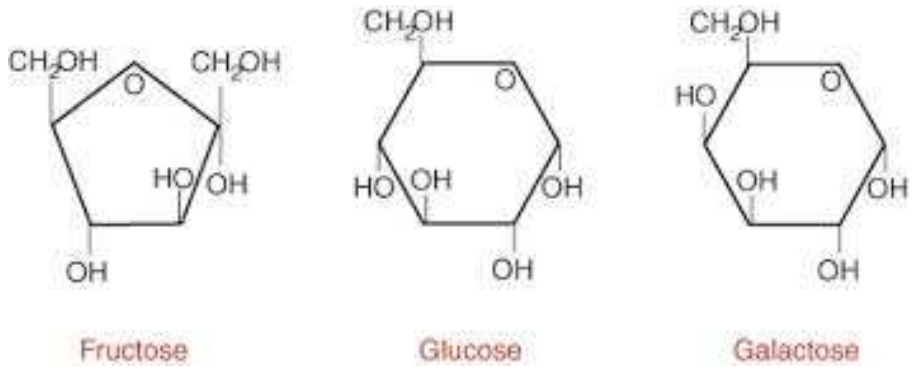
Biomolecules

Today's class

- Important biomolecules
  - Genetic molecules: discussed last class
  - Carbohydrates, lipids, and proteins
  - Enzymes
  - Enzyme reactivity and inhibition of enzyme reactions
  - Coenzymes
  - Adenosine phosphates

Carbohydrates

- Energy source, building materials for cells
- Monomers, dimers, polymers
  - Monosaccharides: building blocks

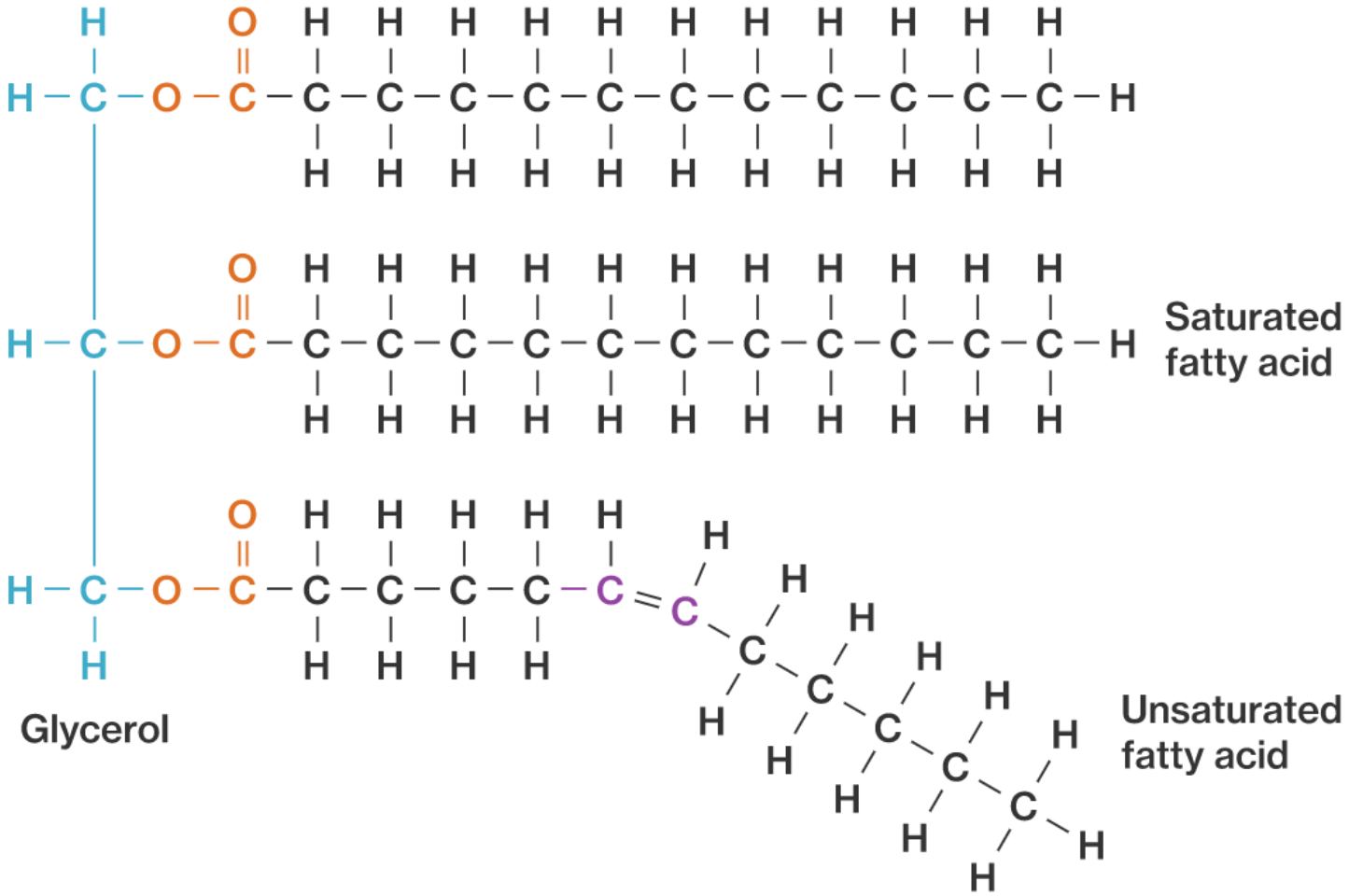


  - Disaccharides: sucrose, lactose, maltose
  - Polysaccharides: >10 of monosaccharides

