Michaelis-Menten Kinetics
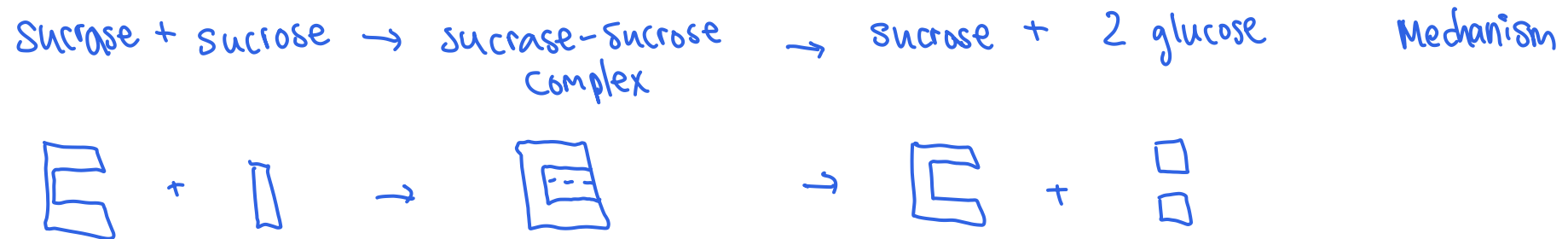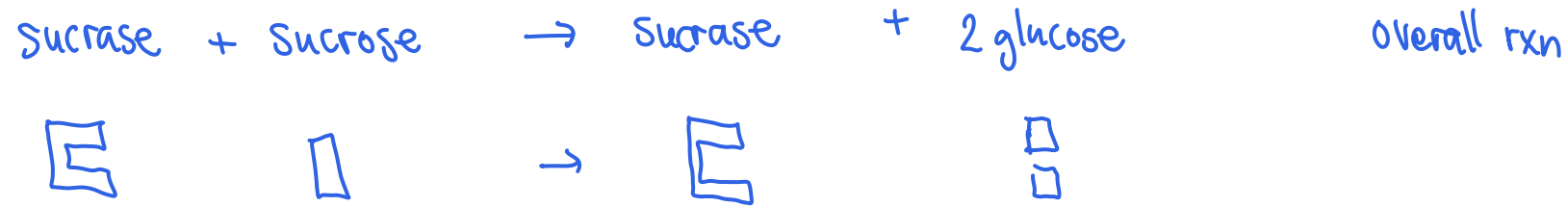
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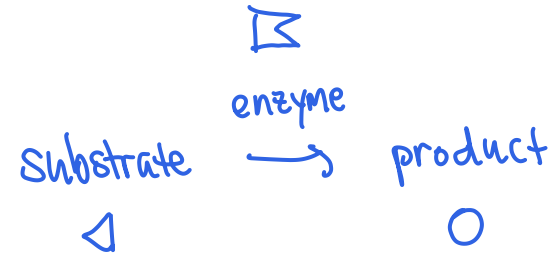**Chemical Reaction Engineering**

Enzyme are proteins that speeds up biological reactions without being used up

- **Catalyzer** - substances that speeds up reactions without being used up
- **Enzyme** - proteins that catalyzes reactions
  - E.g. Sucrase - digestive enzyme that breaks down sucrose into glucose

Sucrase + Sucrose → Sucrase + 2 glucose   Overall rxn

Sucrase + Sucrose → Sucrase-Sucrose Complex → Sucrose + 2 glucose   Mechanism
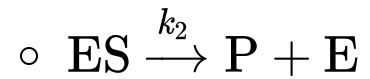
Michaelis-Menten kinetics describes simple enzymatic reactions
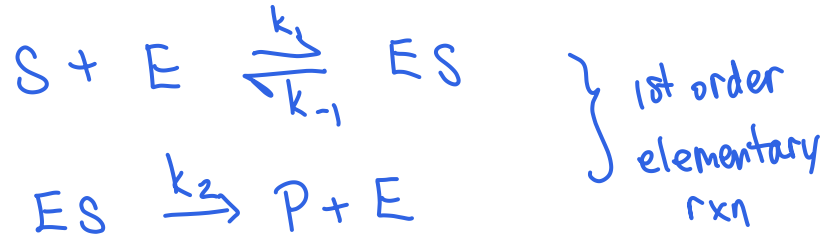
- Overall reaction
  - $S \xrightarrow{E} P$

