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Bioenergitics

Energy & why do we need it?

- ➤ **Definition: Capacity to perform work**
- ➤ **Types of energy:**
  - ✓ **1- Kinetic: Energy in the process of doing work or Energy of motion**

  - ✓ **2- Potential: Energy content stored in a matter**
- ➤ **Why products are more stable than the reactants?**
- ➤ **Whether a reaction occurs or not!**

Thermodynamics/ Bioenergetics

➢ **Thermodynamics: the study of energy transformations that occur in a collection of matter**

➢ **Bioenergetics: studying thermodynamics (energy) in living organisms**

➢ **First Law of thermodynamics: Energy cannot be created or destroyed, but only converted to other forms. Energy of universe is constant**

➢ **Second Law: All energy transformations are inefficient**
   1. systems tend to increase in disorder
   2. systems lose usable energy as heat

Why Do Chemical Reactions Occur? Concept of Free Energy, *Gibbs Equation*

➢ **Free energy change: the total energy change in a system with respect to its temperature**
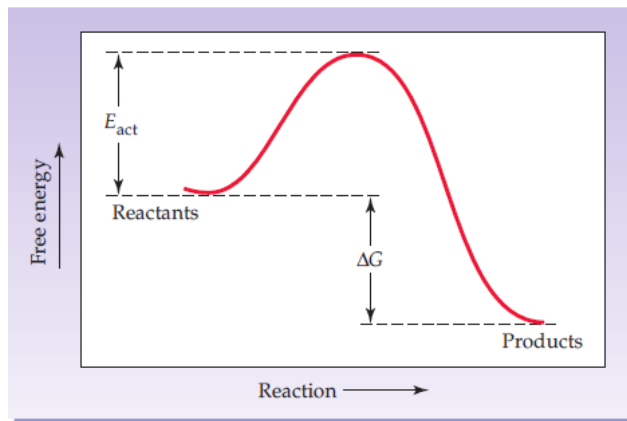
Free-energy change

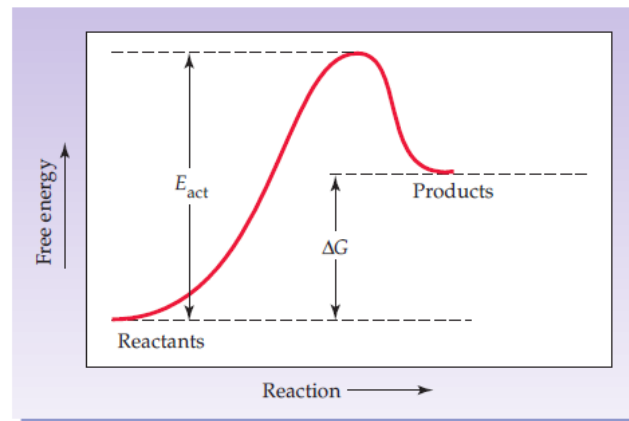Heat of reaction | Temperature (in kelvins) | Entropy change

$$\Delta G = \Delta H - T\Delta S$$

➢ **Exergonic vs. endergonic**
➢ **The value of the free-energy change determines spontaneity**
➢ **The concept of activation energy**

(a) An exergonic reaction

(b) An endergonic reaction

Energy of reactions

➢ **Enthalpy (H & ΔH): A measure of the amount of energy associated with substances involved in a reaction**

➢ **Exothermic & endothermic vs. Spontaneous & non-spontaneous – NOT always**

➢ **Entropy (S, ΔS): The amount of disorder in a system (solid, liquid & gas)**

➢ **Favorable enthalpy & entropy vs. favorable reaction**

✓ **ΔG= GB-GA**

✓ **ΔH= HB-HA**

✓ **ΔS= SB-SA**

H_A { S_A G_A → H_B { S_B G_B

A → B
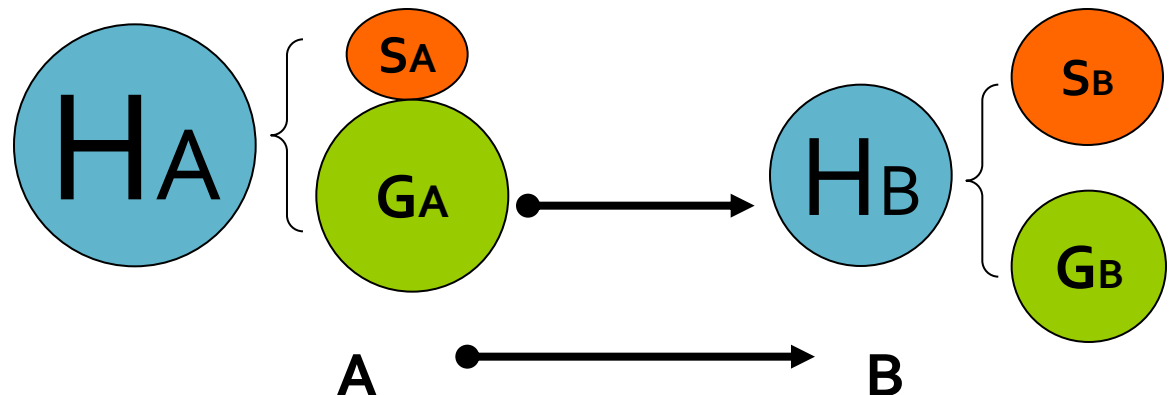
The different free energy terms

➤ ΔG = the free energy difference of a system at any condition

➤ ΔG^o = the free energy difference of a system at standard conditions ($25C^o$ & 1 atmospheric pressure, 1M concentration of reactants & products, pH = 7)

➤ Which one of these terms determine the feasibility of the reaction?