Lipids

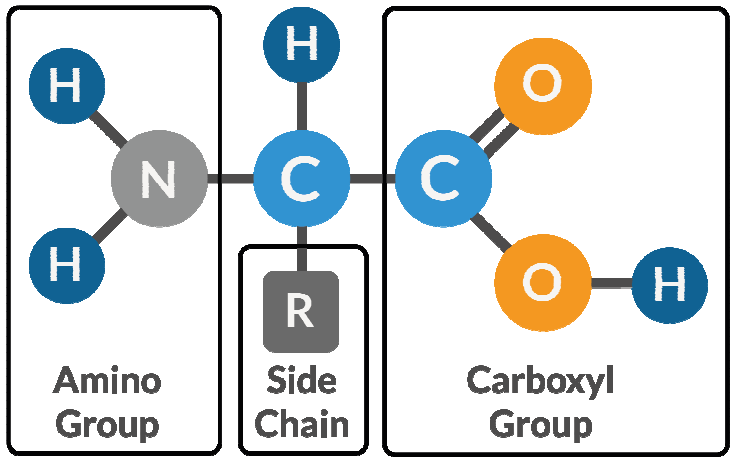
- Not polymeric (no monomers, dimers, polymers)
- Various structures
- Common characteristic: hydrophobic (repulsion of water)
- Fats, phospholipids, and steroids
  - fats: store energy
  - phospholipids: major component of cell membranes
  - steroids: signaling (ex: steroid hormones)

- Fat = fatty acid + glycerol
- Saturated fat vs. Unsaturated fat



Proteins

- Affect almost all cellular functions (enzymes, immunoglobulins, hemoglobins, etc.)
- Structural support of organisms
- Monomers: amino acids (20) / polymers: polypeptides



A GUIDE TO THE TWENTY COMMON AMINO ACIDS

AMINO ACIDS ARE THE BUILDING BLOCKS OF PROTEINS IN LIVING ORGANISMS. THERE ARE OVER 500 AMINO ACIDS FOUND IN NATURE - HOWEVER, THE HUMAN GENETIC CODE ONLY DIRECTLY ENCODES 20. 'ESSENTIAL' AMINO ACIDS MUST BE OBTAINED FROM THE DIET, WHILST NON-ESSENTIAL AMINO ACIDS CAN BE SYNTHESISED IN THE BODY.

