Chapter 29

Reaction Mechanisms

29.1 TST and Overview of Mechanisms

- Overview of key concepts.

    - Reaction mechanisms can involve more than one elementary step.
    - Reactions can be sequential (single- or multi-step).
    - To establish a mechanism, we use several techniques, approaches, assumptions, and approximations.
    - Establish rate determining steps: The rate law and rate constants associated with these steps tend to dominate the kinetics of the overall reaction.
    - Invoke the steady-state approximation to help solve the complicated mathematics of reaction kinetics.
   - Enzyme kinetics, Michaelis-Menten mechanism involves an SS approximation.

- Oftentimes, reactions are of the form

$$\text{E} + \text{S} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \xrightarrow{k_r} \text{P} + \text{E}$$
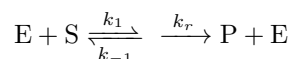
    - Note that this form is very much analogous to the form analyzed in TST.

- **Elementary reaction**: A reaction that does not involve the formation of a reaction intermediate; the products must be formed directly from the reactants.

    - Denoted by the double arrow.
    - An elementary reaction can still be reversible.

- **Molecularity** (of an elementary reaction): The number of reactant molecules involved in the chemical reaction.
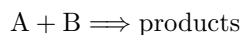
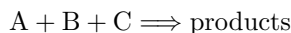- **Unimolecular** (reaction): An elementary reaction with molecularity one. *General form*

$$\text{A} \Longrightarrow \text{products}$$
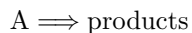
    Rate law

$$v = k[\text{A}]$$

- **Bimolecular** (reaction): An elementary reaction with molecularity two. *General form*

$$\text{A} + \text{B} \Longrightarrow \text{products}$$

    Rate law

$$v = k[\text{A}][\text{B}]$$

- **Termolecular** (reaction): An elementary reaction with molecularity three. *General form*

$$A + B + C \Longrightarrow products$$

  Rate law

$$v = k[A][B][C]$$

- No elementary reaction with molecularity greater than three is known, and the overwhelming majority of elementary reactions are bimolecular.

- When a complex reaction is at equilibrium, the rate of the forward process is equal to the rate of the reverse process for each and every step of the reaction mechanism.

  - We denote a reversible elementary reaction as follows.

$$A + B \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} C + D$$
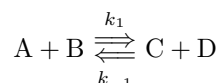
  - A reversible elementary reaction signifies that the reaction occurs in both the forward and reverse directions to a significant extent and that the reaction in each direction is an elementary reaction.
  - The rate laws are

$$v_1 = k_1[A][B] \qquad\qquad v_{-1} = k_{-1}[C][D]$$
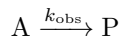
  - At equilibrium,

$$k_1[A]_{eq}[B]_{eq} = k_{-1}[C]_{eq}[D]_{eq}$$
$$\frac{k_1}{k_{-1}} = \frac{[C]_{eq}[D]_{eq}}{[A]_{eq}[B]_{eq}} = K_c$$

- **Principle of detailed balance**: The following relationship, which holds for all reversible elementary reactions. *Given by*

$$K_c = \frac{k_1}{k_{-1}}$$

29.2   The Two-Step Consecutive Reaction Mechanism

4/20:
- Consider the general complex reaction

$$A \xrightarrow{k_{obs}} P$$

  - Suppose that the reaction occurs by the two step mechanism

$$A \xrightarrow{k_1} I \qquad\qquad\qquad I \xrightarrow{k_2} P$$

  - Because each step of this mechanism is an elementary reaction, the rate laws for each species are

$$\frac{d[A]}{dt} = -k_1[A] \qquad \frac{d[I]}{dt} = k_1[A] - k_2[I] \qquad \frac{d[P]}{dt} = k_2[I]$$

  - Thus, assuming that the initial concentrations at time $t = 0$ are $[A] = [A]_0$ and $[I]_0 = [P]_0 = 0$, we have that

$$[A] = [A]_0 e^{-k_1 t}$$
$$[I] = \frac{k_1[A]_0}{k_2 - k_1}(e^{-k_1 t} - e^{-k_2 t})$$
$$[P] = [A]_0 - [A] - [I] = [A]_0 \left\{ 1 + \frac{1}{k_1 - k_2}(k_2 e^{-k_1 t} - k_1 e^{-k_2 t}) \right\}$$

- Distinguishing the two-step consecutive reaction mechanism unambiguously from the one-step reaction.

