

The rates of chemical reactions

Chemical kinetics – the branch of physical chemistry concerned with the rates of chemical reactions. Chemical kinetics deals with how rapidly reactants are consumed and products are formed, how reaction rates respond to changes in the conditions or presence of a catalyst, and the identification of the steps by which a reaction takes place.

The reason to study the rates of reactions – it is practically important to predict how quickly the reaction mixture approaches equilibrium. The rate might depend on variables we can control – the pressure, the temperature – we might be able to optimize it by the appropriate choice of conditions. Another reason – the study of reaction rates leads to an understanding of the **mechanism** of a reaction, its analysis into a sequence of elementary steps. By analyzing the rate of a biochemical reaction we may discover how an enzyme acts. **Enzyme kinetics** – the study of the effect of enzymes on the rates of reactions – shows how these proteins work.

Empirical chemical kinetics

The first stage in the study of the rate and mechanism of a reaction – to determine the overall stoichiometry of the reaction and to identify any side reactions. The next step – to determine how the concentrations of the reactants and products change with time after the reaction has been initiated. The rates of chemical reactions are sensitive to temperature – therefore, the temperature of the reaction mixture must be held constant throughout the course of the reaction because otherwise the observed rate would be a meaningless average of the rates at different temperatures.

Experimental techniques

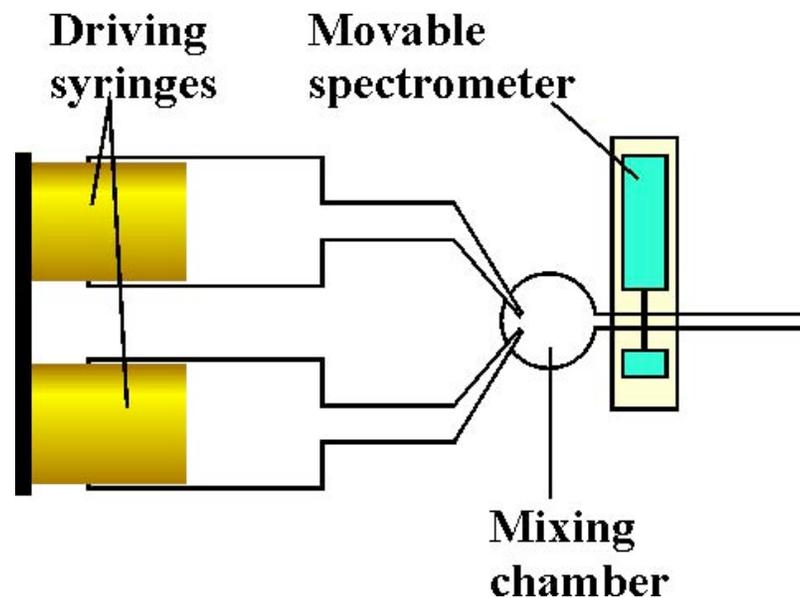
The method used to monitor the concentrations of reactants and products and their variation with time depends on the substances involved and the rapidity with which their concentrations change.

Spectrophotometry – the measurement of the intensity of absorption in a particular spectral region – widely used to monitor concentration. Useful when one substance in the reaction mixture has a strong characteristic absorption. If a reaction changes the number or type of ions in a solution – concentrations may be followed by monitoring the conductivity of the solution. Reactions that change the concentration of hydrogen ions may be studied by monitoring the pH with a glass electrode. Other methods – the detection of fluorescence and phosphorescence, titration, mass spectrometry, gas chromatography, magnetic resonance (EPR and NMR), and polarimetry.

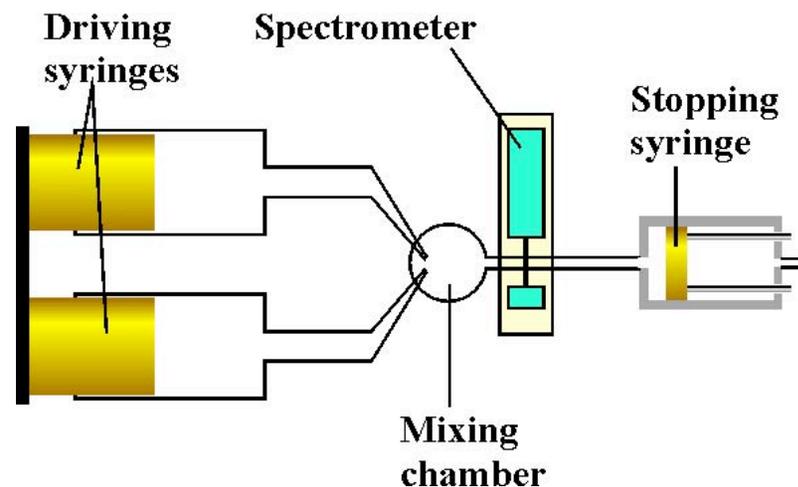
Applications of the techniques

A **real-time analysis** – the composition of the system is analyzed while the reaction is in progress by direct spectroscopic observation of the reaction mixture. The **quenching method** – the reaction is stopped after it has been allowed to proceed for a certain time and then the composition is analyzed. The quenching can be achieved by cooling suddenly, by adding the mixture to a large amount of solvent, or by rapid neutralization of an acid reagent. The method is suitable only for the reactions that are slow enough for there to be little reaction during the time it takes to quench the mixture.

The **flow method** – the reactants are mixed as they flow together in a chamber. The reaction continues as the thoroughly mixed solutions flow through a capillary outlet tube, and different point along the tube correspond to different times after the start of the reaction. Spectroscopic determination of the composition at different positions along the tube is equivalent to the determination of the composition of the reaction mixture at different times. A disadvantage – a large volume of reactant solution is necessary because the mixture must flow continuously through the apparatus.



The **stopped-flow method** – the two solutions are mixed very rapidly (in less than 1 ms) by injecting them into a mixing chamber designed to ensure that the flow is turbulent and that complete mixing occurs very quickly. Behind the reaction chamber there is an observation cell fitted with a plunger that moves back as the liquids flood in, but which comes against a stop after a certain volume has been admitted. The filling of the chamber corresponds to the sudden creation of an initial sample of the reaction mixture. The reaction then continues in the thoroughly mixed solution and is monitored spectrophotometrically.



Flash photolysis – the gaseous or liquid sample is exposed to a brief photolytic or photoactivating flash of light or ultraviolet radiation, and then the contents of the reaction chamber are monitored spectrophotometrically. Lasers can be used to generate nanosecond flashes routinely, picosecond flashes quite readily, and flashes as brief as a few femtosecond in special arrangements. Either emission or absorption spectroscopy can be used to monitor the reaction, and the spectra are recorded electronically at a series of times following the flash.

A **relaxation technique** – the reaction mixture is initially at equilibrium but is then disturbed by a rapid change of conditions – a sudden increase in temperature (a **temperature-jump experiment**) or pressure (a **pressure-jump experiment**). The equilibrium composition before the application of perturbation becomes the initial state for the return of the system to its equilibrium composition at the new temperature or pressure, and the return to equilibrium – the relaxation of the system – is monitored spectroscopically.

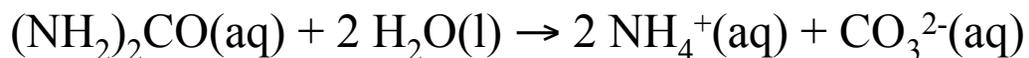
Reaction rates

The raw data from experiments to measure reaction rates – the concentrations of reactants and products at a series of times after the reaction is initiated. Ideally, information on any intermediates should also be obtained, but often they cannot be studied because they are short-lived or their concentration is too low. More information about the reaction can be extracted if data are obtained at a series of different temperatures.

The definition of rate

The rate of a reaction – the rate of change of the concentration of a designated species. The rates at which reactants are consumed and products are formed change in the course of a reaction – it is necessary to consider the **instantaneous rate** of the reaction, its rate at a specific instant. The instantaneous rate of consumption of reactant – the slope of a graph of its molar concentration plotted against time – the slope is evaluated at the instant of interest. The steeper the slope, the greater the rate of consumption of the reactant. The rate of formation of a product – the slope of the graph of its concentration plotted against time. With the concentration measure in mol L⁻¹ and the time in seconds, the reaction rate is reported in mol L⁻¹ s⁻¹.

In general, the various reactants in a given reaction are consumed at different rates and the various products are formed at different rates.

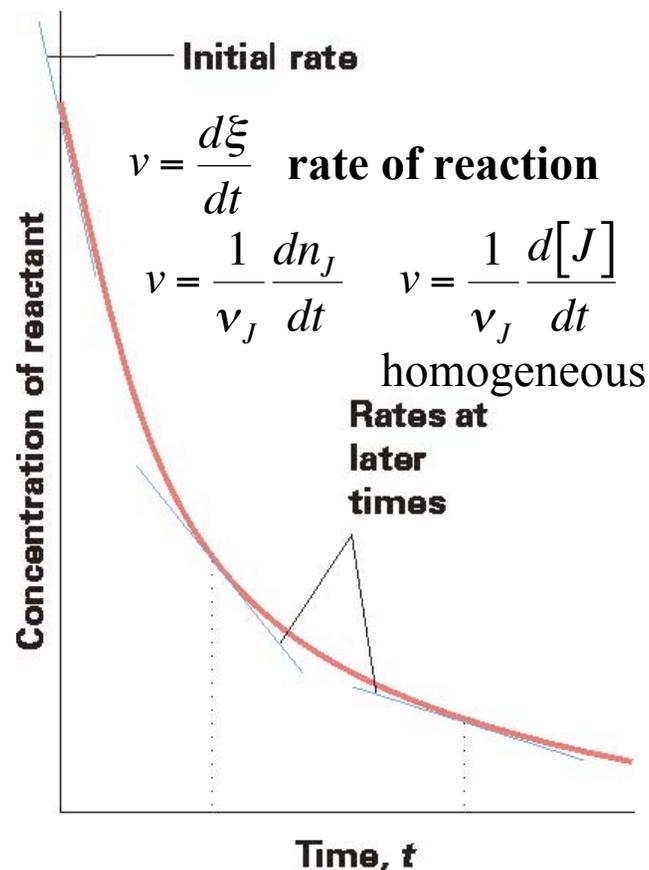


Provided any intermediates are not present the rate of formation of NH₄⁺ is twice the rate of disappearance of (NH₂)₂CO, because, for 1 mol (NH₂)₂CO consumed, 2 mol NH₄⁺ is formed. Once we know the rate of formation or consumption of one substance, we can use the reaction stoichiometry to deduce the rates of formation or consumption of the other participants in the reaction.

Rate laws and rate constants

The rate of reaction is often found to be proportional to the molar concentrations of the reactants raised to a simple power.

Rate of reaction = $k[\text{A}]^p[\text{B}]^q$ k – the **rate constant**



The rate constant is independent of the concentration of the species taking part in the reaction but depends on the temperature. An *experimentally determined* equation is called the ‘rate law’ of the reaction. A **rate law** is an equation that expresses the rate of reaction in terms of the molar concentrations of the species in the overall reaction (including, possibly, the products).

The units of k are always such as to convert the product of concentrations into a rate expressed as a change of concentration divided by time.

$$k \times [A] \times [B] = \text{Rate}$$

$\text{L mol}^{-1} \text{s}^{-1} \times \text{mol L}^{-1} \times \text{mol L}^{-1} = \text{mol L}^{-1} \text{s}^{-1}$

Once we know the rate law and the rate constant of the reaction, we can predict the rate of the reaction for any given composition of the reaction mixture. We can use a rate law to predict the concentrations of the reactants and products at any time after the start of the reaction. A rate law is also an important guide to the reaction mechanism – any proposed mechanism must be consistent with the observed rate law.

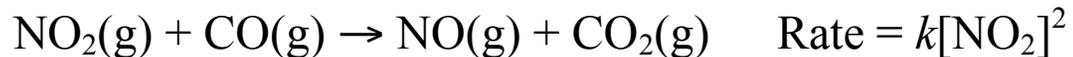
Reaction order

Reactions are classified according to their kinetics (rate laws). The classification is based on their **order** – the power to which the concentrations of a species is raised in the rate law.

$$\text{Rate} = k[A][B] - \textit{first-order} \text{ both in A and B}$$

$$\text{Rate} = k[A]^2 - \textit{second-order} \text{ in A}$$

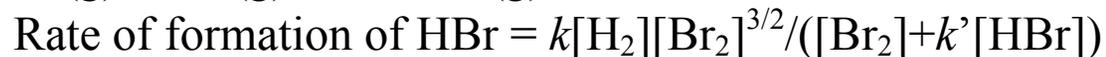
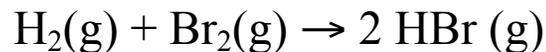
The **overall order** – the sum of the orders of all the components (2 for both reactions above).



The reaction is second-order in NO_2 and second-order overall. The rate is independent of $[\text{CO}]$ provided that some CO is present – the reaction is *zero-order* in CO .



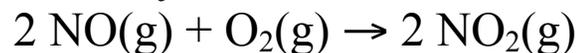
Half-order in A, first-order in B, and three-halves order overall. If a rate law is not in the form $[\text{A}]^x[\text{B}]^y[\text{C}]^z \dots$ then the reaction does not have an overall order.



It is determined experimentally that the reaction is first order in H_2 and it has an indefinite order with respect to both Br_2 and HBr and an indefinite order overall.

A rate law is established experimentally and cannot in general be inferred from the chemical equation for the reaction.

The reaction of hydrogen and bromine, for example, has a very simple stoichiometry but its rate law is very complicated. In some cases, the rate law does happen to reflect the reaction stoichiometry:



The oxidation of nitrogen oxide NO under certain conditions is found to have a third-order rate law.

The determination of the rate law

The determination of a rate law is simplified by the **isolation method** – all the reactants except one are present in large excess. We can find the dependence of the rate on reactants by isolating each of them in turn – and piecing together a picture of the overall rate law. For example, if a reactant B is in large excess, it is a good approximation to take its concentration as constant throughout the reaction. Then, although the true rate law might be

$$\text{Rate} = k[\text{A}][\text{B}]^2$$

we can approximate [B] by its initial value [B]₀:

$$\text{Rate} = k'[\text{A}], \text{ with } k' = k[\text{B}]_0^2$$

Because the true rate law has been forced into first-order form by assuming a constant B concentration, the effective rate law is classified as **pseudofirst-order** and k' is called the **effective rate constant** for a given, fixed concentration of B. If, instead, the concentration of A were in large excess, and hence effectively constant, the rate law would simplify to

$$\text{Rate} = k''[\text{B}]^2, \text{ with } k'' = k[\text{A}]_0$$

This **pseudosecond-order rate law** is easier to analyze and identify than the complete law.

In a similar manner, a reaction may even appear to be zeroth-order. For instance, the oxidation of ethanol to acetaldehyde by NAD⁺ in the liver in the presence of enzyme liver alcohol dehydrogenase



is zeroth-order overall as the ethanol is in excess and the concentration of NAD⁺ is maintained at a constant level by normal metabolic processes. Many reactions in aqueous solution that are reported as first- or second-order are actually pseudofirst- or pseudosecond order: the solvent water participates in the reaction but it is in such large excess that its concentration remains constant.

