

Chem 344--Physical Chemistry for Biochemists II --F'09

I. Introduction → see syllabus

II. Chemical kinetics – (Engel, Ch.25 sect 1-3, 5)

How fast is reaction?

Rate of **formation of product** or **loss of reactant**

– non-equilibrium

– kinetics is path dependent

--shift from thermodynamics

(equilibrium and path independent)

Experimental characterization – rate laws / reaction order

Simplest example: **A → B**

r = -d[A]/dt = d[B]/dt – rate: concentration vs. time

only need to monitor A or B; coupled by stoichiometry

or more general example:

aA + bB → cC + dD

r = -1/a dA/dt = -1/b dB/dt = 1/c dC/dt = 1/d dD/dt

Methods – start reaction by mixing reagents (t = 0)

1. Aliquot – periodically analyze portion – slow reaction

2. Quench – stop reaction in the aliquot – measure later

3. Dynamically monitor some property

must be proportional to concentration

(e.g. pressure / spectra / pH / ε (redox) / ...)

4. Change equilibrium (T-jump) / photolysis / other

Monitor properties during response to stimulus

Rate Equations – experimental observable - not derived

$$r = k[A]^x [B]^y [C]^z [D]^w$$

determine the exponents empirically -- (x,y,z,w)

both sign (+/–) and size (integer or fraction)

order of reaction = $x + y + z + w$, x = order w/r/t A etc.

(Note: rate law does not need to have a simple order,

e.g. $r = k [E][S]/(k_m + [S])$ → typical for enzymes, but usually has limiting behavior - e.g. high or low [S])

Idea → measure r, the rate (monitor $-d[A]/dt$ for example)

→ double [A], re-measure r → behavior gives x

→ same for others [B], [C], etc. → y,z etc.

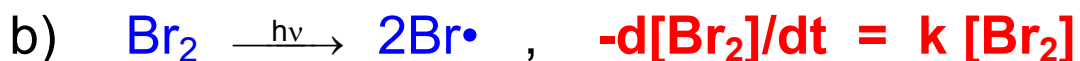
Example: a) $^{238}\text{U} \rightarrow ^{234}\text{Th} + \alpha (^4\text{He}^{+2})$

If you had twice as much ^{238}U , you would get twice as many α particles--twice as radio active

Thus:

$$-d[\text{U}]/dt = k [^{238}\text{U}] \rightarrow \text{1st order}$$

– independent of anything else, simple

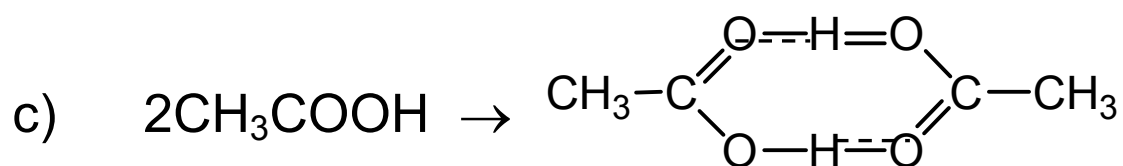


– more $\text{Br}_2 \rightarrow$ more $\text{Br}\cdot$ in linear relation

or $d[\text{Br}_2]/dt$ depends on how much Br_2

– also simple → unimolecular

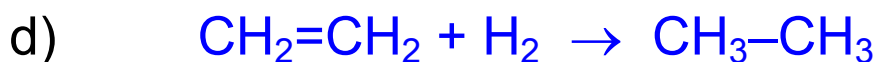
(Note: assume $h\nu$ - light intensity - constant – alternate view - could treat as reagent, not typical)



Ac = acetone

Here if double amount, [Ac] lost 4x faster

$$-1/2 \frac{d[\text{Ac}]}{dt} = k [\text{Ac}]^2 \quad - \text{2nd order}$$



double [e] or [H₂], double rate: $-\frac{d[e]}{dt}$

$$r = k [e] [\text{H}_2] \quad - \text{2nd order overall, [e]=ethene}$$

- but 1st w/r/t [e] or [H₂]

However



$$r = -\frac{d[\text{Br}_2]}{dt} = k [\text{H}_2][\text{Br}_2]/(1 + k' [\text{HBr}]/[\text{Br}_2])$$

Note: at beginning [HBr] = 0 $\Rightarrow r_{\text{init}} = k [\text{H}_2] [\text{Br}_2]$

overall 2nd order initial rate, but later [HBr] build up
at end: 1st [H₂], (-)1st [HBr], 2nd [Br₂]