➤ ΔG depends only on initial state and final state of biochemical pathways

➤ ΔG is not affected by the mechanism of the reaction

$$A \xrightarrow{\text{Enzyme 1}} B \xrightarrow{\text{Enzyme 2}} C \xrightarrow{\text{Enzyme 3}} \ldots$$
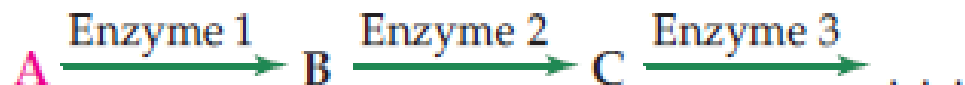
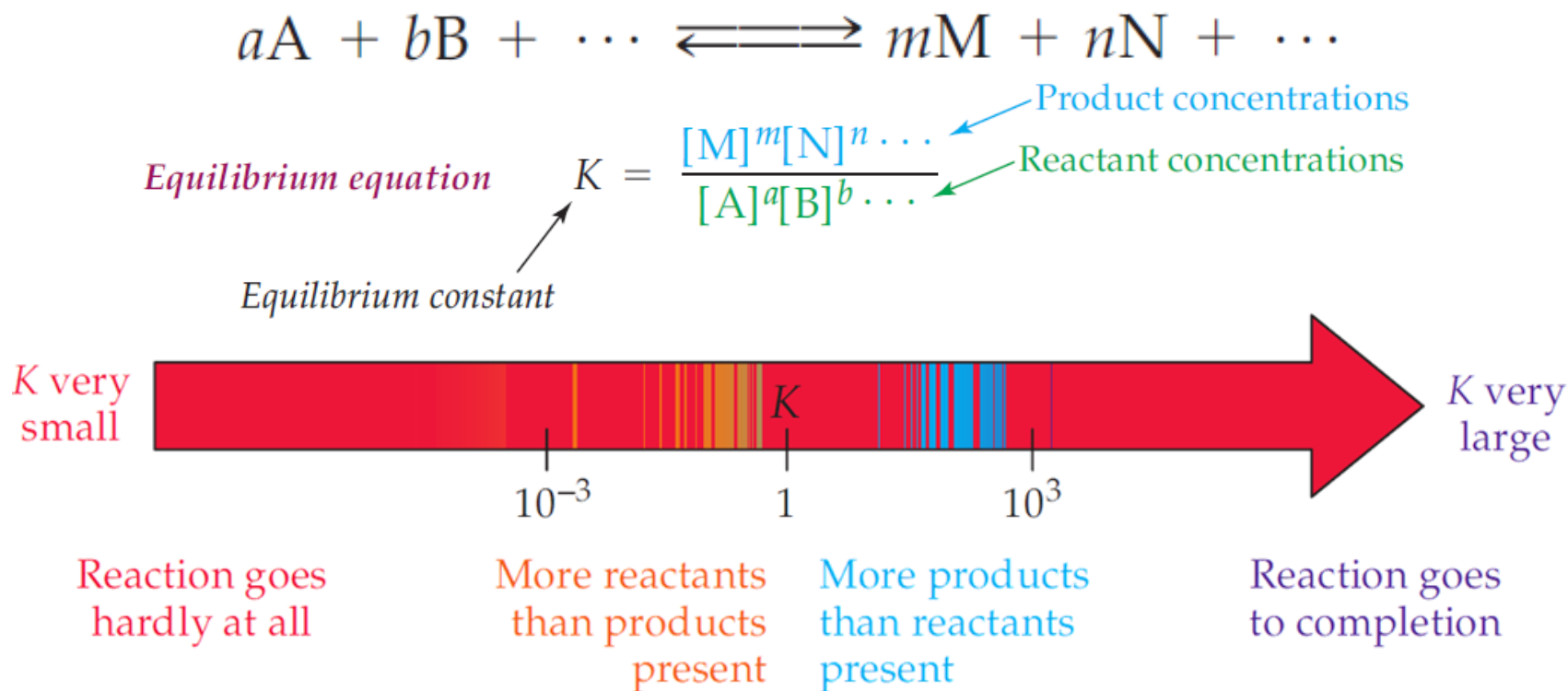# How Do Chemical Reactions Occur?

- Favorability vs. rates of reactions (thermodynamic vs. kinetic)
- Do all favorable reactions occur at room temperature? "The theory of collision"
- Effect of temperature, concentration & catalysts
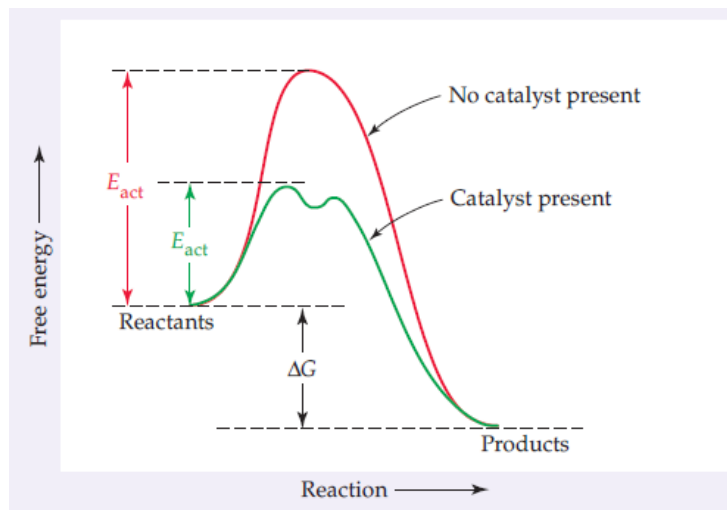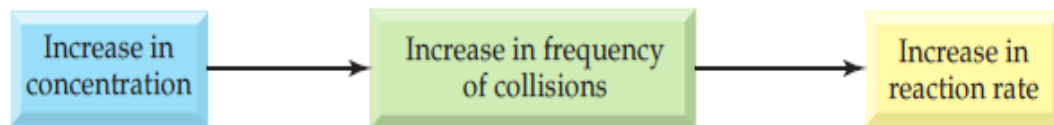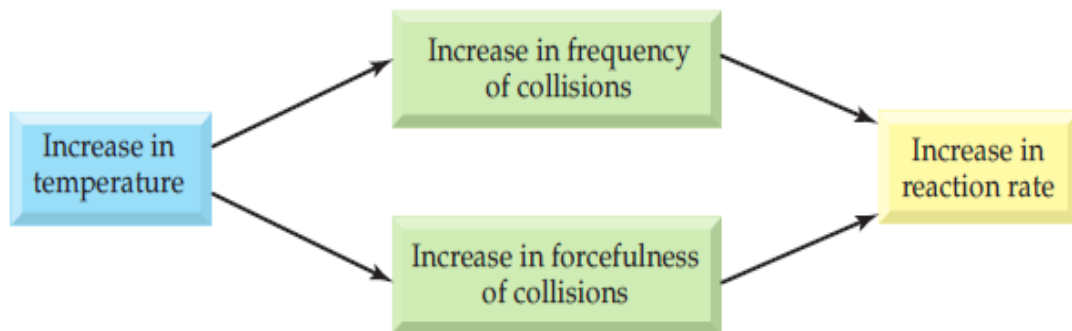
Reversible Reactions & Chemical Equilibrium

- ➢ **What is a reversible reaction?**
- ➢ **What is the chemical equilibrium? Chemical equilibrium is an active, dynamic condition**
- ➢ **At equilibrium, are concentrations equal?**

$$aA + bB + \cdots \rightleftharpoons mM + nN + \cdots$$

Equilibrium equation

$$K = \frac{[M]^m[N]^n \cdots}{[A]^a[B]^b \cdots}$$

Product concentrations

Reactant concentrations

Equilibrium constant

K very small ——————— K ——————— K very large

10^{-3} 1 10^3

Reaction goes hardly at all

More reactants than products present

More products than reactants present

Reaction goes to completion

ΔG & K_{eq}

➤ At equilibrium, $\Delta G = 0$
➤ Can a reaction has a + ΔG^o & still be favorable?

For a reaction $A + B \leftrightarrow C + D$

$$\Delta G = \Delta G^{o\prime} + RT \ln\left(\frac{[C]\,[D]}{[A]\,[B]}\right)$$

$$\Delta G = \Delta G^{o\prime} + RT \ln\left(\frac{[C]\,[D]}{[A]\,[B]}\right)$$

$$0 = \Delta G^{o\prime} + RT \ln\left(\frac{[C]\,[D]}{[A]\,[B]}\right)$$

$$\Delta G^{o\prime} = -RT \ln\left(\frac{[C]\,[D]}{[A]\,[B]}\right)$$

defining $K^{\prime}_{eq} = \left(\dfrac{[C]\,[D]}{[A]\,[B]}\right)$

$$\Delta G^{o\prime} = -RT \ln K^{\prime}_{eq}$$

$K^{\prime}_{eq}$	$\Delta G^{o\prime}$ kJ/mol	Starting with 1 M reactants & products, the reaction:
10^4	- 23	proceeds forward (spontaneous)
10^2	- 11	proceeds forward (spontaneous)
$10^0 = 1$	0	is at **equilibrium**
10^{-2}	+ 11	reverses to form "reactants"
10^{-4}	+ 23	reverses to form "reactants"