  - For a single step reaction,
    $$[P] = [A]_0(1 - e^{-k_1 t})$$

  - The two-step consecutive reaction mechanism has the following alternate form.

    $$[P] = [A]_0 \left\{ 1 + \frac{1}{k_1 - k_2}(k_2 e^{-k_1 t} - k_1 e^{-k_2 t}) \right\}$$

  - However, if $k_2 \gg k_1$, then

    $$[P] = [A]_0 \left\{ 1 + \frac{1}{k_1 - k_2}(k_2 e^{-k_1 t} - k_1 e^{-k_2 t}) \right\}$$
    $$\approx [A]_0 \left\{ 1 + \frac{1}{-k_2}k_2 e^{-k_1 t} \right\}$$
    $$= [A]_0(1 - e^{-k_1 t})$$

  - If $k_1 \gg k_2$, he reaction reduces to
    $$[P] \approx [A]_0(1 - e^{-k_2 t})$$

  - Thus, the only ambiguous situation is $k_2 \gg k_1$.

- The steady-state approximation simplifies rate expressions.

  - We assume that $d[I]/dt = 0$, where I is a reaction intermediate.
  - Given the above differential equation for $d[I]/dt$, making the above assumption yields
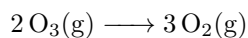
    $$[I]_{SS} = \frac{k_1[A]}{k_2}$$

  - It follows that

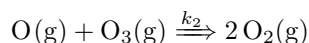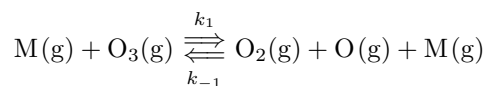 $$[I]_{SS} = \frac{k_1}{k_2}[A]_0 e^{-k_1 t}$$

  - Thus,

    $$\frac{d[I]_{SS}}{dt} = \frac{-k_1^2}{k_2}[A]_0 e^{-k_1 t}$$

  - We get $k_2 \gg k_1^2[A]_0$ and $[P] = [A]_0(1 - e^{-k_1 t})$.

- Example: Decomposition of ozone.
  $$2\,O_3(g) \longrightarrow 3\,O_2(g)$$

  - The reaction mechanism is

    $$M(g) + O_3(g) \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} O_2(g) + O(g) + M(g)$$

    $$O(g) + O_3(g) \overset{k_2}{\Longrightarrow} 2\,O_2(g)$$

    where M is a molecule that can exchange energy with the reacting ozone molecule through a collision, but M itself does not react.

  - The rate equations for $O_3(g)$ and $O(g)$ are

    $$\frac{d[O_3]}{dt} = -k_1[O_3][M] + k_{-1}[O_2][O][M] - k_2[O][O_3]$$
    $$\frac{d[O]}{dt} = k_1[O_3][M] - k_{-1}[O_2][O][M] - k_2[O][O_3]$$

– Invoking the steady-state approximation for the intermediate O yields

$$[O] = \frac{k_1[O_3][M]}{k_{-1}[O_2][M] + k_2[O_3]}$$

– Substituting this result into the rate equation for O_3 gives

$$\frac{d[O_3]}{dt} = -\frac{2k_1k_2[O_3]^2[M]}{k_{-1}[O_2][M] + k_2[O_3]}$$

29.3 Complex Reactions

4/22:
- Expect the midterm to be 2 hours in length, available all next week, and to incorporate largely HW-like questions but also some open-ended, design-an-experiment questions. Completely open note.

- The rate law for a complex reaction does not imply a unique mechanism.
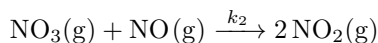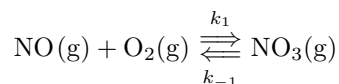
  – Consider the reaction
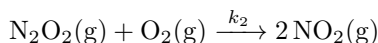 $$2\,NO(g) + O_2(g) \xrightarrow{k_{obs}} 2\,NO_2(g)$$
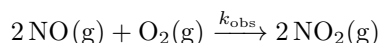
  – The rate law is
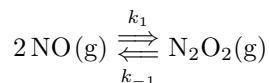 $$\frac{1}{2}\frac{d[NO_2]}{dt} = k_{obs}[NO]^2[O_2]$$

  – Experimental studies confirm that the reaction is not an elementary reaction, but we can propose multiple mechanisms that would both yield the same rate law. Here are two examples.
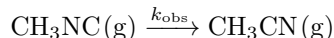
    ■ Mechanism 1.

    $$NO(g) + O_2(g) \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} NO_3(g)$$

    $$NO_3(g) + NO(g) \xrightarrow{k_2} 2\,NO_2(g)$$

    ■ Mechanism 2.

    $$2\,NO(g) \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} N_2O_2(g)$$

    $$N_2O_2(g) + O_2(g) \xrightarrow{k_2} 2\,NO_2(g)$$

  – One experiment to design is to capture or otherwise detect the intermediate species.
  – Through such an experiment, we can verify Mechanism 2.

