Overview of Metabolism

Metabolism

Issues:

- Thermodynamics and biochemistry; carbon/oxygen cycle & nitrogen cycle
- Common organic chemistry principles in biochemistry
- Some biomolecules are "high energy" with respect to their hydrolysis and group transfers.
- Energy stored in reduced organic compounds can be used to reduce cofactors such as NAD^+ and FAD, which serve as universal electron carriers and lead to ATP formation.

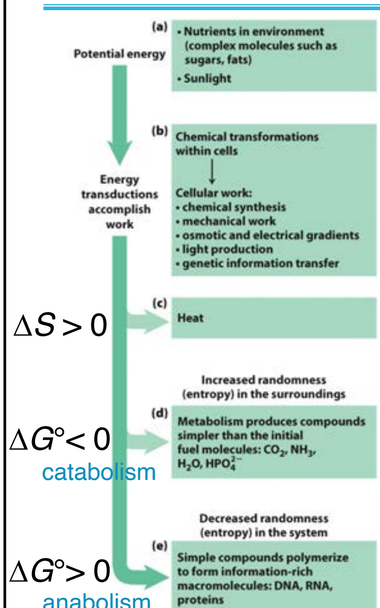
"Now, in the *second* law of thermodynamics . . ."

Metabolism

- Living organisms cannot create energy from nothing.
- Living organisms cannot destroy energy into nothing.
- Living organism may transform energy from one form to another.

- In the process of transforming energy, living organisms must increase the entropy of the universe.
- In order to maintain organization within themselves, living systems must be able to extract useable energy from their surroundings and release useless energy (heat) back to their surroundings.

Organisms Use the First Law Big-Time (perform energy transformations) to Stay Alive

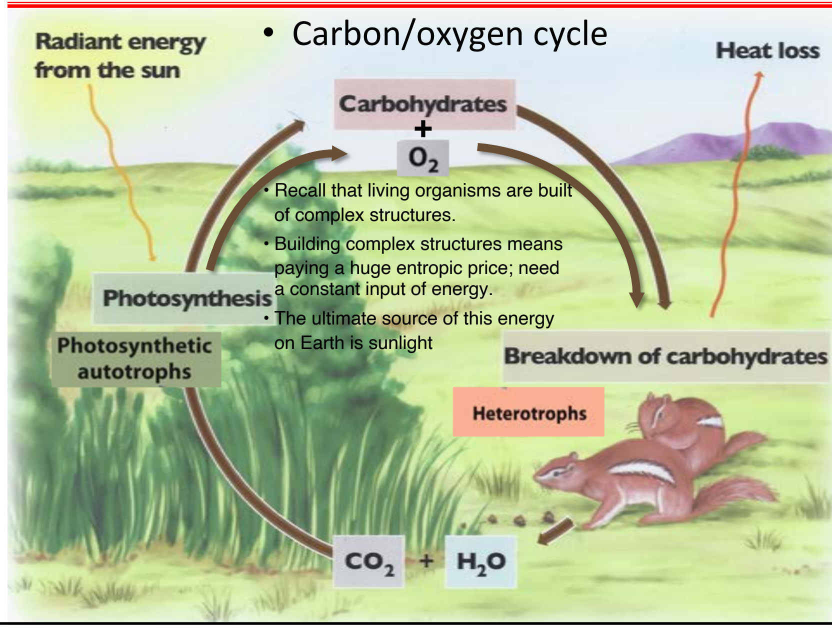


Favorable and Unfavorable Reactions

- The breakdown of some metabolites releases a significant amount of energy (**exergonic**).
  - Their cellular concentration is far higher than their equilibrium concentration.
  - Metabolites, such as ATP, NADH, NADPH, can be synthesized using the energy from sunlight and fuels…..
- Synthesis of complex molecules and many other metabolic reactions requires energy (**endergonic**).
  - A reaction might be thermodynamically unfavorable ($\Delta G° > 0$).
    - Creating order requires work and energy.
- Biochemistry **couples** exergonic with endergonic reactions to insure organisms continue to grow and divide.