The Effect of Changing Conditions on Equilibria

$$\text{defining } K'_{eq} = \left[\frac{[C][D]}{[A][B]}\right]$$

$$\Delta G^{o\prime} = -RT \ln K'_{eq}$$

$$aA + bB + \cdots \rightleftharpoons mM + nN + \cdots$$
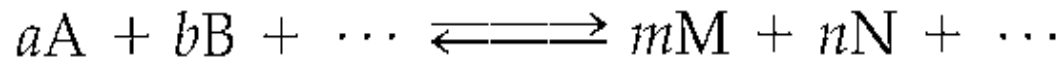
➢ **When a stress is applied to a system at equilibrium, the equilibrium shifts to relieve the stress**

➢ **Stress: any change that disturbs the original equilibrium**

➢ **Effect of Changes in Concentration**

✓ **What happens if a reactant/product is continuously supplied/ removed?**

✓ **Metabolic reactions sometimes take advantage of this effect**

➢ **Effect of Changes in Temperature**

✓ **Endothermic/exothermic are favored by increase/decrease in temperature, respectively.**

➢ **Effect of a catalyst on equilibrium**

Energy and metabolic pathways

➢ **Anabolic Pathways (Endergonic reactions):**
   Those that <u>consume</u> energy to <u>build</u> biomolecules (Protein, Glycogen & lipids)

➢ **Catabolic Pathways (Exergonic reactions):**
   Those that <u>release</u> energy by <u>breaking down</u> complex molecules into simpler compounds such as glycolysis

➢ **Metabolism is essentially a linked series of chemical reactions (biochemical pathways)**
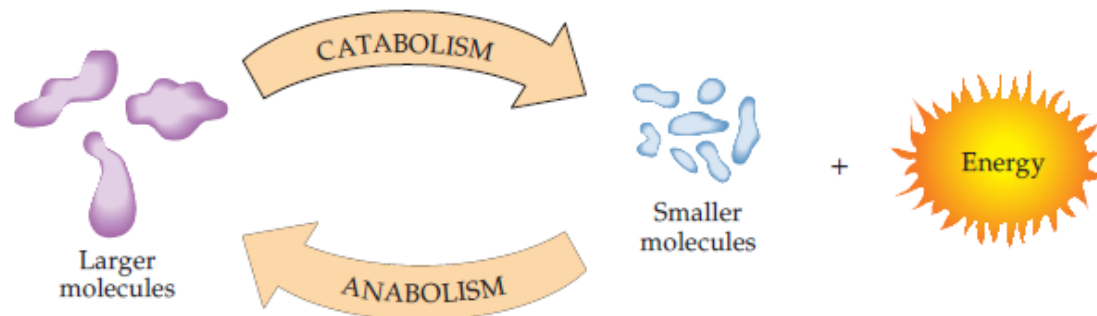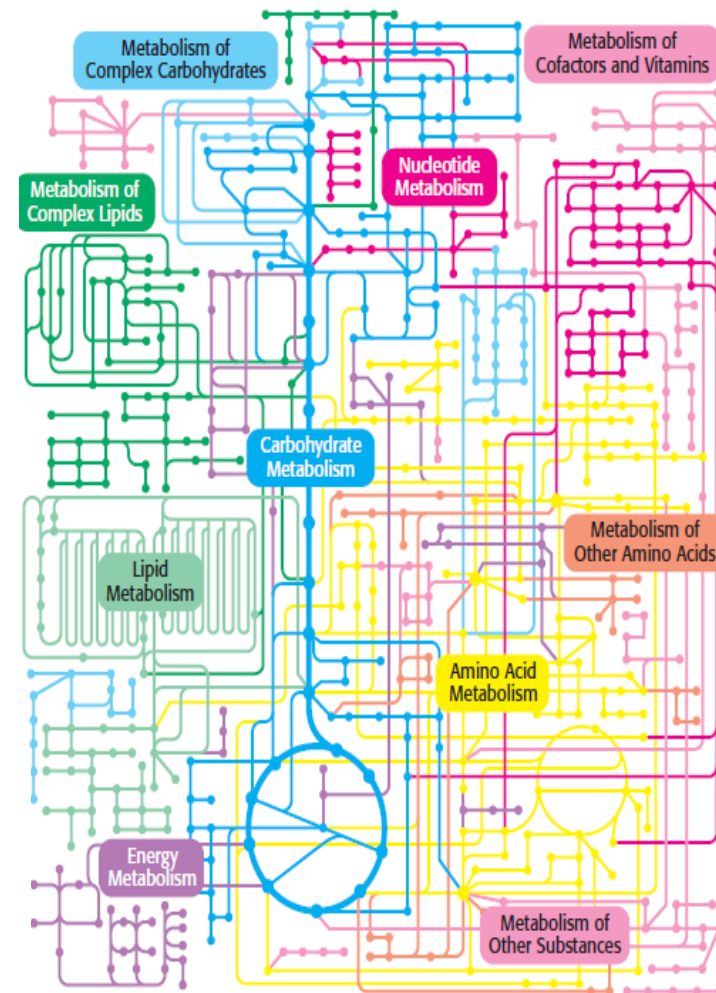
Biochemical (metabolic) pathways

➤ **Are** <u>interdependent</u>
➤ **Are subjected to thermodynamics laws**
➤ **Their activity is coordinated by sensitive means of communication**
➤ <u>**Allosteric enzymes**</u> **are the predominant regulators**
➤ **Biosynthetic & degradative pathways are** <u>**almost always distinct**</u> **(regulation)**
➤ **Metabolic pathways are** <u>linear, cyclic or spiral</u>

The energy machinery of the cell

➢ **Prokaryotic cells vs. eukaryotic cells**

➢ **The mitochondria (singular, mitochondrion) (90% of the body's energy ATP)**

➢ **The number of mitochondria is greatest in eye, brain, heart, & muscle, where the need for energy is greatest**

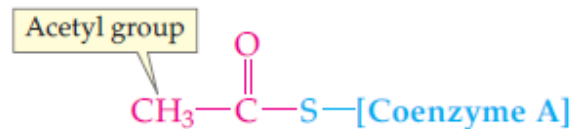➢ **The ability of mitochondria to reproduce (athletes)**

➢ **Maternal inheritance**
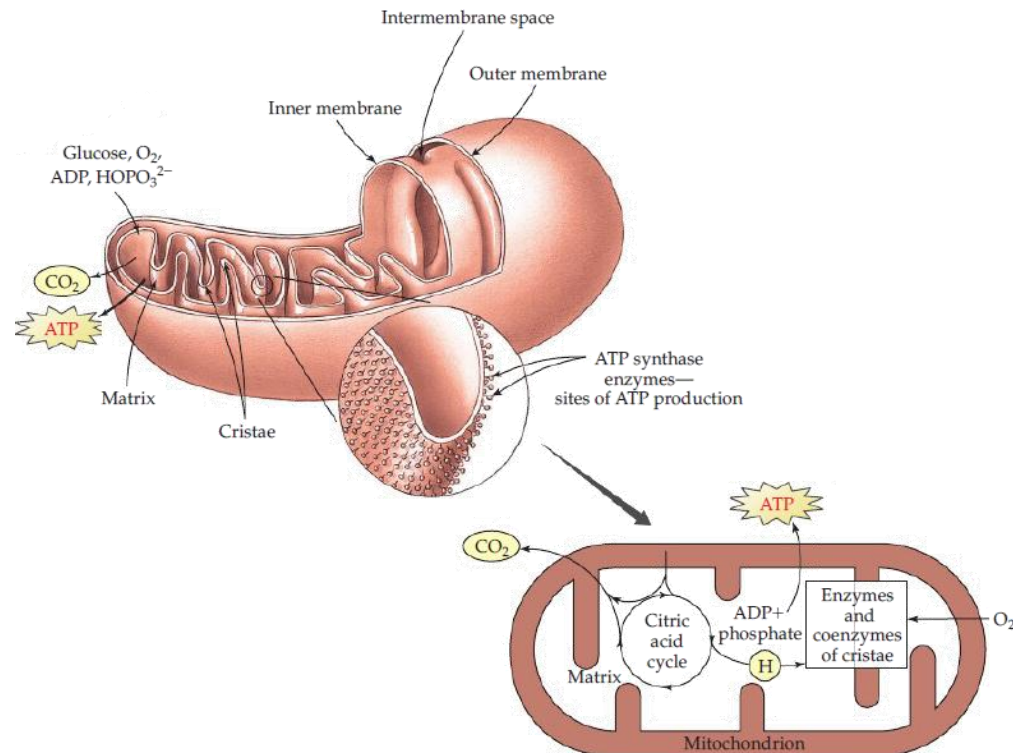
Stages of Energy Production