In the method of **initial rates**, the instantaneous rate is measured at the beginning of the reaction for several different initial concentrations of reactants. Suppose the rate law for a reaction with A isolated

$$r = k' [A]^a$$

Then the initial rate of the reaction is given by the initial concentration of A:

$$r_0 = k' [A]_0^a$$

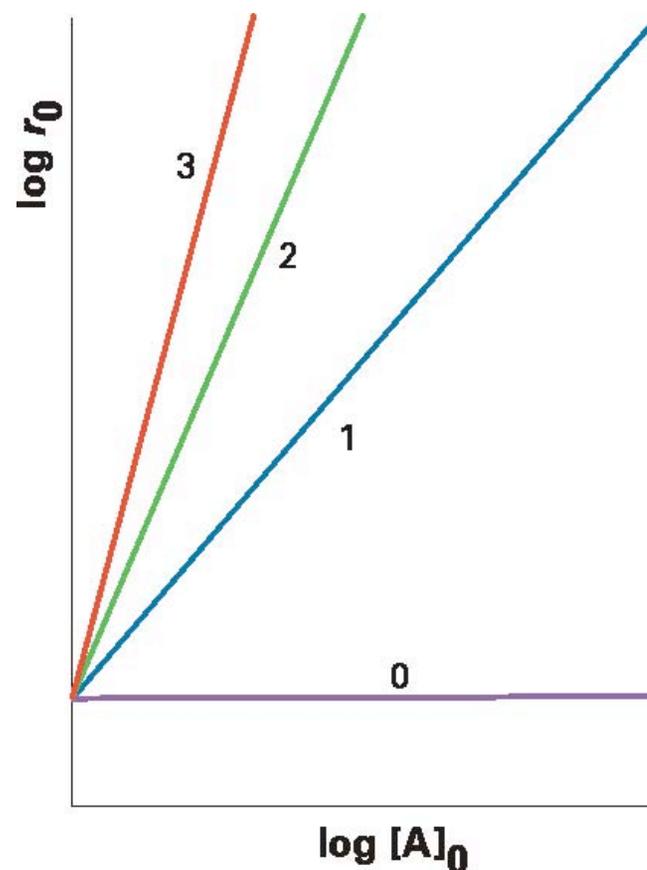
$$\log r_0 = \log k' + a \log [A]_0$$

$$y = \text{intercept} + \text{slope} \times x$$

$$y = \log r_0$$

$$x = \log [A]_0$$

$$\log r_0 = \log k' + a \log [A]_0$$



For a series of initial concentrations, a plot of the logarithms of the initial rates against the logarithms of the initial concentration of A should be a straight line, and that the slope of the graph will be a , the order of the reaction with respect to the species A.

Using the method of initial rates

The recombination of I atoms in the gas phase in the presence of argon was investigated and the order of the reaction was determined by the method of initial rates. The initial rates of reaction of $2 \text{I}(\text{g}) + \text{Ar}(\text{g}) \rightarrow \text{I}_2(\text{g}) + \text{Ar}(\text{g})$ were as follows:

$[\text{I}]_0 / (10^{-5} \text{ mol L}^{-1})$	1.0	2.0	4.0	6.0
$r_0 / (\text{mol L}^{-1} \text{ s}^{-1})$ (a)	1.070×10^{-3}	3.48×10^{-3}	1.39×10^{-2}	3.13×10^{-2}
(b)	4.35×10^{-3}	1.74×10^{-2}	6.96×10^{-2}	1.57×10^{-1}
(c)	1.069×10^{-2}	3.47×10^{-2}	1.38×10^{-1}	3.13×10^{-1}

The Ar concentrations in mol L^{-1} are (a) 1.0×10^{-3} , (b) 5.0×10^{-3} , (c) 1.0×10^{-2} . Find the orders of reaction with respect to I and Ar and the rate constant.

For constant $[\text{Ar}]_0$, the initial rate law has the form $r_0 = k' [\text{I}]_0^a$, with $k' = k [\text{Ar}]_0^b$

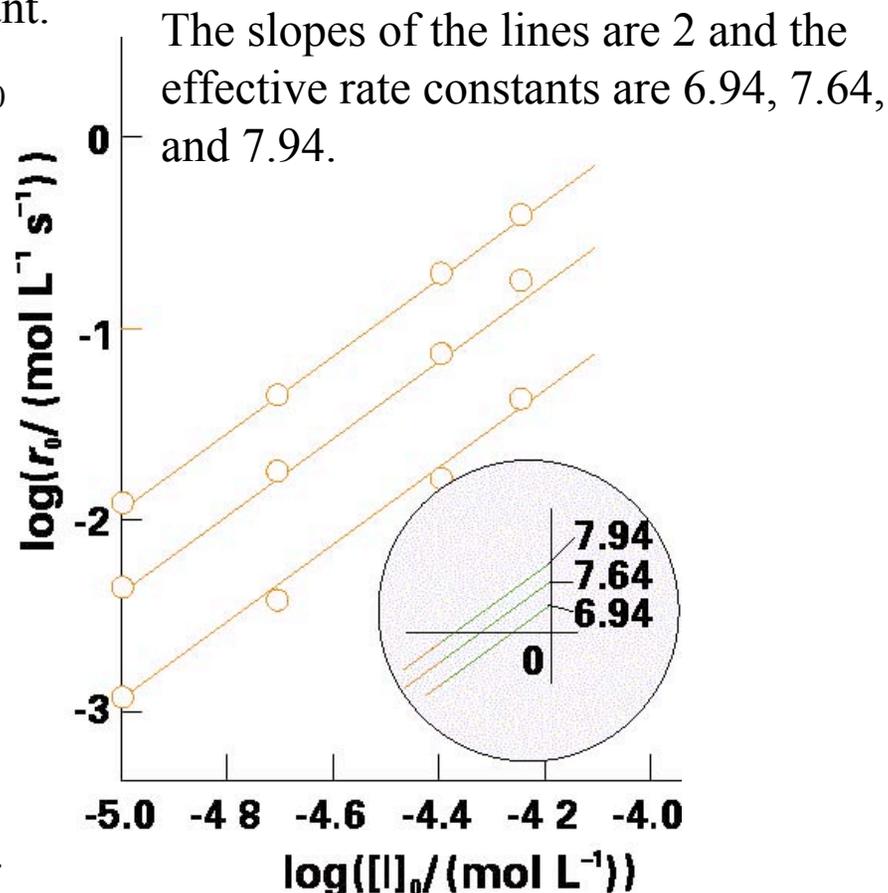
$$\log r_0 = \log k' + a \log [\text{I}]_0$$

We need to make plot of $\log r_0$ against $\log [\text{I}]_0$ and find the order a from the slope and the value k' from the intercept at $\log [\text{I}]_0 = 0$.

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

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

$\log ([\text{I}]_0 / \text{mol L}^{-1})$	-5.00	-4.70	-4.40	-4.22
$\log ([r]_0 / \text{mol L}^{-1} \text{ s}^{-1})$ (a)	-2.971	-2.458	-1.857	-1.504
(b)	-2.362	-1.760	-1.157	-0.804
(c)	-1.971	-1.460	-0.860	-0.504



$\log([\text{Ar}]_0/\text{mol L}^{-1})$	-3.00	-2.30	-2.00
$\log(k'/\text{mol}^{-1} \text{ L s}^{-1})$	6.94	7.64	7.94

If we plot $\log k'$ against $\log [\text{Ar}]_0$, we find that the slope is 1, so $b = 1$. The intercept at $\log [\text{Ar}]_0 = 0$ is $\log k = 9.94$, so $k = 8.7 \times 10^9 \text{ mol}^{-2} \text{ L}^2 \text{ s}^{-1}$. The overall (initial) rate law is

$$r = k[\text{I}]_0^2[\text{Ar}]_0$$

The method of initial rates may not reveal the entire rate law – in a complex reaction the products themselves might affect the rate.

Integrated rate laws

A rate law tells us the rate of the reaction at a given instant (at a particular composition of the reaction mixture). We may want to know the composition of the reaction mixture at a given time given the varying rate of the reaction. An **integrated rate law** – an expression that gives the concentration of a species as a function of the time.

Two principal uses: (1) to predict the concentration of a species at any time after the start of the reaction; (2) to help find the rate constant and order of the reaction.

The reaction rates are rarely measured directly because slopes are difficult to determine accurately. Almost all experimental work in chemical kinetics deals with integrated rate laws – they are expressed in terms of the experimental observables of concentrations and time.

Computers can be used to find numerical versions of the integrated form of even the most complicated rate laws. In a number of simple cases analytical solutions can be obtained.

First-order integrated rate laws

The slope of the plot of $[A]$ against t is the derivative of $[A]$ with respect to t , $d[A]/dt$. The rate of consumption of a reactant, a positive quantity, is defined as the negative of this slope, $-d[A]/dt$.

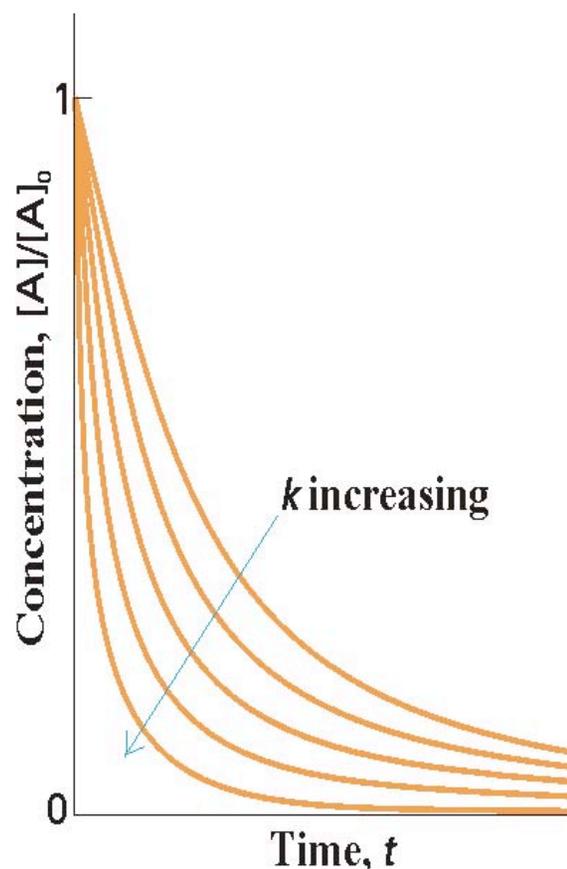
$$-d[A]/dt = k[A] \quad -d[A]/[A] = k dt$$

$$\int_{[A]_0}^{[A]} \frac{d[A]}{[A]} = -k \int_0^t dt$$

$$\ln ([A]_0/[A]) = kt \quad \ln [A] = \ln [A]_0 - kt$$
$$[A] = [A]_0 \exp(-kt) \quad \text{exponential decay}$$

The concentration of the reactant decays exponentially with time.

If we plot $\ln [A]$ against t , then we will get a straight line if the reaction is first-order. If the experimental data do not give a straight line when plotted in this way, the reaction is not first-order. If the line is straight, its slope is $-k$, so we can also determine the rate constant from the graph.



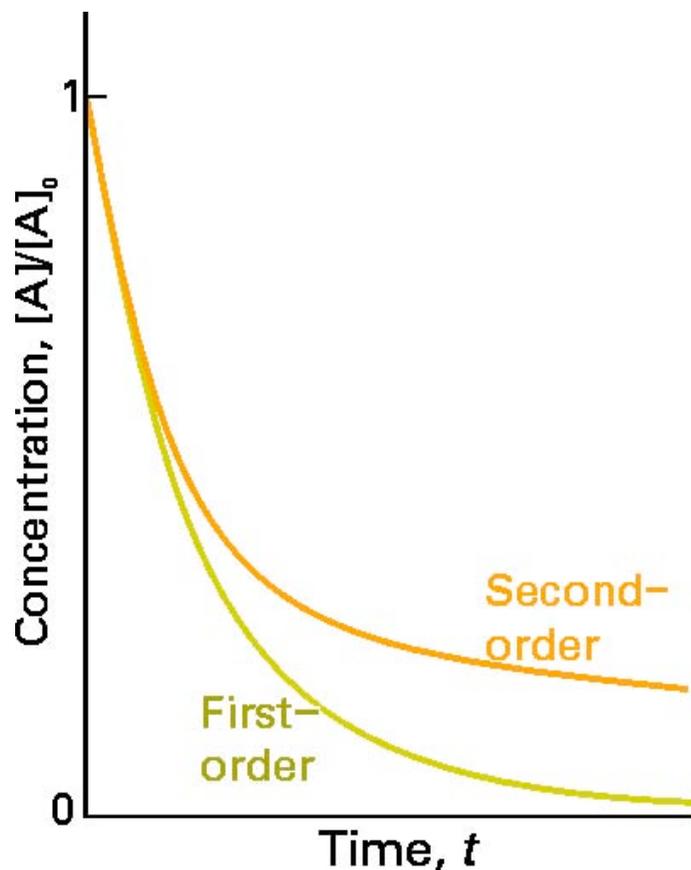
Second-order reaction with the rate law:

$$\text{Rate of consumption of A} = k[A]^2$$

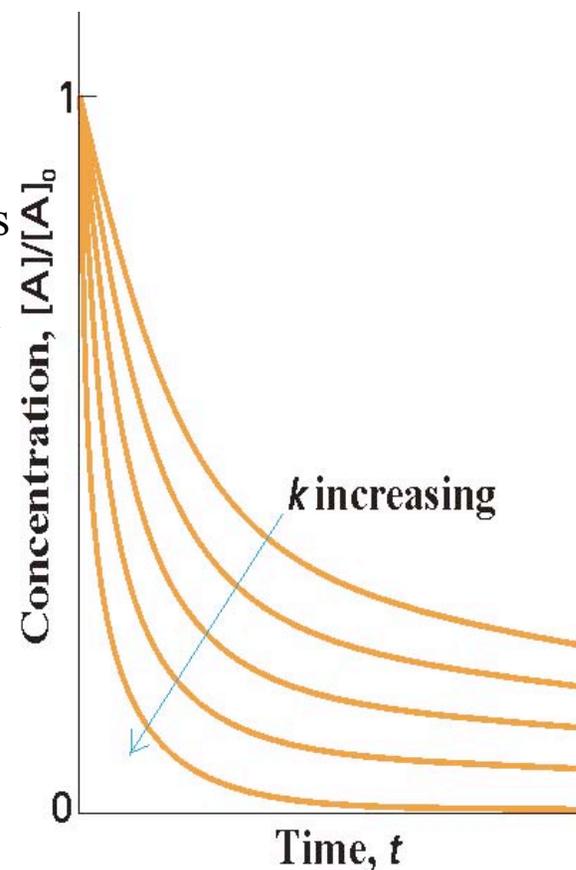
We suppose that the concentration of A at $t = 0$ is $[A]_0$. The differential equation for the rate law is $-d[A]/dt = k[A]^2$

$$\int_{[A]_0}^{[A]} \frac{d[A]}{[A]^2} = -k \int_0^t dt \quad \frac{1}{[A]_0} - \frac{1}{[A]} = kt \quad \frac{1}{[A]} = \frac{1}{[A]_0} + kt \quad [A] = \frac{[A]_0}{1 + kt[A]_0}$$

To test for a second order reaction we should plot $1/[A]$ against t and expect a straight line. If the line is straight, the reaction is second-order in A and the slope of the line is equal to the rate constant.



When $[A]$ is plotted against t , the concentration of A approaches zero more slowly than the first-order reaction with the same initial rate. Reactants that decay by a second-order process die away more slowly at low concentrations than would be expected if the decay were first-order – pollutants commonly disappear by second-order processes, so it takes a very long time for them to decline to acceptable levels.



Half-lives

A useful indication of the rate of a first-order chemical reaction is the **half-life**, $t_{1/2}$, of a reactant – the time it takes for the concentration of the species to fall to half its initial value. We can find the half-life of a species A that decays in a first-order reaction by substituting $[A] = \frac{1}{2} [A]_0$ and $t = t_{1/2}$ into the integrated rate law.

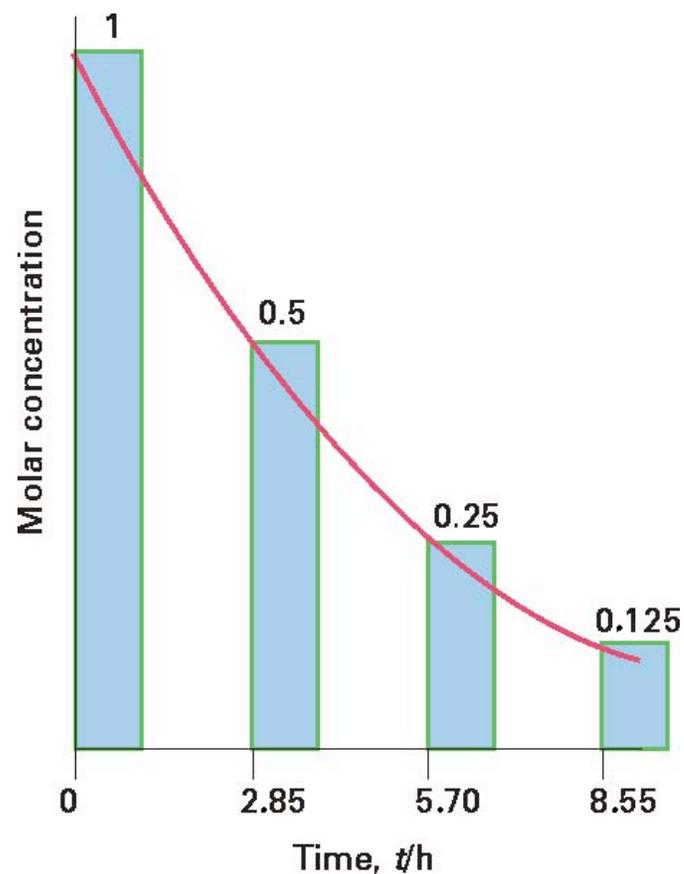
$$kt_{1/2} = \ln([A]_0 / \frac{1}{2}[A]_0) = \ln 2$$

$$t_{1/2} = \ln 2 / k$$

For example, because the rate constant for the first-order reaction



Rate of consumption of $\text{N}_2\text{O}_5 = k[\text{N}_2\text{O}_5]$ is equal to $6.76 \times 10^{-5} \text{ s}^{-1}$ at 25°C , the half-life of N_2O_5 is 2.85 h. The concentration of N_2O_5 falls to half its initial value in 2.85 h, and then to half that concentration again in further 2.85 h, and so on.