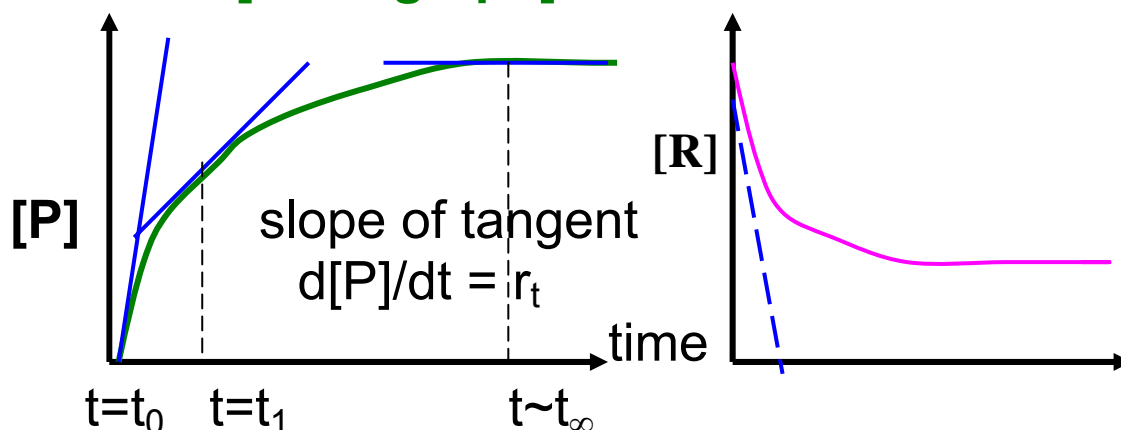
Molecularity: if reaction one step, order reflect stoichio.

unimolecular: $\text{A} \rightarrow \text{P}$, $-\frac{d[\text{A}]}{dt} = k[\text{A}]$

bimolecular: $2\text{A} \rightarrow \text{P}$, $-\frac{1}{2} \frac{d[\text{A}]}{dt} = k[\text{A}]^2$

$\text{A} + \text{B} \rightarrow \text{P}$, $-\frac{d[\text{A}]}{dt} = k[\text{A}][\text{B}]$

termolecular: $\text{A} + \text{B} + \text{C} \rightarrow \text{P}$ rare since imply 3-body coll.

Behavior **[draw graph]**

as time increases the change in product [P] is less
 → approach equilibrium, same for reactant

at $t = 0$ the slope is $d[P]/dt$ or $d[R]/dt \Rightarrow$ initial r_0
 at $t = \infty$ the slope is zero, $r = 0 = -d[R]/dt = d[P]/dt$
 rates of forward and reverse reactions equal
 concentrations cease to change

Initial rates, r_0 : $R \rightarrow P$ Initial concentration is R_0 or P_0
 so: $r_0 = k [R_0]^x \rightarrow$ slope = dR/dt (recall, $P_0 = 0$)
 if vary R_0 & measure r_0 , can determine x , order
 same is true for P , etc. (know all initial conc. - fixed)

How to get slope, r_0 at $[R_0]$ (note any $[R]$ can be $[R_0]$):

- approximate $dR/dt \sim \Delta R/\Delta t$ finite differences
 - crude approx. of derivative / has error
 - more/smaller steps can be better
- fit data to a curve (exponential or other)
 - take derivative of fit function
 - extrapolate to R_0 , etc.

Example:Consider hypothetical reaction: $A + 2B \rightarrow P$ assume: $-d[A]/dt = -1/2 d[B]/dt = k [A]^\alpha [B]^\beta$

t/sec	$[A_0] = 0.5$	$[A_0] = 0.25$	
0	1.0	1.0	} Initial conc. $[B_0]$ at t_0 } $[B]$ vs t } in units of 10^{-3} M
4	0.75	0.87	
8	0.56	0.75	
12	0.42	0.65	
16	0.32	0.56	

initial rate:

$$r_1 = k [0.5]^\alpha [10^{-3}]^\beta$$

$$r_2 = k [0.25]^\alpha [10^{-3}]^\beta$$

use $r \sim \Delta[A]/\Delta t$

$$r_1/r_2 = [0.5/0.25]^\alpha = 2^\alpha$$

$$r_1 \sim -1/2 (0.75-1.0)/(4-0) = 0.25/4 \cdot 2 = \left. \begin{array}{l} \\ \end{array} \right\} r_1/r_2 \sim 1.9$$

$$r_2 \sim -1/2 (0.87-1.0)/(4-0) = 0.13/4 \cdot 2 = \left. \begin{array}{l} \\ \end{array} \right\} \sim 2$$

