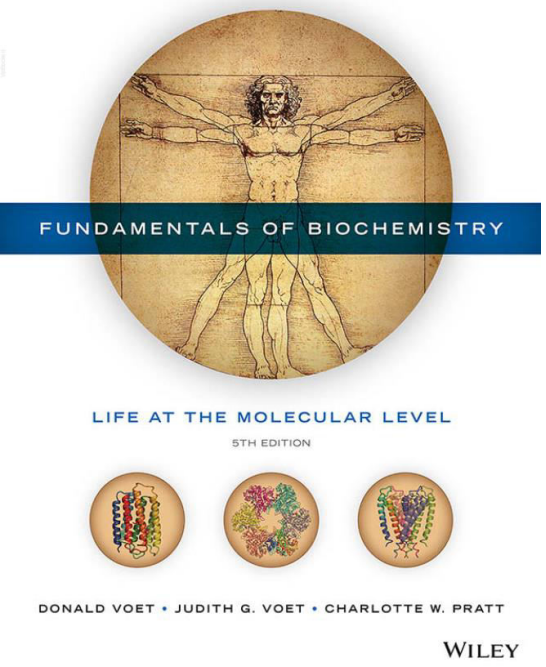
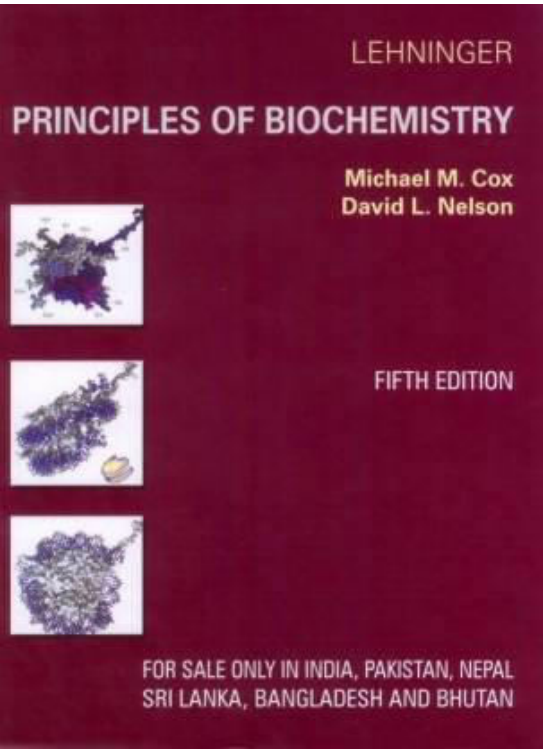