For a first-order reaction, the half-life of a reactant is independent of its initial concentration. It follows that, if the concentration of A at some arbitrary stage of the reaction is [A], then the concentration will fall to $\frac{1}{2}$ [A] after an interval of $0.693/k$ whatever the actual value of [A].

In contrast to first-order reactions, the half-life of a second-order reaction does depend on the initial concentration of the reactant $\{t_{1/2} = 1/(k[A]_0)\}$, and lengthens as the concentration of the reactants falls. Therefore, the half-life is not characteristic of the reaction itself and is rarely used. We can use the half-life of a substance to recognize first-order reactions – if half-life does not change with initial concentration, the reaction is first-order.

Integrated rate laws

Order	Reaction type	Rate law	Integrated rate law
0	$A \rightarrow P$	$r = k$	$[P] = kt$ for $kt \leq [A]_0$
1	$A \rightarrow P$	$r = k[A]$	$[P] = [A]_0(1 - e^{-kt})$
2	$A \rightarrow P$	$r = k[A]^2$	$[P] = \frac{kt[A]_0^2}{1 + kt[A]_0}$
	$A + B \rightarrow P$	$r = k[A][B]$	$[P] = \frac{[A]_0[B]_0(1 - e^{([B]_0 - [A]_0)kt})}{[A]_0 - [B]_0 e^{([B]_0 - [A]_0)kt}}$

The temperature dependence of reaction rates

The rates of most chemical reactions increase as the temperature is raised. As data on reaction rates were accumulated towards the end of 19th century, the Swedish chemist Svante Arrhenius noted that almost all of them showed a similar dependence on the temperature. A graph of $\ln k$, where k is the rate constant for the reaction, against $1/T$, where T is the absolute temperature at which k is measured, gives a straight line with a slope that is characteristic of the reaction.

$$\ln k = \text{intercept} + \text{slope} \times 1/T$$

The **Arrhenius equation**

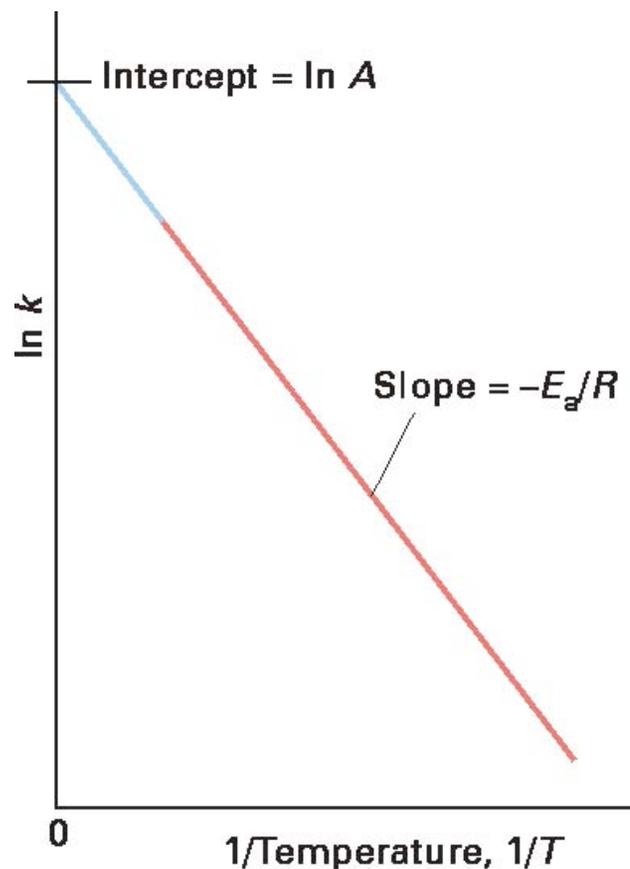
$$\ln k = \ln A - E_a/RT$$

$$k = A \exp(-E_a/RT)$$

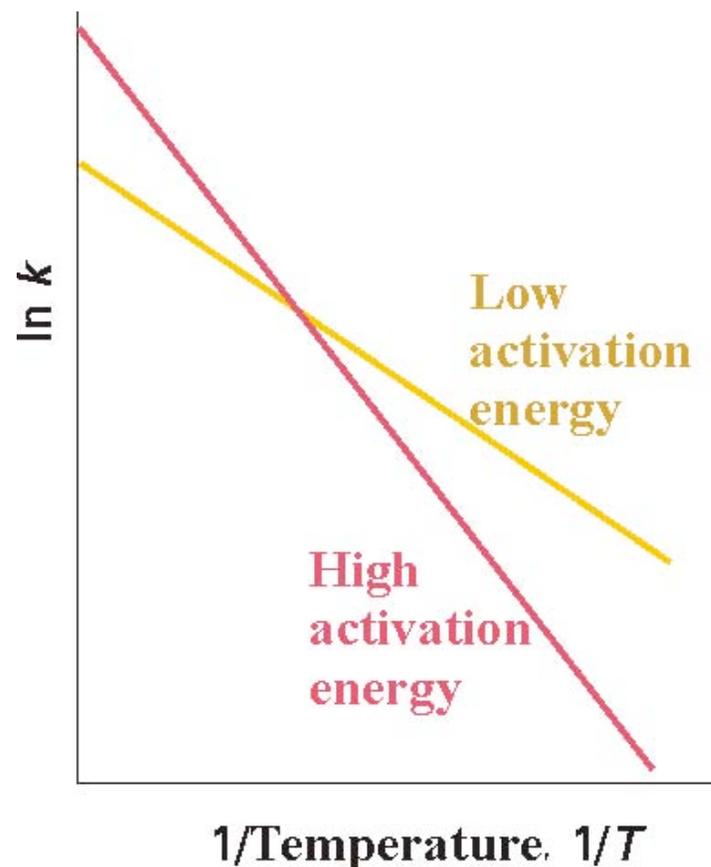
A – the **pre-exponential factor** (has the same units as k)

E_a – the **activation energy** (has the same units as RT , i.e., is a molar energy in kJ mol^{-1})

A, E_a – **Arrhenius parameters**



A high activation energy corresponds to a reaction rate that is very sensitive to temperature (the Arrhenius plot has a steep slope). A small activation energy indicates a reaction rate that varies only slightly with temperature (the slope is shallow). A reaction with zero activation energy (some radical recombination reactions in the gas phase) – the rate is largely independent of temperature.



Once the activation energy of a reaction is known, it is simple to predict the value of a rate constant k' at a temperature T' from its value k at another temperature T :

$$\ln k' = \ln A - E_a/RT \qquad \ln k' - \ln k = -E_a/RT' + E_a/RT \qquad \ln(k'/k) = (E_a/R)(1/T - 1/T')$$

For a reaction with an activation energy of 50 kJ mol^{-1} an increase in the temperature from 25°C to 37°C results in $\ln(k'/k) = (50 \times 10^3 \text{ J mol}^{-1} / 8.3145 \text{ J K}^{-1} \text{ mol}^{-1}) / (1/(298 \text{ K}) - (1/310 \text{ K})) = 0.7812$.

$k' = 2.18 k$ The rate constant is slightly more than doubled.

Determining the Arrhenius parameters

The rate of the second-order decomposition of acetaldehyde (ethanal, CH_3CHO) was measured over the temperature range 700-1000 K, and the rate constants that were found are reported below. Find the activation energy and the pre-exponential factor:

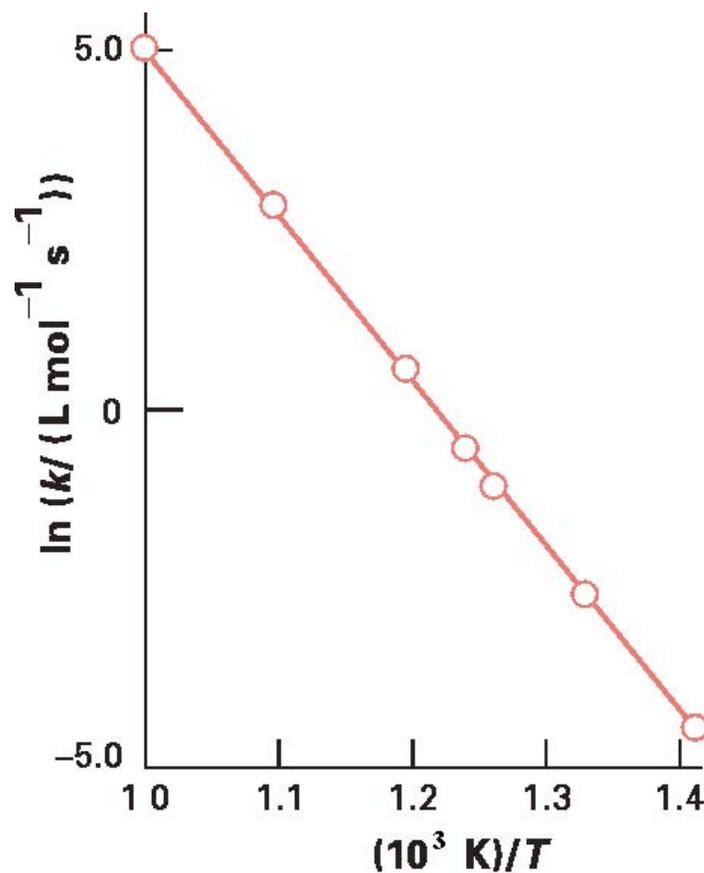
T/K	700	730	760	790	810	840	910	1000
$k/(\text{L mol}^{-1} \text{s}^{-1})$	0.011	0.035	0.105	0.343	0.789	2.17	20.0	145

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 $\ln A$. After plotting the graph, it is best to do a least-squares fit of the data to a straight line. A has the same units as k .

The least-squares best fit of the line has slope -2.265×10^4 and intercept 27.71.

$$E_a = 2.265 \times 10^4 \text{ K} \times 8.3145 \text{ J K}^{-1} \text{ mol}^{-1} = 188 \text{ kJ mol}^{-1}$$

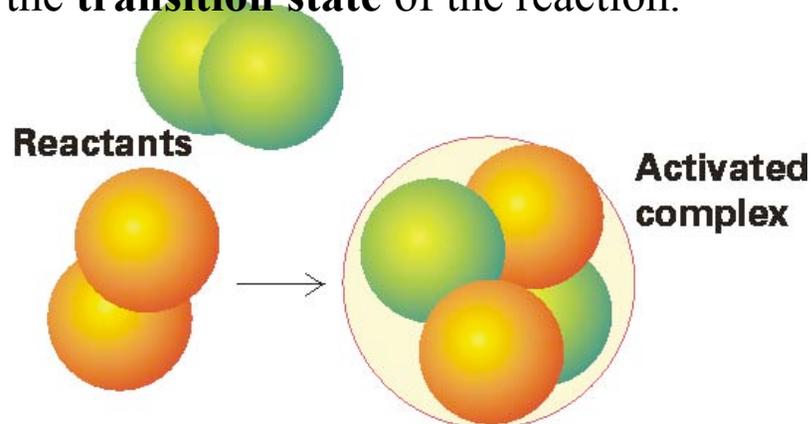
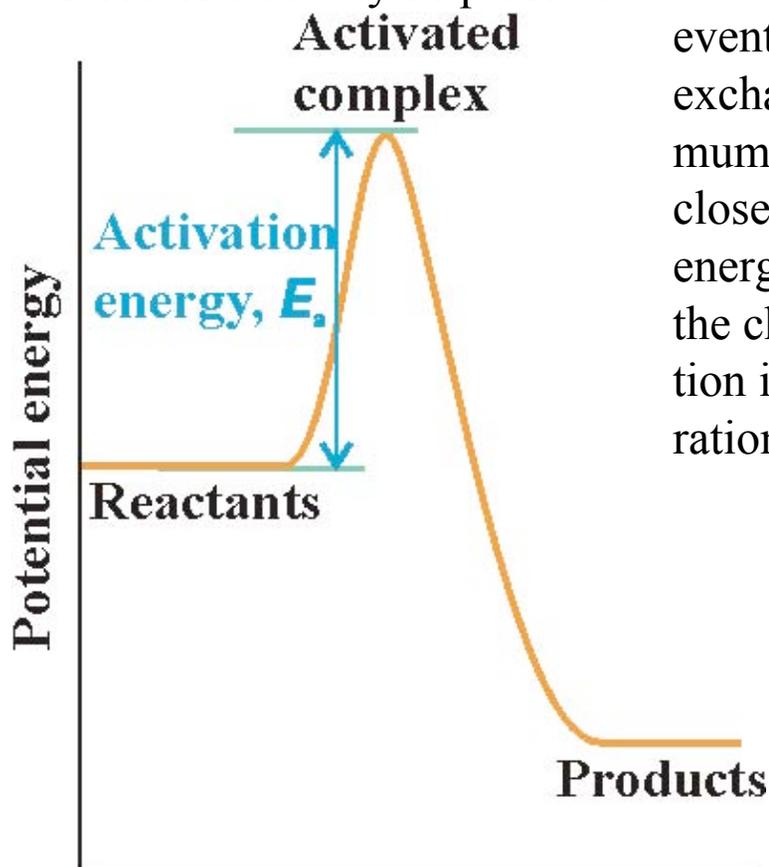
$$A = e^{27.71} \text{ L mol}^{-1} \text{ s}^{-1} = 1.08 \times 10^{12} \text{ L mol}^{-1} \text{ s}^{-1}$$



Activated complex theory

A more sophisticated theory of reaction rates that can be applied to reactions taking place in solution as well as in the gas phase – the **activated complex theory** of reactions. It is supposed that as two reactants approach, their potential energy rises and reaches a maximum. This maximum corresponds to the formation of an **activated complex**, a cluster of atoms that is poised to pass on to products or to collapse back into the reactants from which it was formed. An activated complex is not a reaction intermediate that can be isolated and studied like ordinary molecules. The concept of an activated complex is applicable to reactions in solutions as well as to the gas phase, because we can think of the activated complex as perhaps involving any solvent molecules that may be present.

Initially, only the reactants A and B are present. As the reaction event proceeds, A and B come into contact, distort, and begin to exchange or discard atoms. The potential energy rises to a maximum, and the cluster of atoms that corresponds to the region close to the maximum is the activated complex. The potential energy falls as the atoms rearrange in the cluster, and reaches the characteristic value of the products. The climax of the reaction is at the peak of the potential energy. This crucial configuration is called the **transition state** of the reaction.



