

Nafith Abu Tarboush  
DDS, MSc, PhD  
natarboush@ju.edu.jo  
[www.facebook.com/natarboush](http://www.facebook.com/natarboush)

# Bioenergetics

# 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
- Whether a reaction occurs or not!
- Stability vs. energy



# The major purpose 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

# Why Do Chemical Reactions Occur?

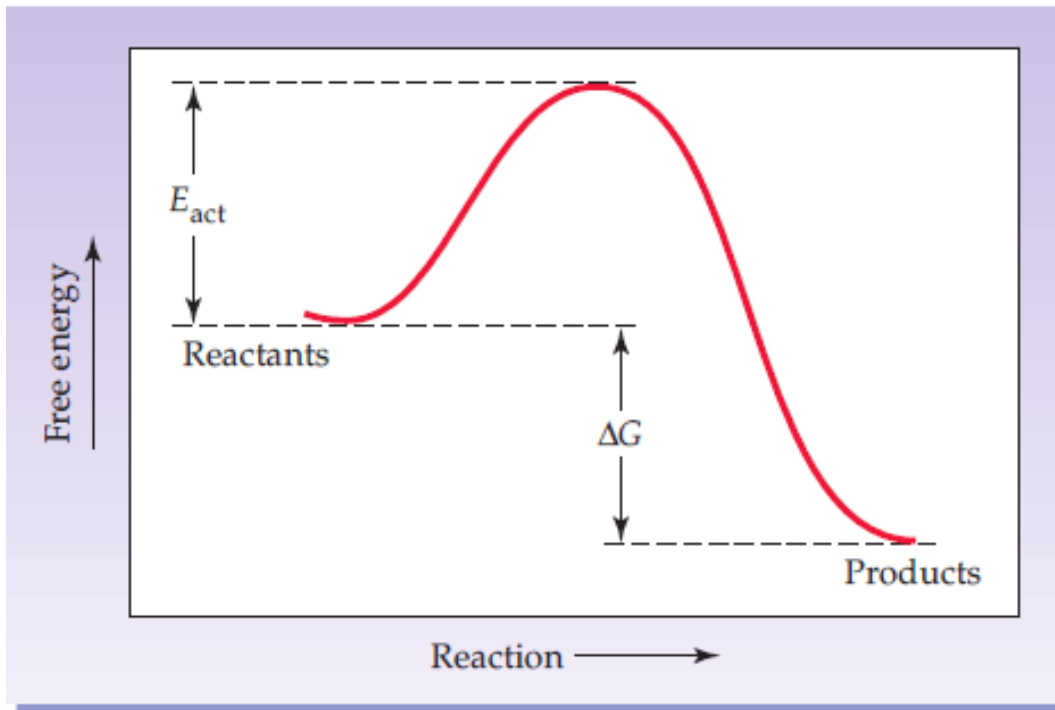
## Concept of Free Energy, Gibbs Equation

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

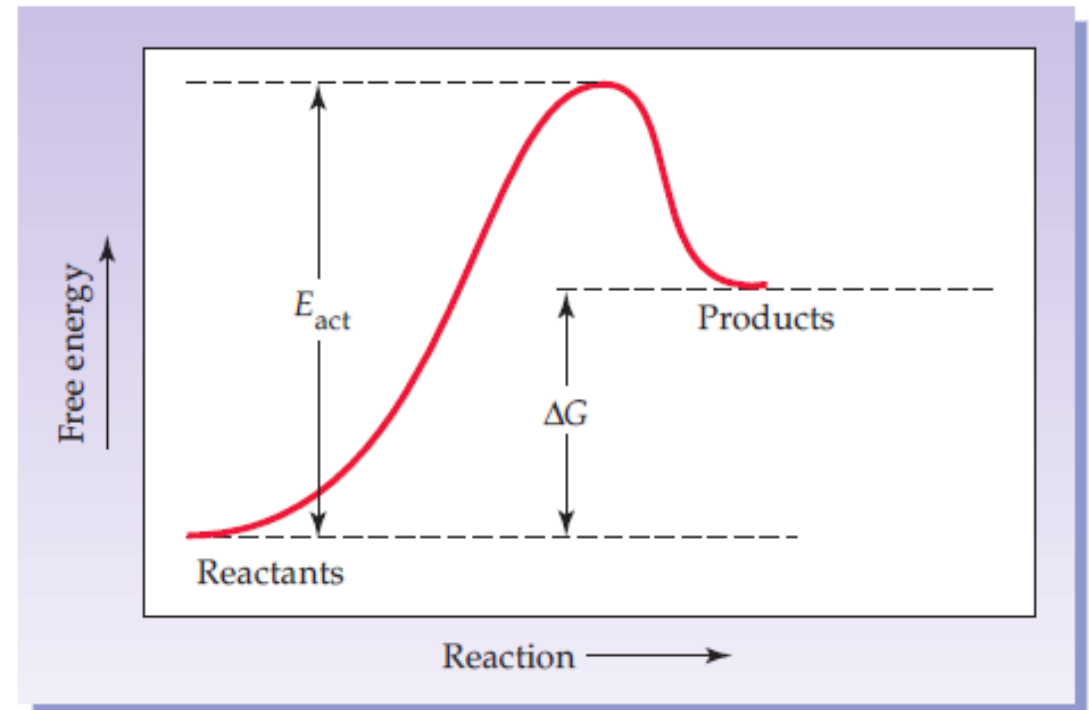
Heat of reaction      Temperature (in kelvins)      Entropy change

*Free-energy change*

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



(a) An exergonic reaction



(b) An endergonic reaction

# The different free energy terms

- $\Delta G$  = the free energy difference of a system at any condition
- $\Delta G^\circ$  = the free energy difference of a system at standard conditions (25°C & 1 atmospheric pressure, 1M concentration of reactants & products, pH = 7)
- Which one of these terms determine the feasibility the reaction?
- $\Delta G$  depends only on initial state and final state of biochemical pathways

# $\Delta G$ is a state function?!

- $\Delta G$  is not affected by the mechanism of the reaction



- $A \rightarrow B \rightarrow C$

$$\Delta G_{A \rightarrow B} = \cancel{GB} - GA$$

$$\Delta G_{B \rightarrow C} = GC - \cancel{GB}$$

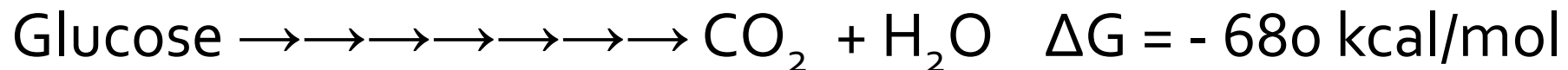
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$$GC - GA = \Delta G_{A \rightarrow C}$$

