Kinetics & Dynamics of Chemical Reactions

Course CH-310

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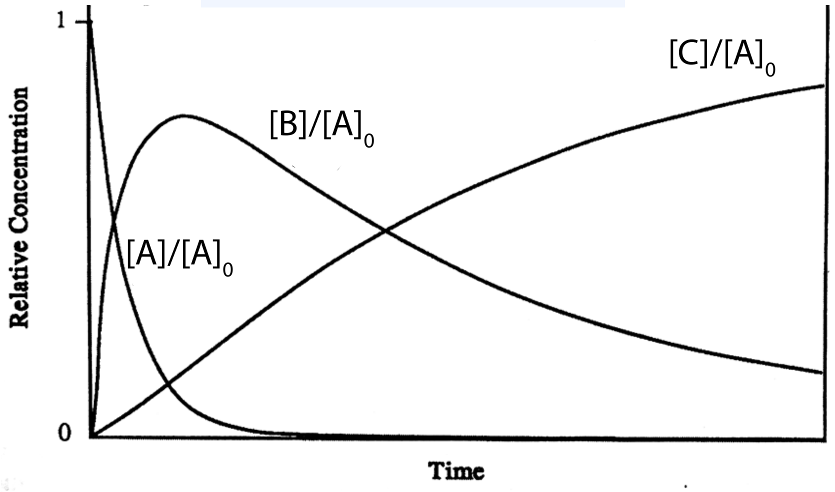
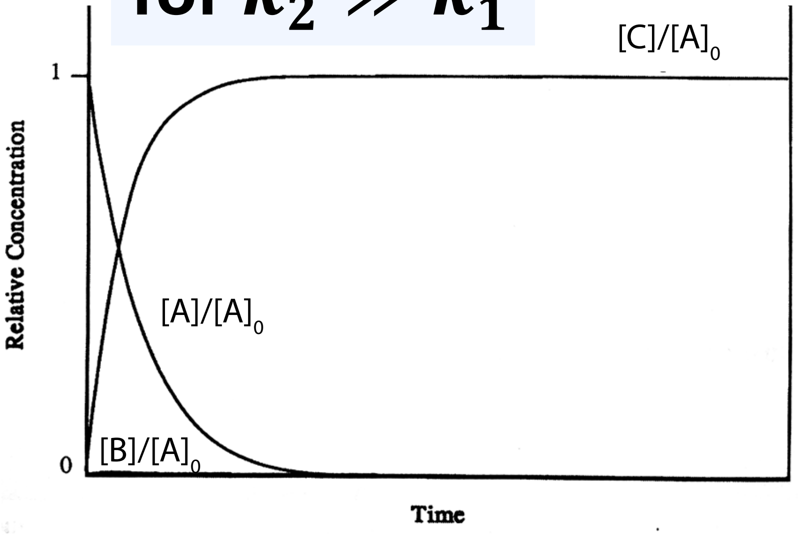
Recap from last session

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

for $k_1 \gg k_2$

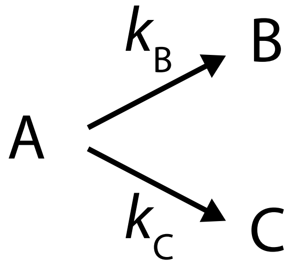


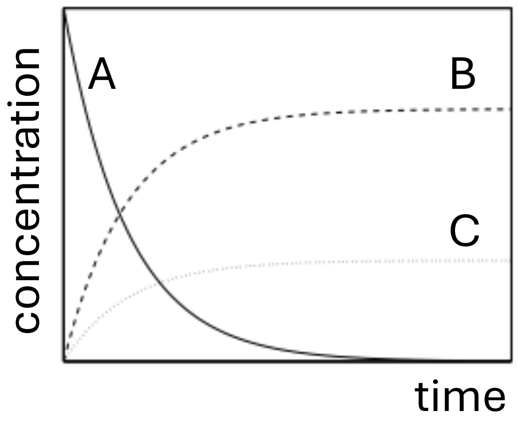
for $k_2 \gg k_1$



Recap from last session

- -Parallel reactions:





