATP to some acceptor molecule — have a requirement for **magnesium ions**.

METAL

ENZYME CONTAINING THE METAL

Zinc

Carbonic anhydrase, carboxy peptidase, alcohol dehydrogenase

Magnesium

Hexokinase, phospho fructo kinase, enolase, glucose-6-phosphatase

Manganese

Phospho gluco mutase, hexokinase, enolase, glycosyl transferases

Copper

Tyrosinase, cytochrome oxidase, lysyl oxidase, superoxide dismutase

Iron

Cytochrome oxidase, catalase, peroxidase, xanthine oxidase

Calcium

Lecithinase, lipase

Molybdenum

Xanthine oxidase

Metallo-enzymes — examples of the metal ion requirements of some enzymes



Organic Cofactors — Coenzymes

The second major class of cofactors comprises **organic cofactors**: coenzymes, many of which are **derivatives of B vitamins**.

EXAMPLE

Carboxylase (enzymes involved in the incorporation of CO₂) requires **biotin**, which is covalently linked to its enzyme.

ENZYME BOUND COFACTOR	TYPE OF REACTION CATALYZED	EXAMPLE OF A COFACTOR-CONTAINING ENZYME	ASSOCIATED PATHWAY
Biotin	Carbon dioxide addition	Acetyl CoA carboxylase	Fatty acid biosynthesis
Factor F430	Methyl transfer	Methyl coenzyme M reductase	Methanogenesis
Flavin mononucleotide	Electron transfer	Cytochrome P450 reductase	Detoxification
Heme	Electron transfer	Cytochrome P450	Detoxification
Lipoic acid	Acyl / methyl amine transfer	2-oxoacid dehydrogenase	Citric acid cycle
MIO cofactor	Carbon-hydrogen bond activation	Phenylalanine ammonia-lyase	Polyphenol biosynthesis
Molybdopterin	Electron transfer	Xanthine oxidase	Purine catabolism
Phosphopantetheine	Acyl carrier	Carboxylic acid reductase	Fatty acid metabolism
Pyridoxal 5' phosphate	Transamination	Glycogen phosphorylase	Glycogenesis
Pyrroloquinoline quinone	Electron transfer	Methanol dehydrogenase	Methane metabolism
Thiamine pyrophosphate	Carbon dioxide removal	Pyruvate ferredoxin / flavodoxin reductase	Pyruvate decarboxylation
Topaquinone	Amine oxidation	Amine oxidase	Urea cycle

Organic cofactors — reactions catalyzed, example enzymes and associated pathways



Coenzymes vs Prosthetic Groups

Coenzymes

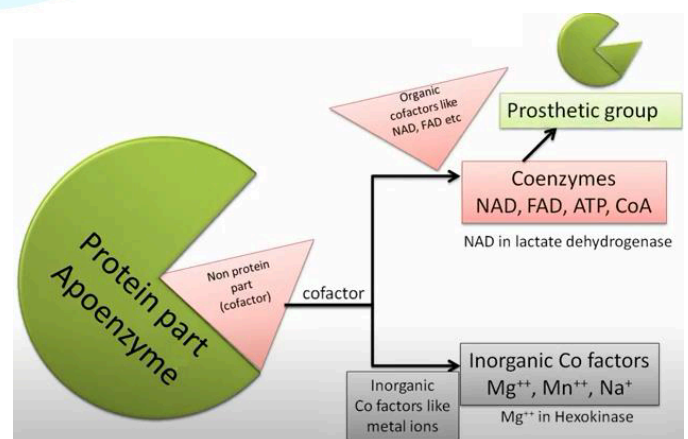
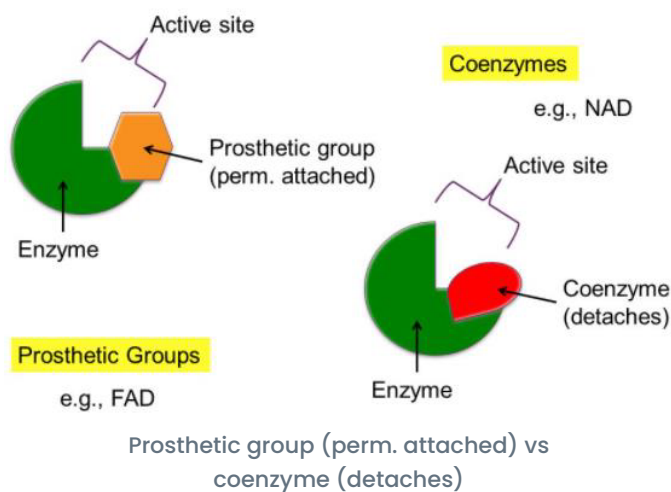
- Bind **reversibly** to the enzyme
- Released** after the catalytic reaction is complete

