

# BIO134: Chemical Kinetics

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## Contents

<b>1</b>	<b>Thermodynamics</b>	<b>3</b>
1.1	The 1st and 2nd Laws . . . . .	3
1.2	Gibbs Free Energy . . . . .	4
1.3	Standard Gibbs Free Energy and Equilibrium Constant . . . . .	5
<b>2</b>	<b>Reaction Rate and Rate Law</b>	<b>7</b>
2.1	Rate of reaction . . . . .	7
2.1.1	Stoichiometry . . . . .	8
2.2	Rate Law . . . . .	9
2.3	Temperature Dependence . . . . .	10
2.3.1	Arrhenius law . . . . .	10
<b>3</b>	<b>Data analysis</b>	<b>12</b>
3.1	Unimolecular reaction $A \rightarrow P$ . . . . .	12
3.1.1	Zero order reaction . . . . .	13
3.1.2	First order reaction . . . . .	13
3.1.3	Second order reaction . . . . .	14
3.1.4	Summary . . . . .	14
3.1.5	Half-life Method . . . . .	15
3.2	More than one species involved . . . . .	17
3.2.1	Isolation Method . . . . .	17
3.2.2	Initial Rate Method . . . . .	17

<b>4</b>	<b>Simple Reactions</b>	<b>20</b>
4.1	Reversible reaction approaching to equilibrium . . . . .	20
4.2	Pre-equilibrium . . . . .	21
4.3	Consecutive reaction . . . . .	23
4.4	Rate-determining process . . . . .	25
<b>5</b>	<b>Steady-state approximation</b>	<b>25</b>
5.1	Application . . . . .	26
5.2	Exercise . . . . .	27
5.3	Michaelis-Menten equation . . . . .	27

## Prerequisites

- Basic knowledge of A-level Kinetics. (e.g., S-Cool AS&A2 Level Chemistry Revision Guide, [http://www.s-cool.co.uk/topic\\_index.asp?subject\\_id=7](http://www.s-cool.co.uk/topic_index.asp?subject_id=7))

## Readings

- Housecroft and Constable, Chemistry, 2nd ed., Prentice Hall, Chapter 14.
- Atkins, The Elements of Physical Chemistry, 3rd ed., Oxford, Chapter 10-11.

## Acknowledgments

Many of the diagrams in this lecture note have been downloaded from the web pages of these textbooks.

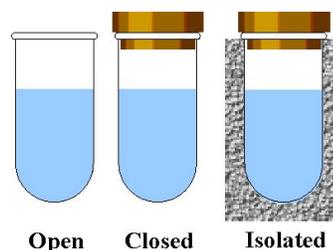
# 1 Thermodynamics

Let us first fix some terminologies.

**Open systems** can exchange both energy (heat) and matter with its surroundings.

**Closed systems** can exchange energy (heat) but not matter with its surroundings.

**Isolated systems** can exchange neither energy (heat) nor matter with its surroundings.



## 1.1 The 1st and 2nd Laws

The 1st and 2nd laws of thermodynamics can be stated as follows. It is important to note that these apply for energy and entropy within an isolated system.

**The 1st law :**

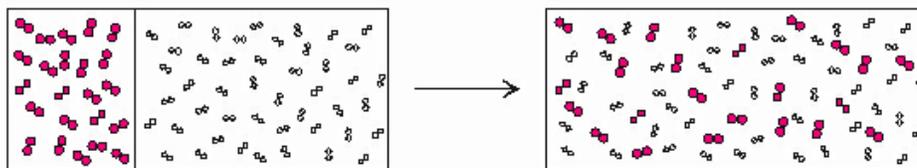
The total energy  $E_{\text{tot}}$  of an isolated system conserves:  $\Delta E_{\text{tot}} = 0$ .

**The 2nd law :**

The total entropy  $S_{\text{tot}}$  of an isolated system tends to increase:  $\Delta S_{\text{tot}} \geq 0$ .

in which  $\Delta E_{\text{tot}}$  and  $\Delta S_{\text{tot}}$  are changes of  $E_{\text{tot}}$  and  $S_{\text{tot}}$  associated with processes occurring in the system.

A typical example of the 2nd law is seen in the diagram below as spontaneous mixing of the two kinds of gases.



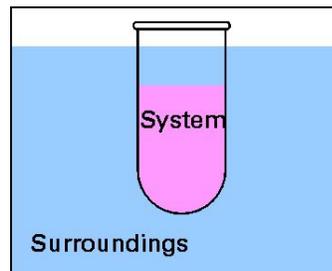
The entropy of the system is closely related to the randomness of the system. In this example of gas mixing, the randomness increases spontaneously, which means that the entropy also increases. In order to define the entropy more precisely in terms of the randomness, we need to learn Statistical Mechanics. However, this is beyond the scope of this lecture course, and we will content with the qualitative connection between the entropy and the randomness.

An important thing to note here is that the spontaneous mixing occurs even when the gases are ideal, i.e., no interaction between the molecules. In this case, there is no energy change (gain or loss) upon mixing of the gases. This means that, the mixing

is not driven by the energy gain but by the entropy gain in terms of the 2nd law of thermodynamics.

## 1.2 Gibbs Free Energy

Let us now consider a System in contact with Surroundings (i.e., heat bath). We assume that the System is closed and the total system of ‘System and Surroundings’ is isolated. The System can thus exchange heat with the Surroundings. The Surroundings is, on the other hand, supposed to be large enough such that its temperature  $T$  is kept constant.