- Reaction mechanism
  - $S + E \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES$

  - $ES \xrightarrow{k_2} P + E$
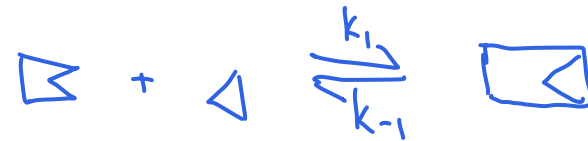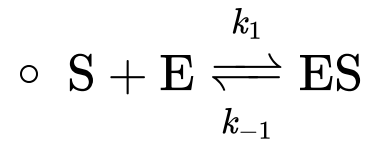
Michaelis-Menten kinetics can be derived with pseudo-steady-state approximation

Ex. Derive the rate of production r_P described by Michaelis-Menten and determine $V_{\max}$ and K_M:

$$S + E \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES$$

$$ES \xrightarrow{k_2} P + E$$

$\left.\begin{array}{c} \\ \\ \end{array}\right\}$ 1st order elementary rxn

$$\boxed{r_P = \frac{V_{\max}[S]}{K_M + [S]}}$$

Measurable : $[S]$, $[P]$, $[E_T]$

NOT measure : $[E]$, $[ES]$
$\Rightarrow$ indirect formula

- Rate expression of rate of production

$$r_P = \frac{d[P]}{dt} = k_2[ES] \qquad \curvearrowleft [ES] \text{ not measurable}$$

- Rate expression of rate of production of intermediate
  - **Pseudo-steady-state approximation** - intermediates are immediately consumed after production, so the net rate of intermediate is zero

$$r_{ES} = \frac{d[ES]}{dt} = k_1[S][E] - k_{-1}[ES] - k_2[ES] \overset{approx}{=} 0$$

Michaelis-Menten kinetics relates rate of production with substrate concentration

$$r_P = \frac{d[P]}{dt} = k_2[ES] \qquad r_{ES} = \frac{d[ES]}{dt} = k_1[S][E] - k_{-1}[ES] - k_2[ES] \overset{approx}{\simeq} 0$$

- Enzyme balance - total amount of enzyme is constant

$$[E_T] = [E] + [ES] \qquad \Rightarrow \qquad [E] = [E_T] - [ES]$$

- Solve for $[ES]$

$$k_1[S]([E_T] - [ES]) - k_{-1}[ES] - k_2[ES] = 0$$

$$[ES] = \frac{k_1[S][E_T]}{k_1[S] + k_{-1} + k_2}$$

- Solve for r_P

$$r_P = k_2[ES] = \frac{k_2 k_1[S][E_T]}{k_1[S] + k_{-1} + k_2}$$

Michaelis-Menten parameters describes reaction properties

- Simplify r_P with
  - **Maximum rate** of reaction
    - $V_{\max} = k_2[\mathrm{E_T}]$
  - **Michaelis-Menten constant** - attraction of enzyme of its substrate
    - $K_M = \dfrac{k_2 + k_{-1}}{k_1}$
  - **Turnover number** - # substrates converted to product per unit time on one enzyme at saturation
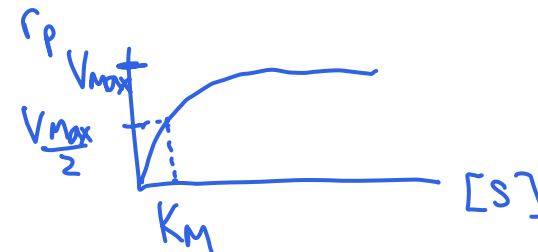   - $k_{\mathrm{cat}} = k_2$

$$r_P = k_2[ES] = \frac{\cdot k_2 k_1 [S][E_T]}{k_1[S] + k_{-1} + k_2} \cdot \frac{/k_1}{/k_1} = \frac{k_2[E_T][S]}{[S] + \frac{k_{-1}}{k_1} + \frac{k_2}{k_1}}$$

