Biochemistry I Fall Term, 2004

Redox Chemistry in Biological Processes

Reading in Campbell: Chapter 17.2 & 12.8-12.9

This page reviews and expands on the above sections of Campbell that were not covered in Lectures 9 & 10. In particular, the equations used to measure reduction/oxidation (redox) reactions found in the oxidative phosphorylation pathways are explained below.

Redox Chemistry

An example of a normal type of redox reaction is:

$$Fe^{3+} + Cu^{+} \text{ <-> } Fe^{2+} + Cu^{2+}$$

This reaction can be broken down into two half reactions:

$$Fe^{3+} + e^{-} \text{ <-> } Fe^{2+}$$

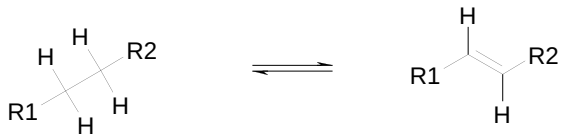
$$Cu^{+} \text{ <-> } Cu^{2+} + e^{-}$$

In this case the iron is reduced from the 3+ state to the 2+ state. In biological oxidations and reductions the electrons are often carried by protons (*i.e.* the the hydrogen atom or hydride, H^{-}). Thus, a general rule for oxidation-reduction is:

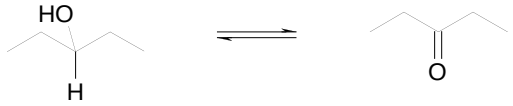
Loss of electrons or hydrogen = oxidation

Gain of electrons or hydrogen = reduction

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 two functional groups. Note that both of these reactions involve a two electron transfer.



alkane alkene



alcohol ketone

Two compounds are widely used in biological oxidations and reductions. These are nicotinamide adenine dinucleotide NAD^+ (and NADH) and flavin adenine dinucleotide, FAD (and $FADH_2$). NAD^+ usually binds reversibly to enzymes, and can thus be considered a substrate. In contrast FAD is tightly bound to enzymes and is thus considered a **cofactor**. In addition to the water soluble reducing/oxidizing agents (NAD^+ and FAD) there are also lipid soluble agents (coenzyme Q) that function to shuttle electrons within lipid membranes.

Thermodynamics of Redox Reactions

The thermodynamics of an oxidation/reduction reaction is the same as that found for any other chemical reaction. The only difference is that the free energies are given in terms of electrical potential with respect to an arbitrary reference state defined by the oxidation/reduction potential of hydrogen. The electrical potential is a measure of the relative energy of an electron on a molecule/atom.

For example, in a battery made of a solution of Fe^{2+}/Fe^{3+} in one cell and hydrogen in the other the following reactions will occur (if the concentration of each species is 1 M). The reaction as written is spontaneous. This indicates that the electron is more stable on the Fe^{2+} than on the Fe^{3+}. The reaction can be written as a sum of two half-reactions.

$$Fe^{3+} + e^- \text{-->} Fe^{2+}$$
$$^1/_2H_2 \text{-->} H^+ + e^-$$

The initial voltage across the cells will be +0.77 volts. As the iron become reduced (and the hydrogen oxidized) the voltage will drop, becoming zero at equilibrium. The net free energy that can be obtained from this reaction is:

$$\Delta G° = -nF\Delta E°$$

The negative sign indicates that the reaction is spontaneous as written.

- n is the number of electrons involved in the transfer (one in this case)
- *F* is the Faraday constant = 96,494 C/mol = 96,494 joules/volt-mol.
- ΔE is the difference between the redox potential of each reaction.

The redox potential is the voltage obtained for a redox reaction relative to that of hydrogen, all reactants being a standard state (1 M). The standard half reaction potential (E^o) is measured relative to reduction of hydrogen at pH 0, 25°C and 1 atm H_2 gas (i.e. E^o for this reaction is zero).

The free energy change of any reaction is given by the following.

$$\Delta G = \Delta G^0 + RT \ln \frac{[\text{products}]}{[\text{reactants}]}$$

$$-nF\Delta E = -nF\Delta E^o + RT \ln \frac{[\text{products}]}{[\text{reactants}]}$$

$$\Delta E = \Delta E^o - \frac{RT}{nF} \ln \frac{[\text{products}]}{[\text{reactants}]}$$

This important equation is called the Nernst equation; it gives the electrical potential that can be obtained from an oxidation-reduction reaction. As with ΔG^o, the standard redox potential (ΔE^0) is the potential that would be observed when the concentration of the products and reactants are 1M.

For any two redox pairs the overall redox potential is calculated according to the following ($E^0_{donor} = 0$ for the reduction of hydrogen) .

$$\Delta E = E^o_{acceptor} - E^o_{donor}$$

The electical potential and free energy change of a number of important redox reactions are listed below.

Reaction (OXIDIZED $\leftrightarrow$ REDUCED**)**	**ΔE^o** (volts)	**ΔG^o** (kJ/mol)
$O_2 + 2\,H^+ + 2e \leftrightarrow H_2O$	0.815	-156
Ubiquinone + $2H^+$+ 2e $\leftrightarrow$ ubiquinol	0.048	-9.2
FAD + $2H^+$ + 2e $\leftrightarrow$ $FADH_2$ (in flavoproteins)	0.000	0.0
$NAD^+ + H^+ + 2e \leftrightarrow NADH$	-0.315	+60.5

Consider the following reaction (the reduction of NAD^+ by $FADH_2$)

$$NAD^+ + FADH_2 \leftrightarrow FAD + NADH$$

The standard reduction potential for this reaction is –0.315 - 0 = -0.315. Alternatively, we can calculate the standard from energy change as +60.5 kJ/mol - 0 kJ/mol = +60.5 kJ/mol. Since ΔE is negative, (alternatively ΔG is positive) the reaction is not spontaneous. Thus, flavin ($FADH_2$) cannot be used to reduce NAD^+. However, the reverse reaction:

$$FAD + NADH \leftrightarrow NAD^+ + FADH_2$$

has a standard reduction potential of 0 - (-0.315) = + 0.315 (ΔG^o = -60.5 kJ/mol) , and is thus spontaneous. Thus, NADH can be used to reduce FAD.

The reduction of molecular oxygen by NADH occurs with the following free energy change:

$$\Delta G = -(2)(96{,}494)(0.815 - (-0.315)) = -218 \text{ kJ/mol}$$

Note that the standard free energy for the formation of ATP from ADP + P_i is approximately 30 kJ/mol. Thus, if the reduction of oxygen by NADH were 100% efficient, then approximately 7 ATP molecules could be synthesized by this reaction. In actual fact a total of 3 ATP molecules result from this redox reaction.

Some Biologically Important Redox Pairs