Physical Principles in Biology
Biology 3550
Spring 2024

Lecture 28

Chemical Thermodynamics Continued: Bimolecular Reactions and Metabolism

Monday, 25 March 2024

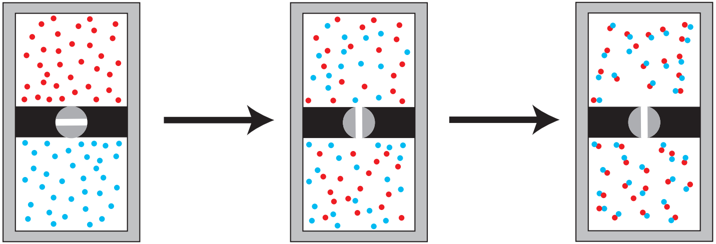
University of Utah
goldenberg@biology.utah.edu

Announcements

- Problem Set 4:
  - Due Monday, 1 April at 11:59 PM
  - Submit pdf file on Gradescope
- Quiz 4:
  - Friday, 29 March
  - 25 min, second half of class
  - Will cover thermodynamics
  - 50 min
- Review Session:
  - 5:15 PM, Thursday, 28 March
  - HEB 2002
  - Come with questions!
- No class on Monday, 8 April

A Hypothetical Example of a Chemical Reaction

- What happens if a chemical reaction takes place in a perfectly insulated chamber?



- $q = 0$ and $w = 0$, so ΔE must be zero.
- Potential energy of the molecules can be converted to kinetic energy (thermal energy), or vice versa.

The Relationship Between Free Energy and the Equilibrium Constant

$$\mathrm{A} \rightleftharpoons \mathrm{B} \qquad\qquad K_{\mathrm{eq}} = \frac{[\mathrm{B}]_{\mathrm{eq}}}{[\mathrm{A}]_{\mathrm{eq}}}$$

- ΔG depends on concentrations of A and B.
  - If $\dfrac{[\mathrm{B}]}{[\mathrm{A}]} < K_{\mathrm{eq}}$, the reaction will try to shift towards B, $\Delta G < 0$
  - If $\dfrac{[\mathrm{B}]}{[\mathrm{A}]} > K_{\mathrm{eq}}$, the reaction will try to shift back to A, $\Delta G > 0$
- Define standard concentrations to specify ΔG:
  - Concentrations of all species are 1 M for solutions or 1 atm for gasses.
  - Free energy change at these concentrations is called ΔG°.

The Relationship Between Free Energy and the Equilibrium Constant

- If reactants and products are at equilibrium concentrations:

$$\Delta G = 0$$

- If reactants and products are at standard state concentrations (1 M):

$$\Delta G \equiv \Delta G^\circ$$

$$\Delta G^\circ = -RT \ln \frac{[\mathrm{B}]_{\mathrm{eq}}}{[\mathrm{A}]_{\mathrm{eq}}} = -RT \ln K_{\mathrm{eq}}$$

ΔG° and K_{eq} convey essentially the same information.

- For other concentrations:

$$\Delta G = \Delta G^\circ + RT \ln \frac{[\mathrm{B}]}{[\mathrm{A}]}$$

The Relationship Between the Standard Free Energy Change and the Equilibrium Constant

$$\Delta G^\circ = -RT \ln K_{\text{eq}} \qquad \text{A} \rightleftharpoons \text{B} \qquad K_{\text{eq}} = \frac{[\text{B}]_{\text{eq}}}{[\text{A}]_{\text{eq}}}$$

- If $K_{\text{eq}} > 1$:
  - Reaction favors B over A.
  - $\Delta G^\circ < 0$
- If $K_{\text{eq}} < 1$:
  - Reaction favors A over B.
  - $\Delta G^\circ > 0$
- If $K_{\text{eq}} = 1$:
  - A and B have equal free energies.
  - $\Delta G^\circ = 0$

Clicker Question #1

For the reaction, A $\rightleftharpoons$ B, the standard free energy change, ΔG°, is -18 kJ/mol at 25°C.

What is the free energy change when the concentrations of A and B are 10 mM and 200 mM, respectively?

