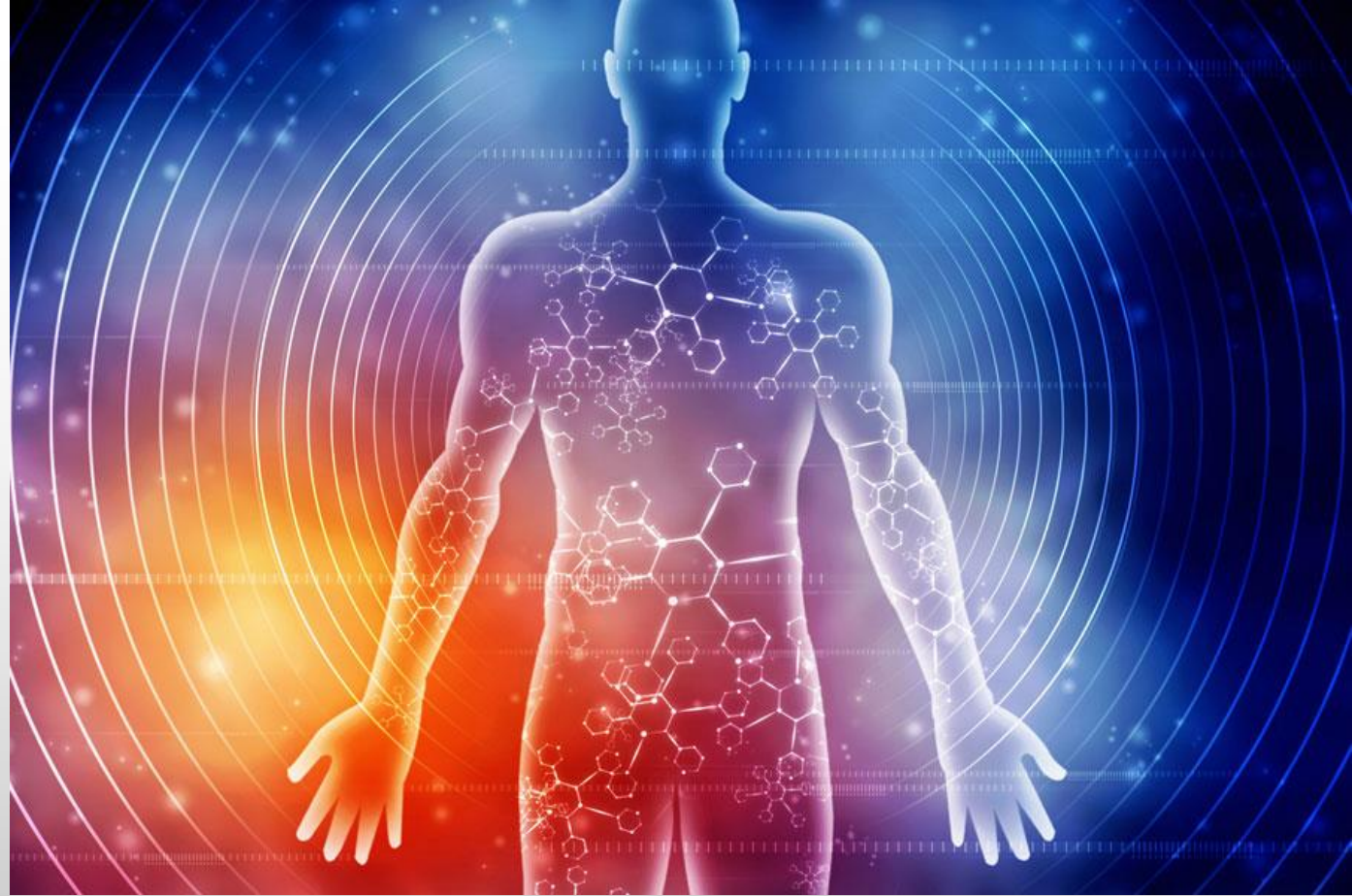


Bioenergetics



Dr. Diala Abu-Hassan, DDS, PhD

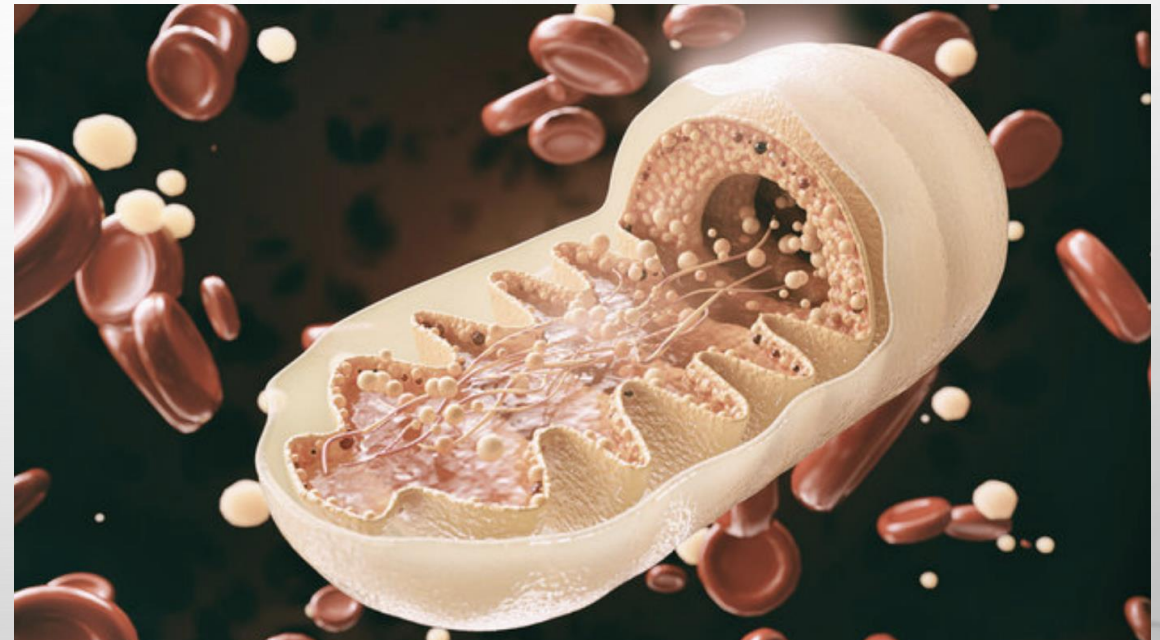
What is ENERGY? Why do we need it?

- ❖ Definition: Capacity to perform work
- ❖ What for? Mechanical, Active transport, Biosynthesis, Heat
- ❖ Types of energy:
 - ✓ 1- Kinetic: Energy in the process of doing work or Energy of motion
 - ✓ 2- Potential: Energy content stored in a matter such as chemical bonds
- ❖ Whether a reaction occurs or not!
- ❖ Bioenergetics describes the transfer and utilization of energy in biologic systems



Purposes of metabolism

- **Metabolism: Sum of all biochemical reactions in living organisms**
- **Mainly for energy generation**
- **Other purposes:**
 - Synthesis of building blocks
 - Synthesis of macromolecules
 - Degradation of biomolecules
- **Bioenergetics: Energy transformations in the cell**



Free energy terms

- ΔG = the free energy difference of a system at any condition
- ΔG° = the free energy difference of a system at standard conditions (25°C & 1 atmospheric pressure, 1M concentration of reactants & products, pH = 7)

Why do chemical reactions occur?

