Notes 11/13

Tuesday, November 13, 2007
10:02 AM

Notes 11...

Audio recording started: 10:03 AM Tuesday, November 13, 2007
8

FINAL VERSON BELOW

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Bioenergetics

Nov. 14, 2007

Outline

- Quick review of Week 6
- Bioenergetics
    - Thermodynamics
    - Show me the money! $$ ATP
    - Biological phosphate compounds
    - Coupled reactions
    - Biological redox reactions

Week 6 Quick Review

- Enzyme regulation
    - Why it is necessary
    - Covalent modification
    - Noncovalent modification
    - Inhibitors
    - Allosteric Enzymes
- Metabolic pathways
    - Metabolites, characteristics, anabolic, catabolic, localization of pathways

Necessary to control reactions and conserve resources

Competitive inhibitors, uncompetitive, mixed, suicide inhibitors

Allosteric enzymes affected by modulator

Difference of modulator and inhibitor
(kinetics are different)

Metabolites are intermediates

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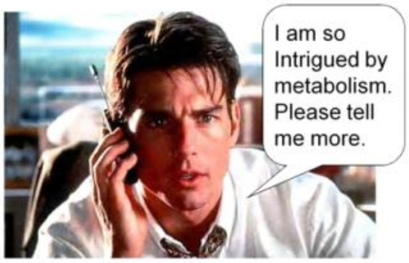

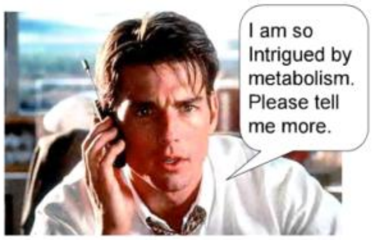

Bioenergetics

- The study of how organisms manage their energy resources

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Cells require sources of free energy

- Heat flow is not an energy source for cells
- Cells use free energy (G)
- Gibbs free-energy
  - Helps us predict direction of rxn
  - Helps us predict equilibrium position

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- Cells are considered isothermal, meaning temperature of cells and organism is uniform

Recall

- Rxn will proceed A-->B only if Gibb's Free Energy of B is lower than that of A

- Catalysis does not influence thermodynamics

- $\Delta G \cdot {}^{\circ\prime} = G_B^{\circ\prime} - G_A^{\circ\prime}$

Recall

- Rxn will proceed A-->B only if Gibb's Free Energy of B is lower than that of A

- Catalysis does not influence thermodynamics

- $\Delta G^{\circ\prime} = G_B^{\circ\prime} - G_A^{\circ\prime}$

Recall

- $G_A = G_A^{\circ\prime} + RT \ln [A]$
- $\Delta G \cdot_{(A \text{-->} B)} = \Delta G \cdot {}^{\circ\prime}_{(A \text{-->} B)} + RT \ln [B]/[A]$
- $R = 8.31 \times 10^{-3}$ kJ/(K mol)
- Standard T = 298 K
- $\ln [B]/[A] = 2.3 \log [B]/[A]$
- At equilibrium, $\Delta G = 0$ and $[B]/[A] = K_{eq}$
- $0 = \Delta G^{\circ\prime} + RT \ln K_{eq}$
- $\Delta G^{\circ\prime}_{(A \text{-->} B)} = -RT \ln K_{eq}$

Recall

- $G_A = G_A^{o'} + RT \ln [A]$
- $\Delta G_{(A\to B)} = \Delta G^{o'}_{(A\to B)} + RT \ln [B]/[A]$
- $R = 8.31 \times 10^{-3}$ kJ/(K mol) do not need to memorize R, will be given
- Standard T = 298 K 25^0C, we are 37C though… numbers use 25C though
- $\ln [B]/[A] = 2.3 \log [B]/[A]$
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$G^{0'}$ - biological standard conditions,
298K, 7pH, 1atm

$\Delta G^{o'}_{(A\to B)} = -RT \ln K_{eq}$

- Biochemical standard free energy change ($\Delta G^{o'}$) of a chemical rxn is simply an alternative way of expressing an equilibrium constant (K_{eq})
- Actual free-energy changes (ΔG) depend on [reactant] and [product]

