

# Week 12

## Experimental Kinetics

### 12.1 Kinetics of Catalytic Reactions

11/19:

- Last week's lectures.
  - Very simple kinetic scenarios.
  - Linearizations allows us to extract essential kinetic parameters for reactions.
  - Kinetic descriptions for multistep processes.
  - Steady-state approximation, quasi-equilibrium approximation.
- Today: Kinetics of Catalytic Reactions.
- Catalysts speed up the rate of reaction without altering the thermodynamics.
- Consider the following balanced chemical reaction.



- Since the catalyst appears on both sides of the reaction, we typically write it over the arrow.
- This notational simplification alides a great deal of multistep complexity.
- Consider a hypothetical potential energy surface.

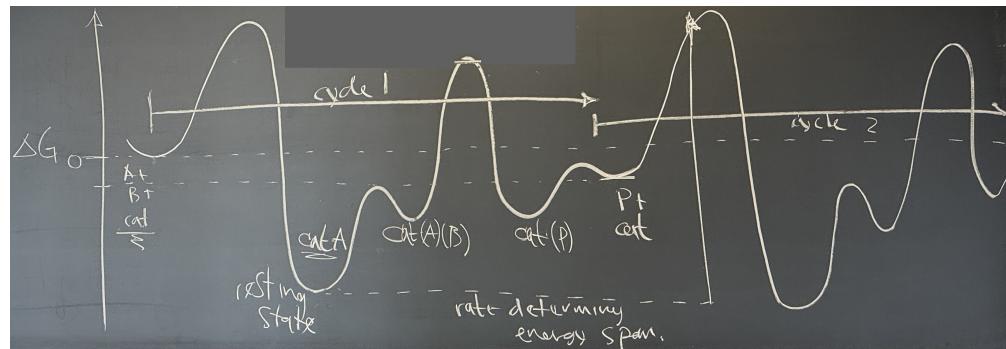


Figure 12.1: Model catalytic potential energy surface.

- Define a reference energy as zero; suppose the starting materials ( $A + B + \text{cat}$ ) begin here.
- Suppose, then, that they proceed through a multistep potential energy surface along our reaction coordinate.

- If this were a stoichiometric reaction, the first step would be rate-determining (highest energy barrier), and the first intermediate would be the product (lowest energy species).
  - But we're catalytic, so we have to consider cycles 2, 3, ...
  - These cycles are driven forward by the ever-so-slight difference in energy  $\Delta G$  between starting materials and products.
- The “first intermediate” is actually the catalyst **resting state**.
  - Indeed, the thing that we throw in may not be the dominant species in solution!
  - It could be  $\text{cat} \cdot (\text{A})$ ,  $\text{cat} \cdot (\text{A})(\text{B})$ , or  $\text{cat} \cdot (\text{P})$ !
- Similarly, the difference in energy between the lowest valley and highest peak is the **rate-determining energy span**.
- Reference (good description of rate-determining energy span): Kozuch and Martin (2011).
- Because continuous potential energy surfaces are not great representations, we typically view catalysts as acting in **catalytic cycles**.

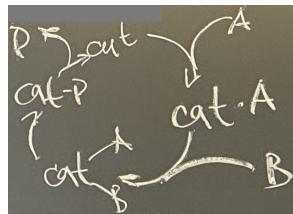


Figure 12.2: Model catalytic cycle.

- This is not that uncommon a catalytic cycle to find!
- Let's now do a kinetic analysis of this model catalytic cycle, using some of the tools developed last lecture.

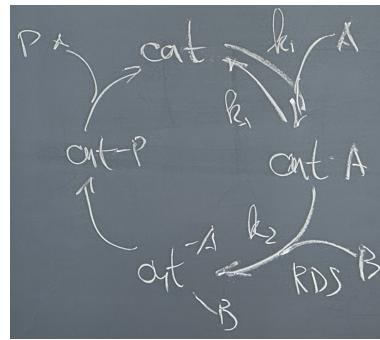


Figure 12.3: Model catalytic cycle (kinetic analysis).