$\therefore \alpha = 1 \rightarrow$ use integer or simple fraction closest to calculated value for exponent

error: always due to use of $\Delta \text{conc.}/\Delta t$ instead of $d[A]/dt$

2 unknowns left: $\beta, k \rightarrow$ consider 1st run:

$$r_0 = k [0.5]^1 [10^{-3}]^\beta \sim 1/2(0.25/4)$$

$$r_4 = k [0.5]^1 [0.75 \times 10^{-3}]^\beta \sim -1/2(0.56-0.75/8-4)=1/2(0.19/4)$$

$$r_0/r_4 = [1/0.75]^\beta \approx 0.25/0.19 \Rightarrow \beta = 1 ; \text{ closest integer}$$

$$k = r_0/[A_0][B_0] = (0.25 \times 10^{-3}/8) / 0.5 \cdot 10^{-3} = \mathbf{0.062 = k}$$

note units: $[\text{conc}]/\text{sec}/[\text{conc}]^2 \rightarrow \text{sec}^{-1}[\text{conc}]^{-1}$

Alternate Bio-example:

See Ex 6.1 – Atkins & de Paula – alternate strategy:

$$r = k [A]^x [B]^y \Rightarrow \log r = \log k + x \log A + y \log B$$

so plot $\log r$ vs $\log A$ get slope = x, etc.

EXAMPLE 6.1 Using the method of initial rates

The following data were obtained on the initial rate of binding of glucose to the enzyme hexokinase:

[glucose] ₀ /(mmol L ⁻¹)	1.00	1.54	3.12	4.02
v ₀ /(mol L ⁻¹ s ⁻¹)	(a) 5.0	7.6	15.5	20.0
	(b) 7.0	11.0	23.0	31.0
	(c) 21.0	34.0	70.0	96.0

The enzyme concentrations are (a) 1.34 mmol L⁻¹, (b) 3.00 mol L⁻¹, and (c) 10.0 mmol L⁻¹. Find the orders of reaction with respect to glucose and hexokinase and the rate constant.

Strategy For constant [hexokinase]₀, the initial rate law has the form $v_0 = k'[\text{glucose}]_0^a$, with $k' = k[\text{hexokinase}]_0^b$, so

$$\log v_0 = \log k' + a \log [\text{glucose}]_0$$

We need to make a plot of $\log v_0$ against $\log [\text{glucose}]_0$ for a given [hexokinase]₀ and find the rate from the slope and the value of k' from the intercept at $\log [\text{glucose}]_0 = 0$. Then, because

$$\log k' = \log k + b \log [\text{hexokinase}]_0$$

plot $\log k'$ against $\log [\text{hexokinase}]_0$ to find $\log k$ from the intercept and b from the slope.

Solution The data give the following points for the graph:

log([glucose] ₀ /mol L ⁻¹)	-3.00	-2.81	-2.51	-2.40
log(v ₀ /mol L ⁻¹ s ⁻¹)	(a) 0.699	0.881	1.19	1.30
	(b) 0.844	1.04	1.36	1.49
	(c) 1.32	1.53	1.85	1.98

The graph of the data is shown in Fig. 6.7. The slopes of the lines are 1 and the effective rate constants k' are as follows:

Figure 6.8 is the plot of $\log k'$ against $\log [\text{hexokinase}]_0$. The slope is 1, so $b = 1$. The intercept at $\log [\text{hexokinase}]_0 = 0$ is $\log k = 6.56$, so $k = 3.6 \times 10^6 \text{ L mol}^{-1} \text{ s}^{-1}$. The overall (initial) rate law is

$$v = k[\text{glucose}]_0[\text{hexokinase}]_0$$

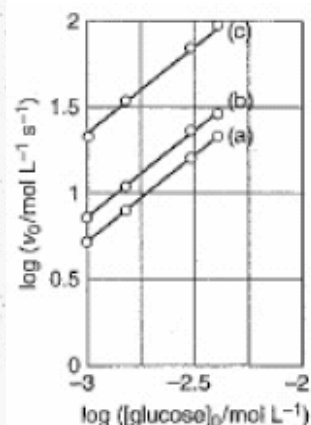


Fig. 6.7 The plots of the data in Example 6.1 for finding the order with respect to glucose.