- Steady-state approximation:

-valid, if conc. of intermediate A_i small. Then can set: $\frac{d[A_i]}{dt} \approx 0$

-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 1^{st} or 2^{nd} step rate-limiting got different results

- Pseudo-first order method (experimental approach)

Chapter 3

Catalysis & Polymerization

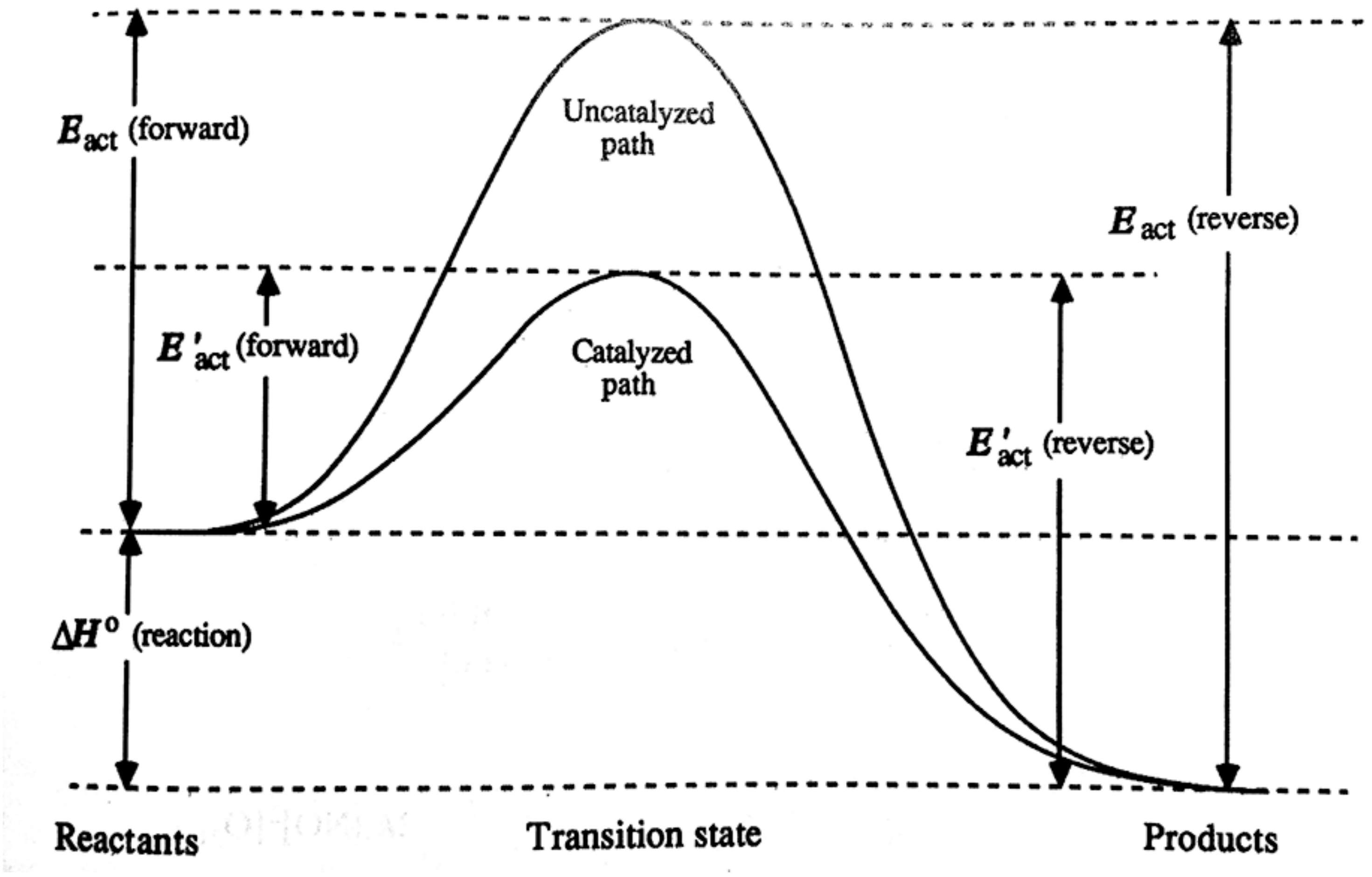