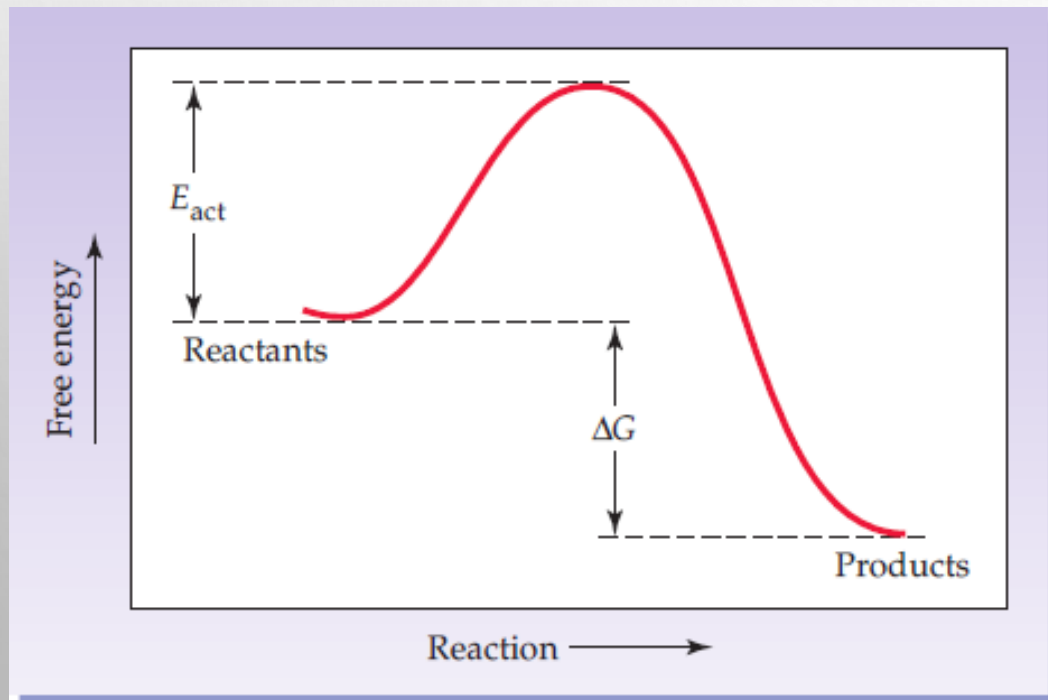
- Free energy change; with respect to its temperature
- Enthalpy; Entropy; Exergonic vs. endergonic; spontaneity
- The concept of activation energy

Heat of reaction Temperature (in kelvins) Entropy change

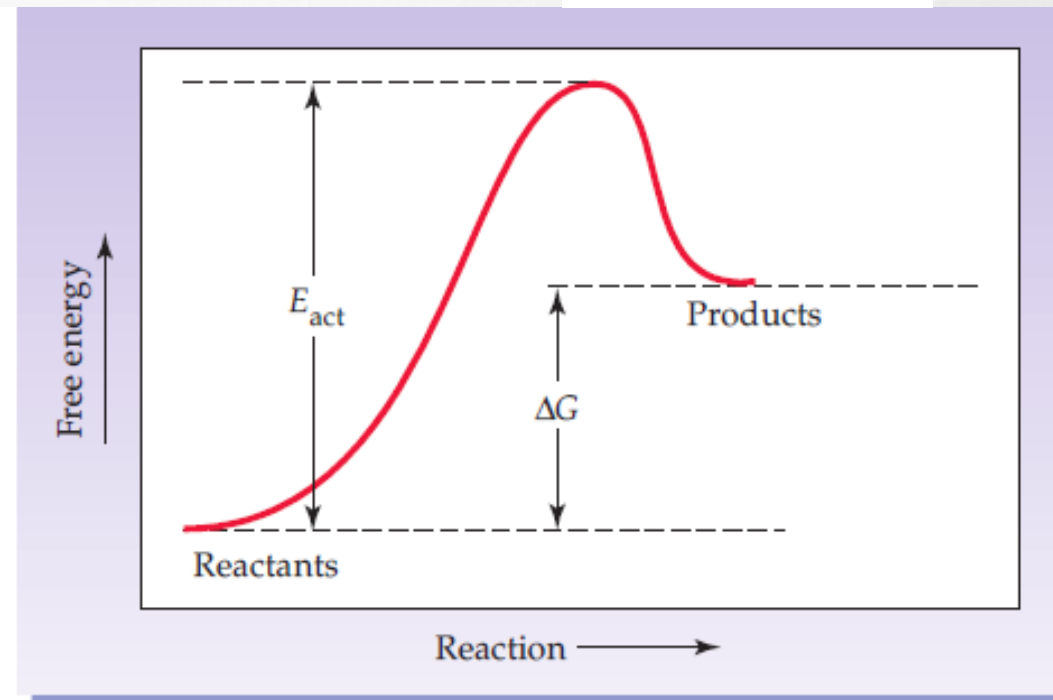
$$\Delta G = \Delta H - T\Delta S$$

Gibbs Equation

Free-energy change



(a) An exergonic reaction



(b) An endergonic reaction

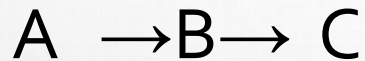
ΔG , GIBBS FREE ENERGY



- This equilibrium is not determined by enzymes but determined by thermodynamics.
- If more equilibrium to A, you will not change the equilibrium by adding any amount of enzyme to the reaction.
- What determines the equilibrium between them? Gibbs free energy.
- ΔG which is related to equilibrium constant and can be used to determine if the reaction is favorable or not:
 - if $\Delta G < 0$, reaction is spontaneous,
 - if $\Delta G > 0$, reaction is not spontaneous
 - if $\Delta G = 0$, reaction is at equilibrium

Is ΔG affected by the mechanism of the reaction?

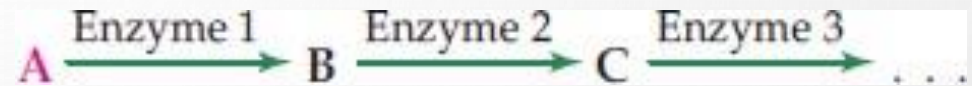
- ΔG is not affected by the mechanism of the reaction
- ΔG depends only on initial state and final state of biochemical pathways



$$\Delta G_{A \rightarrow B} = \cancel{G_B} - G_A$$

$$\Delta G_{B \rightarrow C} = G_C - \cancel{G_B}$$

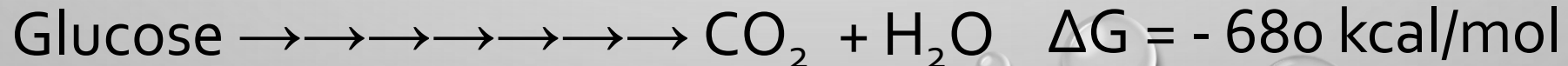
$$G_C - G_A = \Delta G_{A \rightarrow C}$$



- Combustion of glucose in calorimeter



In the cell



ΔG is affected by concentration



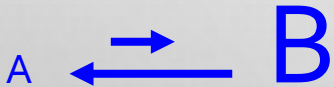
$$\Delta G = \text{---}$$



$$\Delta G = -$$



$$\Delta G = \text{zero}$$



$$\Delta G = ++$$

ΔG measures the tendency of the reaction to proceed towards equilibrium

ΔG° , the standard free energy change

- Concentrations of reactants and products = 1 mole/L

- $\Delta G = \Delta G^\circ + RT \ln \frac{[\text{Products}]}{[\text{Reactants}]}$

R is the gas constant (1.987 cal/mol K)

T is the absolute temperature (K)

- $\Delta G = \Delta G^\circ + RT \ 2.3 \log \frac{[\text{Products}]}{[\text{Reactants}]}$

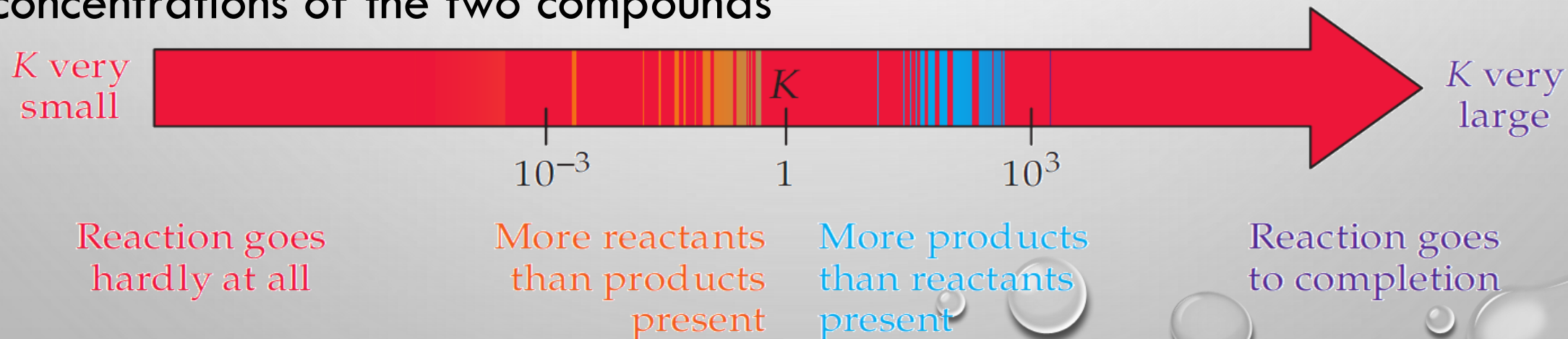
A reaction with a positive ΔG° can proceed in the forward direction if the ratio of products to reactants ($[B]/[A]$) is sufficiently small (that is, the ratio of reactants to products is large) to make ΔG negative.