$\Delta G^{o'}_{(A\to B)} = -RT \ln K_{eq}$

- Standard free energy change ($\Delta G^{o'}$) of a chemical rxn is simply an alternative way of expressing an equilibrium constant (K_{eq})
- Actual free-energy changes (ΔG) depend on [reactant] and [product]

Note the following

- $\Delta G \cdot_{(A\to B)} = \Delta G \cdot^{o'}_{(A\to B)} + RT \ln [B]/[A]$
- $\Delta G^{o'}_{(A\to B)} = -RT \ln K_{eq}$

- The sign of $\Delta G^{o'}$ or ΔG indicates direction of rxn
- Magnitude of $\Delta G^{o'}$ or ΔG is proportional to how far rxn can proceed before reaching equilibrium
- $\Delta G^{o'}$ and ΔG are independent of rxn pathway
- $\Delta G^{o'}$ and ΔG of coupled rxns are additive
- $\Delta G_{A\to B} = -\Delta G_{B\to A}$

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Negative delta G, goes left to right
Positive delta G, goes right to left
Delta G = 0, no change

Table 1. Thermodynamic Relationships

When	Then		And rxn will proceed
$\Delta G_{A\to B} < 0$	$[B]/[A] < K_{eq}$	$k_1[A] > k_2[B]$	To the right
$\Delta G_{A\to B} = 0$	$[B]/[A] = K_{eq}$	$k_1[A] = k_2[B]$	Neither direction (at equil.)
$\Delta G_{A\to B} > 0$	$[B]/[A] > K_{eq}$	$k_1[A] < k_2[B]$	To the left

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spontaneous

Non-spontaneous

Cellular reactions need to be thermodynamically favorable

- A ----> B

- Let's consider three different cellular situations
- $\Delta G^{o'}_{A\to B} <<< 0$
- $\Delta G^{o'}_{A\to B} > 0$ or $\Delta G^{o'}_{A\to B} < 0$
- $\Delta G^{o'}_{A\to B} >>> 0$

Cellular reactions need to be thermodynamically favorable

- A ----> B
  - Let's consider three different cellular situations
  - $\Delta G^{\circ\prime}_{A\text{-->}B} <<< 0$ spontaneous
  - $\Delta G^{\circ\prime}_{A\text{-->}B} > 0$ or $\Delta G^{\circ\prime}_{A\text{-->}B} < 0$ Either way
  - $\Delta G^{\circ\prime}_{A\text{-->}B} >>> 0$ Not spontaneous

$\Delta G^{\circ\prime}_{A\text{-->}B} <<< 0$

- ATP hydrolysis
- ATP + H_2O --> ADP + P_i $\Delta G^{o\prime} = -30.5$ kJ/mol
- $\Delta G^{o\prime} = -RT \ln K_{eq}$
- $\ln K_{eq} = -30.5$ kJ/mol (-K mol/0.0083 kJ) $(298 \text{ K})^{-1}$
- $\ln K_{eq} = 12.3$, $K_{eq} = 2.2 \times 10^5$
- What does this mean?
- $[ADP][P_i]/[ATP] = 220{,}000$ at eq.

$\Delta G^{\circ\prime}_{A\text{-->}B} <<< 0$

$\Delta G^{0\prime}$ is always constant for a particular reaction

- ATP hydrolysis
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- $\Delta G^{o\prime} = -RT \ln K_{eq}$
- $\ln K_{eq} = +30.5 \text{ kJ mol}^{-1} (0.0083 \text{ kJ/K mol})^{-1} (298 \text{ K})^{-1}$
- $\ln K_{eq} = 12.3$, $K_{eq} = 2.2 \times 10^5$
- What does this mean? 2.2×10^5 products per 1 reactant
- $[ADP][P_i]/[ATP] = 220{,}000$ at eq.

