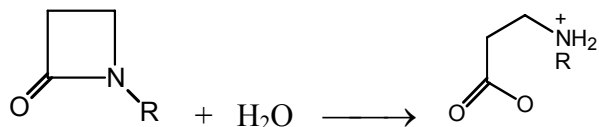


Kinetics Mechanisms (2009-rev) Examples

Engel Ch 25.5-10, Ch 26.1-3

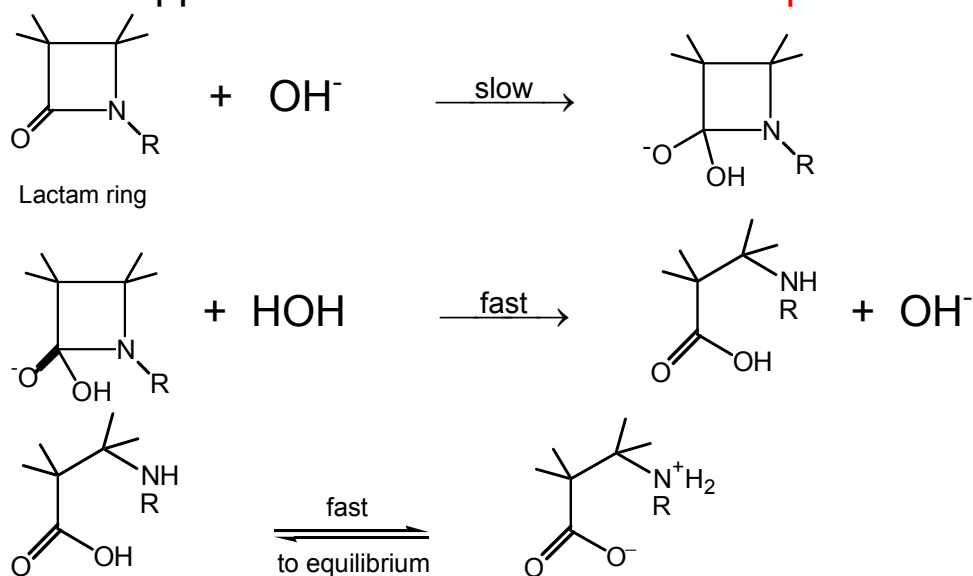
Recall penicillin example—basic chemistry, open ring



We saw observed rate law: 1st order: $r = -d[\text{R}]/dt = k[\text{R}]$

Here R=Lactam, previous used P, confuse with Prod

How might this happen? --mechanism must sense pH



Idea: 1st reaction is slow \rightarrow rate controlling

Once intermediate forms – immediately go to product

this is **steady state model**:

$$d[\text{Int}]/dt \sim 0 = k_{\text{slow}}[\text{Lac}][\text{OH}] - k_{\text{fast}}[\text{Int}][\text{H}_2\text{O}]$$

$$\rightarrow [\text{Int}] = k_{\text{slow}}/k_{\text{fast}}[\text{Lac}][\text{OH}]/[\text{H}_2\text{O}]$$

- but $[\text{H}_2\text{O}] \sim \text{constant} \sim 55 \text{ M} \rightarrow \text{ignore (part of } k)$

$$d[\text{Prod}]/dt = k_{\text{fast}}[\text{Int}] ([\text{H}_2\text{O}]) \sim (k_{\text{fast}} k_{\text{slow}}/k_{\text{fast}})[\text{Lac}][\text{OH}]$$

$$d[\text{Prod}]/dt = (k_{\text{slow}})[\text{Lac}][\text{OH}] \sim k'_{\text{slow}}[\text{Lac}] \text{ in buffer}$$

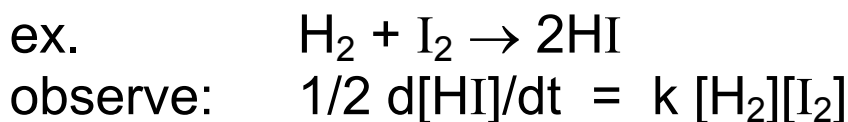
buffers make pH \sim const., $[\text{OH}]$ part of $k'_{\text{slow}} \rightarrow$ senses pH

