Kinetics & Dynamics of Chemical Reactions

Course CH-310

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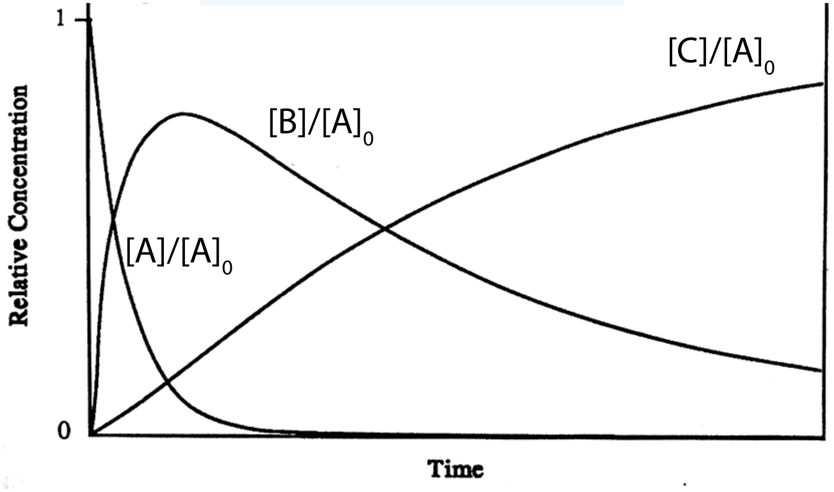
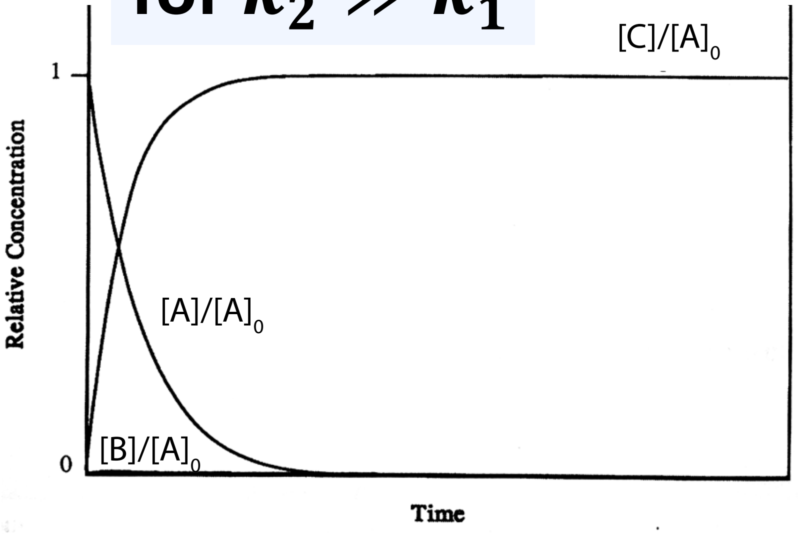
Recap from last session

- Complex (instead of elementary) reactions
- -consecutive reactions: $A \xrightarrow{k_1} B \xrightarrow{k_2} C$
- Two cases:

for $k_1 \gg k_2$

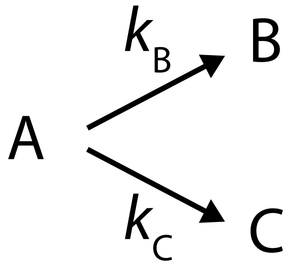


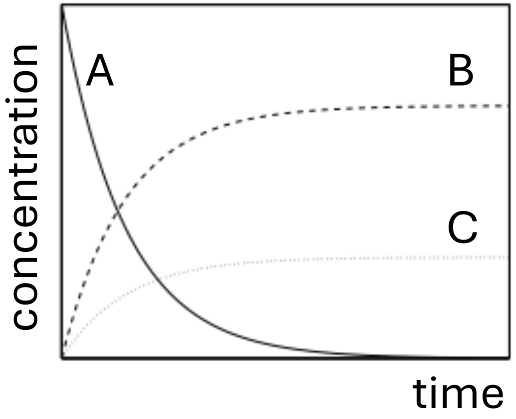
for $k_2 \gg k_1$



Recap from last session

- -Parallel reactions:





- Steady-state approximation:
- -valid, if conc. of intermediate small. Then can set: $\frac{d[\mathrm{A}_i]}{dt} \approx 0$
- -applied it to simple 2-step consecutive reaction with $k_2 \gg k_1$
- -applied it to 2-step consecutive reaction with reversible first step; with cases of 1st or 2nd step rate-limiting got different results
- Pseudo-first order method (experimental approach)