3.1 Catalysis and Equilibrium

- a reaction

$$A \rightarrow B$$

will proceed faster in the presence of a *catalyst* $\mathbf{C}$:

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



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

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

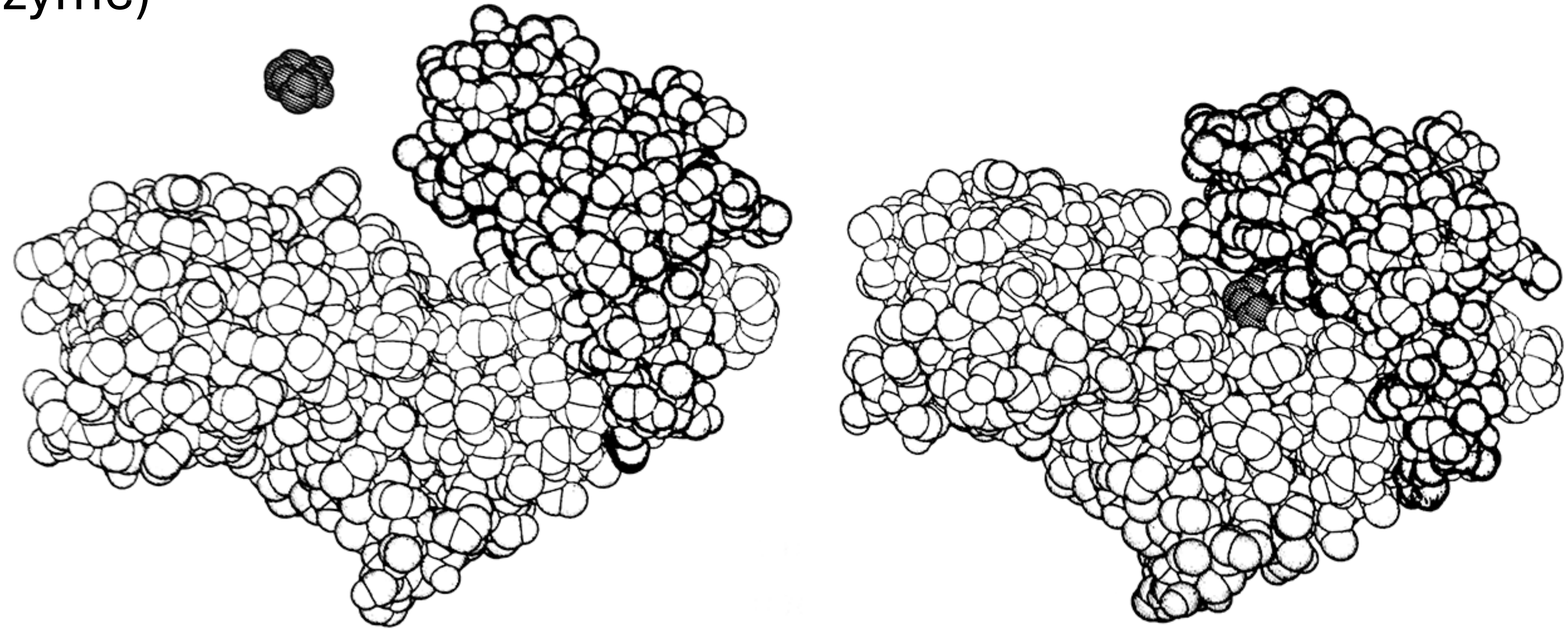
- In equilibrium, with detailed balance, we find