- Combustion of glucose in calorimeter



**In the cell**



# $\Delta G$ is affected by concentration



$$\Delta G = - - -$$



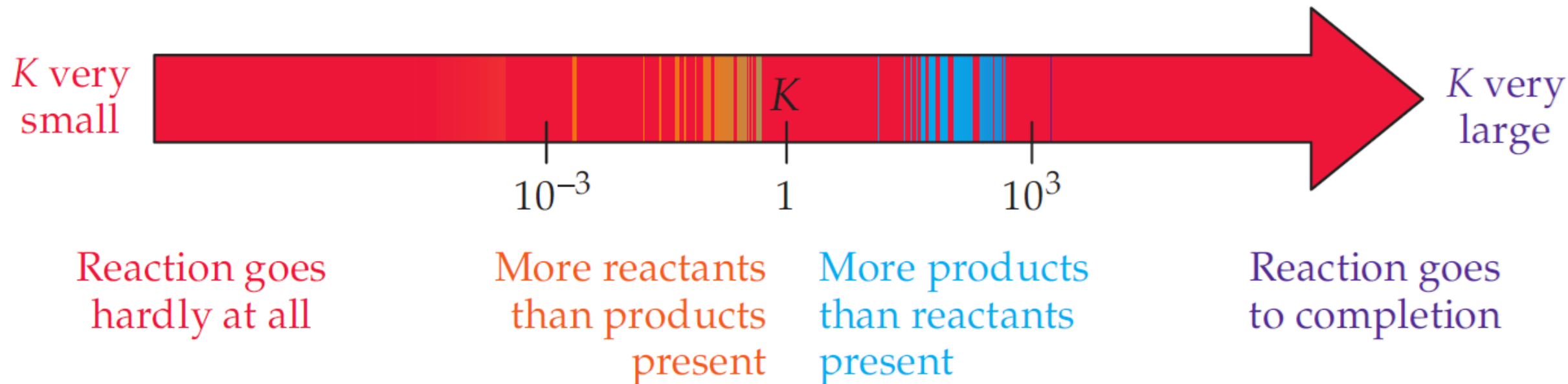
# Standard free energy change $\Delta G^\circ$

- Concentrations of reactants and products = 1 mole/L
- $\Delta G = \Delta G^\circ + RT \ln \frac{[\text{Products}]}{[\text{Reactants}]}$
- $\Delta G = \Delta G^\circ + RT \cdot 2.3 \log \frac{[\text{Products}]}{[\text{Reactants}]}$



# 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?



# Standard free energy change ( $\Delta G^\circ$ ) and equilibrium constant $K_{eq}$

$K_{eq}$  is obtained by dividing [products] by [reactants] when the reaction reaches equilibrium

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

- At equilibrium

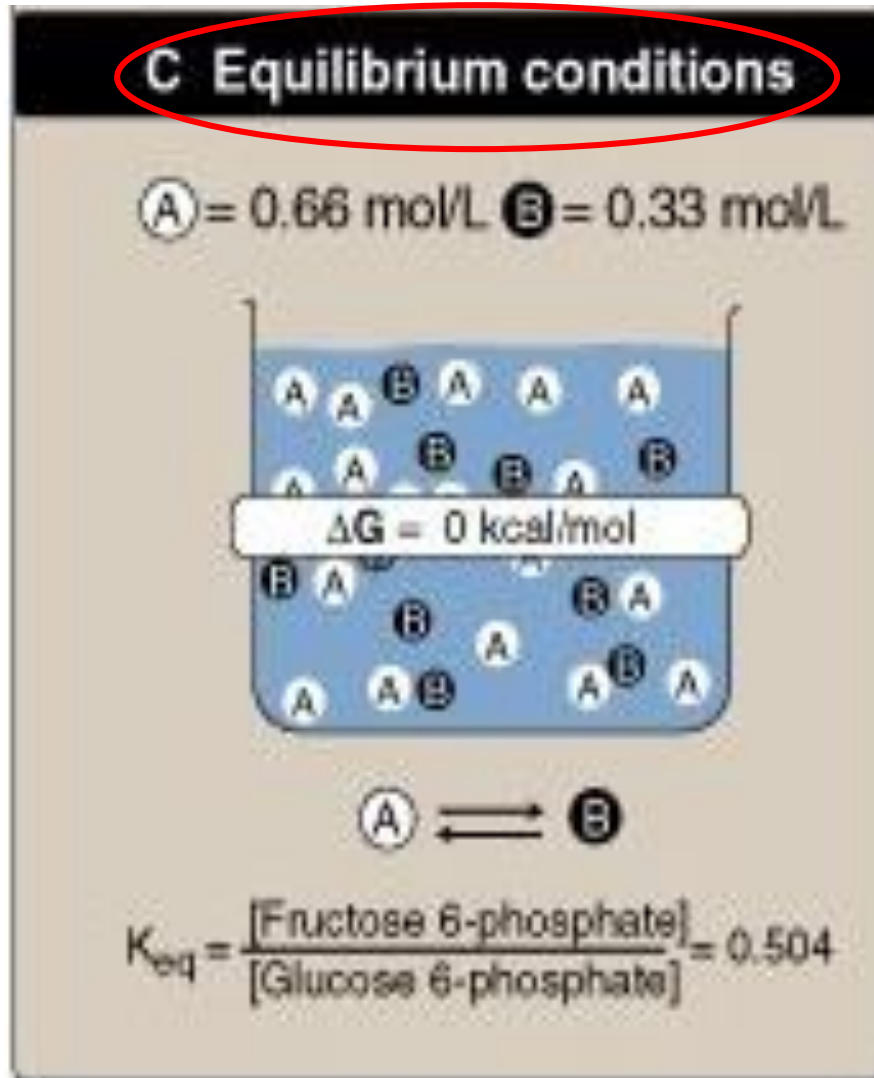
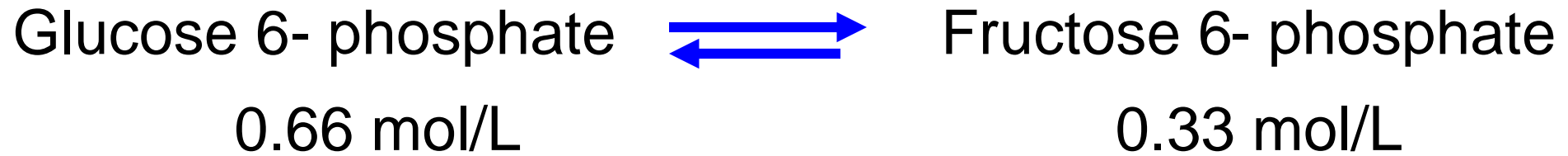
$$0 = \Delta G^\circ + RT \ln K_{eq}$$

