Physical Principles in Biology
Biology 3550
Fall 2018

Lecture 31

Chemical Energy and Metabolism

and

Introduction to Water

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Chemical Energy

- What does “chemical energy” mean?

http://www.caffeineinformer.com http://www.philosophersguild.com

An Energetic Chemical Reaction, Under Some Conditions

$$C_6H_{12}O_6 + 6O_2 \rightleftharpoons 6CO_2 + 6H_2O$$

- Oxidation of glucose (or other hexose) by molecular oxygen.
- Free energy change depends on concentrations.
- Standard state conditions: 1 M glucose, 1 atm O_2 and CO_2
  - $\Delta G^\circ = -2.7\times10^6$ J/mol $= -2,700$ kJ/mol
  - Equilibrium constant:

$$K_{eq} = \frac{[CO_2]_{eq}{}^6}{[C_6H_{12}O_6]_{eq}[O_2]_{eq}{}^6} = e^{-\Delta G^\circ/(RT)} \approx 10^{473}\ \mathrm{M}^{-1}$$

    (Water is ignored in free energy change calculation)

  - Extremely favorable!
- But, this assumes 1 atm O_2 and CO_2.
- Reaction only became favorable about 2.5 billion years ago, when oxygen became abundant on earth.

Nutritional Calories

- Measured as the heat for complete combustions with excess O_2 at constant volume (no work).

  "bomb calorimeter"

- Since, $w = 0$, $q = \Delta E$
- For glucose, $\Delta E = -4\,\text{kcal/g} = -175\,\text{kJ/mol}$, vs $\Delta G^\circ = -2,700\,\text{kJ/mol}$.
- Why are these numbers so different?

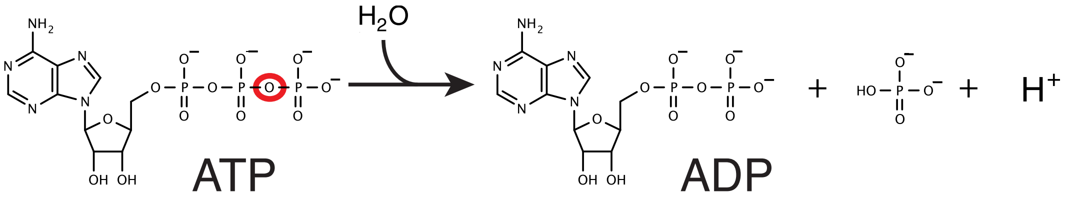
  $$\Delta G = \Delta H - T\Delta S$$

  $$C_6H_{12}O_6 + 6O_2 \rightleftharpoons 6CO_2 + 6H_2O$$

  There is a large increase in entropy, 7 molecules are converted to 12.

- Nutritionists estimate the amount of work required to offset the metabolism of a given number of nutritional calories.

Another “High-energy” Reaction



- $\Delta G^\circ = -30\,\mathrm{kJ/mol}$
- ATP serves as an “energy currency” in metabolism.
- Is there a “high-energy bond”?

Clicker Question #1

What is the equilibrium constant for the reaction?

$$\text{ATP} \rightleftharpoons \text{ADP} + \text{P}_\text{i} \qquad \Delta G^\circ = -30\,\text{kJ/mol}$$

A) $\approx 10^{-5}$ M

B) $\approx 10^{-3}$ M

C) ≈ 10 M

D) $\approx 10^{3}$ M

E) $\approx 10^{5}$ M

$$R = 8.314\,\text{J/(K}\cdot\text{mol)} \qquad T = 298\,\text{K}$$

Calculation of Equilibrium Constant from $\Delta G°$

$$\Delta G° = -30\,\text{kJ/mol} \qquad R = 8.314\,\text{J/(K} \cdot \text{mol)} \qquad T = 298\,\text{K}$$

$$\Delta G° = -RT \ln K_{\text{eq}}$$

$$\ln K_{\text{eq}} = -\Delta G°/(RT)$$

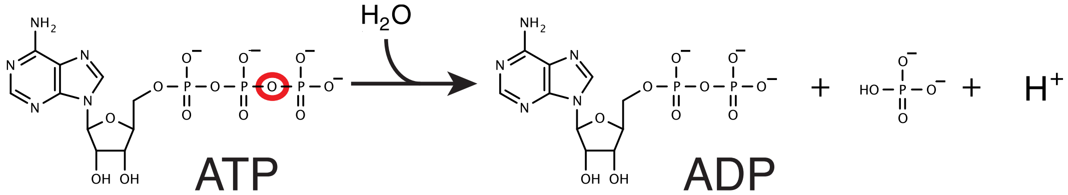
$$K_{\text{eq}} = e^{-\Delta G°/(RT)}$$

$$-\Delta G°/(RT) = 30\,\text{kJ/mol}/\left(8.314\,\text{J/(K} \cdot \text{mol)} \cdot 298\,\text{K}\right)$$

$$= 30{\times}10^3\ \text{J/mol}/2.48{\times}10^3\ \text{J/mol} = 12$$

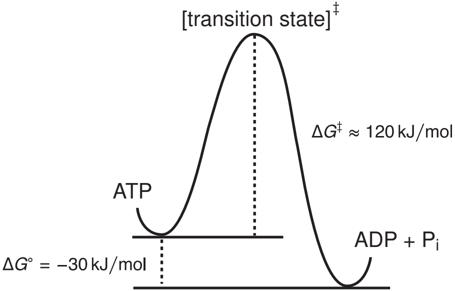
$$K_{\text{eq}} = e^{12} = 1.8{\times}10^5$$