A) -18 kJ/mol

B) -11 kJ/mol

C) -7 kJ/mol

D) 7 kJ/mol

E) 18 kJ/mol

$$\Delta G = \Delta G^\circ + RT \ln \frac{[\mathrm{B}]}{[\mathrm{A}]} = -18,000\,\mathrm{J/mol} + 8.314\,\mathrm{JK^{-1}mol^{-1}} \times 298\,\mathrm{K} \times \ln \frac{200\,\mathrm{mM}}{10\,\mathrm{mM}}$$

$$= 11,000\,\mathrm{J/mol} = -11\,\mathrm{kJ/mol}$$

Reactions with More than One Reactant or Product

- A reaction with two reactants and two products: $\mathrm{aA} + \mathrm{bB} \rightleftharpoons \mathrm{cC} + \mathrm{dD}$

  a, b, c and d represent stoichiometry
- The equilibrium constant:

  $$K_{\mathrm{eq}} = \frac{[\mathrm{C}]_{\mathrm{eq}}^{c}[\mathrm{D}]_{\mathrm{eq}}^{d}}{[\mathrm{A}]_{\mathrm{eq}}^{a}[\mathrm{B}]_{\mathrm{eq}}^{b}}$$

  Products over reactants! (Mrs. Freeman)
- The reaction quotient:

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

  When concentrations are not necessarily at equilibrium.
- $\Delta G = \Delta G^{\circ} + RT \ln Q$

From Two Molecules to One

- A reaction with two reactants and one products: $\mathrm{A} + \mathrm{B} \rightleftharpoons \mathrm{C}$
- The equilibrium constant:

$$K_{\mathrm{eq}} = \frac{[\mathrm{C}]_{\mathrm{eq}}}{[\mathrm{A}]_{\mathrm{eq}}[\mathrm{B}]_{\mathrm{eq}}}$$

- Some problems:
  - The equilibrium constant has units of inverse concentration.
  - The numerical value of K_{eq} will depend on the units that we use for concentration
  - What happens when we try to calculate ΔG°?

$$\Delta G^\circ = RT \ln K_{\mathrm{eq}}$$

Logarithms are functions of pure numbers. How do we take a logarithm of a value with units?

From Two Molecules to One

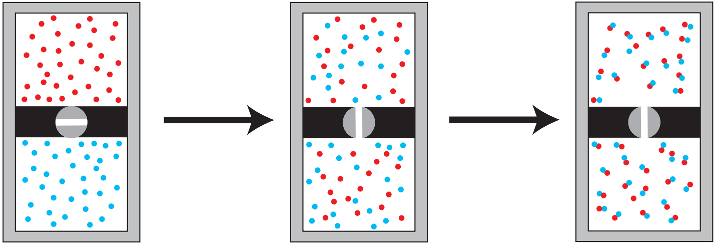
$$\mathrm{A} + \mathrm{B} \rightleftharpoons \mathrm{C}$$

- Defining standard states is important!
  - Standard state concentration is usually defined as 1 M
  - For thermodynamic purposes, refine the definition of the equilibrium constant:

$$K_{\mathrm{eq}} = \frac{\left([\mathrm{C}]_{\mathrm{eq}}/1\,\mathrm{M}\right)}{\left([\mathrm{A}]_{\mathrm{eq}}/1\,\mathrm{M}\right)\left([\mathrm{B}]_{\mathrm{eq}}/1\,\mathrm{M}\right)}$$

  - Now, K_{eq} is dimensionless, and we don't have to feel guilty about taking the logarithm.
  - But, value of ΔG depends on choice of standard state concentrations. Why?

A Hypothetical Example of a Chemical Reaction



- $q = 0$ and $w = 0$, so ΔE must be zero.
- Potential energy of the molecules can be converted to kinetic energy (thermal energy), or vice versa.
- What else changes?

The Entropy Change for a Bimolecular Reaction

- $\mathrm{A} + \mathrm{B} \rightleftharpoons \mathrm{C}$
- Assume a volume made up of N_c little cubes:
  - The number of ways to place a molecule of A and a molecule of B in the volume:

    $\Omega_{\mathrm{A,B}} = N_\mathrm{c}^2$
  - The number of ways to place a molecule of C in the volume:

    $\Omega_\mathrm{C} = N_\mathrm{c}$
- The entropy change

$$\begin{aligned}\Delta S &= k\ln(\Omega_\mathrm{C}) - k\ln(\Omega_{\mathrm{A,B}}) = k\ln(N_\mathrm{c}) - k\ln(N_\mathrm{c}^2)\\ &= k\ln\left(\frac{N_\mathrm{c}}{N_\mathrm{c}^2}\right) = -k\ln(N_\mathrm{c})\end{aligned}$$

- The entropy decreases!

