Fundamentals of Distribution Separations (I)  
(01/09/15)

1. Introduction to Chemical Separation

2. Principles of distribution equilibria  
   -- Driving force for separative displacement

3. Intermolecular interactions  
   -- Major factors controlling equilibrium between phases

This is the base for understanding chemical separations such as chromatography and gel electrophoresis.
1. Introduction to Chemical Separations

a. The essential feature of separations:

b. Driving force for separative transport

c. Limitations for separation

d. Analytical and Preparative Separations
What is Chemical Separation? (I)

1. A complete separation of a mixture of chemical species:

\[(a + b + c + d + e + \ldots) \rightarrow (a) + (b) + (c) + (d) + (e) + \ldots\]

2. A partial separation of a mixture of chemical species:

\[\begin{align*}
(a + b + c + d + e + \ldots) & \rightarrow (a) + (b + c + d + e + \ldots) \\
(a + b + c + d + e + \ldots) & \rightarrow (a + b) + (c + d + e) + \ldots
\end{align*}\]

3. The essential feature of separations:

Components must be transported and redistributed in space in order to realize the goals of the separative operation.
What is Chemical Separation? (II)

4. The transport basics do not stand alone:
   (a) Equilibrium (driving force),
   (b) The macroscopic, microscopic, and molecular structure of the system
   (c) The details of flow
   (d) Mechanics of sample handling

5. Limitations:
   (a) Physical limitations: parameter controlling (e.g., T, P)
   (b) Chemical limitations:
       (i) equilibrium,

\[
\begin{array}{c}
A_1 \\
\leftrightarrow \\
A_2
\end{array}
\]
(ii) thermodynamic limitations: the second law of thermodynamics

Spontaneous direction of change: Entropy: \( \Delta S > 0 \) for an isolated system

\[
(a) + (b) + (c) + (d) \xrightarrow{\text{Mixing (\( \Delta V=0 \))}} (a + b + c + d)
\]

Spontaneous direction of change: Gibbs free energy: \( \Delta G < 0 \)

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

Enthalpy: \( H = U + PV \)

The first law of thermodynamics \( \rightarrow \) Internal energy: \( \Delta U = q + w \)

(a) external work, (b) heat, and (c) dilution

Dilution: \( \Delta S = n R \ln \frac{V_{\text{final}}}{V_{\text{initial}}} \)
Question:

Calculate the entropy change that accompanies the separation of four oligonucleotides from one another in an aqueous containing 0.1 μmole of each. When separated, each component occupies one-quarter of original volume. Deduce from your results whether or not the separation is thermodynamically spontaneous.

four oligonucleotides: (1) AAA-TCA-GA; (2) AGA-TAC-GAT-ATA; (2) ATA-CAC-TGT-AGA-TTT-CTA; (4) AAC-CTC-GTT-AGA-TCC-CTA-TCA

Dilution: \[ \Delta S = n \, R \, \ln \frac{V^{\text{(final)}}}{V^{\text{(initial)}}} \]
What is Chemical Separation? (IV)

6. No absolute separations
   (1) Separation limitations
   (2) Detection limitations

7. General methods
   (1) Named after underlying forces or phenomena:
       extraction, adsorption, crystallization, precipitation, ion exchange,
       diffusion, sedimentation, centrifugation.
   (2) Named after the forms of operation:
       Chromatography, distillation, zone melting, filtration, dialysis, elutriation,
       field-flow fractionation, electrostatic precipitation.
   (3) Both
       Adsorption chromatography, ion exchange chromatography,
       extraction chromatography
Analytical and Preparative Separations (I)

1. General goals of separation: preparative and analytical

2. Preparative separation: for drugs, fuels, metals, chemical feedstock for synthesis....
   Characteristics: (i) continuous in operation and (ii) large in scale
   distillation, extraction, smelting, (many tons per day)
   preparative liquid chromatography (biotechnology industry).

Crude fractionation tower at the Phillips Oil Refinery in Woods Cross, Utah. In this crude fractionator, 25,000 barrels per day of incoming crude oil is divided into six fractions by distillation. (Photo by Alexis Kelner.)