The **reaction coordinate** – an indication of the stage reached in the reaction between the reactants and the products. On the left, we have undistorted, widely separated reactants. On the right are the products. Somewhere in the middle is the stage of the reaction corresponding to formation of the activated complex. At the transition state, motion along the reaction coordinate corresponds to some complicated collective vibration-like motion of all atoms in the complex (and the motion of the solvent molecules if needed)

In a simple form of activated complex theory, we suppose that the activated complex is in equilibrium with the reactants, and that we express the abundance in the reaction mixture in terms of an equilibrium constant, K^\ddagger :

$$A + B \rightleftharpoons C^\ddagger \quad K^\ddagger = [C^\ddagger]/\{[A][B]\}$$

Then, we suppose that the rate at which reactants are formed is proportional to the concentration of the activated complex:

$$\text{Rate of formation of products} \propto [C^\ddagger] = K^\ddagger[A][B]$$

The full activated complex theory gives an estimate of the constant of proportionality as

kT/h , k – Boltzmann's constant ($k = R/N_A$), h – Plank's constant.

$$\text{Rate of formation of products} = (kT/h) \times K^\ddagger [A][B]$$

$$\text{Rate of formation of products} = k_{\text{rate}} [A][B]$$

$$k_{\text{rate}} = (kT/h) \times K^\ddagger$$

An equilibrium constant may be expressed in terms of the standard reaction Gibbs energy ($-RT \ln K = \Delta_r G^\ominus$). In this context, the Gibbs energy is called the **activation Gibbs energy**, $\Delta^\ddagger G$.

$$K^\ddagger = \exp(-\Delta^\ddagger G/RT) \quad \Delta^\ddagger G = \Delta^\ddagger H - T\Delta^\ddagger S$$

$$k_{\text{rate}} = (kT/h) \times \exp\{-(\Delta^\ddagger H - T\Delta^\ddagger S)/RT\} = (kT/h) e^{\Delta^\ddagger S/R} e^{-\Delta^\ddagger H/RT}$$

This expression has the form of the Arrhenius expression, if we identify the **enthalpy of activation**, $\Delta^\ddagger H$, with the activation energy and the term $(kT/h) e^{\Delta^\ddagger S/R}$, which depends on the **entropy of activation**, $\Delta^\ddagger S$, with the pre-exponential factor.

Accounting for the rate laws

Rate laws are a window on to the **mechanism**, the sequence of elementary molecular events that lead from the reactants to the products, of the reaction they summarize. All reactions actually proceed towards a state of equilibrium in which the reverse reaction becomes increasingly important. Moreover, many reactions proceed to products through a series of intermediates.

The approach to equilibrium

All forward reactions are accompanied by their reverse reaction. At the start of the reaction, no or little products are present – the rate of the reverse reaction is negligible. As the concentration of products increases, the rate at which they react to produce reactants also increases. At equilibrium, the reverse rate matches the forward rate and the reactants and the products are present in the abundances given by the equilibrium constant.

Forward: $A \rightarrow B$ rate of formation of B = $k[A]$

Reverse: $B \rightarrow A$ rate of decomposition of B = $k'[B]$

Net rate of formation of B = $k[A] - k'[B]$

If the initial concentrations of A and B are $[A]_0$ and $[B]_0$, at any stage

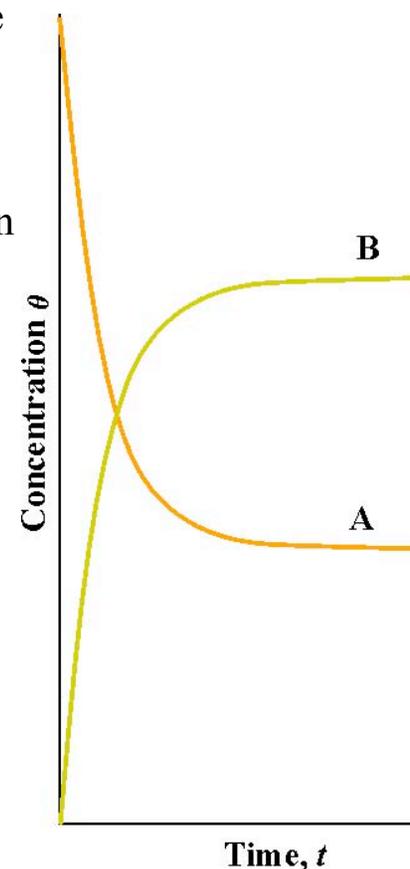
$[A] + [B] = [A]_0 + [B]_0$ $[A] = [A]_0 + [B]_0 - [B]$ Suppose $[B]_0 = 0$

$d[B]/dt = k[A]_0 - k[B] - k'[B]$ The integrate rate law is then

$$[B] = \frac{k(1 - e^{-(k+k')t})[A]_0}{k + k'} \quad [A] = \frac{(k' + e^{-(k+k')t})[A]_0}{k + k'}$$

The equilibrium concentrations are found by setting t equal to infinity and using $e^{-x} = 0$ at $x = \infty$.

$$[B]_{eq} = \frac{k[A]_0}{k + k'} \quad [A]_{eq} = \frac{k'[A]_0}{k + k'}$$



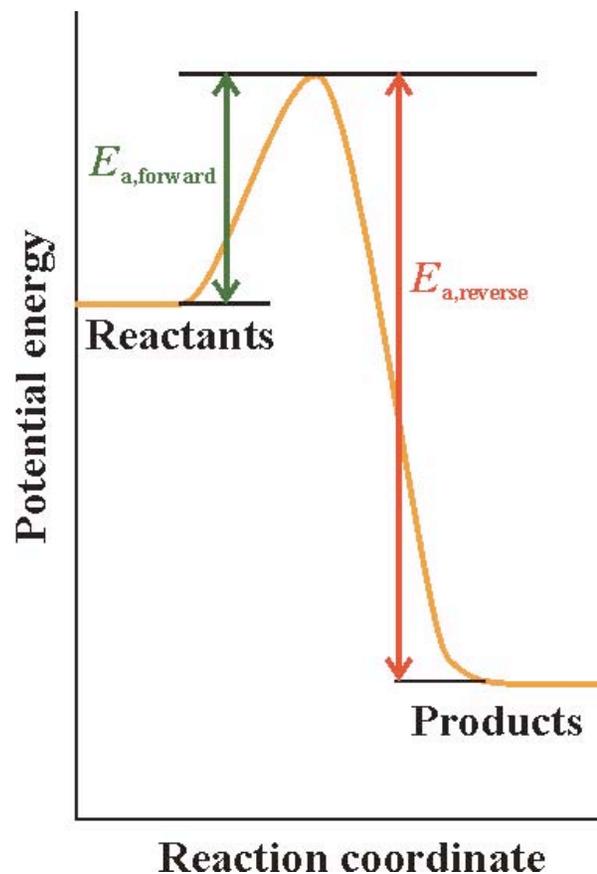
$$K = \frac{[B]_{\text{eq}}}{[A]_{\text{eq}}} = k/k'$$

The equilibrium constant for the reaction is the ratio of the forward and reverse rate constants. If the forward rate constant is much larger than the reverse rate constant, $K \gg 1$. If the opposite is true, then $K \ll 1$. This result is a crucial connection between the kinetics of the reaction and its equilibrium properties. In practice, we may be able to measure the equilibrium constant and one of the rate constants and then can calculate the missing rate constant from the above equation. Alternatively, we can use the relation to calculate the equilibrium constant from kinetic measurements.

Insight into the temperature dependence of equilibrium constants: First, we suppose that both the forward and reverse reactions show Arrhenius behavior. For an exothermic reaction the activation energy of the forward reaction is smaller than that of the reverse reaction.

Therefore, the forward rate constant increases less sharply with temperature than the reverse reaction does. Consequently, when we increase the temperature of a system at equilibrium, k' increases more steeply than k does, and the ratio k/k' , and therefore K , decreases. This is exactly the conclusion we drew earlier from the van't Hoff equation, which was based on thermodynamic arguments:

$$\ln K' - \ln K = \frac{\Delta_r H^\ominus}{R} \left(\frac{1}{T} - \frac{1}{T'} \right)$$



Consecutive reactions

It is commonly the case that a reactant produces an intermediate, which subsequently decays into a product. Let's suppose that the reaction takes place in two steps: (1) the intermediate I is formed from the reactant A in a first-order reaction and (2) I decays in a first-order reaction to form the product P:



For simplicity, we are ignoring the reverse reactions, which is valid if they are slow. A decays with a first-order rate law:

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

The net rate of formation of I is the difference between its rate of formation and its rate of consumption:

$$\text{Net rate of formation of I} = k_1[A] - k_2[I]$$

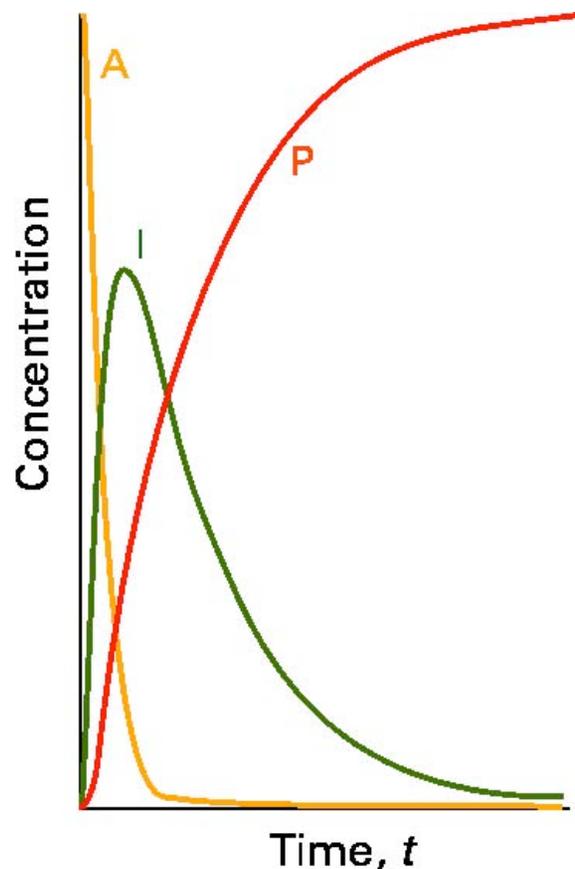
$$[I] = \frac{k_1}{k_2 - k_1} \left(e^{-k_1 t} - e^{-k_2 t} \right) [A]_0$$

We can insert this solution into the rate law for the formation of P and solve the resulting equation to find

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

The intermediate grows in concentration initially, then decays as A is exhausted. The concentration of P rises smoothly to its final value. The intermediate reaches its maximum concentration at

$$t = \frac{1}{k_1 - k_2} \ln \frac{k_1}{k_2}$$

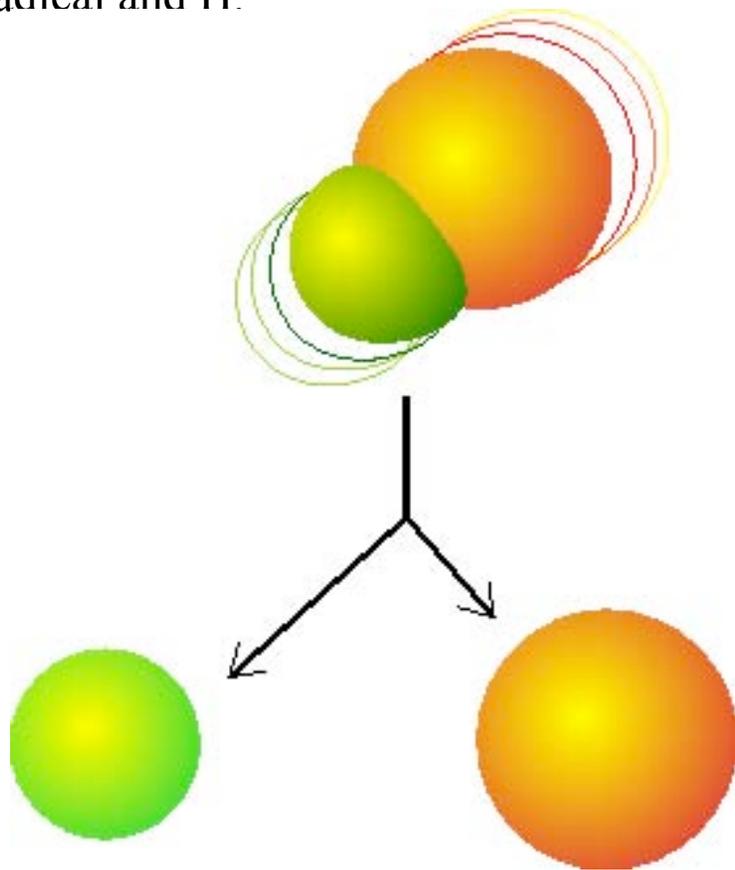


Reaction mechanisms

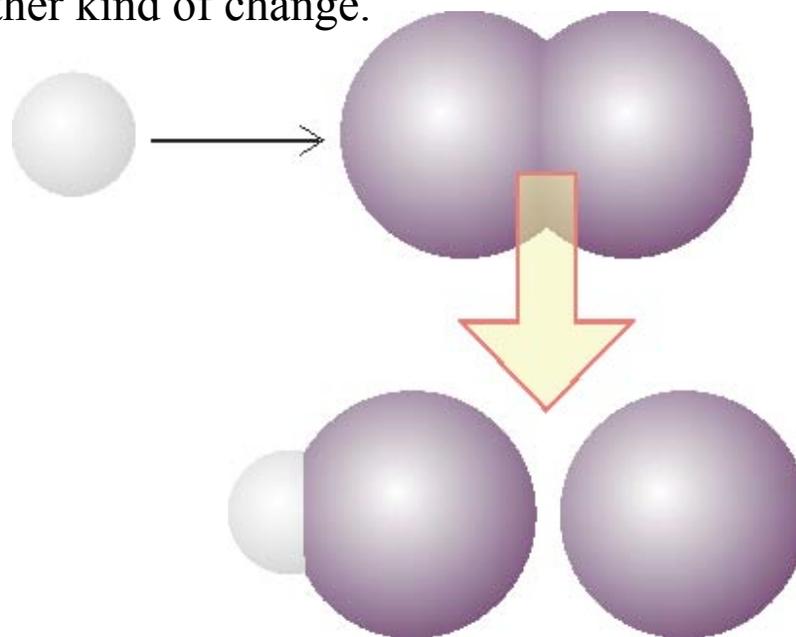
We have seen how two simple types of reactions – approach to equilibrium and consecutive reactions – result in a characteristic dependence of the concentration of time. We can suspect that other variations with time will act as the signatures of other reaction mechanisms.

Elementary reactions. Many reactions occur in a series of steps called **elementary reactions**, each of them involves one or two molecules. Example: $\text{H} + \text{Br}_2 \rightarrow \text{HBr} + \text{Br}$.

The **molecularity** of an elementary reaction – the number of molecules coming together to react. In a **unimolecular reaction** a single molecule shakes itself apart or its atoms into a new arrangement: the isomerization of cyclopropane to propene, dissociation of benzene to phenyl radical and H.



In a **bimolecular reaction**, two molecules collide and exchange energy, atoms, or group of atoms, or undergo some other kind of change.



It is important to distinguish molecularity from order: the *order* of a reaction is an empirical quantity, and is obtained by inspection of the experimentally determined rate law; the *molecularity* of a reaction refers to an individual elementary reaction that has been postulated as a step in a proposed mechanism. Many substitution reactions in organic chemistry (S_N2 nucleophilic substitutions) are bimolecular and involve an activated complex that is formed from two reactant species. Enzyme-catalyzed reactions can be regarded, to a good approximation, as bimolecular – they depend on the encounter of a substrate molecule and an enzyme molecule.

We can write down the rate law of an elementary reaction from its chemical equation.

A unimolecular reaction – in a given interval, 10 times as many A molecules decay when there are initially 1000 A molecules as when there are only 100 A molecules present – the rate of decomposition of A is proportional to its concentration – *a unimolecular reaction is first-order*:



The rate of a bimolecular reaction is proportional to the rate at which the reactants meet, which in turn is proportional to both their concentrations. Therefore, the rate of the reaction is proportional to the product of the two concentrations and *an elementary bimolecular reaction is second-order overall*:

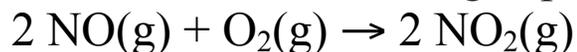


We shall see how to string simple steps together into a mechanism and how to arrive at the corresponding overall rate law.

If the reaction is an elementary bimolecular process, then it has second-order kinetics; however, if the kinetics are second-order, then the reaction could be bimolecular but might be complex.

The formulation of rate laws

Suppose we propose that a particular reaction is the outcome of a sequence of elementary steps. How do we arrive at the rate law implied by the mechanism? As an example, we consider the rate law for the gas-phase oxidation of nitrogen monoxide:



Experimentally, the reaction is found to be third-order overall:

$$\text{Rate of formation of NO}_2 = k[\text{NO}]^2[\text{O}_2]$$

One explanation of the observed reaction order might be that the reaction is a single termolecular (three-molecular) elementary step involving the simultaneous collision of two NO molecules and one O₂ molecule. However, such collisions occur very rarely. Therefore, although termolecular collisions may contribute, the rate of reaction by this mechanism is so slow that another mechanism usually dominates.