✓ ΔG° is constant

✓ ΔG° represents energy changes at non-physiologic concentrations of reactants and products

Reversible reaction and chemical equilibrium

- What is a reversible reaction?
- What is the chemical equilibrium? Chemical equilibrium is an active, dynamic condition
- At equilibrium, no further net chemical change takes place (that is, when A is being converted to B as fast as B is being converted to A)
- At equilibrium, are concentrations equal? No
- At equilibrium, the ratio of [B] to [A] is constant, regardless of the actual concentrations of the two compounds



Standard free energy change (ΔG°) and equilibrium constant K_{eq}

K_{EQ} IS OBTAINED BY DIVIDING [PRODUCTS] BY [REACTANTS] WHEN THE REACTION REACHES EQUILIBRIUM

- At equilibrium

$$0 = \Delta G^\circ + RT \ln K_{eq}$$

$$\Delta G^\circ = -RT \ln K_{eq}$$

$$K_{eq} = \frac{[\text{Products}]}{[\text{Reactants}]}$$

- At standard conditions

$$\Delta G = \Delta G^\circ + RT \ln 1$$

$$\Delta G = \Delta G^\circ$$

- ✓ ΔG° cannot predict the direction of a reaction under physiologic conditions because it is composed solely of constants (R , T , and K_{eq}) and is not, therefore, altered by changes in product or substrate concentrations.

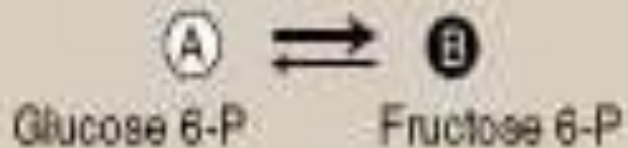
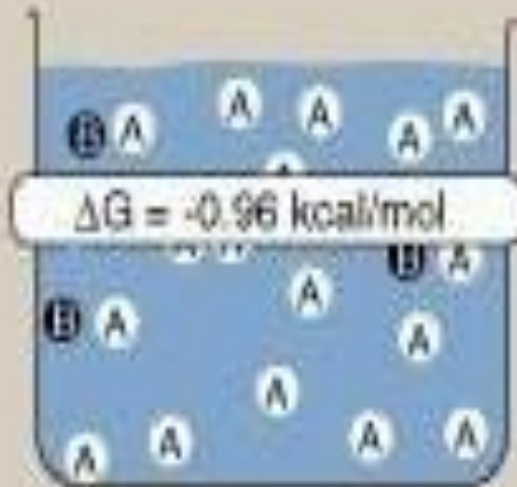
GLUCOSE 6- PHOSPHATE



Fructose 6- phosphate

A Nonequilibrium conditions

A = 0.9 mol/L B = 0.09 mol/L



$$\Delta G^{\circ} = + 0.4 \text{ kcal/mol}$$

$$\Delta G = \Delta G^{\circ} + RT 2.3 \log 0.09/0.9$$

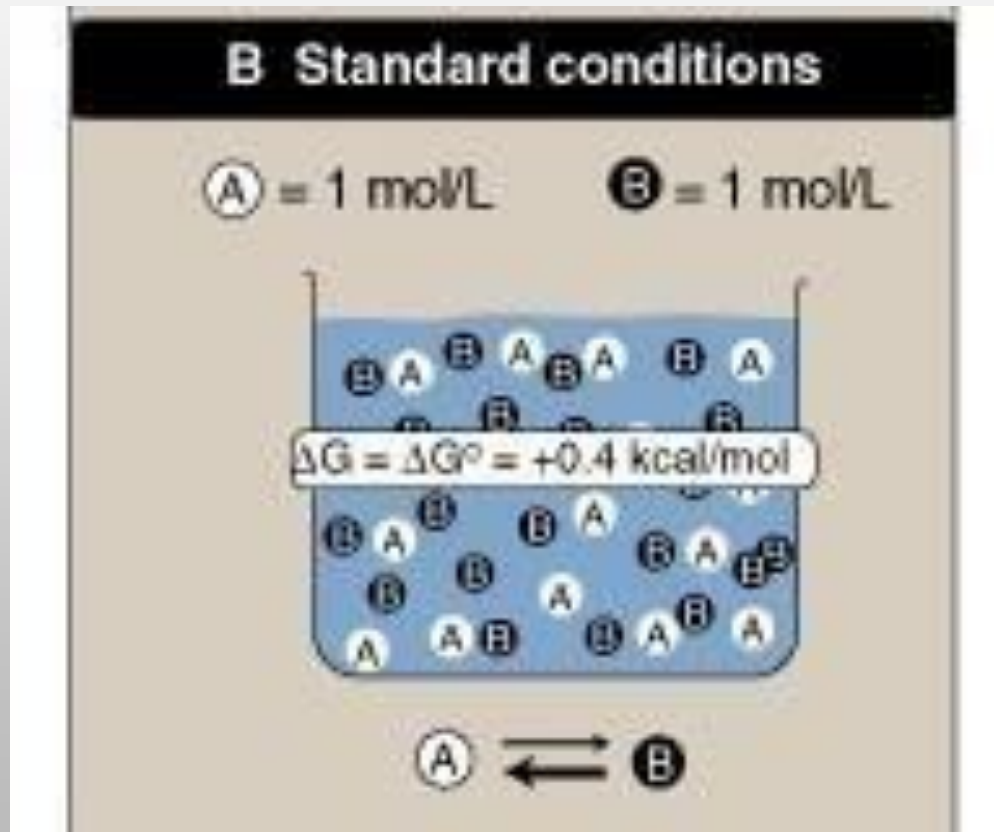
$$\Delta G = - 0.96 \text{ (negative)}$$

Reaction goes forward

Glucose 6-phosphate
1 mol/L



Fructose 6-phosphate
1 mol/L



$$\Delta G = \Delta G^\circ + RT \, 2.3 \log 1/1$$

$$\Delta G = \Delta G^\circ$$

GLUCOSE 6- PHOSPHATE




Fructose 6- phosphate

0.66 mol/L

0.33 mol/L

C Equilibrium conditions

(A) = 0.66 mol/L (B) = 0.33 mol/L



$\Delta G = 0 \text{ kcal/mol}$

(A) \rightleftharpoons (B)

$K_{eq} = \frac{[\text{Fructose 6-phosphate}]}{[\text{Glucose 6-phosphate}]} = 0.504$

$$\Delta G = \Delta G^\circ + RT \ln \frac{0.33}{0.66}$$

$$\Delta G^\circ = + 0.4 \text{ kcal/mol}$$

$$\Delta G = 0$$

ΔG & K_{eq}

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

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

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

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

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

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

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

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

K'_{eq}	$\Delta G^{\circ'}$ 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”

ΔG° and K_{eq}

K_{eq}	ΔG°
10^3	- 4.08
10^2	- 2.72
10^1	- 1.36
1	0
10^{-1}	1.36
10^{-2}	2.72
10^{-3}	4.08