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

- At standard conditions

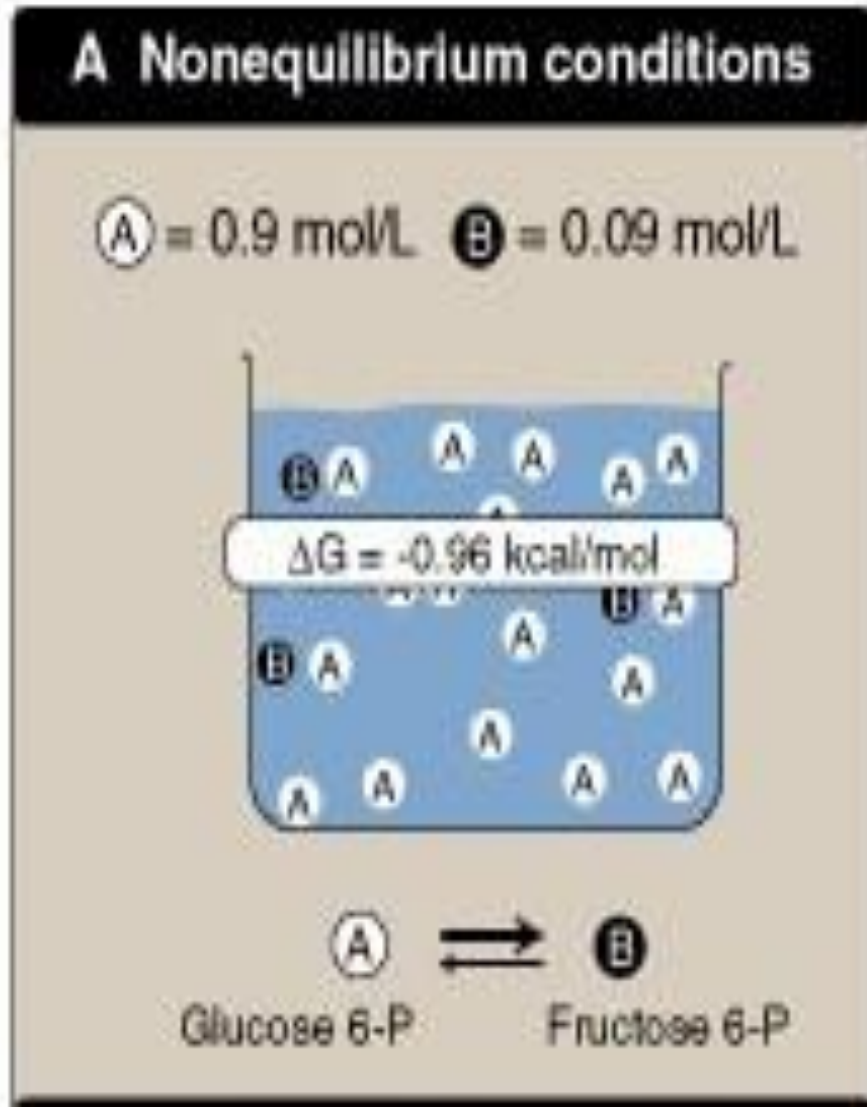
$$\Delta G = \Delta G^\circ + RT \ln 1$$

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



$$\Delta G = \Delta G^\circ + RT \ln 0.33 / 0.66$$

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

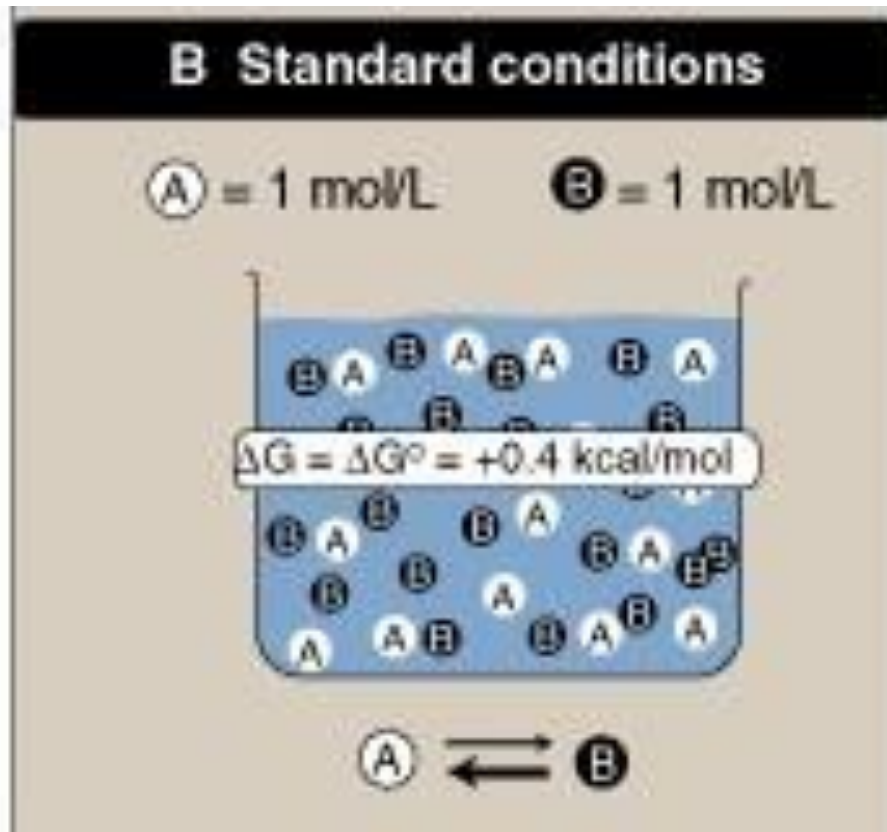


$$\Delta G^{\circ} = + 0.4 \text{ kcal/mol}$$

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

$$\Delta G = - 0.96$$

Glucose 6- phosphate  $\xrightleftharpoons{\hspace{1cm}}$  Fructose 6- phosphate  
 1 mol/L 1 mol/L



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

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

# $\Delta G$ & $K_{eq}$

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

| $K'_{eq}$  | $\Delta G^\circ$<br>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 <b>equilibrium</b>                              |
| $10^{-2}$  | + 11                       | reverses to form “reactants”                          |
| $10^{-4}$  | + 23                       | reverses to form “reactants”                          |