Chart Key: ALIPHATIC · AROMATIC · ACIDIC · BASIC · HYDROXYLIC · SULFUR-CONTAINING · AMIDIC · NON-ESSENTIAL · ESSENTIAL

Chemical Structure — *single letter code*

NAME (A) — *three letter code* — DNA codons

ALANINE (A) — *Ala* — GCT, GCC, GCA, GCG

GLYCINE (G) — *Gly* — GGT, GGC, GGA, GGG

ISOLEUCINE (I) — *Ile* — ATT, ATC, ATA

LEUCINE (L) — *Leu* — CTT, CTC, CTA, CTG, TTA, TTG

PROLINE (P) — *Pro* — CCT, CCC, CCA, CCG

VALINE (V) — *Val* — GTT, GTC, GTA, GTG

PHENYLALANINE (F) — *Phe* — TTT, TTC

TRYPTOPHAN (W) — *Trp* — TGG

TYROSINE (Y) — *Tyr* — TAT, TAC

ASPARTIC ACID (D) — *Asp* — GAT, GAC

GLUTAMIC ACID (E) — *Glu* — GAA, GAG

ARGININE (R) — *Arg* — CGT, CGC, CGA, CGG, AGA, AGG

HISTIDINE (H) — *His* — CAT, CAC

LYSINE (K) — *Lys* — AAA, AAG

SERINE (S) — *Ser* — TCT, TCC, TCA, TCG, AGT, AGC

THREONINE (T) — *Thr* — ACT, ACC, ACA, ACG

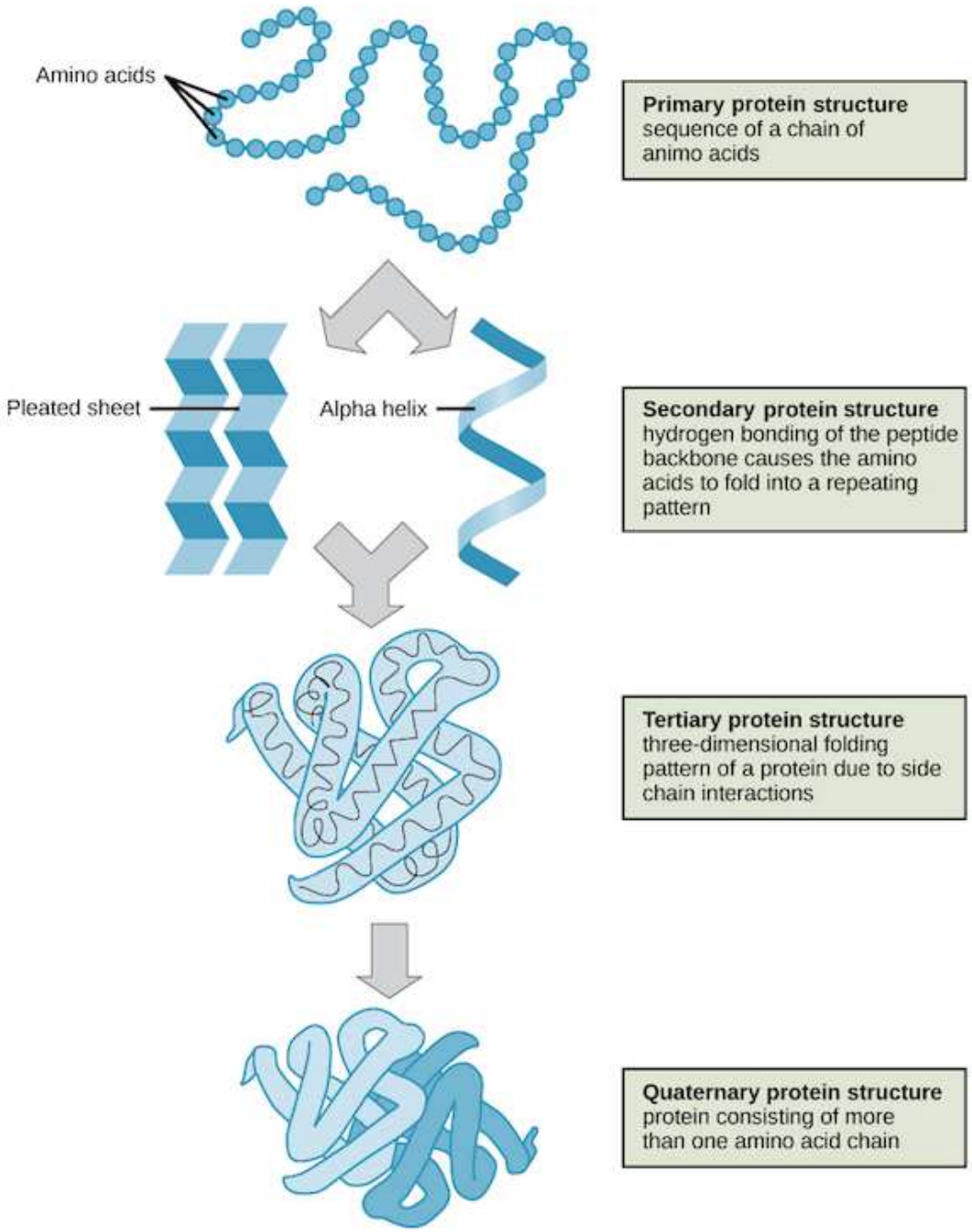
CYSTEINE (C) — *Cys* — TGT, TGC

METHIONINE (M) — *Met* — ATG

ASPARAGINE (N) — *Asn* — AAT, AAC

GLUTAMINE (Q) — *Gln* — CAA, CAG

Note: This chart only shows those amino acids for which the human genetic code directly codes for. Selenocysteine is often referred to as the 21st amino acid, but is encoded in a special manner. In some cases, distinguishing between asparagine/aspartic acid and glutamine/glutamic acid is difficult. In these cases, the codes asx (B) and glx (Z) are respectively used.



- Protein structure
  - Primary
  - Secondary
  - Tertiary
  - Quaternary

Enzymes

- Temperature-sensitive, organic catalysis produced by living cells

- May act outside or inside the cell
  - Intracellular vs. Extracellular

- May be produced continuously or produced on demand in response to external stimulation
  - Constitutive vs. Inducible

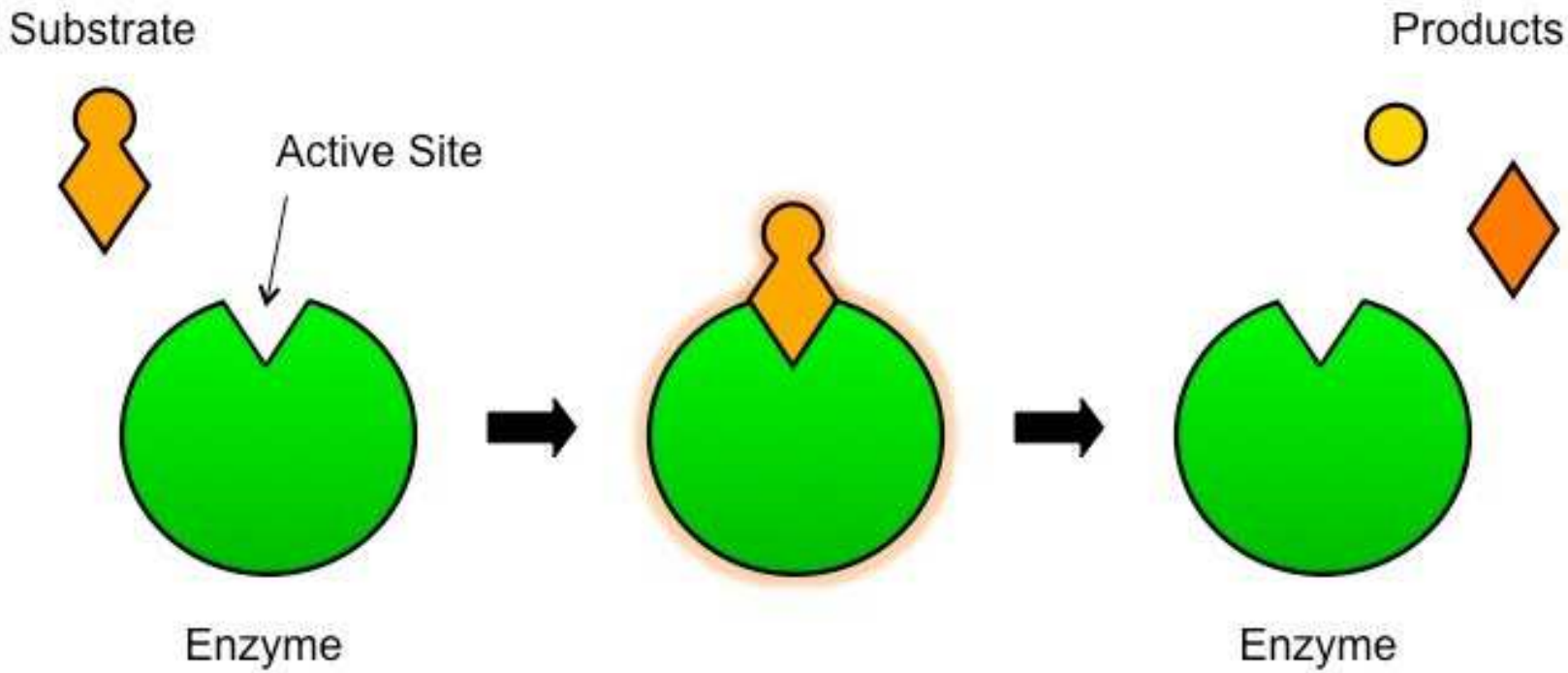
Classification of enzymes

Enzyme	Substrate	Products
Hydrolases		
1. Carbohydrases:		
a. Glycosidases (sugar splitters):		
Sucrase	Sucrose	Glucose + fructose
Maltase	Maltose	Glucose
Lactase	Lactose	Glucose + galactose
b. Amylases (starch splitters):		
Diatase	Starch	Maltose
Ptyalin		
c. Cellulsase	Cellulose	Cellobiose
2. Esterases:		
a. Lipases:		
Lipase	Glycerides	Glycerol + fatty acids
b. Phosphatases	Phosphoric esters	H_3PO_4 + alcohols
3. Proteases:		
a. Proteinases:		
Pepsin	Proteins	Polypeptides
Trypsin		
b. Peptidases	Polypeptides	Amino acids
4. Amidases:		
a. Urease	Urea	NH_3 + CO_2
5. Deaminases:	Amino acids	NH_3 + organic acids