ATP Hydrolysis



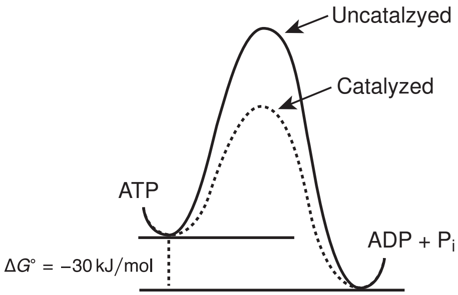
- $\Delta G^{\circ} = -30\,\mathrm{kJ/mol}$
- Why is the reaction so favorable?
  - High density of negative phosphate charges is reduced.
  - More resonance stabilization in ADP and P_i.
  - More favorable interaction with water by ADP and P_i.

Kinetics of ATP Hydrolysis



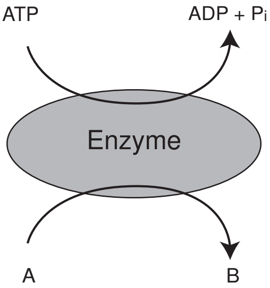
- Half-time is ≈ 20 days at neutral pH and 60°C.
- Transition state is a high energy state with equal probability of breaking down in either direction.
- Reaction rate is proportional to probability of forming the transition state.
- See the lobby of the Henry Eyring Building!

Catalysis of ATP Hydrolysis



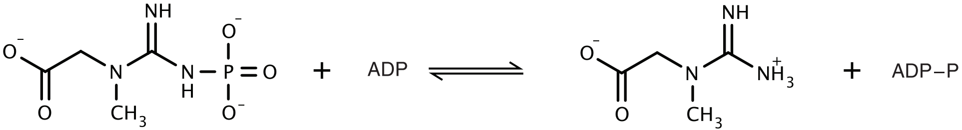
- Enzymes catalyze chemical reactions by lowering transition-state energy.
- Enzymes create micro-environments that favor forming the transition state.
- Simply catalyzing ATP hydrolysis is not useful!

Enzymatic Coupling



- Enzyme mechanistically couples reactions.
- $ATP \longrightarrow ADP + P_i$ can't occur without $A \longrightarrow B$
- $A \longrightarrow B$ can't occur without $ATP \longrightarrow ADP + P_i$
- Coupled "reaction" can be physical motion or transport across membranes.

Enzymatic Coupling: Creatine Kinase



Creatine phosphate (CP)

Creatine (C)

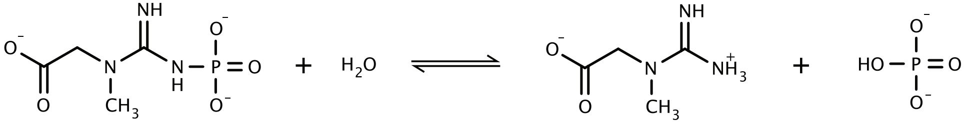
- Coupled reactions

$$ADP + P_i \rightleftharpoons ATP$$
$$CP \rightleftharpoons C + P_i$$

$$ADP + CP \rightleftharpoons ATP + C$$

Enzymatic Coupling: Creatine Kinase

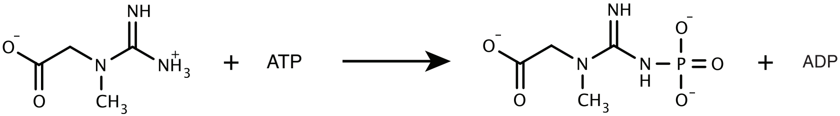
- Hydrolysis of creatine phosphate:

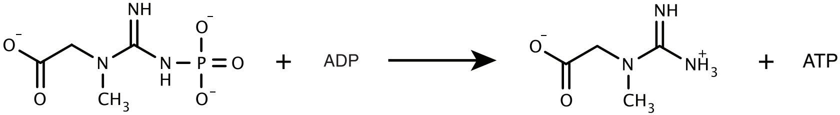


$\Delta G^\circ = -43\,\mathrm{kJ/mol}$; more favorable than ATP hydrolysis.

Clicker Question #2

In which direction is the reaction favorable under standard-state conditions?

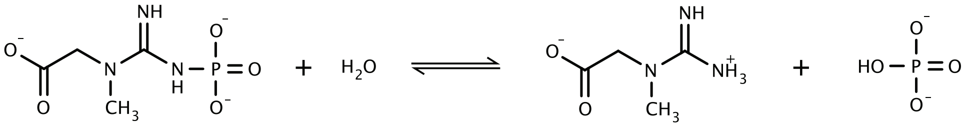
A) 

B) 

C) Neither direction is more favorable than the other.