Chapter 3

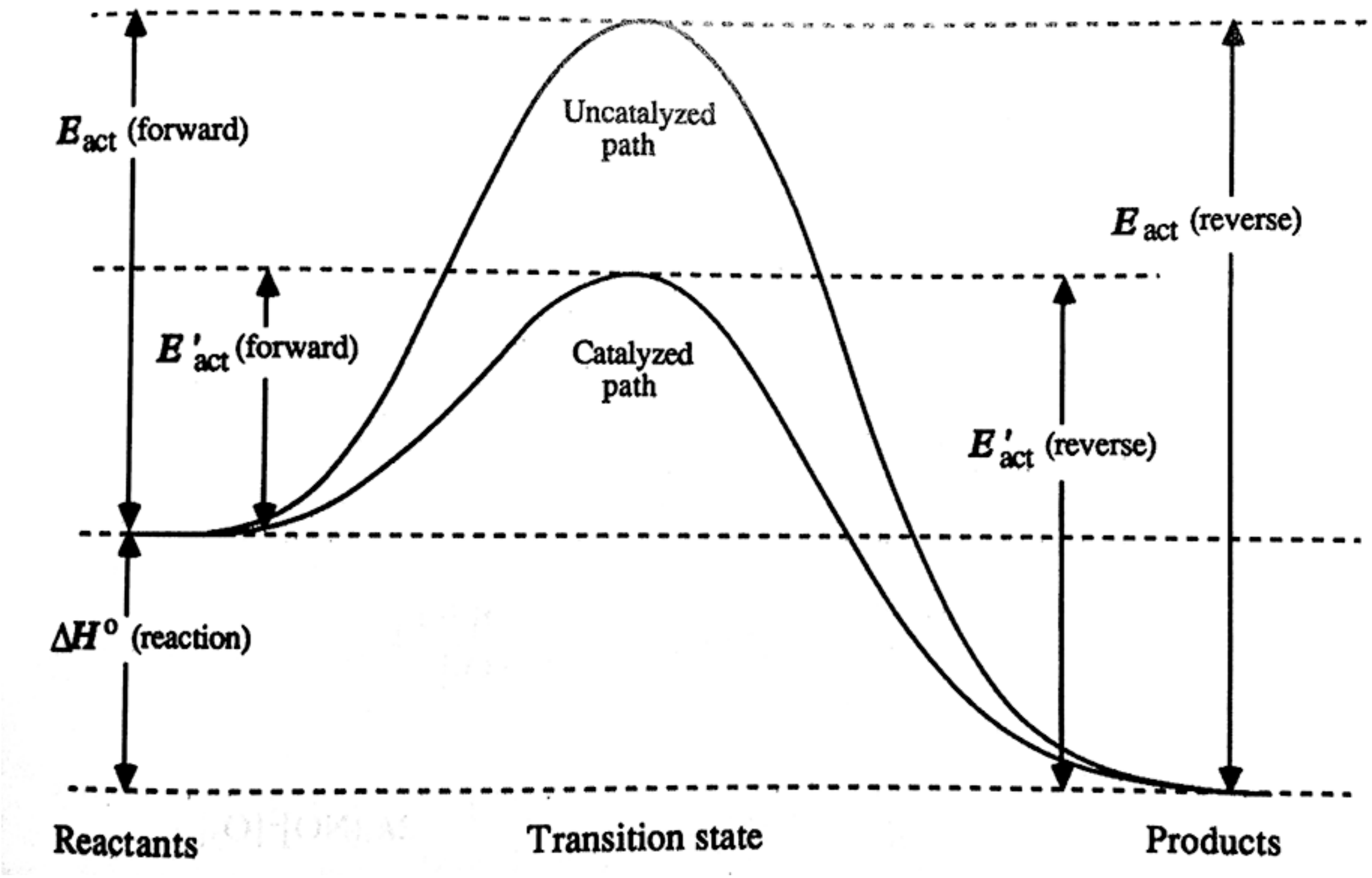
Catalysis & Polymerization

3.1 Catalysis and Equilibrium

- A reaction $\mathrm{A} \rightarrow \mathrm{B}$

will proceed faster in the presence of a catalyst C:

$$\mathrm{A} + \mathrm{C} \rightarrow \mathrm{B} + \mathrm{C}$$



- Reversible reaction in equilibrium: $\mathrm{A} \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} \mathrm{B}$

- Catalyzed: $\mathrm{A} + \mathrm{C} \underset{k'_{-1}}{\overset{k'_1}{\rightleftarrows}} \mathrm{B} + \mathrm{C}$

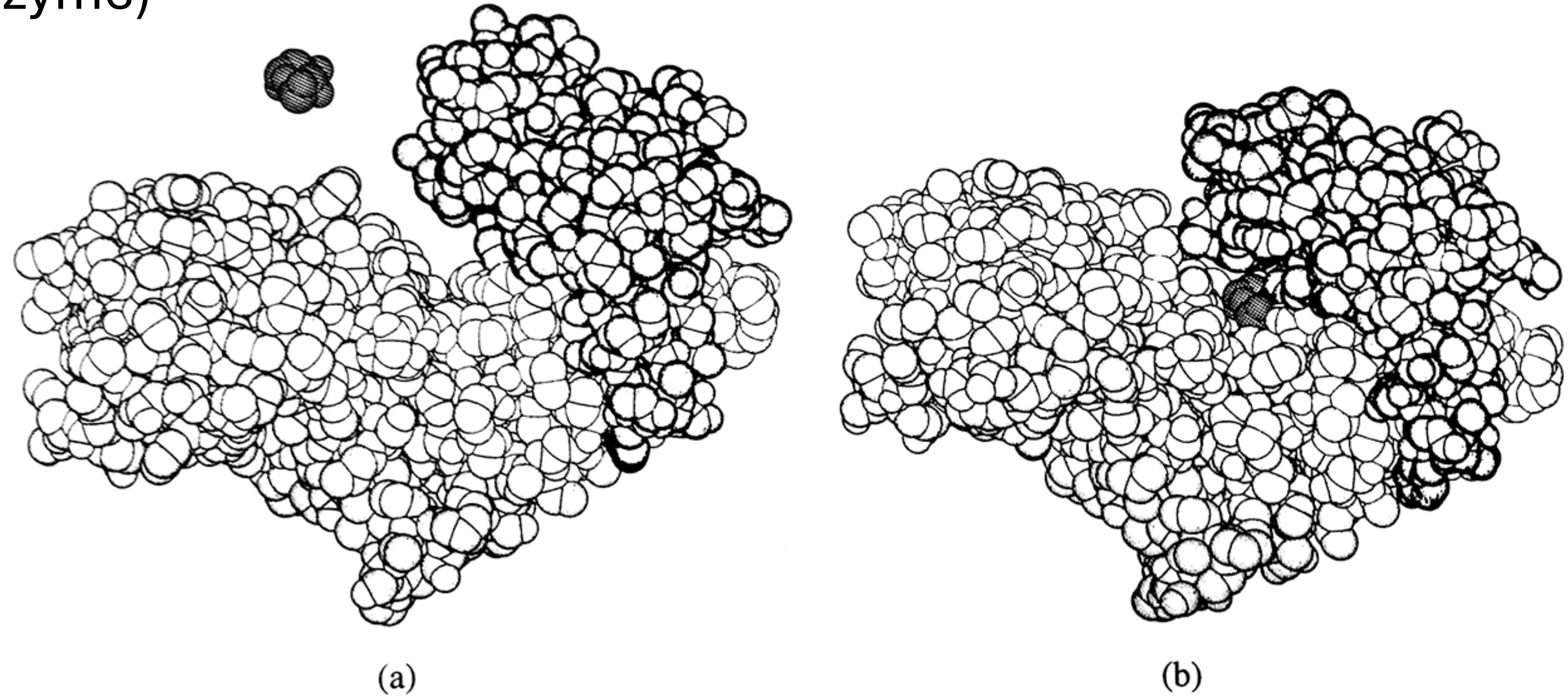
- In equilibrium, with detailed balance, we find