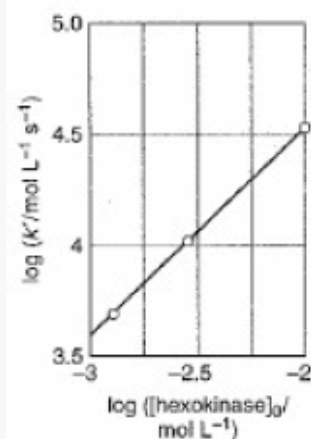


Fig. 6.8 The plots of the data in Example 6.1 for finding the order with respect to hexokinase.

Note: Experience of students is that these numbers do not all work
Enzyme concentration (a) should be ~2.0 mM for 1st order

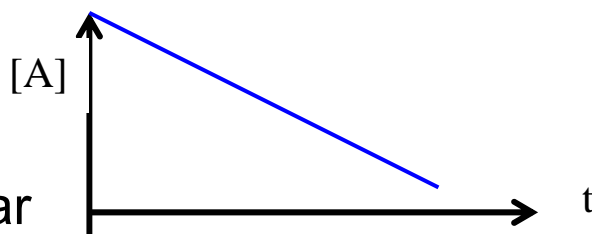
Integrated rate laws – (Engel Ch25.5)

Traditional analysis – use all data - find a linear form

0th order: $-d[A]/dt = k$,
integrate: $[A] - [A_0] = kt$
rate is constant,

change in concentration is linear

ex. catalysis reaction rate can be independent of reagent

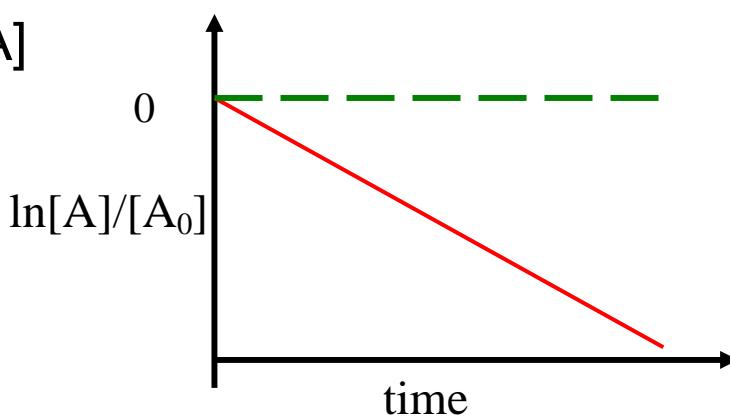


1st order: $-d[A]/dt = k [A]$

$$\int_{A_0}^A d[A]/[A] = - \int_0^t k dt$$

integral of $1/[A]$ is $\ln[A]$

$$\ln ([A]/[A_0]) = -kt$$

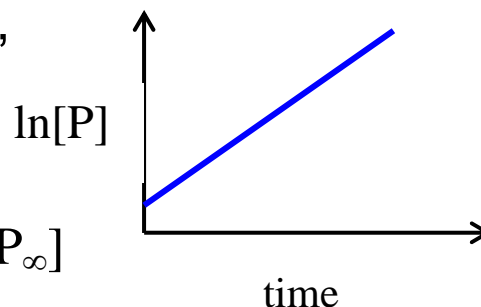


Slope = $-k$

Intercept = 0, i.e. $[A] = [A_0]$ at $t=0$,
so $\ln ([A]/[A_0]) = 0$

Note: if dP/dt slope = $+k$

$t=0$ has no meaning, ref: $\ln[P]/[P_\infty]$

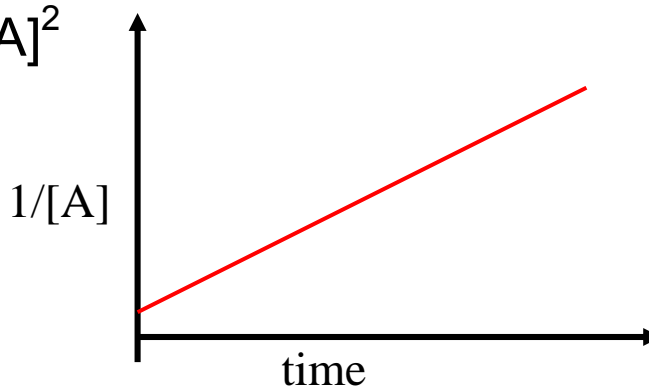


2nd order: $-d[A]/dt = k [A]^2$

$$- \int_{A_0}^A d[A]/[A]^2 = \int_0^t k dt$$

$$1/[A] - 1/[A_0] = kt$$

slope = k



general: $-d[A]/dt = k [A]^n \Rightarrow 1/(n-1) [1/[A]^{n-1} - 1/[A_0]^{n-1}] = kt$