- Assume that the first step is a reversible binding to A.
- Recall that the rate-determining step follows the resting state. Thus,

$$\text{rate} = \frac{d[\text{P}]}{dt} = -\frac{d[\text{A}]}{dt} = k_2[\text{cat} \cdot \text{A}][\text{B}]$$

- We can then apply our rule of thumb for the steady-state approximation.

$$\text{rate} = \frac{k_1 k_2 [\text{A}][\text{B}][\text{cat}]}{k_{-1} + k_2 [\text{B}]}$$

- Going forward, it will be useful to define the total concentration of catalyst

$$[\text{cat}]_T := [\text{cat}] + [\text{cat} \cdot A] + [\text{cat} \cdot AB] + [\text{cat} \cdot P]$$

- To derive the rate law for Figure 12.3 in terms of  $[\text{cat}]_T$  — an observable — we'd need a system of equations.
- Let's now consider a different (simpler) catalytic cycle to develop some core ideas.

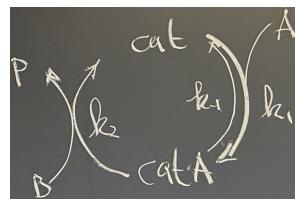
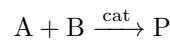


Figure 12.4: Model two-step catalytic cycle (kinetic analysis).

- This cycle pertains to a reaction



- If the second step is rate-determining, then

$$\text{rate} = k_2[\text{cat} \cdot A][B]$$

- It will also be useful to have the assumption

$$[\text{cat}]_T = [\text{cat}] + [\text{cat} \cdot A]$$

- Let's now evaluate this catalytic cycle using the quasi-equilibrium assumption.

- Warning: Lots of algebra coming up!
  - Squiggly lines on the board mean abbreviations.
- The quasi-equilibrium assumption tells us that

$$K = \frac{k_1}{k_{-1}} = \frac{[\text{cat} \cdot A]}{[\text{cat}][A]}$$

- We first solve for the concentration of the catalyst.

$$[\text{cat}] = \frac{[\text{cat} \cdot A]}{K[A]}$$

- We can drop this into our expression for the total catalyst.

$$[\text{cat}]_T = \frac{[\text{cat} \cdot A]}{K[A]} + [\text{cat} \cdot A]$$

- We can factor out the  $[\text{cat} \cdot A]$ 's.

$$[\text{cat}]_T = [\text{cat} \cdot A] \left( \frac{1}{K[A]} + 1 \right)$$

- Rearrange this to solve for  $[\text{cat} \cdot A]$ .

$$[\text{cat} \cdot A] = \frac{[\text{cat}]_T}{1/K[A] + 1}$$

- Remove this fractional denominator via multiplication by a clever form of 1 (namely,  $K[A]/K[A]$ ).

$$[\text{cat} \cdot A] = \frac{K[A][\text{cat}]_T}{1 + K[A]}$$

- We can now drop this back into the rate expression to get an expression for the rate in terms of the overall catalyst concentration, which is more useful because that's an observable (we know how much we put in!).

$$\text{rate} = \frac{k_2 K[A][B][\text{cat}]_T}{1 + K[A]}$$

- Note that we could also write the  $K$ 's above as  $K_{\text{eq}}$ 's.

- Let's now derive an analogous expression for the catalytic cycle in Figure 12.4, but this time under the steady-state approximation.

- We initially obtain

$$[\text{cat} \cdot A] = \frac{k_1[A][\text{cat}]}{k_{-1} + k_2[B]}$$

- Rearranging yields

$$[\text{cat}] = \frac{[\text{cat} \cdot A](k_{-1} + k_2[B])}{k_1[A]}$$

- Using the fact that  $[\text{cat}] = [\text{cat}]_T - [\text{cat} \cdot A]$ , we obtain

$$\frac{[\text{cat} \cdot A](k_{-1} + k_2[B])}{k_1[A]} = [\text{cat}]_T - [\text{cat} \cdot A]$$

- We get rid of the denominator by multiplying both sides by  $k_1[A]$ , collect a couple of terms, and rearrange into

$$[\text{cat} \cdot A](k_1[A] + k_{-1} + k_2[B]) = k_1[A][\text{cat}]_T$$

- Then divide both sides by the term in parentheses on the left.

$$[\text{cat} \cdot A] = \frac{k_1[A][\text{cat}]_T}{k_1[A] + k_{-1} + k_2[B]}$$

- This substitution can now be dropped back into our rate law.

$$\begin{aligned} \text{rate} &= k_2[\text{cat} \cdot A][B] \\ &= \frac{k_1 k_2 [A][B][\text{cat}]_T}{k_{-1} + k_2[B] + k_1[A]} \end{aligned}$$

- We now multiply by another clever form of 1 (namely the inverse of  $k_{-1}$  on both top and bottom).

$$\text{rate} = \frac{\frac{k_1}{k_{-1}} k_2 [A][B][\text{cat}]_T}{1 + \frac{k_2}{k_{-1}} [B] + \frac{k_1}{k_{-1}} [A]}$$

- This is known as the **one plus rate form** of the rate law because of the “1+” in the denominator.