The following mechanism has been proposed:

Step 1: Two NO molecules combine to form a dimer:



This step is plausible because NO is an odd-electron species, a radical, and two radicals can form a covalent bond when they meet. The N₂O₂ dimer is also known in the solid – this also makes the suggestion plausible: it is often a good strategy to decide whether a proposed intermediate is the analogue of a known compound.

Step 2: The N₂O₂ dimer decomposes into NO molecules:



This step, the reverse of step 1 – a unimolecular decay: the dimer shakes itself apart.

Step 3: Otherwise, an O₂ molecule collides with the dimer and results in the formation of NO₂:



$$\text{rate of consumption of N}_2\text{O}_2 = k_b[\text{N}_2\text{O}_2][\text{O}_2]$$

$$\text{rate of formation of NO}_2 = 2k_b[\text{N}_2\text{O}_2][\text{O}_2] \text{ (see stoichiometry)}$$

The steady-state approximation

The rate of formation of product comes directly from step 3:

$$\text{rate of formation of NO}_2 = 2k_b[\text{N}_2\text{O}_2][\text{O}_2]$$

However, this expression is not an acceptable overall rate law because it is expressed in terms of the concentration of intermediate N_2O_2 : an acceptable rate law for an overall reaction is expressed solely in terms of the species that appear in the overall reaction – we need to find an expression for the concentration of N_2O_2 . To do so, we consider the net rate of formation of the intermediate, the difference between its rates of formation and decay:

$$\text{Net rate of formation of N}_2\text{O}_2 = k_a[\text{NO}]^2 - k_a'[\text{N}_2\text{O}_2] - k_b[\text{N}_2\text{O}_2][\text{O}_2]$$

Notice that formation terms occur with a positive sign and decay terms occur with a negative sign – they reduce the net rate of formation.

We introduce the **steady-state approximation**: *the concentrations of all intermediates remain constant and small throughout the reaction* (except right at the beginning and right at the end). An **intermediate** – any species that does not appear in the overall reaction but has been invoked in the mechanism.

$$k_a[\text{NO}]^2 - k_a'[\text{N}_2\text{O}_2] - k_b[\text{N}_2\text{O}_2][\text{O}_2] = 0$$

$$[\text{N}_2\text{O}_2] = k_a[\text{NO}]^2 / (k_a' + k_b[\text{O}_2])$$

$$\text{Rate of formation of NO}_2 = 2k_b[\text{N}_2\text{O}_2][\text{O}_2] = 2k_a k_b [\text{NO}]^2 [\text{O}_2] / (k_a' + k_b[\text{O}_2])$$

At this stage, the rate law is more complex than the observed law. We suppose that the rate of decomposition of N_2O_2 is much greater than its rate of reaction with O_2 :

$$k_a'[\text{N}_2\text{O}_2] \gg k_b[\text{N}_2\text{O}_2][\text{O}_2] \quad \text{Then, } k_a' \gg k_b [\text{O}_2] \text{ and}$$

$$\text{Rate of formation of NO}_2 = (2k_a k_b / k_a') [\text{NO}]^2 [\text{O}_2]$$

This expression has the observed overall third-order form and we can identify the observed rate constant as the following combination of rate constants of the elementary reactions:

$$k = 2k_a k_b / k_a'$$

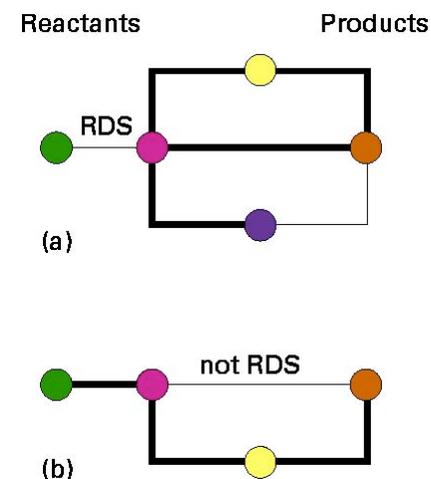
The rate-determining step

The oxidation of nitrogen monoxide introduces another important aspect. Let's suppose that step 3 is very fast, so k_a' may be neglected relative to $k_b[\text{O}_2]$. Then

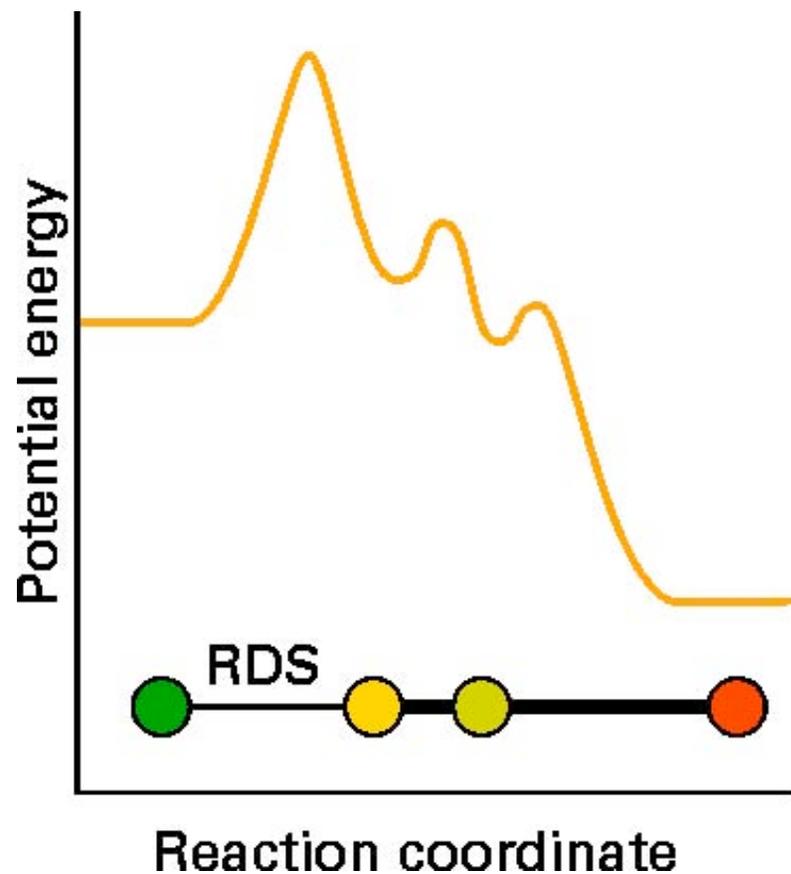
$$\text{Rate of formation of NO}_2 = 2k_a k_b [\text{NO}]^2 [\text{O}_2] / k_b [\text{O}_2] = 2k_a [\text{NO}]^2$$

If this is the case, the reaction is second-order in NO and $[\text{O}_2]$ does not appear in the rate law. The explanation – the rate of reaction of N_2O_2 is so great on account of the high concentration of O_2 in the system that N_2O_2 reacts as soon as it is formed. Under these conditions, the rate of formation of NO_2 is determined by the rate at which N_2O_2 is formed. This step – a **rate-determining step**, the slowest step in a reaction mechanism, which controls the rate of the overall reaction.

The rate determining step is not just the slowest step: it must be slow *and* be a crucial gateway for the formation of products. If a faster reaction can also lead to the products, then the slowest step is irrelevant because the slow reaction can then be side-stepped. The rate-determining step is like a slow ferry crossing between two fast highways: the overall rate at which traffic can reach its destination is determined by the rate at which it can make the ferry crossing.



The rate law of reaction that has a rate-determining step can often be written down by inspection. If the first step in the mechanism is rate-determining, then the rate of the overall reaction is equal to the rate of the first step because all subsequent steps are so fast that once the first intermediate is formed it results immediately in the formation of products. The Figure shows the reaction profile for a mechanism of this kind in which the slowest step is the one with the highest activation energy. Once over the initial barrier, the intermediates cascade into products. However, a rate-determining step may also stem from the low concentration of a crucial reactant or catalyst and need not to correspond to the step with higher activation barrier. A rate-determining step arising from the low activity of a crucial enzyme can sometimes be identified by determining whether or not the reactants and products are in equilibrium: if the reaction is not at equilibrium it suggests that the step may be slow enough to be rate-determining.



Unimolecular reactions

A number of gas-phase reactions follow first-order kinetics – isomerization of cyclopropane: $\text{cyclo-C}_3\text{H}_6 \rightarrow \text{CH}_3\text{CH}=\text{CH}_2$ $\text{Rate} = k[\text{cyclo-C}_3\text{H}_6]$

The problem – the reactant molecule presumably acquires the energy it needs to react by collisions with other molecules. Collisions – simple *bimolecular* events, why first-order then?

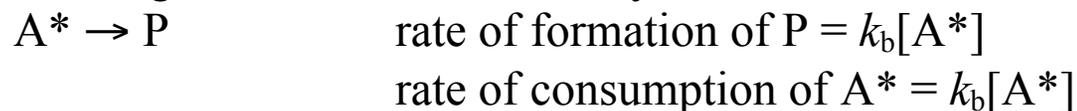
The first successful explanation of unimolecular reactions – Frederick Lindemann (1921).

The Lindemann mechanism:

Step 1 A reactant molecule becomes energetically excited (A^*) by collision with another A molecule: $\text{A} + \text{A} \rightarrow \text{A}^* + \text{A}$ rate of formation of $\text{A}^* = k_a[\text{A}]^2$

Step 2 The energized molecule might lose its excess energy by collision with another molecule: $\text{A} + \text{A}^* \rightarrow \text{A} + \text{A}$ rate of deactivation of $\text{A}^* = k_a'[\text{A}][\text{A}^*]$

Step 3 Alternatively, the excited molecule might shake itself apart and form products P – it might undergo the unimolecular decay:



If the unimolecular step, Step 3, is slow enough to be the rate-determining step, the overall reaction will have first-order kinetics. We can show this by applying the steady-state approximation:

$$\begin{aligned} \text{Net rate of formation of A}^* &= k_a[\text{A}]^2 - k_a'[\text{A}][\text{A}^*] - k_b[\text{A}^*] = 0 \\ [\text{A}^*] &= k_a[\text{A}]^2 / (k_b + k_a'[\text{A}]) \quad \text{P} = k_b[\text{A}^*] = k_a k_b [\text{A}]^2 / (k_b + k_a'[\text{A}]) \end{aligned}$$

Suppose that the rate of deactivation of A^* by its collisions with A is much greater than the rate of unimolecular decay of A^* to products – the unimolecular decay of A^* is the rate determining step. Then, $k_a'[\text{A}][\text{A}^*] \gg k_b[\text{A}^*]$, that is $k_a'[\text{A}] \gg k_b$. If that is the case, we can neglect k_b in the denominator of the rate law:

$$\text{Rate of formation of P} = k[\text{A}], \quad k = k_a k_b / k_a' \text{ – a first-order rate law.}$$

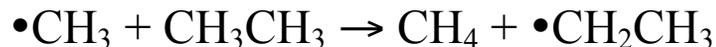
The kinetics of complex reactions

Chain reactions

Many gas-phase reactions and liquid-phase polymerization reactions are **chain reactions** – reactions in which an intermediate produced in one step generates a reactive intermediate in a subsequent step, then that intermediate generates another reactive intermediate, and so on.

The intermediates responsible for the propagation of a chain reaction – **chain carriers**. In a **radical chain reaction** the chain carriers are radicals. Ions may also propagate chains, and in nuclear fission the chain carriers are neutrons.

The first chain carriers are formed in the **initiation step** of the reaction – Cl atoms are formed by the dissociation of Cl₂ either as a result of vigorous intermolecular collisions in a thermolysis reaction or as a result of absorption of a photon in a photolysis reaction. The chain carriers produced in the initiation step attack other reactant molecules in the **propagation steps** – each attack gives rise to a new chain carrier:

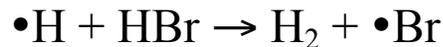


The attack may result in the production of more than one chain carrier – a **branching step**:



The attack of one O atom on an H₂O molecule forms two OH.

The chain carrier might attack a product molecule formed earlier in the reaction – this attack decreases the net rate of formation of product – a **retardation step**. For example, in a photochemical reaction in which HBr is formed from H₂ and Br₂, an H atom might attack an HBr molecule:



retardation does not end the chain – one radical (H) gives rise to another (Br), but it does deplete the concentration of the product.

Elementary reactions in which radicals combine and end the chain – **termination steps**:



In an **inhibition step**, radicals are removed other than by chain termination – by reaction with the walls of the vessel or with foreign radicals:



The NO molecule has an unpaired electron and is a very efficient chain inhibitor.

The rate laws of chain reactions

A chain reaction can have a simple rate law. A first example: the **pyrolysis** (thermal decomposition in the absence of air of acetaldehyde CH_3CHO), which is found to be three-halves order in CH_3CHO :



Some ethane is also detected. The **Rice-Herzfeld mechanism** is as follows:



The chain carriers $\cdot\text{CH}_3$ and $\cdot\text{CHO}$ are formed in the initiation step. For simplicity, we ignore the subsequent reactions of $\cdot\text{CHO}$ – they give rise to the formation CO and the by-product H_2 .

The chain carriers $\cdot\text{CH}_3$ attacks other reactants molecules in the propagation steps. Radicals combine and end the chain in the termination step.

To test the proposed mechanism we need to show that it leads to the observed rate law. According to the steady-state approximation, the net rate of change of the intermediates ($\bullet\text{CH}_3$ and $\text{CH}_3\text{CO}\bullet$) may be set equal to zero:

$$\frac{d[\text{CH}_3]}{dt} = k_i[\text{CH}_3\text{CHO}] - k_p[\text{CH}_3][\text{CH}_3\text{CHO}] + k_p'[\text{CH}_3\text{CO}] - 2k_t[\text{CH}_3]^2 = 0$$

$$\frac{d[\text{CH}_3\text{CO}]}{dt} = k_p[\text{CH}_3][\text{CH}_3\text{CHO}] - k_p'[\text{CH}_3\text{CO}] = 0$$

The sum of the two equations is $k_i[\text{CH}_3\text{CHO}] - 2k_t[\text{CH}_3]^2 = 0$

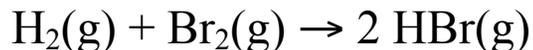
$$[\text{CH}_3] = \left(\frac{k_i}{2k_t}\right)^{1/2} [\text{CH}_3\text{CHO}]^{1/2} \quad \text{the steady-state concentration of CH}_3 \text{ radical}$$

It follows that the rate of formation of CH_4 is

$$\frac{d[\text{CH}_4]}{dt} = k_p[\text{CH}_3][\text{CH}_3\text{CHO}] = k_p \left(\frac{k_i}{2k_t}\right)^{1/2} [\text{CH}_3\text{CHO}]^{3/2}$$

$$k = k_p \left(\frac{k_i}{2k_t}\right)^{1/2}$$

In many cases, a chain reaction leads to a complicated rate law.

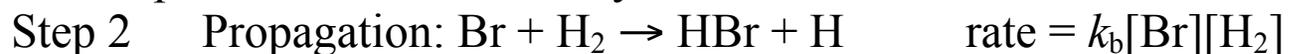


$$\text{Rate of formation of HBr} = k[\text{H}_2][\text{Br}_2]^{3/2}/([\text{Br}_2] + k'[\text{HBr}])$$

The complexity of the rate law suggests that a complicated mechanism is involved.



At low pressures this elementary reaction is bimolecular and second-order in Br_2 .



The 'third body', M, a molecule of an inert gas, removes the energy of recombination; the constant concentration of M has been included into the rate constant k_d . Other possible termination steps include the recombination of H atoms to H_2 and the combination of H and Br atoms; however, only Br atom recombination appears to be important.

HBr is formed in step 2 and consumed in step 3:

$$\text{Net rate of formation of HBr} = k_b[\text{Br}][\text{H}_2] + k_b'[\text{H}][\text{Br}_2] - k_c[\text{H}][\text{HBr}]$$

We apply the steady-state approximation to find [H] and [Br]:

$$\text{Net rate of formation of H} = k_b[\text{Br}][\text{H}_2] - k_b'[\text{H}][\text{Br}_2] - k_c[\text{H}][\text{HBr}] = 0$$

$$\text{Net rate of formation of Br} = 2k_a[\text{Br}_2] + k_b'[\text{H}][\text{Br}_2] + k_c[\text{H}][\text{HBr}] - 2k_d[\text{Br}]^2 = 0$$

$$[\text{Br}] = (k_a[\text{Br}_2]/k_d)^{1/2} \quad [\text{H}] = k_b(k_a/k_d)^{1/2}[\text{H}_2][\text{Br}_2]^{1/2}/(k_b'[\text{Br}_2] + (k_c/k_b)[\text{HBr}])$$

We substitute these concentrations into the equation for net rate of formation of [HBr]:

$$\text{Rate of formation of HBr} = 2k_b(k_a/k_d)^{1/2}[\text{H}_2][\text{Br}_2]^{3/2}/([\text{Br}_2] + (k_c/k_b')[\text{HBr}])$$

This equation is in the same form as the empirical rate law with $k = 2k_b(k_a/k_d)^{1/2}$ $k' = k_c/k_b'$

The proposed mechanism is consistent with the observed rate law. Additional support for the mechanism would come from the detection of the proposed intermediates (by spectroscopy), and the measurement of individual rate constants for the elementary steps and confirming that they correctly reproduced the observed composite rate constants.