Alternate: $-d[A]/dt = k [A] [B]$ if $A + B \rightarrow P$
 Second order overall, but 1st order w/r/t A and B

Let $A = A_0 - x$, $B = B_0 - x$
 $-dx/dt = k [A_0 - x] [B_0 - x]$

$$\int_0^t k dt = \int_0^x dx/[A_0 - x] [B_0 - x]$$

$$kt = 1/([A_0] - [B_0]) \ln [A][B_0]/[B][A_0]$$

* concept focus on one compound by excess in other compound in excess ~constant, so can determine order w/r/t the compound of lower concentration

$$\ln [A] = [A_0 - B_0] kt + \ln [A_0] + \ln [B_0]/[B]$$

Graphical Method →

plot: $[A]$, $\ln [A]$, $1/[A]$, etc. vs. t
 linear one tells order w/r/t $[A]$, etc.

$k \rightarrow$ slope of plot but may include other values

example: if $r = k [A] [B]$

then behave like 1st order in $[A]$, if $B \sim$ constant (large)

“excess of one reagent – other is variable”

$$\text{slope} = k [B_0] = k^1$$

Previous example: $A + 2B \rightarrow \text{Product}$

$\ln [B]$ vs t linear \rightarrow 1st order in $[B]$ when $[A] \gg [B]$

slope = $-2k'$ (2 from stoichiometry)

$$\frac{1}{2} \frac{d[B]}{dt} = k'[B]^\beta \quad k' = k [A_0]^\alpha \quad \text{recall } [B] \text{ is mM}$$

since 1st order in $B \rightarrow \beta = 1$ and $k' \sim \text{const}$

Now for 2 values of $[A_0]$ – determine k' for each

use: $k' = k [A_0]^\alpha$: get $\alpha = 1$ from the following \Rightarrow

$$[0.036/0.018] = [k'_1/k'_2] = [A_0]_1/[A_0]_2^\alpha = [0.5/0.25] = 2^\alpha = 2$$

then $k = k'/A_0 = 0.036 \text{ s}^{-1}/0.5 = \mathbf{0.072 \text{ M}^{-1} \text{ s}^{-1}}$ (2nd order)

Note \rightarrow use of slope averages data

Half-life if $\ln [A] = \ln [A_0] - kt$ (1st order)

at $\tau_{1/2} =$ time to go to $[A_0]/2$

$$k\tau_{1/2} = \ln [A_0]/[A_0/2] = \ln 2 = 0.693$$

Thus for 1st order: $\tau_{1/2} = 0.693/k$

* (work out for other rate laws:)

Example again $A + 2B \rightarrow \text{Product}$

run #1 $\tau_{1/2} \sim 10 \text{ s} \Rightarrow 2k'_1 \approx 0.069 \text{ s}^{-1}$

run #2 $\tau_{1/2} \sim 18\text{-}20 \text{ s} \Rightarrow 2k'_2 \sim 0.035 \text{ s}^{-1}$

again: $k'_1/k'_2 = 2k [A_0]_1^\alpha / 2k [A_0]_2^\alpha = 2^\alpha = 2 \Rightarrow \alpha = 1$

$$k = k'/[A_0] \Rightarrow 0.069 \text{ s}^{-1} \text{ M}^{-1} \quad \text{similar to graph slope}$$

CASE STUDY 6.1 Pharmacokinetics

Pharmacokinetics is the study of the rates of absorption and elimination of drugs by organisms. In most cases, elimination is slower than absorption and is a more important determinant of availability of a drug for binding to its target. A drug can be eliminated by many mechanisms, such as metabolism in the liver, intestine, or kidney followed by excretion of breakdown products through urine or feces.

As an example of pharmacokinetic analysis, consider the elimination of beta adrenergic blocking agents (beta blockers), drugs used in the treatment of hypertension. After intravenous administration of a beta blocker, the blood plasma of a patient was analyzed for remaining drug, and the data are shown below, where c is the drug concentration measured at a time t after the injection.

t/min	30	60	120	150	240	360	480
$c/(\text{ng mL}^{-1})$	699	622	413	292	152	60	24

To see if the removal is a first-order process, we draw up the following table:

t/min	30	60	120	150	240	360	480
$\ln(c/(\text{ng mL}^{-1}))$	6.55	6.43	6.02	5.68	5.02	4.09	3.18

The graph of the data is shown in Fig. 6.12. The plot is straight, confirming a first-order process. Its least-squares best-fit slope is -7.6×10^{-3} , so $k = 7.6 \times 10^{-3} \text{ min}^{-1}$ and $t_{1/2} = 91 \text{ min}$ at 310 K, body temperature.

