Kinetics

Kinetic data gives insight into reaction mechanisms

A kinetic analysis will describe a relationship between concentrations of all chemical species before the rate determining step in a given reaction and the rate of the reaction

Consider an irreversible unimolecular reaction

\[ \begin{array}{c} \text{A} \\ \searrow \end{array} \quad \text{B} \quad \text{A} \xrightarrow{k} \text{B} \]

The rate equation will describe the change in concentration versus rate

\[ -\frac{d[A]}{dt} = k[A] \]

Can also describe in terms of appearance of B

\[ \frac{d[B]}{dt} = k[A] \]

[A] however is dependent on [B]

\[ [B] = [A]_0 - [A] \]

Need to have variable of [B], not in [A] if solve \( \frac{d[B]}{dt} \)

\[ [A]_0 = \text{concentration of A at time 0} \]

\[ \frac{d[B]}{dt} = k([A]_0 - [B]) \]
Kinetics

What about a reversible unimolecular reaction?

\[
\begin{align*}
& \text{A} \quad \xrightleftharpoons[\kappa_2]{\kappa_1} \quad \text{B} \\
& [A] = [A]_o, [B] = 0 \text{ at time } 0
\end{align*}
\]

Disappearance of [A]

\[-d[A]/dt = k_1[A] - k_2[B] \quad \text{Cannot solve for } d[A]/dt \text{ having a variable of } [B]\]

\[ [B] = [A]_o - [A] \]

\[-d[A]/dt = k_1[A] - k_2([A]_o - [A]) \]

\[-d[A]/dt = (k_1 + k_2)[A] - k_2[A]_o \]
Kinetics

Consider an irreversible bimolecular reaction

\[
\begin{array}{ccc}
A & B & k \\
\end{array}
\]

\[
-d[A]/dt = k[A][B]
\]

\[
[A]_o - [A] = [B]_o - [B]
\]

\[
[B] = [A] - [A]_o + [B]_o
\]

\[
-d[A]/dt = k[A][A] - [A]_o + [B]_o)
\]

Consider a dimerization

\[
\begin{array}{ccc}
A & A & k \\
\end{array}
\]

\[
-d[A]/dt = k[A]^2
\]

In order to make \(d[A]/dt\) solvable, need to have only \([A]\) as a variable

Overall therefore a solvable rate equation should be relatively straightforward to write, just remember to understand the relationships present so the only variable is the term being integrated...
Kinetics

The kinetic order of a rate equation is the sum of all exponents of the concentrations appearing in the term

\[-d[A]/dt = k[A]\]

Therefore first order

\[-d[A]/dt = k[A][B]\]

Therefore second order

Can also classify by the order of a given reactant

The overall second order reaction above is thus second order overall, but first order with respect to [A] and first order with respect to [B]
Kinetics

An important experimental determination for a reaction is once a rate equation is written, how to determine the actual value of rate constant (k)

Reconsider the irreversible first order reaction

\[ A \xrightarrow{k} B \]

\[-d[A]/dt = k[A] \]

Rearrange equation to place like terms on same side

\[ d[A]/[A] = -k \, dt \]

Need to integrate equation

\[ \int d[A]/[A] = \int -k \, dt \]

\[ \ln[A] - \ln[A]_o = -kt \]

\[ [A] = [A]_o e^{-kt} \]

Therefore to determine the value of k need to measure the concentration of [A] versus time
A straightforward observation (if not always seen at first) is that if a graph of $\ln [A]$ versus time yields a straight line, then the reaction must have been a first order reaction.

The slope of this graph will be the $-k$ value and the intercept will be $\ln [A]_o$ (which can be used to double check accuracy since this value should be known).

Can also use this data to determine the half-life ($T_{\frac{1}{2}}$) for a reaction

At $T_{\frac{1}{2}}$, $[A] = \frac{1}{2}[A]_o$

$$\ln([A]_o/2) - \ln[A]_0 = -kt_{\frac{1}{2}}$$

$$T_{\frac{1}{2}} = \frac{1}{k} \ln \left( \frac{[A]_0}{\frac{[A]_0}{2}} \right) = \frac{1}{k} \ln 2$$
Kinetics

Consider how determination of rate constant changes if reaction is reversible

\[
A \xrightleftharpoons[k_2]{k_1} B
\]

\[-\frac{d[A]}{dt} = (k_1 + k_2)[A] - k_2[A]_o\]

Need to integrate equation

\[-\int \frac{d[A]}{(k_1 + k_2)[A] - k_2[A]_o} = \int dt\]

At equilibrium

\[\ln \frac{(k_1 + k_2)[A] - k_2[A]_o}{k_1[A]_o} = -(k_1 + k_2)t\]

Leads to two equations

1) \[\frac{k_2[A]_o}{k_1 + k_2} = [A]_e\]

2) \[\ln \frac{[A]_o - [A]_e}{[A] - [A]_e} = (k_1 + k_2)t\]
Kinetics

1) \[ [A]_e = \frac{k_2[A]_o}{k_1 + k_2} \]

2) \[ \ln \frac{[A]_o - [A]_e}{[A] - [A]_e} = (k_1 + k_2)t \]

In order to solve for the \( k_1 \) and \( k_2 \) values:

\( k_1 + k_2 \) can be determined from equation 2 by measuring \([A]\) versus time and knowing the \([A]_o\) and \([A]_e\) terms

The individual \( k_1 \) and \( k_2 \) values are then determined from equation 1

This is for only a relatively simple reversible unimolecular reaction!