Preparative scale liquid chromatography unit with 6 ft (1.8 m) long column (in center) having an inner diameter of 6 in (15 cm). Up to 2 L of sample solution can be injected and processed in a single 90-min run. (Courtesy Thomas J. Filipi and Whatman Chemical Separation Division.)
Analytical and Preparative Separations (II)

2. Analytical separations:

Goal: understanding of mechanisms of separation, sample analysis, and for subsequent detection.

Characteristics: (i) High purity and (ii) small scale

😊 Chromatography techniques

(i) A physical separation technique

(ii) Components partition between two phases:
  Stationary phase: does not move
  Mobile phase: does move

(iii) Solutes separated in the two phases due to differences in how they interact with the phases.
Group Projects

A. Michelle Reid and Robin Kemperman
   Quantitative detection of Hg in fish

B. Weijia Niu and Jiamin Liang
   Rapid detection of HIV in blood samples

C. Emily Louise Gil and Jeremy Koelmel
   Detection of prostate cancer

D. Qiao Ruan and Juliette Experton.
   Diagnosis of brain-eating amoeba infections

E. Song Yang and Yindong
   Detection of single-nucleotide a single human cell

F. Kaitlyn Flower; Xigao Chen
   Real-time measurement of the level of a specific m-RNA in single cells
2. Principles of distribution equilibria
   -- Driving force for separative displacement

Two Important Classes of Equilibrium

(a) Mechanical equilibrium: the resting place of macroscopic bodies

(b) Molecular equilibrium: the spatial distribution of molecules and colloids at equilibrium
1. With macroscopic bodies, it is unnecessary to worry about the thermal (Brownian) motion, which greatly complicates the equilibrium in microscopic (molecular) systems.

2. Entropy effect is negligible

3. Mechanical equilibrium is subject to the simple criterion (no balanced forces)

\[ \frac{dp}{dx} = 0, \text{ potential energy } p \]
Molecular Equilibrium in Closed Systems (I)

A closed system is one with boundaries across which no matter may pass, either in or out. However other changes may occur, including expansion, contraction, heating and cooling.

\[ dU = q + w \]  
\[ w = -p \cdot dV \]
\[ dS \geq \frac{q}{T} \]
\[ dU \leq T \cdot dS - p \cdot dV \]
\[ G = H - TS = U + pV - TS \]
\[ dG \leq -S \cdot dT + V \cdot dP \]
Molecular Equilibrium in Closed Systems (II)

\[ dG \leq -S \cdot dT + V \cdot dP \]

At the typical separation conditions, T and p are constant.

Then, \( dG \leq 0 \)

\( dG = 0 \), ............ molecular equilibrium

- Ice-water equilibrium
  - Reversible, \( dG = 0 \)

- Spontaneous irreversible
  - Melting, \( dG < 0 \).
Molecular Equilibrium in Open Systems (I)

An open system is one which can undergo all the changes in the close system. In addition, it allows mass transfer across its boundaries.

\[ dG = -S \, dT + V \, dP \quad \text{Equilibrium point for a close system} \]

\[ dG = \left( \frac{\partial G}{\partial n_i} \right)_{T, p, n_i} \, dn_i \quad dn_i \text{ mole of } i \text{ molecules enter the system, } T \text{ & } p \text{ are constant,} \]

\[ \mu_i = \left( \frac{\partial G}{\partial n_i} \right)_{T, p, n_i} \quad \text{Chemical potential} \]

\[ dG = \mu_i \, dn_i \]
Molecular Equilibrium in Open Systems (I)

\[ dG = \sum \mu_i dn_i \]

General equilibrium expression

\[ dG = -S \cdot dT + V \cdot dP + \sum \mu_i dn_i \quad \text{(if } T, p \text{ are allowed to vary)} \]

entering: \(dn\) is positive
Leaving: \(dn\) is negative

Two-phase open system:

\[ \alpha + \beta \longrightarrow \text{a close system} \]

For transfer component \(i\) from \(\alpha\) to \(\beta\) at equilibrium

\[ dG = dG^\beta + dG^\alpha = (\mu_i^\beta - \mu_i^\alpha) \ dn_i = 0 \]

\[ \mu_i^\beta = \mu_i^\alpha \]
The Nature of Chemical Potential ($\mu_i$)