Rate determining step is 1st one: $r \sim k_{\text{eff}}[\text{Lac}]$

since $[\text{OH}]$ constant– set by pH ($\sim 1^{\text{st}}$ order in Lac)

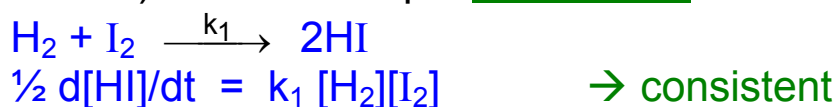
Test: Mechanism always is a model, show consistent with data → change pH / see affect on rate

Examples: Mechanisms are combination of parallel, opposed and chain steps

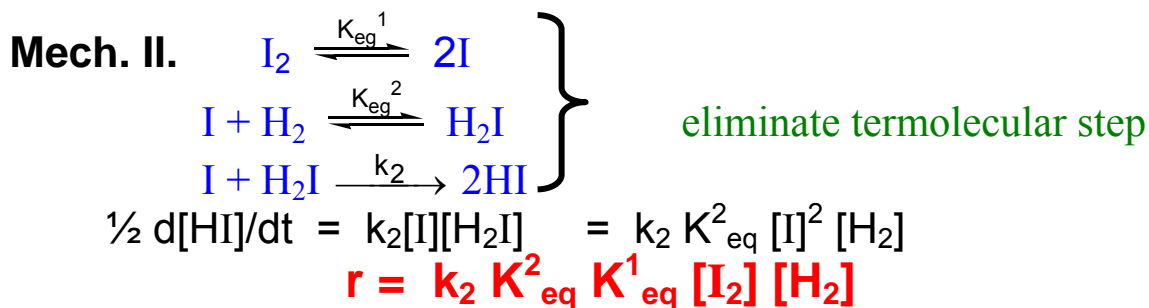
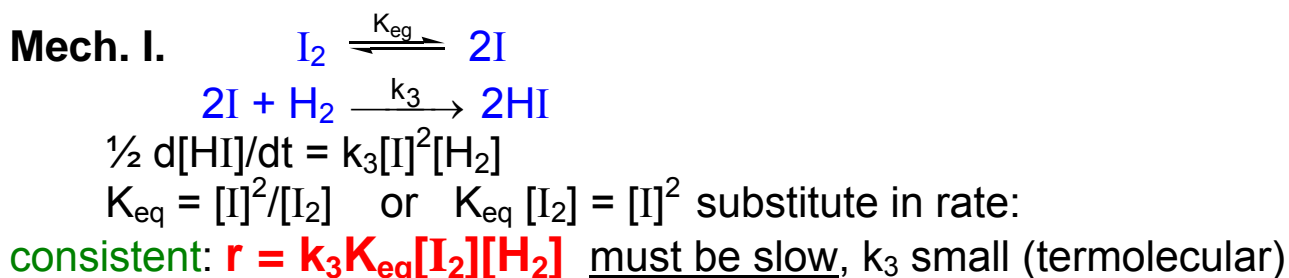


devise consistent mechanism:

a. (old idea) assume simple bimolecular:



b. Fast equilibrium idea (subsequently detected intermediate)



Mech. II also consistent, more flexible rate law (K_{eq} 's),

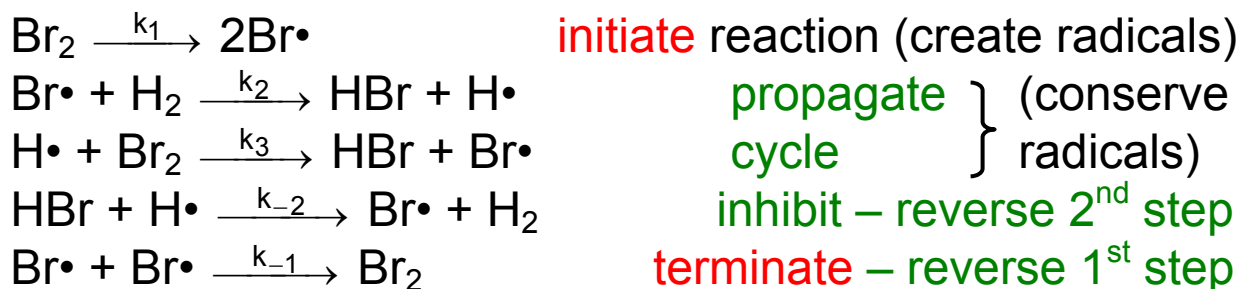
Test by detection of H_2I radical intermediate

c. Steady state example (Chain propagation)