Explosions

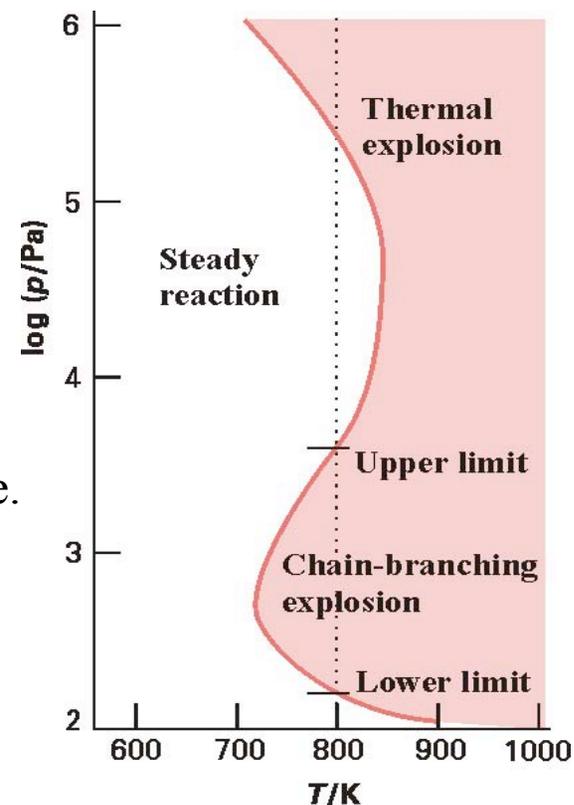
A **thermal explosion** is due to the rapid increase of reaction rate with temperature. If the energy released in an exothermic reaction cannot escape, the temperature of the reaction system rises – the reaction goes faster – faster rise of temperature – the reaction goes even faster, catastrophically fast. A **chain-branching explosion** – may occur when there are chain branching steps in a reaction – the number of chain carriers grows exponentially – the rate of reaction may cascade into an explosion.



Although the net reaction is very simple, the mechanism is very complex: a chain reaction is involved and the chain carriers include H, O, OH, and O₂H radicals. Some steps are:



The occurrence of an explosion depends on the temperature and pressure of the system – **explosion regions**. At very low pressures, the system is outside the explosion region – the mixture reacts smoothly. At these pressures the chain carriers produced in the branching steps can reach the walls and combine. Increasing the pressure takes the system through the **lower explosion limit** (for $T > 730 \text{ K}$). The mixture then explodes because the chain carriers react before reaching the walls – the branching reactions are explosively efficient. The reaction is smooth when the pressure is above the **upper explosion limit**.

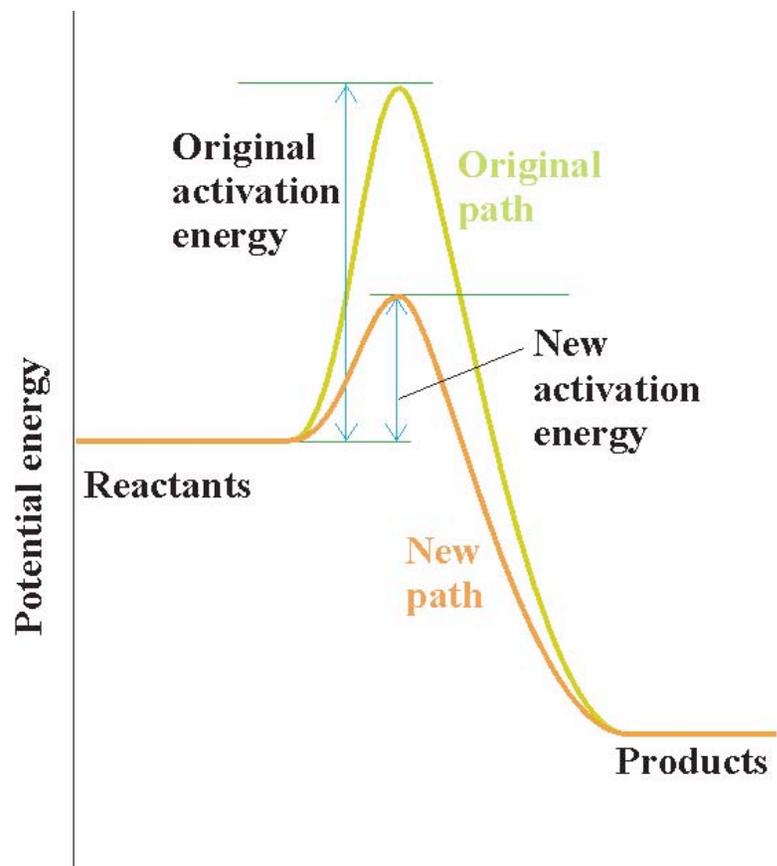


The concentration of molecules in the gas is then so great that the radicals produced in the branching reaction combine in the body of the gas: the $\text{O}_2 + \text{H} \rightarrow \text{O}_2\text{H}$ reaction can occur facilitated by third-body collisions – the third body (M) can remove the excess energy and allow the formation of the bond. The O₂H radical is relatively unreactive and can reach the walls, where it is removed. At lower pressures three-particle collisions are unimportant and recombination is much slower. At higher pressures, when three-particle collisions are important, the explosive propagation of the chain by the radicals is partially quenched. If the pressure is further increased, the reaction rate increases so much that a thermal explosion occurs.

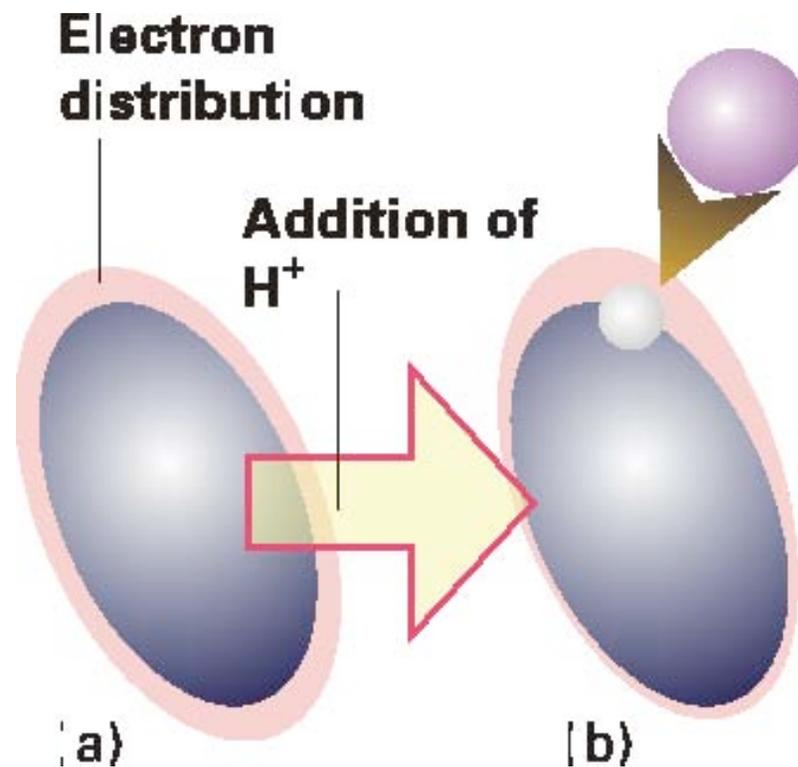
Catalysis

Raising temperature is one way of accelerating a reaction. Another way – to find a means of lowering the activation energy – then at the same temperature a higher proportion of molecules would be able to pass over the activation barrier. The height of the activation barrier for a given path is outside our control: it is determined by the electronic structures of the reactants and the arrangement of atoms in the activated complex. To change an activation barrier, we need to provide another route for the reaction – another reaction mechanism.

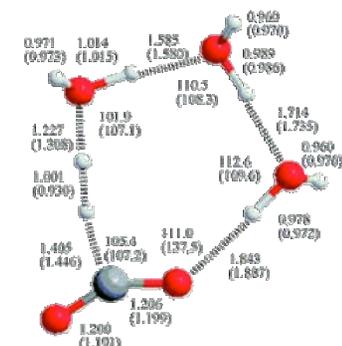
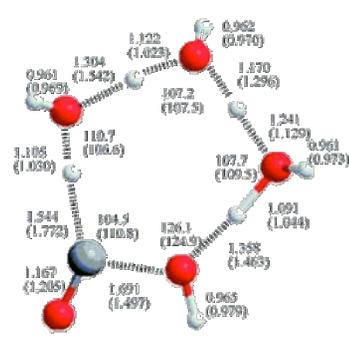
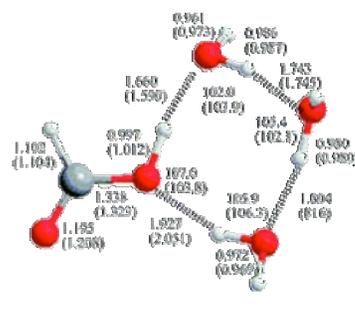
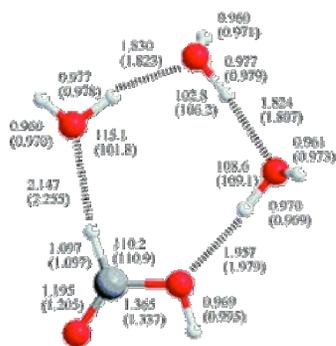
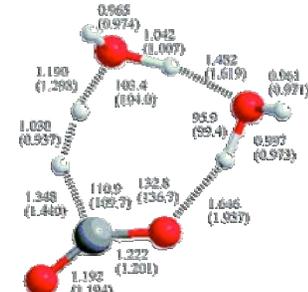
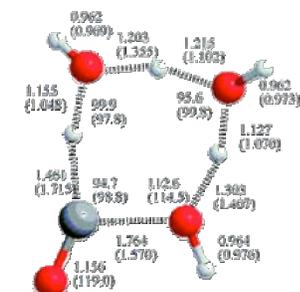
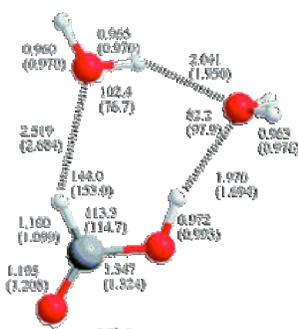
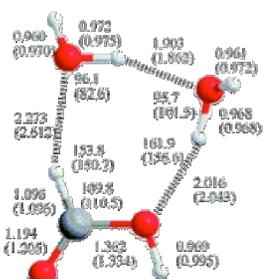
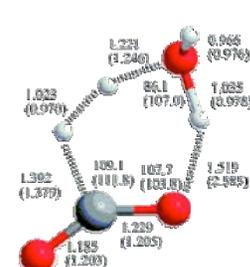
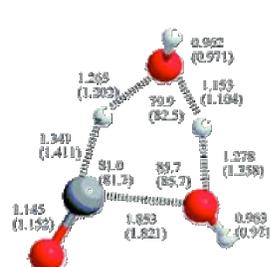
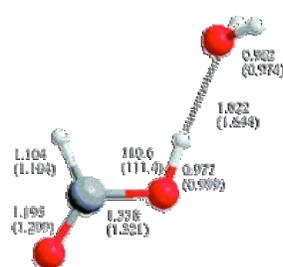
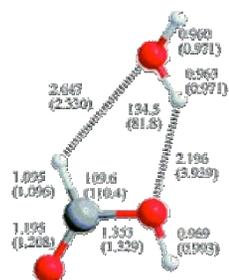
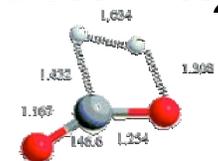
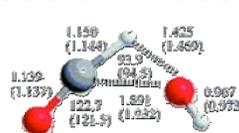
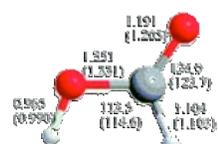
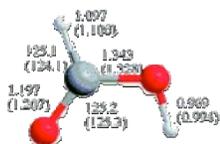
A **catalyst**, a species that increases the reaction rate but is not itself consumed in a reaction, acts by providing an alternative reaction path with a lower activation energy. A catalyst that is in the same phase as the reactants (for example, is dissolved in the same solvent) – a **homogeneous catalyst**. A catalyst that is in a different phase – most commonly a solid introduced into a gas-phase reaction – a **heterogeneous catalyst**. Many industrial processes make use of heterogeneous catalysts, which include platinum, rhodium, zeolites, and various metal oxides, but increasingly attention is turning to homogeneous catalysts, partly because they are easier to cool.



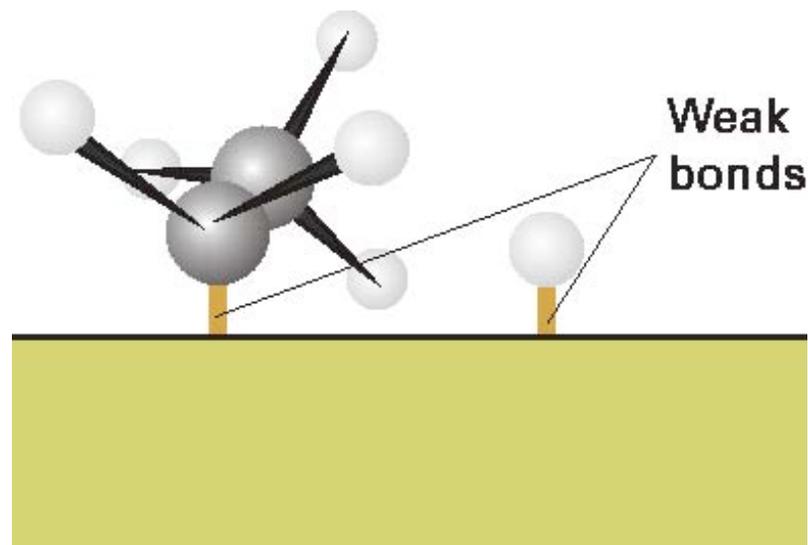
A strong acid can act as a homogeneous catalyst for some reactions, and its action illustrates the general principle of catalysis, that a new reaction pathway is being provided. A strong acid can donate a proton to an organic species, and the resulting cation (the conjugate acid of the organic compound) may have a lower activation energy for reaction with another reactant.



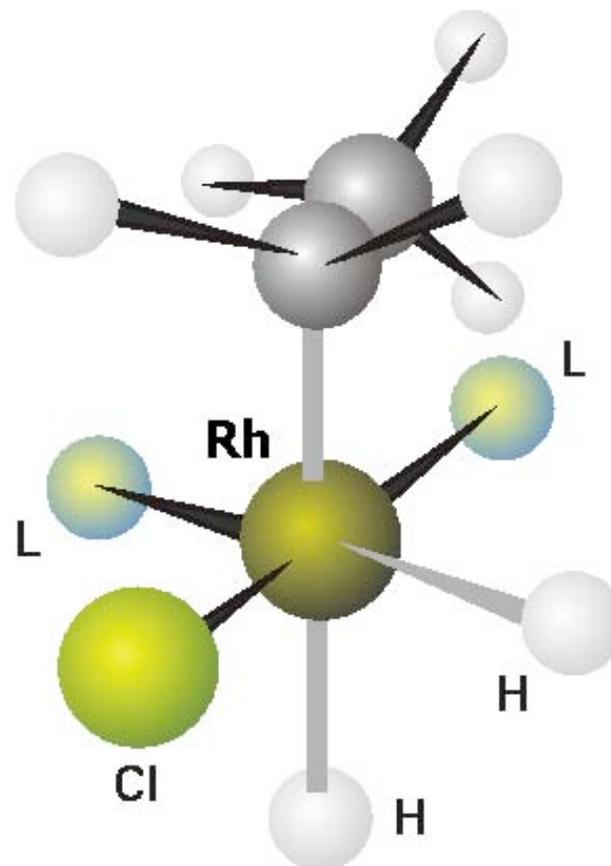
Catalysis by water molecules in solution: decomposition of formic acid



A metal acts as a heterogeneous catalyst for certain gas-phase reactions by providing a surface to which a reactant can attach by **chemisorption**, the formation of chemical bonds to a surface. For example, hydrogen molecules may attach as atoms to a nickel surface, and these atoms react much more readily with another species (such as a hydrocarbon) than the original molecules. The chemisorption step therefore results in a reaction pathway with a lower activation energy than in the absence of the catalyst.