An Introduction to Enzymes



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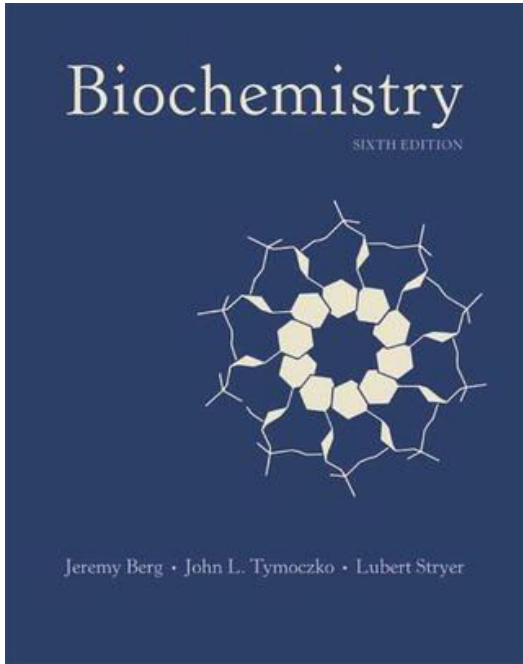
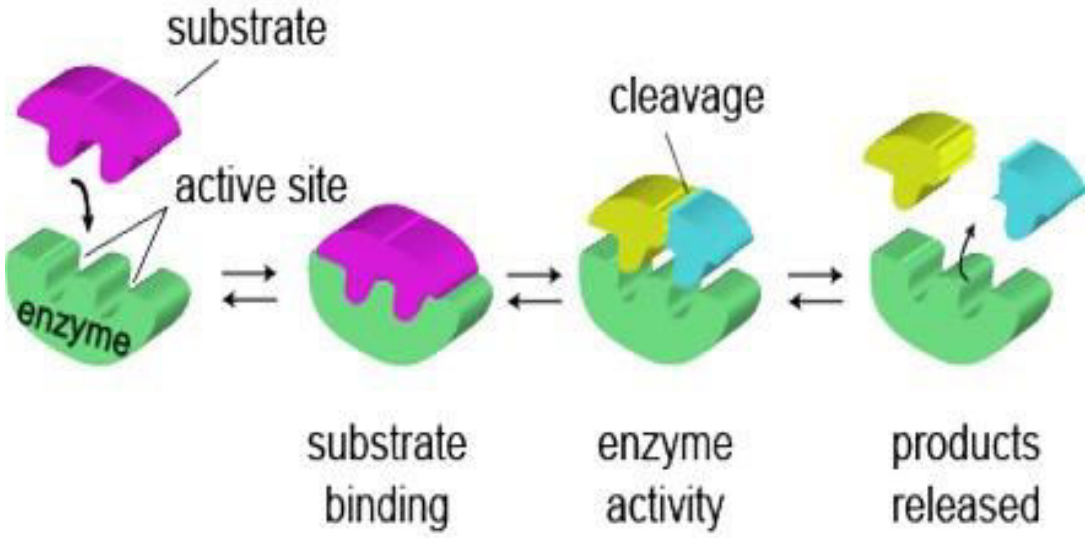
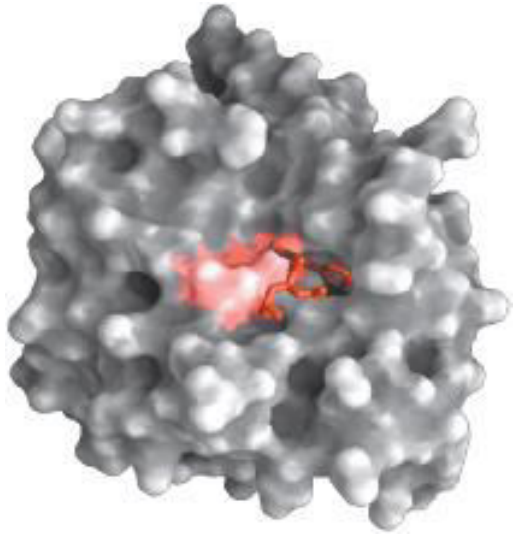
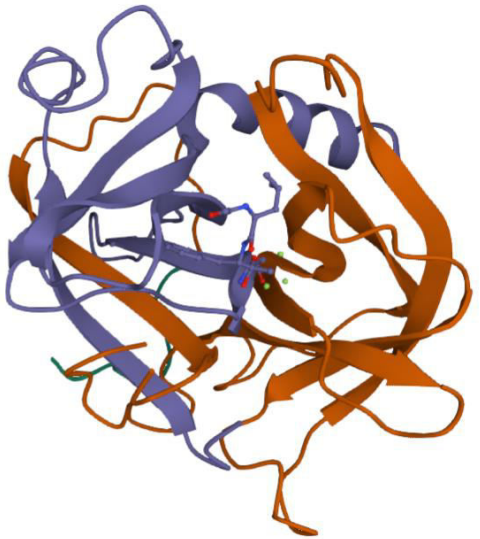


An Introduction to Proteins and Enzymes





Chymotrypsin
(PDB ID- 7GCH)



