Physical Principles in Biology
Biology 3550
Spring 2025

Lecture 27

Enthalpy, the Gibbs Free Energy and Equilibrium Constants

Friday, 21 March 2025

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)

- Enthalpy, H, is closely related to the internal energy, E.

  $$H = E + PV$$

  The product PV has the units of energy or work.

- For a process at constant pressure:

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

  $P\Delta V$ is work done by the system due to a change in volume at constant pressure.

- Two new quantities:

  - $w_p = -P\Delta V =$ work done on the system in constant pressure process
  - $q_p =$ heat absorbed by system in constant pressure process

- From the first law:

  $$\Delta E = q_p + w_p = q_p - P\Delta V$$
  $$P\Delta V = q_p - \Delta E$$
  $$\Delta H = \Delta E + P\Delta V = \Delta E + (q_p - \Delta E) = q_p$$

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 $\Delta H = \Delta E$.
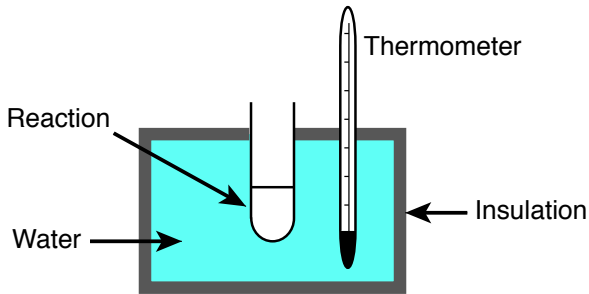
- The heat absorbed during the constant pressure process:

  $$\Delta H = q_p$$

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

  ΔH can be experimentally measured.

Measuring ΔH with a Calorimeter

- The water bath represents the "surroundings".

- If $\Delta H < 0$, heat flows from the reaction vessel and warms the water.

- If $\Delta H > 0$, heat flows into the reaction vessel, and water temperature decreases.

$$\Delta H = -\frac{\Delta T_{\text{water}}}{\text{mass of water (g)}} \qquad \text{(in calories)}$$

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 $\Delta S_{\text{surr}} = -q/T$, at constant pressure:

$$\Delta S_{\text{surr}} = -q_{\text{p}}/T$$
$$T\Delta S_{\text{surr}} = -q_{\text{p}} = -\Delta H$$
$$\Delta H = -T\Delta S_{\text{surr}}$$
$$\Delta G = -T\Delta S_{\text{surr}} - T\Delta S_{\text{sys}} = -T(\Delta S_{\text{surr}} + \Delta S_{\text{sys}})$$
$$\Delta G = -T\Delta S_{\text{univ}}$$

- 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 <u>reverse</u> 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 change in Helmholtz free energy, as previously defined:

$$\Delta F = w_{\text{rev}}$$

  $-w_{\text{rev}}$ is the maximum work available from a spontaneous process.

- From the first law:

$$\Delta E = q_{\text{rev}} + w_{\text{rev}}$$
$$w_{\text{rev}} = \Delta E - q_{\text{rev}}$$
$$\Delta F = \Delta E - q_{\text{rev}}$$

- For a constant-temperature process:

$$\Delta S_{\text{sys}} = \frac{q_{\text{rev}}}{T}$$
$$q_{\text{rev}} = T\Delta S_{\text{sys}}$$
$$\Delta F = \Delta E - T\Delta S_{\text{sys}}$$

The Helmholtz and Gibbs Free Energy Functions

- For a constant temperature process:

$$\Delta F = \Delta E - T\Delta S_{\text{sys}}$$

- The standard definition of the Helmholz free energy:

$$F = E - TS_{\text{sys}}$$

- Compare to:

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

- Since $\Delta H = \Delta E - w_{\text{p}}$:

$$\Delta G = \Delta F - w_{\text{p}}$$

  $-\Delta G$ is the maximum work available from a process $(-\Delta F)$ minus the work due to volume change at constant pressure.

The Helmholtz Free Energy

- From previous slide:

$$\Delta G = \Delta F - w_{\mathrm{p}}$$

- If volume change is small, and w_{p} can be ignored:

  - $\Delta G \approx \Delta F$

  - If $\Delta G < 0$: Process is favorable, and the maximum work available from the process is: $-\Delta F = -\Delta G - w_{\mathrm{p}} \approx -\Delta G$

  - If $\Delta G > 0$: Process is unfavorable, and the minimum work required to drive the process is: $\Delta F = \Delta G + w_{\mathrm{p}} \approx \Delta G$

- Commonly made assumptions for chemical reactions in dilute solutions:

  - $P\Delta V = -w_{\mathrm{p}} \approx 0$

  - $\Delta H \approx \Delta E$: ΔH Represents change in internal energy.

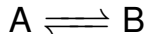 - $\Delta G \approx \Delta F$: $-\Delta G$ Represents maximum work from a spontaneous process.

