Lecture 28: Biochemical Energetics

3. Non-Equilibrium Thermodynamics:

\[ \Delta G^0, \text{ the standard energy, is the energy released when one mole of reactants are converted to one mole of products.} \]

\[ \mu_A^0 - \mu_B^0 = \Delta G^0 = -RT \ln K_{eq} = -RT \ln \frac{[B]_{eq}}{[A]_{eq}} \]

\[ \Delta G^0 = G_{products} - G_{reactants} \]

It is defined by the equilibrium position of the reaction and it depends on the difference in the intrinsic energies of the two compounds:

\[ \mu_A^0 = \text{chemical energy of pure compound A} \]
\[ \mu_B^0 = \text{chemical energy of pure compound B} \]

\[ \Delta G^0, \text{ is insufficient to describe energy changes in metabolism because the concentrations of intermediates in a biochemical pathway are seldom at their equilibrium concentrations.} \]

The Gibbs free energy, \( \Delta G \), is used to describe non-equilibrium conditions. It is the difference between the chemical potential of each compound (\( \mu \)).

For the reaction \( A \rightarrow B \):

\[ \Delta G = \mu_B - \mu_A = (\mu_B^0 + RT \ln[B]) - (\mu_A^0 + RT \ln[A]) \]
\[ = (\mu_B^0 - \mu_A^0) + RT \ln[B] - RT \ln[A] \]
\[ = \Delta G^0 + RT \ln \frac{[B]}{[A]} \]

- \( \Delta G \) indicates the spontaneous direction of the reaction.
- \( |\Delta G| \) is a measure of the energy released by the system as it approaches equilibrium.

\( \Delta G = 0 \) the reaction is at equilibrium, the difference in the chemical potentials of \( A \) and \( B \) is zero, no energy can be gained converting \( A \) to \( B \) or \( B \) to \( A \).

\( \Delta G < 0 \) The potential of \( A \) is larger than \( B \), therefore \( A \rightarrow B \) is spontaneous and \( |\Delta G| \) amount of energy is released as it goes to equilibrium.

\( \Delta G > 0 \) The potential of \( B \) is larger than \( A \), the system will spontaneously move: \( B \rightarrow A \) and \( |\Delta G| \) of energy will be released as it goes to equilibrium.
Case 1: At equilibrium.
\[ \Delta G = (\mu_B^0 + RT \ln[B]_\text{eq}) - (\mu_A^0 + RT \ln[A]_\text{eq}) \]
\[ = (\mu_B^0 - \mu_A^0) + RT \ln[B]_\text{eq} + RT \ln[A]_\text{eq} \]
\[ = -RT \ln \frac{[B]_\text{eq}}{[A]_\text{eq}} \]
\[ \Delta G = 0 \]

Case 2: \([A]\) higher than its equilibrium point by \(\delta\).
\[ \Delta G = (\mu_B^0 + RT \ln[B]_\text{eq} - \delta) - (\mu_A^0 + RT \ln[A]_\text{eq} + \delta) \]
\[ = (\mu_B^0 - \mu_A^0) + RT \ln[B]_\text{eq} - RT \ln[A]_\text{eq} - \delta \]
\[ = -RT \ln \frac{[B]_\text{eq}}{[A]_\text{eq}} + \delta \]
\[ \Delta G < 0 \]

Both \(\ln\) terms are <1, therefore \(\Delta G\) is <0.

Case 3: \([B]\) higher than its equilibrium point by \(\delta\).
\[ \Delta G = (\mu_B^0 + RT \ln[B]_\text{eq} + \delta) - (\mu_A^0 + RT \ln[A]_\text{eq} - \delta) \]
\[ = (\mu_B^0 - \mu_A^0) + RT \ln[B]_\text{eq} - RT \ln[A]_\text{eq} + \delta \]
\[ = RT \ln \frac{[B]_\text{eq}}{[A]_\text{eq}} + \delta \]
\[ \Delta G > 0 \]

Both \(\ln\) terms are >1, therefore \(\Delta G\) is >0.

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 $\Delta G^\circ$. This energy barrier is 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 hexokinase, converts glucose to glucose-6-phosphate. The high energy of ATP is used to drive this unfavorable reaction by direct coupling – the phosphate group is transferred directly from ATP to glucose.

\[ \Delta G = \Delta G^\circ + RT \ln \left( \frac{[B]}{[A]} \right) \]

Indirect Coupling: By lowering the concentration of the product below its equilibrium position, a reaction can be made spontaneous; the $\Delta G$ becomes $< 0$. This generally implies that a reaction further down the pathway has a large negative $\Delta G^\circ$, such that the last compound in the pathway is kept below equilibrium concentration.

Example of Indirect Coupling:

In the pathway: $A \rightarrow B$:
- Concentration of $[A]$ is 1 mM under normal metabolic conditions.
- Standard free energy, $\Delta G^\circ$, of the first reaction ($A \rightarrow B$) is +5.75 kJ/mol.

What is the direction of the reaction if the concentration of $[B]$ is $10^{-5}$ M?

\[ \Delta G = \Delta G^\circ + RT \ln \left( \frac{[B]}{[A]} \right) \]

\[ \Delta G = 5.75 + RT \ln \left( \frac{10^{-5}}{1} \right) \]

\[ \Delta G = 5.75 + 2.5 \ln 10^{-2} \]

\[ \Delta G = 5.75 - 11.51 \]

\[ \Delta G = -5.76 \]
Electron counting rules for determining whether a redox reaction has occurred with organic molecules.

- Order of electronegativity: H<C<S<N<O. The atom that is more electronegative will be counted as having (or owning) the electrons or they are shared between two of the same atoms.

- For example, when you are looking at a C-C bond, the Carbon atoms share the electrons, so each carbon would be allotted one electron for a single bond, two for a double bond. When looking at a C-H bond, the carbon is more electronegative than H, so both electrons in the bond are counted for the carbon. When looking at a C-O bond, the oxygen is more electronegative and thus both electrons are counted towards the oxygen and none for the carbon.

Example 1: ethane CH₃-CH₃ → ethene CH₂=CH₂

Each carbon in ethane has 1 electron counted from the C-C bond and 2 each from the C-H bonds for a total of 7 per carbon or 14 for the molecule.

Each carbon in ethene has 2 electrons counted from the C=C bond and 2 each from the C-H bonds for a total of 6 per carbon or 12 for the molecule.

So to balance the equation it would be CH₃-CH₃ → CH₂=CH₂ + 2H⁺ + 2e⁻

While you can count electrons on the entire molecule, you only need to look at the portion of the molecule where a change has been made.

Example 2: alcohol to a ketone

Only the carbon with the –OH group changes, so you can focus just on the one carbon in this molecule.

In the alcohol you would count 1 electron for each C-C bond (2*1) plus 2 electrons for each C-H bond (2) and no electrons for the C-O bond (0). In sum it would be counted as "owning" a total of 4 electrons.

In the ketone, the carbon of interest still has the two C-C bonds (2*1) but now has a C=O bond (0) and no C-H bonds. In sum it has a total of 2 electrons and thus has been oxidized.