Enzyme	Substrate	Products
Oxido-reductases (redox reactions)		
1. Dehydrogenases		
2. Hydroxylase		
3. Reductive dehalogenase	Tetrachloroethylene	Trichloroethylene
4. Oxidases		
5. Oxygenases		
6. Methane monooxygenase	Methane	Methanol
7. Toluene monooxygenase	Phenol	Catechol
8. Toluene dioxygenase	Benzene	Dihydroxy benzene
	Toluene	Dihydroxy toluene
9. Ammonia monooxygenase	Ammonia	Hydroxylamine
Transferases (transfer of functional group)		
1. Transaminases		
2. ATP		
Lyases (addition to double bonds)		
Isomerase (isomerization reactions)		
Ligase (formation of bonds by ATP)		

Enzyme reactivity

- Works in lock-and-key fashion



Modeling enzyme reactions

Step 1: The free enzyme (E) reacts with substrate (S) to form an enzyme-substrate complex (ES)

$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES$$

Step 2: The enzyme-substrate complex (ES) breaks down to form free enzyme and products (P)

$$ES \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} E + P$$

Assumptions

1) *The total concentration of enzyme ($[E]_{total}$) in the system is constant*
2) *Step 2 is essentially irreversible*
3) *[ES] does not change over time (pseudo-steady state)*

Use assumption 2) & 3):

rate of ES-producing reactions = rate of ES-consuming reactions

$$k_1[E][S] = k_{-1}[ES] + k_2[ES] \quad \Rightarrow \quad [E] = K_M \frac{[ES]}{[S]}$$

where $K_M = \frac{k_{-1} + k_2}{k_1}$

The rate of enzyme reaction (v)

= The rate of the reaction to produce "P"

(step 2 forward reaction)

$$v = k_2[ES]$$

Maximum "v" achievable in the system (v_m):

$$v_m = k_2[E]_{total}$$

Mass balance for enzyme in the system

$$[E]_{total} = [E] + [ES]$$

$[E]_{total}$ is constant by assumption 1)

Compare v and v_m:

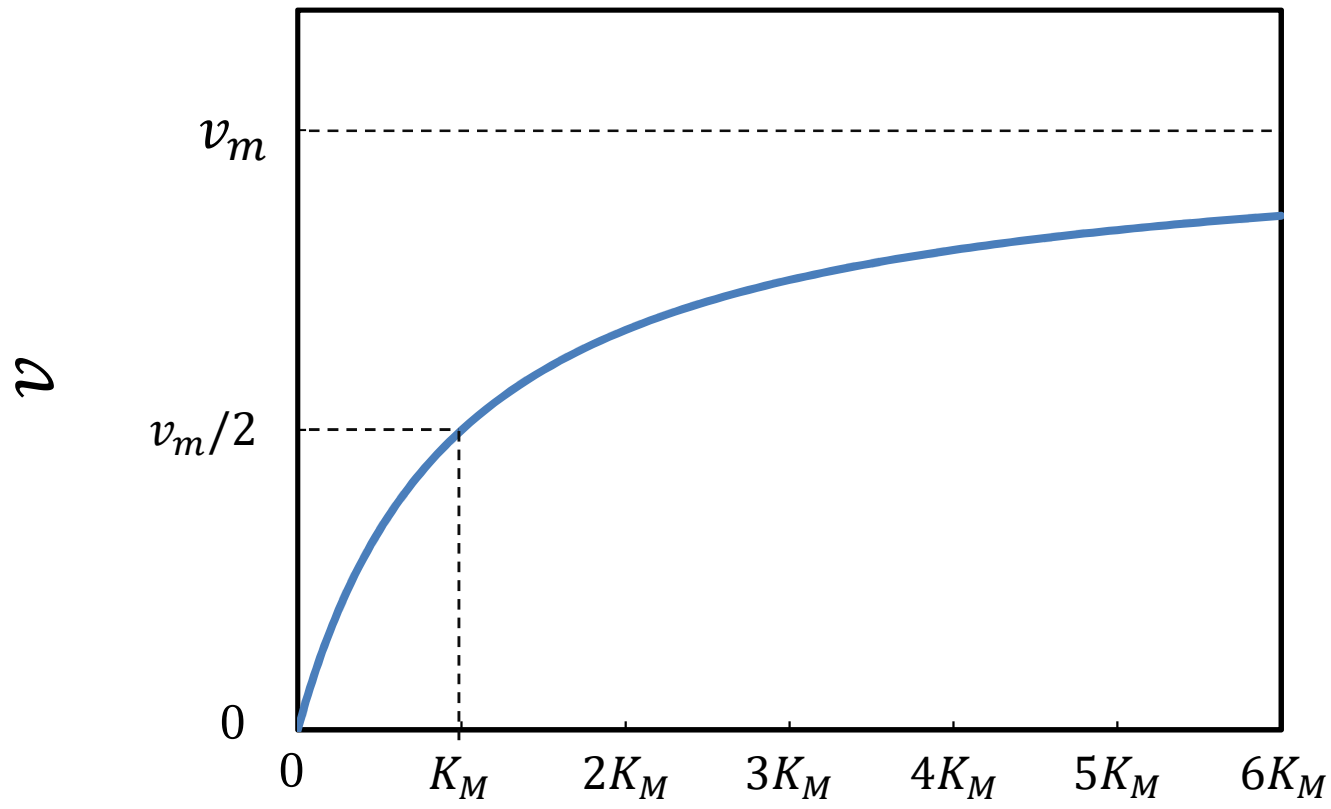
$$\frac{v}{v_m} = \frac{k_2[ES]}{k_2[E]_{total}} = \frac{[ES]}{[E]_{total}} = \frac{[ES]}{[E] + [ES]} = \frac{[ES]}{K_M \frac{[ES]}{[S]} + [ES]} = \frac{[S]}{K_M + [S]}$$

Finally we get:

$$v = v_m \frac{[S]}{K_M + [S]}$$

Michaelis-Menten equation

M-M eq.: [*S*] vs. *v*



K_M = half-velocity constant;
value of $[S]$ *to achieve* $v_m/2$

Inhibition of enzyme reactions

- Chemical agents can reduce the activity of an enzyme by binding to it

- Reversible vs. irreversible inhibition
  - Reversible inhibition
    - An inhibitor binds to enzymes with non-covalent interactions
    - The effect of inhibition disappears when the inhibitor is removed
  - Irreversible inhibition
    - An inhibitor binds to enzymes with covalent interactions
    - The enzymes are made permanently inactive