- We can now compare the two rate laws we've derived.

- We do this by assuming that  $k_{-1} \gg k_2$ , which is exactly the scenario in which the quasi-equilibrium assumption would apply!
- We approach a limit where we can ignore the  $k_2/k_{-1}$  term in the denominator, and  $k_1/k_{-1} = K_{\text{eq}}$  (as established previously).

- Let's consider some limiting scenarios.

- This will help us partially eliminate complexity.
- First, let's consider the scenario in which

$$1 \gg \frac{k_2}{k_{-1}}[B] \approx \frac{k_1}{k_{-1}}[A]$$

- In this case, the denominator vanishes and the simplified rate law is

$$\text{rate} = \frac{k_1}{k_{-1}}[A][B][\text{cat}]_T$$

- Since this constraint implies that  $k_{-1} \gg k_2$ , the second step must be rate-determining.
- It also follows that  $[\text{cat}]_T \approx [\text{cat}]$ , and hence the resting state of the catalyst is the unbound catalyst!
- We can also say that the second step is **turnover-limiting**.

- Second, let's consider the scenario in which

$$\frac{k_2}{k_{-1}}[B] \gg \text{others}$$

- By "others," we mean the other two terms in the denominator.
- In this case, the simplified rate law is

$$\text{rate} = k_1[A][\text{cat}]_T$$

- This constraint implies that the first step is rate-determining.
- Hence, the reaction with B (zero-order) is post-rate limiting.
- It follows additionally that once again, the resting state of the catalyst is the unbound catalyst!

- Third, let's consider the scenario in which

$$\frac{k_1}{k_{-1}}[A] \gg \text{others}$$

- In this case, the simplified rate law is

$$\text{rate} = k_2[B][\text{cat}]_T$$

- Zero-order dependence on [A] implies that the catalyst is fully saturated with [A].
- Hence, the second step is rate-determining and the resting state is the bound catalyst.

- Fourth, everything matters.

- This scenario is not limiting but is, unfortunately, common.
- This implies a kinetic pathway in which all species are at roughly similar energies with roughly similar transition structures.
- This is often a good thing for catalysis, but we'll get there.

- Aside: The one plus rate form.

$$\text{rate} = \frac{c_1[A][B][\text{cat}]_T}{1 + c_2[A] + c_3[A][B] + c_4[P]}$$

- The rate law takes on the above general structure.
- We have a constant (the "kinetic term")  $c$  modified by the concentrations of the inputs in the numerator, collectively referred to as the potential terms (because they reflect something about the TST with respect to the ground state).

- The denominator — the **adsorption term** — consists of all the forms that the catalyst can take.
- What do the constants tell us?
  - $c_1$  tells us about the naked catalyst.
  - $c_2[A]$  can tell us about the  $\text{cat} \cdot A$  complex.
  - $c_3[A][B]$  can tell us about the  $\text{cat} \cdot AB$  complex.
  - $c_4[P]$  can tell us about the  $\text{cat} \cdot P$  complex.
- Goal of this exercise: Gain intuition for the algebra.
  - The best kineticists can easily see the chemistry in rate laws the way that most organic chemists can see it in Lewis structures.
    - Donna Blackmond at Scripps is one of Alex's favorite kineticists.
  - Similarly, spectroscopists can see chemistry in derivative waveforms; “what a power to have!”
- How do we increase the rate, i.e., max out the rate law?
  - We want to get the denominator to go away.
  - This gives Scenario 3, in which all of the substrate is bound to the catalyst and it's doing it's thing as fast as it can.<sup>[1]</sup>

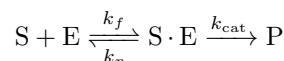
$$\text{rate}_{\max} = k_2[B][\text{cat}]_T$$