- $$K'_{\text{eq}} = \frac{k'_1}{k'_{-1}} = \frac{[B]_{\text{eq}}[C]}{[A]_{\text{eq}}[C]} = \frac{[B]_{\text{eq}}}{[A]_{\text{eq}}} = \frac{k_1}{k_{-1}} = K_{\text{eq}}$$

- Thermodynamics remain unchanged, as is equ. const. *K*

3.2 Enzymatic Catalysis & the Michaelis-Menten Mechanism

- Reaction proceeds through an intermediate (substrate docks to enzyme)



$$\mathrm{E + S \rightleftarrows ES \rightleftarrows EZ \rightleftarrows EP \rightleftarrows E + P}$$

- We simplify this for MMM to

$$\mathrm{E + S} \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} \mathrm{ES} \xrightarrow{k_2} \mathrm{E + P}$$

MMM Assumptions:

- **1**): only 2 steps
- **2**): no reverse reaction (or restrict to initial stage of reaction where back-reaction neglectable)

- **3**): steady-state approximation for intermediate ES
- **4**): [E] << [S]

$$\mathrm{E} + \mathrm{S} \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} \mathrm{ES} \xrightarrow{k_2} \mathrm{E} + \mathrm{P}$$

- Using the assumptions, we can write

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

- simplify further using that $[\mathrm{E}]_0 = [\mathrm{E}] + [\mathrm{ES}]_\mathrm{S}$

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

$$\mathrm{E} + \mathrm{S} \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} \mathrm{ES} \xrightarrow{k_2} \mathrm{E} + \mathrm{P}$$

- Since $[\mathrm{ES}] \approx [\mathrm{E}] \ll [\mathrm{S}]$, we can approximate $[\mathrm{S}]_0 = [\mathrm{S}] + [\mathrm{P}]$, so that

$$v = -\frac{d[\mathrm{S}]}{dt} \approx \frac{d[\mathrm{P}]}{dt} = k_2[\mathrm{ES}]_\mathrm{S} = \frac{k_1 k_2 [\mathrm{E}]_0 [\mathrm{S}]}{k_1[\mathrm{S}] + k_{-1} + k_2}$$

as [E]<<[S]

Rewrite to yield ***Michaelis-Menten Equation***:

$$v = \frac{k_2[\mathrm{E}]_0}{1 + \frac{k_{-1} + k_2}{k_1[\mathrm{S}]}} = \frac{v_{\mathrm{max}}}{1 + \frac{K_M}{[\mathrm{S}]}}$$

$$\mathrm{E} + \mathrm{S} \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} \mathrm{ES} \xrightarrow{k_2} \mathrm{E} + \mathrm{P}$$

***MME*:** maximum rate

$$v = \frac{\overbrace{k_2[\mathrm{E}]_0}^{v_{\max}}}{1 + \underbrace{\frac{k_{-1} + k_2}{k_1[\mathrm{S}]}}} = \frac{v_{\max}}{1 + \frac{K_M}{[\mathrm{S}]}}$$

Michaelis constant $K_M = (k_{-1} + k_2)/k_1$

(units of concentration)

$$\mathrm{E} + \mathrm{S} \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} \mathrm{ES} \xrightarrow{k_2} \mathrm{E} + \mathrm{P}$$

MME:

$$v = \frac{k_2[\mathrm{E}]_0}{1+\frac{k_{-1}+k_2}{k_1[\mathrm{S}]}} = \frac{v_{\max}}{1+\frac{K_M}{[\mathrm{S}]}}$$

- **Two limiting cases:**
- **1**): For $[\mathrm{S}] \ll K_M$, we find

$$v = \frac{v_{\max}}{K_M}[\mathrm{S}]$$

reaction becomes 1st order in S.