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

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

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

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

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

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

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

# $\Delta G^\circ$ and $K_{eq}$

|   |   |
|---|---|
|   |   |
| 1 | 0 |
|   |   |

How much change in  $\Delta G$   
compared to changes in  $K_{eq}$

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

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

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

# The Effect of Changing Conditions on Equilibria

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

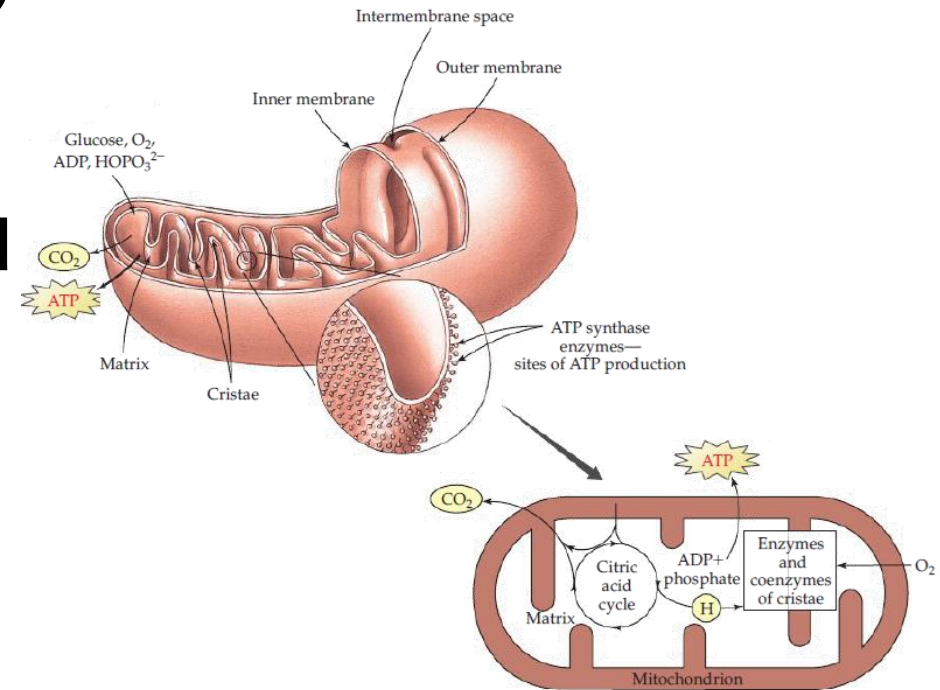
$$\Delta G^{\circ'} = -RT \ln K'_{eq}$$

- 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



# 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

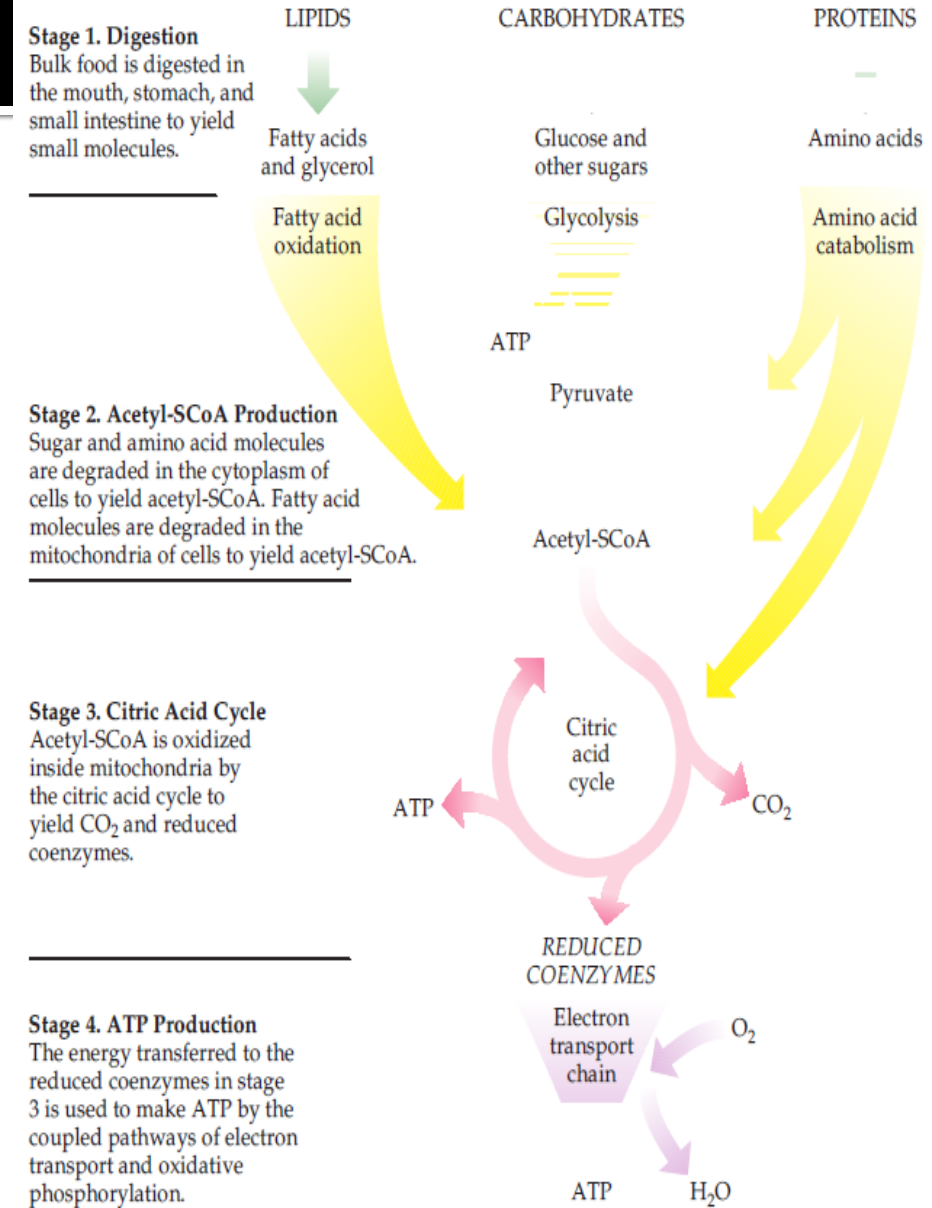
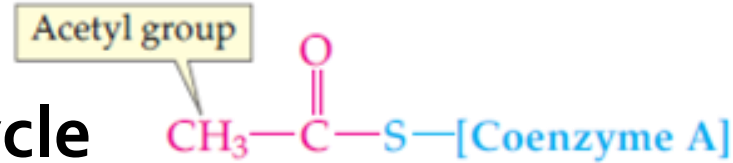
## ➤ Stage 1 (Digestion):

- ✓ 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)