At $t=0 \rightarrow [\text{HBr}]=0 \rightarrow r \sim k[\text{Br}_2]^{1/2}[\text{H}_2]$ but at $t=\infty r \sim k[\text{Br}_2]^{3/2}[\text{H}_2]/[\text{HBr}]$
apparent order change with time

mechanism:



Steady state on radicals \rightarrow very reactive, never build up

a. $d[\text{H}]/dt \sim 0 = k_2[\text{Br}][\text{H}_2] - k_3[\text{H}][\text{Br}_2] - k_{-2}[\text{HBr}][\text{H}]$
 $[\text{H}] = k_2[\text{Br}][\text{H}_2]/(k_3[\text{Br}_2] + k_{-2}[\text{HBr}])$ -- source of denom.

b. $d[\text{Br}]/dt \sim 0 = 2k_1[\text{Br}_2] - k_2[\text{Br}][\text{H}_2] + k_3[\text{H}][\text{Br}_2] + k_{-2}[\text{HBr}][\text{H}] - k_{-1}[\text{Br}]^2$

Subst. [H] result into $d[\text{Br}]/dt$ eqn., 3rd and 4th terms,
2nd, 3rd and 4th terms will cancel – sum to 0:

$$0 = 2k_1[\text{Br}_2] - k_{-1}[\text{Br}]^2 \Rightarrow [\text{Br}] = (2k_1/k_{-1} [\text{Br}_2])^{1/2}$$

substitute [Br] into [H] equation (eliminates all radicals):

$$[\text{H}] = k_2[\text{H}_2] (2k_1/k_{-1})^{1/2}/(k_3[\text{Br}_2] + k_{-2}[\text{HBr}])$$

rate of product formation – depends on [H] and [Br]:

$$d[\text{HBr}]/dt = k_2[\text{Br}][\text{H}_2] + k_3[\text{H}][\text{Br}_2] - k_{-2}[\text{HBr}][\text{H}]$$

Algebra – substitute in:

$$d[\text{HBr}]/dt = k_2(2k_1/k_{-1})^{1/2} [\text{Br}_2]^{1/2} [\text{H}_2] + k_3k_2(2k_1/k_{-1})^{1/2} [\text{H}_2][\text{Br}_2]^{3/2}/D \\ - k_{-2}k_2(2k_1/k_{-1})^{1/2} [\text{H}_2][\text{Br}_2]^{1/2} [\text{HBr}]/D$$

where $D = k_3[\text{Br}_2] + k_{-2}[\text{HBr}] \rightarrow$ the denominator in [H] eqn.

next put 1st term over D, sum the numerators:

$$d[\text{HBr}]/dt = \{k_2(2k_1/k_{-1})^{1/2} [\text{H}_2][\text{Br}_2]^{1/2} (k_3[\text{Br}_2] + k_{-2}[\text{HBr}] + k_3[\text{Br}_2] - k_{-2}[\text{HBr}])\}/D$$

divide top and bottom by $k_3[\text{Br}_2]$ - goal simplify denom.:

$$\therefore d[\text{HBr}]/dt = \frac{2k_2 \left(\frac{2k_1}{k_{-1}}\right)^{1/2} [\text{H}_2][\text{Br}_2]^{1/2}}{1 + \frac{k_{-2}}{k_3} [\text{HBr}] / [\text{Br}_2]} \rightarrow \text{fits experiment!}$$

$$k = 2k_2(2k_1/k_{-1})^{1/2}, \quad k' = k_{-2}/k_3$$

gives back experimental form: $r = \frac{k [\text{H}_2][\text{Br}_2]^{1/2}}{1 + k'[\text{HBr}]/[\text{Br}_2]}$

Comments:

1. reaction example of radical species propagating and enhancing rate but only exists as an intermediate