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

- Note: Thermodynamics remain unchanged, as is eq. const. *K*

3.2 Enzymatic Catalysis & the Michaelis-Menten Mechanism

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



(a)   (b)

$$E + S \rightleftarrows ES \rightleftarrows EZ \rightleftarrows EP \rightleftarrows E + P$$

- We simplify this for MMM to

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

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: $\frac{d[ES]}{dt} \approx 0$

4): [E] << [S]

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

- 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***:

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

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

***MME*:**

maximum rate v_{max}

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

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

[units of concentration]

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

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

- **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

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

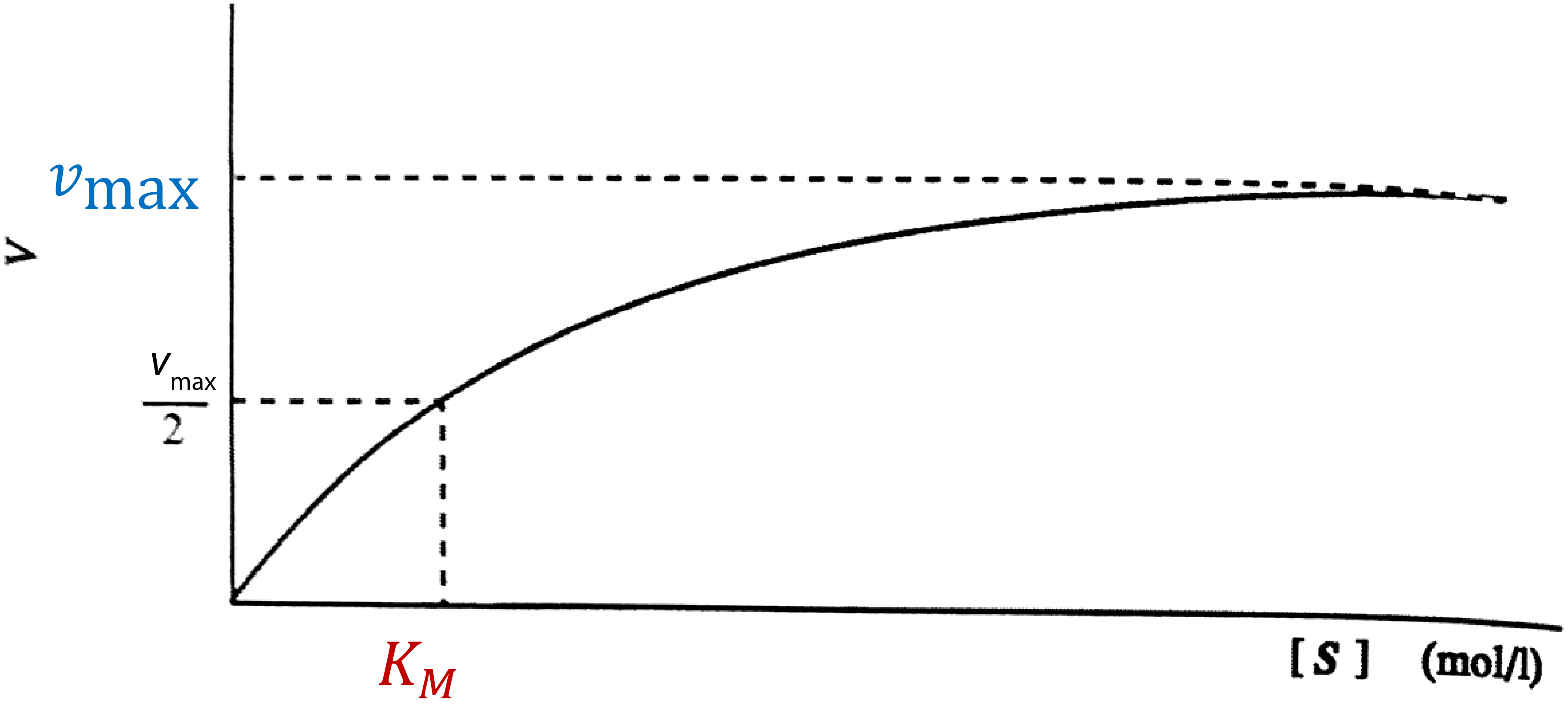
reaction becomes 0th order in S.