$\Delta G^{\circ\prime}_{A\text{-->}B} > 0$, or $\Delta G^{\circ\prime}_{A\text{-->}B} < 0$

- Glucose-6-P <-----> Glucose-1-P
- $K_{eq} = 1/19$
- $\Delta G^{\circ\prime} = -RT \ln K_{eq}$
- $\Delta G^{\circ\prime} = (-0.00831 \text{ kJ/K mol})(298 \text{ K}) \times \ln(1/19)$
- $\Delta G^{\circ\prime} = +7.3$ kJ/mol
- What does this mean?
- What if the actual cellular [B] and/or [A] are different?
- $\Delta G \cdot_{(A\text{-->}B)} = \Delta G \cdot^{\circ\prime}_{(A\text{-->}B)} + RT \ln [B]/[A]$

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What if the actual cellular [Glucose-6-P] and [Glucose-1-P] are different?

- [Glucose-6-P] = 0.199 M
- [Glucose-1-P] = 0.001 M
- $\Delta G \cdot_{(A\text{-->}B)} = \Delta G \cdot^{\circ\prime}_{(A\text{-->}B)} + RT \ln [B]/[A]$
- $\Delta G = +7.3 \text{ kJ/mol} + (0.00831 \text{ kJ/K mol})(298 \text{ K}) \times \ln(0.001/0.199)$
- $\Delta G = -5.8$ kJ/mol

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$$\Delta G = \Delta G^{o\prime} = RT \ln \left(\frac{.001}{.199} \right)$$

Standard free-energy change

- What does it tell us?
- Tells us:
  - The direction for a given rxn
  - How far the rxn must go to reach equil.
- Applies when initial concentration of each component is 1.0 M, pH 7.0, 298 K, 1 atm
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$\Delta G^{o'}{}_{(A\text{-->}B)}$ >>> 0

Figure 16-21a

			$\Delta G'^{\circ}$ (kJ • mol^{-1})
Endergonic half-reaction 1	P_i + glucose	$\rightleftharpoons$ glucose-6-P + H_2O	+13.8
Exergonic half-reaction 2	ATP + H_2O	$\rightleftharpoons$ ADP + P_i	−30.5
Overall coupled reaction	ATP + glucose	$\rightleftharpoons$ ADP + glucose-6-P	−16.7

Page 567

exergonic vs exothermic endergonic vs endothermic

- -gonic is a broader term and refers to free energy
- -thermic refers to heat energy

$\Delta G \cdot {}^{o'}{}_{(A\text{-->}B)}$ >>> 0

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In other words

$$\begin{array}{lll} & A \text{ ----> } B & \Delta G^{o'}{}_1 \\ & \underline{B \text{ ---->} C \quad \Delta G^{o'}{}_2} & \\ \text{Sum} & A\text{---->}C & \Delta G^{o'}{}_1 + \Delta G^{o'}{}_2 \end{array}$$

Show me the money!

In other words

A ----> B $\Delta G^{o'}_1$

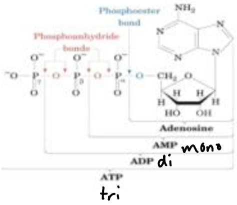
B ---->C $\Delta G^{o'}_2$

Sum A---->C $\Delta G^{o'}_1 + \Delta G^{o'}_2$

Show me the money!

Figure 16-20

ATP is the energy currency



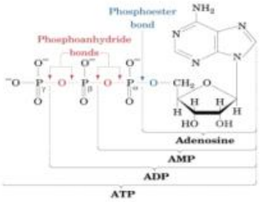
The free-energy change for ATP hydrolysis is large and negative

- chemical energy is donated to endergonic rxns
  - Synthesis
  - Transport
  - Mechanical motion

- Don't confuse bond energy for "high-energy" bonds

Figure 16-20

ATP is energy currency



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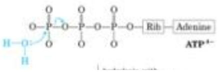
Why are the phosphoryl transfer rxns of ATP so exergonic?

