ChE 344
Reaction Engineering and Design

Lecture 22: Tues, Apr 5, 2022

Pseudo steady-state hypothesis cont., intro to catalysts, enzyme kinetics

Reading for today's Lecture: Chapter 9.2-9.3

Reading for Lecture 22: Chapter 10

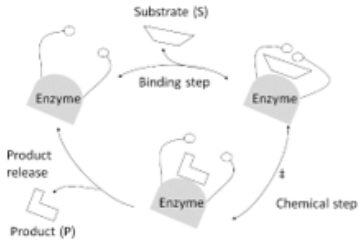
Lecture 22: Enzyme kinetics
Related Text: Chapter 9

Catalyst: A species which itself is not consumed or produced in a reaction, but which affects the rate of reaction. Typically, this comes in the form of interacting with the reactants in a specific way such that the energy associated with a given reaction mechanism is changed. Often catalysts lower activation barriers.

Homogeneous catalysts: Catalysts that are in the same phase (of matter) as the reactants/products*

Heterogeneous catalysts: Catalysts that are in a different phase than the reactants and products

Enzymes are an example of a homogeneous catalyst, specifically biocatalysts. They are usually proteins that fold to create an active center that interacts with the reactants.



The reaction mechanism can be written as:

$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} ES \underset{k_{-2}}{\overset{k_2}{\rightleftarrows}} EP \xrightarrow{k_3} E + P$$

where E is the enzyme, ES is the substrate bound to the enzyme, and EP is the product bound to the enzyme. Importantly, because enzymes are not consumed we can do a balance on the enzyme, where the total enzyme concentration ($C_{E,total}$) is controlled by how much we put into the reactor. In general, we add much less of the enzyme than the substrate, such that $C_{E,total}$ is low, and we can apply PSSH to E, ES, EP.

Solving for the rate of reaction in the absence of diffusion limitations:

$$v = \frac{r_P}{C_{E,total}} = \frac{v_M C_S}{C_S + K_M}$$

$$v_M = k_2 k_3 (k_3 + k_{-2} + k_2)^{-1}$$

$$K_M = \frac{k_{-1}k_{-2} + k_{-1}k_3 + k_3 k_2}{k_1(k_3 + k_{-2} + k_2)}$$

A simplified case is the Briggs-Haldane mechanism:

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

$$v_{M,BH} \approx k_2$$

$$K_{M,BH} \approx \frac{k_{-1} + k_2}{k_1}$$

Last time: **Postulating rate laws from reaction mechanisms** and using the **pseudo steady state hypothesis**

Overall reaction: $A \rightarrow C$

Reaction mechanism: (two elementary steps) $A \overset{k_1}{\rightarrow} B \overset{k_2}{\rightarrow} C$

'Active intermediate' Low conc., short lived

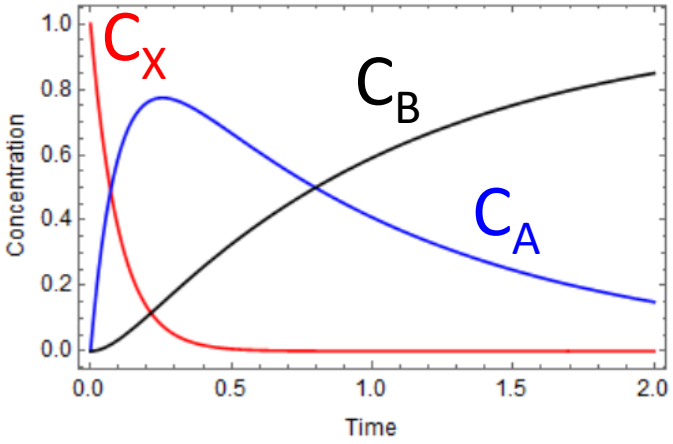
Rules for using PSSH

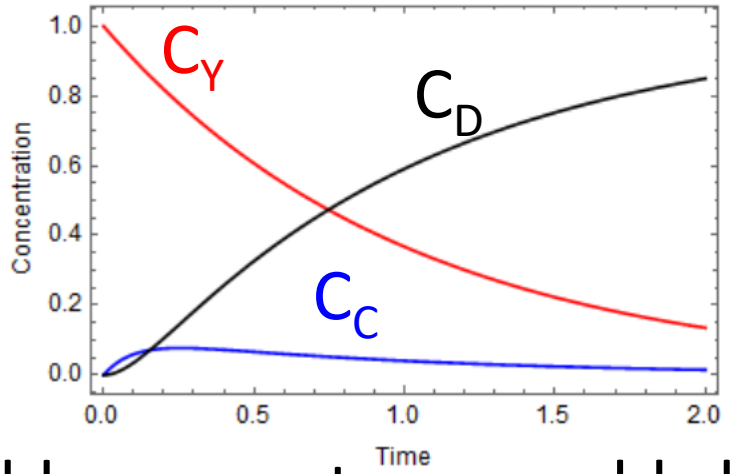
1. PSSH applied to intermediate X yields algebraic equation $r_X = 0$. This should be used to eliminate X, not another intermediate Y.
2. When using PSSH for a long sequence of intermediates start from the 'last' intermediate and work towards the reactant
3. Rate laws from PSSH are inaccurate during the short time while intermediate populations are being established (example from last Thursday, Lecture 21)

