

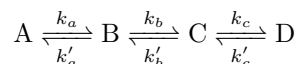
Week 5

Catalysis

5.1 Midterm Review and Intro to Catalysts

4/27: • Example problem 1: Steady-state approximation.

– Let



Suppose $[A]$ is maintained at a fixed value and the product 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 , $[A] = [A]_0$ and $[D] = 0$.
- The hypotheses also imply that we can apply the steady-state approximation to both B and C .
- Thus, we have that

$$\begin{aligned}\frac{d[C]}{dt} &= 0 = k_b[B] - k_c[C] - k'_b[C] \\ [B] &= \frac{k'_b + k_c}{k_b}[C]\end{aligned}$$

so that

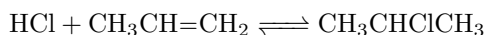
$$\begin{aligned}\frac{d[B]}{dt} &= k_a[A] - k_b[B] - k'_a[B] + k'_b[C] \\ 0 &= k_a[A] - k_b \cdot \frac{k'_b + k_c}{k_b}[C] - k'_a \cdot \frac{k'_b + k_c}{k_b}[C] + k'_b[C] \\ [C] &= \frac{k_a k_b}{k_b k_c + k'_a k'_b + k'_a k_c}[A]\end{aligned}$$

and therefore

$$\begin{aligned}\frac{d[D]}{dt} &= k_c[C] - k'_c \cdot 0 \\ &= \frac{k_a k_b k_c}{k_b k_c + k'_a k'_b + k'_a k_c}[A]\end{aligned}$$

• Example problem 2.

– Consider the reaction



which proceeds by the mechanism

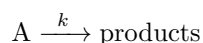
1. $\text{HCl} + \text{HCl} \rightleftharpoons (\text{HCl})_2$ (equilibrium constant K_1).
 2. $\text{HCl} + \text{CH}_3\text{CH}=\text{CH}_2 \rightleftharpoons \text{complex}$ (equilibrium constant K_2).
 3. $(\text{HCl})_2 + \text{complex} \rightleftharpoons \text{CH}_3\text{CHClCH}_3 + \text{HCl} + \text{HCl}$ (equilibrium constant K_3).
- The equilibrium constants for the two pre-equilibria are

$$K_1 = \frac{[(\text{HCl})_2]_{\text{eq}} c^\circ}{[\text{HCl}]_{\text{eq}}^2} \qquad K_2 = \frac{[\text{complex}]_{\text{eq}} c^\circ}{[\text{HCl}]_{\text{eq}} [\text{CH}_3\text{CH}=\text{CH}_2]_{\text{eq}}}$$

- 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

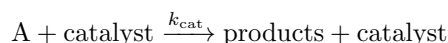
$$\begin{aligned} v &= \frac{d[\text{CH}_3\text{CHClCH}_3]}{dt} \\ &= k_r [(\text{HCl})_2] [\text{complex}] \\ &\approx k_r [(\text{HCl})_2]_{\text{eq}} [\text{complex}]_{\text{eq}} \\ &= k_r \cdot \frac{K_1 [\text{HCl}]_{\text{eq}}^2}{c^\circ} \cdot \frac{K_2 [\text{HCl}]_{\text{eq}} [\text{CH}_3\text{CH}=\text{CH}_2]_{\text{eq}}}{c^\circ} \\ &= \frac{k_r K_1 K_2}{(c^\circ)^2} [\text{HCl}]_{\text{eq}}^3 [\text{CH}_3\text{CH}=\text{CH}_2]_{\text{eq}} \end{aligned}$$

- 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



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



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

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

- 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

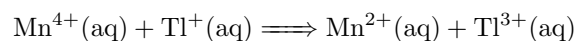


- In the absence of a catalyst,

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

and the mechanism is a termolecular elementary reaction.

- However, with Mn^{2+} as the catalyst, we have the mechanism



where the step with k_{cat} is the rate-determining step.

- Thus, for this mechanism, we have that

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

- The overall rate law for this reaction is therefore

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

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 H^{+} .
- **Substrate:** The reactant molecule acted upon by an enzyme.

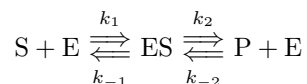
- **Active site:** The region of the enzyme where the substrate reacts.
- **Lock-and-key model:** The active site and substrate have complementary three-dimensional structures and dock without the need for major atomic rearrangements.
- **Induced fit model:** Binding of the substrate induces a conformation 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., $[S]_0 \ll [E]_0$) and the enzyme-substrate affinity is strong (but not so strong that the enzyme-substrate complex is energetically favorable), then we expect $v_{\text{initial}} \propto [S]_0$ because we'd think that all of the substrate will immediately be absorbed and transformed.
 - If the substrate concentration is large (i.e., $[S]_0 \gg [E]_0$) and the enzyme-substrate affinity is strong, then we expect $v_{\text{initial}} \propto [E]_0$ and, importantly, $v_{\text{initial}} \not\propto [S]_0$.

- Mathematical derivation.

- Experimental studies reveal that the rate law for many enzyme-catalyzed reactions has the form

$$-\frac{d[S]}{dt} = \frac{k[S]}{K + [S]}$$

- This is the final goal of the derivation.
- The mechanism is



- Thus,

$$\begin{aligned} -\frac{d[S]}{dt} &= k_1[E][S] - k_{-1}[ES] \\ -\frac{d[ES]}{dt} &= (k_2 + k_{-1})[ES] - k_1[E][S] - k_{-2}[E][P] \\ \frac{d[P]}{dt} &= k_2[ES] - k_{-1}[E][P] \end{aligned}$$

- Note that

$$[E]_0 = [ES] + [E]$$

- Plugging that equation into the rate law for the enzyme-substrate complex and applying the steady-state approximation yields

$$\begin{aligned} -\frac{d[ES]}{dt} = 0 &= [ES](k_1[S] + k_{-1} + k_2 + k_{-1}[P]) - k_1[S][E]_0 - k_2[P][P]_0 \\ [ES] &= \frac{k_1[S] + k_{-1}[P]}{k_1[S] + k_{-2}[P] + k_{-1} + k_2} [E]_0 \end{aligned}$$

- 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,

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

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

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