**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.



|  |  |
| --- | --- |
| **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).