Discuss with neighbors: $X \xrightarrow{k_1} A \xrightarrow{k_2} B$ $Y \xrightarrow{k_3} C \xrightarrow{k_4} D$

If $k_1 \gg k_2, k_3 \ll k_4$

You should be able to sketch the concentrations in a batch reactor (vs. time) or PFR (vs. space time) assuming you start with only X or only Y. (Elementary steps)





To which chemical species would you most reasonably be able to apply PSSH?

A) Species A

B) Species B

C) Species C

D) Species D

Advantages of PSSH

1. Fewer ODEs to solve (in batch reactor)
2. Remaining species involve smaller rate constants so can use bigger timesteps in solving
3. Eliminate rate constants of hard to measure intermediates

Reaction mechanisms and tools like PSSH are useful for understanding reactions related to:

- Drug delivery
- Electrochemistry
- Crystal growth
- Photochemistry
- Polymerization
- Epidemiology
- Nucleation
- Nanoparticle synthesis
- Systems biology
- Solid state diffusion
- Catalysis!

Lets finish our example, nitric oxide oxidation to NO_2

$$2NO + O_2 \rightarrow 2NO_2$$

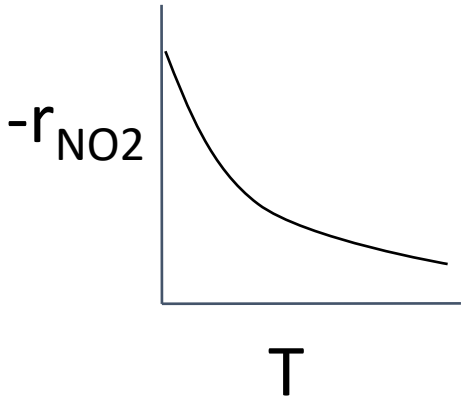
This reaction is very unlikely to happen in one step

It has an elementary rate law

$$r_{NO_2} = k_{empirical} C_{NO}^2 C_{O_2}$$

But unlikely to occur in a single elementary step

The rate of reaction decreases with increasing temperature (non-Arrhenius behavior). Let's use PSSH to find out why



Reaction mechanism broken down into elementary steps.
Each elementary step obeys an elementary rate law

1) $NO + O_2 \rightarrow NO_3$

2) $NO_3 \rightarrow NO + O_2$

3) $NO_3 + NO \rightarrow 2NO_2$

We will see why in a moment

$$r_{1NO_3} = r_1 = k_1 C_{NO} C_{O_2}$$

$$r_{2NO_3} = -r_2 = -k_2 C_{NO_3}$$

$$r_{3NO_3} = -r_3 = -k_3 C_{NO_3} C_{NO}$$

$$r_{NO_2} = 2r_3 = -2r_{3NO_3}$$

Lets consider the intermediate NO_3, and apply the PSSH to it such that the net reaction rate of NO_3 is zero

$$r_{1NO_3} = k_1 C_{NO} C_{O_2};\ r_{2NO_3} = -k_2 C_{NO_3}; r_{3NO_3} = -k_3 C_{NO_3} C_{NO}$$

$$r_{NO_3} = r_{1NO_3} + r_{2NO_3} + r_{3NO_3} \approx 0$$

$$r_{NO_3} = k_1 C_{NO} C_{O_2} - k_2 C_{NO_3} - k_3 C_{NO_3} C_{NO} \approx 0$$

$$k_1 C_{NO} C_{O_2} - C_{NO_3}(k_2 + k_3 C_{NO}) \approx 0$$

$$C_{NO_3} \approx \frac{k_1 C_{NO} C_{O_2}}{(k_2 + k_3 C_{NO})}$$

We can use this to get the rate of NO_2 formation

$$r_{NO_2} = -2r_{3NO_3} \qquad r_{3NO_3} = -k_3 C_{NO_3} C_{NO}$$

From PSSH on NO_3: $C_{NO_3} = \dfrac{k_1 C_{NO} C_{O_2}}{(k_2 + k_3 C_{NO})}$

$$r_{NO_2} = -2r_{3NO_3} = -2\left(-k_3 C_{NO_3} C_{NO}\right)$$

$$r_{NO_2} = 2k_3 C_{NO} \frac{k_1 C_{NO} C_{O_2}}{(k_2 + k_3 C_{NO})} = 2\frac{k_1 k_3 C_{NO}^2 C_{O_2}}{(k_2 + k_3 C_{NO})}$$

If $k_2 >> k_3 C_{NO}$

Actually does appear in denominator!

$$r_{NO_2} \approx 2\frac{k_1 k_3}{k_2} C_{NO}^2 C_{O_2} = k_{effective} C_{NO}^2 C_{O_2}$$

But this "effective" rate constant is not a true elementary rate constant.

$$k_{effective} = 2\frac{k_1 k_3}{k_2} = 2\frac{A_1 A_3}{A_2}\exp\left[\frac{-\overbrace{\left(-E_{a2} + (E_{a1} + E_{a3})\right)}^{E_{a,eff}}}{RT}\right]$$

If $E_{a2} > (E_{a1} + E_{a3})$, our effective activation energy is negative

This is why the rate decreases with increasing temperature for our rate of NO_2 production. A negative activation energy is a flag that a reaction is not a single elementary step.

