# Lecture 28: Biochemical Energetics

**1. Phosphate Hydrolysis:**

**2. Electrons (Redox Chemistry)**



An example of a redox reaction involving inorganic metals: Fe3+ + Cu+ ↔ Fe2+ + Cu2+

This reaction can be broken down into two balanced half reactions:

Fe3++e- ↔ Fe2+

Cu+ ↔ Cu2++ e-

In this case the iron is reduced from the 3+ state to the 2+ state while the copper is oxidized from the 1+ state to the 2+  state.

In biological oxidations and reductions the electrons are often carried by protons (i.e. hydrogen atom). Thus a general rule for oxidation-reduction are:

**Loss of electrons or hydrogen atom (H+ + e-) = oxidation**

**Gain of electrons or hydrogen atom = reduction**

There are several common acronyms to help you remember the above, here are two:

LEO GER - lose electrons oxidation, gain electron reduction.

OIL RIG - oxidation involves loss, reduction involves gain.

In the case of biological systems the redox state of an organic molecule may be difficult to discern. The following shows the oxidation (loss of hydrogen atoms) of three functional groups. Note that all of these reactions involve a *two* electron transfer.



Balancing organic redox reactions. It can be difficult to determine whether a change in an organic compound is an oxidation or not. The two steps for balancing an organic redox reaction are:

i) If oxygen is needed to balance the reaction, use H2O.

ii) Use H+, or H+ + *e-*, or *e-* to balance hydrogen atoms and/or charge.

A redox reaction has occurred if electrons are consumed or released.



Example: Is the conversion of ethene to ethanol a redox reaction?

**Organic Electron Carriers:** Two compounds are widely used in biological reductions and oxidations. These are nicotinamide adenine dinucleotide (**NAD**) and flavin adenine dinucleotide (**FAD**). If these compounds are involved it’s a good bet that a 2 electron oxidation/reduction has occurred.

* NAD is loosely bound to enzymes and can thus be considered a true substrate (only the functional group that undergoes a redox change is shown).



* FAD is tightly bound to enzymes and is thus considered a **cofactor**. (only the functional group that undergoes a redox change is shown).

**3. Non-Equilibrium Thermodynamics**:

**ΔGo, the standard energy**, is the energy released when one mole of reactants are converted to products. 

The standard free energy difference between products and reactants, ΔGo, is insufficient to describe energy changes in metabolism because the concentrations of intermediates in a biochemical pathway are seldom at their equilibrium concentrations. The Gibbs free energy, ΔG is used instead.

Each species in a reaction (e.g. A and B) has an intrinsic free energy associated with it, called the **chemical potential:**



**ΔG, Gibbs Free Energy**, is the difference in chemical potential, ΔG = Δµ = µB - µA.

Assuming the usual direction for the reaction of A→B, where A is the reactant and B is the product.





* ΔG is a measure of the potential energy of the system, or its ability to do work (release energy).
* ΔG indicates the spontaneous direction of the reaction.

**ΔG = 0** the reaction is at equilibrium, the difference in the potential energies of A and B is zero, no energy can be gained converting A to B or B to A.

**ΔG < 0** the reaction is spontaneous, and energy will be released as the system approaches equilibrium, the potential of A is larger than B, A→B is spon.

**ΔG > 0** the reaction is not spontaneous, energy had to be added to the system to reach this state (the reverse reaction is spontaneous). The potential of B is larger than A, the system will spontaneously move: B→A.

**Case 1:** At equilibrium.





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| **Case 2 :** [A] higher than its equilibrium point.    Both *ln* terms are <1, therefore ΔG is <1. | **Case 3:** [B] higher than its equilibrium point.    Both *ln* terms are >1, therefore ΔG is >1 |

**4. Flux and Coupling of Reactions:** A key feature of all biochemical pathways is that there is a constant flux of material through the pathway. To insure a constant flux through the pathway it is necessary to insure that the Gibbs energy of the products are lower in energy than the substrates, such that the natural flow is always from substrates to products.



**Direct Coupling:** Many steps in biochemical pathways involve reactions that are extremely unfavorable, i.e. a large positive ΔGo. This energy barrier reduced by the **direct coupling** of the unfavorable reaction to a favorable one, with both reactions occurring at the same time **in the active** site of one enzyme.The energetics of each reaction are most easily seen by considering the half-reactions. For example, the first reaction in glycolysis, catalyzed by the enzyme hexosekinase, converts glucose to glucose-6-phosphate. The high energy of ATP is used to drive this unfavorable reaction by direct coupling..

Reactions of this type are often called **“group transfer reactions”** since a group (phosphate) is transferred from one substrate to another.

**Indirect Coupling:** By lowering the concentration of the product, a reaction can be made spontaneous; the ΔG becomes < 0. This generally implies that a reaction further down the pathway has a large negative ΔGo, such that [B] is kept low.



**Example problem in indirect coupling:** In the pathway: A→B:

Concentration of [A] is 1 mM under normal metabolic conditions.

Standard free energy, ΔGo, of the first reaction (A→B) is +5.75 kJ/mol. What is the *direction* of the reaction if the concentration of [B] is 10-5 M? Assume RT=2.5 kJ/mol (T~300K).