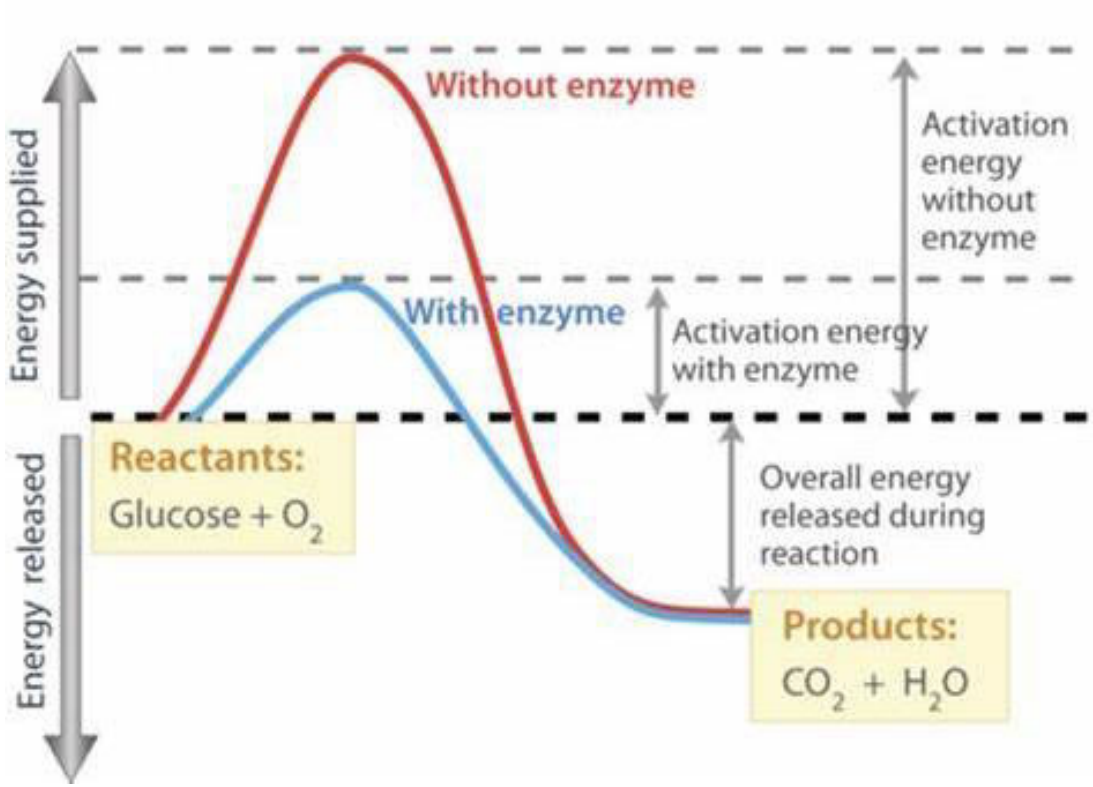


TABLE 11-1 Catalytic Power of Some Enzymes

Enzyme	Nonenzymatic Reaction Rate (s^{-1})	Enzymatic Reaction Rate (s^{-1})	Rate Enhancement
Carbonic anhydrase	1.3×10^{-1}	1×10^{6}	7.7×10^{6}
Chorismate mutase	2.6×10^{-5}	50	1.9×10^{6}
Triose phosphate isomerase	4.3×10^{-6}	4300	1.0×10^{9}
Carboxypeptidase A	3.0×10^{-9}	578	1.9×10^{11}
AMP nucleosidase	1.0×10^{-11}	60	6.0×10^{12}
Staphylococcal nuclease	1.7×10^{-13}	95	5.6×10^{14}

Source: Radzicka, A. and Wolfenden, R., *Science* **267**, 91 (1995).

History

- Biological catalysis was first recognized and described in the late 1700s, in studies on the digestion of meat by secretions of the stomach.

- In the 1850s, Louis Pasteur concluded that fermentation of sugar into alcohol by yeast is catalyzed by "ferments."

- He postulated that these ferments were inseparable from the structure of living yeast cells; this view, called vitalism, prevailed for decades.

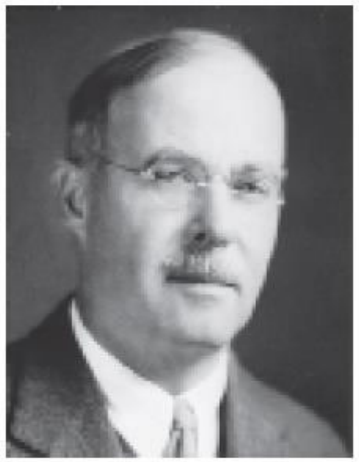
- Then in 1897 Eduard Buchner discovered that yeast extracts could ferment sugar to alcohol, proving that fermentation was promoted by molecules that continued to function when removed from cells.

- Frederick W. Kühne called these molecules enzymes.

- As vitalistic notions of life were disproved.

- The isolation and crystallization of urease by James Sumner in 1926 provided a breakthrough in early enzyme studies.