Note: Often you'll see concentrations written as $[NO_2]$ rather than C_{NO_2}, especially when dealing with reaction mechanisms and kinetics

Today we'll start our last topic: Catalysis

Catalysts control rates but are not consumed during reaction e.g., oxygen can accelerate combustion, but since O_2 is consumed it is not a catalyst! Catalysts *can* change during reaction but must return to starting state (catalytic cycle)

Homogeneous catalysis examples (today's Lecture)

- Biocatalysis (enzymes)
- Acid/base catalysis

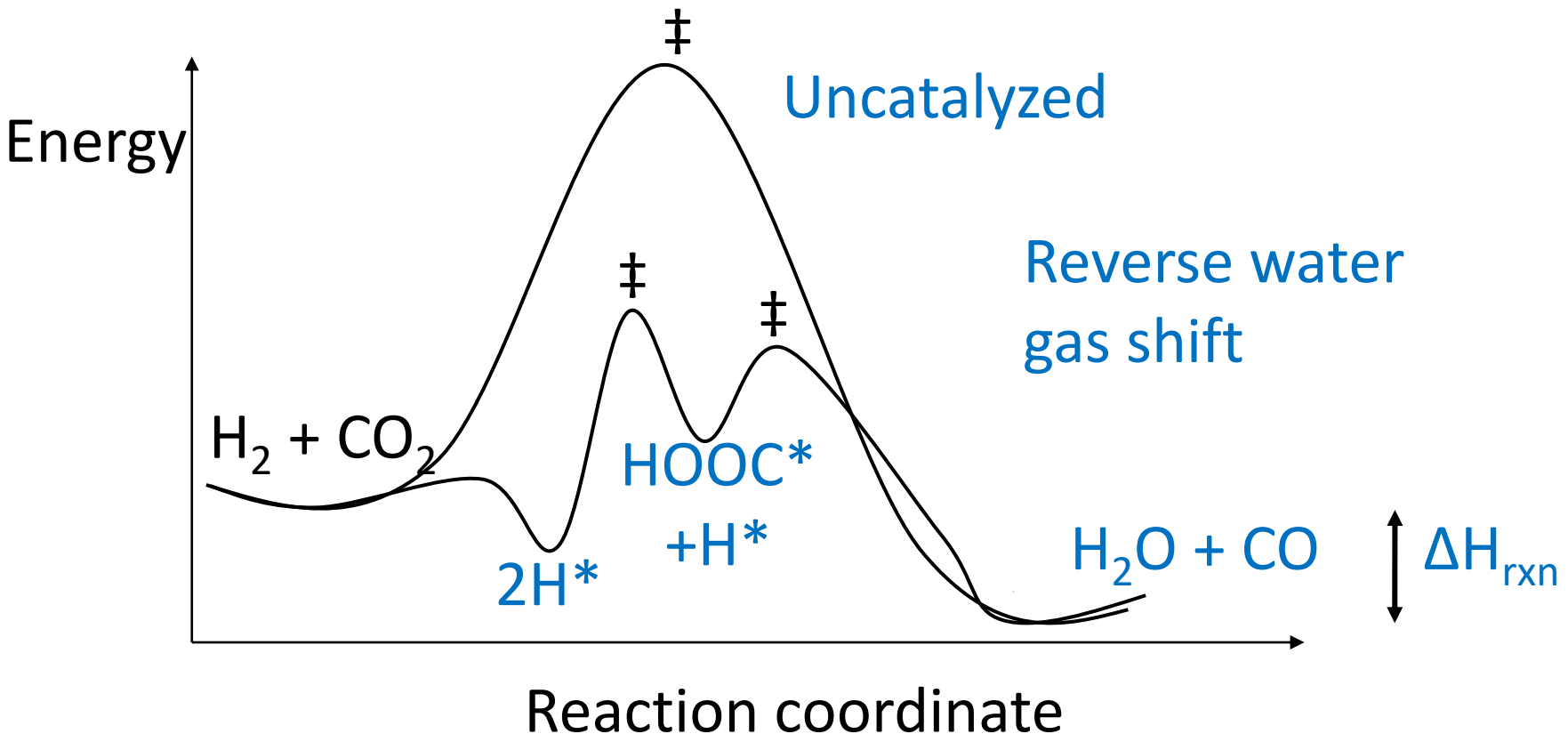
Generally for fine chemicals (10^2-10^4 tonnes per year), pharmaceuticals (10-10^2 tonnes per year)

Heterogeneous catalysis examples (Lectures 22-24)

- Gas-phase reactions on solid surfaces
- Electrocatalysis

Production of bulk chemicals (10^4 – 10^6 tonnes per year)

In nearly all cases a catalyst lowers transition states/intermediates energy so that a large barrier is replaced by a smaller barrier (or barriers). Catalysts do not affect thermodynamics of the overall reaction



When would you want to increase an activation barrier?