From the 1st law of thermodynamics,\* the enthalpy change of the total system is zero:  $\Delta H_{\text{tot}} = 0$ . Because the total enthalpy change is the sum of the enthalpy change of the System and the Surroundings,  $\Delta H_{\text{tot}} = \Delta H_{\text{sys}} + \Delta H_{\text{surr}}$ , it follows that

$$\Delta H_{\text{sys}} = -\Delta H_{\text{surr}} \quad (1)$$

In other words, the heat is exchanged solely between the System and the Surroundings and goes nowhere else (because the total system is isolated). The enthalpy gain of the System is precisely equal to the loss of the Surroundings.

On the other hand, the 2nd law predicts that the entropy of the total system tends to increase;

$$\Delta S_{\text{total}} = \Delta S_{\text{sys}} + \Delta S_{\text{surr}} \geq 0 \quad (2)$$

However, this does not appear very useful as it only deals with the total system and not the System in which the processes of our interest are taking place. We are more interested in predicting what will happen in the System rather than in the total system that include the Surroundings. We therefore wish to separate our discussion on the System from the Surroundings. To this end, it is useful to define the **Gibbs Free Energy** of the System by

$$\Delta G_{\text{sys}} = \Delta H_{\text{sys}} - T\Delta S_{\text{sys}} \quad (3)$$

This is useful because we can show that the 2nd law  $\Delta S_{\text{tot}} \geq 0$  is essentially equivalent to  $\Delta G_{\text{sys}} \leq 0$ . Thanks to this, we only need to look at the quantities (enthalpy and entropy) of the System and do not have to be bothered by the Surroundings.

The equivalence of  $\Delta S_{\text{tot}} \geq 0$  and  $\Delta G_{\text{sys}} \leq 0$  can be demonstrated as follows. The essential point is that the heat bath (= the Surroundings) is large enough such that the

---

\* Here we assume to be dealing with solution phase systems, as is usually the case in biochemistry, such that the volume change of the system may be neglected. In this case, it would be justified to consider that the enthalpy and the internal energy are identical. In other words, we neglect  $pV$  in  $H = U + pV$ .

equilibrium is maintained in the Surroundings in the course of the processes occurring in the System. Therefore, we may put

$$\Delta G_{\text{surr}} \cong 0 \quad \Rightarrow \quad \Delta H_{\text{surr}} \cong T \Delta S_{\text{surr}} \quad (4)$$

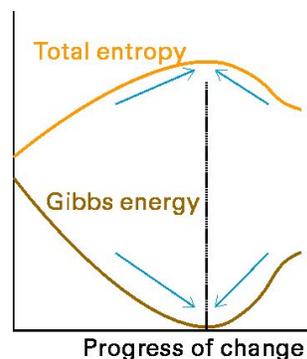
Putting this and Eq (1) into Eq (5), it follows

$$\Delta G_{\text{sys}} = -T(\Delta S_{\text{surr}} + \Delta S_{\text{sys}}) = -T \Delta S_{\text{tot}} \quad (5)$$

Because the absolute temperature  $T$  (in Kelvin) is always positive, Eq (5) means that the 2nd law  $\Delta S_{\text{total}} \geq 0$  is equivalent to  $\Delta G_{\text{sys}} \leq 0$ . In other words, we can consider that  $\Delta G_{\text{sys}}$  effectively contains the influences from the Surroundings, as can be understood from the derivation above.

In summary, the direction of the chemical processes is related to the Gibbs free energy change such that

- The reaction in the System occurs spontaneously only if  $\Delta G_{\text{sys}} < 0$
- The System is in equilibrium when  $\Delta G_{\text{sys}} = 0$



### 1.3 Standard Gibbs Free Energy and Equilibrium Constant

Let us consider a reaction between  $x$  moles of X and  $y$  moles of Y producing  $z$  moles of Z.



The Gibbs free energy change of the reaction is given by

$$\Delta G = \Delta G^\circ + RT \ln Q = \Delta G^\circ + RT \ln \left[ \frac{(a_Z)^z}{(a_X)^x (a_Y)^y} \right] \quad (7)$$

where  $a_{X,Y,Z}$  are the activities of X, Y and Z,  $Q$  is the reaction **quotient**,  $R$  ( $= 8.314 \times 10^{-3} \text{kJ mol}^{-1} \text{K}^{-1}$ ) is the gas constant, and  $\Delta G^\circ$  is the **standard free energy of the reaction**. At equilibrium, the free energy change of the reaction vanishes,  $\Delta G = 0$ , and the reaction quotient  $Q$  is equal to the **equilibrium constant**  $K$ . Then, Eq (7) becomes

$$0 = \Delta G^\circ + RT \ln K \quad \Rightarrow \quad \Delta G^\circ = -RT \ln K \quad (8)$$

Out of equilibrium, the reaction quotient  $Q$  is not equal to the equilibrium constant  $K$ ; in other words, the activities  $a_{X,Y,X}$  are different from their equilibrium values.  $\Delta G$  is then not equal to zero, and its sign determines the spontaneous direction of the reaction: forward or backward reaction when  $\Delta G < 0$  or  $> 0$ , respectively.