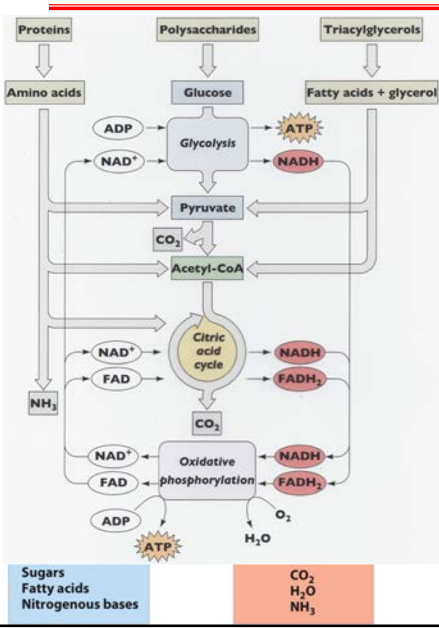
Metabolism

- Carbon/oxygen cycle

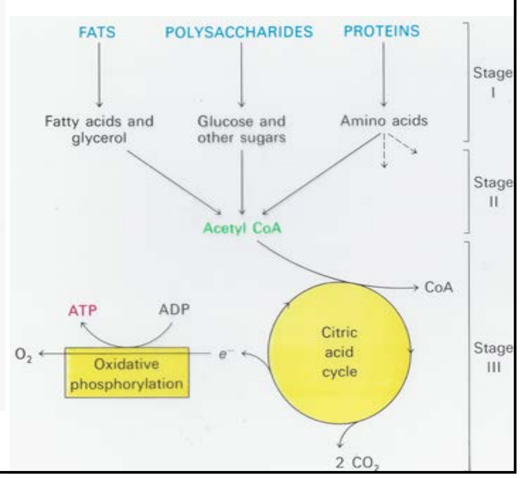


- Recall that living organisms are built of complex structures.
- Building complex structures means paying a huge entropic price; need a constant input of energy.
- The ultimate source of this energy on Earth is sunlight

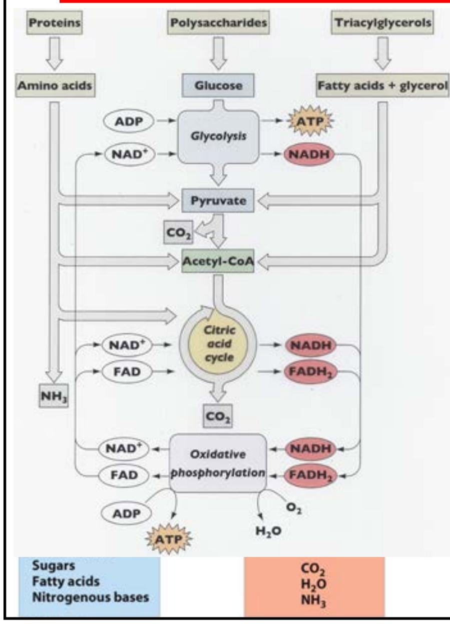
Metabolism



- In biochemistry, the oxidation of reduced fuels with O_2 is stepwise and controlled.
- Recall that being thermodynamically favorable is not the same as being kinetically rapid.



Metabolism



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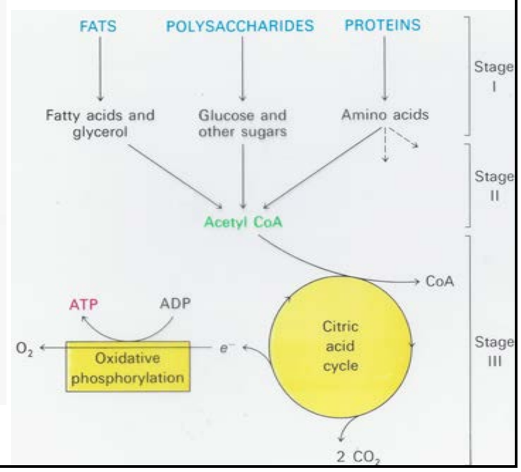


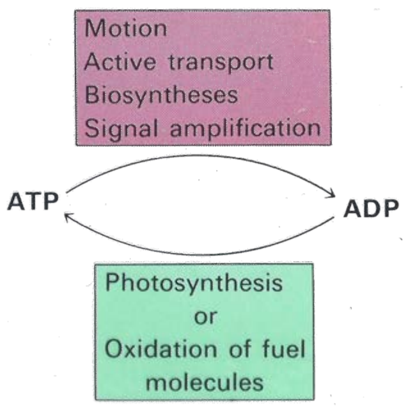
Metabolism

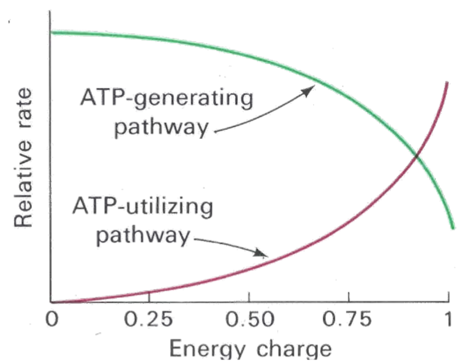
NAD and NADP Are Common Redox Cofactors

- These are commonly called pyridine nucleotides.
- They can dissociate from the enzyme after the reaction.
- In a typical biological oxidation reaction, hydride from an alcohol is transferred to NAD^+, giving NADH.