Selectivity!

Industrial Catalysis:

$10 billion annual sales of catalysts globally

1/3 is for fuel refining → 90% of processes are catalytic for fuels and chemicals

1/3 chemical production

1/3 depollution

Catalyst cost is generally 0.1% of product value

Approx. 30% of GDP is from catalytic processes

Additionally: Nobel prizes (at least 20) in both biocatalysts and heterogeneous

Both in Chemistry and Physiology or Medicine

Chemistry 2018 Frances Arnold "directed evolution of enzymes"

Discuss with your neighbor:

Homogeneous catalysts are usually molecular and have uniform active sites. Heterogeneous catalysts are generally non-molecular, have lower separation costs, but have non-uniform active sites.

Which of the following processes that we've mentioned during class uses a homogeneous catalyst?

A) Car exhaust flows through Pt catalyst PBR aka catalytic converter (Lecture 8)

B) Sulfuric acid for propylene oxide + water (CSTR startup)

C) Iron metal for $NH_3(g)$ synthesis (Lecture 1)

D) Ethylene epoxidation over Cs-Ag (HW 5)

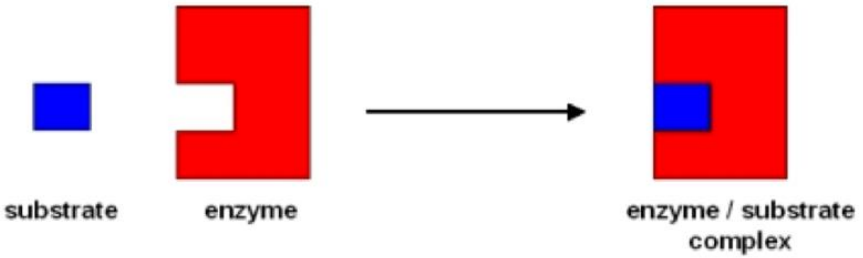
Homogeneous (enzyme)

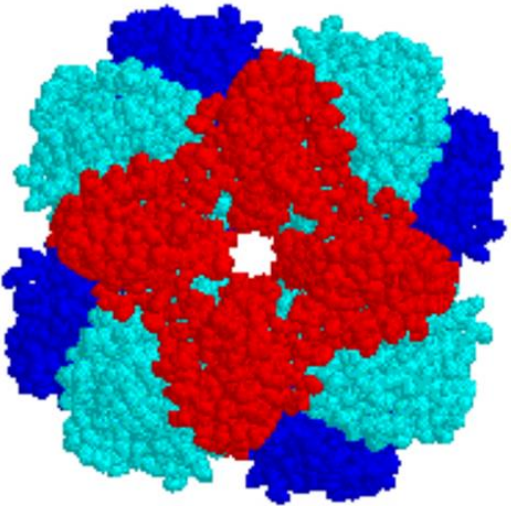
Enzymes are a big topic in catalysis. Cheap and abundant metals, big in industry, high selectivity.

Enzymes are proteins that fold to create an active site.

Often metal ion and ligands are in the active site. Enzymes run the range of extremely picky (of what they react) to applicable to a range of reactions

