Week 12 Recitation

Chapter 9: Kinetics (final)

Chapter 10: Enzyme Kinetics (intro)

Updates

- Grading is late because I was concussed most of last week.

- Plan to wrap up Chapter 9 content and introduce Chapter 10.

- Shorter lecture today, will keep Zoom open to answer questions.

- First office hours will be held tomorrow, barring car accidents.

# Questions?

Objectives

1. Non-ideality and TS theory

2. Relaxation kinetics

3. Introduction to enzyme kinetics

Review

Our understanding of reaction kinetics is sophisticated enough to consider:

- Chemical species
- Stoichiometry
- Rate constants and rate expressions (diff. eq. and integrated)
- Interdependent equilibria
- Relative rates of reaction (i.e. when to apply certain approximations)
- Multi-step processes

Such that the following is trivial to solve:

$$2A \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} B \overset{k_2}{\rightarrow} P$$

slow   fast
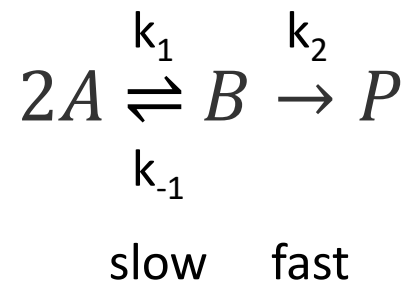
Non-ideality

The rate of reaction can be affected by non-reacting species.

Ex. 9.7: Consider the ionic strength dependence of formic acid denaturation of CO-hemoglobin in sodium formate buffer.

$$P_N + H^+ \xrightarrow{k} P_D$$

Data of half-life /min. as a function of salt (Na^+) concentration:

NaOOCH /M	$t_{1/2}$ /min.
0.007	20.2
0.010	13.6
0.015	8.1
0.020	5.9

Recall: The eq. for half-life can be determined by integrating the rate expression $\therefore$ Na^+ has an effect on the rate of unfolding.

Note: non-reacting $\neq$ non-interacting

If Na^+ affects unfolding, then there must be some physiochemical interaction occurring.

Non-ideality and TS Theory

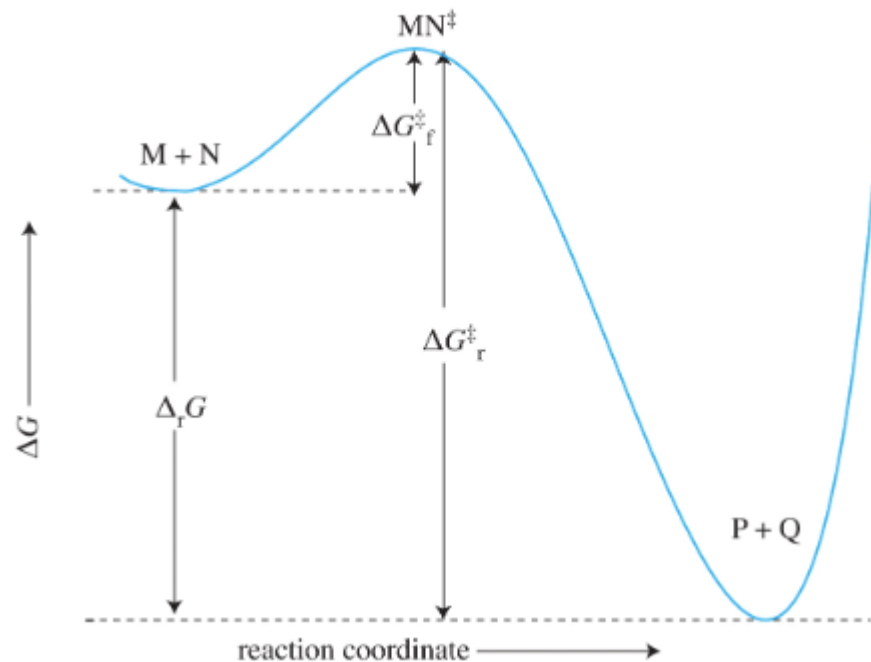TS theory allows modeling non-ideal behavior by including activity coefficients:

$$M + N \rightleftharpoons MN^{\ddagger} \rightleftharpoons P + Q$$

$$v = k_{c_M c_N} = k[M][N] \text{ (w/o TS theory)}$$

$$v = k^{\ddagger} c^{\ddagger} = \frac{k_B T}{h} c^{\ddagger} \text{ (w/ TS theory)}$$

$$K^{\ddagger} = \frac{[MN^{\ddagger}]}{[M][N]} = \frac{c^{\ddagger}\gamma^{\ddagger}}{c_M \gamma_M c_N \gamma_N}$$

$$v = \frac{k_B T}{h} K^{\ddagger} \frac{\gamma_M \gamma_N}{\gamma^{\ddagger}} c_M \gamma_M$$

1. Solve for γ based on charge of each species (M, N, and $MN^{\ddagger}$) using DH eq.

2. Plot log(k) as a function of sqrt(I)

log(k) = log(k_0) + 2(0.51)$Z_M Z_N$sqrt(I) [y = b + mx]

Non-ideality and TS Theory cont.

Conclusions:

Strong like charge accumulation?

Greatly decreased rate
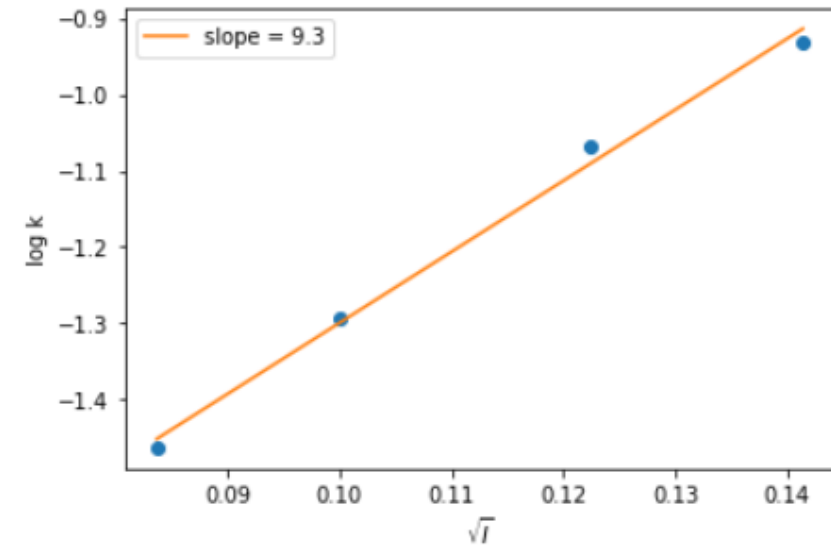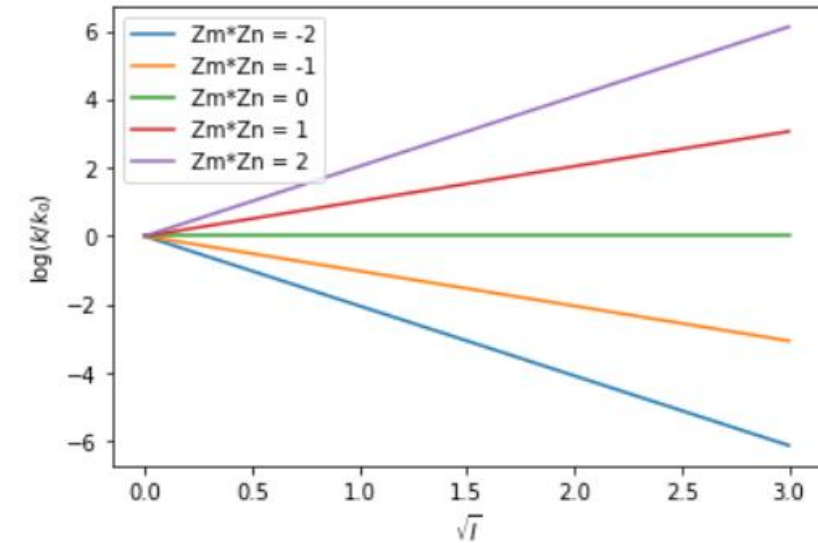
Weak like charge accumulation?

Slightly decreased rate

Weak opposite charge accumulation?

Slighting increased rate

Strong opposite charge accumulation?