**Question:** The equilibrium constant of a reaction,

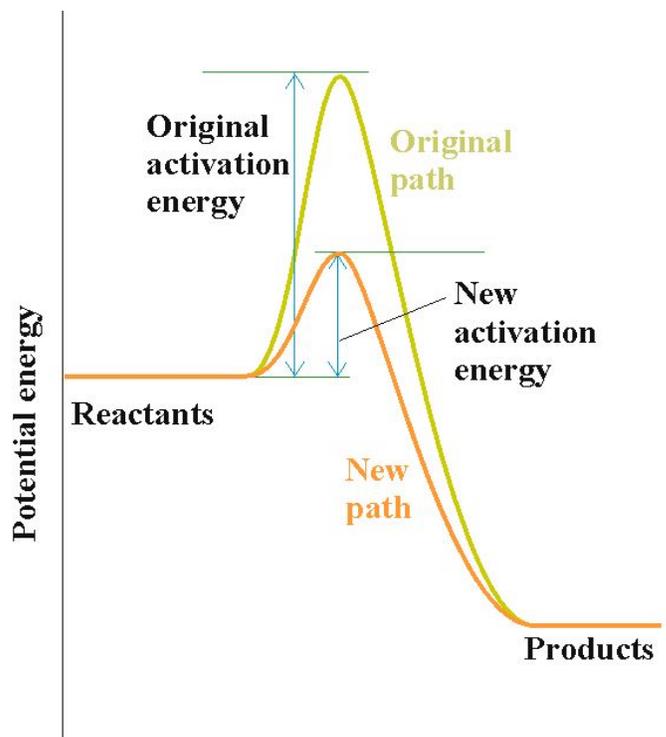


is  $K = 1.3 \times 10^{-10}$  at 298 K.

**Q1.** Calculate  $\Delta G^\circ$ .

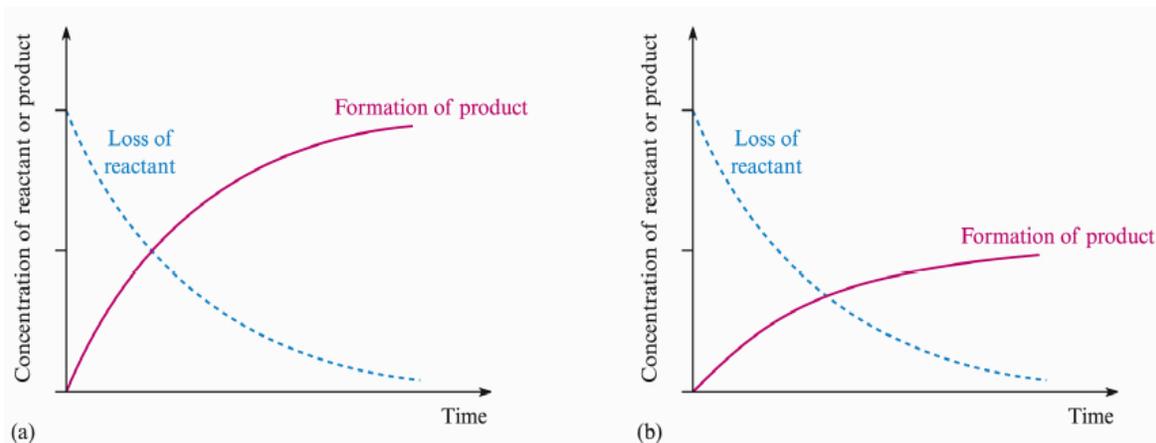
**Q2.** A mixture of  $[\text{C}_6\text{H}_5\text{OH}] = 0.1 \text{ mol dm}^{-3}$  and  $[\text{C}_6\text{H}_5\text{O}^-] = [\text{H}^+] = 10^{-5} \text{ mol dm}^{-3}$  was prepared. Will the reaction occur spontaneously?

In this way,  $\Delta G$  determines the **direction** of the reaction. However, it is important to note that the **rate** of the reaction is not determined by  $\Delta G$ .



## 2 Reaction Rate and Rate Law

### 2.1 Rate of reaction



The graphs above show the change along time of the concentrations of the reactant and the product. The rate of the loss of the reactant at a particular moment is given by the slope of the tangent of the graph at that moment. (See also the diagram below.)

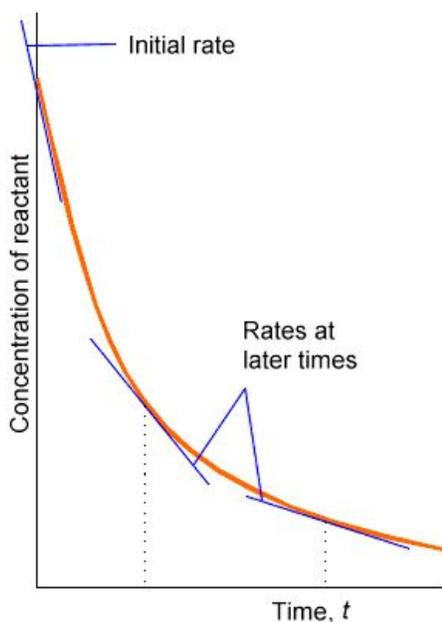
$$\text{Rate of loss of reactant (R)} = -\frac{d[\text{R}]}{dt} \quad (9)$$

Similarly, the rate of the formation of the product at that moment is given by

$$\text{Rate of formation of product (P)} = +\frac{d[\text{P}]}{dt} \quad (10)$$

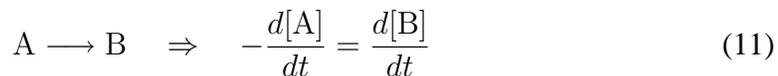
Note the minus sign in (9): the reactant concentration [R] is decaying along time so that its derivative  $d[\text{R}]/dt$  is negative, and therefore Eq (9) overall is positive.

