Catalysis

1. Background
   a) Motivation for Catalysis -- The reaction $A \rightleftharpoons B$ is slow because of a large $E_a$. How do we accelerate product formation? Raise the reaction temperature? This is a possible solution, but suppose the reaction is exothermic ($\Delta H < 0$). Then,

   \[ \frac{d \ln K_{eq}}{dT} = \frac{\Delta H^0}{RT^2}; \quad K_{eq} = \frac{[B]}{[A]} \]

   decreases with $T$.

   Thus, the yield of product goes down as the rate increases! How do we maintain the yield and concurrently increase the rate? Often it is possible to find a catalyst which will accomplish this goal. For example, instead of

   \[ A \xrightarrow{k_1} B \xleftarrow{k_{-1}} \]

   we utilize

   \[ A + C \xrightarrow{k_2} B + C \xleftarrow{k_{-2}} \]

   Where $k_2 > k_1$ because of the catalyst $C$. In general the catalyst, is not destroyed by the reaction.

   b) Effectiveness of Catalyst -- Catalyst can be very effective at accelerating reaction rates. Consider the reaction

   \[ H_2O_2 \xrightarrow{\text{Catalase}} H_2O + \frac{1}{2}O_2 \]

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Velocity ($-d[H_2O_2]/dt$)</th>
<th>$E_a$ (kJ/mole)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>$10^{-8}$</td>
<td>71</td>
</tr>
<tr>
<td>HBr</td>
<td>$10^{-4}$</td>
<td>50</td>
</tr>
<tr>
<td>Fe$^{2+}$/Fe$^{3+}$</td>
<td>$10^{-3}$</td>
<td>42</td>
</tr>
<tr>
<td>Catalase (enzyme)</td>
<td>$10^7$</td>
<td>8</td>
</tr>
</tbody>
</table>

   Reaction velocity accelerates by a factor of $10^{15}$!
\[(\text{NH}_2 \text{C}=\text{O} + \text{H}_2\text{O}) \xrightarrow{\text{Urease}} \text{CO}_2 + \text{NH}_2\]

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>-d[Urea]/dt</th>
<th>(E_a) (kJ/mole)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>No reaction</td>
<td>.</td>
</tr>
<tr>
<td>(\text{H}_3\text{O}^+)</td>
<td>10(^{-8})</td>
<td>100</td>
</tr>
<tr>
<td>Urease</td>
<td>10(^7)</td>
<td>7</td>
</tr>
</tbody>
</table>

Again, an acceleration of \(10^{15}\)!

As illustrated above enzymes are very effective catalysts. Sometimes they are very specific -- ie, a small change in the substrate will disable their function. Others react with large classes of molecules -- phosphatase cleaves a large number of different phosphate esters.

2) Function of a Catalyst -- a catalyst lowers \(E_a\) and therefore accelerates the reaction. Often the mechanism of the reaction is also altered.

In the case above \(E_a\) is lowered from 71 to 8 kJ/mole, However, for the reaction

\[
A + C \xrightleftharpoons{<k_2}> B + C
\]

the equilibrium constant is

\[
K_{eq} = \frac{k_2}{k_{-2}} = \frac{[B][C]}{[A][C]} = \frac{[B]}{[A]}
\]

Thus, the position of the equilibrium is not altered by the presence of \(C\)!
3) Types of Catalysts -- Catalyst and catalytic processes are divided into two categories:

   a) **Homogeneous catalyst** occupies the same phase as the reactants: thus,

   \[
   \text{H}_2\text{O}_2 \xrightarrow{\text{Catalase}} \text{H}_2\text{O} + \frac{1}{2}\text{O}_2
   \]

   \[
   \text{CH}_3\text{C} - \text{OEt} + \text{H}_2\text{O} \xrightarrow{\text{H}^+} \text{CH}_3\text{COOH} + \text{EtOH}
   \]

   b) **Heterogeneous Catalyst** is in a different phase than the reactants: for example a liquid (reactants)-solid (catalyst) or gas (reactants)-solid (catalyst)

   \[
   3\text{H}_2 + \text{CO} \xrightarrow{\text{Ni}/\text{Al}_2\text{O}_3} \text{CH}_4 + \text{H}_2\text{O}
   \]

   \[\text{DG}_\infty (500 \text{ K}) = -94.4 \text{ kJ/mole, } K_{\text{eq}} \sim 1.2 \times 10^{10}\text{ but in the absence of a catalyst, the rate is very slow.}\]

   How does the catalyst function -- mechanism of \(3\text{H}_2 + \text{CO}\) on Ni.