Chemical potential, $\mu_i$, for solute $i$ in give phase depends on two factors (a) intrinsic thermodynamic affinity of solute to the phase, (b) dilution of Solute (affect $\mu_i$ through entropy: entropy of dilution).

$$\mu_i = \mu_i^0 + RT \ln c_i$$

$\mu_i^0$: standard-state chemical potential

$$\left(\frac{c_i^\beta}{c_i^\alpha}\right) = \exp\left(-\frac{\Delta\mu_i^0}{RT}\right)$$

$$\Delta\mu_i^0 = \mu_i^0,\beta - \mu_i^0,\alpha$$

$$K = \exp\left(-\frac{\Delta\mu_i^0}{RT}\right)$$, distribution coefficient

$$\mu_i = \mu_i^0 + RT \ln c_i$$

$\gamma_i$: active coefficient

$$\mu_i = \mu_i^0 + RT \ln \gamma_i c_i$$

for gas

$$\mu_i = \mu_i^0 + RT \ln \rho_i$$
Example: Sufficiently diluted, ethyl acetate has an equilibrium concentration at 20 °C in an isobutanol-rich phase that is 7.20 times higher than that in a water-rich phase (that is, the distribution coefficient $K$ for isobutanol/$\text{H}_2\text{O}$ is 7.20). What is the value of $\Delta \mu^o$ for the transfer of ethyl acetate from water to isobutanol solutions?
Equilibrium in External Fields

Common fields: electric, magnetic, sedimentation

\[ dG = -S \* dT + V \* dP + \Sigma \mu_i \, dn_i \]

\[ dG = -S \* dT + V \* dP + \Sigma (\mu_i^{\text{int}} + \mu_i^{\text{ext}}) \, dn_i \]

Electric field

\[ dG = dG^{\beta} + dG^{\alpha} \]

\[ = (\mu_i^{\text{int}, \beta} + \mu_i^{\text{ext}, \beta} - \mu_i^{\text{int}, \alpha} - \mu_i^{\text{ext}, \alpha}) \, dn_i = 0 \]

\[ \mu_i^{\text{int}} = \mu_i^{0} + RT \ln c_i \]
Equilibrium in External Fields (II)

\[
\left( \frac{c_i^\beta}{c_i^\alpha} \right) = \exp \left( \frac{-\Delta \mu_i^0 - \Delta \mu_i^\text{ext}}{RT} \right)
\]

\[
\Delta \mu_i^0 = \mu_i^\beta - \mu_i^\alpha
\]

\[
\Delta \mu_i^\text{ext} = \mu_i^\text{ext, } \beta - \mu_i^\text{ext, } \alpha
\]

\[
K = \exp \left( \frac{-\Delta \mu_i^0 - \Delta \mu_i^\text{ext}}{RT} \right)
\]

Comparison: \(\Delta \mu_i^0\) & \(\Delta \mu_i^\text{ext}\)

(1) Equal in a mathematical sense

(2) Dissimilar in a physical sense: changes at phase boundaries

\[
\begin{cases} 
\Delta \mu_i^0, \text{abrupt} \\
\Delta \mu_i^\text{ext}, \text{continuous}
\end{cases}
\]
The Nature of Chemical Potential ($\mu_i^0$)

$$\Delta\mu_i^0 = \Delta\hat{H}_i^0 - T\Delta\hat{S}_i^0$$

$\Delta\hat{H}_i^0$, $\Delta\hat{S}_i^0$: the partial molar enthalpy and entropy under standard conditions.

$\Delta\hat{S}_i^0$: randomness of the immediate molecular environment of a species

For general separation system involving a partition of components between phases

$$|\Delta\hat{H}_i^0| >> |T\Delta\hat{S}_i^0|$$

Intermolecular interactions
What we have learnt:

1. Two Classes of Equilibria
2. Molecular Equilibrium in Closed Systems
3. Molecular Equilibrium in Open Systems
4. The Nature of Chemical Potential ($\mu_i$)
5. Equilibrium in External Fields
6. Comparison of $\Delta \mu_i^0$ and $\Delta \mu_i^{\text{ext}}$
7. The Nature of Chemical Potential ($\mu_i^0$)