In general, reaction rates change along time. As the graph below shows, the rate is usually the largest at the beginning ( $t = 0$ ) and gradually decreases along time as the reaction proceeds and the concentrations approach to their asymptotic (equilibrium) values.

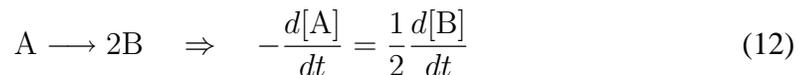


### 2.1.1 Stoichiometry

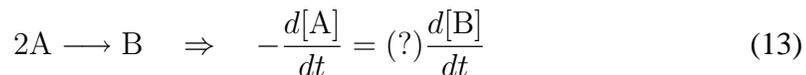
Let us consider a reaction  $A \rightarrow B$ , where one mole of A produces one mole of B. The rates of the loss of A and the formation of B are related as



Now, how should (or should not) this be modified for a different reaction  $A \rightarrow 2B$ ? In this case, because two moles of B is produced as one mole of A is lost, the rate of the former is twice as large as the latter. Therefore, we find



Similarly, for a reaction  $2A \rightarrow B$ ,



(Find the numerical coefficient.)

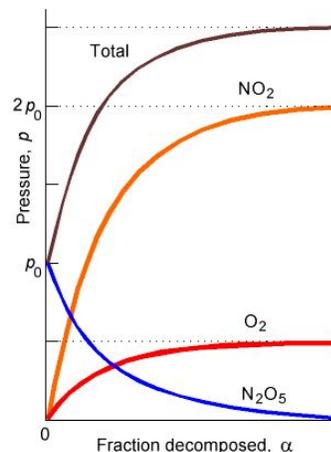
### Question:

Consider the reaction

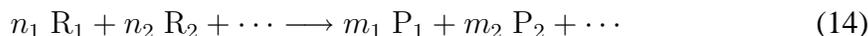


Find the numerical coefficients in

$$-\frac{d[\text{N}_2\text{O}_5]}{dt} = (?) \frac{d[\text{NO}_2]}{dt} = (?) \frac{d[\text{O}_2]}{dt}$$



Here is a useful formula for general reactions



We simply put the inverse of the molar coefficients in front of the derivatives  $d[\text{R}]/dt$  etc., remembering the minus signs for the reactants;

$$-\frac{1}{n_1} \frac{d[\text{R}_1]}{dt} = -\frac{1}{n_2} \frac{d[\text{R}_2]}{dt} = \dots = +\frac{1}{m_1} \frac{d[\text{P}_1]}{dt} = +\frac{1}{m_2} \frac{d[\text{P}_2]}{dt} = \dots \quad (15)$$

## 2.2 Rate Law

As we have seen, the reaction rates changes along time, normally decreases along with the progress of the reaction. This implies that the rate decreases as the number of reactant molecules decreases. Normally, as the concentrations <sup>†</sup> of the reactants decreases, the chance of their reactive encounter will also decrease. (On the other hand, the increase of the product concentrations may inhibit the reaction.)

We **often** observe that the reaction rates are proportional to the concentrations or the square of the concentrations of the reactants. We **sometimes** observe the reaction rates proportional to the cube or the square-root of the concentrations. These may be described in a form,

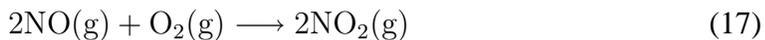
$$\text{Rate} = k[\text{A}]^n[\text{B}]^m \dots \quad (16)$$

where the coefficient  $k$  is called the **rate constant** of the reaction.  $n$  and  $m$  are the **orders** with respect to the reactants A and B, respectively. They are most often 1 or 2, and sometimes 3 or 1/2. We also define the **overall order** by  $n + m$ .

<sup>†</sup>For gas phase reactions, we usually consider partial pressures of the species instead of concentrations. The partial pressure is proportional to the concentration for ideal gases at a given temperature and volume,  $pV = nRT \Rightarrow p = RT(n/V)$ .

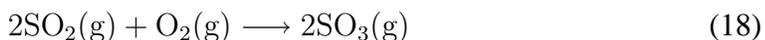
It is very important to note that the orders cannot be predicted simply from the stoichiometry of the reaction. Let us see the following two examples:

**Example 1.**



$$\text{Observed rate law: Rate} = k[\text{NO}]^2[\text{O}_2]$$

**Example 2.**



$$\text{Observed rate law: Rate} = k[\text{SO}_2][\text{SO}_3]^{-\frac{1}{2}} = k \frac{[\text{SO}_2]}{\sqrt{[\text{SO}_3]}}$$

Note that these two reactions have the same stoichiometry of



but the observed rate laws (the orders) are totally different. This means that we cannot predict the rate law just by looking at the equation of the reaction. Generally, the rate laws must be determined from experiments. The experimental methods and their theoretical background will be discussed in the next section.

As we will see in the subsequent discussions, different rate laws come from different **mechanisms** of the reaction. Namely, different involvements of the **elementary steps** and the associated **intermediate species**. In other words, by carefully examining the rate law, we expect to be able to clarify the mechanism of the reaction. This is indeed the major motivation to study Chemical Kinetics. From the analysis of the rate laws derived from experiments, we can discuss and infer the mechanism of the reactions.

**Question:** State the orders with respect to each specie and the overall order for Examples 1 and 2. Does the rate increase or decrease as the concentration of  $\text{SO}_3$  increases in Example 2? What could be the chemical reason for this?