MME:

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

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

- *Michaelis-Menten Plot*:



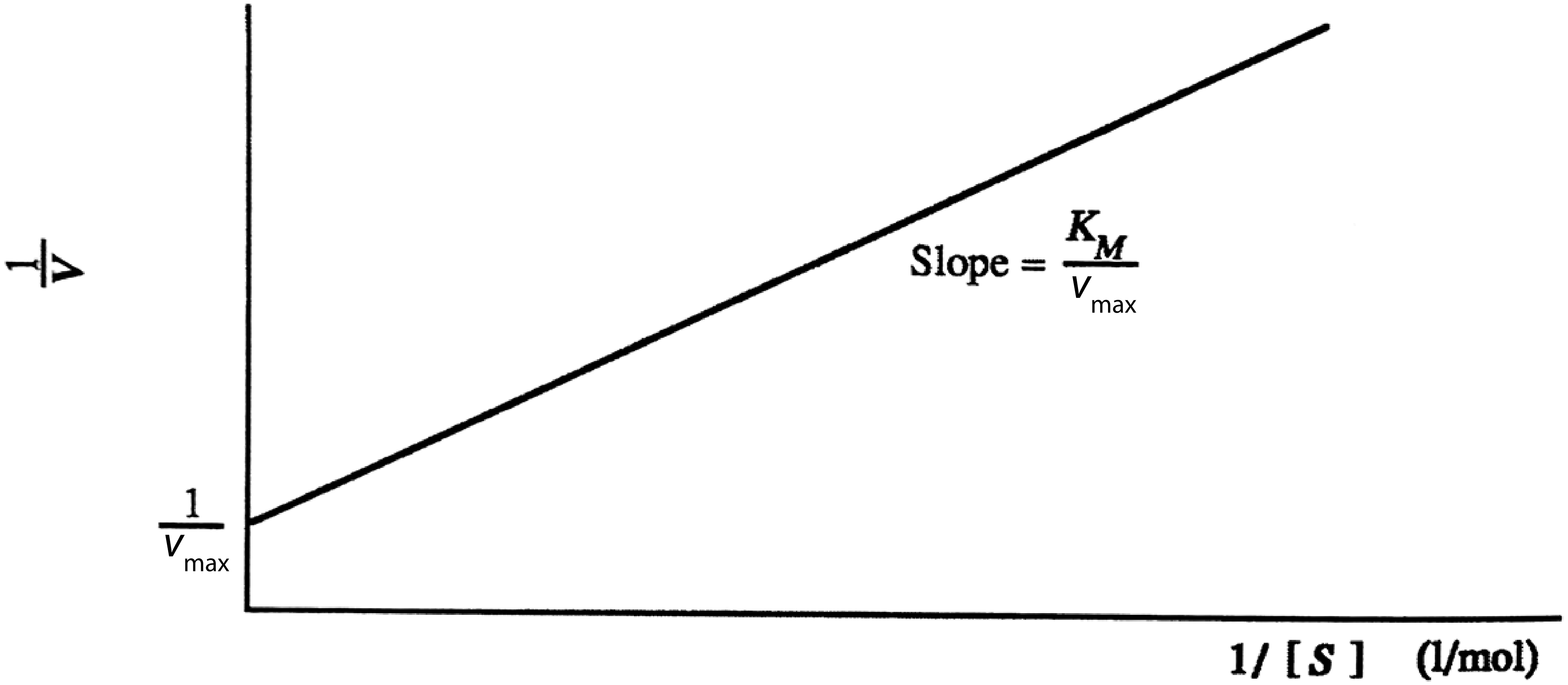
- Brain teaser: How can we determine all 3 rate constants?