Most drugs are eliminated from the body by a first-order process. An essential aspect of drug development is the optimization of the half-life of elimination, which needs to be long enough to allow the drug to find and act on its target organ but not so long that harmful side effects become important. ■

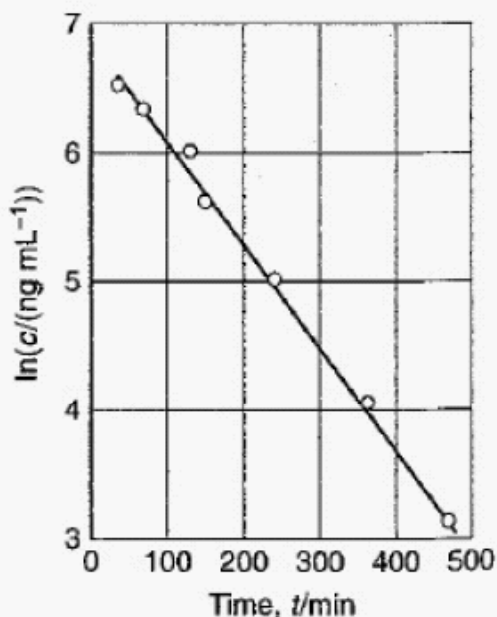
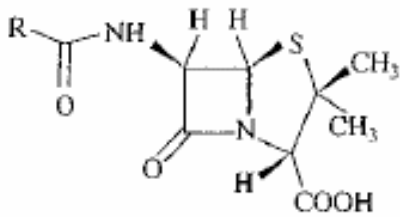
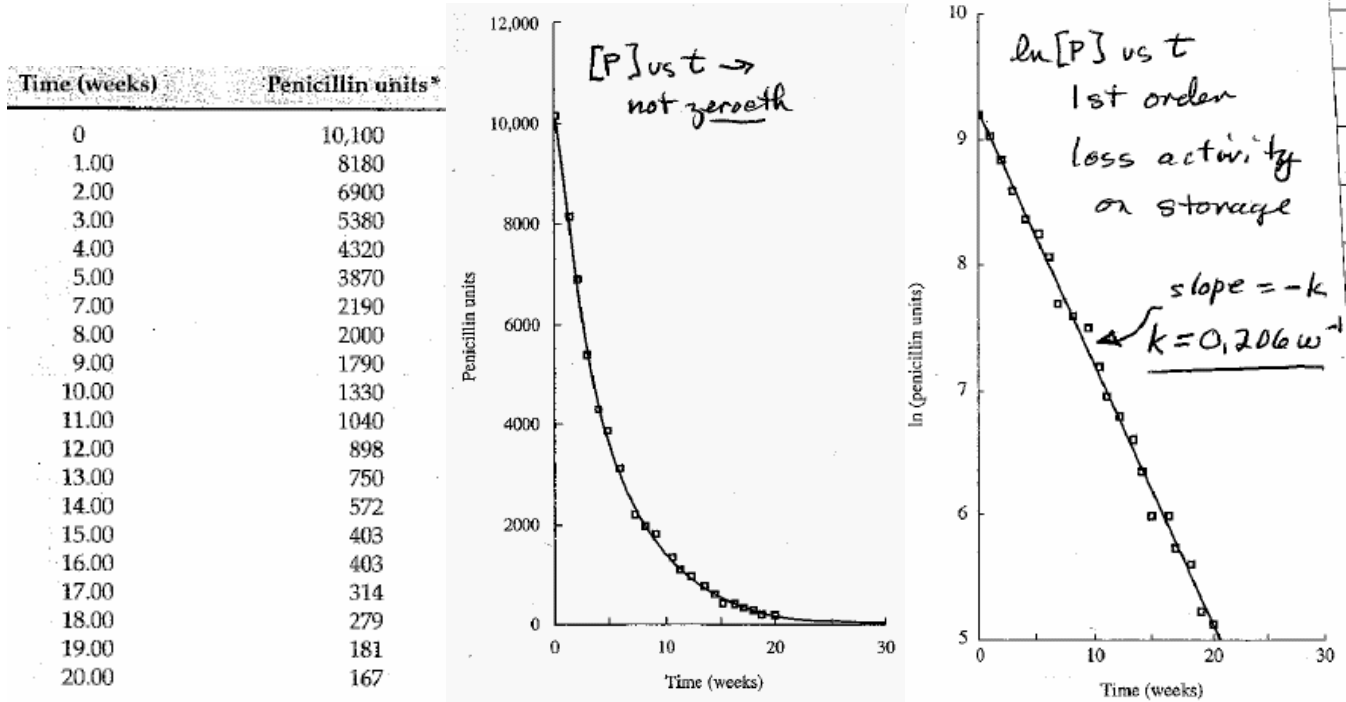


Fig. 6.12 The determination of the rate constant of a first-order reaction. A straight line is obtained when $\ln c$ is plotted against t ; the slope is $-k$. The data are from Case study 6.1.