* Can easily realize that this kinetic analysis will become very difficult as the complexity of the reactions increase

* Need approximations to solve more complex reactions
Kinetics

As an example consider again a second order reaction

\[
\begin{array}{c}
A & \underset{k}{\rightarrow} & C \\
\end{array}
\]

\[-d[A]/dt = k[A]([A] - [A]_0 + [B]_0)\]

Integrate equation

\[
\frac{1}{[B]_0 - [A]_0} \ln \frac{[A]_0([B]_0 - [A]_0 + [A])}{[A][B]_0} = kt
\]

What if we start reaction with one reagent in great excess?

\[[B]_0 \gg [A]_0, \text{ which also means } [B]_0 \gg [A]\]

If apply to integral

\[
\frac{1}{[B]_0} \ln \frac{[A]_0}{[A]} = kt
\]
Kinetics

\[
\frac{1}{[B]_o} \ln \frac{[A]_o}{[A]} = kt
\]

\[
\ln \frac{[A]_o}{[A]} = [B]_o kt
\]

Let \([B]_o k = k_{obs}\)

(often done in practice, all constants are combined into a \(k_{obs}\) term which is the actually measured value)

\[
\ln \frac{[A]}{[A]_o} = -k_{obs} t
\]

* Identical to irreversible first order reaction
  (called \textit{pseudo first order} kinetics)

For second order reactions, if one reagent is used in great excess (need > 10 fold) then that reagent will not appear in rate equation
Kinetics

Excess reagent term, however, will affect the observed rate constant

$$A \quad B \quad \overset{k}{\rightarrow} \quad C$$

If $[B]$ is in excess

$$-\frac{d[A]}{dt} = k_{obs}[A]$$

$$k_{obs} = k_1[B]$$

As $[B]$ increases, the $k_{obs}$ will also increase

$$\ln[A] - \ln[A]_o = -k_{obs}t$$

With pseudo first order approximation, a second order reaction will follow first order behavior and the observed rate constant can be obtained from a graph of $\ln [A]$ versus time.
Kinetics

Another common approximation to use in kinetic analysis is called a *steady-state approximation*

Consider a reaction of the type shown

\[
\begin{align*}
\text{A} & \xrightleftharpoons[k_2]{k_1} \text{B} \\
& \xrightarrow{k_3} \text{C}
\end{align*}
\]

rate equations

Step 1

\[-d[A]/dt = k_1[A] - k_2[B]\]

Step 2

\[d[C]/dt = k_3[B]\]

Considering [B]

\[-d[B]/dt = k_3[B] + k_2[B] - k_1[A]\]

Now we assume \(d[B]/dt = 0\)  *Steady-state approximation*

Therefore [B] does not change appreciably over time

Can occur if either \(k_2 \gg k_1\) or \(k_3 \gg k_1\)
Kinetics

Means that any reactive intermediate B will not accumulate in concentration over time

Change in concentration of B is small compared to change in concentration of either A or C over time

\[-\frac{d[B]}{dt} = 0 = k_3[B] + k_2[B] - k_1[A]\]

Solve for [B]

\[[B] = \frac{k_1[A]}{k_3 + k_2}\]

Remember rate equations

\[-\frac{d[A]}{dt} = k_1[A] - k_2[B]\]

\[\frac{d[C]}{dt} = k_3[B]\]

Can substitute for solvable integral

\[\frac{d[C]}{dt} = -\frac{d[A]}{dt} = \frac{k_3k_1[A]}{k_3 + k_2}\]

Therefore \[-\frac{d[A]}{dt} = k_{\text{obs}}[A]\] Obtain first order equation
Kinetics

Can also use steady-state approximation for nonunimolecular reactions

\[ \begin{align*}
A & \xrightleftharpoons[k_2]{k_1} B \\
B & \xrightarrow{k_3} C \\
C & \rightarrow D
\end{align*} \]

Merely pay attention to properly write rate equations

\[-\frac{d[A]}{dt} = k_1[A] - k_2[B] \]

\[-\frac{d[B]}{dt} = 0 = k_3[B][C] + k_2[B] - k_1[A] \]

\[\frac{d[D]}{dt} = k_3[B][C] \]

\[ [B] = \frac{k_1[A]}{k_2 + k_3[C]} \]

\[\frac{d[C]}{dt} = -\frac{d[A]}{dt} = \frac{k_3[C]k_1[A]}{k_2 + k_3[C]} \]

\[-\frac{d[A]}{dt} = k_{\text{obs}}[A] \]

The \( k_{\text{obs}} \) term now includes \([C]\) (which means you would need to run in excess), but otherwise is identical to steady-state approximation for unimolecular case.
Kinetics

Examples of mechanistic questions answered by proper kinetic analysis

1) Does a reaction proceed through an intermediate?