➢ **Stage 1 (Digestion):**

✓ **Mouth, stomach, & small intestine**

✓ **Carbohydrates to glucose & other sugars**

✓ **Proteins to amino acids**

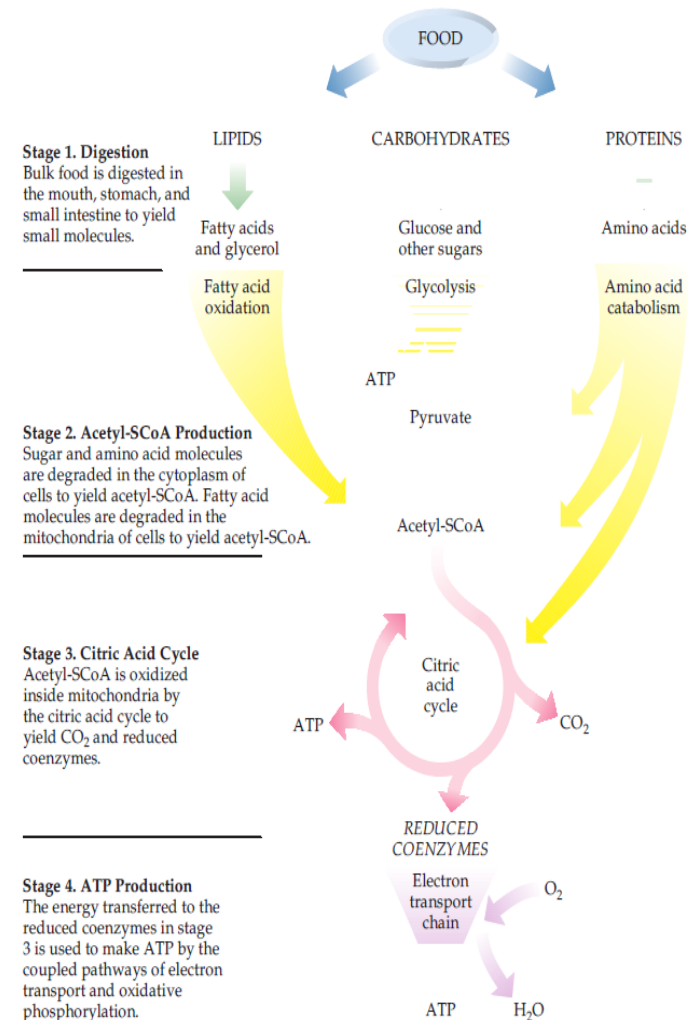✓ **Triacylglycerols to glycerol plus fatty acids**

✓ **From there to blood**

➢ **Stage 2 (Acetyl-coenzyme A)**
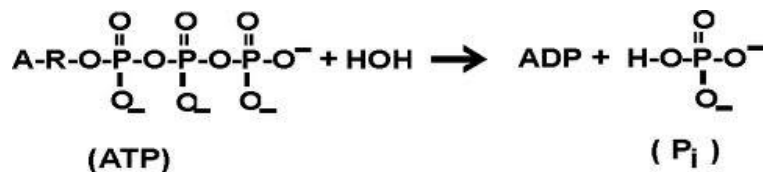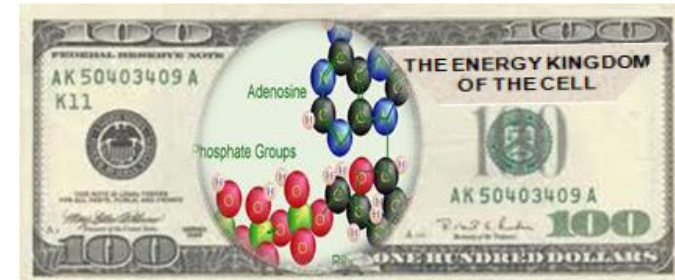
Attachment of acetyl group to coenzyme A

Acetyl group

$$CH_3 - C - S - [Coenzyme \ A]$$

with O double-bonded to C

➢ **Stage 3: citric acid cycle**

➢ **Stage 4: electron transfer chain & oxidative phosphorylation**

FOOD

Stage 1. Digestion
Bulk food is digested in the mouth, stomach, and small intestine to yield small molecules.

LIPIDS   CARBOHYDRATES   PROTEINS

Fatty acids and glycerol   Glucose and other sugars   Amino acids

Fatty acid oxidation   Glycolysis   Amino acid catabolism

ATP

Pyruvate

Stage 2. Acetyl-SCoA Production
Sugar and amino acid molecules are degraded in the cytoplasm of cells to yield acetyl-SCoA. Fatty acid molecules are degraded in the mitochondria of cells to yield acetyl-SCoA.

Acetyl-SCoA

Stage 3. Citric Acid Cycle
Acetyl-SCoA is oxidized inside mitochondria by the citric acid cycle to yield CO_2 and reduced coenzymes.

ATP   Citric acid cycle CO_2

REDUCED COENZYMES

Stage 4. ATP Production
The energy transferred to the reduced coenzymes in stage 3 is used to make ATP by the coupled pathways of electron transport and oxidative phosphorylation.