## 2.3 Temperature Dependence

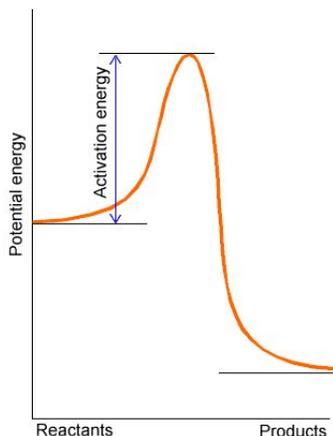
### 2.3.1 Arrhenius law

Normally, the reaction rates increase by raising the temperature. This sounds natural since the reactant molecules will move more actively in higher temperature, and hence the chance of their reactive encounter will be larger. It was found from a number of

experiments that this situation is described quantitatively by the following formula for the rate constant

$$k = Ae^{-E_a/RT} \quad (20)$$

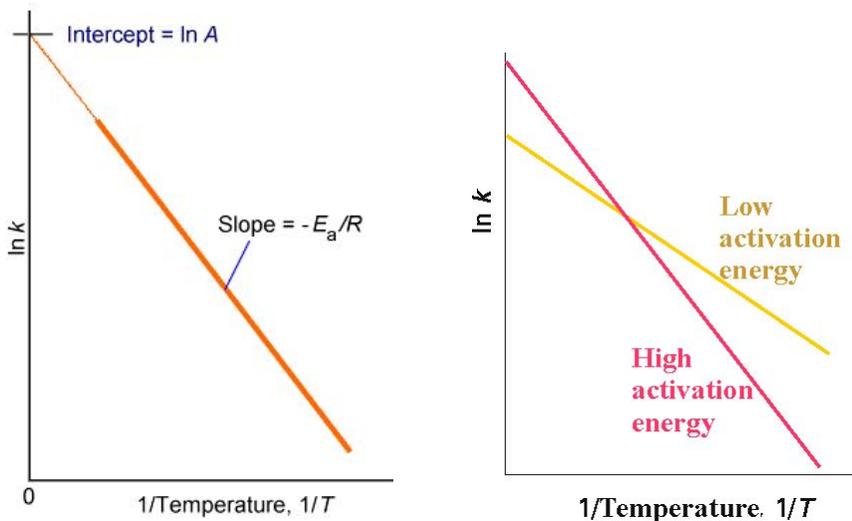
in which  $E_a$  and  $A$  are called an activation energy and a pre-factor.<sup>‡</sup>  $R$  is the gas constant ( $= 8.314 \times 10^{-3} \text{ kJ mol}^{-1} \text{ K}^{-1}$ ).



By taking the natural logarithms ( $\log_e$  or  $\ln$ ) of both sides,

$$\ln k = \ln A - \frac{E_a}{RT} \quad (21)$$

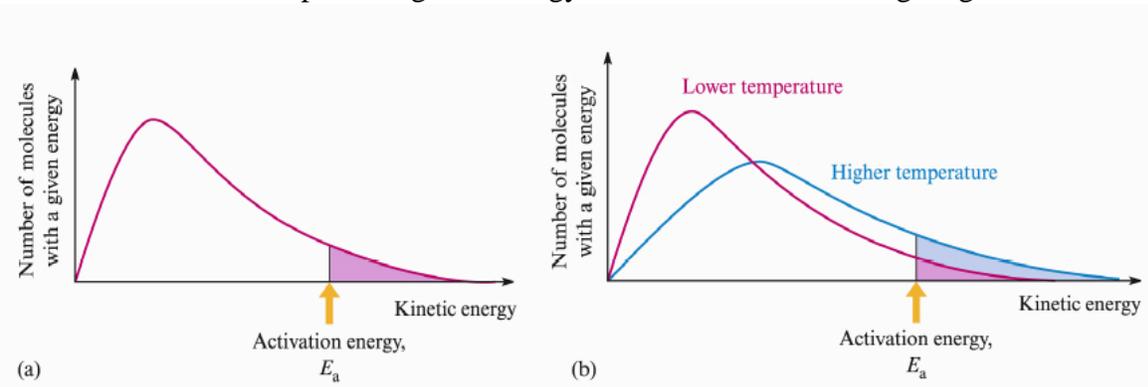
Therefore, by plotting  $\ln k$  against  $1/T$ , we will obtain a straight line as shown in the next diagrams. From the slope and the intercept of the plot we can calculate the activation energy  $E_a$  and the pre-factor  $A$ .



<sup>‡</sup> The pre-factor  $A$  is sometimes called a frequency factor.

Equations (20) and (21) are called the **Arrhenius equation** and the plot of  $\ln k$  against  $1/T$  the **Arrhenius plot**.

The Arrhenius law is closely related to the **Boltzmann's law**. In thermal equilibrium at temperature  $T$ , the molecules can take various energies.<sup>§</sup> The distribution of the number of molecules plotted against energy  $E$  will look the following diagrams.



As seen, the number of molecules decreases as the energy increases (in the high energy region). According to the picture of the activation energy barrier lying between the reactant and product states, the reaction rate will be proportional to the number of molecules having higher energy than  $E_a$ , i.e., in the shaded area of the diagram. By raising the temperature the molecules will receive energy from the surroundings, and then the distribution graph will shift toward the right, i.e., toward the higher energy. This results in an increase of the number of molecules above  $E_a$  and hence the increase of the reaction rate. This behaviour is described quantitatively by the Arrhenius equation (20) or (21).