- **2**): For $[\mathrm{S}] \gg K_M$, we find

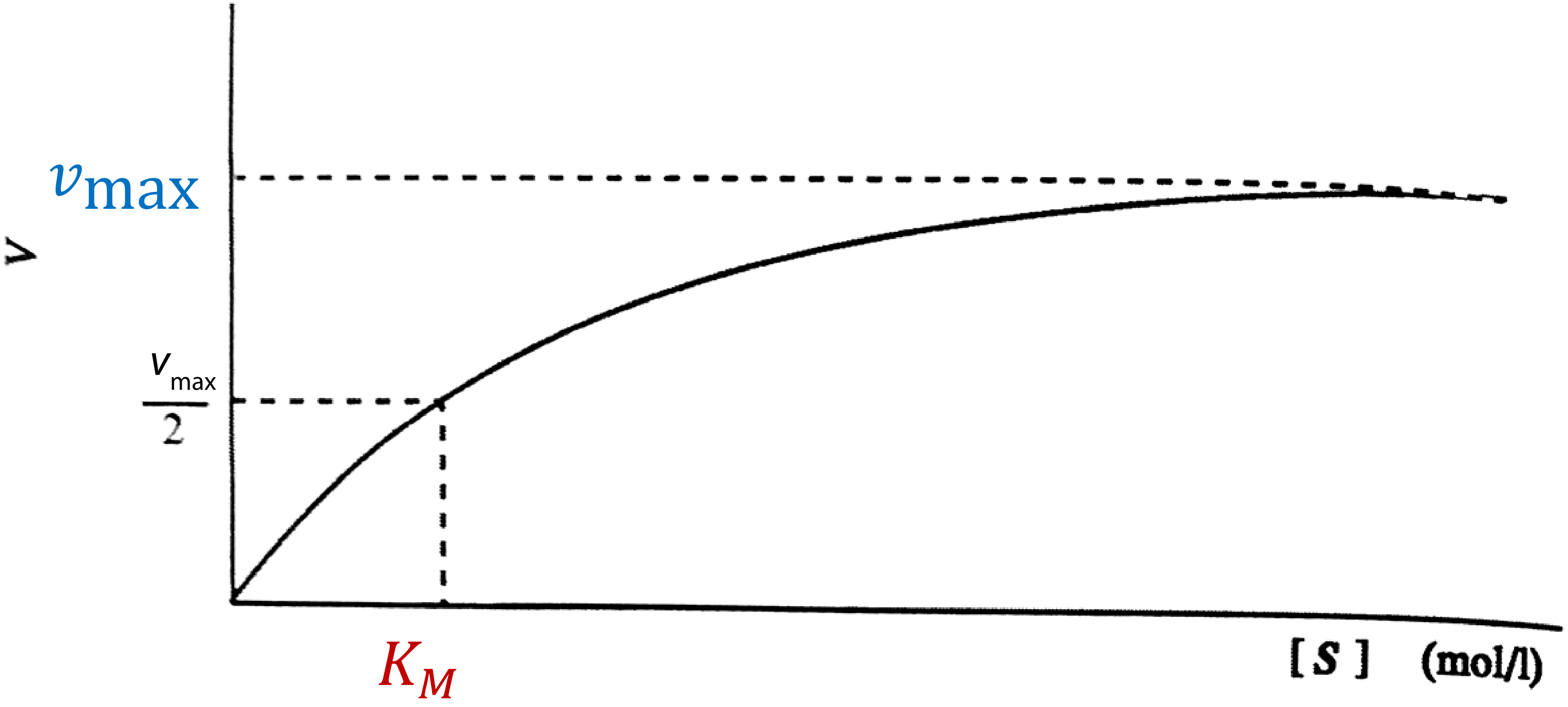
$$v = v_{\max} = k_2[\mathrm{E}]_0$$

reaction becomes 0th order in S.

MME: $$v = \frac{k_2[\mathrm{E}]_0}{1+\frac{k_{-1}+k_2}{k_1[\mathrm{S}]}} = \frac{v\mathrm{max}}{1+\frac{K_M}{[\mathrm{S}]}}$$

$$\mathrm{E} + \mathrm{S} \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} \mathrm{ES} \xrightarrow{k_2} \mathrm{E} + \mathrm{P}$$

- *Michaelis-Menten Plot*:

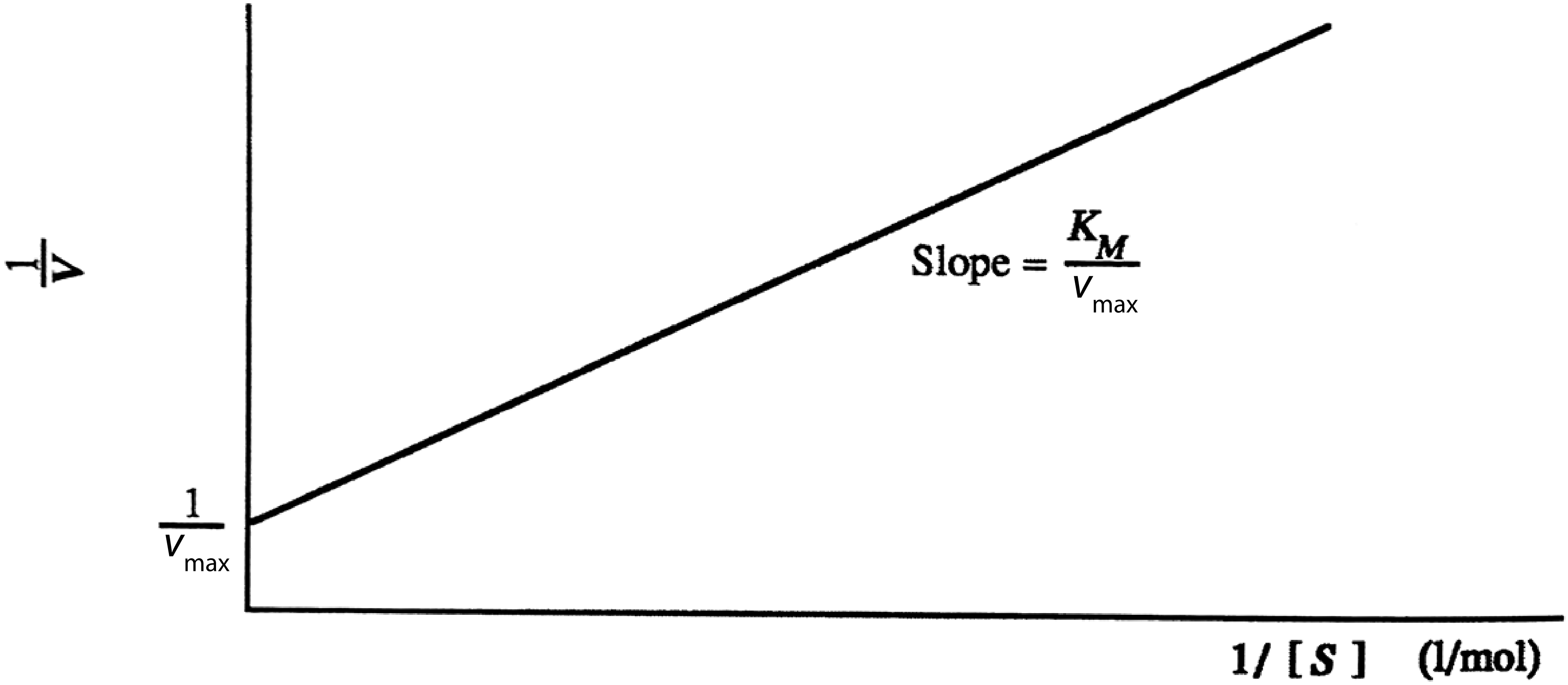


- But how can we extract all 3 rate constants?

$$\mathrm{E} + \mathrm{S} \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} \mathrm{ES} \xrightarrow{k_2} \mathrm{E} + \mathrm{P}$$

MME: $$v = \frac{k_2[\mathrm{E}]_0}{1+\frac{k_{-1}+k_2}{k_1[\mathrm{S}]}} = \frac{v\mathrm{max}}{1+\frac{K_M}{[\mathrm{S}]}}$$

- *Lineweaver-Burk Plot:* $\frac{1}{v} = \frac{K_M}{v\mathrm{max}}\frac{1}{[\mathrm{S}]} + \frac{1}{v\mathrm{max}}$

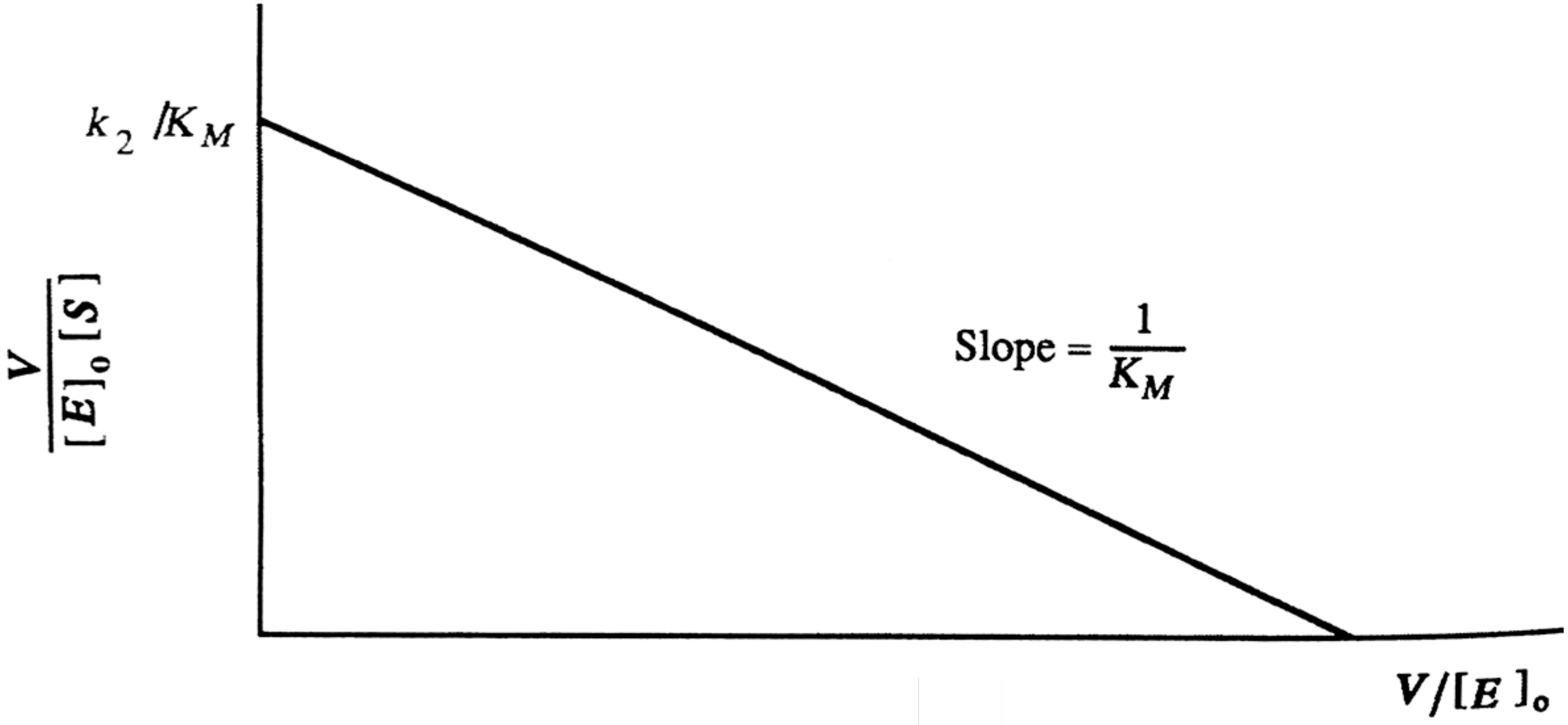


$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} ES \xrightarrow{k_2} E + P$$