Electron transport chain O_2
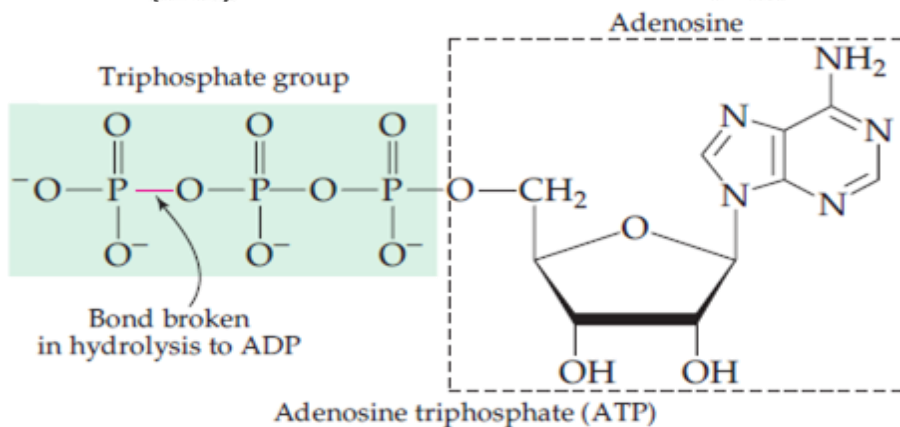
ATP H_2O

ATP

- ➤ **ATP is the energy currency of the cell**
- ➤ **What is a high energy molecule?**
- ➤ **Why ATP?**
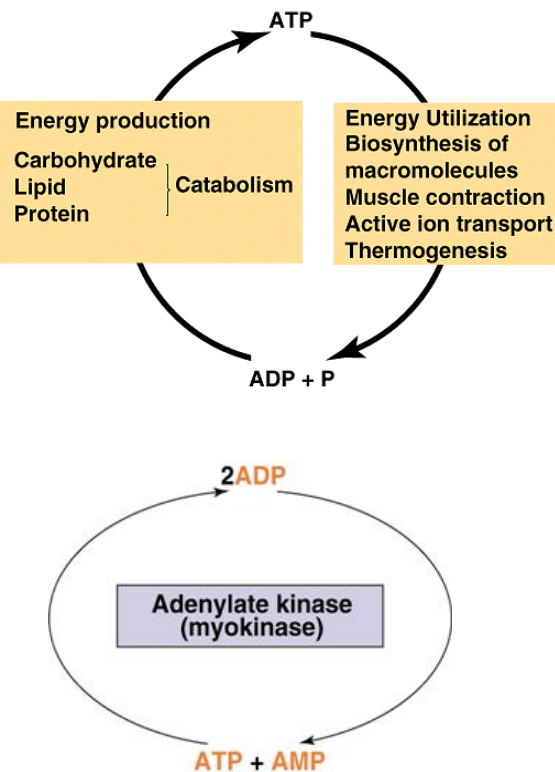 - ➤ **Has an intermediate energy value, so can be coupled**

-7.3 kcal/mole
-3.4 kcal/mole

(ATP) (P_i)

Triphosphate group

Bond broken in hydrolysis to ADP

Adenosine

Adenosine triphosphate (ATP)

Compound $+H_2O$	Product + phosphate	$\Delta G°$
Phosphoenol pyruvate	Pyruvate	-14.8
1,3 bisphosphoglycerate	3 phosphoglycerate	-11.8
Creatine phosphate	Creatine	- 10.3
ATP	**ADP**	**- 7.3**
Glucose 1- phosphate	Glucose	-5.0
Glucose 6- phosphate	Glucose	-3.3

Is ATP a good long-term energy storage molecule?

➤ **As food in the cells is gradually oxidized, the released energy is used to re-form the ATP so that the cell always maintains a supply of this essential molecule**

ATP

Energy production

Carbohydrate
Lipid   Catabolism
Protein

Energy Utilization
Biosynthesis of
macromolecules
Muscle contraction
Active ion transport
Thermogenesis

ADP + P

2ADP

Adenylate kinase
(myokinase)

ATP + AMP

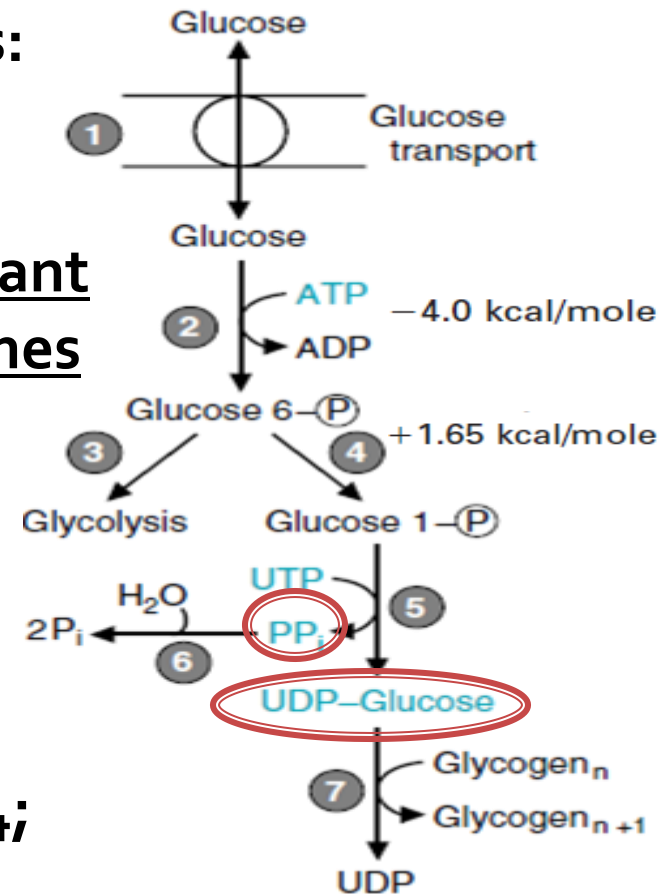| Tissue	ATP turnover (mole/day)
Brain	20.4
Heart	11.4
Kidney	17.4
Liver	21.6
Muscle	19.8
Total	90.6

90.6 * 551 (g/mole)
=
49,920 g ATP

How do our cells get energy for unfavorable biochemical work?
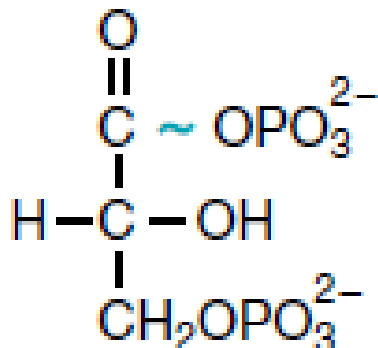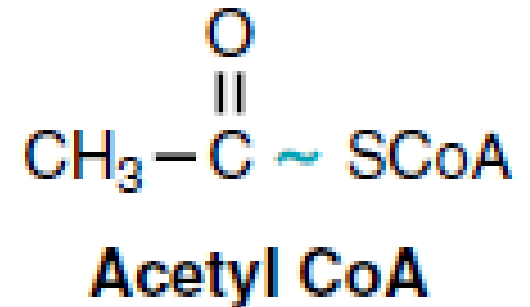
➢ **The concept of coupling**
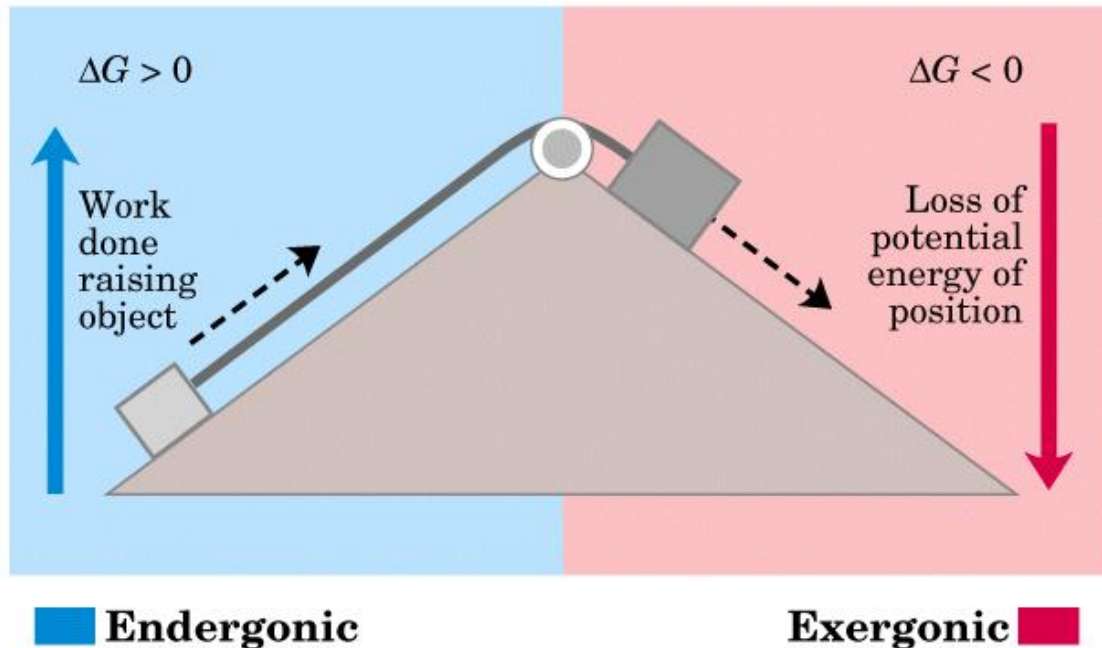
How do our cells get energy for unfavorable biochemical work?