Metabolism

THE ATP CYCLE

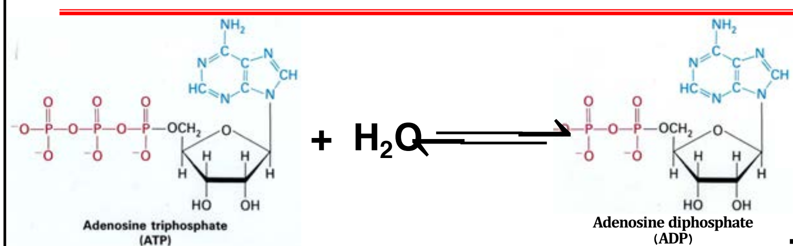




This "buffering" of energy in the cell keeps the [ATP] high enough to keep fighting the second law of thermodynamics.

$$\text{Energy Charge} = \frac{[ATP^{-4}] + \frac{1}{2}[ADP^{-3}]}{[ATP^{-4}] + [ADP^{-3}] + [AMP^{-2}]}$$

Metabolism



+ HPO_4^{2-}
+
H^+
(at pH 7)

If this reaction is allowed to come to equilibrium, what is the ΔG?

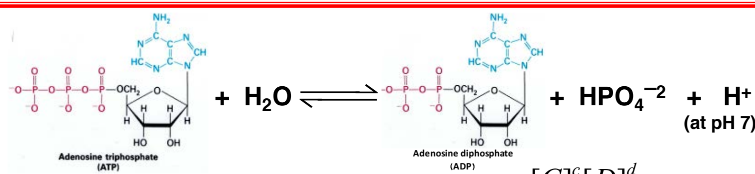
Recall, at equilibrium, ΔG=0

Also, recall that the actual free-energy change of a reaction depends on:
- A constant (the standard change in free energy, ΔG°)
- actual concentrations of products and reactants
- For the reaction aA + bB ⇌ cC + dD:

$$\Delta G' = \Delta G^{\circ\prime} + RT \ln \frac{[C]^c[D]^d}{[A]^a[B]^b}$$

[In biochemistry, we add a prime (′) because we pull [H^+] out of the expression and set it to 10^{-7}, not 1 M]

Metabolism



At equilibrium, ΔG=0

$$\Delta G' = \Delta G^{\circ\prime} + RT \ln \frac{[C]^c[D]^d}{[A]^a[B]^b}$$

BUT, if we are at equilibrium, this equation becomes:

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

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

For the above reaction (hydrolysis of ATP):

$$\Delta G^{\circ\prime} = -7.3 \text{ kcal/mole}$$

TABLE 13-3 Relationships among K'_{eq}, $\Delta G'^{\circ}$, and the Direction of Chemical Reactions

When K'_{eq} is . . .	$\Delta G'^{\circ}$ is . . .	Starting with all components at 1 M, the reaction . . .
>1.0	negative	proceeds forward
1.0	zero	is at equilibrium
<1.0	positive	proceeds in reverse

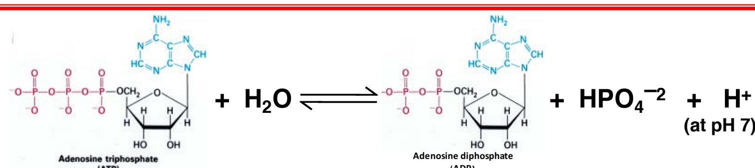
But, what is the actual $\Delta G'$ of ATP Hydrolysis IN THE CELL?

TABLE 13-2 Relationship between Equilibrium Constants and Standard Free-Energy Changes of Chemical Reactions

	$\Delta G'^{\circ}$	
K'_{eq}	(kJ/mol)	(kcal/mol)[a]
10^3	–17.1	–4.1
10^2	–11.4	–2.7
10^1	–5.7	–1.4
1	0.0	0.0
10^{-1}	5.7	1.4
10^{-2}	11.4	2.7
10^{-3}	17.1	4.1
10^{-4}	22.8	5.5
10^{-5}	28.5	6.8
10^{-6}	34.2	8.2

[a] Although joules and kilojoules are the standard units of energy and are used throughout this text, biochemists and nutritionists sometimes express $\Delta G'^{\circ}$ values in kilocalories per mole. We have therefore included values in both kilojoules and kilocalories in this table and in Tables 13-4 and 13-6. To convert kilojoules to kilocalories, divide the number of kilojoules by 4.184.