Prosthetic groups

- Are **covalently bound** to the enzyme
- Not released** after completion of the reaction

	COENZYMES	PROSTHETIC GROUPS
Binding to enzyme	Reversible	Covalent
After the reaction	Released	Not released

The prosthetic group may be **organic** — such as a vitamin, sugar, RNA, phosphate or lipid — or **inorganic**, such as a metal ion; **Heme (iron)**.



Cofactors of the apoenzyme: coenzymes, prosthetic and inorganic



Coenzymes and Their Vitamins

Coenzymes are **derivatives of B vitamins** — each one carries a specific group or reaction type.

COENZYME OR PROSTHETIC GROUP	VITAMIN	REACTIONS
Lipoic acid	Lipoic acid	Hydrogen and acyl group acceptor
Tetrahydrofolic acid (THF)	Folic acid	One carbon transfer
Biotin	Biotin	Carboxylation
Thiamin pyrophosphate (TPP)	Thiamine B1	Oxidative decarboxylation
Flavin mononucleotide (FMN)	Riboflavin B2	Oxidation / Reduction
Flavin adenine dinucleotide (FAD)	Riboflavin B2	Oxidation / Reduction
Nicotinamide adenine dinucleotide (NAD ⁺)	Niacin B3	Oxidation / Reduction
Nicotinamide adenine dinucleotide phosphate (NADP ⁺)	Niacin B3	Oxidation / Reduction
Coenzyme A (CoA)	Pantothenic acid B5	Acetyl or acyl group transfer
Pyridoxal phosphate (PALP)	Pyridoxine B6	Aminotransferases, amino acid decarboxylases, racemases
Cobamide	Cobalamin B12	One carbon transfer



Apoenzyme and Holoenzyme

APOENZYME

An enzyme that requires a cofactor — a non-protein molecule — **to participate in the reaction.**

Apoenzyme (inactive)

+

Cofactor

→

Holoenzyme (active)

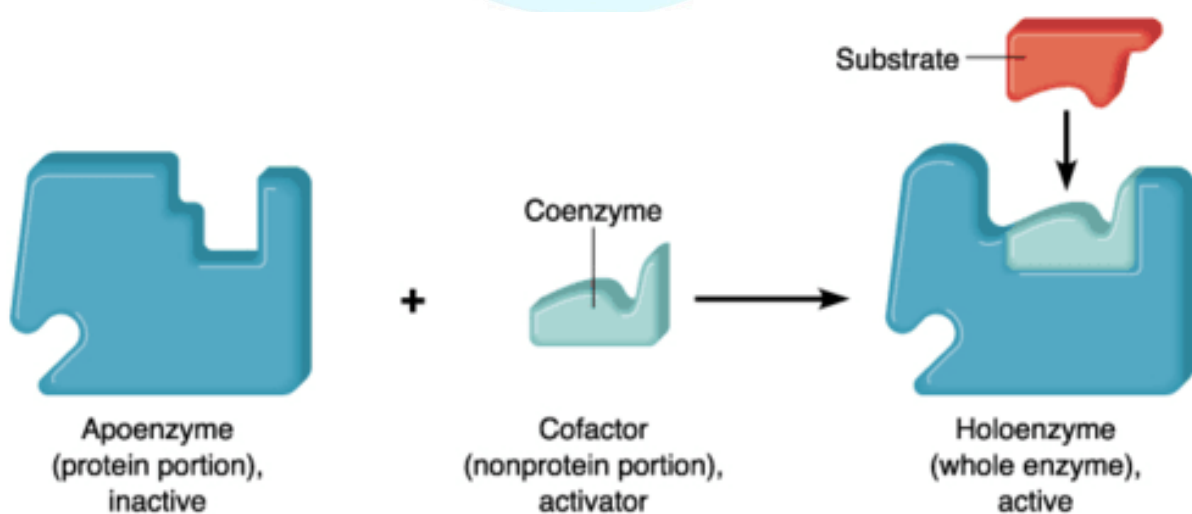
Apoenzyme are **inactive by themselves** — they must be activated by cofactors.