I. **ΔG° Values are additive**

  i. **Through phosphoryl transfer reactions:**
- ✓ **Step 2 (+3.3 vs. -4 kcal/mole)**
- ✓ **Step 2 + 4 = -2.35 kcal/mole**
- ✓ <u>**The net value for synthesis is irrelevant to the presence or absence of enzymes**</u>

  ii. **Activated intermediates (step 4 is facilitated by steps 5&6)**

II. **ΔG Depends on Substrate and Product Concentration (step 4 has a ratio of 6/94; +1.65 kcal/mol, if 3/94; -0.4kcal/mol)**

Glucose

Glucose transport — 1

Glucose

ATP / ADP — 2   −4.0 kcal/mole

Glucose 6–P

Glycolysis — 3

4   +1.65 kcal/mole

Glucose 1–P

UTP — 5

H_2O PP$_i$ 2P$_i$ — 6

UDP–Glucose
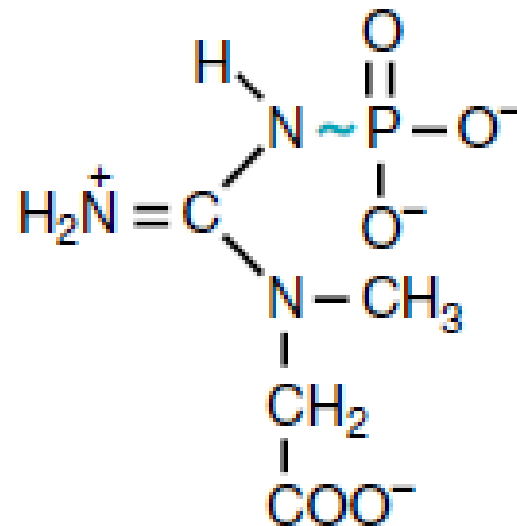
Glycogen$_n$ — 7 — Glycogen$_{n+1}$

UDP

How do our cells get energy for unfavorable biochemical work?

III. **Activated Intermediates other than ATP; UTP is used for combining sugars, CTP in lipid synthesis, and GTP in protein synthesis**
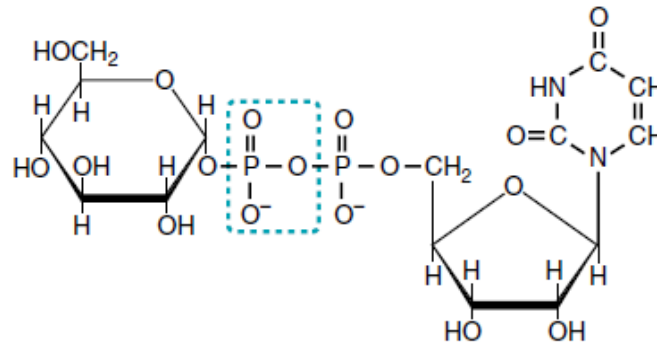
$$CH_3 - \overset{\overset{\displaystyle O}{\|}}{C} \sim SCoA$$

Acetyl CoA

$$\overset{\overset{\displaystyle O}{\|}}{C} \sim OPO_3^{2-}$$
$$H - C - OH$$
$$CH_2OPO_3^{2-}$$

1,3–Bisphosphoglycerate

$$H_2\overset{+}{N} = C \begin{cases} \overset{H}{\underset{}{N}} \sim \overset{\overset{\displaystyle O}{\|}}{P} - O^- \\ \quad\; O^- \\ N - CH_3 \\ CH_2 \\ COO^- \end{cases}$$
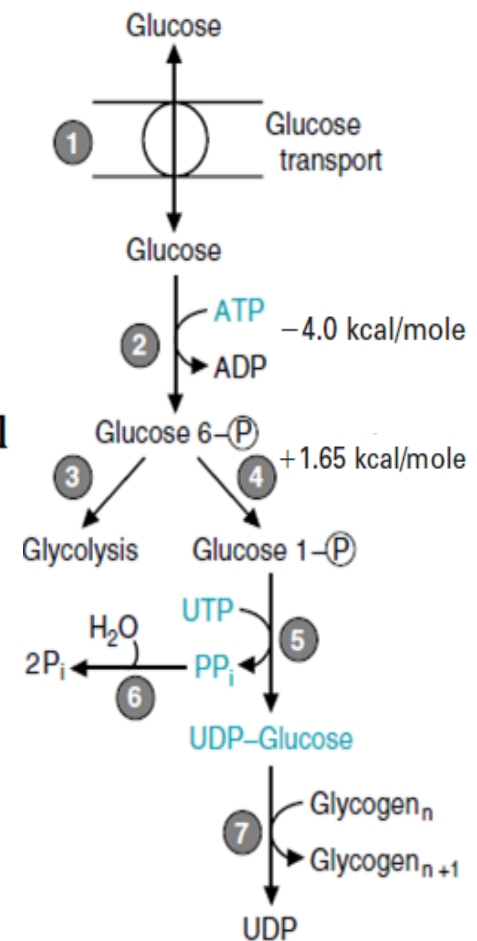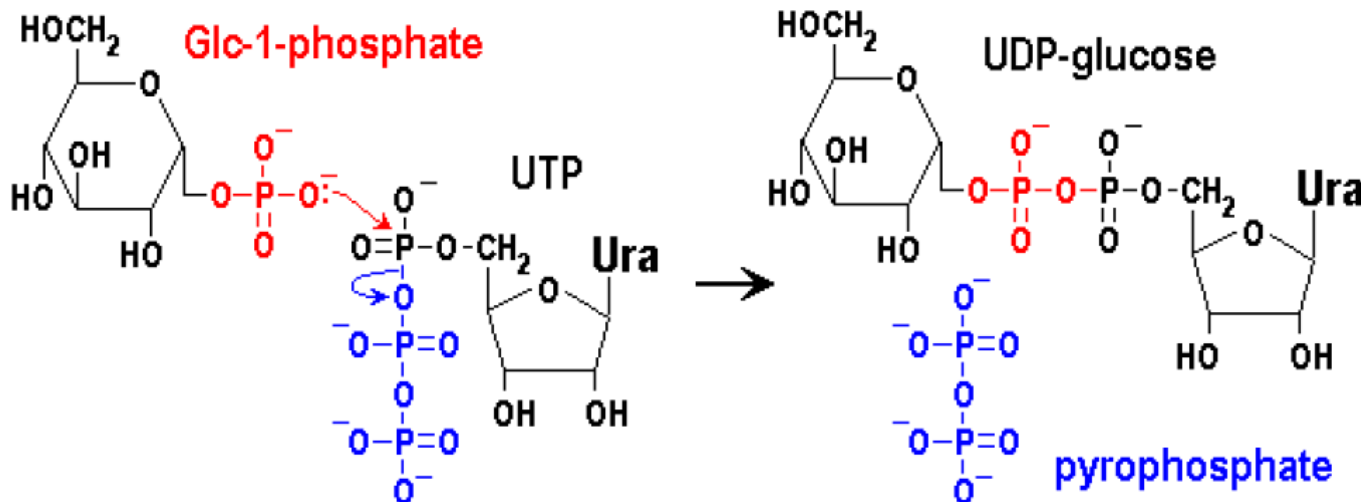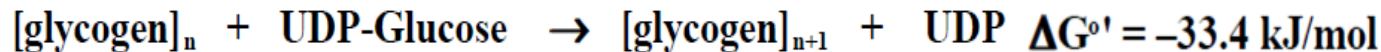
Creatine phosphate