Modern homogeneous catalysts include complexes of rhodium or palladium, which can form bonds to organic molecules, and enable them to undergo rearrangements at temperatures far below those required in the absence of a catalyst. These complexes can be regarded as the limit of a metal surface – their active site is just a single metal atom.



Nature produced catalysts long before chemists. Natural catalysts are the protein molecules called *enzymes*. Despite the complexity of these large molecules, the central mode of action is the same as described above. The enzyme provides a reaction pathway with a low activation energy and accelerates the reaction for which it has evolved.

Enzyme reactions

The mechanism of enzyme action

One of the earliest descriptions of the action of enzymes – the **Michaelis-Menten mechanism**:

Step 1 The bimolecular formation of a combination, ES, of the enzyme and a substrate:



Step 2 The unimolecular decomposition of the complex:



Step 3 The unimolecular formation of products and the release of the enzyme from its combination with the substrate:



The Michaelis-Menten rate law

The product is formed (irreversibly) in step 3: rate of formation of P = $k_b[ES]$

To calculate the concentration [ES] we write an expression for the net rate of formation of ES allowing for its formation in step 2 and its removal in steps 2 and 3. Net rate is then set to zero (the steady-state approximation):

Net rate of formation of ES = $k_a[E][S] - k_a'[ES] - k_b[ES] = 0$ $[ES] = k_a[E][S]/(k_a' + k_b)$
[E] and [S] – molar concentrations of the *free* enzyme and *free* substrate. If $[E]_0$ is the total concentration of enzyme, then $[E] + [ES] = [E]_0$

Only a little enzyme is added – the free substrate concentration is almost the same as the total substrate concentration and we can ignore the slight difference between [S] and $[S] + [ES]$.

$$[ES] = k_a([E]_0 - [ES])[S]/(k_a' + k_b) \quad [ES] = k_a[E]_0[S]/(k_a' + k_b + k_a[S])$$

Rate of formation of P = $k[E]_0$ with $k = k_b[S]/([S] + K_M)$

$K_M = (k_a' + k_b)/k_a$ – the **Michaelis constant**.

$$P = k[E]_0 \quad k = k_b[S]/([S] + K_M) \quad K_M = (k_a' + k_b)/k_a$$

The rate of enzymolysis is first-order in the enzyme concentration, but the effective rate constant k depends on the concentration of substrate. When $[S] \ll K_M$, the effective rate constant is $k_b[S]/K_M$ – the rate increases linearly with $[S]$ at low concentrations. When $S \gg K_M$, the effective rate constant is k_b :

$$\text{rate of formation of P} = k_b[E]_0$$

In this case, the rate is independent of $[S]$ because there is so much substrate present that it remains at effectively the same concentration even though products are being formed.

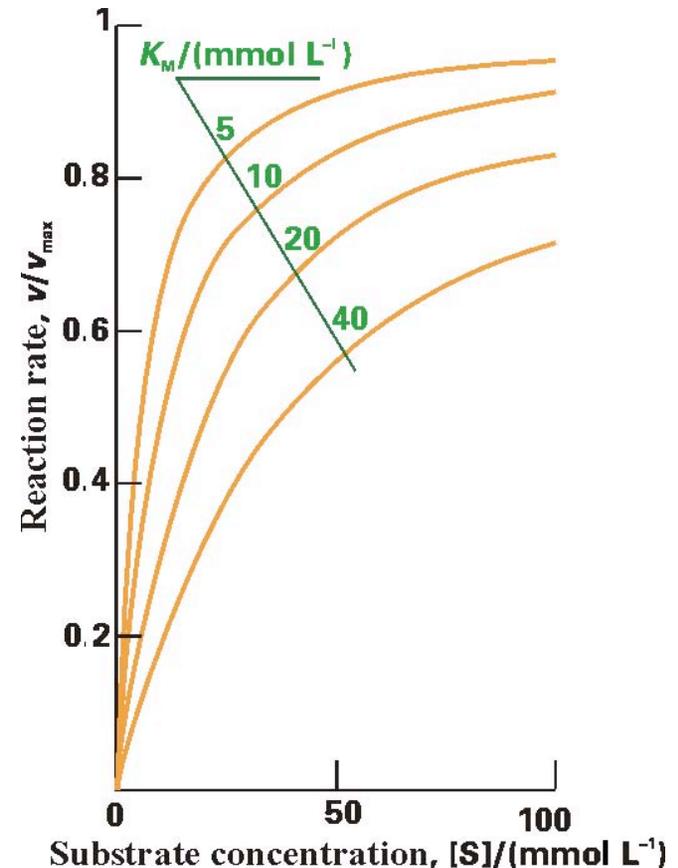
Under these conditions, the rate of formation of product is a maximum – $k_b[E]_0$ is called the **maximum velocity**, v_{\max} , of the enzymolysis:

$$v_{\max} = k_b[E]_0$$

k_b – the **maximum turnover number**. The rate-determining step is step 3, because there is ample ES present (because S is so abundant) – the rate is determined by the rate at which ES reacts to form the product.

The reaction rate v at a general substrate composition:

$$v = [S]v_{\max}/([S] + K_M)$$



$$v = [S]v_{\max}/([S] + K_M)$$

This equation is the basis of the analysis of enzyme kinetic data by using a **Lineweaver-Burk plot** – a graph of $1/v$ (the reciprocal of the reaction rate) against $1/[S]$ (the reciprocal of substrate concentration).

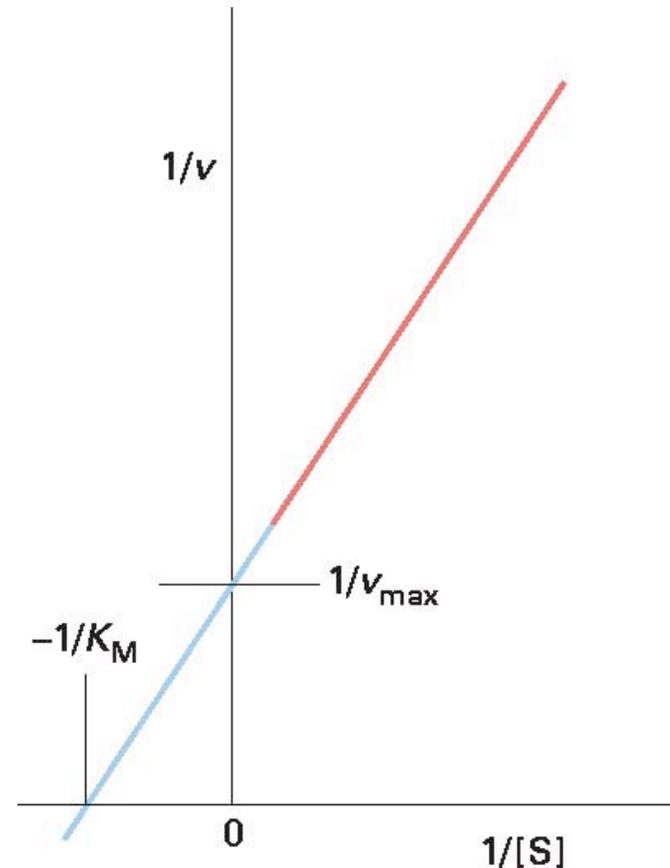
$$\frac{1}{v} = \frac{[S] + K_M}{[S]v_{\max}} = \frac{1}{v_{\max}} + \left(\frac{K_M}{v_{\max}}\right) \frac{1}{[S]}$$

This expression has the form

$$y = \text{intercept} + \text{slope} \times x$$

$$y = 1/v \quad x = 1/[S]$$

We expect to obtain a straight line when we plot $1/v$ against $1/[S]$. The slope of the straight line is K_M/v_{\max} and the extrapolated intercept at $1/[S] = 0$ is $1/v_{\max}$. Therefore, the intercept can be used to find v_{\max} , and then that value combined with the slope to find the value of K_M . Alternatively, the extrapolated intercept with the horizontal axis (where $1/v = 0$) occurs at $1/[S] = -1/K_M$.



Analyzing a Lineweaver-Burk plot

Several solutions containing a substrate at different concentrations were prepared and the same small amount of enzyme was added to each one. The following data were obtained on the initial rates of the formation of product:

$[S]/(\mu\text{mol L}^{-1})$	10.0	20.0	40.0	80.0	120.0	180.0	300.0
$v/(\mu\text{mol L}^{-1} \text{s}^{-1})$	0.32	0.58	0.90	1.22	1.42	1.58	1.74

Determine the maximum velocity and the Michaelis constant for the reaction.

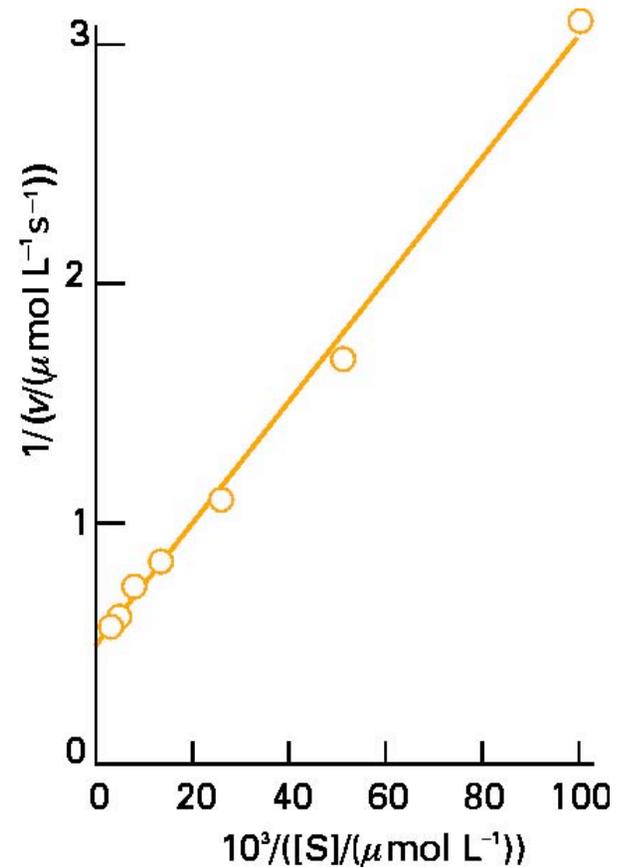
We construct a Lineweaver-Burk plot by drawing up a table of $1/[S]$ and $1/v$. The intercept at $1/[S] = 0$ is $1/v_{\text{max}}$ and the slope of the line through the points is K_M/v_{max} . K_M is found from the slope divided by the intercept:

$10^3/[S]/(\mu\text{mol L}^{-1})$	100	50.0	25.0	12.5	8.33	5.56	3.33
$1/v/(\mu\text{mol L}^{-1} \text{s}^{-1})$	3.1	1.7	1.1	0.820	0.704	0.633	0.575

A least-square analysis gives an intercept at 0.476 and a slope at 26.17. It follows that

$$v_{\text{max}}/(\mu\text{mol L}^{-1} \text{s}^{-1}) = 1/\text{intercept} = 1/0.476 = 2.10$$

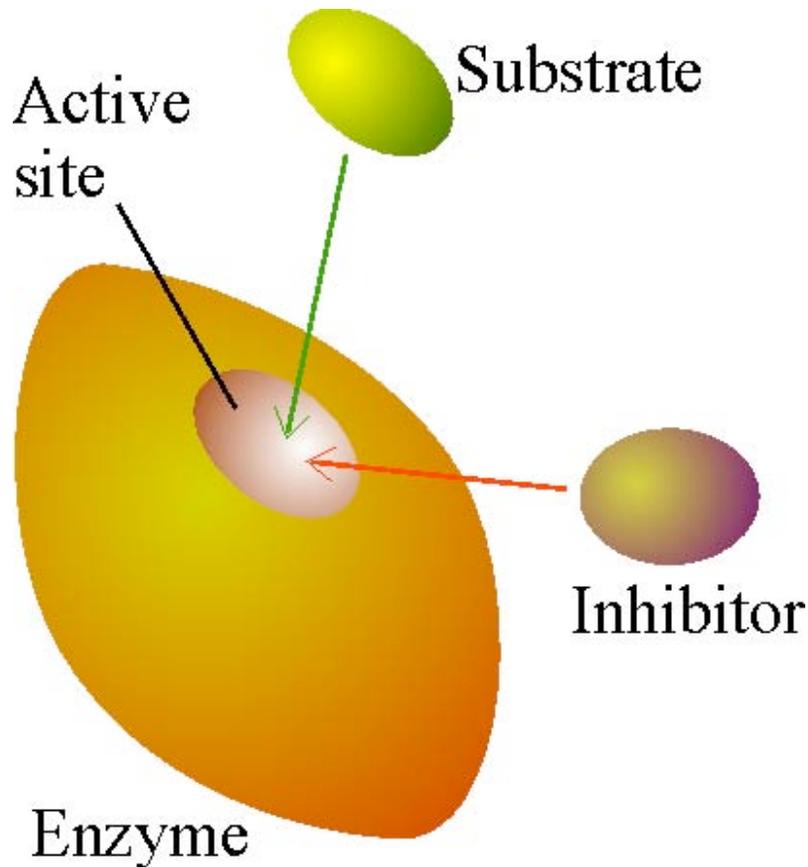
$$K_M/(\mu\text{mol L}^{-1}) = \text{slope}/\text{intercept} = 26.17/0.476 = 55.0$$



Enzyme inhibition

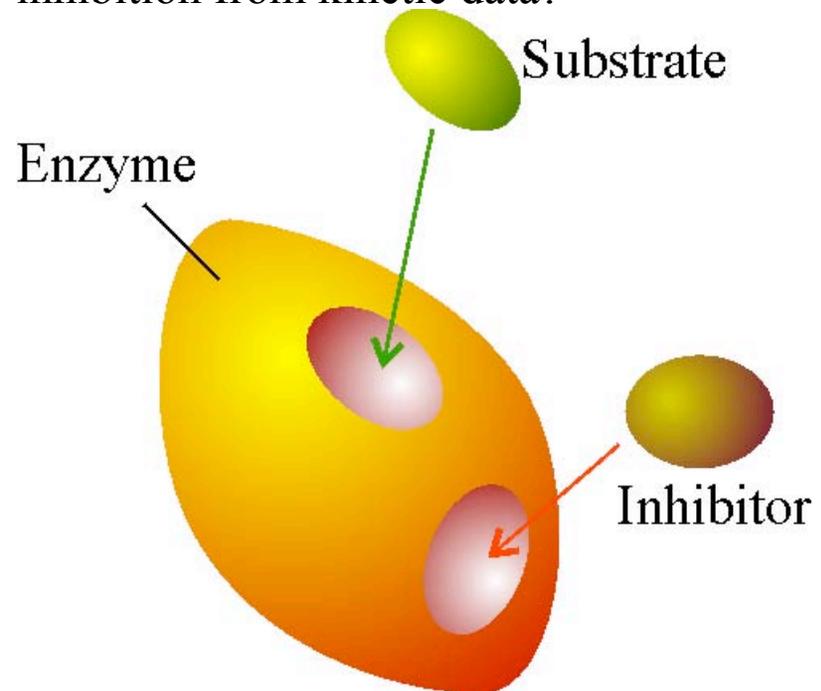
The action of an enzyme may be partially suppressed by the presence of a foreign substance – an **inhibitor**. An inhibitor (I) may be a poison that has been administered to the organism, or it may be a substance naturally present in the cell and involved in its regulatory mechanism.

In **competitive inhibition** the inhibitor competes for the active site and reduces the ability of the enzyme to bind substrate.



In **noncompetitive inhibition** the inhibitor attaches to another part of the enzyme molecule, thereby distorting it and reducing its ability to bind the substrate.