Enzymatic Coupling: Creatine Kinase

- Hydrolysis of creatine phosphate:



$\Delta G^\circ = -43\,\mathrm{kJ/mol}$; more favorable than ATP hydrolysis.

- Coupled reactions

$$
\begin{aligned}
\mathrm{ADP} + \mathrm{P_i} &\rightleftharpoons \mathrm{ATP} & \Delta G^\circ &= 30\,\mathrm{kJ/mol} \\
\mathrm{CP} &\rightleftharpoons \mathrm{C} + \mathrm{P_i} & \Delta G^\circ &= -43\,\mathrm{kJ/mol}
\end{aligned}
$$

$$\mathrm{ADP} + \mathrm{CP} \rightleftharpoons \mathrm{ATP} + \mathrm{C} \qquad \Delta G^\circ = -13\,\mathrm{kJ/mol}$$

Phosphorylation of ADP by creatine phosphate is favored.

(at standard-state concentrations!)

Creatine Kinase in Muscle Cells

$$\mathrm{ADP} + \mathrm{CP} \rightleftharpoons \mathrm{ATP} + \mathrm{C} \qquad \Delta G^\circ = -13\,\mathrm{kJ/mol}$$

- Typical concentrations in resting muscle cells:

  4 mM ATP
  0.013 mM ADP
  25 mM creatine phosphate
  13 mM creatine

- Calculate ΔG for these concentrations:

$$\Delta G = \Delta G^\circ + RT \ln \frac{[\mathrm{ATP}][\mathrm{C}]}{[\mathrm{ADP}][\mathrm{CP}]}$$

$$= -13\,\mathrm{kJ/mol} + RT \ln \frac{4\,\mathrm{mM} \cdot 13\,\mathrm{mM}}{0.013\,\mathrm{mM} \cdot 25\,\mathrm{mM}}$$

$$\approx 0$$

- Because enzyme keeps reaction at equilibrium!

Creatine Kinase in Muscle Cells

$$\text{ADP} + \text{CP} \rightleftharpoons \text{ATP} + \text{C} \qquad \Delta G^\circ = -13\,\text{kJ/mol}$$

- If 1 mM ATP is converted to ADP:

  4 mM ATP → 3 mM ATP
  0.013 mM ADP → 1 mM ADP
  25 mM creatine phosphate
  13 mM creatine

- Calculate ΔG for these concentrations:

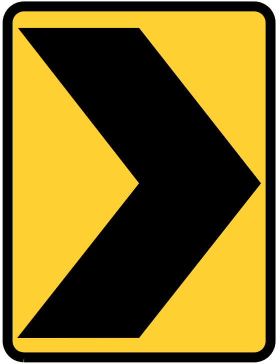
$$\Delta G = \Delta G^\circ + RT \ln \frac{[\text{ATP}][\text{C}]}{[\text{ADP}][\text{CP}]}$$

$$= -13\,\text{kJ/mol} + RT \ln \frac{3\,\text{mM} \cdot 13\,\text{mM}}{1\,\text{mM} \cdot 25\,\text{mM}}$$

$$\approx -12\,\text{kJ/mol}$$

- Creatine phosphate provides emergency reserve of free energy.

Warning!



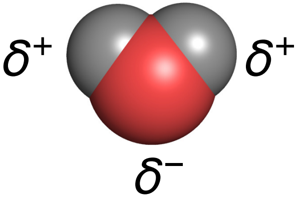
Direction Change

Water: What Makes it Special?

- Unusually high boiling temperature.
  - Boiling temperature is point where vapor pressure reaches atmospheric pressure.
  - Generally, boiling temperature reflects strength of interactions between molecules.
  - Generally, boiling temperature increases with size of molecules, because larger molecules have larger surfaces for interaction.
  - Boiling temperature of water is high for its size.
- Melting temperature of solid (ice) is also relatively high for size.
- Does not mix well with many other liquids, especially hydrocarbons.

Water Molecules are Polar

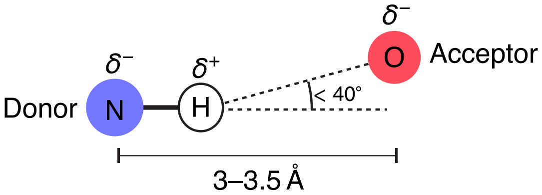
- Chemical bonds represent “sharing” of electrons between atoms.
- In some bonds, sharing is quite even: C-C, O-O, C-H
- Some elements are “greedy” for electrons: Electronegative elements: Oxygen and Nitrogen
- Some elements are “generous” with electrons: Electropositive elements: H, metals
- Water is particularly polar:



Oxygen has partial negative charge, and hydrogens have partial positive charges.

Hydrogen Bonds

- Form between a hydrogen atom covalently bonded to an electronegative atom and a second electronegative atom.



- Electronegative atoms are usually nitrogen or oxygen in biological molecules.
- Largely accounted for by electrostatic interaction between partial positive and negative charges, but there is probably also a small degree of covalent character to hydrogen bonds.
- Significant variability in geometry and strength of hydrogen bonds.