[Tinoco Fig 7.3]—Penicillin after storage



Penicillin Assay— monitor surviving colonies of bacteria
 (killing rate \sim activity \rightarrow express as units
 more ability to kill bacteria, more units)

Note: decrease by $\frac{1}{2}$ in 3-4 weeks, \rightarrow half-life
 then to $\frac{1}{4}$ in \sim 8 weeks, i.e. 2^{nd} $\tau_{1/2} \sim$ 4weeks
 constant half-life \Rightarrow 1st order
 consistent with graphical result

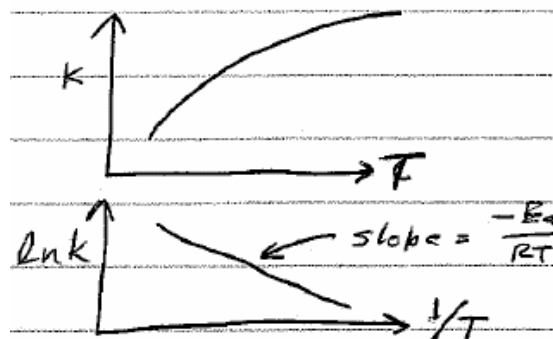
Temperature variation of rates – (Engel Ch.25-9)

Arrhenius observed rates increase with temperature

rate law: $\ln k \sim 1/T$

empirical relation

$$k = (\text{const})e^{-\gamma/T} = Ae^{-E_a/RT}$$



behave like barrier, enough energy could go over barrier

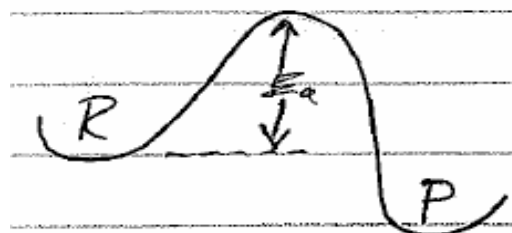
E_a – activation energy

$T \Rightarrow$ average K.E.

A – “pre-exponential factor” (T-independent)

Analysis: plot $\ln k$ vs $1/T$

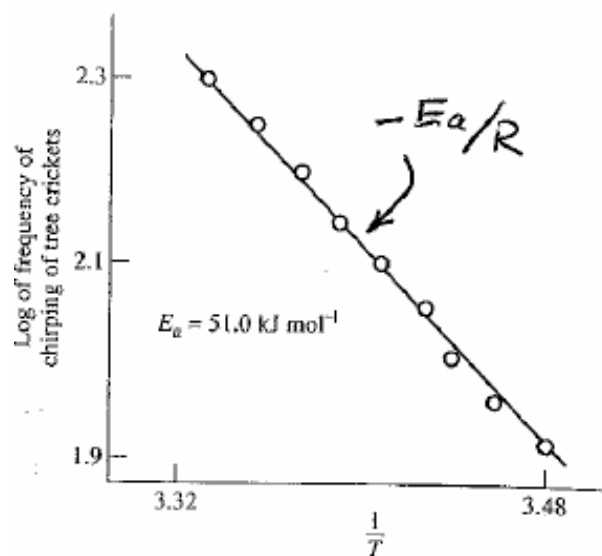
$$\begin{cases} \text{slope} = -E_a/RT \\ \text{intercept} = \ln A \end{cases}$$



Example: Biological Thermometer

Cricket chirping frequency (rate of biological process) changes by >2 over 285 to 300 K (54 \rightarrow 81° F)

Plot \ln (frequency) vs $1/T$
slope = $-E_a/R \Rightarrow E_a = 51 \text{ kJ/mol}$



Example 6.2 – sucrose hydrolysis—Atkins & dePaula

EXAMPLE 6.2 Determining the Arrhenius parameters

The rate constant of the acid hydrolysis of sucrose discussed in Section 6.6a varies with temperature as follows. Find the activation energy and the pre-exponential factor.