- ATP ---> ADP + P_i
- Hydrolysis
  - Separates negatively charged phosphates
  - Relieves electrostatic repulsion
  - P_i (HPO_4^{2-}) orthophosphate is resonance stabilized
  - ADP^{2-} ionizes

ATP Hydrolysis



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  - Separates negatively charged phosphates
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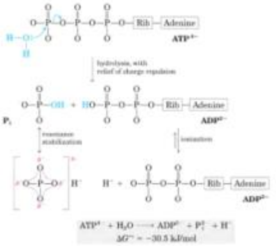
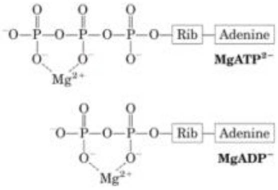
  - ADP^{2-} ionizes into a medium of low pH

ATP Hydrolysis



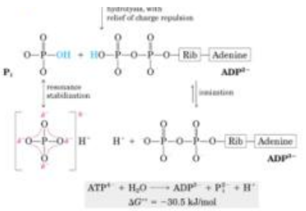
Actual free-energy change for ATP Hydrolysis



Has magnesium ions, Mg changes delta G

Keeping it real: The real cost of doing metabolic business

- Phosphphorylation potential (ΔG_p) is the cellular ΔG for ATP hydrolysis
- Calculate the the ΔG_p in human erythrocytes. Assume ATP, ADP, and P_i are 2.25, 0.25, and 1.65 mM, respectively. The pH is 7.0 and the temperature is 25 ºC. next slide



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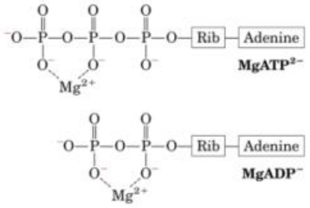

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- ΔG_p = -30,500 J/mol + (8.315 J/ mol K)(298 K) x ln (2.50 x 10^{-4})(1.65 x 10^{-3})/(2.25 x 10^{-3})
- ΔG_p = -51.8 kJ/mol

ATP Provides Energy by Group Transfers, not by Simple Hydrolysis

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ATP Provides Energy by Group Transfers, not by Simple Hydrolysis

- ATP ---> ADP + P_i

- ATP hydrolysis generates heat

- In reality, ATP participates covalently in an enzyme catalyzed rxn

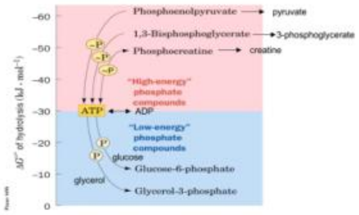
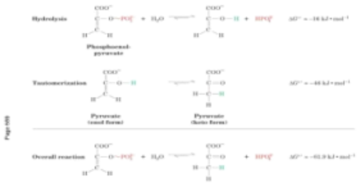


Figure 16-25 modified

Figure 16-21b

Figure 16-23



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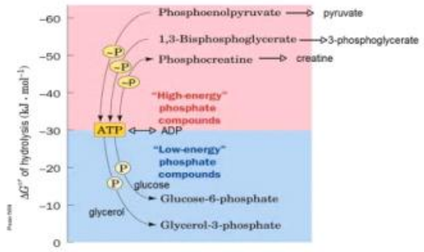

Figure 16-25 modified

Compound	ΔG (kJ · mol⁻¹)
Phosphoenolpyruvate	−61.9
1,3-Bisphosphoglycerate	−49.4
Acetyl phosphate	−43.1
Phosphocreatine	−43.1
PP_i	−33.5
ATP (→ AMP + PP_i)	**−32.2**
ATP (→ ADP + P_i)	**−30.5**
Glucose-1-phosphate	−20.9
Fructose-6-phosphate	−13.8
Glucose-6-phosphate	−13.8
Glycerol-3-phosphate	−9.2

Source: Jencks, W.P., in Fasman, G.D. (Ed.), *Handbook of Biochemistry and Molecular Biology* (3rd ed.), *Physical and Chemical Data,* Vol. I, pp. 296–304, CRC Press (1976).

Table 16-3