   Thus, heterogeneous or surface catalysis involves adsorption of reactants on active sites.

   Sometimes the distinction between homogeneous and heterogeneous catalysis is not clear. For example, many **membrane bound enzymes** are involved in catalysis. Is this hetero- or homogenous catalysis?

4) Enzyme Catalysis

   a) **Michaelis-Menten Equation**

   Enzymes are large molecules (\(\text{mw} = 10^4\text{-}10^6\)) which catalyze biochemical reactions. Typically, they are \(\sim 10\text{-}100\) nm diameter and are sometimes immobilized in membranes. Two typical experimental observations are
(a) Product formation is linear in [E]
(b) For fixed [E], velocity a [S] and rate approaches a maximum or saturating velocity.
(c) We will consider the initial rate regime.

Consider the general reaction

\[
E + S \xrightarrow{k_1} ES \xrightarrow{k_{-1}} E + P
\]

In most experimental circumstances

\[ [E] \ll [S] \text{ and } [ES] \ll [S] \]

therefore, steady state approximation is valid.

\[
d[ES]/dt = k_1 [E] [S] - k_{-1} [ES] - k_2 [ES] + k_{-2} [E] [P] = 0
\]

We often do not know [E], but we do know

\[
[E]_0 = [E] + [ES] \quad \text{and} \quad [E] = [E]_0 - [ES]
\]

\[
([E]_0 - [ES]) \left[ k_1 [S] + k_{-2} [P] \right] - (k_{-1} + k_2) [ES] = 0
\]

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

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

The reaction rate is \(-d[S]/dt\), which yields
\[ V = \frac{-d[S]}{dt} = k_1 [E][S] - k_{-1} [ES] \]
\[ = k_1 ([E]_0 - [ES]) [S] - k_{-1} [ES] \]
\[ V = k_1 [E]_0 [S] - (k_1 [S] + k_{-1}) [ES] \]

Since \([ES] \sim 0\),
\[ - \frac{d[S]}{dt} = \frac{d[P]}{dt} \]
\[ V = k_1 [E]_0 [S] - (k_1 [S] + k_{-1}) \left( \frac{k_1 [S] + k_2 [P]}{k_{-1} + k_2 + k_1 [S] + k_{-2} [P]} [E]_0 \right) \]

which yields
\[ V = \frac{k_1 k_2 [S] - k_{-1} k_{-2} [P]}{k_{-1} + k_2 + k_1 [S] + k_{-2} [P]} [E]_0 \]

In the initial rate regime \([P] \sim 0\) (and \([S] \sim [S]_0\))

**Michaelis-Menton Equation:**

\[ V = \frac{k_2 [S]}{[S] + \frac{k_{-1} + k_2}{k_1} [E]_0} \]

where

\[ K_m = \frac{k_{-1} + k_2}{k_1} \text{ Michaelis Constant} \]

Some limiting cases of importance:

\[
\begin{align*}
[S] &> > K_m & V &= k_2 [E]_0 = V_{\text{max}} \\
[S] &< < K_m & V &= \frac{V_{\text{max}}}{K_m} [S] \\
[S] &\sim K_m & V &= \frac{V_{\text{max}}}{2}
\end{align*}
\]
The Michaelis Constant, $K_m$, equals $[S]$ that yields half the maximum velocity! Small $K_m$ means that the enzyme binds the substrate tightly, and small $[S]$’s are sufficient to saturate the enzyme and to approach maximum catalytic efficiency.