Warning!
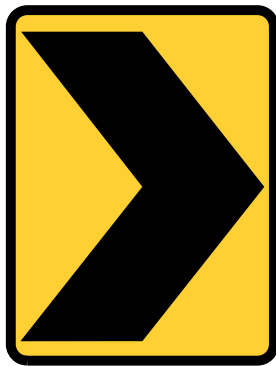
Direction Change

Equilibrium Constants

The Equilibrium Constant for a Chemical Reaction

$$A \rightleftharpoons B$$

- The reaction can occur in either direction. (at least in principle)

- The probability that any molecule of A will be converted to a molecule of B is the same as for any other molecule of A.
  - The total rate of conversion of A to B is proportional to the concentration of A.
  - Similarly, the total rate of conversion of B to A is proportional to the concentration of B.

- A differential equation:

$$\frac{d[A]}{dt} = -k_f[A] + k_r[B]$$

The constants k_f and k_r are called rate constants.

The Equilibrium Constant for a Chemical Reaction

$$A \underset{k_r}{\overset{k_f}{\rightleftharpoons}} B$$
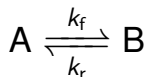
- From the previous slide:

$$\frac{d[A]}{dt} = -k_f[A] + k_r[B]$$

- Whatever the starting concentrations, [A] and [B] will eventually adjust so that they no longer change.

- At equilibrium:

$$\frac{d[A]}{dt} = -\frac{d[B]}{dt} = 0$$

The Equilibrium Constant for a Chemical Reaction

$$A \underset{k_r}{\overset{k_f}{\rightleftharpoons}} B$$

- At equilibrium:

$$\frac{d[A]}{dt} = -\frac{d[B]}{dt} = -k_f[A]_{eq} + k_r[B]_{eq} = 0$$

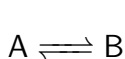$[A]_{eq}$ and $[B]_{eq}$ are the concentrations of A and B at equilibrium.

- Rearranging:

$$k_r[B]_{eq} = k_f[A]_{eq}$$

$$\frac{[B]_{eq}}{[A]_{eq}} = \frac{k_f}{k_r} = K_{eq}$$

K_{eq} is defined as the equilibrium constant.

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

- At equilibrium, a little bit of work can push the reaction in either direction.

  This defines the condition where $\Delta G = 0$
  No work can be done!

- Definition of ΔG for a chemical reaction:

  The free energy change for converting one mole of reactants to one mole of products, at specified concentrations, without significantly changing concentrations(!).

  Implies a very, very large volume!

  Or, a mechanism that restores concentrations continuously.

The Relationship Between Free Energy
and the Equilibrium Constant

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

- ΔG depends on concentrations of A and B.

  - If $\quad \dfrac{[B]}{[A]} < K_{eq}$, the reaction will try to shift towards B, $\quad \Delta G < 0$

  - If $\quad \dfrac{[B]}{[A]} > K_{eq}$, the reaction will try to shift back to A, $\quad \Delta G > 0$

- 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):

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

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

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

- For other concentrations:

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

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

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

- If $K_{eq} > 1$:
  - Reaction favors B over A.
  - $\Delta G^\circ < 0$

- If $K_{eq} < 1$:
  - Reaction favors A over B.
  - $\Delta G^\circ > 0$

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

For a hypothetical reaction, $A \rightleftharpoons B$, $K_{eq} = 1500$ at 25°C.

What is the standard free energy change at this temperature?

$$R = 8.314 \, \text{JK}^{-1}\text{mol}^{-1}$$

A) -8 kJ/mol

B) -18 kJ/mol

C) 0 kJ/mol

D) 8 kJ/mol

E) 18 kJ/mol

$$\Delta G^\circ = -RT \ln K_{eq} = -8.314 \, \text{JK}^{-1}\text{mol}^{-1} \times 298 \, \text{K} \times \ln 1500$$

$$= -18,000 \, \text{J/mol} = -18 \, \text{kJ/mol}$$

For a different hypothetical reaction, C $\rightleftharpoons$ D, $\Delta G^\circ = 5\,\text{kJ/mol}$ at 25°C.

What is the equilibrium constant at this temperature?

A) -1

B) -0.13

C) 0.13

D) 1

E) 7.5

$K_{eq} = e^{-\Delta G^\circ/(RT)} = e^{-5,000\,\text{J/mol}/(8.314\,\text{JK}^{-1}\text{mol}^{-1} \times 298\,\text{K})} = 0.13$

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

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

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

Reactions with More than One Reactant or Product

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

  a, b, c and d represent stoichiometry

- The equilibrium constant:

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

  Products over reactants! (Mrs. Freeman)

- The reaction quotient:

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

  When concentrations are not necessarily at equilibrium.

- $\Delta G = \Delta G^{\circ} + RT \ln Q$