# The UDP-glucose as an example

> **UDP Carries the activated sugar**

Uridine diphosphate glucose
(UDP−glucose)

Glycogen synthase

$$[glycogen]_n + \text{UDP-Glucose} \rightarrow [glycogen]_{n+1} + \text{UDP} \quad \Delta G^{o\prime} = -33.4 \text{ kJ/mol}$$

Glc-1-phosphate

UTP

UDP-glucose

Ura

pyrophosphate

Glucose

Glucose transport

Glucose

ATP -4.0 kcal/mole
ADP

Glucose 6–(P) $+1.65$ kcal/mole

Glycolysis   Glucose 1–(P)

H_2O UTP
$2P_i$ PP_i

UDP–Glucose

Glycogen$_n$

Glycogen$_{n+1}$

UDP

The acetyl CoA as an example

➢ **Coenzyme A is a universal carrier (donor) of Acyl groups**
➢ **Forms a thio-ester bond with carboxyl group**
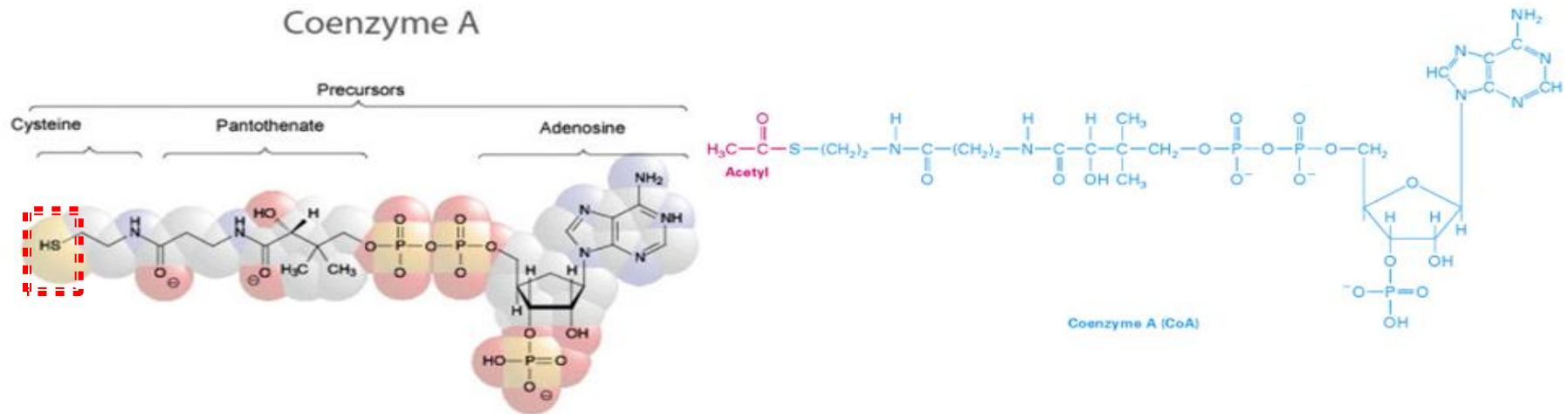
➢ Acetyl CoA + H_2O ⟶ Acetate + CoA $\Delta G^o = -7.5$kcal
➢ Acetylcholine + H_2O ⟶ Acetate + Choline $\Delta G^o = -3$ kcal

➢   + Choline ⟶ Acetylcholine + $\Delta G^o = +3$ kcal
➢ Acetyl CoA +   ⟶   + CoA $\Delta G^o = -7.5$ kcal

➢ Acetyl CoA + Choline ⟶ Acetylcholine + COA
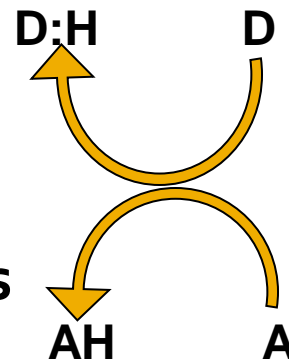
Oxidation-Reduction reactions (Redox)

➢ **Oxidation:**
  ✓ **Gain of Oxygen**
  ✓ **Loss of Hydrogen**
  ✓ **Loss of electrons**

➢ *Reduction:*
  ✓ **Gain of Hydrogen**
  ✓ **Gain of electron**
  ✓ **Loss of Oxygen**

➢ *E*= **redox Potential:** **it is a POTENTIAL ENERGY that measures the tendency of oxidant/reductant to gain/lose electrons, to become reduced/oxidized**

D:H   D

➢ **Electrons move from compounds with lower reduction potential (more negative) to compounds with higher reduction potential (more positive)**

AH   A

➢ **Oxidation and reduction must occur simultaneously**

Oxidation-Reduction reactions (Redox)

➢ $\Delta E = E_A - E_D$

➢ ΔE = Redox difference of a system in any condition

➢ ΔE^o = Redox difference of a system in standard condition ($25C^o$ and 1 atmosphere pressure, pH = 7)