- Let's plop  $\text{rate}_{\max}$  into our steady-state approximation rate law, and multiply it by  $1 = k_{-1}/k_{-1}$ .

$$\text{rate} = \frac{\text{rate}_{\max} k_1[A]}{k_{-1} + k_2[B] + k_1[A]}$$

- Now define
- $$\frac{1}{K_m} = \frac{k_1}{k_{-1} + k_2[B]}$$
- It follows that
- $$\text{rate} = \frac{\text{rate}_{\max}[A]}{K_m + [A]}$$
- Under the quasi-equilibrium assumption, we can assume something else.
- $$\text{rate} = \frac{\text{rate}_{\max} K_{\text{eq}}[A]}{1 + K_{\text{eq}}[A]}$$
- Now define
- $$K_D = \frac{1}{K_{\text{eq}}}$$
- as the dissociation constant for the  $\text{cat} \cdot A$  complex.
- It follows that
- $$\text{rate} = \frac{\text{rate}_{\max}[A]}{K_D + [A]}$$
- $K_m$  takes us into **Michaelis-Menten kinetics**.

- Defined in the early twentieth century to guide our emerging understanding of biochemical kinetics.
- Using the historical nomenclature (substrate and enzyme), we have




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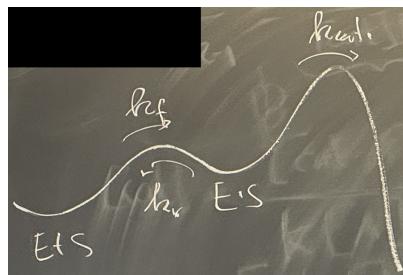
<sup>1</sup>Why should this scenario give the fastest rate??

- There is a relationship here to saturation kinetics, defined in the limiting scenarios with Figure 12.4.
- Michaelis and Menten talked about a kinetic velocity  $v_{\max}$  where we go from asymptotic speed down to a first-order dependence on  $[S]$ .
- Other relevant expressions:

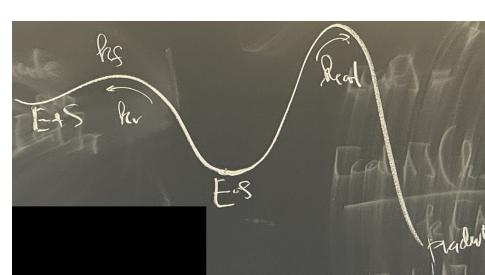
$$K_m = \frac{k_r + k_{cat}}{k_f} \quad v = \frac{v_{\max}[S]}{K_m + [S]}$$

- If  $K_m = [S]$ , then  $v = v_{\max}/2$ .
- We can experimentally determine the Michaelis constant by assaying a bunch of different initial rates at different concentrations.

- What's the point of Michaelis-Menten kinetics?



(a) Zeroeth-order.



(b) First-order.

Figure 12.5: Michaelis-Menten kinetic regimes.

- Enzymes can be characterized according the Michaelis constant  $K_m$  and the intrinsic rate constant  $k_{cat}$ .
- When we're zeroeth order in the substrate, we have one kinetic regime.
- When we're first-order in the substrate, we have a kinetic regime that's more like quasi-equilibrium!
- How well the enzyme binds the substrate is a measure of how efficient the catalyst is.

- When  $k_r \gg k_{cat}$ ,

$$K_m \approx \frac{k_r}{k_f} = K_D$$

- This ratio measures how well the enzyme binds to the substrate.

- When  $k_{cat} \gg k_r$ ,

$$K_m \approx \frac{k_{cat}}{k_m} =: \text{specificity constant}$$

- These ratios can be analyzed as the specificity constant for a specific enzyme.
- Describes an enzyme's preference (both in terms of binding and reactivity) for one substrate over another.

- Example: Fumerase (responsible for redox transport).

- $K_m = 5 \times 10^{-6}$ , and  $k_{cat} = 8 \times 10^2$ , so SC is  $10^7$ .

- Example: Carbonic anhydrase.

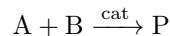
- $K_m = 2.6 \times 10^{-2}$ , and  $k_{cat} = 4 \times 10^5$ , so SC is  $10^8$ .