- The Lindemann Mechanism explains how unimolecular reactions occur.

  – Consider the reaction
  $$CH_3NC(g) \xrightarrow{k_{obs}} CH_3CN(g)$$

  – The following rate law is only correct at $[CH_3NC]$.
  $$\frac{d[CH_3NC]}{dt} = -k_{obs}[CH_3NC]$$

  – At low $[CH_3NC]$, we have
  $$\frac{d[CH_3NC]}{dt} = -k_{obs}[CH_3NC]^2$$
  which is not the rate law for a unimolecular reaction.

– The Lindemann mechanism for unimolecular reactions of the form $A(g) \longrightarrow B(g)$ is

$$A(g) + M(g) \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} A(g)^* + M(g)$$

$$A(g)^* \xrightarrow{k_2} B(g)$$
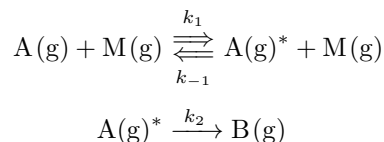
– The symbol $A(g)^*$ represents an energized reactant molecule. $M(g)$ is the collision partner.

– By the steady-state approximation, we have that

$$\frac{d[A^*]}{dt} = 0 = k_1[A][M] - k_{-1}[A^*][M] - k_2[A^*]$$

$$[A^*] = \frac{k_1[M][A]}{k_2 + k_{-1}[M]}$$

so that

$$\frac{d[B]}{dt} = k_2[A^*]$$

$$-\frac{d[A]}{dt} = \frac{d[B]}{dt} = \underbrace{\frac{k_2 k_1 [M]}{k_2 + k_{-1}[M]}}_{k_{obs}}[A]$$

– At high $[M]$, we have that $k_{-1}[M][A^*] \gg k_2[A^*]$, or $k_{-1}[M] \gg k_2$. Thus,

$$k_{obs} = \frac{k_1 k_2}{k_{-1}}$$

– At low $[M]$, we have that $k_2 \gg k_{-1}[M]$ so that
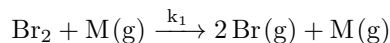
$$\frac{d[B]}{dt} = k_1[M][A]$$
$$= k_1[A]^2$$

– This mechanism was proposed by the British chemists J. A. Christiansen in 1921 and F. A. Lindemann in 1922. Their work underlies the current theory of unimolecular reaction rates.
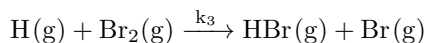
• Some reaction mechanisms involve chain reactions.

– Chain reactions involve amplification.

– For example, $H_2(g) + Br_2(g) \rightleftharpoons 2\,HBr(g)$ follows the ensuing mechanism.

■ Initiation.
$$Br_2 + M(g) \xrightarrow{k_1} 2\,Br(g) + M(g)$$

■ Propagation.

$$Br(g) + H_2(g) \xrightarrow{k_2} HBr(g) + H(g)$$
$$H(g) + Br_2(g) \xrightarrow{k_3} HBr(g) + Br(g)$$

■ Inhibition.

$$HBr(g) + H(g) \xrightarrow{k_{-2}} Br(g) + H_2(g)$$
$$HBr(g) + Br(g) \xrightarrow{k_{-3}} H(g) + Br_2(g)$$

■ Termination.

$$2\,\mathrm{Br} + \mathrm{M\,(g)} \xrightarrow{\mathrm{k_{-1}}} \mathrm{Br_2\,(g)} + \mathrm{M\,(g)}$$
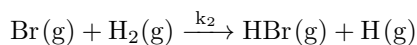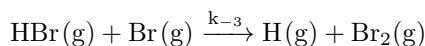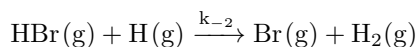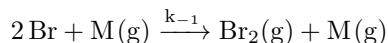
– The fifth step can be ignored.

– Notice that the inhibition and termination reactions are the reverse reactions of the propagation and initiation reaction(s), respectively.

■ Termination does not need to be the reverse of initiation, though. Termination just kills any reactive species.

■ Inhibition is the reverse of propagation, though.