Eduard Buchner,
1860–1917

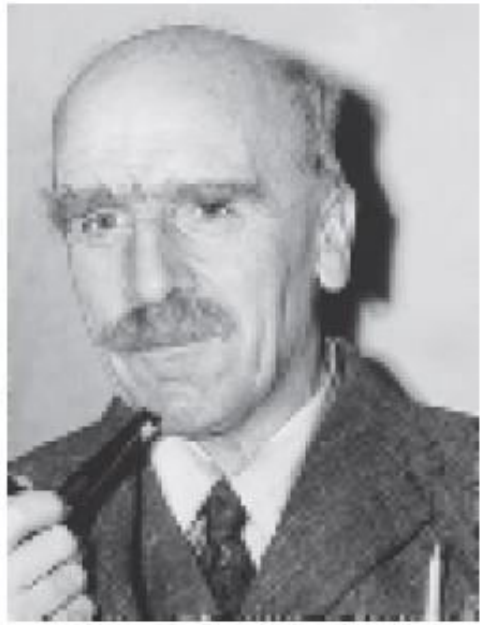


James Sumner,
1887–1955

- Sumner found that urease crystals consisted entirely of protein, and he postulated that all enzymes are proteins.

- Only in the 1930s was Sumner's conclusion widely accepted, after John Northrop and Moses Kunitz crystallized pepsin, trypsin, and other digestive enzymes and found them also to be proteins.

- Haldane made the remarkable suggestion that weak bonding interactions between an enzyme and its substrate might be used to catalyze a reaction. This insight lies at the heart of our current understanding of enzymatic catalysis.



J. B. S. Haldane,
1892–1964

General structure

Holoenzyme= Apoenzyme + co-factors

Co-factors

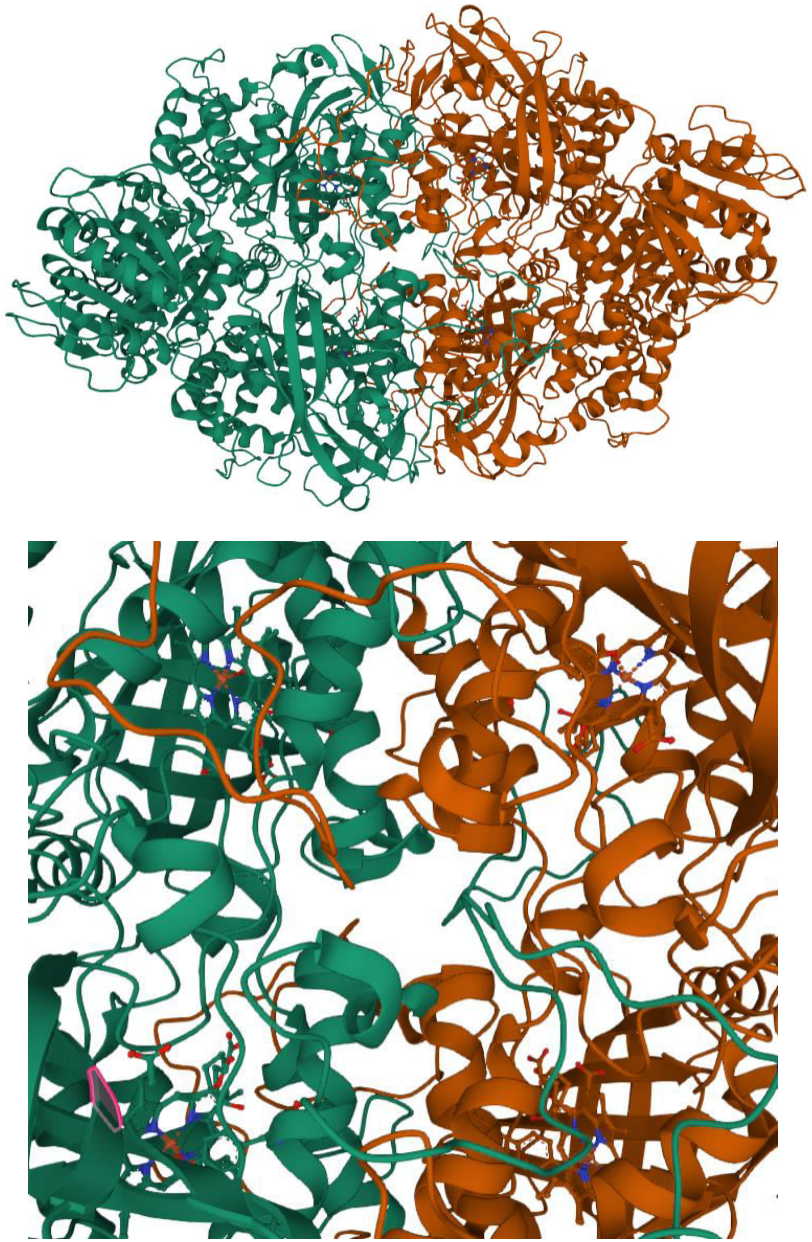
- **Co-enzymes (Small organic molecules)**
- **Inorganic metal ions**