MME:

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

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

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

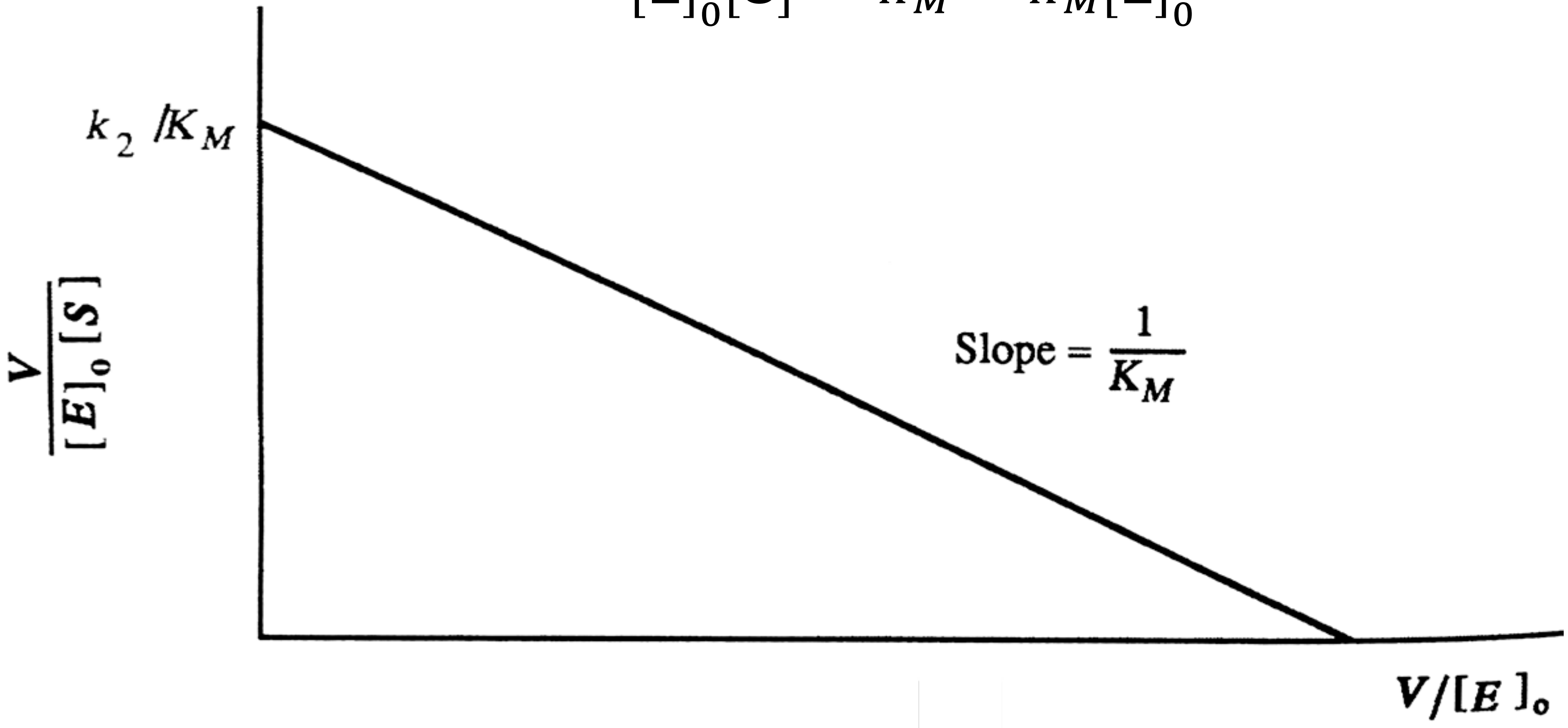


MME:

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

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

- *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-catalyzed reaction:

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

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

competitive $\quad$ EI $\qquad$ ESI $\quad$ uncompetitive

"mixed"

- Rate of product formation in presence of inhibitor?