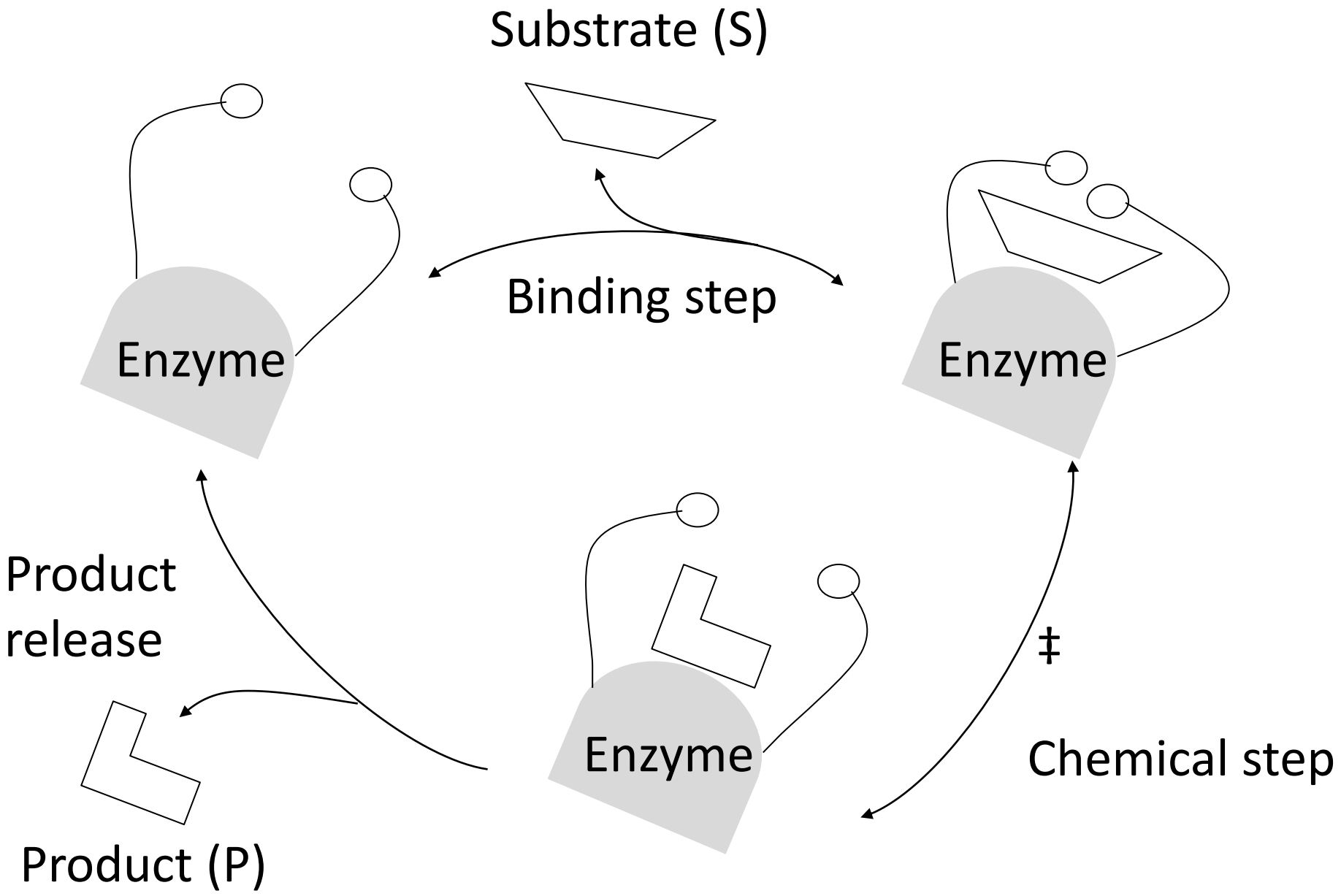
"Lock and key" binding





Example:
RuBisCO (photosynthesis)

Enzyme catalytic cycle



Enzymes rate equations

Simplest mechanism is substrate binding step, chemical step, product release.

Generally can apply the pseudo steady state hypothesis where the enzyme concentration is much lower than reactants (bound species are intermediates)

$$E + A \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} EA \underset{k_{-2}}{\overset{k_2}{\rightleftarrows}} EB \xrightarrow{k_3} E + B$$

$E = enzyme$

$EA = enzyme - species\ (substrate)\ complex$

Net overall reaction: A ⇄ B

Enzyme balance:

Constant number of total enzymes ($C_E + C_{EA} + C_{EB}$ = constant)

Can do $r_E \approx 0$, $r_{EA} \approx 0$ and $r_{EB} \approx 0$, but only two would be linearly independent as we have enzyme balance now.

$$r_E = -k_1 C_E C_A + k_{-1} C_{EA} + k_3 C_{EB} \approx 0$$

$$r_{EA} = k_1 C_E C_A - k_{-1} C_{EA} - k_2 C_{EA} + k_{-2} C_{EB} \approx 0$$

$$C_{E,total} = C_E + C_{EA} + C_{EB}$$

$$r = r_B = k_3 C_{EB}$$

Need to solve for the concentrations of our intermediates.

From r_E

$$-k_1 C_E C_A + k_{-1} C_{EA} + k_3 C_{EB} = 0$$

$$k_1 C_E C_A - k_{-1} C_{EA} = k_3 C_{EB}$$

From r_{EA}

$$k_1 C_E C_A - k_{-1} C_{EA} - k_2 C_{EA} + k_{-2} C_{EB} = 0$$

$$k_3 C_{EB} - k_2 C_{EA} + k_{-2} C_{EB} = 0$$

$$C_{EB}(k_3 + k_{-2}) = k_2 C_{EA}$$

$$C_{EB} = \frac{k_2 C_{EA}}{k_3 + k_{-2}}$$

Plug C_{EB} back into r_E equation:

$$-k_1 C_E C_A + k_{-1} C_{EA} + k_3 \frac{k_2 C_{EA}}{k_3 + k_{-2}} = 0$$

$$k_1 C_E C_A = \left(k_{-1} + k_3 \frac{k_2}{k_3 + k_{-2}} \right) C_{EA}$$

$$\frac{k_1 C_E C_A}{\left(k_{-1} + k_3 \frac{k_2}{k_3 + k_{-2}} \right)} = C_{EA}$$

$$C_{EB} = \frac{k_2 C_{EA}}{k_3 + k_{-2}} = \frac{k_2}{k_3 + k_{-2}} \frac{k_1 C_E C_A}{\left(k_{-1} + k_3 \frac{k_2}{k_3 + k_{-2}}\right)}$$