- So for great catalysis, you want the catalyst to find substrate quickly and immediately turn it over.
  - These two catalysts operate near the diffusion limit (which is ideal); they are near-perfect.
- References.
  - Knowles (1991).
  - A beautiful piece of literature; the touchstone for biological catalysis, per Alex.

## 12.2 Techniques for Kinetics Determinations

11/21:

- Today: Experimental techniques for kinetic determination.
  - In contrast to last time's algebra, we'll figure out today that many of those algebraic techniques were unnecessary.
  - Many techniques of kinetic analysis can be done with just a few observational experiments.
  - Goal of today: Convince us that kinetic analysis can be easy... and even fun!
- Consider the following reaction from last time.



- Recall from last time that kinetics can be used to elucidate the transition state structure.
- Recall from last week that linearizing data can give us the reaction order.
- However, we can access rate constant data without regression by using the **method of initial rates**.
- **Method of initial rates:** Assume that rate =  $k[A]^a[B]^b[\text{cat}]^c$ , take time courses, and make plots as in Figure 11.7 to extract  $k$ .

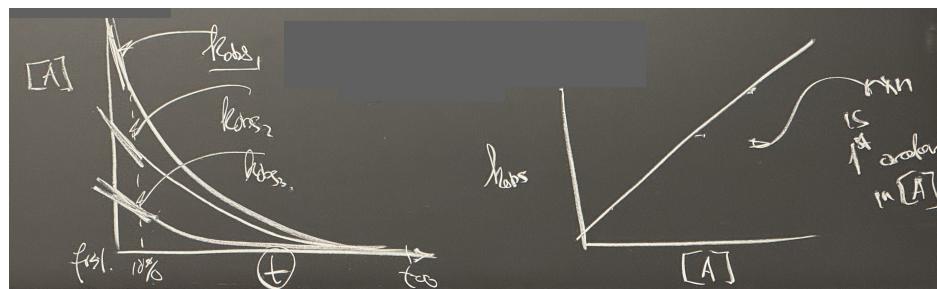


Figure 12.6: Method of initial rates.

- Begin by taking a time course for  $[A]$ .
- We can extract  $k_{\text{obs}}$  from initial slopes

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

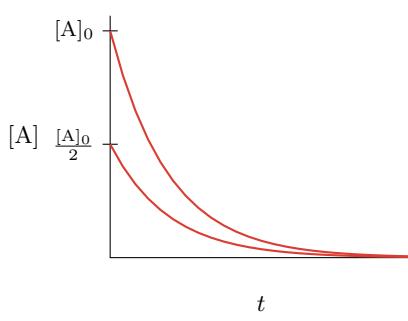
- if we're in a regime where all of the other concentrations are basically constant.
- If we consider the first, say, 10% of the reaction, then this approximate initial slope gives us  $k_{\text{obs}}$  directly.
- We can vary the initial concentration of  $[A]$  to get multiple values of  $k_{\text{obs}}$ .
- Then — as in Figure 11.7 — we can plot  $k_{\text{obs}}$  vs.  $[A]$  to learn the order of our reaction.

- The time domain matters a lot.
  - If  $t \in [10^2 \text{ s}, 10^6 \text{ s}]$ , we're in the “conventional” range for reaction speed.
    - Techniques like NMR are applicable here. These can allow us to assign concentration and structure in one experiment.
    - UV-Vis can also be good here.
    - FT-IR is also nice; it's very fast.
    - GC-MS is another recommended one in the conventional time domain.
  - If  $t \in [10^{-3} \text{ s}, 10^1 \text{ s}]$ , our reactions are too fast to pull out an aliquot.
    - As such, we need stopped flow kinetics.
  - If  $t \in [10^{-12} \text{ s}, 10^{-6} \text{ s}]$ , our reactions are too fast for mechanical injection into a compartment.
    - As such, use **flash photolysis**: Flash a light and follow the course with (typically) UV-Vis.
- How can we directly read out rate data from a reaction?
  - Calorimetry: The flow of heat from the vessel is directly related to the rate.
  - Mass transport and gas flow: Also good direct measurements.
- Usefulness of the method of initial rates.
  - Pros.
    - No complex math.
    - Direct access to  $k_{\text{obs}}$ .
    - Easy.
      - You've already got the starting materials, so just set up one more reaction!
    - Useful for trickier reactions with more complex kinetic scenarios, e.g., heterogeneous catalysis.
  - Cons.
    - Prone to error ( $\pm 10\%$  at best).
      - We've got only a few data points from a short window in which not much has happened.
    - The first 10% of the reaction course may not be representative of the entire reaction.
      - In fact, there are many cases where the first 10% is patently *not* representative of the entire reaction (see Figure 12.8).
      - Example: A burst of speed at the very beginning due, for example, to a catalyst turning over very quickly because there's a large amount of it unbound early on.
      - Example: An **induction period** before the reaction begins in earnest.
    - Can be labor intensive.
      - We need several measurements of  $k_{\text{obs}}$ ; two measurements define a straight line, technically, but at least three are needed to be experimentally viable.
- Alex has personally done such initial rate experiments, despite the difficulties. But in the computer age, the method of initial rates has been outpaced by **whole-reaction kinetics**.
  - We can take a bunch of data points, and the computer can just fit it to a curve.
  - We can then transform this into a linear plot of  $d[A]/dt$  vs.  $[A]$ .
  - Curve fitting via polynomial regression: Fit