Prosthetic group- A coenzyme or metal ion that is very tightly or even covalently bound to the enzyme protein is called a prosthetic group.

Co-factors

TABLE 6–1 Some Inorganic Elements That Serve as Cofactors for Enzymes

Cu^{2+}	Cytochrome oxidase
Fe^{2+} or Fe^{3+}	Cytochrome oxidase, catalase, peroxidase
K^{+}	Pyruvate kinase
Mg^{2+}	Hexokinase, glucose 6-phosphatase, pyruvate kinase
Mn^{2+}	Arginase, ribonucleotide reductase
Mo	Dinitrogenase
Ni^{2+}	Urease
Se	Glutathione peroxidase
Zn^{2+}	Carbonic anhydrase, alcohol dehydrogenase, carboxypeptidases A and B

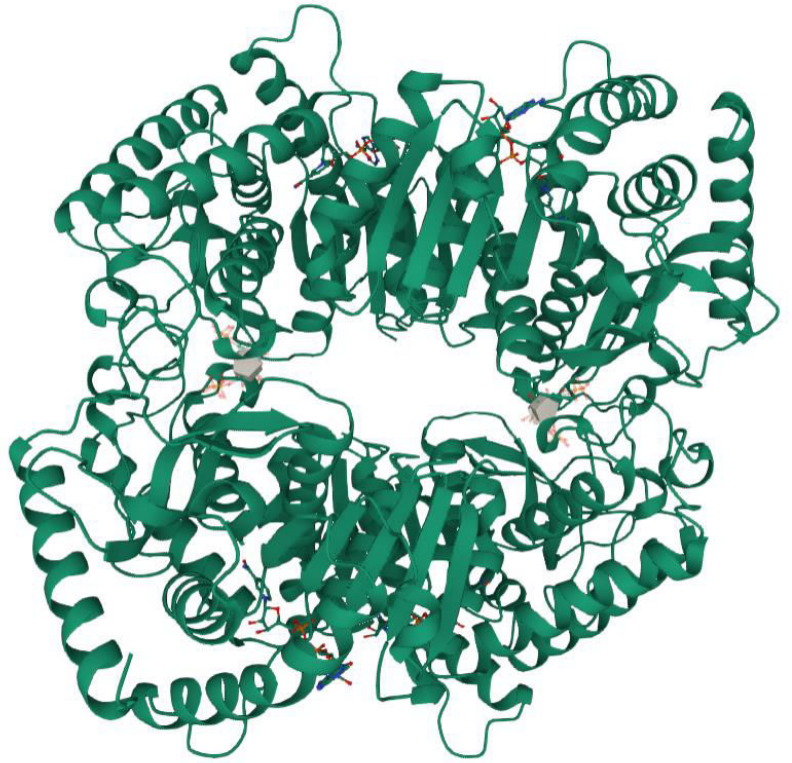


Crystal structure of the catalase-1 from *Neurospora crassa*, native structure at 1.75A resolution.