Now we have C_{EA}, C_{EB}, so will plug into enzyme balance:

$$C_{E,total} =$$

$$C_E + \frac{k_1 C_E C_A}{\left(k_{-1} + k_3 \frac{k_2}{k_3 + k_{-2}}\right)} + \frac{k_2}{k_3 + k_{-2}} \frac{k_1 C_E C_A}{\left(k_{-1} + k_3 \frac{k_2}{k_3 + k_{-2}}\right)}$$

$$C_{E,total} = C_E \left(1 + \frac{k_1 C_A}{\left(k_{-1} + k_3 \frac{k_2}{k_3 + k_{-2}}\right)} \left(1 + \frac{k_2}{k_3 + k_{-2}}\right)\right)$$

$$\frac{C_{E,total}}{1+\frac{k_1 C_A}{\left(k_{-1}+k_3\frac{k_2}{k_3+k_{-2}}\right)}\left(1+\frac{k_2}{k_3+k_{-2}}\right)} = C_E$$

Plug C_E into C_{EA} equation

$$C_{EA} = \frac{k_1 C_E C_A}{\left(k_{-1}+k_3\frac{k_2}{k_3+k_{-2}}\right)} = \frac{k_1 C_A}{\left(k_{-1}+k_3\frac{k_2}{k_3+k_{-2}}\right)}$$

$$\frac{C_{E,total}}{1+\frac{k_1 C_A}{\left(k_{-1}+k_3\frac{k_2}{k_3+k_{-2}}\right)}\left(1+\frac{k_2}{k_3+k_{-2}}\right)}$$

Use C_{EB} equation:

$$C_{EB} = \frac{k_2 C_{EA}}{k_3 + k_{-2}} =$$

$$\frac{\frac{k_2}{k_3 + k_{-2}} \frac{k_1 C_A}{\left(k_{-1} + k_3 \frac{k_2}{k_3 + k_{-2}}\right)} C_{E,total}}{1 + \frac{k_1 C_A}{\left(k_{-1} + k_3 \frac{k_2}{k_3 + k_{-2}}\right)} \left(1 + \frac{k_2}{k_3 + k_{-2}}\right)}$$

Now we have C_{EB} in terms of $C_{E,total}$ and C_A, both of which we can measure/know.

Can use these expressions to give rate

$$r = k_3 C_{EB} = k_3 k_2 \frac{C_A C_{E,total}(k_3 + k_{-2} + k_2)^{-1}}{\frac{(k_{-1}(k_3 + k_{-2}) + k_3 k_2)}{k_1(k_3 + k_{-2} + k_2)} + C_A}$$

$$r = k_3 k_2 \frac{C_A C_{E,total}(k_3 + k_{-2} + k_2)^{-1}}{\frac{k_{-1}k_{-2} + k_{-1}k_3 + k_3 k_2}{k_1(k_3 + k_{-2} + k_2)} + C_A}$$

$$r = k_3 C_{EB} = k_3 \frac{k_2}{k_3 + k_{-2}} \frac{k_1 C_A}{\left(k_{-1} + k_3 \frac{k_2}{k_3 + k_{-2}}\right)}$$

$$\frac{C_{E,total}}{1 + \frac{k_1 C_A}{\left(k_{-1} + k_3 \frac{k_2}{k_3 + k_{-2}}\right)}\left(1 + \frac{k_2}{k_3 + k_{-2}}\right)}$$

Skipped in class

$$r = k_3 C_{EB} = k_3 k_2 \frac{k_1 C_A}{(k_{-1}(k_3 + k_{-2}) + k_3 k_2)}$$

$$\frac{C_{E,total}}{1 + \frac{k_1 C_A}{\left(\frac{k_{-1}(k_3 + k_{-2}) + k_3 k_2}{k_3 + k_{-2}}\right)}\left(\frac{k_3 + k_{-2} + k_2}{k_3 + k_{-2}}\right)}$$

$$r = k_3 C_{EB} = k_3 k_2 \frac{k_1 C_A}{1}$$

$$\frac{C_{E,total}}{(k_{-1}(k_3 + k_{-2}) + k_3 k_2) + k_1 C_A (k_3 + k_{-2}) \left(\frac{k_3 + k_{-2} + k_2}{k_3 + k_{-2}} \right)}$$

Skipped in class

$$r = k_3 C_{EB}$$

$$= k_3 k_2 \frac{C_A C_{E,total}}{\frac{(k_{-1}(k_3 + k_{-2}) + k_3 k_2)}{k_1} + C_A (k_3 + k_{-2} + k_2)}$$

$$r = k_3 C_{EB} = k_3 k_2 \frac{C_A C_{E,total} (k_3 + k_{-2} + k_2)^{-1}}{\frac{(k_{-1}(k_3 + k_{-2}) + k_3 k_2)}{k_1 (k_3 + k_{-2} + k_2)} + C_A}$$

$$r = k_3 k_2 \frac{(k_3 + k_{-2} + k_2)^{-1} C_A C_{E,total}}{\frac{k_{-1} k_{-2} + k_{-1} k_3 + k_3 k_2}{k_1 (k_3 + k_{-2} + k_2)} + C_A}$$