Metabolism



Go back the original equation: $\Delta G' = \Delta G^{\circ\prime} + RT \ln \frac{[C]^c[D]^d}{[A]^a[B]^b}$

In RBCs = 1.5×10^{-4} M

$$\Delta G' = \Delta G^{\circ\prime} + RT \ln \frac{[ADP^{-3}]\,[HPO_4^{-2}]}{[ATP^{-4}]}$$

$$\Delta G = \Delta G^{\circ\prime} + RT \ln \frac{[MgADP^-]\cdot[P_i]}{[MgATP^{2-}]}$$

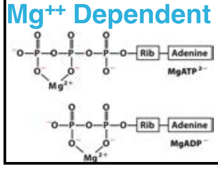
At 25 °C: $\Delta G' = \Delta G^{\circ\prime} + 0.59 \ln \frac{[ADP^{-3}]\,[HPO_4^{-2}]}{[ATP^{-4}]}$

$\Delta G^{\circ\prime}$ **of ATP Hydrolysis is Mg^{++} Dependent**

$$\Delta G' = \Delta G^{\circ\prime} + 1.36 \log (1.5 \times 10^{-4})$$

$$\Delta G' = (-7.3) + (-5.2)$$

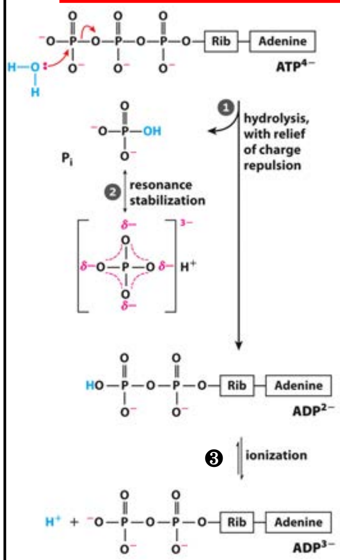
$$\Delta G' = -12.5 \text{ kcal/mole}$$



WOW!

Other than concentrations, what makes the $\Delta G'$ of ATP so high?

Metabolism



$ATP^{4-} + H_2O \longrightarrow ADP^{3-} + HPO_4^{2-} + H^+$

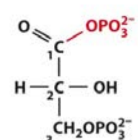
$\Delta G'^\circ = -30.5$ kJ/mol

- Contributions of the incredible favorability of the ATP hydrolysis reaction:
  - Better charge separation in products (relief of charge repulsion)
  - More favorable resonance stabilization of products
  - Ionization of products (ADP or P_i)

$H_2PO_4^- \rightleftharpoons HPO_4^{2-} + H^+$ (at pH 7)

Are there other compounds in the cell with high negative $\Delta G^{\circ\prime}$ of hydrolysis?

Metabolism



1,3-bisphosphoglycerate

$\Delta G^{\circ\prime} = -12$ kcal/mole

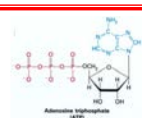
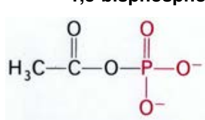
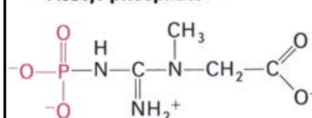


TABLE 13-4 Standard Free-Energy Changes of Some Chemical Reactions	$\Delta G'^\circ$	
Reaction type	(kJ/mol)	(kcal/mol)
Hydrolysis reactions		
Acid anhydrides		
Acetic anhydride + H_2O → 2 acetate	–91.1	–21.8
ATP + H_2O → ADP + P_i	–30.5	–7.3
ATP + H_2O → AMP + PP_i	–45.6	–10.9
PP_i + H_2O → $2P_i$	–19.2	–4.6
UDP-glucose + H_2O → UMP + glucose 1-phosphate	–43.0	–10.3
Esters		
Ethyl acetate + H_2O → ethanol + acetate	–19.6	–4.7
Glucose 6-phosphate + H_2O → glucose + P_i	–13.8	–3.3
Amides and peptides		
Glutamine + H_2O → glutamate 1 NH_4^+	–14.2	–3.4
Glycylglycine + H_2O → 2 glycine	–9.2	–2.2
Glycosides		
Maltose + H_2O → 2 glucose	–15.5	–3.7
Lactose + H_2O → glucose + galactose	–15.9	–3.8
Rearrangements		
Glucose 1-phosphate → glucose 6-phosphate	–7.3	–1.7
Fructose 6-phosphate → glucose 6-phosphate	–1.7	–0.4
Elimination of water		
Malate → fumarate + H_2O	3.1	0.8
Oxidations with molecular oxygen		
Glucose + $6O_2$ → $6CO_2$ + $6H_2O$	–2,840	–686
Palmitate + $23O_2$ → $16CO_2$ + $16H_2O$	–9,770	–2,338