2. $t = 0$ rate $\sim k [\text{H}_2][\text{Br}_2]^{1/2}$

initial rate is a clue right away to complexity,

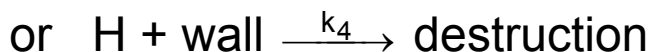
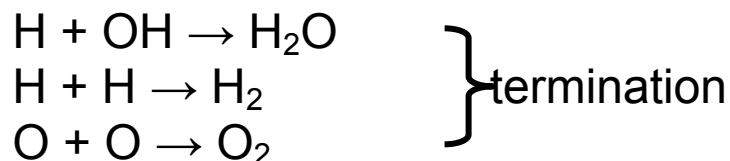
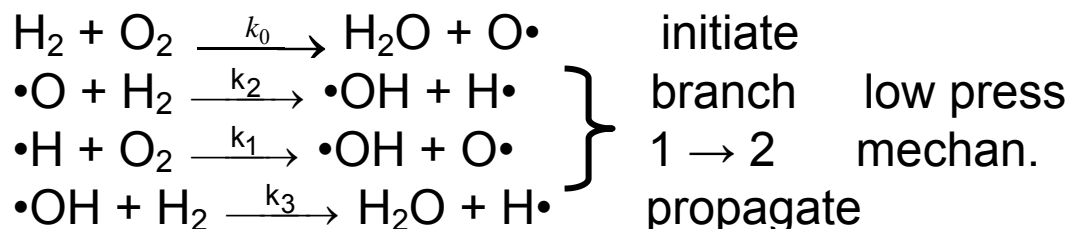
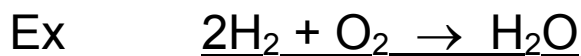
$[\]^{1/2}$ from termination step – signal for radical formation
(i.e. opposing step has a different order)

3. denominator is result of inhibitor step

d. Branching chain reaction – see Fried p. 651-54
—here just aiming for the idea, not details

In above example always got a radical from radical (1→1)
or terminated chain (1→0 or 2→0)

Branching –step in chain that generates more radicals:



Point is that branching creates high level of unstable species (radicals) → reaction then driven very fast – explodes
i.e., mech. has denom., when = 0 → branching out of control

Solve by steady state on all radicals: H, O and OH

Combining them with significant algebra gives OH yielding:

$$r_{\text{H}_2\text{O}} = k_3[\text{OH}][\text{H}_2] = (k_0[\text{H}_2][\text{O}_2])(2k_1[\text{O}_2]) / \{k_4 - 2k_1[\text{O}_2]\}$$

alternate:

$$r_{\text{H}_2\text{O}} \sim r_0 \beta / (\delta - \beta) \quad r_0\text{-initiate, } \beta\text{-branch factor, } \delta\text{-destroy chain}$$