Get a 'maximum rate parameter'

$$v_M = k_2 k_3 (k_3 + k_{-2} + k_2)^{-1}$$

And a Michaelis constant:

$$K_M = \frac{k_{-1} k_{-2} + k_{-1} k_3 + k_3 k_2}{k_1 (k_3 + k_{-2} + k_2)}$$

And can define this as a turnover frequency compared to the total enzyme: $v = r/C_{E,total}$

$$v = \frac{v_M C_A}{C_A + K_M}$$

Should v be dependent on the $C_{E,total}$?

Why or why not?

Rough values

10^{-7} M < K_M < 10^{-1} M

1 s^{-1} < v_M < 10^5 s^{-1}

Can get cases where diffusion controlled rate of reaction

Special case is the Briggs-Haldane mechanism:

$$E + A \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} EA \xrightarrow{k_2} E + B$$

In turnover frequency compared to the total enzyme:

$v = r/C_{Etotal}$

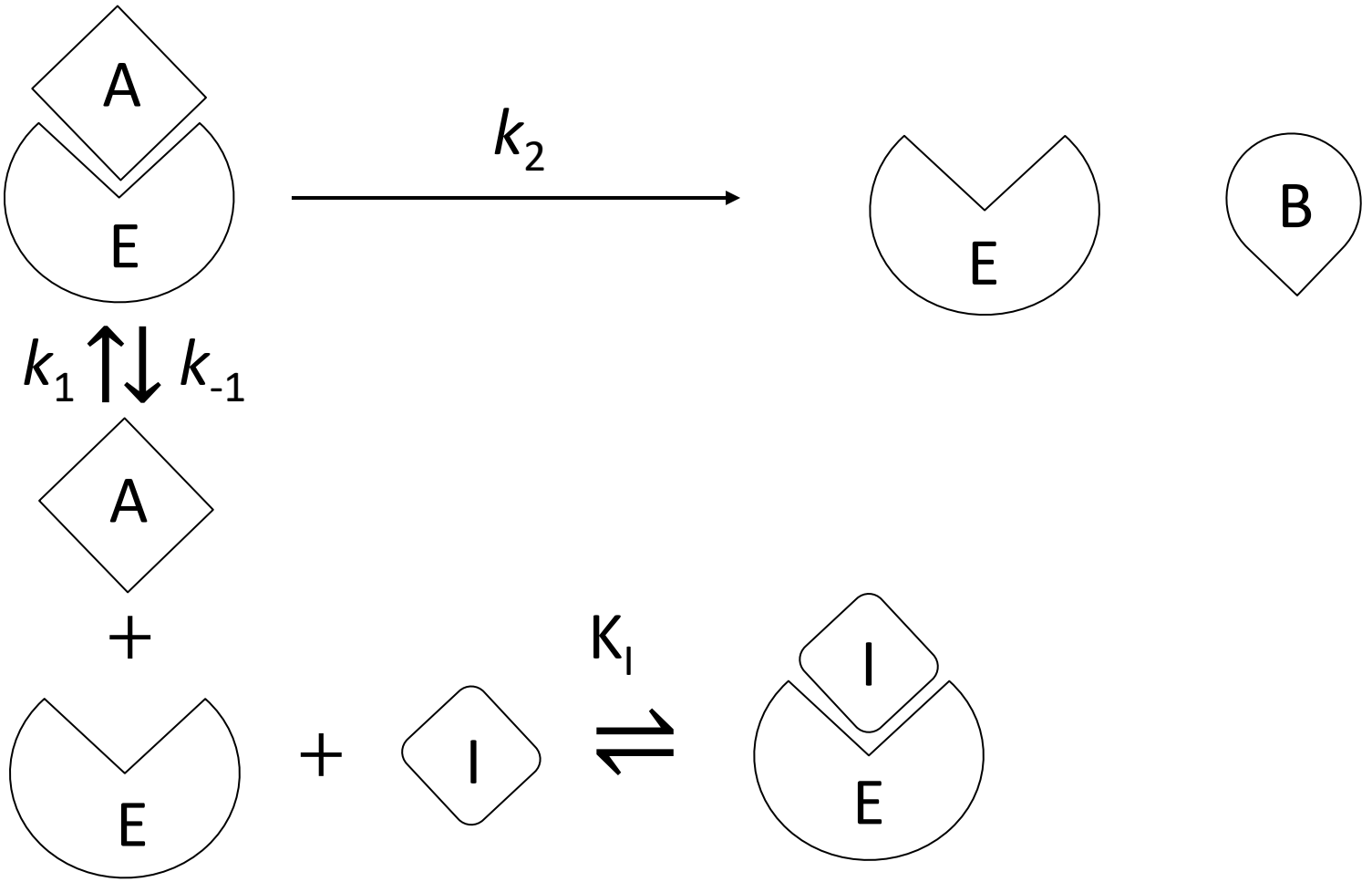
$$v = \frac{v_M C_A}{C_A + K_M}$$

$$v_{M,BH} \approx k_2$$

$$K_{M,BH} \approx \frac{k_{-1} + k_2}{k_1}$$

Also can have cases with "inhibitors"

