Week 5

Catalysis

5.1 Midterm Review and Intro to Catalysts

4/27:

- Example problem 1: Steady-state approximation.
  - Let
$$\mathrm{A} \underset{k_a'}{\overset{k_a}{\rightleftharpoons}} \mathrm{B} \underset{k_b'}{\overset{k_b}{\rightleftharpoons}} \mathrm{C} \underset{k_c'}{\overset{k_c}{\rightleftharpoons}} \mathrm{D}$$
    Suppose [A] is maintained at a fixed value and the produce D is removed from the reaction as it is formed. Find the rate at which the product is formed in terms of [A].
  - By hypothesis, we have that at all times t, $[\mathrm{A}] = [\mathrm{A}]_0$ and $[\mathrm{D}] = 0$.
  - The hypotheses also imply that we can apply the steady-state approximation to both B and C.
  - Thus, we have that
$$\begin{aligned}\frac{\mathrm{d}[\mathrm{C}]}{\mathrm{d}t} = 0 &= k_b[\mathrm{B}] - k_c[\mathrm{C}] - k_b'[\mathrm{C}] \\ [\mathrm{B}] &= \frac{k_b' + k_c}{k_b}[\mathrm{C}]\end{aligned}$$
    so that
$$\begin{aligned}\frac{\mathrm{d}[\mathrm{B}]}{\mathrm{d}t} &= k_a[\mathrm{A}] - k_b[\mathrm{B}] - k_a'[\mathrm{B}] + k_b'[\mathrm{C}] \\ 0 &= k_a[\mathrm{A}] - k_b \cdot \frac{k_b' + k_c}{k_b}[\mathrm{C}] - k_a' \cdot \frac{k_b' + k_c}{k_b}[\mathrm{C}] + k_b'[\mathrm{C}] \\ [\mathrm{C}] &= \frac{k_a k_b}{k_b k_c + k_a' k_b' + k_a' k_c}[\mathrm{A}]\end{aligned}$$
    and therefore
$$\begin{aligned}\frac{\mathrm{d}[\mathrm{D}]}{\mathrm{d}t} &= k_c[\mathrm{C}] - k_c' \cdot 0 \\ &= \frac{k_a k_b k_c}{k_b k_c + k_a' k_b' + k_a' k_c}[\mathrm{A}]\end{aligned}$$
- Example problem 2.
  - Consider the reaction
$$\mathrm{HCl} + \mathrm{CH_3CH{=}CH_2} \rightleftharpoons \mathrm{CH_3CHClCH_3}$$
    which proceeds by the mechanism

1. $\mathrm{HCl} + \mathrm{HCl} \rightleftharpoons (\mathrm{HCl})_2$ (equilibrium constant K_1).
2. $\mathrm{HCl} + \mathrm{CH_3CH{=}CH_2} \rightleftharpoons$ complex (equilibrium constant K_2).
3. $(\mathrm{HCl})_2 + \text{complex} \rightleftharpoons \mathrm{CH_3CHClCH_3} + \mathrm{HCl} + \mathrm{HCl}$ (equilibrium constant K_3).

– The equilibrium constants for the two pre-equilibria are

$$K_1 = \frac{[(\mathrm{HCl})_2]_{\mathrm{eq}} c^\circ}{[\mathrm{HCl}]_{\mathrm{eq}}^2} \qquad K_2 = \frac{[\text{complex}]_{\mathrm{eq}} c^\circ}{[\mathrm{HCl}]_{\mathrm{eq}}[\mathrm{CH_3CH{=}CH_2}]_{\mathrm{eq}}}$$

– We can divide the mass-action expression for K_1 by $(c^\circ)^2$ to get each concentration over c° within its exponent.

– The rate of product formation is

$$\begin{aligned} v &= \frac{\mathrm{d}[\mathrm{CH_3CHClCH_3}]}{\mathrm{d}t} \\ &= k_r[(\mathrm{HCl})_2][\text{complex}] \\ &\approx k_r[(\mathrm{HCl})_2]_{\mathrm{eq}}[\text{complex}]_{\mathrm{eq}} \\ &= k_r \cdot \frac{K_1[\mathrm{HCl}]_{\mathrm{eq}}^2}{c^\circ} \cdot \frac{K_2[\mathrm{HCl}]_{\mathrm{eq}}[\mathrm{CH_3CH{=}CH_2}]_{\mathrm{eq}}}{c^\circ} \\ &= \frac{k_r K_1 K_2}{(c^\circ)^2}[\mathrm{HCl}]_{\mathrm{eq}}^3[\mathrm{CH_3CH{=}CH_2}]_{\mathrm{eq}} \end{aligned}$$

■ There's a key assumption with the steady state and something about being able to apply the equilibrium concentration of the intermediate as the steady-state quantity.

■ This question wants to let you know that an equilibrium constant like K_1 might indicate a steady-state approximation.