$$v = \delta - \beta \quad \text{net destruction factor}$$

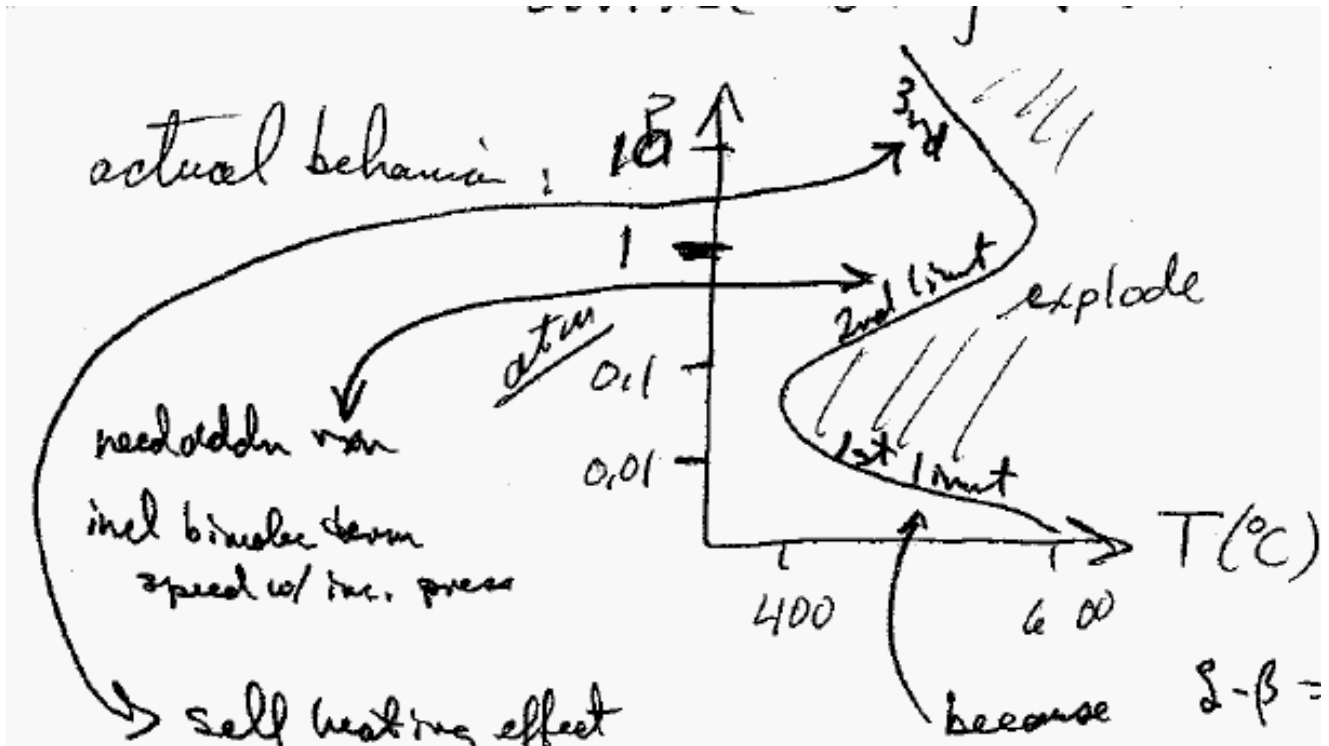
sensitive to container (wall collisions deactivate) and buffer gas and pressure (enhance termination)

$$v = \delta - \beta = 0 \text{ explosion limit - H}_2\text{O produce at infinite rate} \\ = k_4(T) - 2k_1(T) \cdot (3RT)^{-1} P$$

-last term use ideal gas law for conc. of O_2

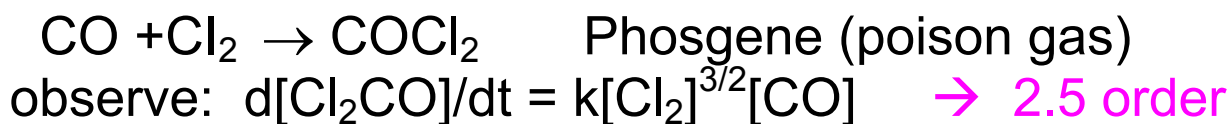
\Rightarrow T + P balance

but each rate constant depends on T

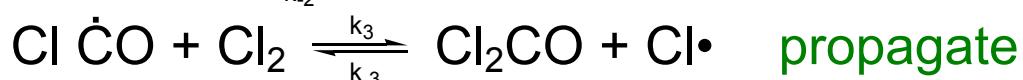


govern by wall termination
depend on size and shape

e. Practice problem—test methods:



propose mechanism



$$\text{rate: } d[\text{Cl}_2\text{CO}]/dt = k_3[\text{Cl}\dot{\text{C}}\text{O}][\text{Cl}_2] - k_{-3}[\text{Cl}_2\text{CO}][\dot{\text{C}}\text{Cl}]$$

rate limit \rightarrow if k_3 limit then this will be the correct form,
but has intermediate

NOTE due to propagation steps, $\text{Cl}\cdot$ conc. will be signif.