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

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

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

  meaning all other species are in *pre-equilibrium*

- To find expression for $[ES]_S$ write down mass balance again:
$$[\mathrm{E}]_0 = [\mathrm{E}] + [\mathrm{EI}] + [\mathrm{ES}]_\mathrm{S} + [\mathrm{ESI}]$$

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

- Under pre-equilibrium condition we can define dissociation constants (eq. constants):

$$K_{\mathrm{ES}} = \frac{k_{-1}}{k_1} = \frac{[\mathrm{E}][\mathrm{S}]}{[\mathrm{ES}]}; \quad K_{\mathrm{EI}} = \frac{[\mathrm{E}][\mathrm{I}]}{[\mathrm{EI}]}; \quad K_{\mathrm{ESI}} = \frac{[\mathrm{ES}][\mathrm{I}]}{[\mathrm{ESI}]}$$

- 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:

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

- so that

$$\lim_{\substack{K_{EI}\to\infty,\\ K_{ESI}\to\infty}} v = \frac{v_{max}}{1 + \frac{K_{ES}}{[\mathrm{S}]}}$$

$$K_M = \frac{k_{-1} + k_2}{k_1} \approx K_{\mathrm{ES}} = \frac{k_{-1}}{k_1}$$

↑ if $k_{-1} \gg k_2$

in pre-equilibrium

Competitive inhibition

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

$\uparrow\downarrow K_{EI}$

EI

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

Uncompetitive inhibition

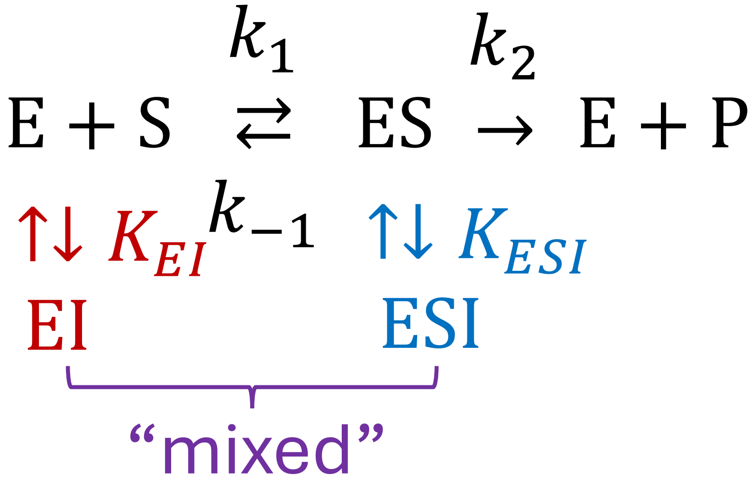
$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} ES \overset{k_2}{\rightarrow} E + P$$

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

$$ESI$$

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

<u>Mixed (noncompetitive) inhibition</u>



- $\alpha > 1$ and $\alpha' > 1$

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

- 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 $\int_0^x \frac{dX}{([\mathrm{A}]_0 - x)(x + [\mathrm{B}]_0)} = \int_0^t k dt$ ...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
- $\int_0^x \frac{dX}{([\mathrm{A}]_0 - x)(x + [\mathrm{B}]_0)} = \frac{1}{[\mathrm{A}]_0 + [\mathrm{B}]_0} \left\{ \int_0^x \frac{dX}{([\mathrm{A}]_0 - x)} + \int_0^x \frac{dX}{(x + [\mathrm{B}]_0)} \right\}$
- $= \frac{1}{[\mathrm{A}]_0 + [\mathrm{B}]_0} \ln \left| \frac{[A]_0 (x + [B]_0)}{[B]_0 ([A]_0 - x)} \right| = kt$

