Derive Michaelis-Menten reaction rate expression. Many assumptions lead to the same saturation form.

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Method #1 Equilibrium Assumption.

$$S + E \underset{k_i}{\overset{k_1}{\longleftrightarrow}} ES \xrightarrow{k_2} P + E$$

Legend
- S ... substrate
- P ... product
- E ... unbound enzyme
- ES ... enzyme-substrate complex

Given

1. dp/dt=rate=v $\quad v = k_2 \cdot ES$
2. Conservation of enzyme species $\quad E_0 = E + ES$
3. **Equilibrium Assumption** for the first step. $\quad k_1 \cdot S \cdot E = k_i \cdot ES$

(Just set up the equations and let Mathcad do the rest. We have three equations, and we can choose to solve for any of the three unknowns -- E, ES, and v) Find the analytical expression (via Math|SmartMath|).

$$\mathrm{Find}(E, ES, v) \rightarrow \begin{bmatrix} \dfrac{1}{(k_1 \cdot S + k_i)} \cdot k_i \cdot E_0 \\ E_0 \cdot k_1 \cdot \dfrac{S}{(k_1 \cdot S + k_i)} \\ k_2 \cdot E_0 \cdot k_1 \cdot \dfrac{S}{(k_1 \cdot S + k_i)} \end{bmatrix}$$

Thus, the last row is the analytical expression for v.

$$k_2 \cdot k_1 \cdot S \cdot \frac{E_0}{(k_1 \cdot S + k_i)}$$

Dividing the numerator and denominator by k_1 gives:

$$v = \frac{k_2 \cdot E_0 \cdot S}{\dfrac{k_i}{k_1} + S}$$

Thus, by defining: $v_m = k_2 \cdot E_0 \quad K_m = \dfrac{k_i}{k_1}$ we reach the Michaelis-Menten form:

$$v(s) = \frac{v_m \cdot s}{K_m + s}$$

Method #2 Sequential Irreversible Reaction Assumption.

$$S + E \xrightarrow{k_1} ES \xrightarrow{k_2} P + E$$

Given

1. dp/dt=rate=v $\qquad v = k_2 \cdot ES$
2. Conservation of enzyme species $\qquad E_0 = E + ES$
3. Irreversible first step without accumulation of intermediate species ES. $\qquad k_1 \cdot S \cdot E = k_2 \cdot ES$

$$\text{Find}(E, ES, v) \rightarrow \begin{bmatrix} \dfrac{1}{(k_1 \cdot S + k_2)} \cdot k_2 \cdot E_0 \\ E_0 \cdot k_1 \cdot \dfrac{S}{(k_1 \cdot S + k_2)} \\ k_2 \cdot E_0 \cdot k_1 \cdot \dfrac{S}{(k_1 \cdot S + k_2)} \end{bmatrix}$$

Thus, by defining: $v_m = k_2 \cdot E_0 \quad K_m = \dfrac{k_2}{k_1}$ we reach the Michaelis-Menten form: $v(s) = \dfrac{v_m \cdot s}{K_m + s}$

Method #3 Quasi-Steady State Assumption. (Briggs & Haldane)

$$S + E \underset{k_i}{\overset{k_1}{\longleftrightarrow}} ES \xrightarrow{k_2} P + E$$

Given

1. dp/dt=rate=v $\qquad v = k_2 \cdot ES$
2. Conservation of enzyme species $\qquad E_0 = E + ES$
3. Quasi-Steady State Assumption (for the intermediate species ES) d(ES)/dt=0

$$k_1 \cdot S \cdot E - k_i \cdot ES - k_2 \cdot ES = 0$$

$$\text{Find}(E, ES, v) \rightarrow \begin{bmatrix} E_0 \cdot \dfrac{(k_i + k_2)}{(k_1 \cdot S + k_i + k_2)} \\ E_0 \cdot k_1 \cdot \dfrac{S}{(k_1 \cdot S + k_i + k_2)} \\ k_2 \cdot E_0 \cdot k_1 \cdot \dfrac{S}{(k_1 \cdot S + k_i + k_2)} \end{bmatrix}$$

Thus, by defining: $v_m = k_2 \cdot E_0 \quad K_m = \dfrac{k_i + k_2}{k_1}$ we reach the Michaelis-Menten form: $v(s) = \dfrac{v_m \cdot s}{K_m + s}$

This last form contains the first two assumptions:

For $k_2 << k_i$, $K_m \rightarrow k_i/k_1$ (which is Assumption #1)

For $k_2 >> k_i$, $K_m \rightarrow k_2/k_1$ (which is Assumption #2)