MME:

$$v = \frac{k_2[\mathrm{E}]_0}{1+\frac{k_{-1}+k_2}{k_1[\mathrm{S}]}} = \frac{v\mathrm{max}}{1+\frac{K_M}{[\mathrm{S}]}}$$

- *Eadie-Hofstee Plot:* $\frac{v}{[\mathrm{E}]_0[\mathrm{S}]} = \frac{k_2}{K_M} - \frac{v}{K_M[\mathrm{E}]_0}$



3.3 Inhibition of Enzymatic Reactions

- An inhibitor decreases the rate of an enzyme-catalysed reaction

$$\mathrm{E} + \mathrm{S} \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} \mathrm{ES} \overset{k_2}{\rightarrow} \mathrm{E} + \mathrm{P}$$

$$\uparrow\downarrow K_{EI} \qquad\qquad \uparrow\downarrow K_{ESI}$$

$$\text{competitive} \quad \underbrace{\mathrm{EI} \qquad\qquad \mathrm{ESI}}_{\text{“mixed”}} \quad \text{uncompetitive}$$

- Rate of product formation in presence of inhibitor?

- Inhibition of $\mathrm{E} + \mathrm{S} \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} \mathrm{ES} \xrightarrow{k_2} \mathrm{E} + \mathrm{P}$

- In SSA we find $v = -\frac{d[\mathrm{S}]}{dt} = \frac{d[\mathrm{P}]}{dt} = k_2[ES]_S$

- Moreover, assume last step $\mathrm{ES} \xrightarrow{k_2} \mathrm{E} + \mathrm{P}$ is *slow*

- meaning all other species in *pre-equilibrium*

- To find expression for $[ES]_S$ write down mass balance again:

$$[\mathrm{E}]_0 = [\mathrm{E}] + [\mathrm{EI}] + [\mathrm{ES}]_\mathrm{S} + [\mathrm{ESI}]$$

$$[\mathrm{E}]_0 = [\mathrm{E}] + [\mathrm{EI}] + [\mathrm{ES}]_{\mathrm{S}} + [\mathrm{ESI}]$$

- Under pre-equilibrium condition we can define dissociation constants (equil. constants):
- $K_{\mathrm{ES}} = \frac{k_{-1}}{k_1} = \frac{[\mathrm{E}][\mathrm{S}]}{[\mathrm{ES}]}$; $K_{\mathrm{EI}} = \frac{[\mathrm{E}][\mathrm{I}]}{[\mathrm{EI}]}$; $K_{\mathrm{ESI}} = \frac{[\mathrm{ES}][\mathrm{I}]}{[\mathrm{ESI}]}$

- Substitute and simplify to
- $[\mathrm{E}]_0 = [\mathrm{E}] + \frac{[\mathrm{E}][\mathrm{I}]}{K_{EI}} + [\mathrm{ES}] + \frac{[\mathrm{ES}][\mathrm{I}]}{K_{ESI}} = [\mathrm{E}]\alpha + [\mathrm{ES}]\alpha'$

where $\alpha = 1 + \frac{[\mathrm{I}]}{K_{\mathrm{EI}}}$ and $\alpha' = 1 + \frac{[\mathrm{I}]}{K_{\mathrm{ESI}}}$

- Further substitute using our K_{ES} from above

$$[E] = [ES]\, K_{ES}/[\mathrm{S}]$$

- yields $[\mathrm{E}]_0 = [\mathrm{ES}]\left(\alpha' + \alpha \frac{K_{\mathrm{ES}}}{[\mathrm{S}]}\right)$

- To finally obtain the expression for the rate:

$$v = k_2[\mathrm{ES}] = \frac{k_2[\mathrm{E}]_0}{\alpha' + \alpha \frac{K_{ES}}{[\mathrm{S}]}} = \frac{v_{\max}}{\alpha' + \alpha \frac{K_{ES}}{[\mathrm{S}]}}$$

- Let's compare this to our MME (without inhibition):

$$v_{MM} = \frac{v_{\max}}{1 + \frac{K_M}{[\mathrm{S}]}}$$

- Actually, the above equation is the more general case, and the MME is a special case of it! When do we retrieve the MME?
- We retrieve the MME, if dissoc. consts. for inhibitor become huge:

$$\lim_{K_{EI} \to \infty} \alpha = 1; \qquad \lim_{K_{ESI} \to \infty} \alpha' = 1$$

- so that

$$\lim_{\substack{K_{EI} \to \infty, \\ K_{ESI} \to \infty}} v = \frac{v_{max}}{1 + \frac{K_{ES}}{[\mathrm{S}]}} \qquad K_M = \frac{k_{-1} + k_2}{k_1} \underset{\substack{\uparrow \\ \text{if } k_{-1} \gg k_2}}{\approx} K_{\mathrm{ES}} = \frac{k_{-1}}{k_1}$$