Greatly increased rate

Relaxation Kinetics

For brevity, this slide contains information that will not be discussed in extensive detail.

$$A + B \rightleftharpoons P$$

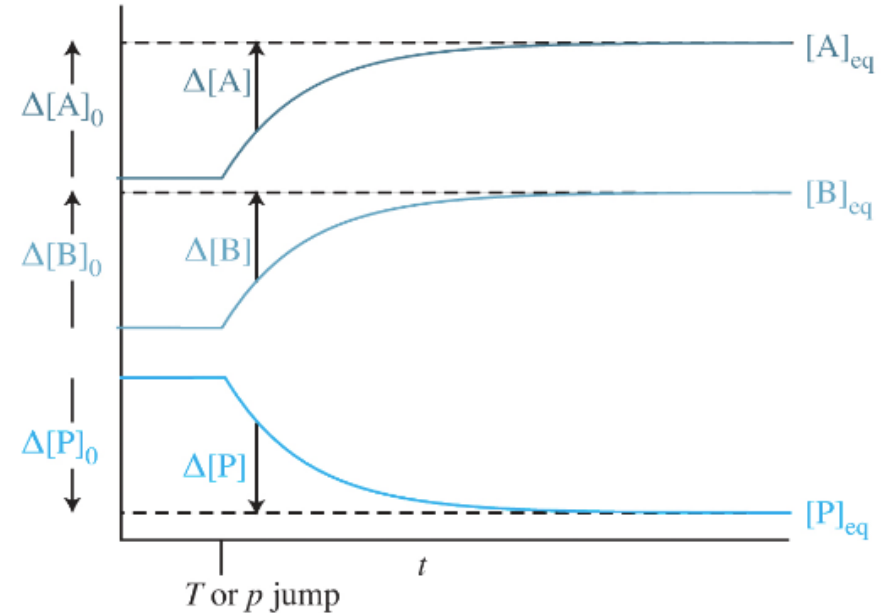$$\frac{d[P]}{dt} = k_1[A][B] - k_{-1}[P] = 0$$

$$K = \frac{k_1}{k_{-1}} = \frac{[P]_{eq}}{[A]_{eq}[B]_{eq}}$$

Use mass balance for A, B, and P:

$$\frac{d[P]}{dt} = k_1([A]_{eq} - \Delta[P])([B]_{eq} - \Delta[P]) - k_{-1}([P]_{eq} - \Delta[P])$$

If equilibrium shifts are small, the above quadratic (dP^2) reduces to:

$$-\frac{d[P]}{dt} = \{k_1([A]_{eq} + [B]_{eq} + k_{-1}\}\Delta[P]) = \frac{\Delta[P]}{\tau} \equiv \Delta[P] = \Delta[P]_0 e^{-\frac{t}{\tau}}$$

Chapter 10: Enzyme Kinetics

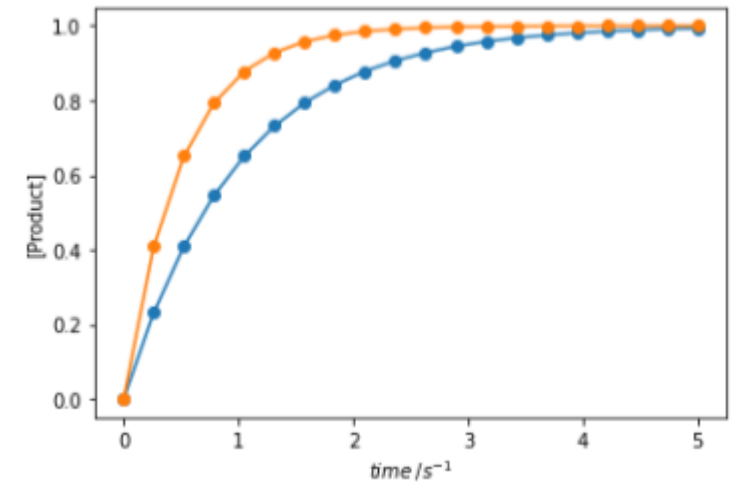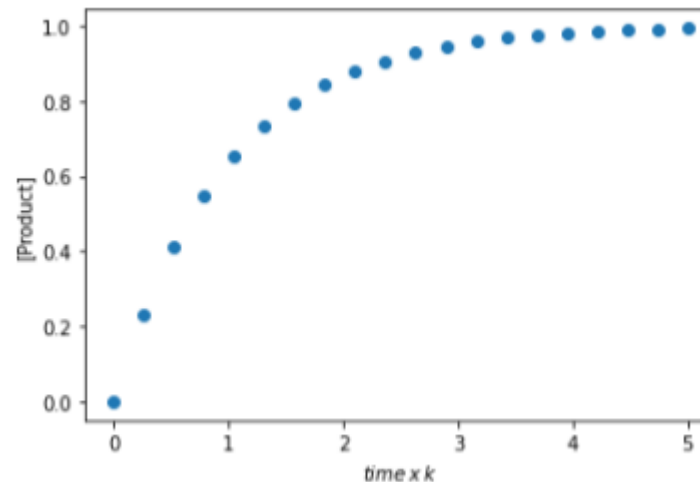Definition: Biological catalysts that enhance the rate of chemical reactions.