Or does starting material react directly to product?

If the intermediate is reactive and cannot be detected spectroscopically, how can an experimentalist determine whether it occurs or not?
Kinetics

Presence of intermediate can be detected by the kinetic analysis

Write the rate equations for the two possible mechanisms:

With intermediate

\[
\begin{align*}
\text{A} & \xrightarrow{k_1} \text{B} \quad \text{B} \xrightarrow{k_3} \text{D} \\
& \xleftarrow{k_2} \quad & \text{D} \rightarrow \text{P}
\end{align*}
\]

\(D\) represent “alkene”

\[
\begin{align*}
-d[B]/dt &= 0 = k_3[B][D] + k_2[B] - k_1[A] \\
\frac{d[P]}{dt} &= -\frac{d[A]}{dt} = \frac{k_3[D]k_1[A]}{k_2 + k_3[D]} \\
\frac{-d[A]}{dt} &= k_{\text{obs}}[A]
\end{align*}
\]

Direct reaction

\[
\begin{align*}
\text{A} & \xrightarrow{k} \text{D} \quad \text{D} \rightarrow \text{P}
\end{align*}
\]

\[
\begin{align*}
-d[A]/dt &= k[D][A] \\
\frac{-d[A]}{dt} &= k_{\text{obs}}[A]
\end{align*}
\]

How to detect difference between direct reaction and pathway with intermediate? (both simplify to pseudo first order when approximations are applied)
Kinetics

Often an issue when trying to distinguish pathways, how to run experiment to differentiate between possible pathways?

In this case, report experiments with a double reciprocal plot

With intermediate

\[ k_{\text{obs}} = \frac{k_3[D]k_1}{k_2 + k_3[D]} \]

\[ \frac{1}{k_{\text{obs}}} = \frac{k_2}{k_1k_3[D]} + \frac{1}{k_1} \]

Direct reaction

\[ k_{\text{obs}} = k[D] \]

\[ \frac{1}{k_{\text{obs}}} = \frac{1}{(k[D])} \]

Whether the intercept passes through the origin (direct reaction) or has a finite value (with intermediate) in double reciprocal plot will distinguish possible mechanisms.
Kinetics

2) Another question that a proper kinetic analysis can answer is how to increase the rate of a reaction

Consider the synthesis of benzhydrol in a sodium chloride solution

\[
d[C]/dt = k_3[H_2O][B]
\]

Use pseudo first order approximation with water

\[
d[C]/dt = k_{obs}[B]
\]

Since B is a reactive intermediate, can apply steady-state approximation for the [B] term
Kinetics

\[
d[B]/dt = 0 = k_1[A] - k_2[B][Cl^-] - k_3[H_2O][B]
\]

\[
[B] = \frac{k_1[A]}{k_3[H_2O] + k_2[Cl^-]}
\]

\[
d[C]/dt = -d[A]/dt = k_3[H_2O][B]
\]

\[
-d[A]/dt = \frac{k_1k_3[H_2O][A]}{k_3[H_2O] + k_2[Cl^-]}
\]

\[
k_{obs} = \frac{k_1k_3[H_2O]}{k_3[H_2O] + k_2[Cl^-]}
\]

Therefore rate becomes slower as concentration of chloride ion increases

* Known as *common ion rate depression*
Kinetics

3) What does kinetics indicate if we change the type of trapping agent in question 1?

![Kinetics Diagram]

Assume pathway with intermediate

\[ k_{\text{obs}} = \frac{k_3[D]k_1}{k_2 + k_3[D]} \]

\[ \frac{1}{k_{\text{obs}}} = \frac{k_2}{k_1k_3[D]} + \frac{1}{k_1} \]

If trapping agent is more reactive, then the \(k_3\) rate will be faster.

Therefore slope in double reciprocal plot will be less, but the intercept will be the same.
Kinetics

What occurs if no longer have steady-state conditions when an intermediate is formed?

A \[\xrightarrow{k_1} \] B \[\xrightarrow{k_2} \] C

The kinetics become much more complicated

\[ A = [A]_0 e^{-k_1 t} \]

\[ B = \frac{[A]_0 k_1}{k_2-k_1} \left( e^{-k_1 t} - e^{-k_2 t} \right) \]

\[ C = [A]_0 \left\{ 1 + \frac{1}{(k_1-k_2)} \left[ k_2 e^{-k_1 t} - k_1 e^{-k_2 t} \right] \right\} \]

The concentration of A, B and C do not follow as simple of relationship as when a reactive intermediate is present.
Kinetics

If \( k_1 = 0.001/s \) and \( k_2 = 0.0005/s \), then \([B]_{\text{max}} = 0.46 [A]_0\) and \( T_{[B]_{\text{max}}} = 15 \text{ min}\)

If we want to synthesize B, but it can decompose to another product C, then we would need to determine the \( k_1 \) and \( k_2 \) rate constants and then find out when \([B]_{\text{max}}\) occurs to stop reaction and then isolate B.