### 3 Data analysis

Suppose that we have carried out a series of experiments to observe changes along time of the concentrations of the reactants and products as in the diagrams in Section 2.1. From these and other supplementary data, we attempt to determine the rate law, i.e., the orders with respect to the species involved and the rate constant.

#### 3.1 Unimolecular reaction $A \rightarrow P$

We begin with a very simple reaction in which only one specie  $A$  is involved in the reactant.



<sup>§</sup>The temperature  $T$  is proportional to the **average** kinetic energy of the molecules. The energy of each molecule may deviate from this average.

We do not consider the backward reaction. We also assume that there is no intermediate species or intermediate steps involved in the reaction. That is, (22) is a single step reaction. This is an example of the **elementary** reaction.

In this case, the rate law will contain only the concentration of A,

$$\text{Rate} = k[\text{A}]^n \quad (23)$$

Because the reaction rate is that of the loss of A,  $-d[\text{A}]/dt$ , the above equation is a simple differential equation

$$-\frac{d[\text{A}]}{dt} = k[\text{A}]^n \quad (24)$$

which can be integrated mathematically.

### 3.1.1 Zero order reaction

Let us first consider the zero order case,  $n = 0$ . Because  $[\text{A}]^0 = 1$ , (24) becomes

$$-\frac{d[\text{A}]}{dt} = k \quad (25)$$

This means that the gradient  $d[\text{A}]/dt$  is a constant  $-k$ . Therefore, [A] decays at a constant rate and the plot of [A] along time will be a straight line.

$$[\text{A}]_t = [\text{A}]_0 - kt \quad (26)$$

Here and hereafter, we denote the concentration of A by  $[\text{A}]_t$  when we wish to emphasize its dependence on time. The initial concentration at  $t = 0$  is  $[\text{A}]_0$ .

### 3.1.2 First order reaction

For  $n = 1$ , we have

$$\frac{d[\text{A}]}{dt} = -k[\text{A}] \quad (27)$$

The solution<sup>¶</sup> is an exponential function

$$[\text{A}]_t = [\text{A}]_0 e^{-kt} \quad (28)$$

This is equivalent to

$$\ln[\text{A}]_t = \ln[\text{A}]_0 - kt \quad (29)$$

Therefore, the plot of  $\ln[\text{A}]_t$  against time  $t$  is a straight line.

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<sup>¶</sup> For simplicity we write  $A(t)$  instead of  $[\text{A}]_t$ . It follows from (27) that

$$\frac{dA}{dt} = -kA \Rightarrow \int \frac{dA}{A} = -k \int dt \Rightarrow \ln A(t) = -kt + C$$

Putting  $t = 0$ , we find  $C = \ln A(0)$ . We thus get (29) which is equivalent to (28).

### 3.1.3 Second order reaction

For  $n = 2$ ,

$$\frac{d[A]}{dt} = -k[A]^2 \quad (30)$$

The solution is<sup>||</sup>

$$[A]_t = \frac{[A]_0}{1 + kt[A]_0} \quad (31)$$

Or equivalently,

$$\frac{1}{[A]_t} = \frac{1}{[A]_0} + kt \quad (32)$$

Therefore, the plot of  $1/[A]_t$  against time  $t$  is a straight line.

### 3.1.4 Summary

- 0th order: Rate =  $-\frac{d[A]}{dt} = k$   
 $\Rightarrow [A]_t = [A]_0 - kt$   
 $\Rightarrow$  Plot of  $[A]_t$  against time  $t$  is linear
- 1st order: Rate =  $-\frac{d[A]}{dt} = k[A]$   
 $\Rightarrow [A]_t = [A]_0 \exp(-kt) \quad \Rightarrow \ln[A]_t = \ln[A]_0 - kt$   
 $\Rightarrow$  Plot of  $\ln[A]_t$  against time  $t$  is linear
- 2nd order: Rate =  $-\frac{d[A]}{dt} = k[A]^2$   
 $\Rightarrow [A]_t = \frac{[A]_0}{1 + kt[A]_0} \quad \Rightarrow \frac{1}{[A]_t} = \frac{1}{[A]_0} + kt$   
 $\Rightarrow$  Plot of  $1/[A]_t$  against time  $t$  is linear

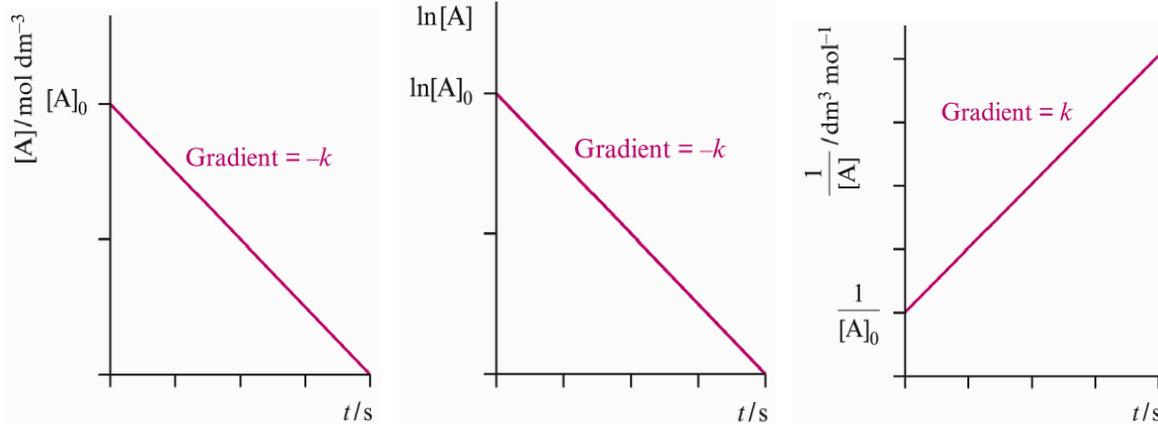
In this way, the order  $n$  and the rate constant  $k$  can be determined from the graphs of  $[A]$ ,  $\ln[A]$  or  $1/[A]$  against time. Suppose we have obtained from experiments the concentration of A as a function of time. We then plot  $[A]$ ,  $\ln[A]$  or  $1/[A]$  against time. If one of these was found to be a straight line, the order  $n$  is 0, 1 or 2, respectively.