SOME COFACTORS ARE

- **Metal ions**
- **Organic molecules** — also called coenzymes, and are derived from vitamins

BINDING RESULT

Binding of apoenzyme to cofactor produces a **holoenzyme** — the whole, active enzyme.



Apoenzyme (protein portion, inactive) + cofactor (nonprotein portion, activator) = holoenzyme (whole enzyme, active)



Specificity Classes & Isoenzymes

Absolute specificity

Act on a **specific substrate**.

Broad specificity

Act on a **group of related substrates**.

ISOENZYMES

Enzymes that catalyze the **same reaction** but have different physical properties — e.g. amino acid or subunit composition, or cofactors.

EXAMPLE — CREATINE KINASE (CK), A DIMER OF B (BRAIN) AND M (MUSCLE)

BB

Brain

MM

Skeletal muscle

MB

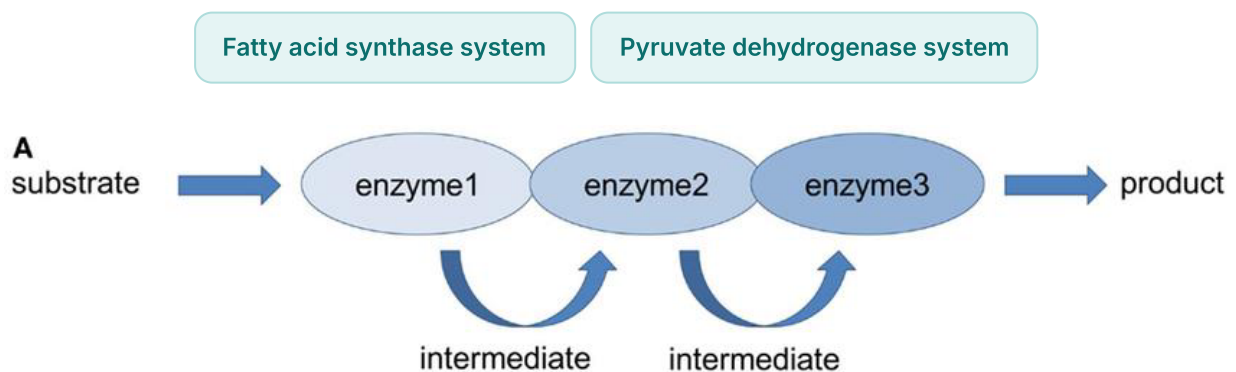
Heart muscle

The appearance of **CK MB in serum** indicates **injury to the myocardium**.



Multienzyme Systems

Stable assemblies of **more than one enzyme**, generally involved in **sequential catalytic transformations**.



Sequential catalysis: intermediates pass from one enzyme to the next



How Do We Name Enzymes?

Enzymes are named by adding the suffix **-ase** to the name of the substrate that they modify, or the type of reaction they catalyze.