b) Lineweaver-Burke Analysis

Rewriting $V$ in terms of $V_{\text{max}}$, we obtain

$$V = \frac{V_{\text{max}} [S]}{K_m + [S]}$$

**Lineweaver-Burke Equation:**

$$\frac{1}{V} = \frac{K_m}{V_{\text{max}} [S]} + \frac{1}{V_{\text{max}}}$$

which leads to a **Lineweaver-Burke Plot**

$$\text{Turnover Number} = \frac{\text{Number moles product}}{\text{Number moles binding site} \cdot \text{sec}}$$

$$= \frac{V_{\text{max}}}{[E_0]} k_{2\text{cat}}$$
c) **Comments about Michaelis-Menton:**

(a) $M^2$ is an oversimplification. In many situations EP and other ES complexes exist.

(b) $M^2$ was developed when enzyme's were rare and difficult to obtain. With genetic engineering, E's are readily available and kinetic analysis will change.

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**Relaxation Kinetics**

*(M. Eigen--Nobel Prize, 1967)*

Steady state treatment above is not applicable to fast reactions. However, relaxation techniques can be used to perturb the equilibrium and observed the return to a new equilibrium. The techniques are particularly useful for enzymes. Generally, they involve T (temperature) jump, P (pressure) jump, etc.

Consider the reversible reaction

$$A + B \overset{k_1}{\underset{k_{-1}}{\rightleftharpoons}} P$$

where

$$\frac{d[P]}{dt} = k_1 [A][B] - k_{-1} [P] \quad K = \frac{k_1}{k_{-1}} = \frac{[P]}{[A][B]}$$

Now, apply a T or P jump to the system and establish a new equilibrium according to

$$\left(\frac{\partial \Delta G}{\partial T}\right)_P = -\Delta S \quad \text{and} \quad \left(\frac{\partial \Delta G}{\partial P}\right)_T = \Delta V$$

$$\left(\frac{\partial \ln K}{\partial T}\right)_P = \frac{\Delta H^0}{RT^2} \quad \text{and} \quad \left(\frac{\partial \ln K}{\partial P}\right)_T = -\frac{\Delta V^0}{RT^2}$$

Experimentally a $5 \approx 10 \approx C$ or $10^{-3}$ atm change in $10^{-8} - 10^{-6}$ sec is achievable
For the above example,

\[ [P] = [\text{P}] + \delta[P] \]

where \([\text{A}] & [\text{B}]\) are equilibrium values

\[ [A] = [\text{A}] + \delta[A] = [\text{A}] - \delta[P] \]

\[ [B] = [\text{B}] + \delta[B] = [\text{B}] - \delta[P] \]

\[
\frac{d[P]}{dt} = \frac{d}{dt} ([P] + \delta[P]) = \frac{d(\delta[P])}{dt}
\]

\[
\frac{d[P]}{dt} = 0 -- \text{small changes}
\]

\[
= k_1 [\text{A}][\text{B}] - k_{-1} [P]
\]

\[
= k_1 ([\text{A}] - \delta[P])([\text{B}] - \delta[P]) - k_{-1} ([P] + \delta[P])
\]

\[
= k_1 [\text{A}][\text{B}] - k_{-1} [P] - k_1 ([\text{A}] \delta[P] + [\text{B}] \delta[P] - (\delta[P])^2) k_{-1} \delta[P]
\]

which yields

\[
- \frac{d(\delta[P])}{dt} = (k_1 ([\text{A}] + [\text{B}]) + k_{-1}) \delta[P]
\]

or

\[
- \frac{d(\delta[P])}{dt} = \frac{\delta[P]}{\tau}
\]

where

\[
\frac{1}{\tau} = k_1 ([\text{A}] + [\text{B}]) + k_{-1}
\]

Integrating

\[
\delta[P] = \delta[P]_0 e^{-t/\tau}
\]

where
\[ \tau = \frac{1}{k_1 ([A] + [B]) + k_{-1}} \]  

Relaxation Time

An experiment typically consists of a T jump followed by a spectroscopic observation of relaxation.

Follow the optical absorbance, ESR line, NMR line, etc., after the T jump. Fit the experimental data to an exponential decay to obtain \( \tau \).