– When you want to design a chain reaction species, make sure you have a reactive species (like bromine) for the initiation step. Notice, for instance, that hydrogen does not initiate.

– This leads to the experimentally determined rate law

$$\frac{1}{2}\frac{\mathrm{d[HBr]}}{\mathrm{d}t} = \frac{k[\mathrm{H_2}][\mathrm{Br_2}]^{1/2}}{1 + k'[\mathrm{HBr}][\mathrm{Br_2}]^{-1}}$$

– Deriving said rate law.

■ We have that

$$\frac{\mathrm{d[HBr]}}{\mathrm{d}t} = k_2[\mathrm{Br}][\mathrm{H_2}] - k_{-2}[\mathrm{HBr}][\mathrm{H}] + k_3[\mathrm{H}][\mathrm{Br_2}]$$

$$\frac{\mathrm{d[H]}}{\mathrm{d}t} = k_2[\mathrm{Br}][\mathrm{H_2}] - k_{-2}[\mathrm{HBr}][\mathrm{H}] - k_3[\mathrm{H}][\mathrm{Br_2}]$$

$$\frac{\mathrm{d[Br]}}{\mathrm{d}t} = 2k_1[\mathrm{Br_2}][\mathrm{M}] - k_{-1}[\mathrm{Br}]^2[\mathrm{M}] - k_2[\mathrm{Br}][\mathrm{H_2}] + k_{-2}[\mathrm{HBr}][\mathrm{H}] + k_3[\mathrm{H}][\mathrm{Br_2}]$$

■ We can apply the SS approximation to the second and third equations above, which both describe intermediate species.

$$0 = k_2[\mathrm{Br}][\mathrm{H_2}] - k_{-2}[\mathrm{HBr}][\mathrm{H}] - k_3[\mathrm{H}][\mathrm{Br_2}]$$

$$0 = 2k_1[\mathrm{Br_2}][\mathrm{M}] - k_{-1}[\mathrm{Br}]^2[\mathrm{M}] - k_2[\mathrm{Br}][\mathrm{H_2}] + k_{-2}[\mathrm{HBr}][\mathrm{H}] + k_3[\mathrm{H}][\mathrm{Br_2}]$$

■ Solving the two equations above for [H] and [Br], respectively, is made substantially easier by noting that the negative of the first expression appears in its entirety in the second expression. Thus, we may simply substitute the former into the latter and solve to find an expression for [Br].

$$0 = 2k_1[\mathrm{Br_2}][\mathrm{M}] - k_{-1}[\mathrm{Br}]^2[\mathrm{M}] - 0$$

$$[\mathrm{Br}] = \left(\frac{k_1}{k_{-1}}\right)^{1/2}[\mathrm{Br_2}]^{1/2}$$

$$[\mathrm{Br}] = (K_{c,1})^{1/2}[\mathrm{Br_2}]^{1/2}$$

■ Resubstituting yields an expression for [H].

$$0 = k_2[\mathrm{Br}][\mathrm{H_2}] - k_{-2}[\mathrm{HBr}][\mathrm{H}] - k_3[\mathrm{H}][\mathrm{Br_2}]$$

$$0 = k_2(K_{c,1})^{1/2}[\mathrm{Br_2}]^{1/2}[\mathrm{H_2}] - (k_{-2}[\mathrm{HBr}] + k_3[\mathrm{Br_2}])[\mathrm{H}]$$

$$[\mathrm{H}] = \frac{k_2(K_{c,1})^{1/2}[\mathrm{Br_2}]^{1/2}[\mathrm{H_2}]}{k_{-2}[\mathrm{HBr}] + k_3[\mathrm{Br_2}]}$$
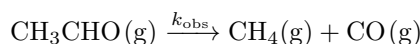
∎ Substituting these two expressions back into the original differential equation for [HBr] yields

$$\frac{d[HBr]}{dt} = k_2[Br][H_2] - k_{-2}[HBr][H] + k_3[H][Br_2]$$

$$= k_2(K_{c,1})^{1/2}[Br_2]^{1/2}[H_2] - k_{-2}[HBr] \cdot \frac{k_2(K_{c,1})^{1/2}[Br_2]^{1/2}[H_2]}{k_{-2}[HBr] + k_3[Br_2]}$$

$$+ k_3 \cdot \frac{k_2(K_{c,1})^{1/2}[Br_2]^{1/2}[H_2]}{k_{-2}[HBr] + k_3[Br_2]} \cdot [Br_2]$$