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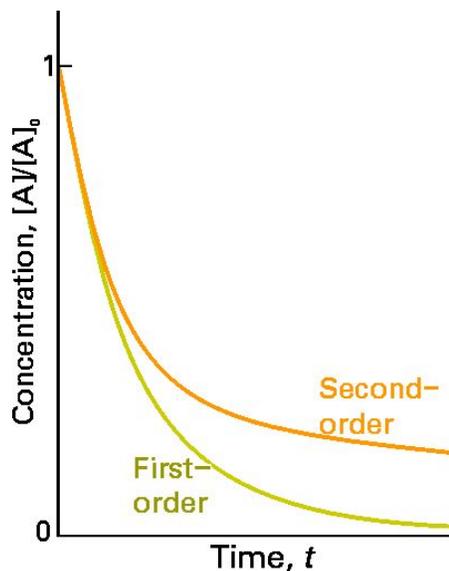
<sup>||</sup> From (30),

$$\frac{dA}{dt} = -kA^2 \quad \Rightarrow \quad - \int \frac{dA}{A^2} = k \int dt \quad \Rightarrow \quad \frac{1}{A(t)} = kt + C$$

Putting  $t = 0$ , we find  $C = 1/A(0)$ . This immediately gives (32) and after rearranging we get (31).



For the first and second order reactions, the raw data of  $[A]_t$  will look like

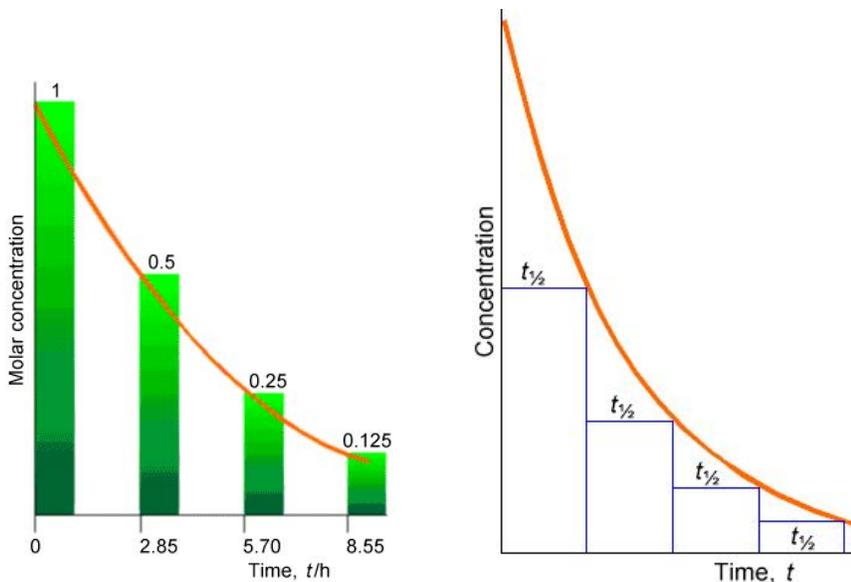


Both curves show smooth decay in which the gradient (= rate) decreases along time as the concentration  $[A]$  decreases. This is simply because the rate is proportional to  $[A]$  or  $[A]^2$ . In other words, the chance of the reaction will decrease as we lose the reactant molecules along with the progress of the reaction.

### 3.1.5 Half-life Method

The **half-life** is the time taken for the concentration of the reactant  $[A]$  to halve. It may depend on the starting concentration  $[A]$ . For example, for zero order reactions where  $[A]_t$  is a linear function of  $t$ , the half life decreases along time, i.e., as the starting concentration decreases. (Confirm this by drawing a graph.) In contrast, for the first

order reactions the half life is a constant that is independent of the starting concentration. See the diagrams below.



This is a special characteristic of the first order reactions. Let us denote the half life by  $\tau$ . Then Eq (28) at  $t = \tau$  is written as

$$\frac{[A]_0}{2} = [A]_0 \exp(-k\tau) \quad (33)$$

By dividing both sides by  $[A]_0$  and taking the natural logarithms, we find

$$\frac{1}{2} = \exp(-k\tau) \Rightarrow \exp(k\tau) = 2 \Rightarrow k\tau = \ln 2 \Rightarrow \tau = \frac{\ln 2}{k} \quad (34)$$

As seen in the previous diagram, the decay profile of the concentration  $[A]$  for the second order reaction is quite different from the first order reaction. It is easy to show from Eq (32) that the half life for the second order reaction is proportional to the inverse of the starting concentration,  $\tau = 1/k[A]_0$ . This means that the half-life increases as the reaction proceeds.