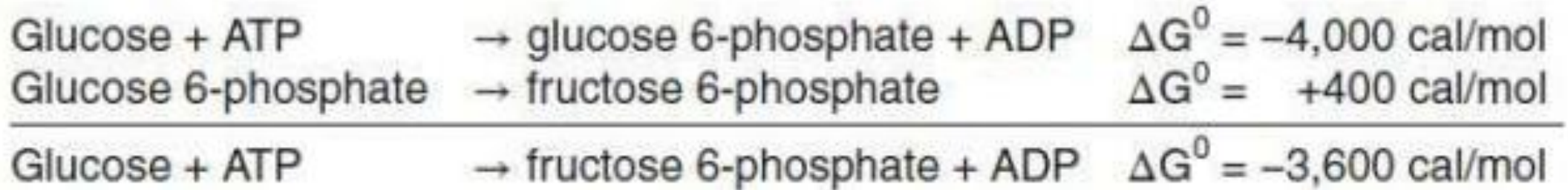
If $K_{eq} = 1$, then $\Delta G^\circ = 0$

If $K_{eq} > 1$, then $\Delta G^\circ < 0$

If $K_{eq} < 1$, then $\Delta G^\circ > 0$

ΔG & ΔG°

- The ΔG° s are additive in any sequence of consecutive reactions, as are the ΔG s

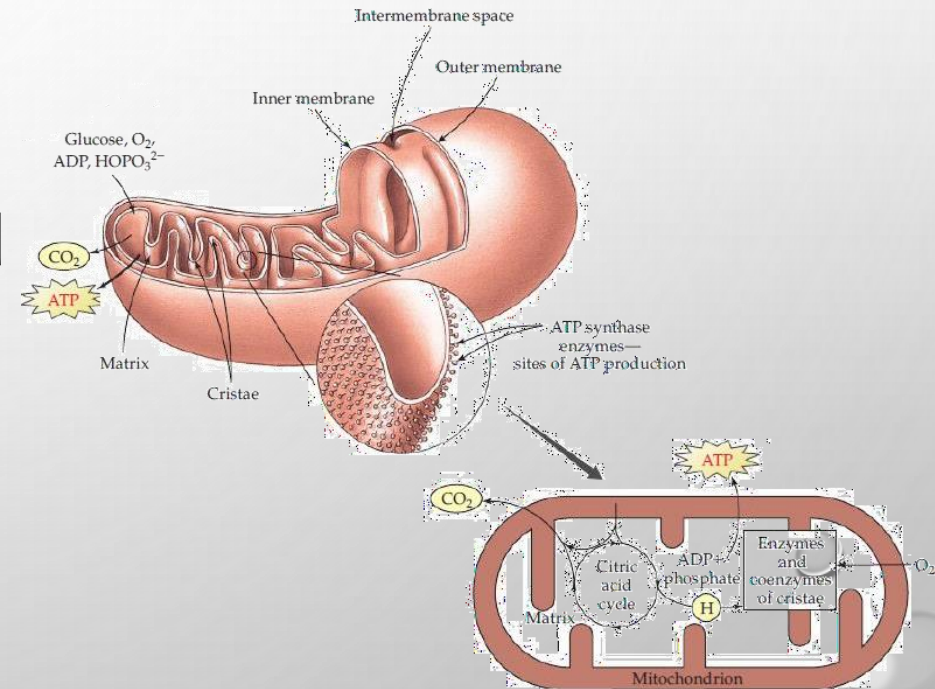


- ΔG s of a pathway: $A \rightarrow B \rightarrow C \rightarrow D \rightarrow \dots$

As long as the sum of the ΔG s of the individual reactions is negative, the pathway can proceed, even if some of the individual reactions of the pathway have a positive ΔG . However, the actual rates of the reactions depend on the lowering of activation energies (E_a) by the enzymes that catalyze the reactions

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



Energy production stages

➤ Stage 1 (Digestion):

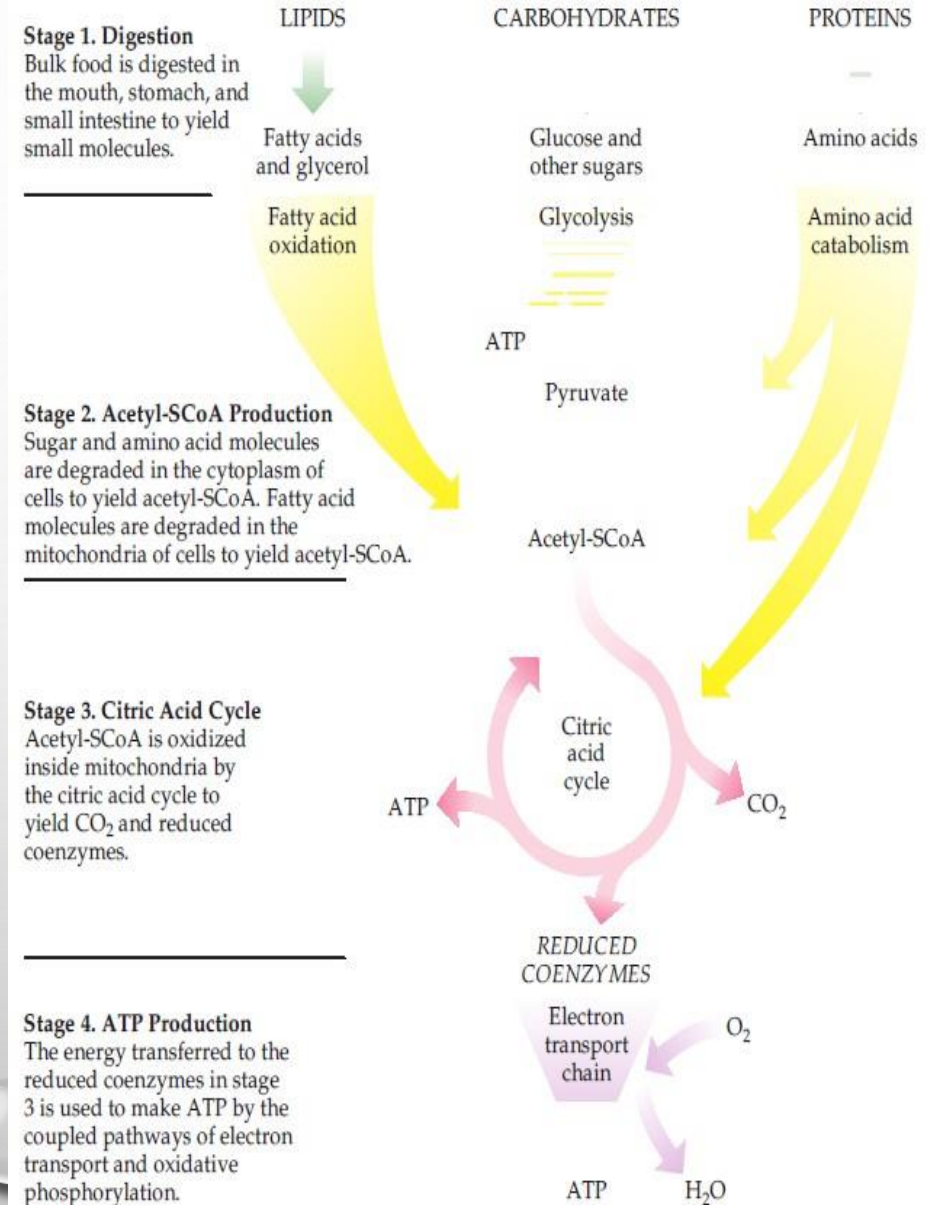
- ✓ Mouth, stomach, & small intestine
- ✓ Carbohydrates to glucose & other sugars
- ✓ Proteins to amino acids
- ✓ Triacylglycerols to glycerol plus fatty acids
- ✓ From there to blood

➤ Stage 2 (Acetyl-coenzyme A)

