Lecture Notes J: Chemical Equilibrium I

1) **Motivation: Binding/Unbinding of biological molecules**

How do we think about reactions where two molecules stick together/unstick together:

\[
\text{Protein + Drug} \rightleftharpoons \text{Protein:Drug}
\]

The larger the binding energy, the more Protein:Drug complex we expect to find.

- Duplex-DNA \rightleftharpoons \text{single strand DNA}

The DNA helix better not be too strongly bound or it will never unravel to expose its sequence for transcription.

2) **Law of Mass Action**

For a reaction: \( aA + bB \rightarrow cC + dD \)

\[
\frac{[C]^c [D]^d}{[A]^a [B]^b} = K
\]

Consider starting with 1 atm of \( H_2 \) and 1 atm of \( I_2 \). These will react according to the following reaction:

\[
H_2(g) + I_2(g) \rightarrow 2HI(g)
\]

At equilibrium, you find 0.213 atm each of \( H_2 \) and \( I_2 \) and 1.573 atm of \( I_2 \):

\[
\begin{align*}
\text{Initially} & \quad 1 \text{ atm} \quad 1 \text{ atm} \quad 0 \\
\text{At equilibrium} & \quad 0.213 \text{ atm} \quad 0.213 \text{ atm} \quad 1.573 \text{ atm}
\end{align*}
\]

If we then add 1 atm of \( I_2 \) (raising it to 1.213 atm), the system will adjust and at equilibrium, the pressures will be as follows,

\[
\begin{align*}
\text{Initially} & \quad 0.213 \text{ atm} \quad 1.213 \text{ atm} \quad 1.573 \text{ atm} \\
\text{At equilibrium} & \quad 0.0612 \text{ atm} \quad 1.061 \text{ atm} \quad 1.878 \text{ atm}
\end{align*}
\]
Concept
Consider the reaction: \( A_2 + B_2 \leftrightarrow 2AB \)
The reactants are mixed together and the following is a plot of the reactant and product concentrations with time:

What is the value of the equilibrium constant?

(A) \( 1/2 \)  (B) 1  (C) 2  (D) 4

\[
k = \frac{[AB]^2}{[A_2][B_2]} = \frac{1}{\left(\frac{1}{2}\right)\left(\frac{1}{2}\right)} = 4
\]

3) Equilibrium is dynamic

\( A_2 + B_2 \rightleftharpoons 2AB \)

Forward rate: \( k_1 [A_2] [B_2] \)

Reverse rate: \( k_1 [AB]^2 \)

At equilibrium:

Forward = Reverse rate

\[
k_1 [A_2] [B_2] = k_1 [AB]^2 \]

\[
\frac{[AB]^2}{[A_2][B_2]} = k = \frac{k_1}{k_1} \]

\[ k > 1 \rightarrow \text{Product} \] \( \rightarrow \text{Real} \] \( \text{spontaneous} \)

\[ k < 1 \rightarrow \text{Product} \] \( \rightarrow \text{Real} \] \( \text{not spontaneous} \)
4) Reaction Quotient

When the mass action expression is not equal to K, its value if denoted Q:

\[ aA + bB \rightarrow cC + dD \]

\[ Q = \frac{[C]^c[D]^d}{[A]^a[B]^b} \]

\( Q = K \) AT EQUIL.

\[ Q = \frac{[C]^c[D]^d}{[A]^a[B]^b} \]

\[ Q > K \] \( \Rightarrow \) \( \text{REACTION MOVES} \)

\[ Q < K \] \( \Rightarrow \) \( \text{REACTION MOVES} \)

Concept Test

Consider the reaction:

\[ \text{N}_2 + 3\text{H}_2 \leftrightarrow 2\text{NH}_3 \]

The equilibrium constant at 400°C is \( K = 0.5 \).

Suppose we make a mixture with the following concentrations:

\[ [\text{NH}_3] = 1.0 \text{M}, [\text{N}_2] = 1.0 \text{M}, [\text{H}_2] = 1.0 \text{M} \]

In which direction will the reaction go?

a) \( \text{N}_2 + 3\text{H}_2 \rightarrow 2\text{NH}_3 \)

b) \( \text{N}_2 + 3\text{H}_2 \leftarrow 2\text{NH}_3 \)

\[ Q = \frac{[\text{NH}_3]^2}{[\text{N}_2][\text{H}_2]^3} = \frac{1^2}{1^3} = 1 \]

5) Heterogenous Equilibrium (a reaction involving more than one phase)

\[ \text{C(s)} + \text{CO}_2(g) \leftrightarrow 2\text{CO}(g) \]

\[ K = \frac{[\text{CO}]^2}{[\text{CO}_2]} \]

As long as there is some A + solid \( \rightarrow \) B

\[ K = \frac{[\text{B}]}{[\text{A}]} \]

\[ \text{AMOUNT OF SOLID DOESN'T MATTER} \]
Concept Test

Consider the equilibrium expression for the following reaction:

\[ \text{CaCO}_3(s) \rightleftharpoons \text{CaO}(s) + \text{CO}_2(g) \]

Which of the following is true:

\( \Rightarrow \)
a) The ratio of \( \text{CaO}(s) \) to \( \text{CaCO}_3(s) \) will be the same in all samples of this solid.

\[ Q = \frac{P_{\text{CO}_2}}{P_{\text{CaO}}} = k \]

\[ K = P_{\text{CO}_2} \]

b) The vapor pressure of \( \text{CO}_2(g) \) above a mixture of \( \text{CaCO}_3(s)/\text{CaO}(s) \) is independent of the relative amount of these two solids.