$$= \frac{V_{\max}[S]}{[S] + K_M}$$

- Given Michaelis-Menten parameters, we can know $r_P([S])$ by Michaelis-Menten eqn:

$$\text{If } r_p = \tfrac{1}{2} V_{\max} = \frac{V_{\max}[S]}{K_M + [S]} \Rightarrow r_p = \tfrac{1}{2} V_{\max}$$

$$[S] = K_M$$

$$\tfrac{1}{2}k_m + \tfrac{1}{2}[S] = [S]$$

$$[S] = K_M$$

$$\boxed{r_P = \frac{V_{\max}[S]}{K_M + [S]}}$$

Michaelis-Menten parameters can be found by linearizing the Michaelis-Menten eqn

$$r_P = \frac{V_{max}[S]}{K_M + [S]}$$
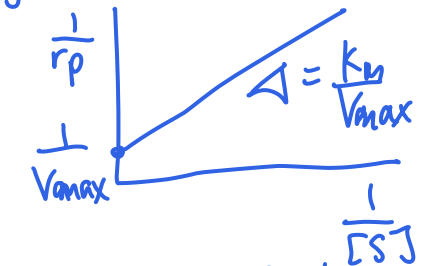
Measureable: r_P, $[S]$

Get: V_{max}, K_M

$$\frac{1}{r_P} = \frac{K_M + [S]}{V_{max}[S]} = \frac{K_M}{V_{max}[S]} + \frac{[S]}{V_{max}[S]}$$

$$\underbrace{\frac{1}{r_P}}_{y} = \underbrace{\frac{K_M}{V_{max}}}_{slope} \underbrace{\frac{1}{[S]}}_{x} + \underbrace{\frac{1}{V_{max}}}_{y-inter}$$

- **Lineweaver-Burk equation**

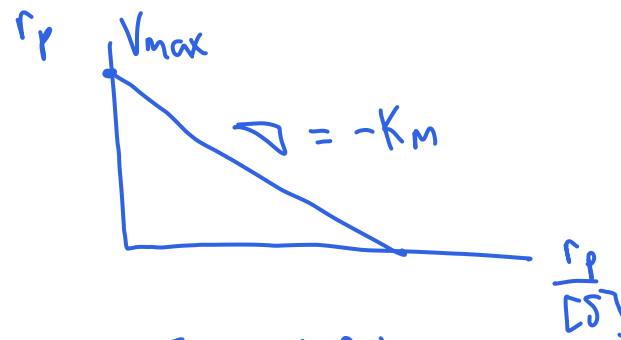 ○ $\dfrac{1}{r_P} = \dfrac{K_M}{V_{max}}\dfrac{1}{[S]} + \dfrac{1}{V_{max}}$

- Eadie-Hofstee equation

  ○ $r_P = V_{max} - K_M \dfrac{r_P}{[S]}$

  $\underbrace{r_P}_{y} = \underbrace{V_{max}}_{y-int} - \underbrace{K_M}_{slope} \underbrace{\dfrac{r_P}{[S]}}_{x}$

- Hanes-Woolf equation

  ○ $\dfrac{[S]}{r_P} = \dfrac{K_M}{V_{max}} + \dfrac{1}{V_{max}}[S]$

  $\underbrace{\dfrac{[S]}{r_P}}_{y} = \underbrace{\dfrac{K_M}{V_{max}}}_{y-inter} + \underbrace{\dfrac{1}{V_{max}}}_{slope} \underbrace{[S]}_{x}$

Lineweaver-Burk (graph: $\frac{1}{r_P}$ vs $\frac{1}{[S]}$, slope $= \frac{K_M}{V_{max}}$, intercept $\frac{1}{V_{max}}$)

Eadie-Hofstee (graph: r_P vs $\frac{r_P}{[S]}$, intercept V_{max}, slope $= -K_M$)

Hanes-Woolf (graph: $\frac{[S]}{r_P}$ vs $[S]$, intercept $\frac{K_M}{V_{max}}$, slope $= \frac{1}{V_{max}}$)