Competitive inhibition

$$\begin{tikzcd} E + S \arrow[r, shift left, "k_1"] \arrow[d, shift left, "K_{EI}"] & ES \arrow[l, shift left, "k_{-1}"] \arrow[r, "k_2"] & E + P \\ EI \arrow[u, shift left] \end{tikzcd}$$

- $\alpha = 1 + \frac{[\mathrm{I}]}{K_{\mathrm{EI}}} > 1$ and $\alpha' \approx 1$
- $v = \frac{v_{\max}}{1 + \alpha \frac{K_{\mathrm{ES}}}{[\mathrm{S}]}}$
- If substrate conc. [S] is low, inhibitor slows down reaction significantly: $v \approx \frac{v_{\max}}{\alpha K_{\mathrm{ES}}} [\mathrm{S}]$
- If $[\mathrm{S}] \rightarrow \infty$ the maximum rate remains unaffected (no significant inhibition) : $v = v_{\max}$

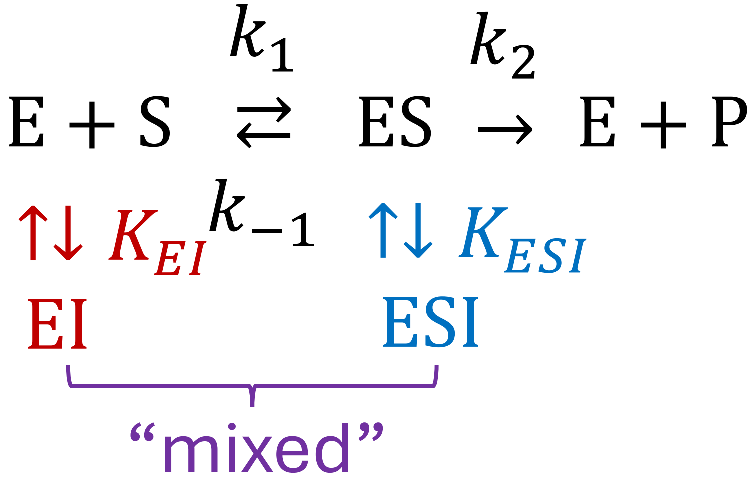
Uncompetitive inhibition

$$\begin{tikzcd} \mathrm{E} + \mathrm{S} \arrow[r, shift left, "k_1"] & \mathrm{ES} \arrow[l, shift left, "k_{-1}"] \arrow[r, "k_2"] \arrow[d, shift left, "K_{ESI}"] & \mathrm{E} + \mathrm{P} \\ & \mathrm{ESI} \arrow[u, shift left] & \end{tikzcd}$$

- $\alpha \approx 1$ and $\alpha' = 1 + \frac{[\mathrm{I}]}{K_{\mathrm{ESI}}} > 1$
- $v = \frac{v_{\max}}{\alpha' + \frac{K_{\mathrm{ES}}}{[\mathrm{S}]}}$
- If low conc. of substrate S, inhibitor does not change reaction rate significantly: $v \approx \frac{v_{\max}}{K_{\mathrm{ES}}}[\mathrm{S}]$
- If $[\mathrm{S}] \to \infty$, so for very large S, the maximum rate is significantly lowered: $v = v_{\max}/\alpha'$

Mixed (noncompetitive) inhibition

- $\alpha > 1 \quad \text{and} \quad \alpha' > 1$



$$\begin{array}{ccccc} \mathrm{E+S} & \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} & \mathrm{ES} & \xrightarrow{k_2} & \mathrm{E+P} \\ \uparrow\downarrow K_{EI} & & \uparrow\downarrow K_{ESI} & & \\ \mathrm{EI} & & \mathrm{ESI} & & \end{array}$$

$$\underbrace{\mathrm{EI} \qquad\qquad \mathrm{ESI}}_{\text{“mixed”}}$$

- $v = \dfrac{v_{\max}}{\alpha' + \alpha \dfrac{K_{\mathrm{ES}}}{[\mathrm{S}]}}$

- To quantify efficiency of an inhibitor (in all cases), i.e. to quantify the alphas:
- measure rates experimentally with and without an inhibitor present

3.4 Autocatalysis

- Occurs, when the product of a reaction appears as the reactant of either the same reaction or a coupled reaction. Simplest case:

$$\mathrm{A} + \mathrm{B} \xrightarrow{k} 2\mathrm{B}$$

- Rate equation for this?

$$\mathrm{v} = \frac{dX}{dt} = -\frac{d[\mathrm{A}]}{dt} = k[\mathrm{A}][\mathrm{B}]$$

- Simplify using $x = [\mathrm{A}]_0 - [\mathrm{A}]_t = [\mathrm{B}]_t - [\mathrm{B}]_0$

- $$\frac{dX}{dt} = k([\mathrm{A}]_0 - x)(x + [\mathrm{B}]_0)$$

$$\mathrm{A} + \mathrm{B} \xrightarrow{k} 2\mathrm{B}$$

- Integrate $\int_0^x \frac{dX}{\left([\mathrm{A}]_0 - x\right)\left(x + [\mathrm{B}]_0\right)} = \int_0^t k dt$ how?
- Method of partial fractions:
- $\frac{1}{([A]_0 - x)(x + [B]_0)} = \frac{A}{([A]_0 - x)} + \frac{B}{(x + [B]_0)}$ yields eventually
- $\int_0^x \frac{dX}{\left([\mathrm{A}]_0 - x\right)\left(x + [\mathrm{B}]_0\right)} = \frac{1}{[\mathrm{A}]_0 + [\mathrm{B}]_0} \left\{ \int_0^x \frac{dX}{\left([\mathrm{A}]_0 - x\right)} + \int_0^x \frac{dX}{\left(x + [\mathrm{B}]_0\right)} \right\}$
- $= \frac{1}{[\mathrm{A}]_0 + [\mathrm{B}]_0} \ln \left| \frac{[A]_0 (x + [B]_0)}{[B]_0 ([A]_0 - x)} \right| = kt$