NAMED FOR THE SUBSTRATE

urease

tyrosinase

NAMED FOR THE REACTION

dehydrogenase

decarboxylase



Enzyme Commission (EC) Number

Enzymes are classified by being assigned an EC number consisting of **four parts (a, b, c, d)**.

EC

a

b

c

d

- a** **1st number** — indicates the **type of reaction catalyzed** and can take values from 1 to 6 according to the classification of reaction types
- b** **2nd number** — indicates the **subclass**, which usually specifies the type of substrate or the bond cleaved more precisely
- c** **3rd number** — indicates the **sub-subclass**, specifies more precisely the reaction catalyzed in terms of the type of electron acceptor or the type of group removed
- d** **4th number** — indicates the **serial number** of the enzyme

Classification is based on the **chemical reaction catalyzed** and **not on the source** (species or tissues) of the enzyme.

Enzyme nomenclature database: enzyme.expasy.org



The Six Classes of Enzymes

Hundreds of reactions in our cells are catalyzed by enzymes. These are classified into **SIX classes** according to the type of reaction they catalyze.

1 · Oxidoreductases

2 · Transferases

3 · Hydrolases

4 · Lyases

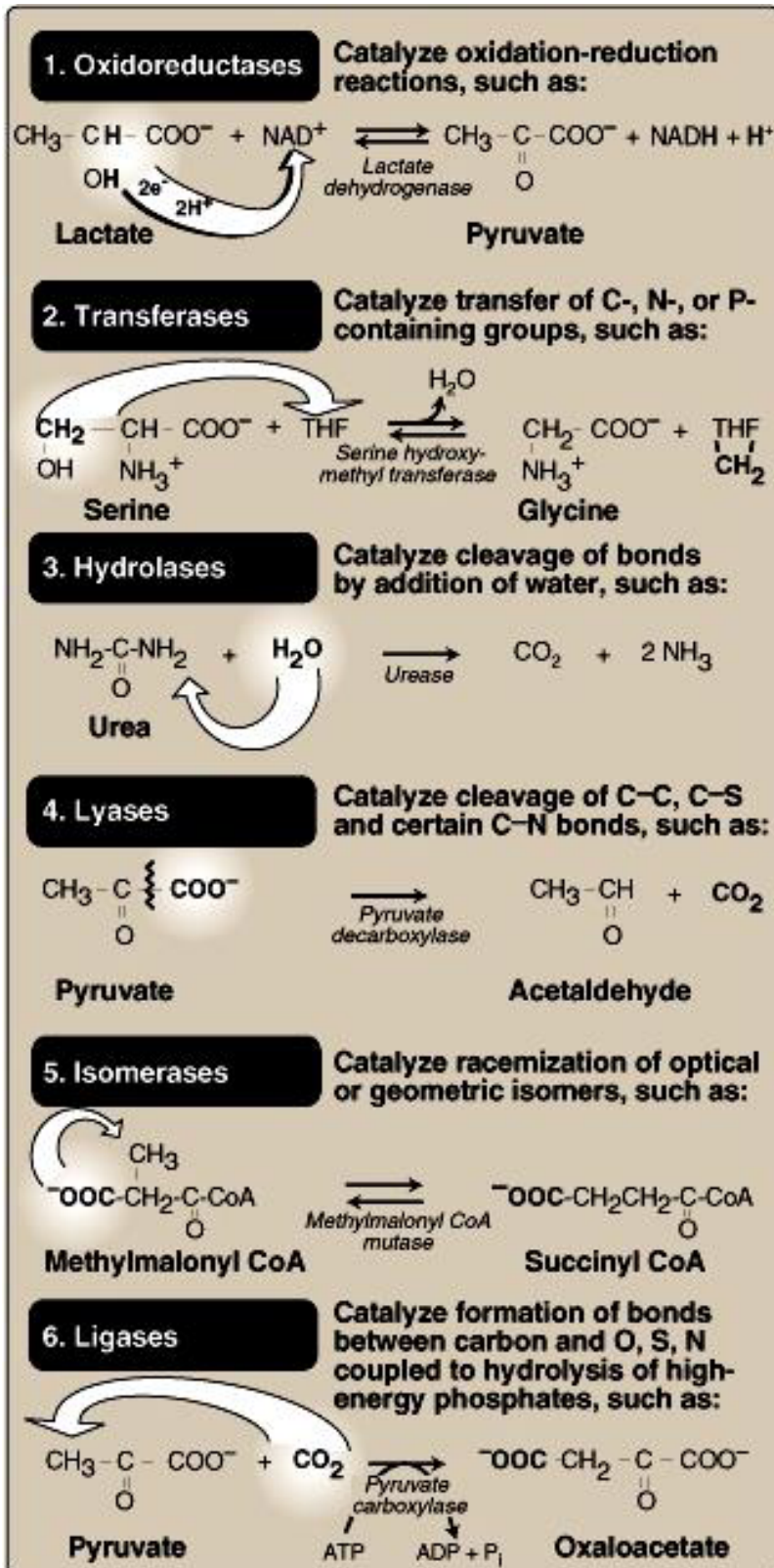
5 · Isomerases

6 · Ligases

CLASS OF ENZYMES	MECHANISM OF REACTION
1) Oxidoreductase	It performs redox reaction by utilizing electron acceptor such as NAD^+ in dehydrogenases, H_2O_2 in peroxidases and oxygen in oxidases.
2) Transferases	It catalyses by transferring groups like amino, phosphoryl, carboxyl, carbonyl etc. between different substrates. Examples — kinases, transaminases, phosphorylases.
3) Hydrolases	It performs reactions by adding water which breaks the bonds — phosphodiester bond is broken down by phosphodiesterases, amide bond is broken down by peptidases.