How to distinguish between the two kinds of inhibition from kinetic data?



Competitive inhibition

Suppose that the inhibitor molecule, I, is in equilibrium with the complex EI it forms when it is bound to the active site.

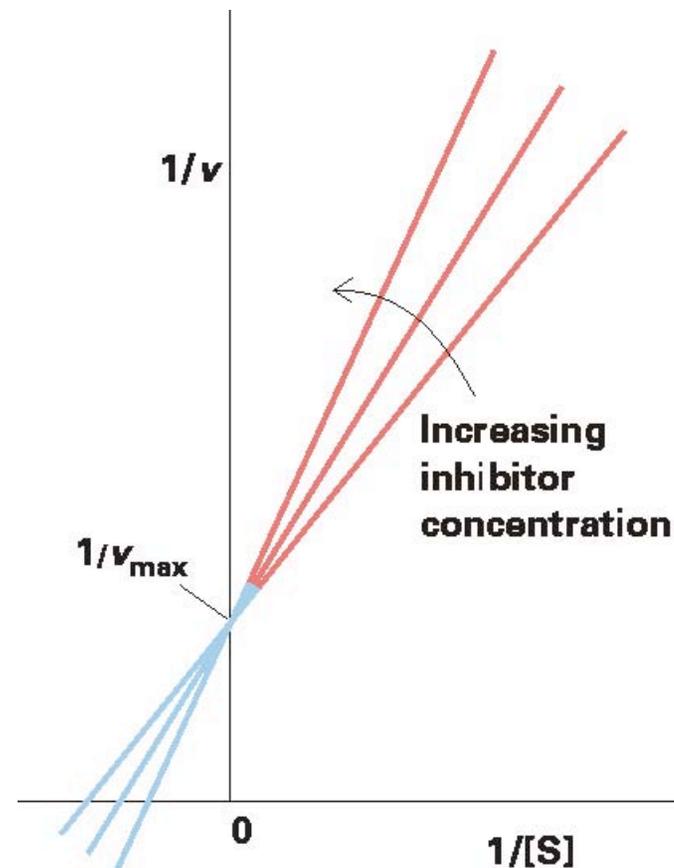
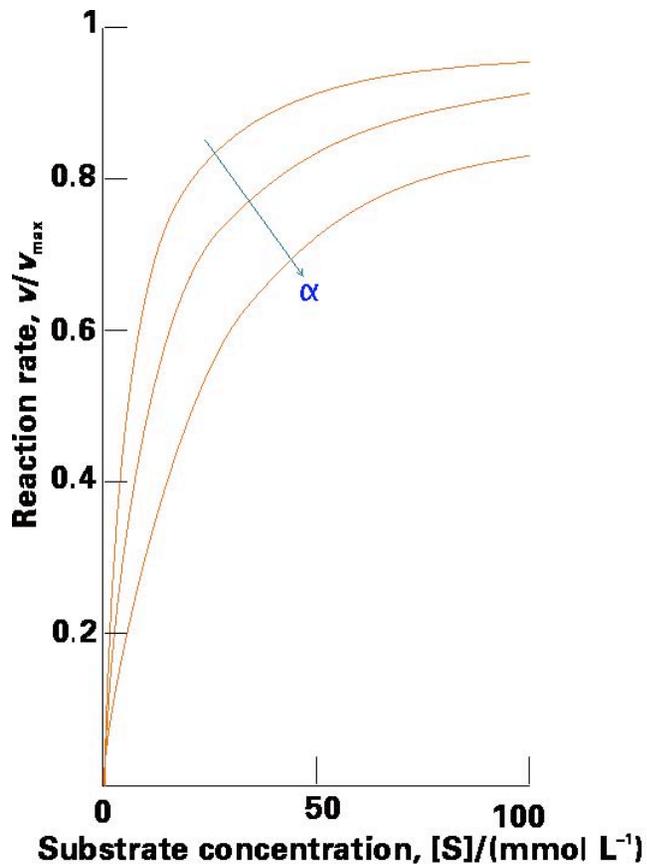


The rate of formation of product turns out to be $v = [S]v_{\max}/([S] + \alpha K_M)$

$$\alpha = 1 + [I]/K_I$$

The role of the inhibitor – to modify K_M to αK_M .

In a Lineweaver-Burk plot, the slope and the intercept with the horizontal axis change as [I] is changed, but the intercept with the vertical axis (the value of $v_{\max} = K_b[E]_0$) remain unchanged.



Noncompetitive inhibition

Suppose that the inhibitor is in equilibrium with a bound state IE, but that site occupied by I is not the active site for the attachment of S. Because I and S are not in competition for the same site, I may also bind to the complex ES to give a complex IES:

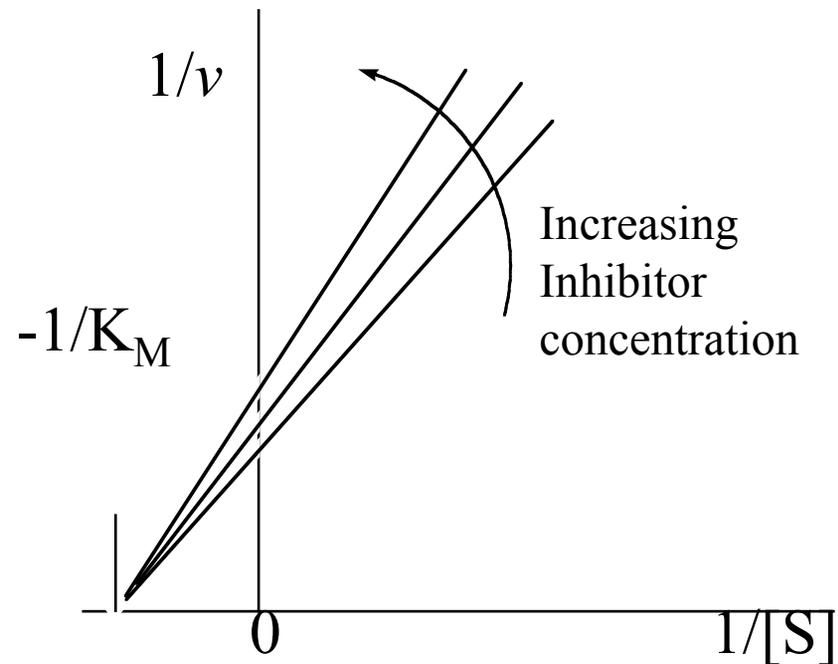


We suppose that, although I and S may both bind to E, the enzyme can bring about change in S only if I is not present – only ES can give rise to products; IES cannot.

The rate of formation of product turns out to be

$$v = [\text{S}]v_{\max} / \alpha([\text{S}] + K_M) \quad \alpha = 1 + [\text{I}]/K_I$$

In a Lineweaver-Burk plot with different values of [I], the straight lines now pass through a common intercept with the horizontal axis (because $1/v = 0$ at $1/[\text{S}] = -1/K_M$ independent of the inhibitor properties), but the slope and the intercept with the vertical axis both increase as the concentration of inhibitor is increased.



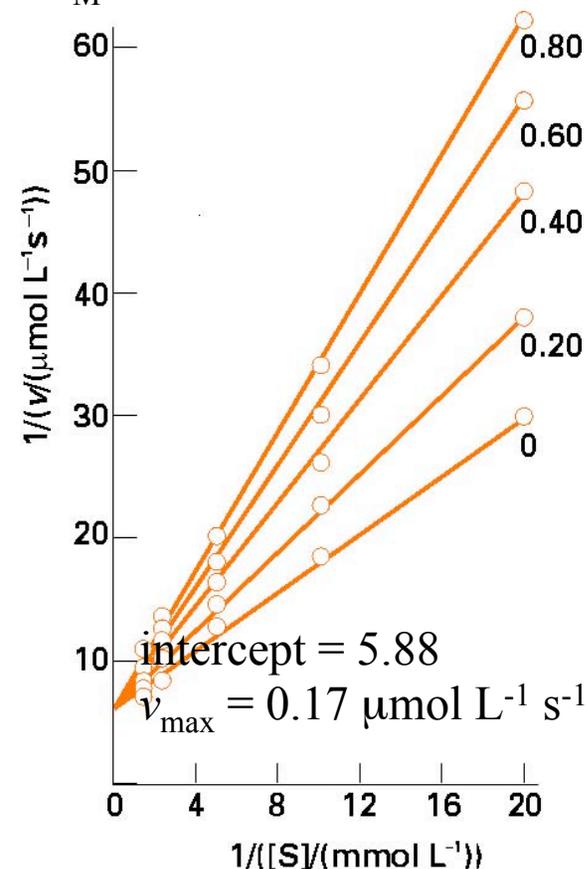
Distinguishing between types of inhibition

Five solutions of a substrate S were prepared with the concentrations given in the first column below and each one was divided into five equal volumes. The same concentration of enzyme was present in each one. An inhibitor I was then added in five different concentrations to the samples, and the initial rate of formation of product was determined with the results given below. Does the inhibitor acts competitively and noncompetitively? Determine K_I and K_M .

[S]/(mmol L ⁻¹)	0	[I]/(mmol L ⁻¹)				
		0.20	0.40	0.60	0.80	
0.050	0.033	0.026	0.021	0.018	0.016	
0.10	0.055	0.045	0.038	0.033	0.029	
0.20	0.083	0.071	0.062	0.055	0.050	
0.40	0.111	0.100	0.091	0.084	0.077	
0.60	0.126	0.116	0.108	0.101	0.094	

We draw a series of Lineweaver-Burk plots for different inhibitor concentrations and from the behavior of the plots determine whether the inhibition is competitive or noncompetitive.

1/[S]/(mmol L ⁻¹)	0	1/v/($\mu\text{mol L}^{-1} \text{s}^{-1}$) for [I]/(mmol L ⁻¹)				
		0.20	0.40	0.60	0.80	
20	30	38	48	56	62	
10	18	22	26	30	34	
5.0	12	14	16	18	20	
2.5	9.01	10.0	11.0	11.9	13.0	
1.7	7.94	8.62	9.26	9.90	10.6	



The five plots pass through same intercept on the vertical axis – the inhibition is competitive.

To find K_I , we need to determine the slope at each value of $[I]$, which is equal to

$$\alpha K_M/v_{\max} = K_M/v_{\max} + K_M[I]/(K_I v_{\max})$$

Then, we plot this slope against $[I]$: the intercept at $[I] = 0$ is the value of K_M/v_{\max} and the slope is $K_M/(K_I v_{\max})$

The slopes of the lines are as follows:

$[I]/(\text{mmol L}^{-1})$	0	0.20	0.40	0.60	0.80
Slope	1.219	1.627	2.090	2.489	2.832

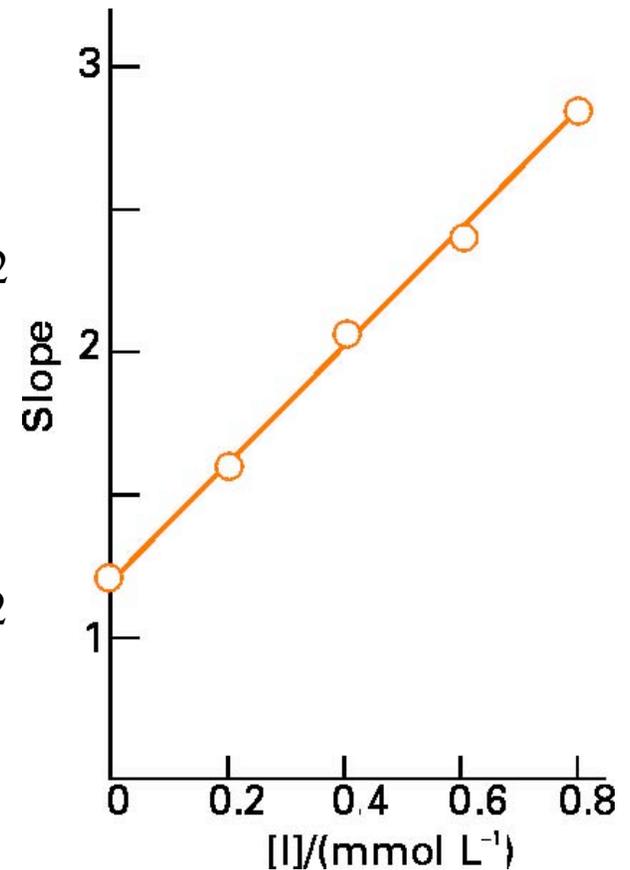
These values are plotted on the right.

The intercept at $[I] = 0$ is 1.235, so

$$K_M = \text{intercept} \times v_{\max} = 0.21 \text{ mmol L}^{-1}$$

The slope of the line is 1.992, so

$$K_I/(\text{mmol L}^{-1}) = K_M/(\text{slope} \times v_{\max}) = 0.21/(1.992 \times 0.17) = 0.62$$



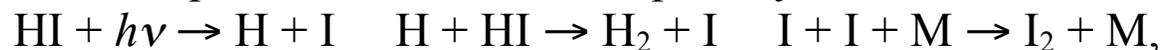
Photochemical processes

Many reactions can be initiated by the absorption of light – photochemical processes capture the Sun's radiant energy. Some of these reactions lead to the heating of the during the daytime by absorption in the ultraviolet region. Other include the absorption of red and blue light by chlorophyll and the subsequent use of energy to bring about the synthesis of carbohydrates from carbon dioxide and water.

Quantum yield

A molecule acquires enough energy to react by absorbing a photon. If the frequency of the radiation is ν , then the energy of each photon is $h\nu$, where h is Planck's constant, $h = 6.62608 \times 10^{-34}$ J s. Therefore, when a molecule absorbs radiation, it acquires the energy brought by the photon and can use that energy to undergo further reaction. However, not every excited molecule may form a specific primary product because there are many ways in which the excitation may be lost other than dissociation or ionization. We therefore speak of the **primary quantum yield**, ϕ – the number of reactant molecules producing specific primary products for each photon absorbed. If each molecule that absorbs a photon undergoes a reaction (for instance, dissociation), $\phi = 1$. If none does, because the excitation energy is lost before the molecule has time to dissociate, $\phi = 0$.

One successfully excited molecule might initiate the consumption of more than one reactant molecules. The **overall quantum yield**, Φ - the number of reactant molecules that react for each photon absorbed. In the photolysis of HI,



the overall quantum yield is 2: the absorption of one photon leads to the destruction of two HI molecules.

In a photochemically initiated chain reaction, Φ may be very large – the values of $\sim 10^4$ are common – the chain reaction acts as a chemical amplifier of the initial absorption step.

Using the quantum yield

The overall quantum yield for the formation of ethane from 4-heptanone with 313 nm light is 0.21. How many molecules of 4-heptanone per second, and what chemical amount per second, are destroyed when the sample is irradiated with a 50 W, 313 nm source under conditions of total absorption?

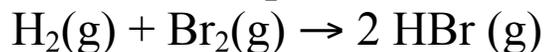
We need to calculate the number of photon emitted by the lamp per second, all are absorbed – this number is the power divided by the energy of a single photon ($E = h\nu$, with $\nu = c/\lambda$):

$$\text{Rate of photon production} = P/(hc/\lambda) = (50 \text{ J s}^{-1}) \times (313 \times 10^{-9} \text{ m}) / \{ (6.62608 \times 10^{-34} \text{ J s}) \times (2.99792 \times 10^8 \text{ m s}^{-1}) \} = 7.9 \times 10^{19} \text{ s}^{-1}$$

$$\text{The number of 4-heptanone molecules destroyed per second} = 0.21 \times 7.9 \times 10^{19} \text{ s}^{-1} = 1.7 \times 10^{19} \text{ s}^{-1} \text{ or } 2.8 \times 10^{-5} \text{ mol s}^{-1}.$$

Photochemical rate laws

Consider the photochemical activation of the reaction



In place of the first step in the thermal reaction we have



I_{abs} – the number of photons of the appropriate frequency divided by the time interval and the volume. Because the thermal reaction mechanism had $k_a[\text{Br}_2]$ in place of I_{abs} , I_{abs} should take place of $k_a[\text{Br}_2]$ in the rate law derived for the thermal reaction scheme:

Rate of formation of HBr =

$$2k_b(1/k_d)^{1/2}[\text{H}_2][\text{Br}_2]I_{\text{abs}}^{1/2}/([\text{Br}_2] + (k_c/k_b')[\text{HBr}])$$

The reaction rate should depend on the square root of the absorbed light intensity.