Reversible inhibition

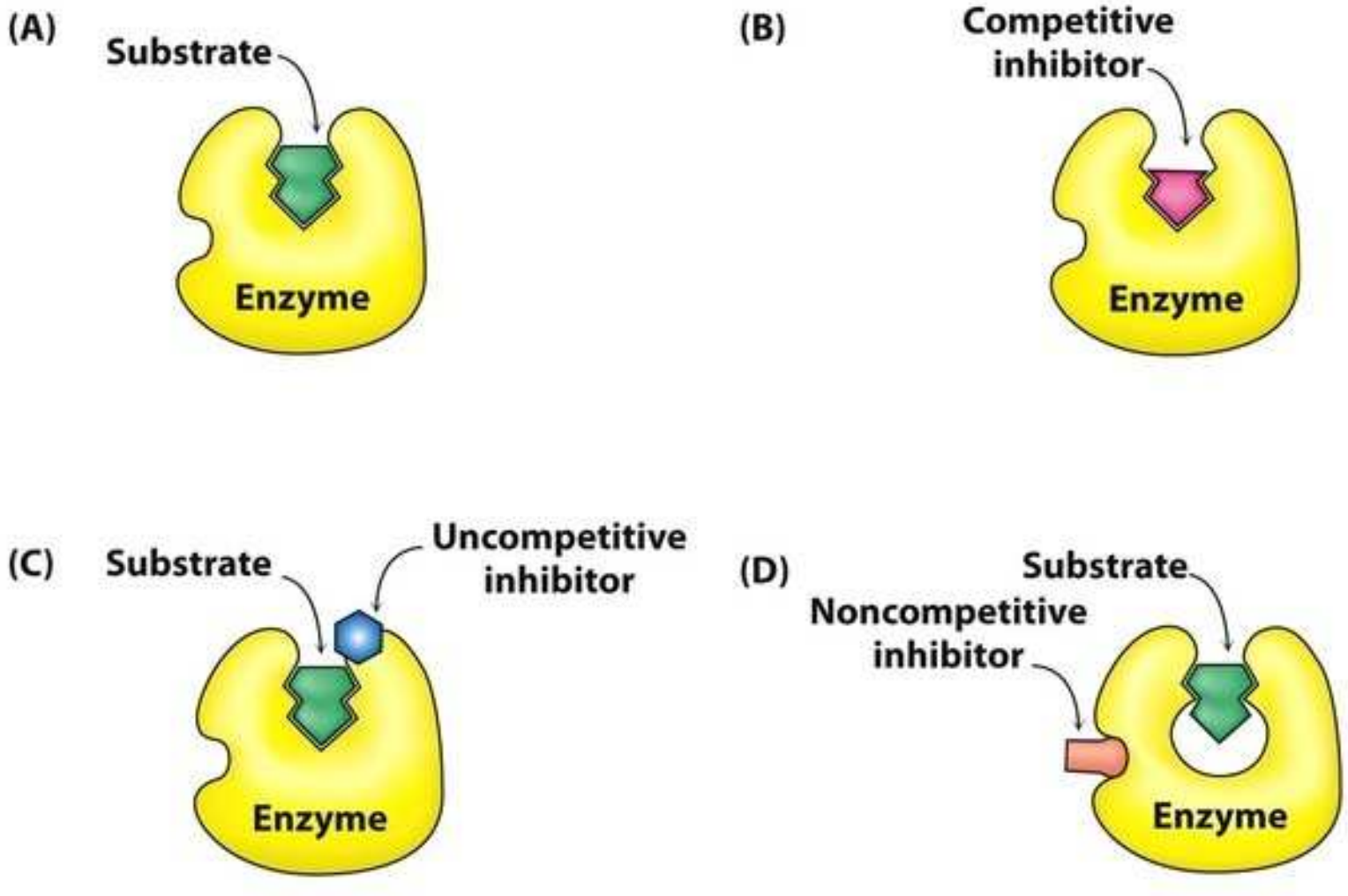


Figure 8.14
Biochemistry, Seventh Edition

Reversible inhibition: Mechanisms & effects

- Competitive inhibition [A]
  - **E** (free enzyme) binds to **I** (inhibitor)
  - v_m unchanged; K_M increased
- Uncompetitive inhibition [B]
  - **I** binds only to **ES** (enzyme-substrate complex)
  - v_m decreased; K_M decreased
- Noncompetitive inhibition [C]
  - **I** binds to both **ES** and **E**
  - v_m decreased; K_M unchanged

Cofactors

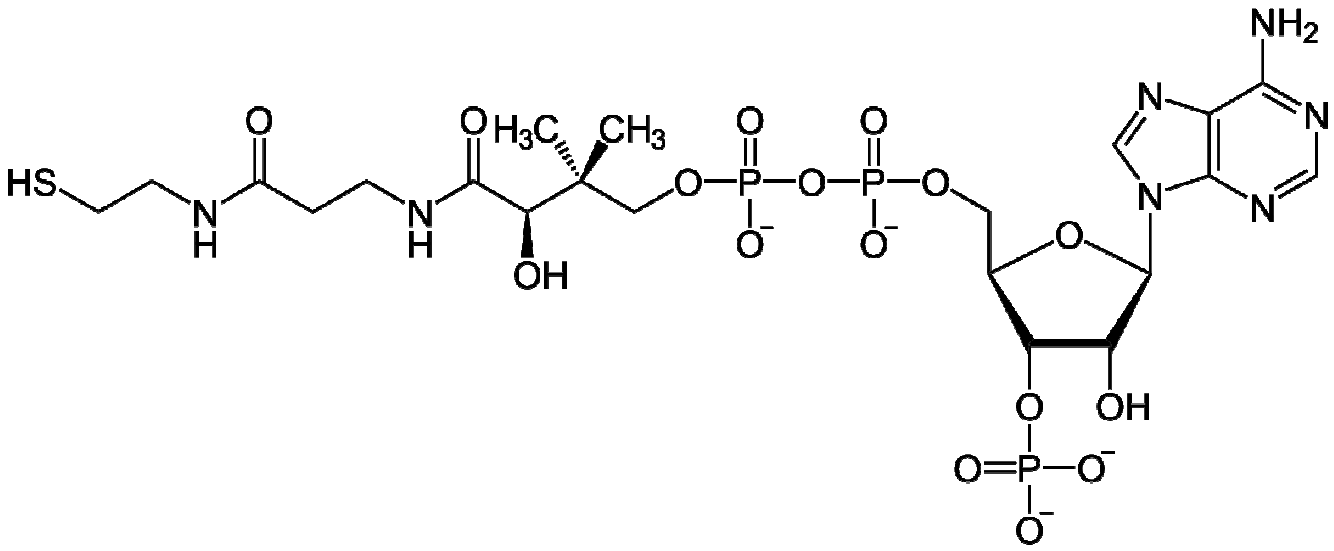
- Some enzymes require nonprotein structures (cofactors) to exhibit their activity
- Cofactors can be a metal ion or a complex organic molecule (coenzyme)
- Metals that may serve as cofactors
  - Zn, Mg, Mn, Fe, Cu, Ni, Co, K, Na, …