- Note: Mind the positive and negative signs when constructing differential rate laws!
- The midterm will be posted this Friday (April 29) and will be available until the following Friday (May 6). There will be a timed 2 hour period to take it.
- **Catalyst**: A substance that participates in the chemical reaction but is not consumed in the process.
  – A catalyst affects the mechanism and activation energy of a chemical reaction.
  – A catalyst can give rise to a reaction path with a negligible activation barrier.
  – The exothermicity or endothermicity of the chemical reaction is not altered by the presence of a catalyst.
- **Homogeneous catalysis**: Catalysis in which the catalyst is in the same phase as the reactants and products.
- **Heterogeneous catalysis**: Catalysis in which the catalyst is in a different phase from the reactants and products.
- Imagine that initially, we have the reaction

$$\mathrm{A} \xrightarrow{k} \text{products}$$

where k is the observed rate constant.

– When a catalyst is introduced into solution, this mechanism continues, but we now also have the new reaction pathway

$$\mathrm{A} + \text{catalyst} \xrightarrow{k_{\mathrm{cat}}} \text{products} + \text{catalyst}$$

  - If each of these competing reactions is an elementary process, then

$$-\frac{\mathrm{d}[\mathrm{A}]}{\mathrm{d}t} = k[\mathrm{A}] + k_{\mathrm{cat}}[\mathrm{A}][\text{catalyst}]$$

  - In most cases, catalysts enhance reaction rates by many orders of magnitude, and therefore only the rate law for the catalyzed reaction need be considered in analyzing experimental data.

- Reviews the Nobel Prizes in 2020 and 2021 (for CRISPR and asymmetric organocatalysis, respectively).
- An example of homogeneous catalysis.
  - Consider the reaction

$$2\,\mathrm{Ce^{4+}(aq)} + \mathrm{Tl^{+}(aq)} \longrightarrow 2\,\mathrm{Ce^{3+}(aq)} + \mathrm{Tl^{3+}(aq)}$$

  - In the absence of a catalyst,

$$v = k[\mathrm{Tl^{+}}][\mathrm{Ce^{4+}}]^2$$

    and the mechanism is a termolecular elementary reaction.
  - However, with $\mathrm{Mn^{2+}}$ as the catalyst, we have the mechanism

$$\mathrm{Ce^{4+}(aq)} + \mathrm{Mn^{2+}(aq)} \xrightarrow{k_{\mathrm{cat}}} \mathrm{Mn^{3+}(aq)} + \mathrm{Ce^{3+}(aq)}$$

$$\mathrm{Ce^{4+}(aq)} + \mathrm{Mn^{3+}(aq)} \Longrightarrow \mathrm{Mn^{4+}(aq)} + \mathrm{Ce^{3+}(aq)}$$

$$\mathrm{Mn^{4+}(aq)} + \mathrm{Tl^{+}(aq)} \Longrightarrow \mathrm{Mn^{2+}(aq)} + \mathrm{Tl^{3+}(aq)}$$

    where the step with k_{cat} is the rate-determining step.
    - Thus, for this mechanism, we have that

$$v = k_{\mathrm{cat}}[\mathrm{Ce^{4+}}][\mathrm{Mn^{2+}}]$$

  - The overall rate law for this reaction is therefore

$$v = k[\mathrm{Tl^{+}}][\mathrm{Ce^{4+}}]^2 + k_{\mathrm{cat}}[\mathrm{Ce^{4+}}][\mathrm{Mn^{2+}}]$$

5.2 Enzymatic Catalysis

4/27:

- Midterm questions:
  - First 10 are T/F. He will test key concepts by making statements that are either true or false.
    - We should expect to spend no more than 30 minutes out of our 2 hours on these.
  - 4 calculation problems.
    - First- and second-order reactions.
    - Collisions.
    - A reaction mechanism problem.
  - Use calculators, do online searches, and use the textbook.
  - Do not talk to your classmates.
  - The midterm will become available Friday at noon.
- Enzymes are protein molecules that catalyze specific biochemical reactions.
  - For example, hexokinase converts glucose and ATP to glucose 6-phosphate, ADP, and $\mathrm{H^{+}}$.
- **Substrate**: The reactant molecule acted upon by an enzyme.