- With $[\mathrm{B}]_t = [\mathrm{B}]_0 + x$, we finally obtain

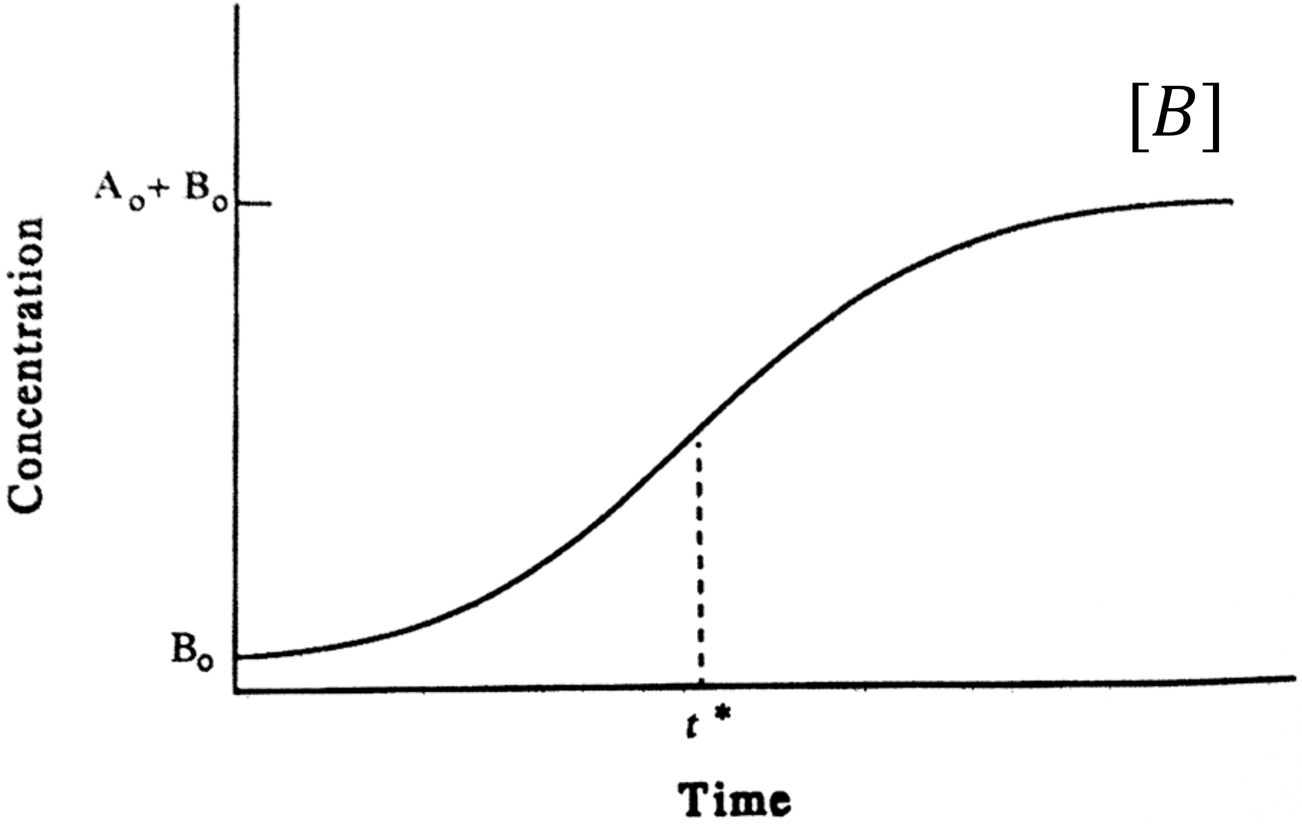
$$[\mathrm{B}]_t = \frac{[\mathrm{A}]_0 + [\mathrm{B}]_0}{1 + \frac{[\mathrm{A}]_0}{[\mathrm{B}]_0} e^{-\left([\mathrm{A}]_0 + [\mathrm{B}]_0\right)kt}}$$

But what does this mean if we plot it?

$$[\mathrm{B}]_t = \frac{[\mathrm{A}]_0+[\mathrm{B}]_0}{1+\frac{[\mathrm{A}]_0}{[\mathrm{B}]_0}\ e^{-([\mathrm{A}]_0+[\mathrm{B}]_0)kt}}$$

$$\mathrm{A} + \mathrm{B} \xrightarrow{k} 2\mathrm{B}$$

- How does this look at t_0?
- e-function term = 1 , meaning
- $[B]_{t=0} = \frac{[\mathrm{A}]_0+[\mathrm{B}]_0}{\frac{[B]_0+[A]_0}{[B]_0}} = [B]_0$
- How does this look at very late times?
- $[B]_{t\to\infty} = [A]_0 + [B]_0$



$[B]_t$ shows a typical *S Curve*:

$$A + B \xrightarrow{k} 2B$$

- *Induction period*: rate of reaction increases
- Rate reaches maximum at inflection point t^*
- Reaction then slows down and approaches its end at v. late times
- Example: Growth of bacteria population with limited food supply