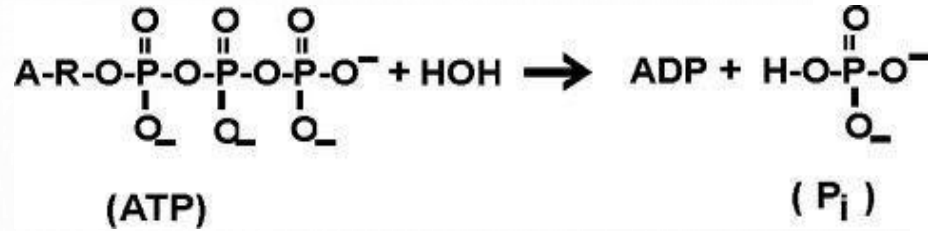
➤ Stage 3: citric acid cycle

➤ Stage 4: electron transport chain & oxidative phosphorylation

Acetyl group



ATP



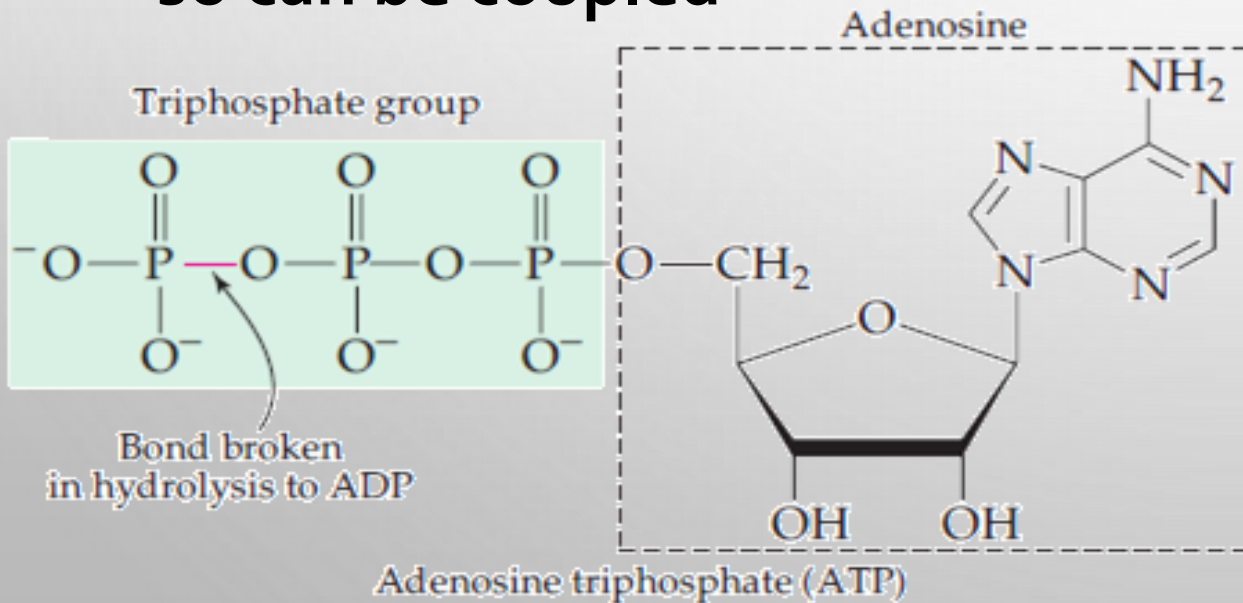
- ATP is the energy currency of the cell
- What is a high energy molecule?
- Why ATP?
- Has an intermediate energy value, so can be coupled

ATP to ADP and ADP to AMP

-7.3 kcal/mole

From AMP to adenosine and phosphate

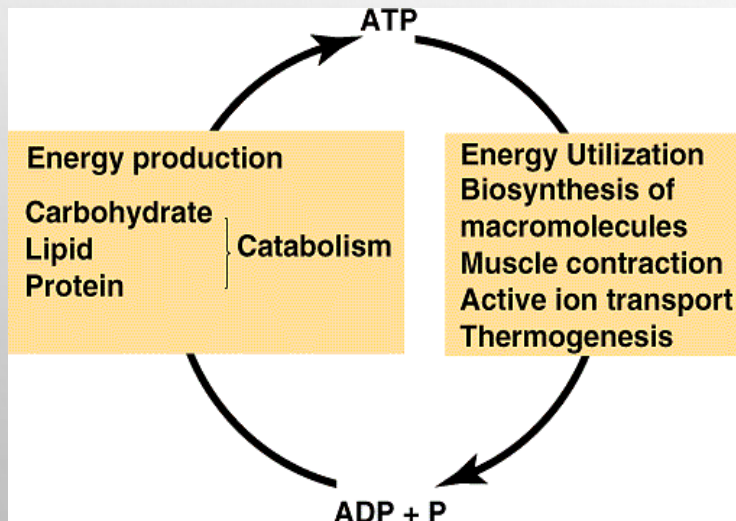
-3.4 kcal/mole



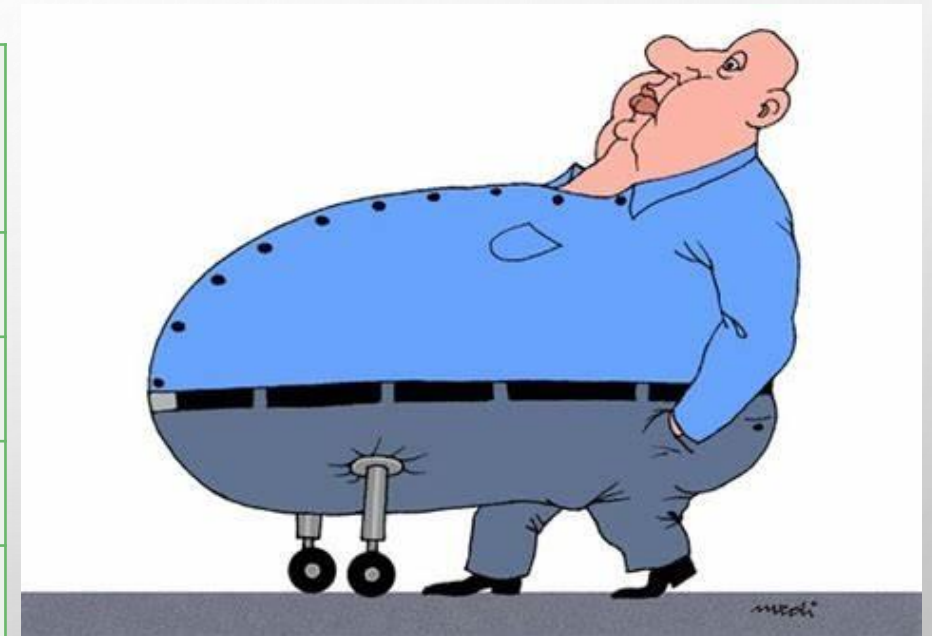
Compound + H ₂ O	Product + phosphate	ΔG°
Phosphoenol pyruvate	Pyruvate	-14.8
1,3 bisphosphoglycerate	3 phosphoglycerate	-11.8
Creatine phosphate	Creatine	- 10.3
ATP	ADP	-7.3
Glucose 1- phosphate	Glucose	-5.0
Glucose 6- phosphate	Glucose	-3.3