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

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

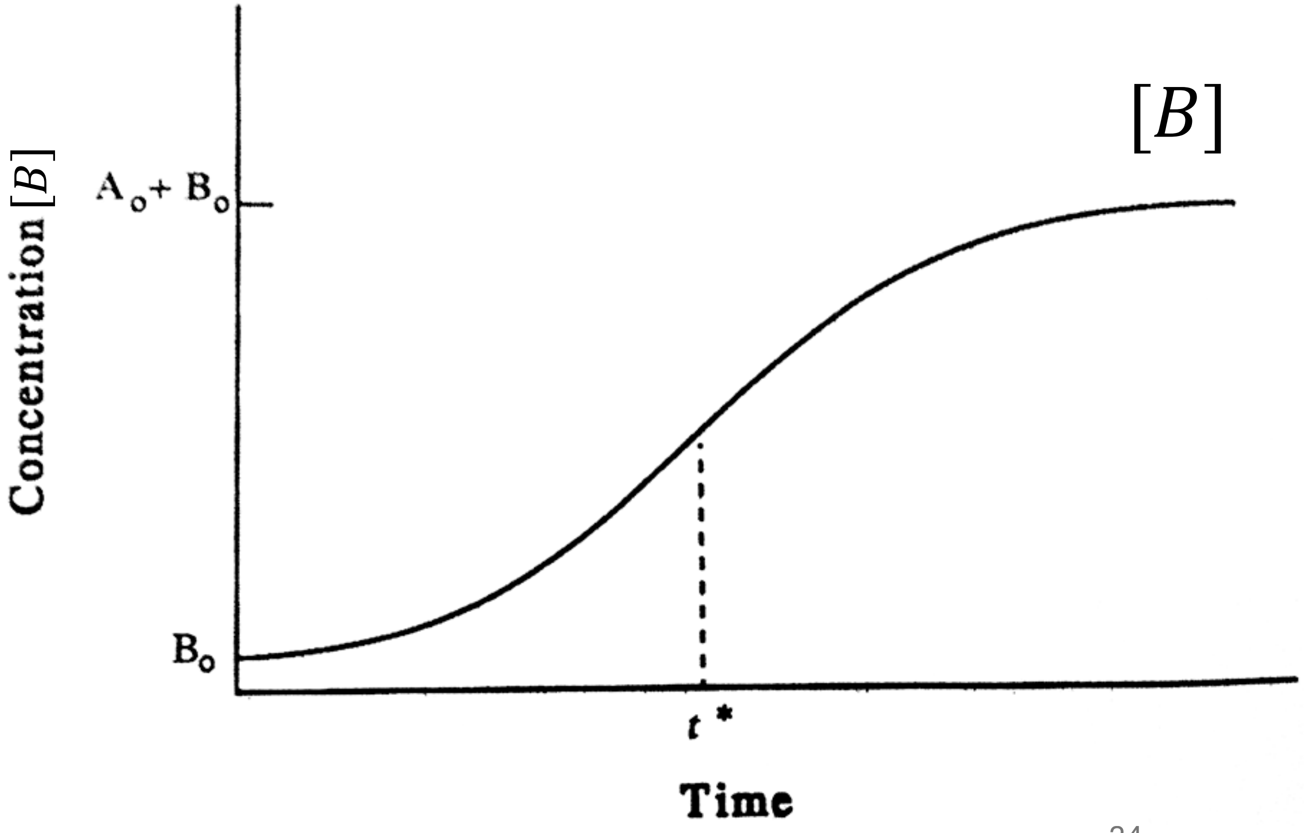
But what does this look like, if we plot it?

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

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

- How does $[B]$ look at earliest times?
- 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 $[B]$ 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 late times
- Example: Growth of bacteria population with limited food supply