Here competitive:



$$C_{E,total} = C_E + C_{EA} + C_{EB} + C_{EI}$$

Types of inhibition:

Competitive:

Prevents binding of the target molecule

Non-competitive:

Binds at a site different than the active site, but reduces activity of the enzyme

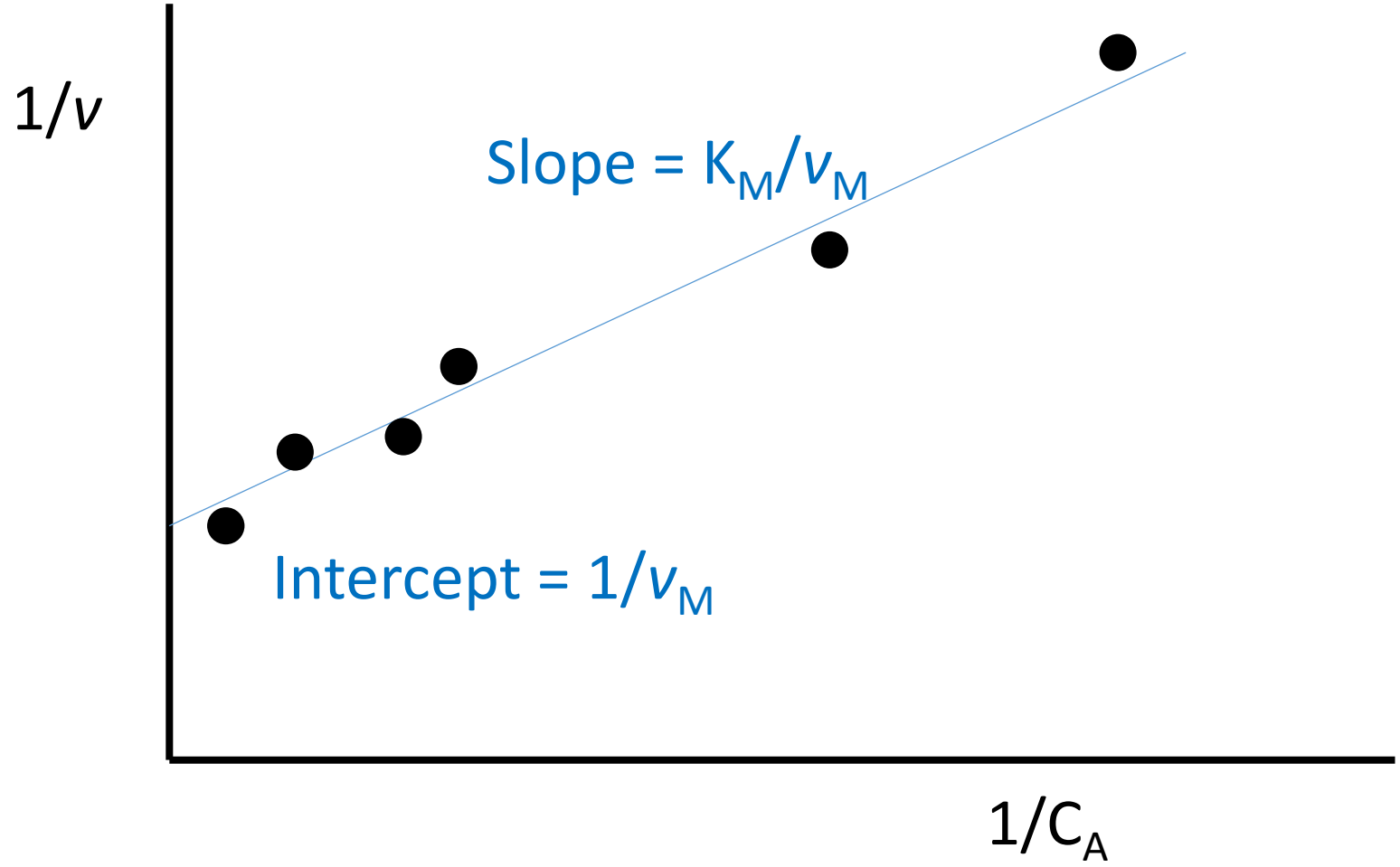
Uncompetitive:

Binds only to the complex formed between enzyme and substrate

Why would you want inhibition?

Sometimes you don’t want to keep making product!

Lineweaver-Burk plot



By plotting data from with and without inhibitor, can be used to determine competitive (same y-intercept), uncompetitive (same slope) and noncompetitive inhibitors