- **Active site**: The region of the enzyme where the substrate reacts.
- **Lock-and-key model**: The active site and substrate have complementary three-dimensional structures and dock without the need for major atomic rearrangements.
- **Induced fit model**: Binding of the substrate induces a conformation change in the active site. The substrate fits well in the active site after the conformational change has taken place.
- The Michaelis-Menten Mechanism is a reaction mechanism for enzyme catalysis.
- Intuition.
  - Imagine we have a solution of enzymes and substrate molecules.
  - Limiting factors of an enzymatically catalyzed reaction.
    - The enzyme-substrate affinity.
    - The turnover number.
  - If the substrate concentration is low (i.e., $[\mathrm{S}]_0 \ll [\mathrm{E}]_0$) and the enzyme-substrate affinity is strong (but not so strong that the enzyme-substrate complex is energetically favorable), then we expect $v_{\text{initial}} \propto [\mathrm{S}]_0$ because we'd think that all of the substrate will immediately be absorbed and transformed.
  - If the substrate concentration is large (i.e., $[\mathrm{S}]_0 \gg [\mathrm{E}]_0$) and the enzyme-substrate affinity is strong, then we expect $v_{\text{initial}} \propto [\mathrm{E}]_0$ and, importantly, $v_{\text{initial}} \not\propto [\mathrm{S}]_0$.
- Mathematical derivation.
  - Experimental studies reveal that the rate law for many enzyme-catalyzed reactions has the form
    $$-\frac{\mathrm{d}[\mathrm{S}]}{\mathrm{d}t} = \frac{k[\mathrm{S}]}{K + [\mathrm{S}]}$$
    - This is the final goal of the derivation.
  - The mechanism is
    $$\mathrm{S} + \mathrm{E} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{ES} \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} \mathrm{P} + \mathrm{E}$$
  - Thus,
    $$\begin{aligned} -\frac{\mathrm{d}[\mathrm{S}]}{\mathrm{d}t} &= k_1[\mathrm{E}][\mathrm{S}] - k_{-1}[\mathrm{ES}] \\ -\frac{\mathrm{d}[\mathrm{ES}]}{\mathrm{d}t} &= (k_2 + k_{-1})[\mathrm{ES}] - k_1[\mathrm{E}][\mathrm{S}] - k_{-2}[\mathrm{E}][\mathrm{P}] \\ \frac{\mathrm{d}[\mathrm{P}]}{\mathrm{d}t} &= k_2[\mathrm{ES}] - k_{-1}[\mathrm{E}][\mathrm{P}] \end{aligned}$$
  - Note that
    $$[\mathrm{E}]_0 = [\mathrm{ES}] + [\mathrm{E}]$$
  - Plugging that equation into the rate law for the enzyme-substrate complex and applying the steady-state approximation yields
    $$\begin{aligned} -\frac{\mathrm{d}[\mathrm{ES}]}{\mathrm{d}t} = 0 &= [\mathrm{ES}](k_1[\mathrm{S}] + k_{-1} + k_2 + k_{-1}[\mathrm{P}]) - k_1[\mathrm{S}][\mathrm{E}]_0 - k_2[\mathrm{P}][\mathrm{P}]_0 \\ [\mathrm{ES}] &= \frac{k_1[\mathrm{S}] + k_{-1}[\mathrm{P}]}{k_1[\mathrm{S}] + k_{-2}[\mathrm{P}] + k_{-1} + k_2}[\mathrm{E}]_0 \end{aligned}$$

– Substituting this and the original expression for $[E]_0$ into the rate law for the substrate yields

$$v = -\frac{d[S]}{dt} = \frac{k_1 k_2 [S] + k_{-1} k_{-2} [P]}{k_1 [S] + k_{-2} [P] + k_{-1} + k_2} [E]_0$$

– If the experimental measurements of the reaction rate are taken during the time period when only a small percentage (1-3%) of the substrate is converted to product, then

$$[S] \approx [S]_0$$

and

$$[P] \approx 0$$

– Using this approximation simplifies the above rate law to

$$v = -\frac{d[S]}{dt} = \frac{k_1 k_2 [S]_0 [E]_0}{k_1 [S]_0 + k_{-1} + k_2} = \frac{k_2 [S]_0 [E]_0}{K_m + [S]_0}$$

where $K_m = (k_{-1} + k_2)/k_1$ is the **Michaelis constant**.

- The Michaelis constant tells you the ration of dissociation of the enzyme-substrate complex to the formation of the enzyme-substrate complex. In other words, it provides information on the enzyme-substrate affinity.
- Note that k_{-2} is not present in the denominator of the Michaelis constant because for a good enzyme, k_{-2} should be very small.
- The unit of K_m should be concentration.
- When $K_m = [S]_0$, $v = v_{max}/2$

– An enzyme-catalyzed reaction is first order in the substrate at low substrate concentrations ($K \gg [S]_0$) and then becomes zero order in the substrate at high substrate concentrations ($K \ll [S]_0$).

– Thus, at low substrate concentrations, the above equation holds, but at high substrate concentrations,

$$-\frac{d[S]}{dt} = k_2 [E]_0 \qquad\qquad v_{max} = k_2 [E]_0$$

resulting in the **Lineweaver-Burk plot**, canonically represented by the second of the two equivalent forms below.

$$v = \frac{v_{max}}{1 + K_m/[S]_0} \qquad\qquad \frac{1}{v} = \frac{1}{v_{max}} + \frac{K_m}{v_{max}} \frac{1}{[S]_0}$$