a) **Pre-equilibrium** -- fast formation of intermediate

$$K_1 = [\dot{\text{C}}\text{Cl}]^2/[\text{Cl}_2] \quad \text{and} \quad K_2 = [\dot{\text{C}}\text{Cl CO}]/[\dot{\text{C}}\text{Cl}] [\text{CO}]$$

$$\text{combine: } [\dot{\text{C}}\text{Cl CO}] = K_2 [\dot{\text{C}}\text{Cl}] [\text{CO}] = K_2 (K_1[\text{Cl}_2])^{1/2} [\text{CO}]$$

$$\text{plug in: } d[\text{Cl}_2\text{CO}]/dt = k_3 \{K_2(K_1[\text{Cl}_2])^{1/2} [\text{CO}]\} [\text{Cl}_2]$$

$$*(\text{assume } k_{-3} \sim 0) = k [\text{Cl}_2]^{3/2} [\text{CO}] \quad \text{consistent}$$

$$k = K_2 K_1^{1/2} k_3$$

note: if assume k_2 rate limiting

$$\text{then } r \sim k_2[\text{Cl}\cdot][\text{CO}] \sim k_2 K_1^{1/2} [\text{Cl}_2]^{1/2} [\text{CO}]$$

but incomplete

* – equivalent to assuming Product very stable and will reform reactant (makes problem easier – okay for initial rate)

b) Alternative – Steady State on $[\dot{\text{Cl}} \text{ CO}]$

$$d[\dot{\text{Cl}} \text{ CO}]/dt = k_2[\dot{\text{Cl}}][\text{CO}] - k_{-2}[\dot{\text{Cl}} \text{ CO}] - k_3[\dot{\text{Cl}} \text{ CO}][\text{Cl}_2] = 0$$

$$[\dot{\text{Cl}} \text{ CO}] = k_2[\dot{\text{Cl}}][\text{CO}]/k_{-2} + k_3[\text{Cl}_2] \quad \text{* (again neglect } k_{-3} \text{)}$$

i) assume fast equilibrium from first step $K_1 = [\text{Cl}]^2/[\text{Cl}_2]$

$$[\dot{\text{Cl}} \text{ CO}] = k_2 \{K_1[\text{Cl}_2]\}^{1/2} [\text{CO}/k_{-2} + k_3 [\text{Cl}_2]]$$

$$\text{rate: } d[\text{Cl}_2\text{CO}]/dt = k_3 \left[k_2 K_1^{1/2} \frac{[\text{Cl}_2]^{1/2} [\text{CO}]}{k_{-2} + k_3 [\text{Cl}_2]} \right] [\text{Cl}_2]$$

2 cases:

a. $k_{-2} \gg k_3[\text{Cl}_2] \Rightarrow r = k [\text{Cl}_2]^{3/2} [\text{CO}]$
 same as before $k = k_3 k_2 K_1^{1/2} / k_{-2} = k_3 K_2 K_1^{1/2}$
 i.e. this works

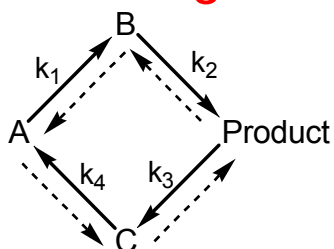
b. $k_3[\text{Cl}_2] \gg k_{-2}$
 $r = k' [\text{Cl}_2]^{1/2} [\text{CO}]$
 does not fit observed rate law

$\therefore k_{-2} \gg k_3[\text{Cl}_2] \rightarrow$ test by vary $[\text{Cl}_2]$
 observed law should deviate high \uparrow

Microscopic Reversibility

Once get to elementary steps the reaction can go forward and back on same path

can not get reversible reaction by cyclic mechanism



Solid line path not enough
dash lines must be included - complete

However – reverse steps may be fast/slow

- equilibria makes rate constants interdependent
- $K_f = P/A = k_1k_2/k_{-1}k_{-2}$ $K_r = A/P = k_3k_4/k_{-3}k_{-4}$
but $K_f = K_r^{-1} \rightarrow k_1k_2/k_{-1}k_{-2} = k_{-3}k_{-4}/k_3k_4$
- rate limiting idea may favor \rightarrow solid line path

But if $k_{-1} = 0$ then $K_f^e = \infty$

or $k_{-2} = 0$ $= k_1k_2/k_{-1}k_{-2}$

clearly then $k_{-3}, k_{-4} \neq 0$ or $K_r^e = \infty \Rightarrow$ impossible!