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



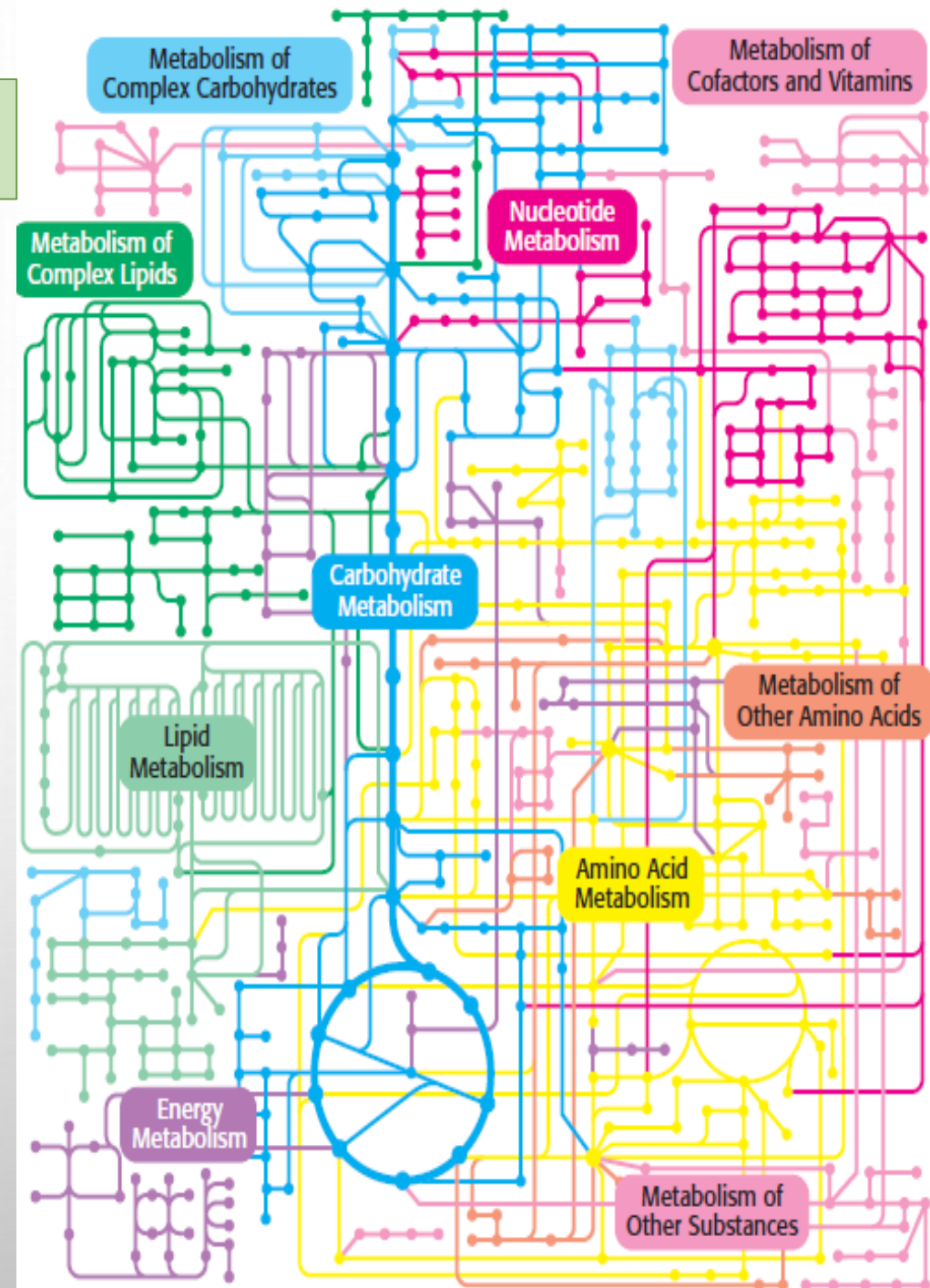
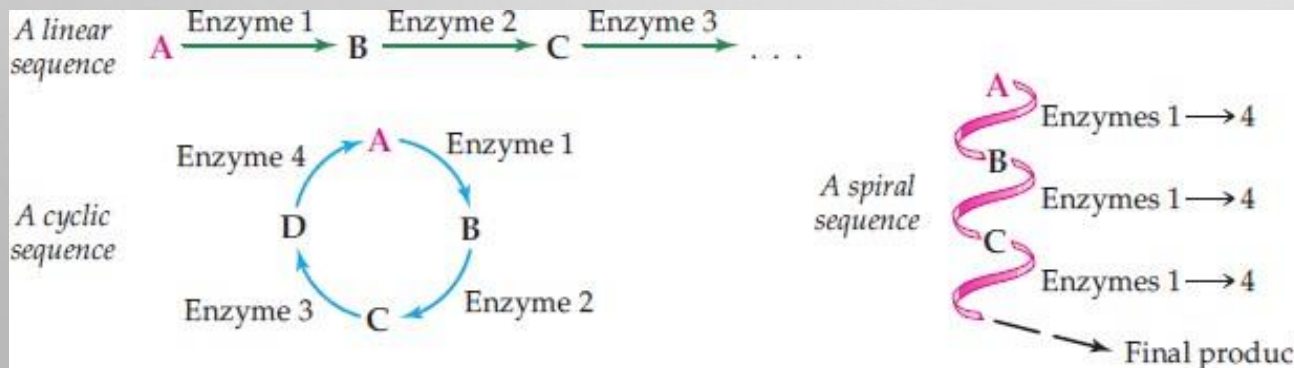
Tissue	ATP turnover (mole/day)
Brain	20.4
Heart	11.4
Kidney	17.4
Liver	21.6
Muscle	19.8
Total	90.6



$$90.6 * 551 \text{ (g/mole)} = 49,920 \text{ g ATP}$$

Biochemical metabolic pathways

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



Exergonic reactions in Biochemistry

- Complex structures → simple structures

Starch → n glucose

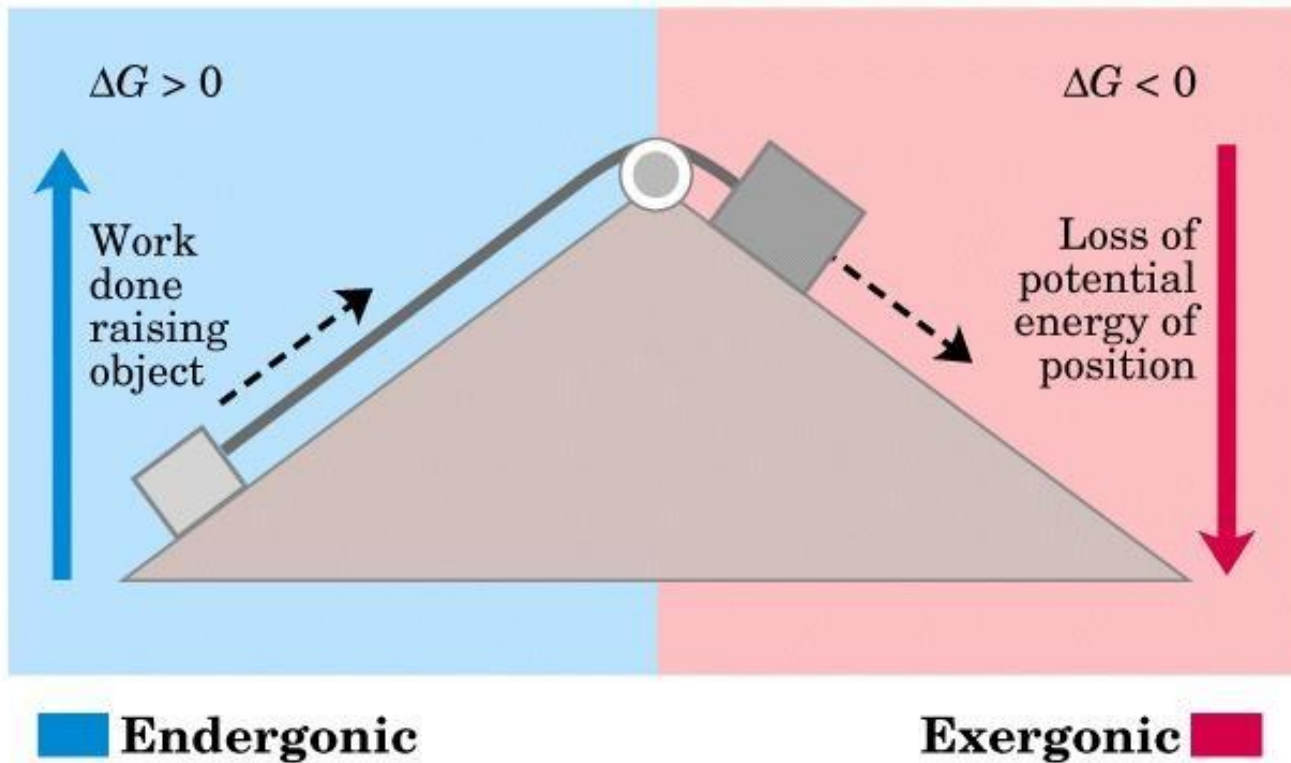
glucose + O₂ → CO₂ + H₂O

Proteins → Amino acids

- More specifically
 - ✓ Hydrolysis reactions
 - ✓ Decarboxylation reactions (release of CO₂)
pyruvate (C3) → acetyl-CoA(C2) + CO₂
 - ✓ Oxidation with O₂

Where do cells get energy for unfavorable biochemical reactions?