➢ **Does ΔE determine the feasibility of a reaction?**

➢ $\Delta G^o = -nf\Delta E^o$

ΔG is related to ΔE

➤ ΔE is directly proportional to ΔG^o
　　　　➤ $\Delta G^o = -nf\Delta E^o$
➤ Where:
➤ n = the number of transferred electron
➤ F = the Faraday constant (96.5 kJ/volt) (23.06 kcal/volt)
➤ E = the reduction potential (volts);
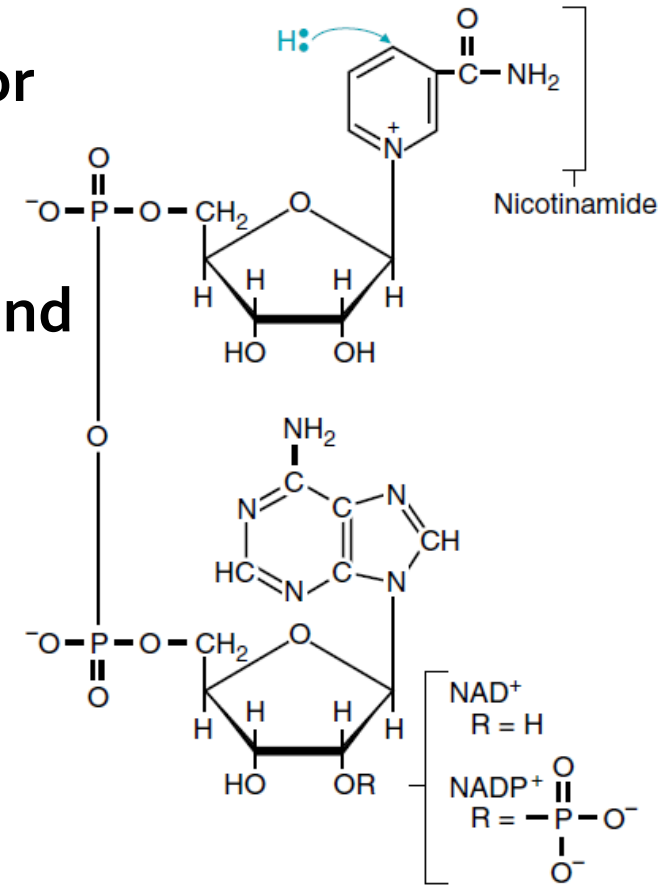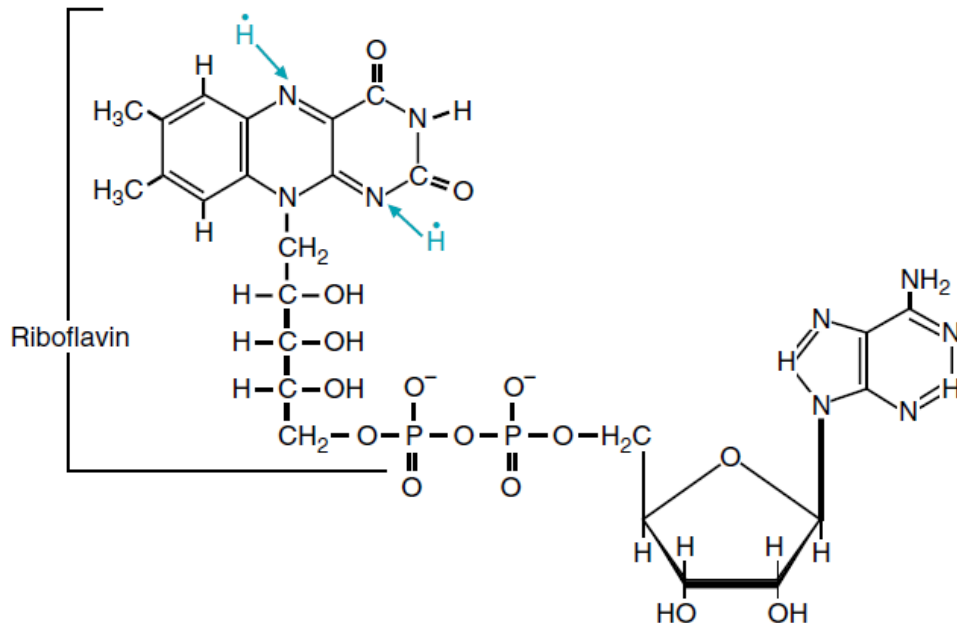➤ G = the free energy (Kcal or KJ)

➤ In other words; energy (work) can be derived from the transfer of electrons
➤ Or
➤ Oxidation of foods can be used to synthesize ATP

Oxidation-Reduction reactions (Redox)

- Always involve <u>a pair</u> of chemicals: an electron donor and an electron acceptor (Food vs. NAD^+)
- NAD^+ vs. FAD
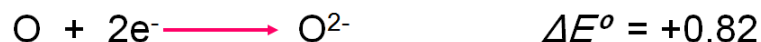- NAD^+ vs. $NADP^+$ (fatty acid synthesis and detoxification reactions)

Oxidation-Reduction reactions (Redox)

➢ **The more negative the reduction potential, the greater is the energy available for ATP generation**

Table 19.4. Reduction Potentials of Some Oxidation-Reduction Half-Reactions

Reduction Half-Reactions	$E^{0\prime}$ at pH 7.0
$1/2\ O_2 + 2H^+ + 2\ e^- \rightarrow H_2O$	0.816
Cytochrome a-Fe^{3+} + 1 $e^- \rightarrow$ cytochrome a-Fe^{2+}	0.290
$CoQ + 2H^+ + 2\ e^- \rightarrow CoQH_2$	0.060
Fumarate + $2H^+ + 2\ e^- \rightarrow$ succinate	0.030
Oxalacetate + $2H^+ + 2\ e^- \rightarrow$ malate	−0.102
Acetaldehyde + $2H^+ + 2\ e^- \rightarrow$ ethanol	−0.163
Pyruvate + $2H^+ + 2\ e^- \rightarrow$ lactate	−0.190
Riboflavin + $2H^+ + 2\ e^- \rightarrow$ riboflavin-H_2	−0.200
$NAD^+ + 2H^+ + 2\ e^- \rightarrow NADH + H^+$	−0.320
Acetate + $2H^+ + 2\ e^- \rightarrow$ acetaldehyde	−0.468

$NADH + 1/2O_2 \longrightarrow NAD^+ + H_2O$ 　　　　　 $FADH_2 + 1/2O_2 \longrightarrow FAD + H_2O$

$NADH \longrightarrow NAD+ + 2e^-$ 　$\Delta E^o = +0.32$ 　　　 $FADH_2 \longrightarrow FAD + 2e^-$ 　$\Delta E^o = +0.20$

$O + 2e^- \longrightarrow O^{2-}$ 　　　　$\Delta E^o = +0.82$ 　　　　 $O + 2e^- \longrightarrow O^{2-}$ 　　　$\Delta E^o = +0.82$

$\Delta G^o \approx -53$ kcal/mol 　　　　　　　　　　 $\Delta G^o \approx -41$ kcal/mol

CALORIC VALUES OF FUELS

➢ **1. Directly related to its oxidation state (ΔG°)= the transfer of electrons from that fuel (C-H and C-C bonds) to O2**

➢ **2. In humans, the enzymes that oxidizes fuels! Burning of wood**
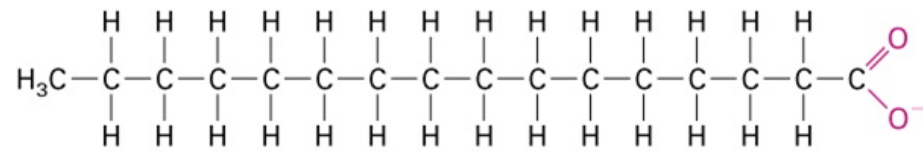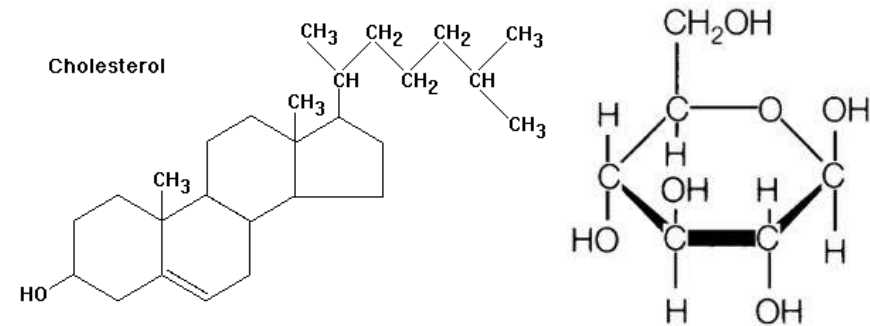
Compound	ΔG° (kcal/mol)	Molecular weight	Caloric value (kcal/g)
Glucose	686	180	3.8
Palmitate	2380	256	9.3
Glycine	234	75	3.1

Cholesterol

Palmitate