Physical Principles in Biology
Biology 3550
Spring 2025

Lecture 28

Chemical Thermodynamics Continued: Bimolecular Reactions and Metabolism

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Announcements

- Quiz 4:
  - Friday, 28 March
  - 25 min, second half of class
  - Will cover material on thermodynamics
- Problem set 4
  - Due Friday, 28 March, 11:59 PM

A New State Function: Enthalpy (H)

Two consistent definitions for ΔH at constant pressure:

- ΔE plus work done by the system due to volume change

  $$\Delta H = \Delta E + P\Delta V$$

  If there is no volume change, then $P\Delta V = 0$, and $\Delta H = \Delta E$.

- The heat absorbed during the constant pressure process:

  $$\Delta H = q_\mathrm{p}$$

  Chemical and biochemical reactions are often studied under conditions of constant (or nearly constant) pressure, and ΔV is usually very small.

- If $\Delta H \approx \Delta E$, ΔH represents change in internal energy.
- ΔH can be experimentally measured.

The Gibbs Free Energy, Another State Function

- $G = H - TS_{\text{sys}}$
- For a process at constant temperature:

$$\Delta G = \Delta H - T\Delta S_{\text{sys}}$$

- Since $\Delta S_{\text{surr}} = -q_{\text{p}}/T$, at constant pressure and temperature:

$$T\Delta S_{\text{surr}} = -q_{\text{p}} = -\Delta H$$

$$\Delta H = -T\Delta S_{\text{surr}}$$

$$\Delta G = -T\Delta S_{\text{surr}} - T\Delta S_{\text{sys}} = -T(\Delta S_{\text{surr}} + \Delta S_{\text{sys}})$$

$$\Delta G = -T\Delta S_{\text{univ}}$$

- Or, $\Delta S_{\text{univ}} = -\Delta G/T$

The Gibbs Free Energy is Used to Apply the Second Law

- From the previous slide:

$$\Delta S_{\text{univ}} = -\Delta G/T$$

- If $\Delta G < 0$
  - $\Delta S_{\text{univ}} > 0$, and the process will be spontaneous.
- If $\Delta G > 0$
  - $\Delta S_{\text{univ}} < 0$, and the reverse process will be spontaneous.
- If $\Delta G = 0$
  - $\Delta S_{\text{univ}} = 0$, and the process is reversible.
    (Can be pushed in either direction.)
  - $\Delta G = 0$ defines a system at equilibrium.
- All based on state functions of the system! (at constant pressure)

  Don't have to worry (explicitly) about the surroundings.

The Relationship Between Free Energy and the Equilibrium Constant for a Chemical Reaction

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

- 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 standard state concentrations (1 M):

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

- For other concentrations:

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

- If reactants and products are at equilibrium concentrations:

$$\Delta G = 0$$

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

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

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.
  - $\Delta G^\circ = 0$

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:

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

  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

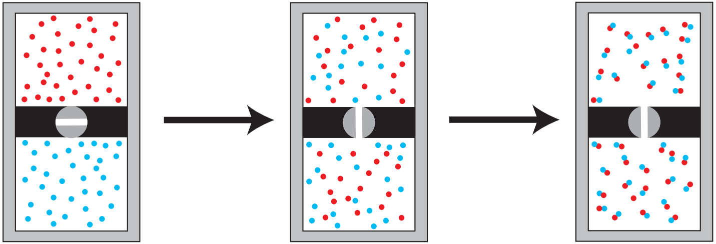
$$\mathrm{A} + \mathrm{B} \rightleftharpoons \mathrm{C}$$

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

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

  - 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?
- How much does the entropy change?

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:

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

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

$$\Delta S = k\ln(\Omega_{\mathrm{C}}) - k\ln(\Omega_{\mathrm{A,B}}) = k\ln(N_c) - k\ln(N_c^2)$$

$$= k\ln\left(\frac{N_c}{N_c^2}\right) = -k\ln(N_c)$$

- The entropy decreases!

The Entropy Change for a Bimolecular Reaction

- From previous slide:

$$\Delta S = -k \ln(N_c)$$

- 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,

$$V_c = (1\,\text{nm})^3 = 1\,\text{nm}^3$$

  - For a volume of 1 L:

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

The Entropy Change for a Bimolecular Reaction

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

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

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

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

- For reactants and products at 1 M concentration:

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

Clicker Question #1

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:

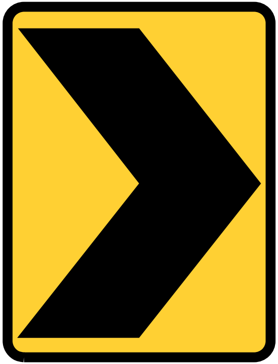
$$\begin{aligned} -T\Delta S &= 298\,\mathrm{K} \times 460\,\mathrm{J/K} \\ &= 140\,\mathrm{kJ/mol} \end{aligned}$$

- 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

- $\mathrm{A} + \mathrm{B} \rightleftharpoons \mathrm{C}$
- $\Delta S = -460\,\mathrm{J/K}$
- $-T\Delta S = 140\,\mathrm{kJ/mol}$
- 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?

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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:

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

    (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, $\Delta E = -4\,\mathrm{kcal/g} = -175\,\mathrm{kJ/mol}$, vs $\Delta G^\circ = -2,700\,\mathrm{kJ/mol}$.
- Why are these numbers so different?

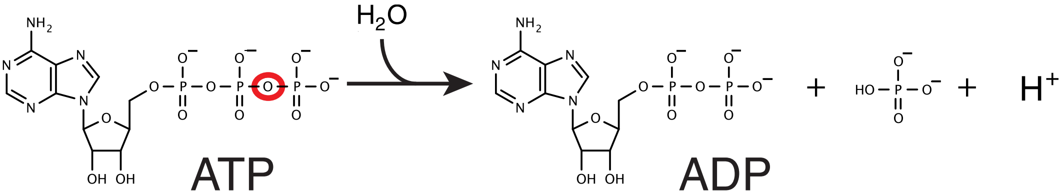
$$\Delta G = \Delta H - T\Delta S$$

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

  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



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