Summary: $r_f = r_r$ at equilibrium { detailed balance

Exponential behavior \rightarrow often analyze [conc] vs. t
by fit to exponential function

1st order: $-dA/dt = kA \rightarrow A = A_0e^{-kt}$

ex. Protein folding \rightarrow vary conditions /protein fold on own
should be 1st order \rightarrow exponential -- if simple
if fit to multiple exponential \rightarrow multi step process

Bio. Mechanism. Tinoco – pp 334-337 Renature DNA

Duplex DNA - complementary strand $A + A' \rightleftharpoons AA'$

High T – unfold and separate

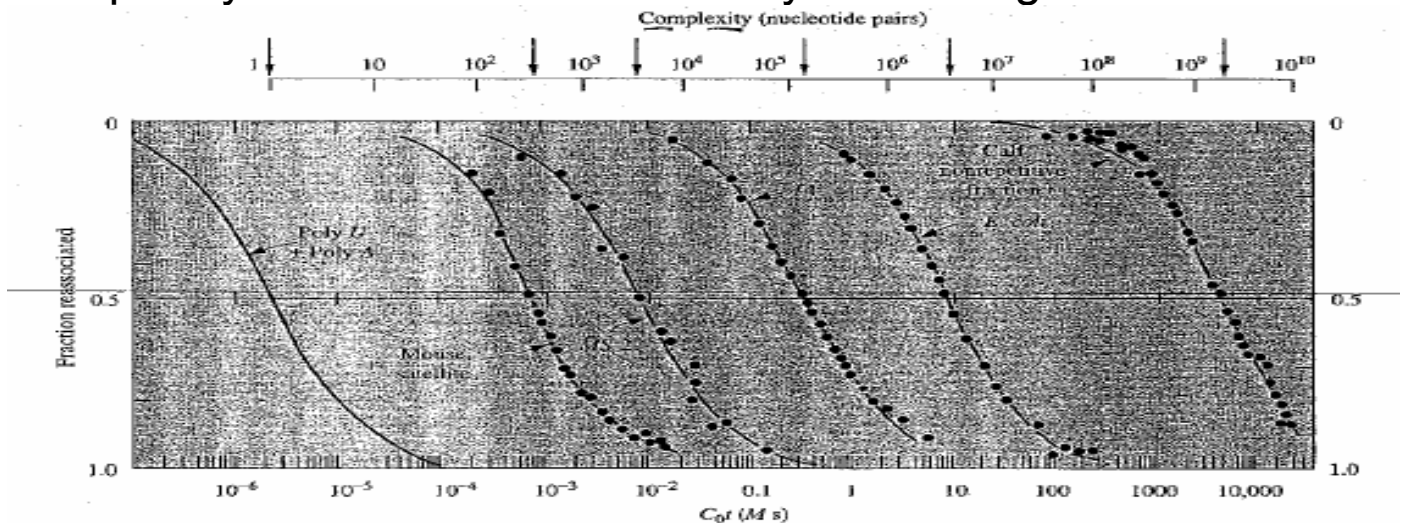
Cool – refold → speed depends on alignment, 2nd order

Sonicate DNA → break into small segments, e.g. ~20 bp
uniqueness depends on the repeat pattern of DNA

→ if “melt” → strand separate and mix,

recombine slow if unique, faster if repeat

Complexity: Recombination rate vary → heterogeneous



1. Break to ~400 bp

2. Denature to ss

3. Cool, renature

Different curves for sequences with increasing complexity,

left to right: polyUpolyA, Mouse, MS-2, T4, e.coli, calf

r – C₀ – conclusion – complexity (arrows)

