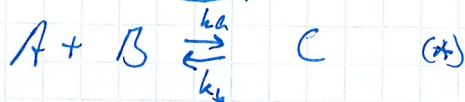


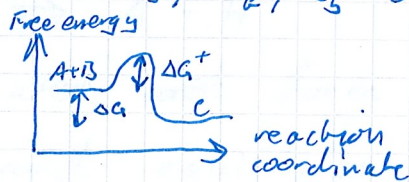
Chemical forces and self assembly.⊗ Introduction

Nelson Chapter 8, 3.2.4, 6.6.2, 10.3-4, (8.5), 8.6  $\Rightarrow$  by SW  
 Problems 8.2, 8.3, 8.5, 8.6

Slides Krebs cycle, ATP-ADP, photosynthesis, signalling, GRN

- Chemical reactions

- reaction rate is proportional to concentration of reactants (Law of mass action)
- rate constants,  $k_f, k_b$  depends on activation barriers



- equilibrium concentrations depend on potential difference
- 'formalized' from statistical mechanics via chemical potentials and 'forces'.

Deterministic description of (\*) (Meanfield)

$$\frac{d c_A}{dt} = -k_f c_A c_B + k_b c_C \quad (\text{concentrations})$$

Stochastic descriptions of (\*)

$$\begin{aligned} P_f(t, t+dt) &= k_f \cdot \frac{N_A}{V} \cdot \frac{N_B}{V} \Rightarrow \begin{cases} N_A \rightarrow N_A - 1 \\ N_B \rightarrow N_B - 1 \\ N_C \rightarrow N_C + 1 \end{cases} \\ P_b(t, t+dt) &= k_b \cdot \frac{N_C}{V} \end{aligned} \quad (\# \text{ Number of molecules})$$

Solved by e.g. Gillespie algorithm:

- select reaction randomly from probabilities
- step forward in time via random distribution



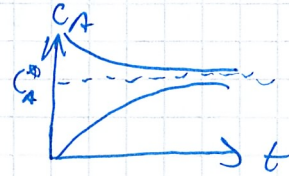
Statistical equilibrium: forward rate equals backward rate

$$\frac{dC_A^*}{dt} = 0 \Rightarrow \frac{C_C^*}{C_A^* \cdot C_B^*} = \frac{k_f}{k_b} \equiv K_{eq} \text{ (equilibrium constant)}$$

↑ depends on T

$$C_A < C_A^* \Rightarrow C_A \uparrow, \quad C_A > C_A^* \Rightarrow C_A \downarrow$$

∴ equilibrium stable fixed point



Multiple reactions can provide complex dynamical behavior

slide TGF $\beta$  pathway

### Dissociation 8.3



- deprotonated and form of ions
- rates and equilibrium depends on pH
- can be used to determine protein composition

slide auxin

### Self assembly 8.4, 8.6

- hydrophobicity (lipidarity) can drive formation of organized structures (decreasing free energy)

slide micelles, membranes

### Michaelis-Menten 10.3, 10.4

Many reactions will not occur spontaneously



Enzymes catalyze reactions "A + E  $\rightarrow$  B + E"



$$\frac{dB}{dt} = \frac{V_{max} A}{K + A}$$

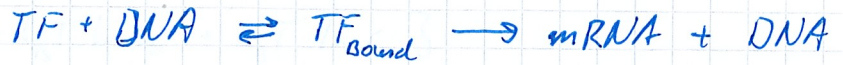
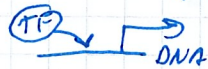


saturation

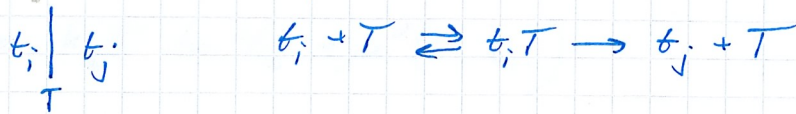


M-M cont

- gene regulation



- mediated transport



slides cell cycle, lac-operon

Reaction-Diffusion

Chemical reactions combined with diffusion can create spatial concentration patterns (Exercise)

slides Brusselator, Turing/PW model, (Turing)

⊗ Chemical potential (8.1)

System with energy  $E$  and  $N_\alpha$  particles of species  $\alpha$  ( $\alpha=1,2,\dots$ )

Entropy  $S(E, \{N_\alpha\})$

Temperature  $\frac{1}{T} = \left. \frac{dS}{dE} \right|_{N_\alpha; \alpha=1,2,\dots}$

Chemical Potential  $\mu_\alpha = -T \left. \frac{dS}{dN_\alpha} \right|_{E, N_\beta, \beta \neq \alpha}$