Important coenzymes

Coenzyme	Description
Coenzyme A	A derivative of pantothenic acid. Functions in fatty-acid oxidation and synthesis.
Coenzyme M	A coenzyme unique to methanogens that is involved in the production of methane, serving as a methyl carrier.
NAD	Nicotinamide adenine dinucleotide. Transfers hydrogen atoms or electrons and participates in the oxidation of organic materials.
NADP	Nicotinamide adenine dinucleotide phosphate. Similar in structure and function to NAD, but has three phosphorus atoms in the structure instead of two.
Flavoproteins	Include flavin adenine dinucleotide (FAD) and flavin mononucleotide (FMN). Important in the transport of hydrogen or electrons from metabolites to oxygen.
F420	A coenzyme contained in methanogens that is involved in the production of methane. Serves as an electron carrier, carrying two electrons per molecule.
F430	A nickel-containing coenzyme present in methanogens and involved in the production of methane. Can also facilitate dichlorination of chlorinated organic compounds.

Coenzyme A (CoA)

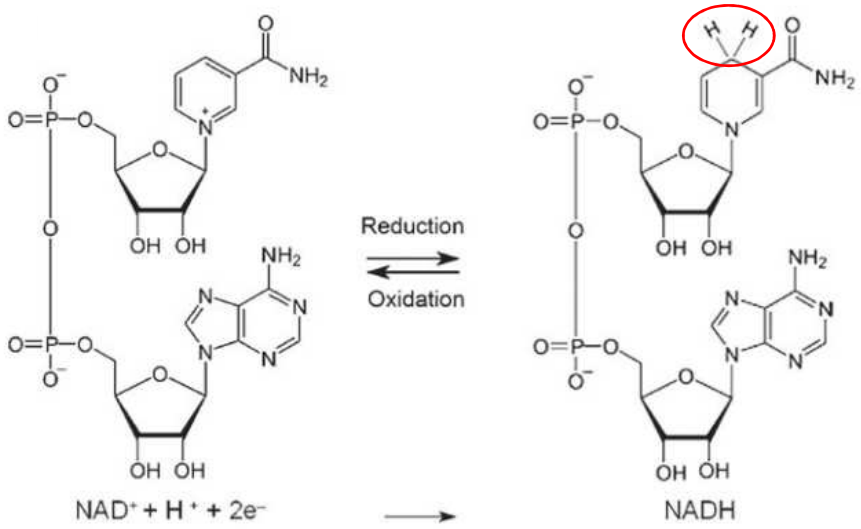
- Involved in
  - The synthesis and oxidation of fatty acids
  - Oxidation of pyruvate



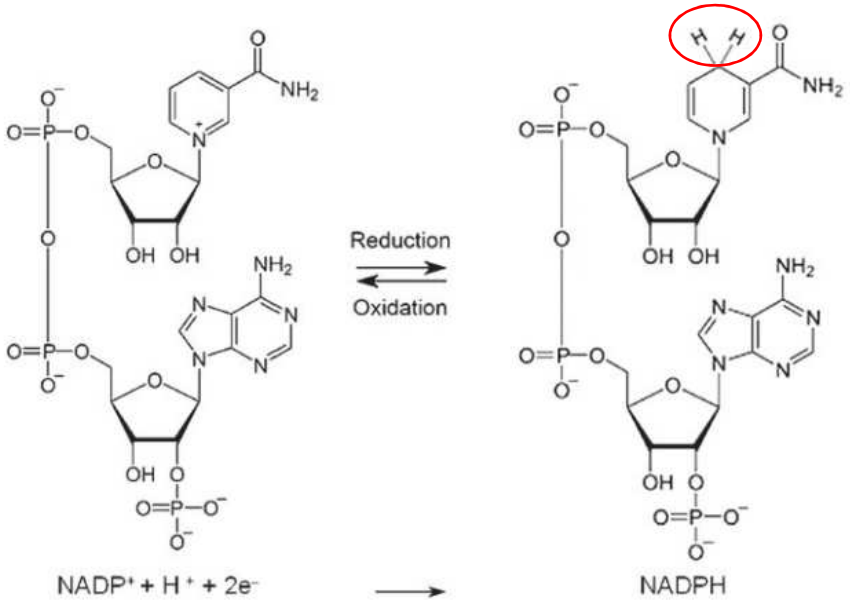
NAD, NADP, Flavoproteins

- Has deprotonated/protonated forms
  - NAD^+/NADP, $NADP^+$/NADPH, FAD/$FADH_2$, FMN/$FMNH_2$

- Involved in redox reactions
  - Takes electrons and/or hydrogen atoms that are generated from one reaction and provide them to another reaction
  - Acts as an “electron battery” (charged – uncharged)



Uncharged **Charged**



ATP, ADP, & AMP

- Adenosine triphosphate / di- / mono-
- A type of nucleotide
  - Contains a nucleobase, ribose (C5) sugar, & phosphate(s)
- Key role in intercellular energy transfer by acting as an "energy battery"