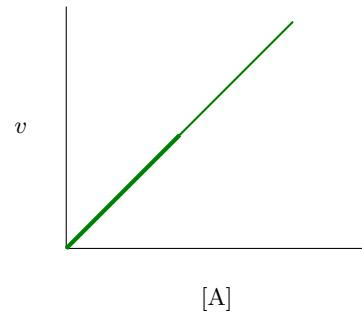
$$[A]_t = f(t) = a + bt + ct^2 + dt^3 + et^4 + ft^5 + \dots$$

- If we have enough terms, we can fit basically anything!
- And polynomials are nice because they're easily differentiated.
- Computers can do all this.

- How can we account for saturation kinetics?
  - Recall that as  $[A]$  decreases, we sometimes switch kinetic regimes.
    - Such data may be hard to manipulate via linear regression.
    - This can be easier to look at on a rate vs. concentration plot than a concentration vs. time plot.
  - Note that on a rate vs. concentration plot, reactions with induction periods show up as humps.
    - This is because the reaction takes a bit to get going (i.e., during the induction period), then accelerates to normal, and then tapers off.
    - We can still polynomial fit these!
- Experimental chemistry offers all manner of complex kinetics, not just simple integrated rate laws.
  - So we need powerful techniques.
- To solve these challenges, use reaction progress kinetic analysis (RPKA).
  - Developed by Donna Blackmond (Scripps) — a modern genius of reaction kinetics.
  - She has a few valuable, albeit impenetrable, pieces of literature.
    - Blackmond (2005).
    - Blackmond (2015).
  - This method does not shoehorn reactions into models that they don't fit.
  - Two relevant techniques.
    - Same excess experiment.
    - Different excess experiment.
- Same excess experiment.



(a) Concentration vs. time plot.



(b) Rate vs. concentration plot.

Figure 12.7: Same excess experiment.

- Recall Figure 12.4, and the corresponding rate law

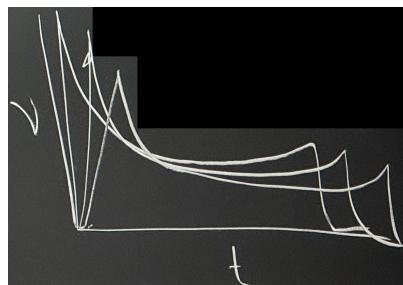
$$\frac{d[P]}{dt} = \frac{k_1 k_2 [A][B][\text{cat}]_T}{k_{-1} + k_2[B] + k_1[A]}$$

- Via the stoichiometry of  $A + B \xrightarrow{\text{cat}} P$ , we know that the following equality holds.