➤ The concept of coupling



Where do cells get energy for unfavorable biochemical reactions?

I. ΔG° Values are additive

i. Through phosphoryl transfer reactions:

✓ Step 2 (+3.3 vs. -4 kcal/mole)

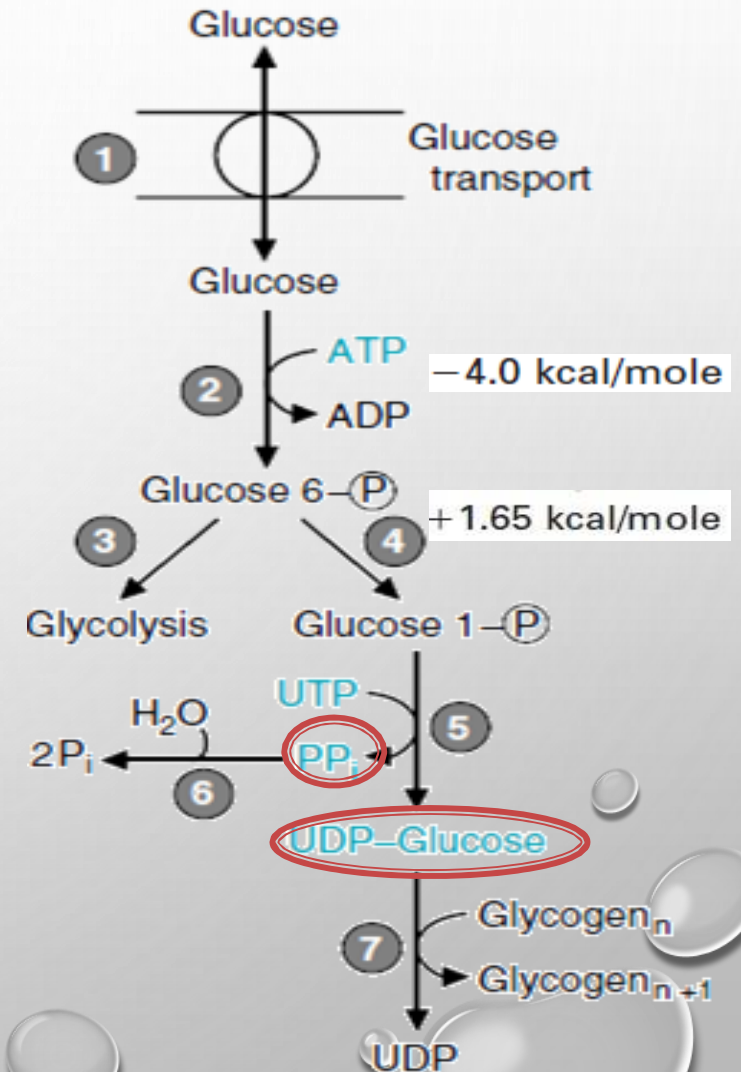
✓ Step 2 + 4 = -2.35 kcal/mole

✓ The net value for synthesis is irrelevant to the presence or absence of enzymes

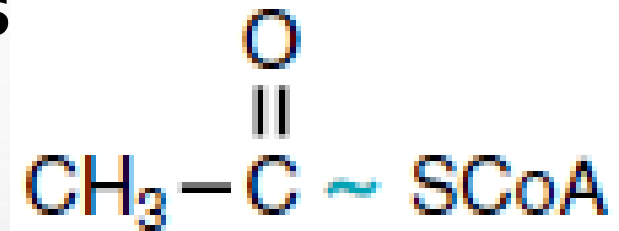
ii. Activated intermediates (step 4 is facilitated by steps 5&6)

II. ΔG Depends on Substrate and Product

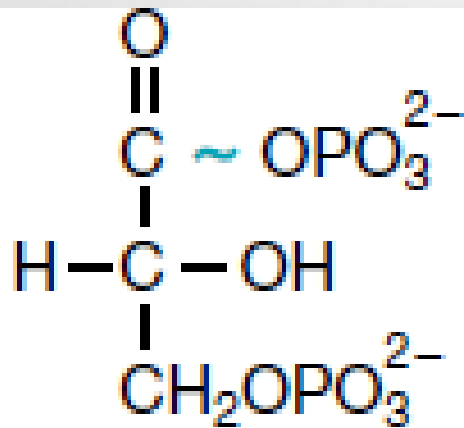
Concentration (step 4 has a ratio of 6/94; +1.65 kcal/mol, if 3/94; -0.4 kcal/mol)



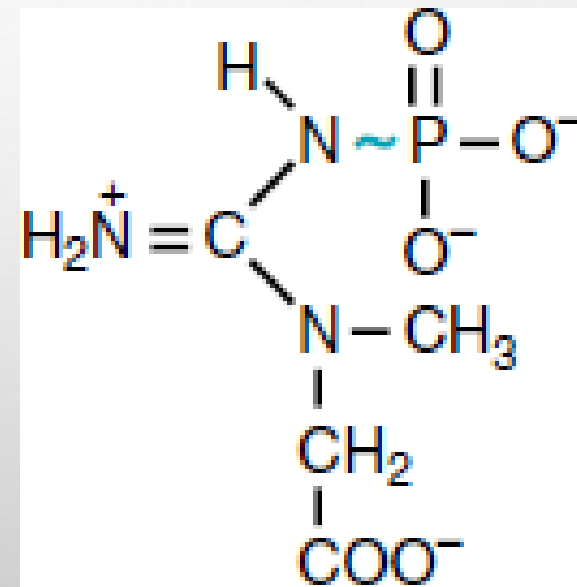
III. Activated Intermediates other than ATP; UTP is used for combining sugars, CTP in lipid synthesis, and GTP in protein synthesis



Acetyl CoA



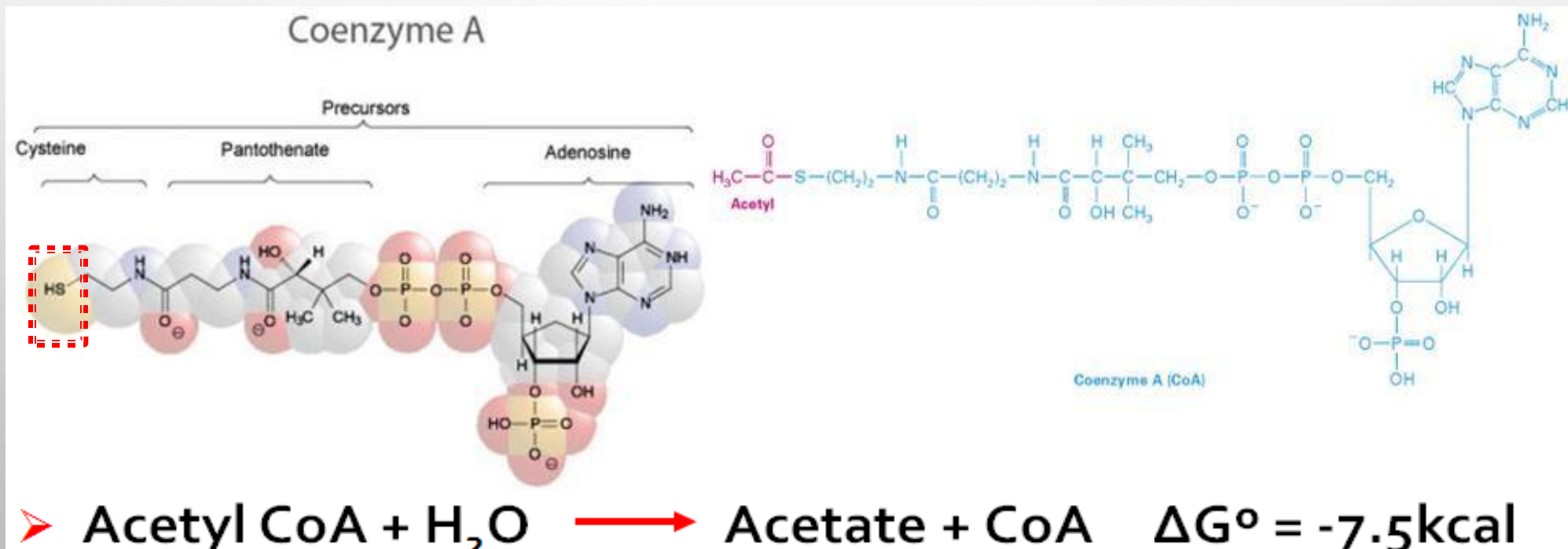
1,3-Bisphosphoglycerate



Creatine phosphate

Acetyl-CoA

- Coenzyme A is a universal carrier (donor) of Acyl groups
- Forms a thio-ester bond with carboxyl group