$\mu_\alpha$  'availability' of particle species  $\alpha$

Ideal gas example ( $S(E, N)$ )

$$S = k_B \ln \left[ \frac{2\pi^{3N/2}}{(2\pi k)^N} (2m E_{kin})^{3N/2} \frac{V^N}{N!} (2\pi k)^{-3N} \frac{1}{2} \right] \quad \begin{matrix} \text{Eq 6.6} \\ \text{Sakur-Tetrode} \\ \text{formula} \end{matrix}$$

molecules have internal energy  $\epsilon$

$$E = E_{kin} + \sum_\alpha N_\alpha \epsilon_\alpha$$

$$\left. \frac{dS}{dN} \right|_E = \left. \frac{dS}{dN} \right|_{E_{kin}} - E \left. \frac{dS}{dE_{kin}} \right|_N \stackrel{\text{8.A}}{=} k_B \frac{3}{2} \ln \left[ \frac{1}{3\pi} \frac{m}{4^2} \frac{E_{kin}}{N} \left( \frac{V}{N} \right)^{2/3} \right] - E k_B \frac{3N}{2E_{kin}}$$

$$\left\{ \frac{E_{kin}}{N} = \frac{3}{2} k_B T, C = \frac{N}{V} \right\} \quad \ln N! = N \ln N - N$$



(Ideal gas cont.)

$$\mu = -T \frac{dS}{dN} \Big|_{\epsilon} = \epsilon + k_B T \ln c - \frac{3}{2} k_B T \ln \frac{m k_B T}{2\pi \hbar^2} \\ \left\{ -k_B T \ln c_0 + k_B T \ln c_0 \right\}$$

$$\mu = k_B T \ln c/c_0 + \mu^{\circ}(T, \epsilon, \dots)$$

ideal gas/dilute solution

$$\mu^{\circ}(T) = \epsilon - \frac{3}{2} k_B T \ln \frac{m k_B T}{2\pi \hbar^2 c_0^{3/2}} \left( = \epsilon - k_B T \ln(k_B T) \right)$$

ideal gas

$\mu^{\circ}$  - standard chemical potential

- depends on  $T, \epsilon, c_0, \dots$

- 'found' in tables

$c_0$  - reference concentration, (aqueous solutions)  $c_0 = 1 \text{ mole/L} =$

-  $c_x / M \equiv [X]$  (Mol/L)

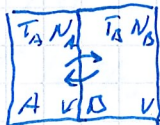
= 1 Molar

### chemical equilibrium

$\mu_{\alpha} = \mu_{\beta}$   $\alpha, \beta$  system is chemical equilibrium

**example**

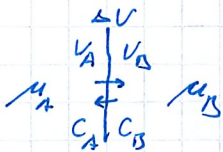
Two containers that exchange Energy and particles



Maximize Entropy  $\begin{cases} T_A = T_B \\ \mu_A = \mu_B \quad (c_A = c_B) \end{cases}$

**example**

Electrochemical potential,  $\mu^{\circ} \rightarrow \mu^{\circ} + qV(\epsilon)$



$$\mu_A = \mu_B : k_B T \ln c_A/c + \mu^{\circ} + qV_A = k_B T \ln c_B/c + \mu^{\circ} + qV_B$$

$$\Delta(\ln c) = -q \Delta V / k_B T \quad (\text{Nernst relation}) \\ \text{Eq. 4.26}$$

**Boltzmann**

$\therefore \mu$ : A molecular species will be highly available for chemical reactions if its concentration  $c$  is big or its internal energy  $\epsilon$  is big, as measured by  $\mu = -T \frac{dS}{dN} \Big|_{\epsilon}$

$$\mu = k_B T \ln c/c_0 + \mu^{\circ}(T, \epsilon) \quad \text{dilute solution}$$



# Boltzmann distribution with particle exchange



$$P_a = \Omega_B(E_{tot} - E_a) P_0 \propto e^{S_B(E_{tot} - E_a, N - N_a) / k_B T}$$

$$S_B(E, N) = S_B(E - E_a, N - N_a) = S_B(E, N) - E_a \frac{dS_B}{dE} - N_a \frac{dS_B}{dN} + \dots$$

$\sim 1/T \cdot E$        $\sim -1/T \cdot N$

$$P_j = \{ \text{prob. of states w. } E_j, N_j \} = \frac{e^{-(E_j - \mu N_j) / k_B T}}{\sum_i e^{-(E_i - \mu N_i) / k_B T}}$$

$\therefore$  {Gibbs grand canonical} distribution

## Chemical reactions (8.2)

Two state system  $X_1 \rightleftharpoons X_2$



$$\left. \begin{matrix} N_1, N_2 \\ E_1 < E_2 \end{matrix} \right\} \mu_1, \mu_2$$

isolated system  $\Delta S_{tot} = -\Delta N_1 \frac{\Delta S}{\Delta N_1} + \Delta N_2 \frac{\Delta S}{\Delta N_2} = (\mu_1 - \mu_2) / T$