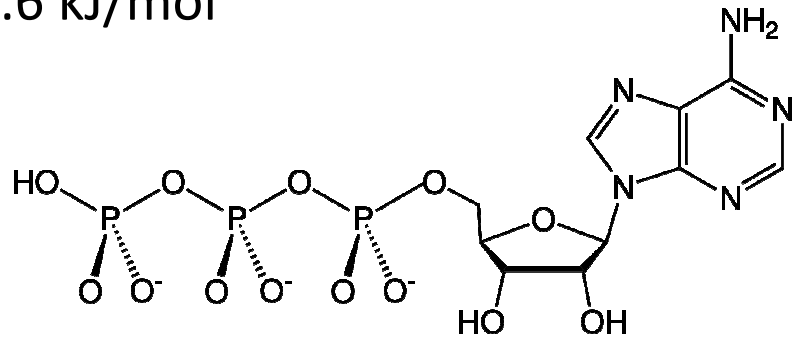
$ATP + H_2O \rightarrow ADP + P_i \quad \Delta G^{0'} = -30.5$ kJ/mol

$ATP + H_2O \rightarrow AMP + PP_i \quad \Delta G^{0'} = -45.6$ kJ/mol

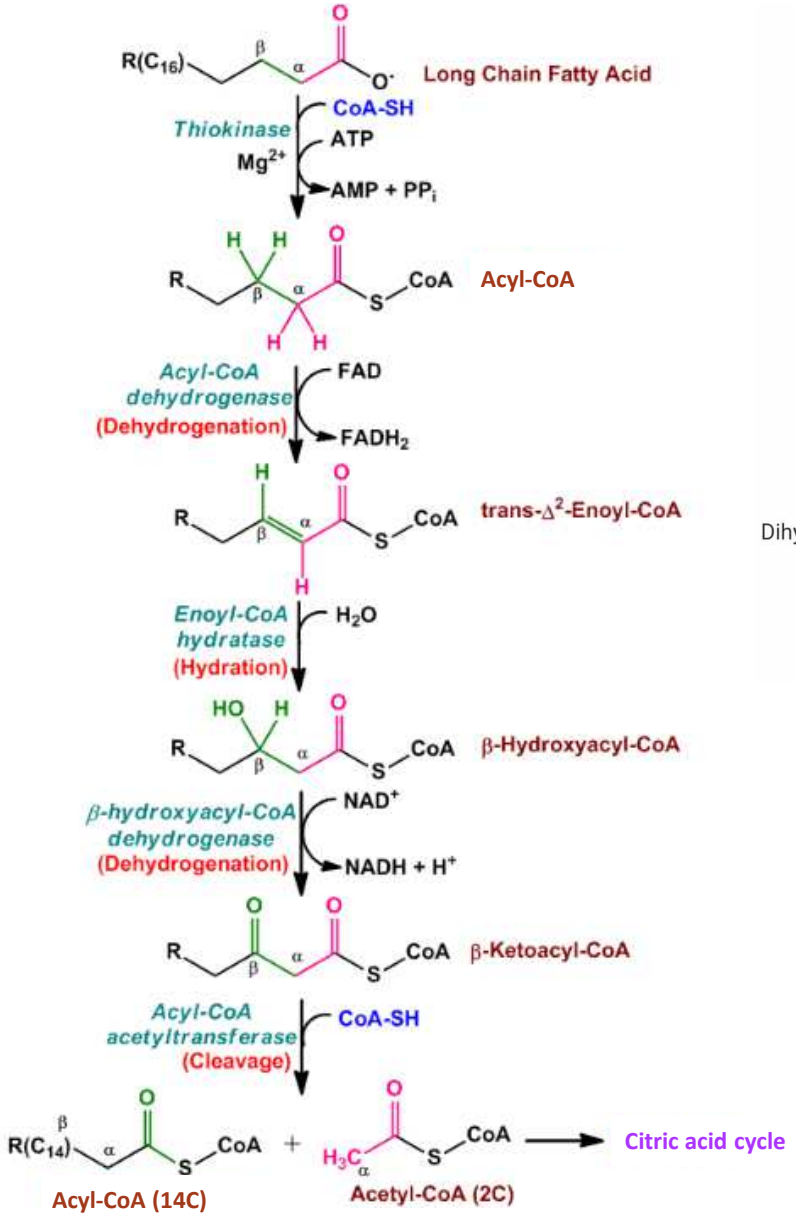
*At near-neutral pH,