True  burn solids present, so \( K = P_{\text{CO}_2} \)

6) Relation between the equilibrium constant and \( \Delta G^0 \).

\[ K = \frac{P_{\text{CO}_2}}{P_{\text{CaO}}} \]

\[ K = e^{-\frac{\Delta G^0}{RT}} \]

\[ \Delta G^0 = \Delta H^0 - T \Delta S^0 \]

\[ RT < \Delta G^0 \quad K < 1 \]

\[ \text{POOR TAKEN} \quad \text{POOR TAKEN} \]

\[ K \geq 1 \]

\[ \text{POOR TAKEN} \quad \text{POOR TAKEN} \]

\[ K \geq 1 \]
The binding constant for a drug-protein interaction is the equilibrium constant for the reaction:

\[
\text{Protein + Drug} \rightleftharpoons \text{Protein:Drug} \quad K_{\text{binding}} \quad \Delta G^\circ_{\text{binding}}
\]

How big must the binding energy (\(\Delta G^\circ_{\text{binding}}\)) be for \(K_{\text{binding}}\) to be equal to 1000 at body temperature?

\[
K = e^{-\Delta G \text{ / } RT}
\]

\[
1000 = e^{-\Delta G \text{ / } RT}
\]

\[
\ln(1000) = -\Delta G \text{ / } RT
\]

\[
\Delta G = -\ln(1000) \cdot RT
\]

\[
= -6.9 \cdot RT \approx -17.8 \text{ kJ / mol}
\]

What range of \(\Delta G^\circ_{\text{binding}}\) gives \(K\) between 1/1000 and 1000?

\[
\ln(K) = -\Delta G \text{ / } RT
\]

\[
\Delta G = -\ln(K) \cdot RT
\]
Concept
If $\Delta G^\circ_{\text{binding}}$ is doubled, what happens to $K_{\text{binding}}$?

a) $K$ stays the same  
   b) new $K = 10,000$  
   c) new $K = 100,000$  
   d) new $K = 1000e^2$

$$K = e^{-\frac{\Delta G^\circ}{RT}} \quad K' = e^{-\frac{2\Delta G^\circ}{RT}}$$
$$K' = (e^{-\Delta G^\circ/RT})^2 = (1000)^2 = (10^3)^2 = 10^6$$

Concept
If $\Delta G^\circ_{\text{binding}}$ is positive, no drug binds to the protein.  

true  
false

7) Properties of Equilibrium Constants:
Consider the following reactions
$$A + 2B \leftrightarrow C$$

$$K_{\text{original}} = \frac{[C]}{[A][B]^2} = e^{-\frac{\Delta G^\circ}{RT}}$$

Multiply reaction coefficients by $n$
$$2A + 4B \leftrightarrow 2C$$

$$K_{\text{new}} = \frac{[C]^2}{[A]^2[B]^4} = (K_{\text{original}})^2 = e^{-2\frac{\Delta G^\circ}{RT}} = (e^{-\Delta G^\circ/RT})^2$$

Reverse reaction
$$C \leftrightarrow A + 2B$$

$$e^{-x} = \frac{1}{e^x}$$

$$K_{\text{new}} = \frac{[A][B]^2}{[C]} = K_{\text{original}} = e^{-\frac{-\Delta G^\circ}{RT}} = (e^{-\Delta G^\circ/RT})^{-1}$$
Add two reactions

1) \[ A + B \rightleftharpoons C \quad \Delta G_1 \]
2) \[ B + C \rightleftharpoons D \quad \Delta G_2 \]
3) \[ A + 2B \rightleftharpoons D \quad \Delta G_3 = \Delta G_1 + \Delta G_2 \]

\[
k_1 = \frac{[C]}{[A][B]} \quad k_2 = \frac{[D]}{[B][C]} \quad k_3 = \frac{[D]}{[A][B]^2} = k_1 k_2
\]

Concept
From a chemical handbook you find the equilibrium constants that give the concentrations of Iodine vapor above water and oil:

\[ I_2(\text{water}) \rightleftharpoons I_2(g) \quad K_{\text{water}} \]
\[ I_2(\text{oil}) \rightleftharpoons I_2(g) \quad K_{\text{oil}} \]

But you want the equilibrium constant for the partitioning of I_2 between water and oil

\[ I_2(\text{water}) \rightleftharpoons I_2(\text{oil}) \quad K \]

You can obtain it as:

- a) \( K = K_{\text{water}} K_{\text{oil}} \)
- b) \( K = K_{\text{water}} K_{\text{oil}} \)
- c) \( K = \frac{K_{\text{water}}}{K_{\text{oil}}} \)
- d) \( K = \frac{K_{\text{oil}}}{K_{\text{water}}} \)

Concept
Hemoglobin can bind up to 4 oxygen molecules. If the equilibrium constant for binding a single oxygen is \( K_1 \), what is the equilibrium constant for binding 4 oxygen molecules?

- a) \( 4K_1 \)
- b) \( K_1^4 \)
- c) \( \sqrt[4]{K_1} \)
- d) \( K_1^2 \)