{define  $\Delta G \equiv \mu_2 - \mu_1$ } =  $-\frac{\Delta G}{T}$

increase entropy  $\left\{ \begin{matrix} \Delta G < 0 & (\mu_1 > \mu_2) \\ \Delta G > 0 & (\mu_1 < \mu_2) \end{matrix} \right\} \begin{matrix} 1 \rightarrow 2 & \text{forward reaction} \\ 2 \rightarrow 1 & \text{backward reaction} \end{matrix}$

$$\mu = k_B T \ln c/c_0 + \mu^0$$

equilibrium  $0 = \Delta G = k_B T \ln c_2/c_0 + \mu_2^0 - k_B T \ln c_1/c_0 - \mu_1^0$

$$\ln(c_2/c_1) = (\mu_1^0 - \mu_2^0) / k_B T$$

$$\frac{c_2}{c_1} = e^{-(\mu_2^0 - \mu_1^0) / k_B T} \equiv K_{eq}$$

equilibrium constant

$$pK \equiv -\log_{10} K_{eq}$$

$\Delta G \equiv \mu_{prod} - \mu_{react} \Rightarrow$

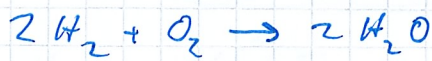
- $-\Delta S$  (entropy)      isolated
- $\Delta F$  (Helmholtz free energy)      closed
- $\Delta G$  (Gibbs free energy)      open

↑  
chemical force (general)  
'drives reactions'



example

Burning hydrogen



$$\Delta G_r \equiv 2\mu_{H_2O} - 2\mu_{H_2} - \mu_{O_2} \quad (\mu = k_B T \ln c/c_0 + \mu^0)$$

equilibrium  $0 = \frac{\Delta G_r}{k_B T} = \frac{2\mu_{H_2O}^0 - 2\mu_{H_2}^0 - \mu_{O_2}^0}{k_B T} + \ln \left[ \left(\frac{c_{H_2O}}{c_0}\right)^2 \left(\frac{c_{H_2}}{c_0}\right)^{-2} \left(\frac{c_{O_2}}{c_0}\right)^{-1} \right]$

$$\frac{c_{H_2O}^2}{c_{H_2}^2 \cdot c_{O_2}} = K_{eq} c_0, \quad K_{eq} \equiv e^{-(2\mu_{H_2O}^0 - 2\mu_{H_2}^0 - \mu_{O_2}^0)/k_B T}$$

(Ideal gas)  $\frac{\mu^0}{k_B T} = \frac{\epsilon}{k_B T} - \ln \left( \frac{m k_B T}{2\pi h^2 c_0} \right)^{3/2}$

$$K_{eq} = \underbrace{e^{-(2\epsilon_{H_2O} - 2\epsilon_{H_2} - \epsilon_{O_2})/k_B T}}_A c_0 \underbrace{\left( \frac{2\pi h^2}{k_B T} \cdot \frac{m_{H_2O}^2}{m_{H_2}^2 m_{O_2}} \right)^{3/2}}_B$$

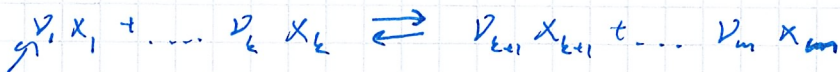
T small  $K_{eq} \gg 1 \quad \frac{c_{H_2O}^2}{c_{H_2}^2 c_{O_2}} \gg 1 \Rightarrow H_2O$

T large  $K_{eq} \ll 1 \quad -11- \ll 1 \Rightarrow H_2 + O_2$

(room T)  $K_{eq}^{Tr} = e^{457 \text{ (kJ/mole)} / k_B T}$

4 kg ~ 2000 mole  $H_2$    
 16 kg ~ 1000 mole  $O_2$    
  $\left\{ \begin{array}{l} Vol \sim 22 m^3 \\ k_B T_r \sim 1.5 \text{ kJ/mole} \end{array} \right\} \Rightarrow \left\{ \begin{array}{l} 4 H_2 \\ 2 O_2 \end{array} \right\}$  at equilibrium

General reaction



stoichiometric coefficients (order)

$$\mu_k = -T \frac{dS}{dN_k} \Big|_{E, N_{j \neq k}} = k_B T \ln c_k/c_0 + \mu_k^0(T, \epsilon_k)$$

$$\Delta G \equiv -\nu_1 \mu_1 - \dots - \nu_k \mu_k + \nu_{k+1} \mu_{k+1} + \dots + \nu_m \mu_m$$

\*  $\Delta G_r$  free energy change for one forward step

$\Delta G < 0 \Rightarrow$  forward

$\Delta G > 0 \Rightarrow$  backward

$\Delta G = 0 \Rightarrow$  equilibrium

$\Delta G^0 \equiv -\nu_1 \mu_1^0 - \dots + \nu_m \mu_m^0$  standard free energy change