$P_i = HPO_4^{2-}$ or $H_2PO_4^-$

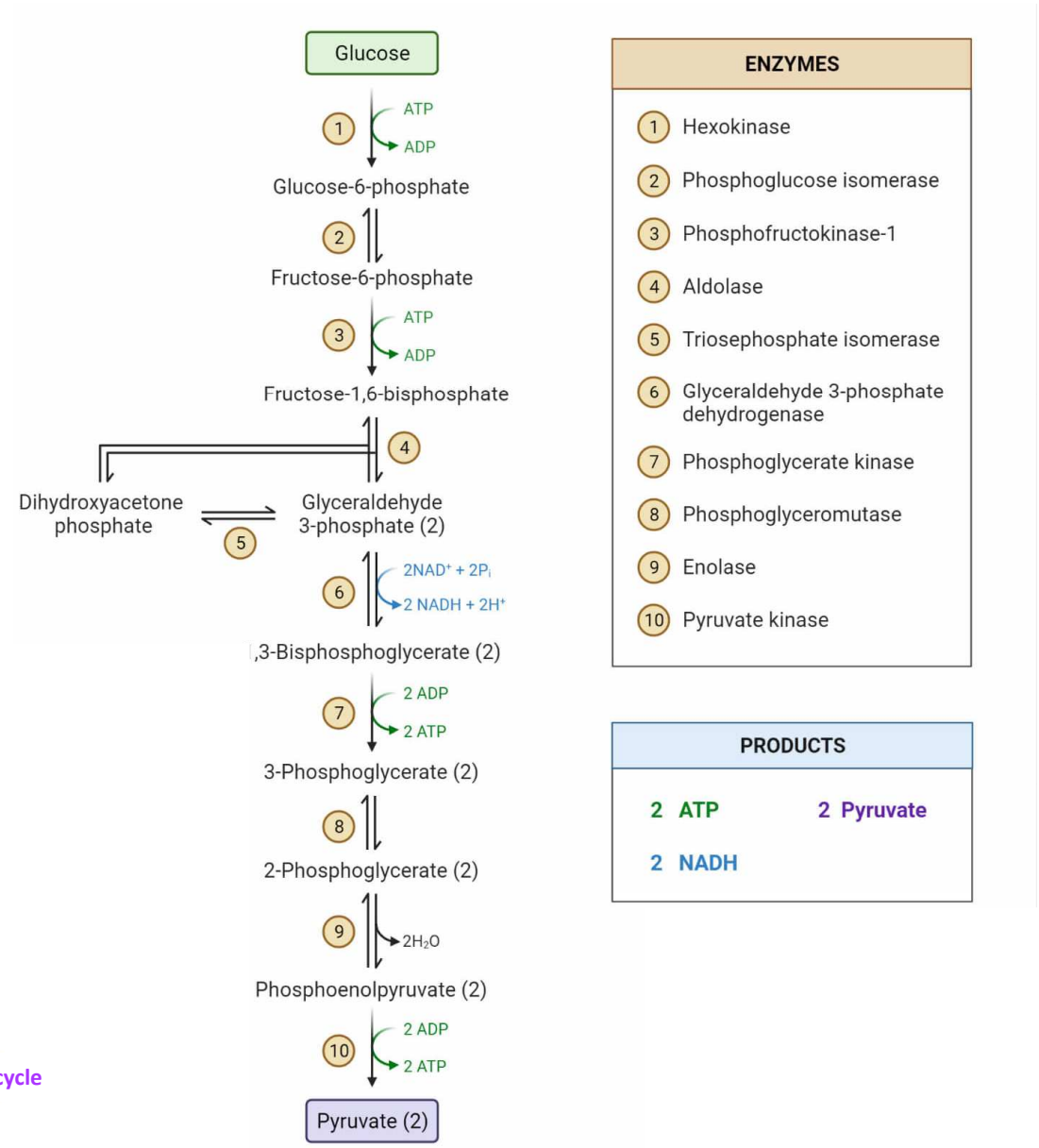
$PP_i = H_2P_2O_7^{2-}$ or $HP_2O_7^{3-}$



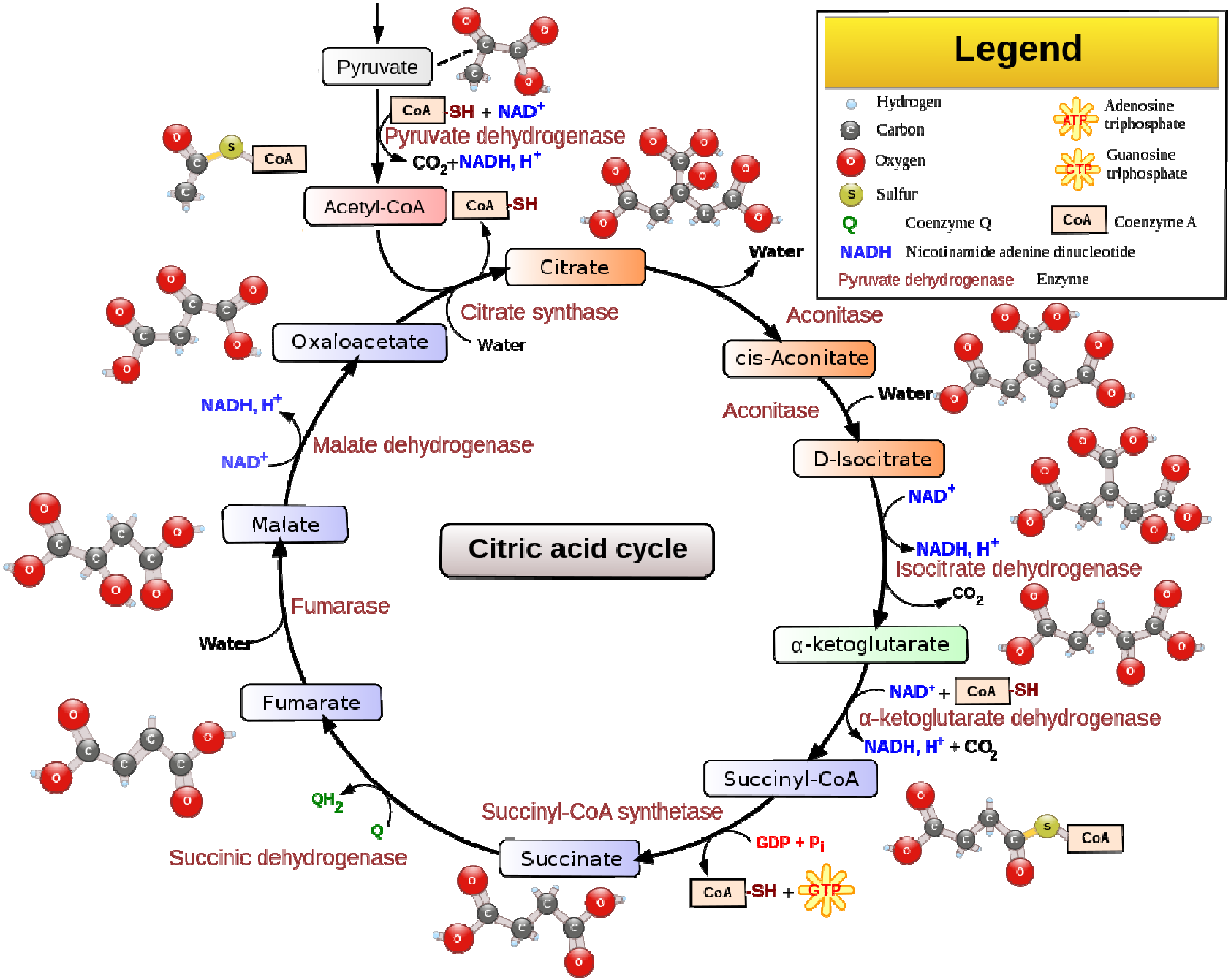
[Molecular structure of ATP]



[β-oxidation of fatty acids]



[Glycolysis]



[Pyruvate oxidation & citric acid cycle]