$$= k_2(K_{c,1})^{1/2}[Br_2]^{1/2}[H_2] - \frac{k_2 k_{-2}(K_{c,1})^{1/2}[HBr][Br_2]^{1/2}[H_2]}{k_{-2}[HBr] + k_3[Br_2]}$$

$$+ \frac{k_2 k_3(K_{c,1})^{1/2}[Br_2]^{3/2}[H_2]}{k_{-2}[HBr] + k_3[Br_2]}$$

$$= k_2(K_{c,1})^{1/2}[Br_2]^{1/2}[H_2] \left(1 - \frac{k_{-2}[HBr]}{k_{-2}[HBr] + k_3[Br_2]} + \frac{k_3[Br_2]}{k_{-2}[HBr] + k_3[Br_2]}\right)$$

$$= k_2(K_{c,1})^{1/2}[Br_2]^{1/2}[H_2] \left(\frac{k_{-2}[HBr] + k_3[Br_2]}{k_{-2}[HBr] + k_3[Br_2]} - \frac{k_{-2}[HBr] - k_3[Br_2]}{k_{-2}[HBr] + k_3[Br_2]}\right)$$

$$= k_2(K_{c,1})^{1/2}[Br_2]^{1/2}[H_2] \cdot \frac{2k_3[Br_2]}{k_{-2}[HBr] + k_3[Br_2]}$$

$$\frac{1}{2}\frac{d[HBr]}{dt} = k_2(K_{c,1})^{1/2}[Br_2]^{1/2}[H_2] \cdot \frac{1}{(k_{-2}/k_3)[HBr][Br_2]^{-1} + 1}$$

$$= \frac{k_2(K_{c,1})^{1/2}[H_2][Br_2]^{1/2}}{1 + (k_{-2}/k_3)[HBr][Br_2]^{-1}}$$

$$= \frac{k[H_2][Br_2]^{1/2}}{1 + k'[HBr][Br_2]^{-1}}$$
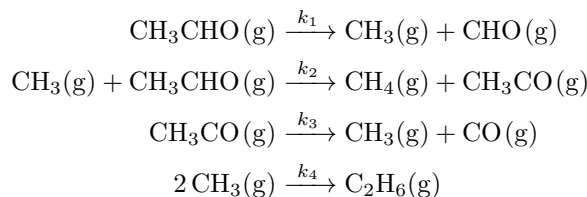
where we have substituted $k = k_2(K_{c,1})^{1/2}$ and $k' = k_{-2}/k_3$ in the last expression.

- Problem 29-24.

  - The reaction

  $$CH_3CHO(g) \xrightarrow{k_{obs}} CH_4(g) + CO(g)$$

  proceeds by the mechanism

  $$CH_3CHO(g) \xrightarrow{k_1} CH_3(g) + CHO(g)$$

  $$CH_3(g) + CH_3CHO(g) \xrightarrow{k_2} CH_4(g) + CH_3CO(g)$$

  $$CH_3CO(g) \xrightarrow{k_3} CH_3(g) + CO(g)$$

  $$2\,CH_3(g) \xrightarrow{k_4} C_2H_6(g)$$

  - The initiation step is the first equation, the propagation steps are the second and third equations, and the termination step is the fourth equation.

  - We can write the rate laws

  $$\frac{d[CH_4]}{dt} = k_2[CH_3][CH_3CHO]$$

  $$\frac{d[CH_3]}{dt} = k_1[CH_3CHO] - k_2[CH_3][CH_3CHO] + k_3[CH_3CO] - 2k_4[CH_3]$$

  $$\frac{d[CH_3CO]}{dt} = k_2[CH_3][CH_3CHO] - k_3[CH_3CO]$$

- Applying the SS approximation to the last second and third equations yields (respectively)

$$[CH_3] = \frac{k_1[CH_3CHO] + k_3[CH_3CO]}{k_2[CH_3CHO] + 2k_4} \qquad [CH_3CO] = \frac{k_2}{k_3}[CH_3][CH_3CHO]$$

- Substituting the right equation above into the left equation above and solving for $[CH_3]$ yields an expression for $[CH_3]$ purely in terms of $[CH_3CHO]$.

$$[CH_3] = \frac{k_1[CH_3CHO] + k_2[CH_3][CH_3CHO]}{k_2[CH_3CHO] + 2k_4}$$
$$k_2[CH_3][CH_3CHO] + 2k_4[CH_3] = k_1[CH_3CHO] + k_2[CH_3][CH_3CHO]$$
$$2k_4[CH_3] = k_1[CH_3CHO]$$
$$[CH_3] = \frac{k_1}{2k_4}[CH_3CHO]$$

- The final result is

$$\frac{d[CH_4]}{dt} = k_2\left(\frac{k_1}{2k_4}[CH_3CHO]\right)[CH_3CHO]$$
$$= k_2\left(\frac{k_1}{2k_4}\right)^{1/2}[CH_3CHO]^{3/2}$$

■ What's the issue here?