Coenzymes

TABLE 6–2 Some Coenzymes That Serve as Transient Carriers of Specific Atoms or Functional Groups

Coenzyme	*Examples of chemical groups transferred*	*Dietary precursor in mammals*
Biocytin	CO_2	Biotin
Coenzyme A	Acyl groups	Pantothenic acid and other compounds
5′-Deoxyadenosylcobalamin (coenzyme B_{12})	H atoms and alkyl groups	Vitamin B_{12}
Flavin adenine dinucleotide	Electrons	Riboflavin (vitamin B_2)
Lipoate	Electrons and acyl groups	Not required in diet
Nicotinamide adenine dinucleotide	Hydride ion ($:H^-$)	Nicotinic acid (niacin)
Pyridoxal phosphate	Amino groups	Pyridoxine (vitamin B_6)
Tetrahydrofolate	One-carbon groups	Folate
Thiamine pyrophosphate	Aldehydes	Thiamine (vitamin B_1)



CRYSTALS OF BACTERIAL L-LACTATE DEHYDROGENASE- 1LTH

Nomenclature and classification of enzyme

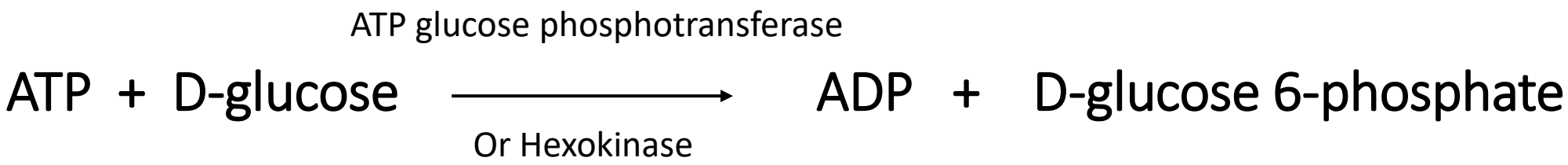
- Many enzymes have been named by adding the suffix "**-ase**" to the name of their substrate or to a word or phrase describing their activity. (Urease, DNase, RNase etc.)

- Other enzymes were named by their discovers for a broad function, before the specific reaction catalyzed was known. (For example, an enzyme known to act in the digestion of foods was named **pepsin**, from the Greek **pepsis**, "digestion," and lysozyme was named for its ability to lyse bacterial cell walls)

