C8863 Free Energy Calculations

Lesson 4
Equilibrium - Practicals

JS/2022 Present Form of Teaching: Rev1

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Overview

macroworld | **microworld**

states

(thermodynamic properties, G, T,...)

phenomenological thermodynamics

equilibrium (equilibrium constant)

kinetics (rate constant)

free energy

(Gibbs/Helmholtz)

partition function

statistical thermodynamics

microstates

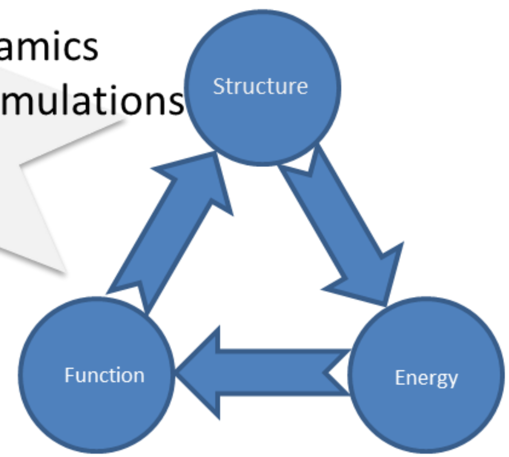
(mechanical properties, E)

Description levels (model chemistry):

- quantum mechanics
  - semiempirical methods
  - ab initio methods
  - post-HF methods
  - DFT methods
- molecular mechanics
- coarse-grained mechanics

Simulations:

- molecular dynamics
- Monte Carlo simulations
- docking
- ...



microstate ≠ microworld

Revisions

- At the given temperature and definition of the standard state, the **equilibrium constant** is determined only by the **standard reaction Gibbs energy**:

$$\Delta G_r^0 = -RT \ln K$$

- The equilibrium constant ***K*** is proportional to activities of all compounds in the equilibrium.

$$K = \prod_{i=1}^{N} a_{r,i}^{v_i}$$

Sign convention for stochiometric coefficients ν_i

products (end state)	- positive value
reactants (initial state)	- negative value

- For ideal (diluted) solutions, activities can be approximated by molar concentrations:

$$K \approx \prod_{i=1}^{N} [X_i]_r^{v_i}$$

Equilibrium

multiple chemical processes

Complex Chemical Mixtures

Composition of the chemical system with multiple reactions is determined by a system of equations. These equations include

- **each equilibrium process**
- **balance of all reacting compounds**

Example:

$$A + 2B \rightleftharpoons AB_2 \qquad K_1 = \frac{[AB_2]}{[A][B]^2}$$

$$2A + C \rightleftharpoons A_2C \qquad K_2 = \frac{[A_2C]}{[A]^2[C]}$$

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equilibria

Unknowns:

$[A], [B], [C], [AB_2], [A_2C]$

$\rightarrow$ 5 equations

initial amount

$$c_{0,A} = [A] + [AB_2] + 2[A_2C]$$

$$c_{0,B} = [B] + 2[AB_2]$$

$$c_{0,C} = [C] + [A_2C]$$

balance

Numerical Solution I

Example:

$$A + 2B \rightleftharpoons AB_2 \qquad K_1 = \frac{[AB_2]}{[A][B]^2}$$

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balance

Only **two components are independent**:

- five components
- three balances

Numerical Solution I, cont.

Find [A] and [B] such that the last two equations are satisfied:

1. Determine dependent parameters:

$$c_{0,A} = [A] + [AB_2] + 2[A_2C]$$

$$c_{0,B} = [B] + 2[AB_2]$$

$$c_{0,C} = [C] + [A_2C]$$

$$[AB_2] = \frac{1}{2} c_{0,B} - \frac{1}{2}[B]$$

$$[A_2C] = \frac{1}{2} c_{0,A} - \frac{1}{2}[A] - \frac{1}{2}[AB_2]$$

$$[C] = c_{0,C} - [A_2C]$$

2. Solve system of independent equations: $f(\boldsymbol{X}) = \boldsymbol{0}$

$$K_1 = \frac{[AB_2]}{[A][B]^2} \qquad 0 = \log([AB_2]) - \log([A]) - 2\log([B]) - \log(K_1)$$

$$K_2 = \frac{[A_2C]}{[A]^2[C]} \qquad 0 = \log([A_2C]) - 2\log([A]) - \log([C]) - \log(K_2)$$

Octave, Matlab: lsqnonlin

Numerical Solution II

Find concentration of all components such that all equations are satisfied:

$[A], [B], [C], [AB_2], [A_2C]$

1. Solve system of equations: $f(\boldsymbol{X}) = \boldsymbol{0}$

$$c_{0,A} = [A] + [AB_2] + 2[A_2C] \qquad 0 = [A] + [AB_2] + 2[A_2C] - c_{0,A}$$

$$c_{0,B} = [B] + 2[AB_2] \qquad 0 = [B] + 2[AB_2] - c_{0,B}$$

$$c_{0,C} = [C] + [A_2C] \qquad 0 = [C] + [A_2C] - c_{0,C}$$

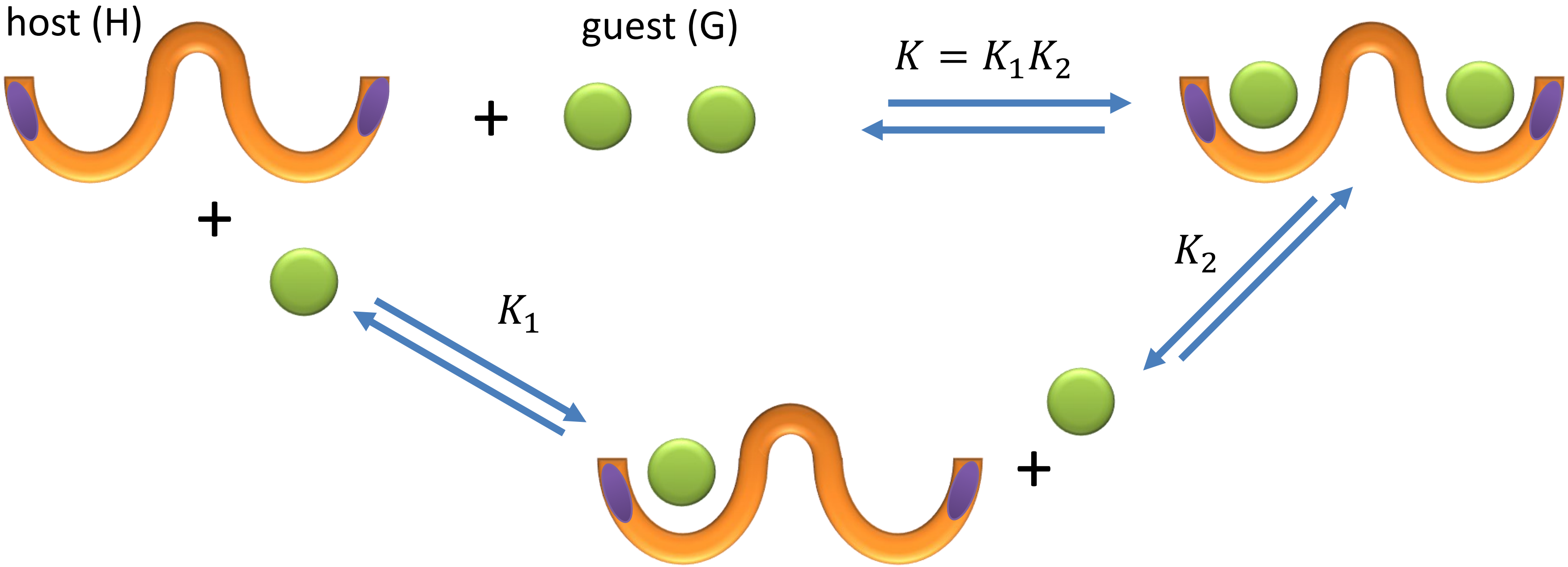
$$K_1 = \frac{[AB_2]}{[A][B]^2} \qquad 0 = \log([AB_2]) - \log([A]) - 2\log([B]) - \log(K_1)$$

$$K_2 = \frac{[A_2C]}{[A]^2[C]} \qquad 0 = \log([A_2C]) - 2\log([A]) - \log([C]) - \log(K_2)$$

this might be numerically less stable

Problems

Host with two binding sites



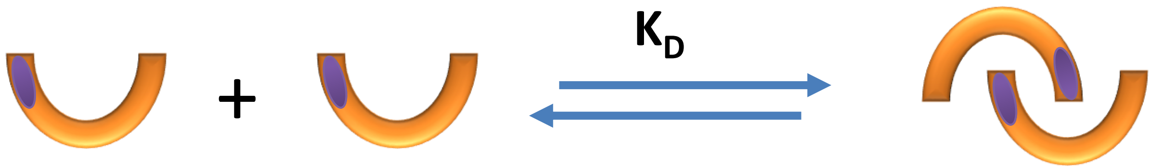
$$H + G \overset{K_1}{\rightleftharpoons} HG \qquad\qquad HG + G \overset{K_2}{\rightleftharpoons} HG_2$$

Note: binding sites are chemically equivalent

Host with two binding sites, tasks

1. Are K_1 and K_2 equal?
2. Determine the composition of the reaction mixture for $c_{0,H} = 1\ mM$ titrated by guest up to 6 molar equivalents for:
   - $K_1 = 10^2$
   - $K_1 = 10^5$
3. Determine Job Plots for $c_{0,H} = 1\ mM$ and
   - $K_1 = 10^1$
   - $K_1 = 10^2$
   - $K_1 = 10^3$
   - $K_1 = 10^4$

Host Dimerization



$$2H \overset{K_D}{\rightleftharpoons} H_2$$

- What is K_D for dimerization process of the host? Selected 1H NMR signal (fast exchange) undergoes the following change during the sample dilution.

  TBA

References

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