See that simple sequences fold faster because

they can find a mate (less complex) for segment

More repeat sequences, less complex

N = number of bp in smallest repeat sequence

Initial concentration $[A_0] \sim C_0/N$ C_0 – concentration all ss

N – poly A poly U = 1 = 1 smallest repeat each bp

E. coli – almost no repeat N = number of bp

So point is $r = -d[A]/dt = k [A][A']$

since $A \sim C/N \rightarrow$ more complex – big N

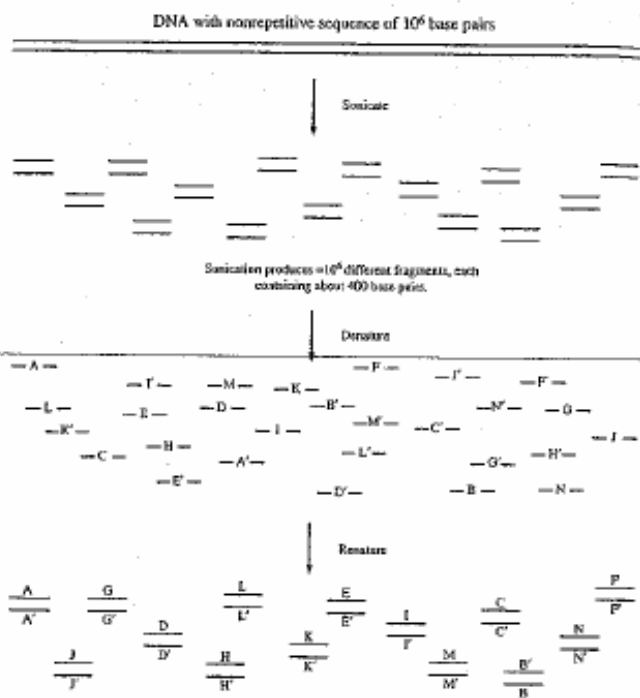
\rightarrow more complex A small / rate slow

Complementarity $[A] = [A']$ from how strands broken

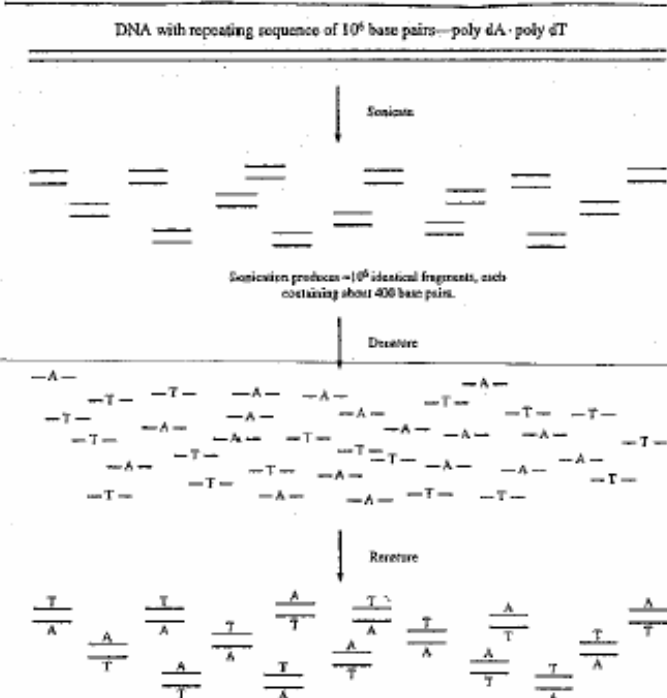
$$-d[A]/dt = k[A]^2 = k(C/N)^2$$

Thus more complex, slows the reaction: $t_{1/2} \sim N/kC_0$
 or half-life varies inversely with complexity

apter 7 Kinetics: Rates of Chemical Reactions



Renaturation is very slow because strands A and A' are in very low concentrations, so any collisions are needed to find complementary partners.



Renaturation is very fast because strands A and T are in high concentrations.

Blood Clotting example – rapid equilibrium – Tinoco, p.347-8

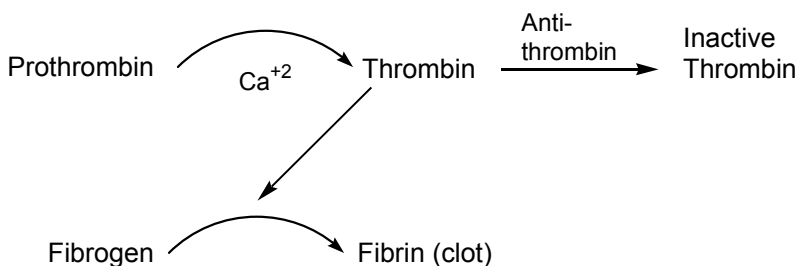
response to wound is very complex but key is

fibrinogen → fibrin which forms clot

To turn this on need Thrombin (proteolytic enzyme)

To get this need “activate” prothrombin by proteolysis

Mechanism:



Thrombin is then an intermediate / build fast – equilibrium → decay