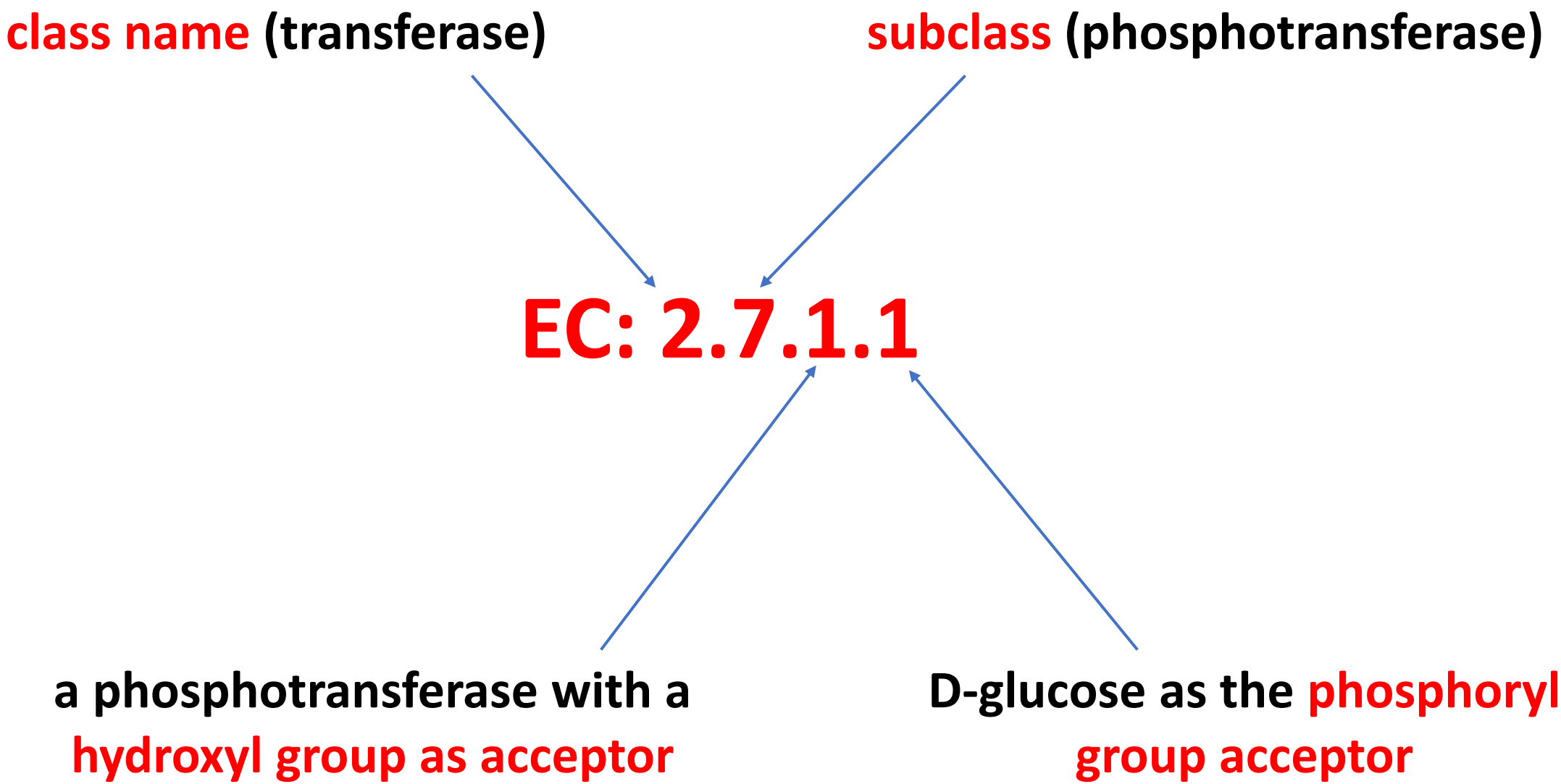
Problem

Sometimes the same enzyme has two or more names, or two different enzymes have the same name.

- Because of such ambiguities, and the ever increasing number of newly discovered enzymes, biochemists, by international agreement, have adopted a system for naming and classifying enzymes.
- This system divides enzymes into six classes, each with subclasses, based on the type of reaction catalyzed.
- Each enzyme is assigned a four-part classification number and a systematic name, which identifies the reaction it catalyzes.



Its Enzyme Commission number (E.C. number) is 2.7.1.1



A complete list and description of the thousands of known enzymes is maintained by the Nomenclature Committee of the International Union of Biochemistry and Molecular Biology (IUBMB).

TABLE 6–3 International Classification of Enzymes

No.	*Class*	*Type of reaction catalyzed*
1	Oxidoreductases	Transfer of electrons (hydride ions or H atoms)
2	Transferases	Group transfer reactions
3	Hydrolases	Hydrolysis reactions (transfer of functional groups to water)
4	Lyases	Addition of groups to double bonds, or formation of double bonds by removal of groups
5	Isomerases	Transfer of groups within molecules to yield isomeric forms
6	Ligases	Formation of C—C, C—S, C—O, and C—N bonds by condensation reactions coupled to ATP cleavage

Class	Reaction catalyzed	Typical reaction	Enzyme example(s) with trivial name
EC 1 Oxidoreductases	Oxidation/reduction reactions; transfer of H and O atoms or electrons from one substance to another	$AH + B \rightarrow A + BH$ (reduced) $A + O \rightarrow AO$ (oxidized)	Dehydrogenase, oxidase
EC 2 Transferases	Transfer of a functional group from one substance to another. The group may be methyl-, acyl-, amino- or phosphate group	$AB + C \rightarrow A + BC$	Transaminase, kinase
EC 3 Hydrolases	Formation of two products from a substrate by hydrolysis	$AB + H_2O \rightarrow AOH + BH$	Lipase, amylase, peptidase, phosphatase
EC 4 Lyases	Non-hydrolytic addition or removal of groups from substrates. C-C, C-N, C-O or C-S bonds may be cleaved	$RCOCOOH \rightarrow RCOH + CO_2$ or $[X\text{-}A{+}B\text{-}Y] \rightarrow [A{=}B + X\text{-}Y]$	Decarboxylase
EC 5 Isomerases	Intramolecule rearrangement, i.e. isomerization changes within a single molecule	$ABC \rightarrow BCA$	Isomerase, mutase
EC 6 Ligases	Join together two molecules by synthesis of new C-O, C-S, C-N or C-C bonds with simultaneous breakdown of ATP	$X + Y + ATP \rightarrow XY + ADP + P_i$	Synthetase