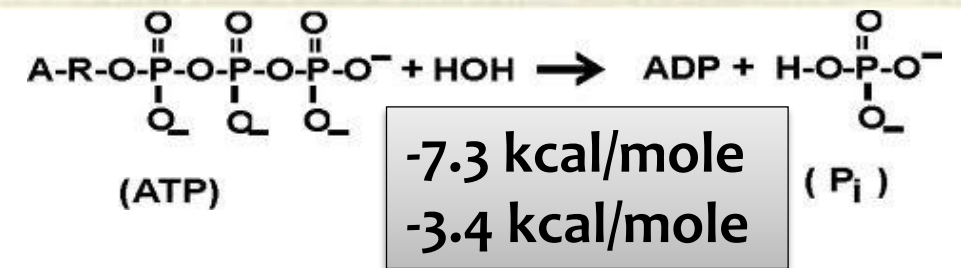
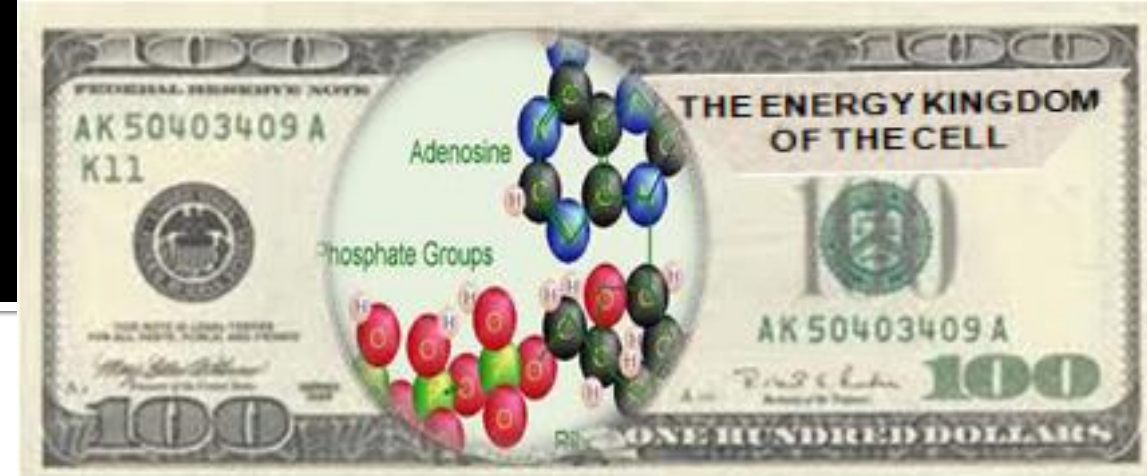
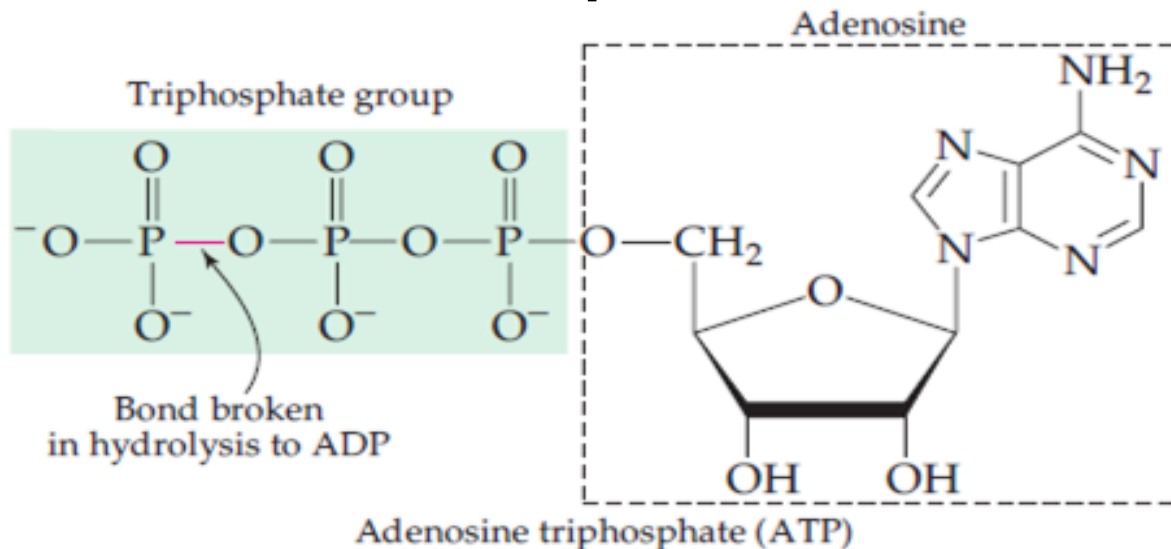
## ➤ Stage 3: citric acid cycle

## ➤ Stage 4: electron transfer chain & oxidative phosphorylation



# ATP

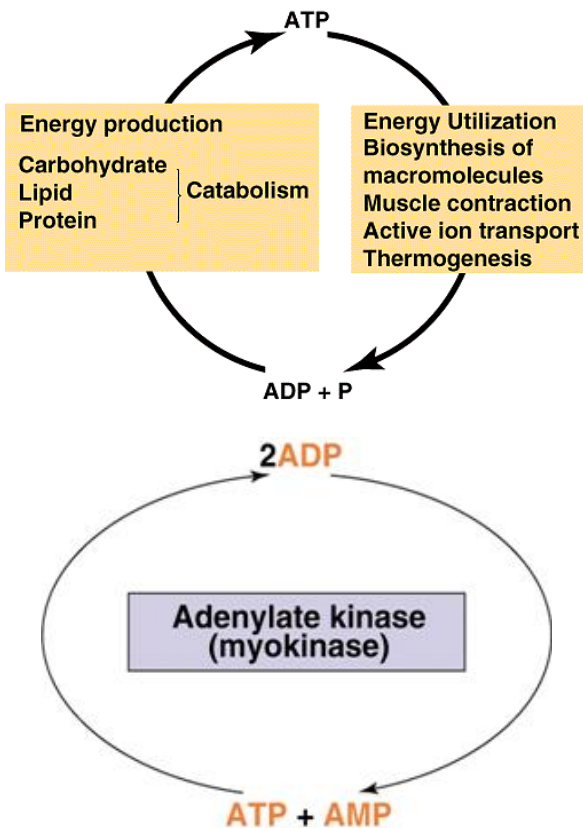
- ATP is the energy currency of the cell
- What is a high energy molecule?
- Why ATP?
  - Has an intermediate energy value, so can be coupled



| Compound + H <sub>2</sub> O | Product + phosphate | ΔG°         |
|-----------------------------|---------------------|-------------|
| Phosphoenol pyruvate        | Pyruvate            | -14.8       |
| 1,3 bisphosphoglycerate     | 3 phosphoglycerate  | -11.8       |
| Creatine phosphate          | Creatine            | -10.3       |
| <b>ATP</b>                  | <b>ADP</b>          | <b>-7.3</b> |
| 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