29.4 Midterm Review and Intro to Catalysts

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

    - Let

$$A \underset{k_a'}{\overset{k_a}{\rightleftharpoons}} B \underset{k_b'}{\overset{k_b}{\rightleftharpoons}} C \underset{k_c'}{\overset{k_c}{\rightleftharpoons}} D$$
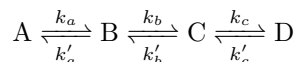
    Suppose $[A]$ is maintained at a fixed value and the produce D is removed from the reaction as it is formed. Find the rate at which the product is formed in terms of $[A]$.

    - By hypothesis, we have that at all times t, $[A] = [A]_0$ and $[D] = 0$.
    - The hypotheses also imply that we can apply the steady-state approximation to both B and C.
    - Thus, we have that

$$\frac{d[C]}{dt} = 0 = k_b[B] - k_c[C] - k_b'[C]$$
$$[B] = \frac{k_b' + k_c}{k_b}[C]$$

    so that

$$\frac{d[B]}{dt} = k_a[A] - k_b[B] - k_a'[B] + k_b'[C]$$
$$0 = k_a[A] - k_b \cdot \frac{k_b' + k_c}{k_b}[C] - k_a' \cdot \frac{k_b' + k_c}{k_b}[C] + k_b'[C]$$
$$[C] = \frac{k_a k_b}{k_b k_c + k_a' k_b' + k_a' k_c}[A]$$

    and therefore

$$\frac{d[D]}{dt} = k_c[C] - k_c' \cdot 0$$
$$= \frac{k_a k_b k_c}{k_b k_c + k_a' k_b' + k_a' k_c}[A]$$

- Example problem 2.
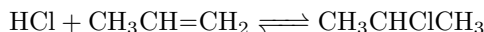
  - Consider the reaction
  $$HCl + CH_3CH{=}CH_2 \rightleftharpoons CH_3CHClCH_3$$
  which proceeds by the mechanism
    1. $HCl + HCl \rightleftharpoons (HCl)_2$ (equilibrium constant K_1).
    2. $HCl + CH_3CH{=}CH_2 \rightleftharpoons$ complex (equilibrium constant K_2).
    3. $(HCl)_2 +$ complex $\rightleftharpoons CH_3CHClCH_3 + HCl + HCl$ (equilibrium constant K_3).
  - The equilibrium constants for the two pre-equilibria are

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

  - 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

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

    ∎ 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

$$A \xrightarrow{k} products$$
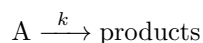
where k is the observed rate constant.

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

$$\text{A} + \text{catalyst} \xrightarrow{k_{\text{cat}}} \text{products} + \text{catalyst}$$
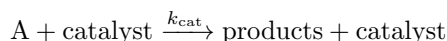
- If each of these competing reactions is an elementary process, then

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

- 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.
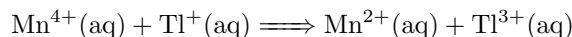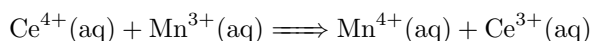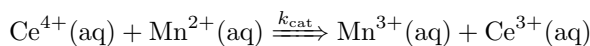
  - Consider the reaction

$$2\,\text{Ce}^{4+}(\text{aq}) + \text{Tl}^{+}(\text{aq}) \longrightarrow 2\,\text{Ce}^{3+}(\text{aq}) + \text{Tl}^{3+}(\text{aq})$$
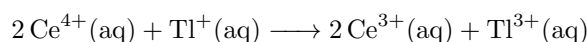
  - In the absence of a catalyst,

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

  and the mechanism is a termolecular elementary reaction.

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

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

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

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

  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

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

29.5   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

    $$S + E \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} P + E$$
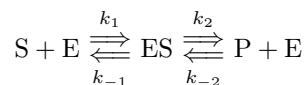
  - Thus,

    $$-\frac{d[S]}{dt} = k_1[E][S] - k_{-1}[ES]$$

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

    $$\frac{d[P]}{dt} = k_2[ES] - k_{-1}[E][P]$$

  - 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

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

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

– 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.

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