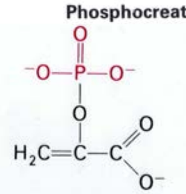
Acetyl phosphate

$\Delta G^{\circ\prime} = -11.8$ kcal/mole



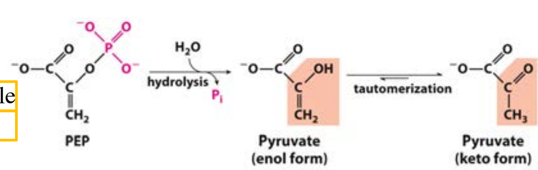
Phosphocreatine

$\Delta G^{\circ\prime} = -10.3$ kcal/mole



Phosphoenolpyruvate (PEP)

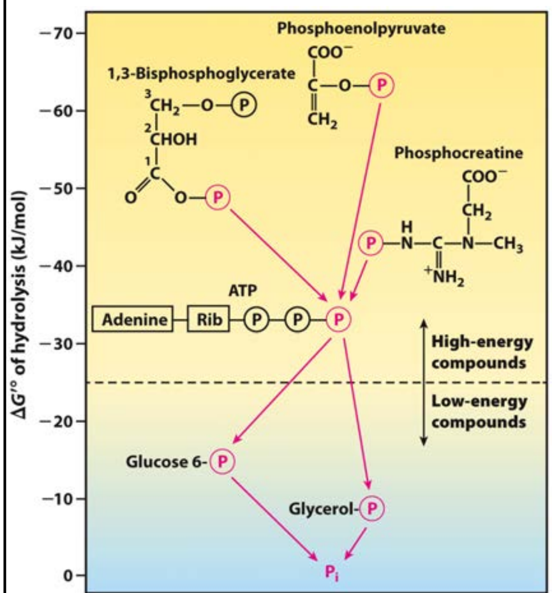
$\Delta G^{\circ\prime} = -14.8$ kcal/mole
$= -61.9$ kJ/mole



$PEP^{3-} + H_2O \longrightarrow pyruvate^- + HPO_4^{2-}$

$\Delta G'^\circ = -61.9$ kJ/mol

Metabolism



Phosphates: Ranking by the *Standard* Free Energy of Hydrolysis

Phosphate can be transferred from compounds with higher $\Delta G^{\circ\prime}$ to those with lower $\Delta G^{\circ\prime}$.

Metabolism

TABLE 13-5 Total Concentrations of Adenine Nucleotides, Inorganic Phosphate, and Phosphocreatine in Some Cells

	Concentration (mM)[a]					
	ATP	ADP[b]	AMP	Energy Charge	P_i	PCr
Rat hepatocyte	3.38	1.32	0.29	0.81	4.8	0
Rat myocyte	8.05	0.93	0.04	0.94	8.05	28
Rat neuron	2.59	0.73	0.06	0.87	2.72	4.7
Human erythrocyte	2.25	0.25	0.02	0.94	1.65	0
E. coli cell	7.90	1.04	0.82	0.86	7.9	0

[a] For erythrocytes the concentrations are those of the cytosol (human erythrocytes lack a nucleus and mitochondria). In the other types of cells the data are for the entire cell contents, although the cytosol and the mitochondria have very different concentrations of ADP. PCr is phosphocreatine, discussed on p. 516.
[b] This value reflects total concentration; the true value for free ADP may be much lower (p. 509).

Cellular ATP concentration is usually far above the equilibrium concentration, making ATP a very potent source of chemical energy.

End of 421

- BI-421 Lab exams (Today); Ch 6 PL's due
- Additional Office hours – Thursday (12/10) & next Wednesday (12/16) at 10:00-11 am
- Review session – next Monday (12/14) 2-3 PM SCI109
- *Final Exam – Thursday 8-11 AM in LAW*