*A linear sequence*

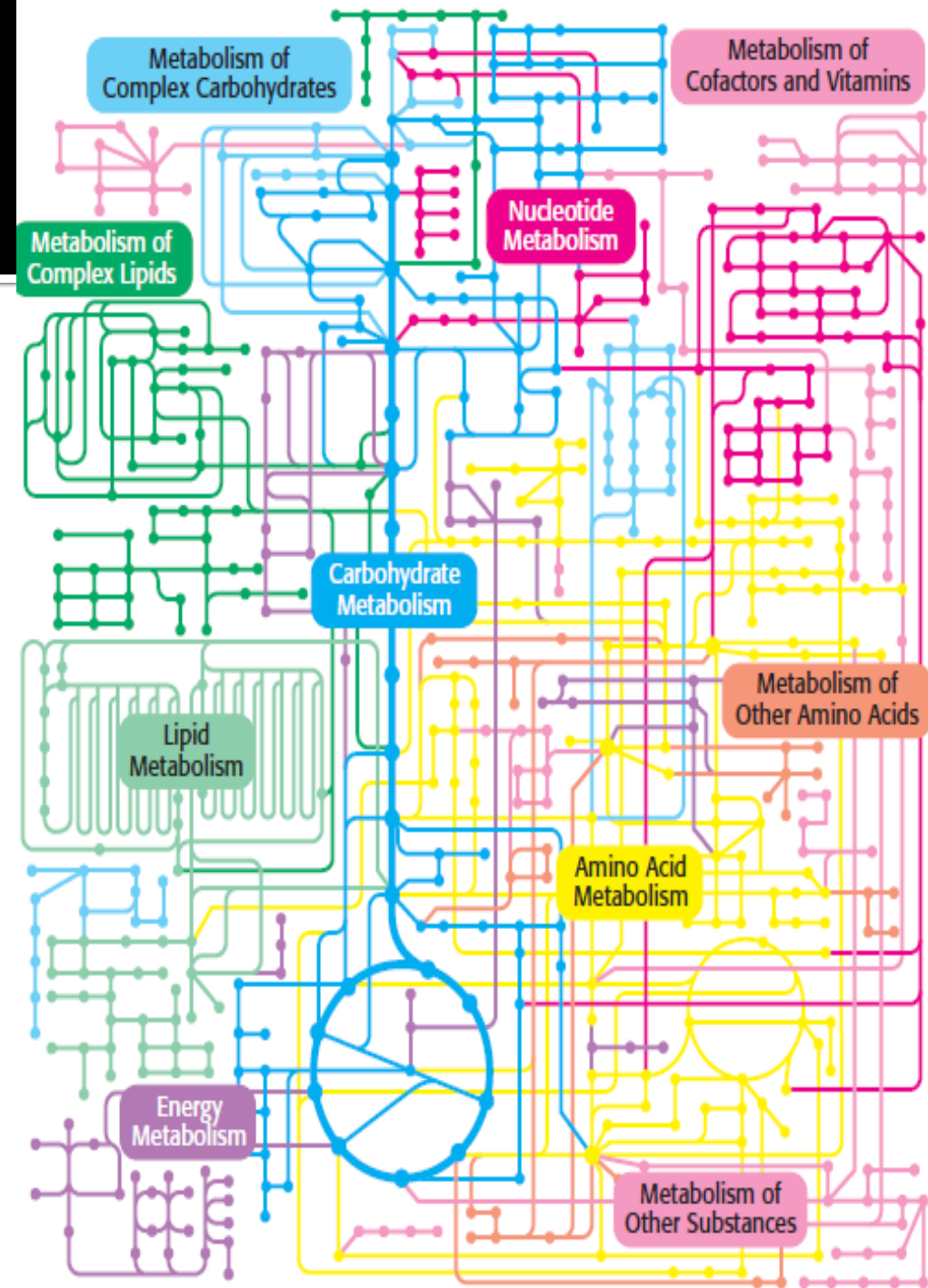
A  $\xrightarrow{\text{Enzyme 1}}$  B  $\xrightarrow{\text{Enzyme 2}}$  C  $\xrightarrow{\text{Enzyme 3}}$  ...

*A cyclic sequence*

Enzyme 4  $\xrightarrow{\text{A}}$  Enzyme 1  $\xrightarrow{\text{B}}$  Enzyme 2  $\xrightarrow{\text{C}}$  Enzyme 3  $\xrightarrow{\text{D}}$  Enzyme 4

*A spiral sequence*

A  $\xrightarrow{\text{Enzymes 1} \rightarrow 4}$  B  $\xrightarrow{\text{Enzymes 1} \rightarrow 4}$  C  $\xrightarrow{\text{Enzymes 1} \rightarrow 4}$  ...  
Final product



# Exergonic reactions in Biochemistry

- Complex structures → simple structures

Proteins → amino acids

Starch → n glucose

glucose + O<sub>2</sub> → CO<sub>2</sub> + H<sub>2</sub>O

- More specifically

- ✓ Hydrolysis reactions

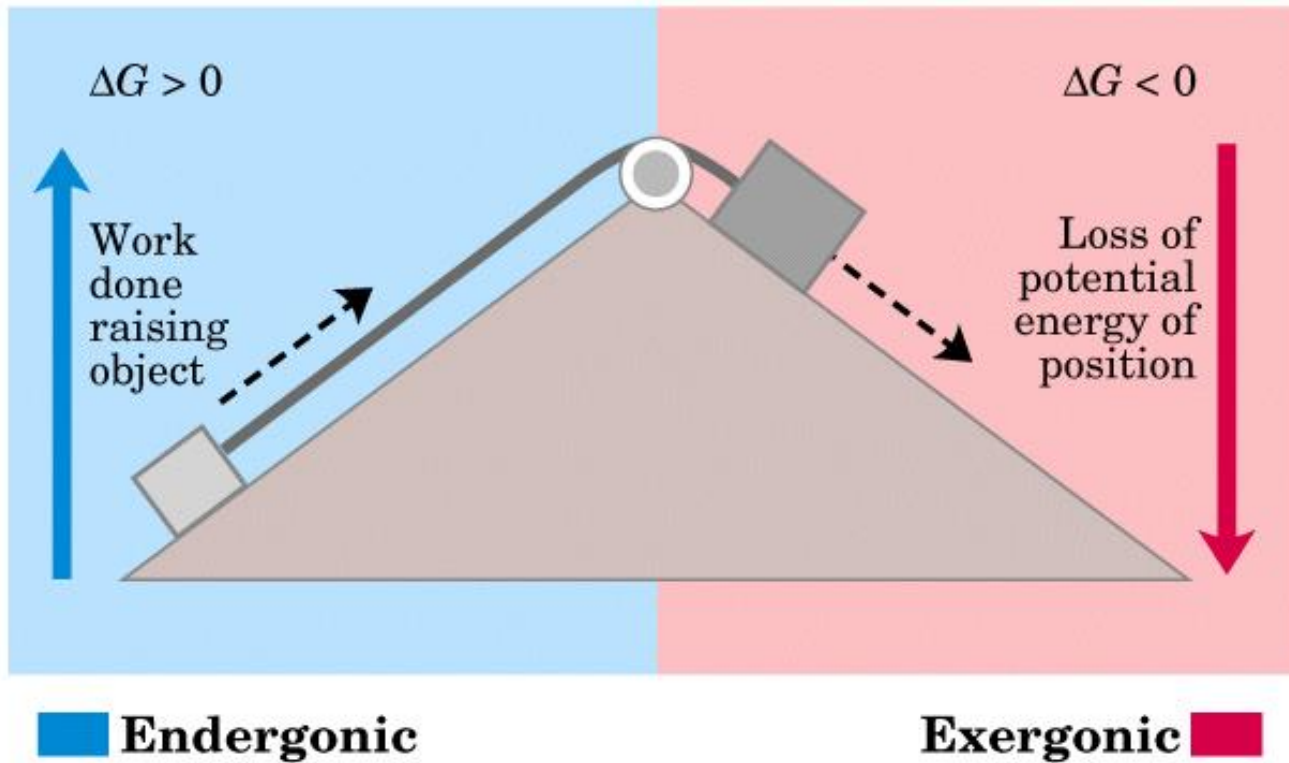
- ✓ Decarboxylation reactions (release of CO<sub>2</sub>)