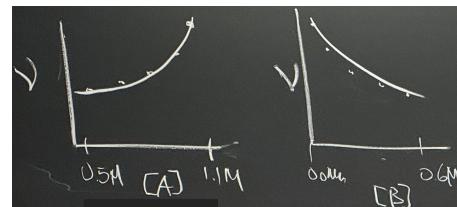
$$[B]_t = \underbrace{[B]_0 - [A]_0}_{\text{"excess"}} + [A]_t$$

- Note that “excess” refers to how much more B there is, relative to A. Because A and B both have coefficients of 1 in the balanced chemical equation, the excess is constant throughout this reaction.
- This substitution also allows us to define reaction progress in terms of only one variable!
- We now run two experiments (Figure 12.7a).
  - Experiment 1: Run the experiment with  $[A]_0 = 0.1 \text{ mmol}$  and a small excess  $[B]_0 = 0.12 \text{ mmol}$ .
    - Then the excess is 0.02 mmol.
  - Experiment 2: Run the experiment with  $[A]_0 = 0.05 \text{ mmol}$  and  $[B]_0 = 0.07 \text{ mmol}$ .
    - The excess is the same as last time: 0.02 mmol!
- If the reaction is behaving in a well-defined way, we should see overlay via visual inspection of the rates in the derivative plot (Figure 12.7b).
  - Thus, we can assay whether the rates of two experiments are the same by whether or not the lines visually overlay.
  - Overlay is commonly the case, but in cases where we *don't* get overlay, we get something really illuminating.
- In what cases does a same excess experiment produce lines that do not overlay?
  - Experiment 2 can proceed in a way such that it doesn't overlay.
  - Case 1: The reaction beginning from 50% conversion is faster. What could explain this?
    - Product inhibition.
      - This is a big one!
      - For example, molecules of the catalyst could be held up by strong binding to the product.
    - Catalyst decomposition.
  - Both of these possibilities suggest new experiments.
    - Start at 50% completion but add 50% product and look for overlay! This would provide evidence for a product inhibition pathway.
    - We could also think about varying catalyst percentage to provide evidence for a decomposition pathway.
  - Case 2: The reaction beginning from 50% conversion is slower. What could explain this?
    - Slow pre-equilibria.
      - For example, there could be an increase in the effective catalyst concentration with time. This could happen if we need, for instance, a retro-dimerization to get the catalyst to its active state.
    - The product could improve rate via some kind of autocatalysis.
      - This is rare, but not impossible.
- The value of visually inspecting rate vs. concentration plots is that they pop out relationships that are otherwise difficult to pull from curves.
  - For example, we may only get a small difference in concentration vs. time curves toward the end of our time courses! This is easy to miss if we're not looking super closely.
- Different excess experiment.
  - Hold the concentration of one of the reagents steady, and change the excess of the other.
  - What if we get overlay here?
    - Then we learn that the rate does not vary with excessive concentrations of B.
    - This means that the reaction is zero-order in B!

- What does no overlay mean?
  - There's a kinetic dependence on B.
  - Mathematically,  $v \approx k_{\text{obs}}[A][B]$ .
  - Thus,  $v/[B] \approx k_{\text{obs}}[A]$ !
  - Manipulating the exponent of [B] then allows us to read out the order of B from what exponent gives us a linear plot with overlay
- Note that overlay yes/no is a binary judgement.
  - But how do we know whether something is overlaying? How close does it have to be before we say, “yes, we're seeing overlay?”
  - There's some room for interpretation here.
- Implication from excess experiments: Only these two experiments tell us everything we need to know, even in wildly complex scenarios.
- A Blackmond paper exemplifying the power of excess experiments: Hein et al. (2011).



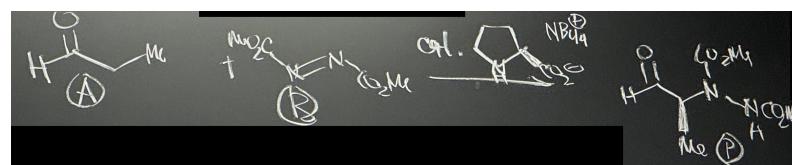
(a) The time course.



(b) The experimental data.

Figure 12.8: A complex time course.

- This paper blew Alex's hair back when he read it.
- The reaction is nominally pretty straightforward: Aldehyde plus azodicarboxylate in the presence of a chiral proline anion organocatalyst, stereoselectively yielding an  $\alpha$ -amination product.