• Rate enhancement is indiscriminate – forward and reverse increased

• An enzyme can be modified, but its catalytic function should not deactivate it

• Selects for the transition state to lower the activation barrier

Consider: $S \rightarrow P$ [Michaelis-Menten]

$$[P] = [S]_0(1 - e^{-kt})$$

Blue is 1x E

Orange is 2x E

Michaelis-Menten (Abridged)
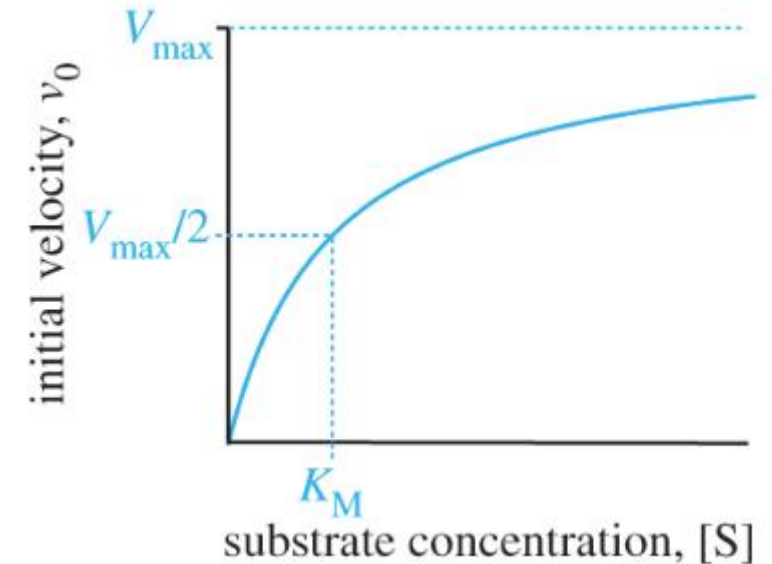
$$v_0 = \frac{V_{max}[S]}{K_M + [S]}$$

- If [S] increase, "distance" from eq. is large
- At very high [S], V_{max} is limited by [E]
- $K_M = V_{max}/2$

$$E + S \rightleftharpoons ES \xrightarrow{k_2} E + P$$

$v_0 = \frac{d[P]}{dt} = k_2[ES]$, you all know how to solve for [ES]...

Considerations:

1. At low [S], $K_M/[S] \gg 1$, so $v_0 = k[S]$
2. At high [S], $v_0 = k_2[E]_0 = V_{max}$ (effectively repeating second bullet point)

Concept Checks

What physiochemical effects would an increase in Na^+ have on the following residues: Ala, His, Asp, Lys

Drawing upon your understanding of hemoglobin unfolding mechanism, explain why Na^+ increases the rate of unfolding.

Understand how a mechanism could be inferred for hemoglobin unfolding by acidic solution.

What is the order of relaxation? What does this mean?

Understand Michaelis-Menten kinetics.

How can these data be linearized? What are the practical benefits of doing so (hint: what can be determined at $[S] = 0$)?

Explain why an enzyme does not shift the equilibrium position of a reaction.

Questions?