pyruvate (C3) → acetyl-CoA(C2) + CO<sub>2</sub>

- ✓ Oxidation with O<sub>2</sub>

# 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. $\Delta G^\circ$ Values are additive

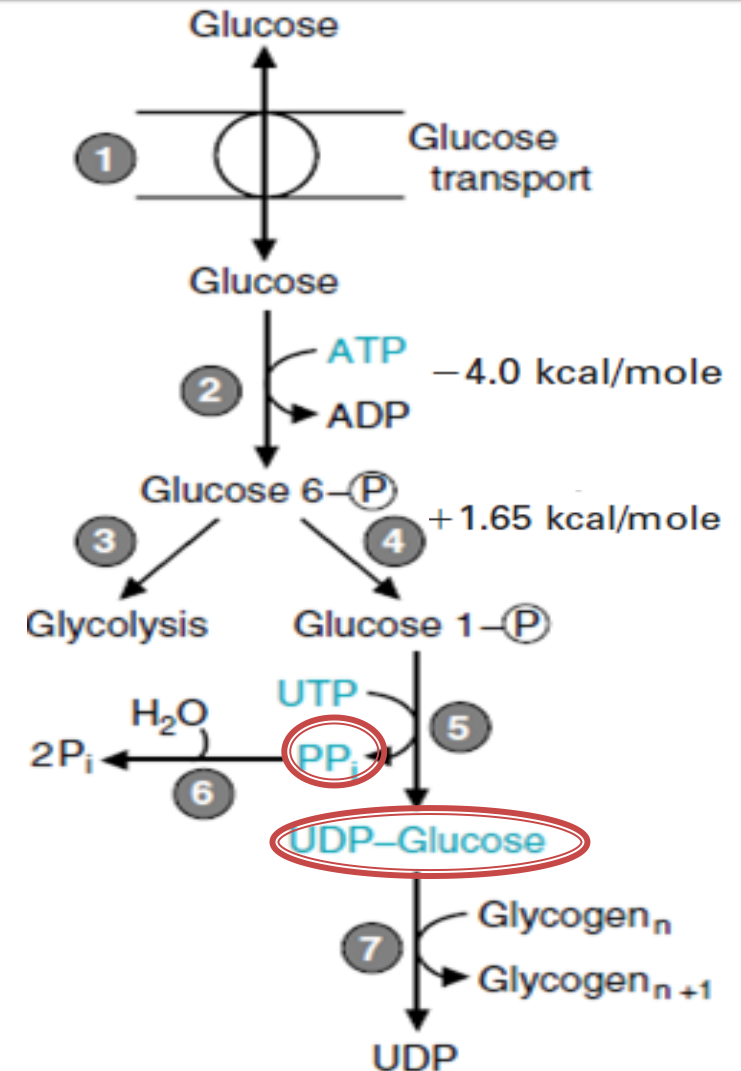
### i. Through phosphoryl transfer reactions:

- ✓ 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. $\Delta G$ Depends on Substrate and Product

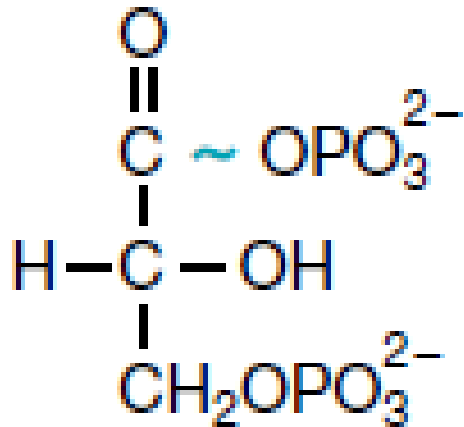
**Concentration** (step 4 has a ratio of 6/94; +1.65 kcal/mol, if 3/94; -0.4 kcal/mol)



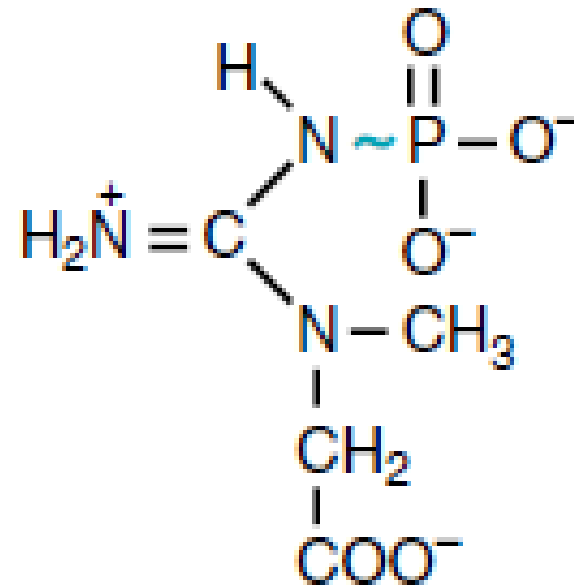


# How do our cells get energy for unfavorable biochemical work?

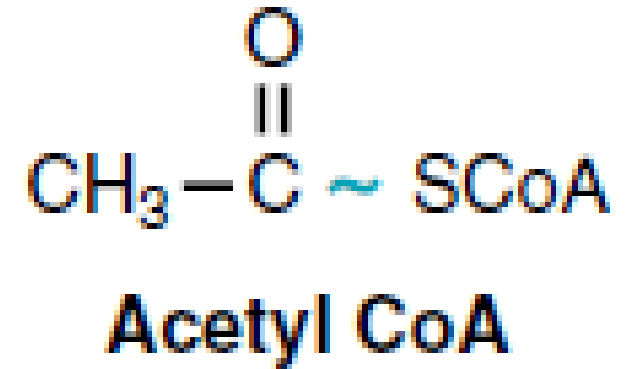
- III. Activated Intermediates other than ATP; UTP is used for combining sugars, CTP in lipid synthesis, and GTP in protein synthesis