The Entropy Change for a Bimolecular Reaction

- From previous slide:

$$\Delta S = -k\ln(N_\mathrm{c})$$

- In this case, the number of little cubes doesn't cancel out, and the size of the cubes matters.
- A plausible estimate:
  - Make the cubes about the right size to hold one or two small molecules,

$$V_\mathrm{c} = (1\,\mathrm{nm})^3 = 1\,\mathrm{nm}^3$$

  - For a volume of 1 L:

$$N_\mathrm{c} = \frac{1\,\mathrm{L}}{1\,\mathrm{nm}^3} \times \frac{10^{-3}\,\mathrm{m}^3}{L} \times \left(\frac{10^9\,\mathrm{nm}}{\mathrm{m}}\right)^3 = 10^{24}$$

The Entropy Change for a Bimolecular Reaction

- For one molecule of A and B converteted to C in a volume of 1 L:

$$\Delta S = -k \ln(N_\text{c}) = -k \ln(10^{24})$$

- For one mole each of A and B converted to C, in 1 L:

$$\begin{aligned}\Delta S &= -N_\text{A} k \ln(10^{24}) \\ &= -R \ln(10^{24})\end{aligned}$$

- For reactants and products at 1 M concentration:

$$\Delta S = -R \ln(10^{24}) = -8.31\,\text{J}/\text{K} \times 53 = -460\,\text{J}/\text{K}$$

Clicker Question #2

If the reaction volume is doubled for the reaction $\mathrm{A} + \mathrm{B} \rightleftharpoons \mathrm{C}$, How will the entropy change be affected?

A) ΔS will be unaffected.

B) [✓ ΔS will become more negative.]

C) ΔS will become less negative.

$$\Delta S = -k \ln(N_\mathrm{c}) = -k \ln(V(\mathrm{L}) \times 10^{24})$$

A Bimolecular Reaction

- $\mathrm{A} + \mathrm{B} \rightleftharpoons \mathrm{C}$
- An estimate of the entropy change for combining two molecules into one:

$$\Delta S = -460\,\mathrm{J/K}$$

- Total free energy change for the reaction:

$$\Delta G = \Delta H - T\Delta S$$

- The contribution of entropy change to the free energy change at 298 K:

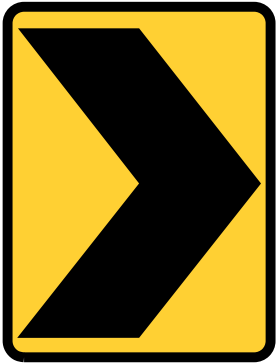
$$\begin{aligned} -T\Delta S &= 298\,\mathrm{K} \times 460\,\mathrm{J/K} \\ &= 140\,\mathrm{kJ/mol} \end{aligned}$$

- This is a large, unfavorable contribution to ΔG.
- For the reaction to be favorable, there must be other factors that make the total free energy change negative.

A Bimolecular Reaction

- $\text{A} + \text{B} \rightleftharpoons \text{C}$
- $\Delta S = -460\,\text{J/K}$
- $-T\Delta S = 140\,\text{kJ/mol}$
- Some caveats:
  - This is a highly simplified treatment.
  - Choice of V_c is not very well justified.
  - Ignores rotational freedom of molecules.
  - Ignores internal motions of molecules.
  - This is a controversial subject!
    But this estimate is within the bounds of the controversy! (at the lower end)
- ΔG°, defined with specific concentration units, contains within it the entropy change at the standard state concentration.
- If the concentrations change, ΔS changes!

Warning!



Direction Change

Chemical Energy and Metabolism

Chemical Energy

- What does “chemical energy” mean?