4) Lyases	Groups like CO_2 , NH_3 are either added or removed from the substrate. Examples — aldolases, synthases, decarboxylases.
5) Isomerases	It catalyses by rearranging the compounds forming isomers. Examples — epimerases, mutases, racemases.
6) Ligases	Ligases form new bonds by utilizing ATP. Examples — carboxylases and synthetases.



Six Classes — Worked Examples



Each class with a worked example reaction

1

Oxidoreductases

Lactate → Pyruvate

lactate dehydrogenase

2

Transferases

Serine → Glycine

serine hydroxymethyl transferase

3

Hydrolases

Urea → CO₂ + 2 NH₃

urease

4

Lyases

Pyruvate → Acetaldehyde + CO₂

pyruvate decarboxylase

5

Isomerases

Methylmalonyl CoA →

Succinyl CoA

methylmalonyl CoA mutase

6

Ligases

Pyruvate + CO₂ → Oxaloacetate

pyruvate carboxylase, ATP → ADP + P_i



To Summarise...

DEFINITION

Catalyst**Enzymes are biological catalysts**

- Speed up the rates of chemical reactions
- Undergo no permanent change
- Majority are proteins; some RNA (ribozymes)

POWER

10¹⁷**Catalytic power**

- Rate increase up to 10¹⁷ fold
- Orders of magnitude faster than chemical catalysts
- Act under mild temperature and pressure

PROPERTIES

3**The three most important properties**

- Catalytic power
- Specificity
- Regulation

BINDING

2**Models of substrate binding**

- Lock and key — Emil Fischer
- Induced fit — Koshland, 1958
- The enzyme is partially flexible

COFACTORS

2**Non-protein components for activity**

- Metal ions — zinc, magnesium, iron
- Organic coenzymes, derived from B vitamins
- Apoenzyme + cofactor = holoenzyme

CLASSIFICATION

6**Naming and classifying**

- Six classes by type of reaction catalyzed
- EC number of four parts (a, b, c, d)
- Named with the suffix -ase

THE SIX CLASSES

Oxidoreductases



Transferases



Hydrolases



Lyases



Isomerases



Ligases