Highlights of Metabolic Control

1. Metabolism is literally the chemistry of life. Schematic diagrams of metabolism are the equivalent of highway maps for a city. Central pathways, like glycolysis, are the equivalent of the main streets.

2. To understand chemical reactions in cells, we must understand the thermodynamics (energy) of the reactions.

3. The free energy of a process is the energy available to do useful work. The free energy of a process is called the Gibbs Free Energy.

4. Most commonly, we are concerned with the change in free energy for a system. For example, for an enzymatically catalyzed reaction, we are interested in the change in free energy between the reactants and the products. The change in free energy (ΔG) indicates the favorability of a process.

a. If the ΔG for a process is negative, the process is favored.

b. If the ΔG for a process is positive, the process is not favored (in fact, the reverse of the process is favored).

c. If the ΔG for a process is zero, the process is at equilibrium.

Example:

For A <=> B,

if ΔG is negative, A->B is favored.

if ΔG is positive, B-> A is favored.

if ΔG is 0, B-> A and A-> B are equally favored. The system is at equilibrium.

5. The chemical potential of a component A is equal to the chemical potential at the standard state plus RT ln[A]. For a reaction of multiple components,

aA + bB <=> cC + dD

6. ΔG zero (usually written as ΔG with a little degree sign above the G, but the browser isn't allowing that) is the ΔG measured under standard conditions (all products and reactants at 1M). Here, $\Delta G = \Delta G$ zero

7. For biological systems, we define a ΔG zero prime (note the prime at the end) to encompass aqueous solutions at pH 7.0.

8. ATP is a source of energy in cells because the ΔG of the hydrolysis reaction is very negative

(releases much free energy). Hydrolysis of ATP directly to yield energy (like burning of wood to heat a house) is not the mechanism used by cells to drive reactions. Instead, hydrolysis of ATP is coupled to energetically unfavorable reactions to make them proceed. We will discuss examples of this later in the term.

9. Cells must have ATP to accomplish work (muscular action), transmit information (nerve signals), signal each other (cellular signaling), and synthesize important biochemicals.

10. Oxidation is used to provide the energy necessary to make ATP. ATP energy is used to provide reduction necessary to biosynthesize compounds like fats and fatty acids.

11. The oxidation state of a molecule is related to its available energy. The higher the oxidation state of a molecule, the less energy that can be obtained from it. Thus, glucose, which has a higher oxidation state than fatty acids, provides less energy to cells than fatty acids.

12. ATP is made from ADP by phosphorylation. There are three types of cellular phosphorylation in nature. Substrate level phosphorylation occurs when high energy phosphate molecules (like creatine phosphate) transfer their phosphate directly to ADP to form ATP. Oxidative phosphorylation occurs as a result of actions in the mitochondria, ultimately caused by oxidation. Photophosphorylation (occurs only in photosynthetic organisms) uses light energy to make ATP.

13. Creatine phosphate is a backup ATP source for muscle cells. This arises from the following reaction

Creatine phosphate + ADP <=> Creatine + ATP($\triangle$ G zero prime = 12 kJ/mol)

Normally when at rest, this reaction moves to the LEFT, due to high ATP concentrations. Upon exercising, however, ATP concentrations drop, and the reaction moves to the right, restoring ATP concentrations.

14. For every oxidation (loss of electrons) by one molecule, there is a reduction (gain of electrons) by another one. In biological systems, electron carriers, such as NAD^+/NADH and FAD/$FADH_2$ are electron carriers. When a biological molecule is oxidized, electrons are given (in pairs) to either NAD^+ or FAD to form NADH or $FADH_2$. NADH and $FADH_2$ can also donate electrons to biological molecules, thus reducing the biological molecules.

15. An example oxidation/reduction reaction that might occur in cells is

Alcohol + NAD^+ <=> Aldehyde/Ketone + NADH + H^+

16. Catabolism generally involves oxidation and/or breakdown of large molecules (proteins, fats, carbohydrates) into smaller ones (many of these converge at acetyl-CoA). Catabolism releases energy that is used to make ATP. Anabolism generally involves reducation and/or synthesis of large molecules from small ones. Anabolism requires an energy source - often from ATP.

17. ATP energy in anabolism is used to drive energetically unfavorable reactions by coupling the hydrolysis of ATP (an energetically favorable process) with the reaction that is energetically unfavored (such as the addition of phosphate to glucose, as noted in class). By doing this coupling, an unfavorable reaction becomes energetically favorable. Thus, the synthesis of large molecules from small ones is not energetically favorable, but when energy from ATP is provided, they become energetically favorable.

18. Besides ATP energy (or GTP or UTP or CTP, as appropriate), other mechanisms available to cells to "drive" reactions forward are to alter the concentrations of reactants and products. I defined the phenomenon of "pushing" a reaction as increasing the amount of reactants. This has the effect of reducing the Δ G value and making a reaction more favorable in the forward direction. I also defined the phenomenon of "pulling" a reaction as decreasing the amount of product. This too has the effect of reducing the value of Δ G and favoring a reaction to go forward.