---

http://www.caffeineinformer.com http://www.philosophersguild.com

An Energetic Chemical Reaction, Under Some Conditions

$$C_6H_{12}O_6 + 6O_2 \rightleftharpoons 6CO_2 + 6H_2O$$

- Oxidation of glucose (or other hexose) by molecular oxygen.
- Free energy change depends on concentrations.
- Standard state conditions: 1 M glucose, 1 atm O_2 and CO_2
  - $\Delta G^\circ = -2.7 \times 10^6\ \mathrm{J/mol} = -2,700\ \mathrm{kJ/mol}$
  - Equilibrium constant:

$$K_{\mathrm{eq}} = \frac{{[CO_2]_{\mathrm{eq}}}^6}{[C_6H_{12}O_6]_{\mathrm{eq}}{[O_2]_{\mathrm{eq}}}^6} = e^{-\Delta G^\circ/(RT)} \approx 10^{473}\ \mathrm{M}^{-1}$$

    (Water is ignored in equilibrium constant.)
  - Extremely favorable!
- But, this assumes 1 atm O_2 and CO_2.
- Reaction only became favorable about 2.5 billion years ago, when oxygen became abundant on earth.

Nutritional Calories

- Measured as the heat for complete combustion with excess O_2 at constant temperature and volume (no work).

  "bomb calorimeter"

- Since, $w = 0$, $q = \Delta E =$ change in potential energy
- For glucose, $\Delta E = -4\,\mathrm{kcal}/\mathrm{g} = -175\,\mathrm{kJ}/\mathrm{mol}$, vs $\Delta G^\circ = -2,700\,\mathrm{kJ}/\mathrm{mol}$.
- Why are these numbers so different?

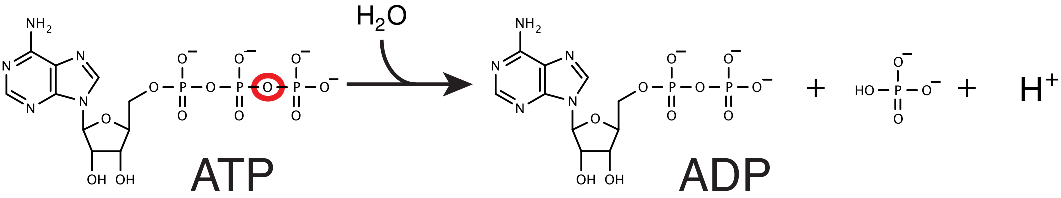
  $$\Delta G = \Delta H - T\Delta S$$

  $$C_6H_{12}O_6 + 6O_2 \rightleftharpoons 6CO_2 + 6H_2O$$

  There is a large increase in entropy, 7 molecules are converted to 12.

- Nutritionists estimate the amount of work required to offset the metabolism of a given number of nutritional calories.

Another “High-energy” Reaction



- $\Delta G^\circ = -30\,\mathrm{kJ/mol}$

Clicker Question #3

What is the equilibrium constant for the reaction?

$$\mathrm{ATP} \rightleftharpoons \mathrm{ADP} + \mathrm{P_i} \qquad \Delta G^\circ = -30\,\mathrm{kJ/mol}$$

A) $\approx 10^{-5}\,\mathrm{M}$

B) $\approx 10^{-3}\,\mathrm{M}$

C) $\approx 10\,\mathrm{M}$

D) $\approx 10^{3}\,\mathrm{M}$

E) $\boxed{\approx 10^{5}\,\mathrm{M}}$

$$R = 8.314\,\mathrm{J/(K \cdot mol)} \qquad T = 298\,\mathrm{K}$$

Calculation of Equilibrium Constant from ΔG°

$$\Delta G^\circ = -30\,\text{kJ/mol} \qquad R = 8.314\,\text{J/(K}\cdot\text{mol)} \qquad T = 298\,\text{K}$$

$$\Delta G^\circ = -RT \ln K_{\text{eq}}$$
$$\ln K_{\text{eq}} = -\Delta G^\circ/(RT)$$
$$K_{\text{eq}} = e^{-\Delta G^\circ/(RT)}$$

$$-\Delta G^\circ/(RT) = 30\,\text{kJ/mol}/\big(8.314\,\text{J/(K}\cdot\text{mol)}\cdot 298\,\text{K}\big)$$
$$= 30 \times 10^3\,\text{J/mol}/2.48 \times 10^3\,\text{J/mol} = 12$$

$$K_{\text{eq}} = e^{12} = 1.8 \times 10^5\,\text{M}$$