- This is literally the same type of reaction as in Figure 12.4.
- The rate was measured via calorimetry in a relevant concentration domain (we didn't have to do weird flooding as with Figure 11.7).
- Result: We have a complex positive order in [A], and a complex *inverse* order in [B] (i.e., at higher concentrations of B, the reaction goes slower).
- The time course (rate vs. time) is fast acceleration, then slowing down, then speeding up, then dead.
  - Here, the full rate course data is *essential* to figuring out what's going on. We would be so wrong it's not even funny if we tried to do method of initial rates here!
  - As an experimentalist, Alex would first think that his calorimeter is horribly broken. But this is rigorous at different concentrations; this *is* the kinetics!
- You can simulate time courses using software packages like COPASI.

- The full mechanism that Blackmond and colleagues ended up determining.

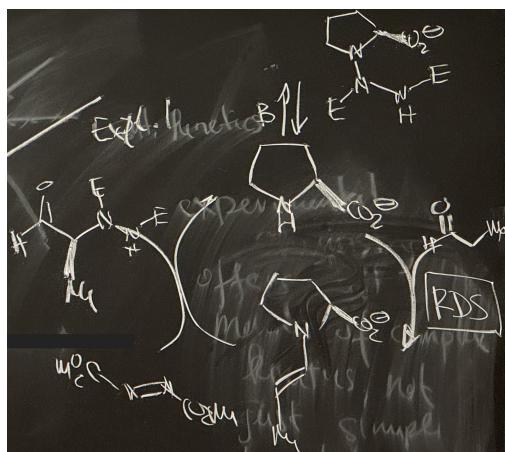


Figure 12.9: Mechanism underlying an example complex time course.

- This involves an off-cycle equilibrium of the catalyst being sequestered by one of the reagents.
- Formation of the enamine is rate-determining.
- How important is this whole paper? Alex doesn't know. The beauty of the process may be lost on you if you're a synthetic organic chemist and only care about getting the product.
- Challenges with RPKA: Measuring rates directly is difficult, and converting concentration data to rate data propagates some error.
- Spiritual successor to RPKA: Variable time normalization analysis (VTNA).



Figure 12.10: Variable time normalization analysis.

- Reference: Work by Jordi Burés.
  - Initial set of papers: Burés (2016).
  - A really useful tutorial: Nielsen and Burés (2019).
- Collect concentration vs. time data (e.g., via GC-MS aliquots as per usual).
- Change the total catalyst concentration  $[\text{cat}]_T$  and look how the rates change.
- Key insight:  $[\text{cat}]_T$  is basically constant during the reaction, so just treat it as a parameter of the system.
- Normalize to  $[\text{cat}]^n$  by varying  $n$  until you get overlay and call that the order!

- Using VTNA, you can also normalize not only to something that's constant, but to something that's variable.

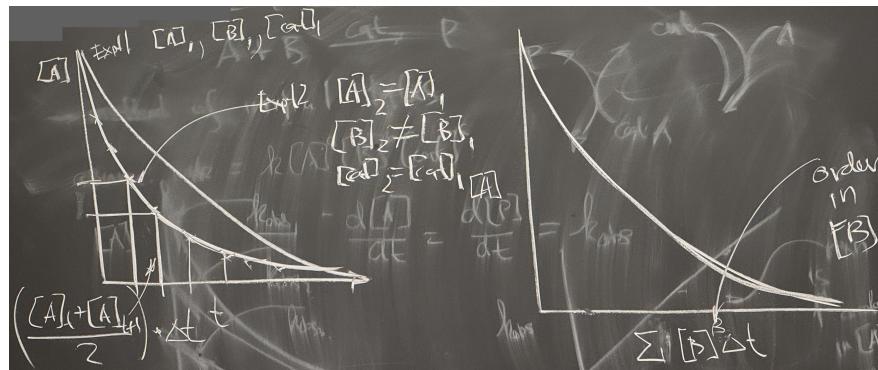


Figure 12.11: Variable time normalization analysis (different excess experiment).

- Do a different excess experiment.
- Experiment 1: Run it with  $[A]_1$ ,  $[B]_1$ , and  $[cat]_1$ .
- Experiment 2: Keep  $[A]_2 = [A]_1$  and  $[cat]_2 = [cat]_1$ , but change  $[B]_2 \neq [B]_1$ .
- $[B]$  is being consumed during the reaction, so it's changing in a stoichiometric fashion.
- Use the trapezoid rule to integrate under the Experiment 2 curve. Then plot  $[A]$  vs. our new time-normalized  $x$ -axis, and vary  $\beta$  until we get the correct reaction order.