1,3-Bisphosphoglycerate

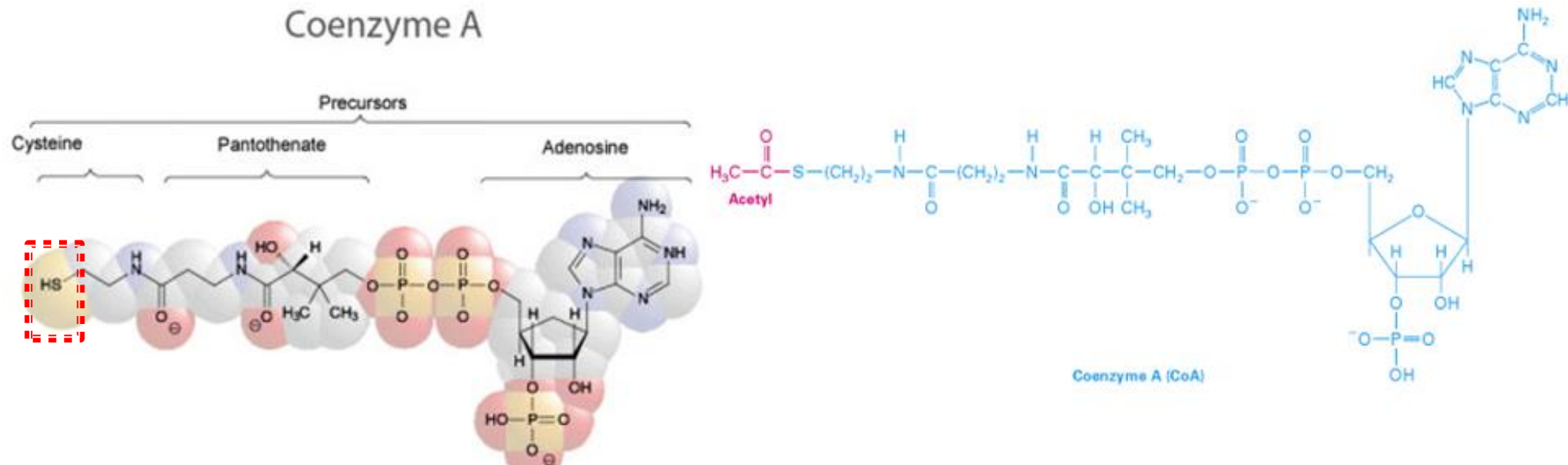


Creatine phosphate



# The acetyl CoA as an example

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



- $\text{Acetyl CoA} + \text{H}_2\text{O} \longrightarrow \text{Acetate} + \text{CoA} \quad \Delta G^\circ = -7.5 \text{ kcal}$
- $\text{Acetylcholine} + \text{H}_2\text{O} \longrightarrow \text{Acetate} + \text{Choline} \quad \Delta G^\circ = -3 \text{ kcal}$

# THERMOGENESIS

- The first law of thermodynamics
- Heat production is a natural consequence of “burning fuels”
- Thermogenesis refers to energy expended for generating heat ( $37^{\circ}\text{C}$ ) in addition to that expended for ATP production
- Shivering thermogenesis (ATP utilization): responding to sudden cold with asynchronous muscle contractions
- Non-shivering thermogenesis (ATP production efficiency)



# Oxidation-Reduction reactions (Redox)

## ➤ Oxidation:

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

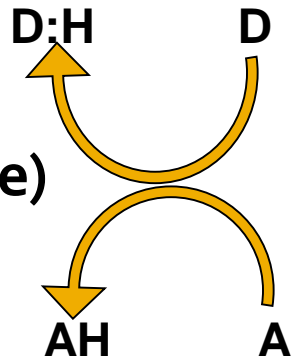
## ➤ Reduction:

- ✓ 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



Type of reaction

What determine the direction of the reaction?



Type of reaction

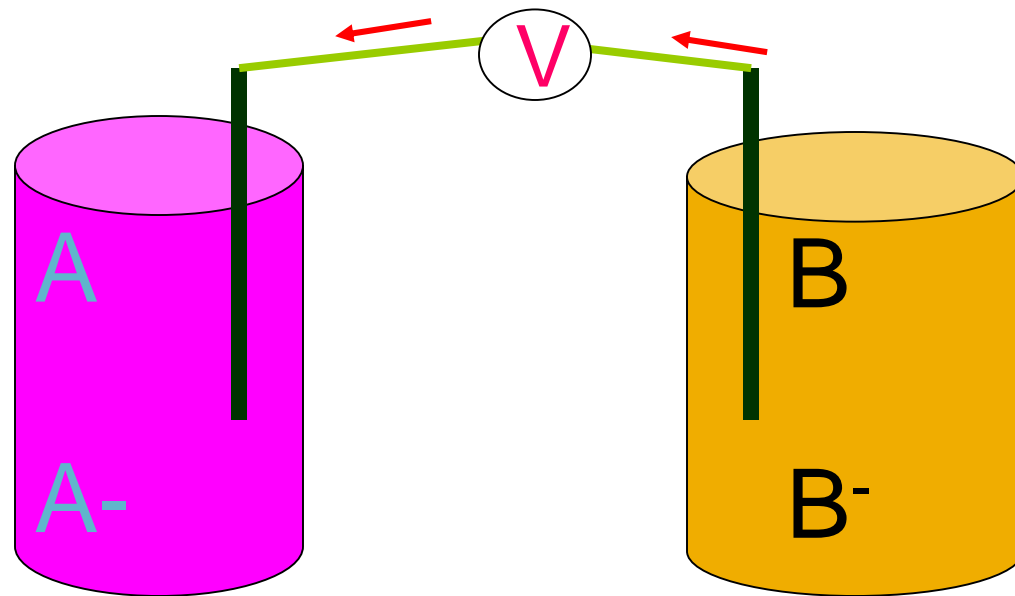
What determine the direction of the reaction?

# Reduction potential and direction of the reaction

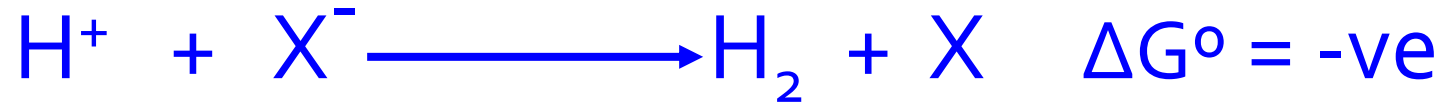


B oxidized form  
B<sup>-</sup> reduced form

Redox couple



# Reduction potential and direction of the reaction



X oxidized form

X<sup>-</sup> reduced form

Redox couple

X<sup>-</sup> has higher tendency to loose electrons than H<sub>2</sub> does



Negative reduction potential

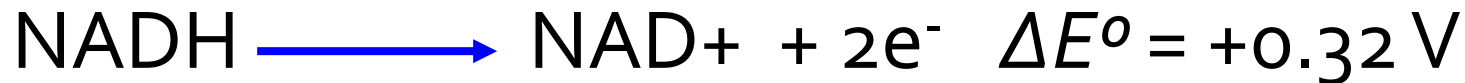
# Reduction potential: Ability to accept electrons

| Oxidized + e <sup>-</sup> | → Reduced                | $\Delta E^{\circ}$ (V) |
|---------------------------|--------------------------|------------------------|
| Succinate                 | $\alpha$ ketoglutarate   | - 0.67                 |
| Acetate                   | Acetaldehyde             | - 0.60                 |
| <b>NAD<sup>+</sup></b>    | <b>NADH</b>              | <b>- 0.32</b>          |
| Acetaldehyde              | Ethanol                  | - 0.20                 |
| Pyruvate                  | Lactate                  | - 0.19                 |
| Fumarate                  | Succinate                | + 0.03                 |
| Cytochrome <sup>+3</sup>  | Cytochrome <sup>+2</sup> | + 0.22                 |
| <b>oxygen</b>             | <b>water</b>             | <b>+ 0.82</b>          |



# Calculation of $\Delta G^\circ$ from $\Delta E^\circ$

- $\Delta G^\circ = - n f \Delta E^\circ$ 
  - $F$  = Farady constant = 23.06 kcal/Volt
- Calculate  $\Delta G^\circ$  of the following reaction



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

# Oxidation-Reduction reactions (Redox)

- $\Delta E = E_A - E_D$
- $\Delta E$  = Redox difference of a system in any condition
- $\Delta E^\circ$  = Redox difference of a system in standard condition (25C° and 1 atmosphere pressure, pH = 7)
  - Does  $\Delta E$  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.  $\text{NAD}^+$ )
- $\text{NAD}^+$  vs. FAD
- $\text{NAD}^+$  vs.  $\text{NADP}^+$  (fatty acid synthesis and detoxification reactions)