T/K	297	301	305	309	313
$k/(10^{-3} \text{ L mol}^{-1} \text{ s}^{-1})$	4.8	7.8	13	20	32

Strategy We plot $\ln k$ against $1/T$ and expect a straight line. The slope is $-E_a/R$ and the intercept of the extrapolation to $1/T = 0$ is $\ln A$. It is best to do a least-squares fit of the data to a straight line. Note that A has the same units as k .

Solution The Arrhenius plot is shown in Fig. 6.18. The least-squares best fit of the line has slope -1.10×10^4 and intercept 31.7 (which is well off the graph). Therefore,

$$E_a = -R \times \text{slope}$$

$$= -(8.3145 \text{ J K}^{-1} \text{ mol}^{-1}) \times (-1.10 \times 10^4 \text{ K}) = 91.5 \text{ kJ mol}^{-1}$$

and

$$A = e^{31.7} \text{ L mol}^{-1} \text{ s}^{-1} = 5.8 \times 10^{13} \text{ L mol}^{-1} \text{ s}^{-1}$$

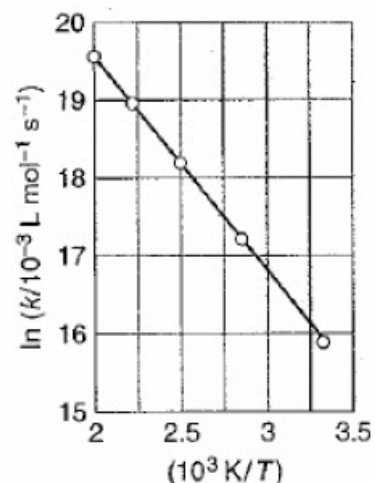
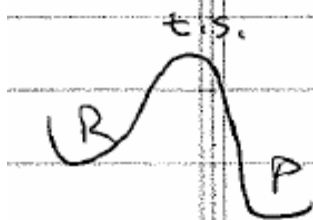


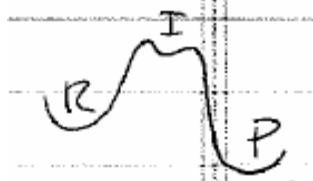
Fig. 6.18 The Arrhenius plot for the acid hydrolysis of sucrose, and the best (least-squares) straight line fitted to the data points. The data are from Example 6.2.

Meaning: reactants must rearrange to form product,
process must increase energy if R stable



top of curve – high energy point –
transition state -- can fall to R or P
getting there like Boltzman $\sim e^{-E_a/RT}$

Structure – activated complex can be
close to reactant or to product



Partially stable at top– **reaction intermediate**

To go faster \Rightarrow Catalyst / Enzyme – lower E_a
increase probability to cross barrier
-- also could increase temperature

Alternate approach: re-express: $k = Ae^{-E_a/RT}$

measure k at 2 temperatures

$$k'_1/k'_2 = \exp [-E_a/R (1/T_1 - 1/T_2)]$$

take \ln : $\ln k_1 - \ln k_2 = -E_a/R (1/T_1 - 1/T_2)$

Example: Urea decomposition in 0.1 M HCl

$\text{NH}_2\text{CONH}_2 + 2\text{H}_2\text{O} \xrightarrow{\text{(acid)}} 2\text{NH}_4^+ + \text{CO}_3^{2-}$			
T (°C)	k (min ⁻¹)	$\ln k$	1/T (K ⁻¹)
61	$.713 \times 10^{-5}$	-11.85	2.922×10^{-3}
71.2	2.77×10^{-5}	-10.49	2.904×10^{-3}

$$E_a = \frac{8.314 \text{ JK}^{-1} \text{ mol}^{-1} (-11.85 + 10.49)}{(2.922 - 2.904) \times 10^{-3} \text{ K}^{-1}} = 1.28 \times 10^5 \text{ J mol}^{-1}$$

(128 kJ mol⁻¹)

$$\ln A = \ln k \sim E_a/RT = -10.49 + \frac{1.28 \times 10^5 \text{ J mol}^{-1}}{(8.314 \text{ Jk}^{-1} \text{ mol}^{-1})(344.4 \text{ K})}$$

$$A = 8.28 \times 10^{14} \text{ min}^{-1} = 1.38 \times 10^{13} \text{ s}^{-1}$$

Note: -- A reflects max rate, i.e. $T \rightarrow \infty$, $e^{-E_a/RT} \rightarrow 1$
 this A is order vibrational motion – fast as atoms move

-- Precision in Temperature affects answer