Thermogenesis

- Heat production is a natural consequence of “burning fuels”
- Thermogenesis refers to energy expended for generating heat (37°C) in addition to that expended for ATP production
- Shivering thermogenesis (ATP utilization): activation of exothermic reactions by responding to sudden cold with asynchronous muscle contractions
- Non-shivering thermogenesis (ATP production efficiency)
 - In the first 6 months of life
 - It is associated with brown adipose tissue



Oxidation reduction reactions (Redox)

➤ Oxidation:

- ✓ Gain of Oxygen
- ✓ Loss of Hydrogen
- ✓ Loss of electrons

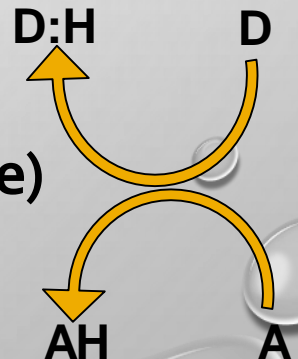
➤ Reduction:

- ✓ 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

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

➤ Oxidation and reduction must occur simultaneously

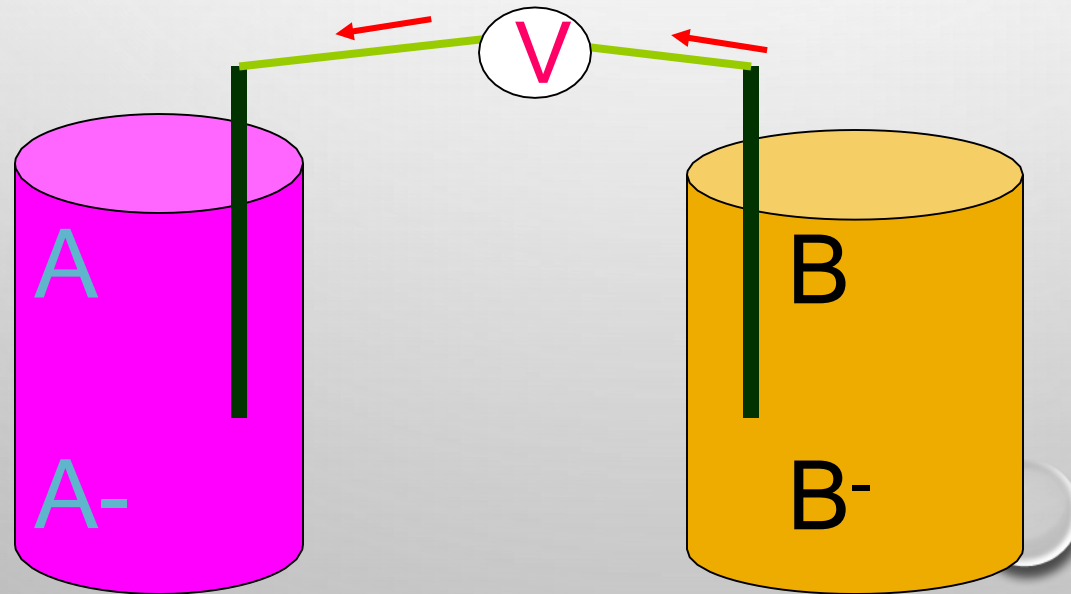


Reduction Potential and the direction of reaction

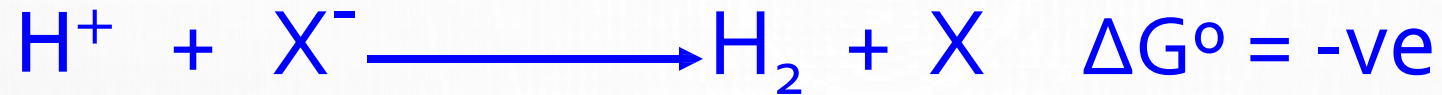


B oxidized form
B⁻ reduced form

Redox couple



Reduction Potential and the direction of reaction



X oxidized form

X⁻ reduced form

Redox couple

V

X

H⁺

H₂

X⁻ has higher tendency to loose electrons than H₂ does



Negative reduction potential

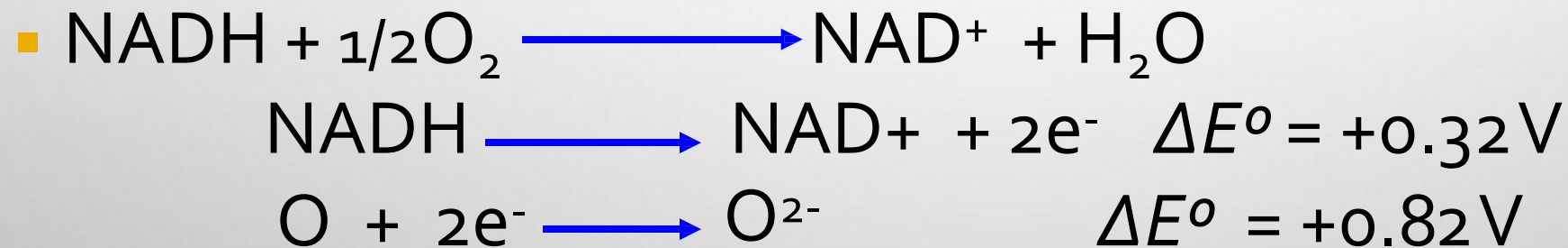
X⁻

Reduction Potential: the ability to accept electrons

Oxidized + e ⁻	→ Reduced	ΔE° (V)
Succinate	α ketoglutarate	- 0.67
Acetate	Acetaldehyde	- 0.60
NAD⁺	NADH	- 0.32
Acetaldehyde	Ethanol	- 0.20
Pyruvate	Lactate	- 0.19
Fumarate	Succinate	+ 0.03
Cytochrome ⁺³	Cytochrome ⁺²	+ 0.22
oxygen	water	+ 0.82

Calculation of ΔG° and ΔE°

- $\Delta G^\circ = - nF\Delta E^\circ$
 - $F =$ Farady constant = 23.06 kcal/Volt
 - n is the number of moles of electrons transferred in the redox reaction
- Calculate ΔG° of the following reaction



$$\Delta G^\circ = - 52.6 \text{ kcal/mol}$$

Oxidation reduction reactions (Redox)

- ΔE° = Redox difference of a system in standard condition (25C° and 1 atmosphere pressure, pH = 7)
 - Does ΔE° determine the feasibility of a reaction?
 - $\Delta G^\circ = -nf\Delta E^\circ$
- In other words; energy (work) can be derived from the transfer of electrons **Or**
- Oxidation of food can be used to synthesize ATP

Oxidation reduction reactions (Redox)

- Always involve a pair of chemicals: an electron donor and an electron acceptor (Food vs. NAD^+)
- NAD^+ vs. FAD (hydride vs H-atom, number, energy)
- NAD^+ vs. NADP^+ (fatty acid synthesis and detoxification reactions)