In summary,

- 0th order: half-life =  $[A]_0/2k \propto [A]_0$
- 1st order: half-life =  $\ln 2/k$  independent of  $[A]_0$
- 2nd order: half-life =  $1/k[A]_0 \propto 1/[A]_0$

**Question:** Confirm these behaviours (qualitatively) on graphs. Derive these mathematical formulas of the half-life from Eqs (26) - (32).

## 3.2 More than one species involved

In the previous section we assumed that only one reactant specie A is involved in the reaction. This is of course too restrictive; in reality we much more often encounter reactions involving more than one species. This implies that the data analysis will be more complicated. For example, how can we determine the orders  $n$  and  $m$  when the rate law is given by

$$\text{Rate} = k[A]^n[B]^m \quad (35)$$

which means that the differential equation now contains two unknown time-dependent variables  $[A]_t$  and  $[B]_t$ ? Two representative strategies to work around this problem are the **isolation method** and the **initial rate method**.

### 3.2.1 Isolation Method

Suppose that we have prepared a large excess of one of the reactants, say A, compared to B. That is, the initial concentrations are such that  $[A]_0 \gg [B]_0$ . In this case, we may consider that  $[A]$  will stay large in the course of the reaction so that its concentration change may be neglected approximately.

$$[A]_t \simeq [A]_0 \quad (= \text{constant})$$

Then the rate law will be approximated as

$$\text{Rate} \simeq k[A]_0^n[B]^m \equiv k'[B]^m$$

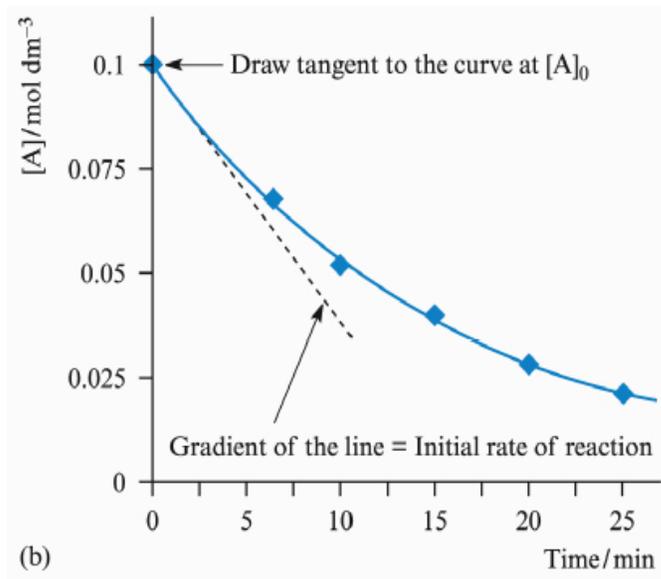
where  $k'$  is defined by  $k' = k[A]_0^n$ . In this way, the unknown variable  $[A]$  has been (approximately) eliminated from the rate law. Now we can apply the methods in the previous section in order to determine the order  $m$  and the new rate constant  $k'$ .

In the next set of experiments, we prepare a large excess of B compared to A, and repeat similar procedure to determine the order  $n$ . Finally, from  $n$  and  $k'$  we determine the original rate constant  $k$ .

In this way, the contributions from each of the reactant species can be **isolated** one by one.

### 3.2.2 Initial Rate Method

Another method to avoid the complication coming from the involvement of multiple species is to consider only the **initial rates** (rates at  $t = 0$ ).

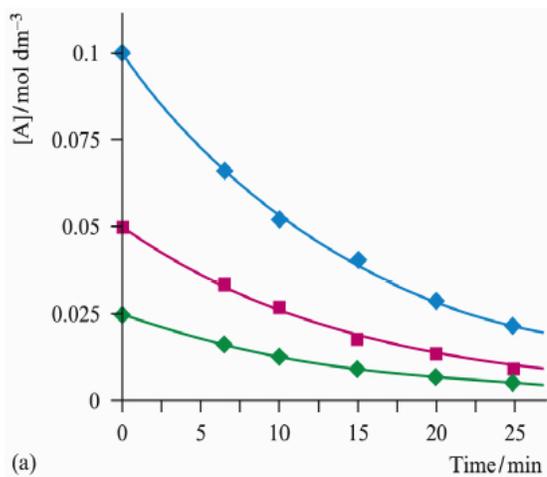


The essential point is that the concentrations of all the reactant species are precisely known at  $t = 0$  as we have prepared them.

$$(\text{Initial Rate}) = k[A]_0^n[B]_0^m$$

Therefore, we do not have to be concerned with the complicated changes of the concentrations of the multiple species that will occur in  $t > 0$ .

For example, to determine the order  $n$ , we measure the initial rate of the decay of  $[A]$ , that is,  $-d[A]/dt$  at  $t = 0$ . We repeat this for different initial concentrations  $[A]_0$  as shown in the diagram below. It is important to keep  $[B]_0$  to the same value in this series of experiments. (Otherwise we will mess up the analysis!)



**Example:** The following data have been obtained for a reaction  $A + B \rightarrow P$ .

$[A]_0$ / mol dm <sup>-3</sup>	$[B]_0$ / mol dm <sup>-3</sup>	Initial Rate / mol dm <sup>-3</sup> s <sup>-1</sup>
0.2	0.2	$5 \times 10^{-5}$
0.4	0.2	$1 \times 10^{-4}$
0.2	0.6	$1.5 \times 10^{-4}$

Find the orders with respect to A and B and the rate constant  $k$ .

As illustrated by this Example, the analysis is easy when the orders are immediately found to be simple integers. For otherwise and more general cases, the following procedure is useful.

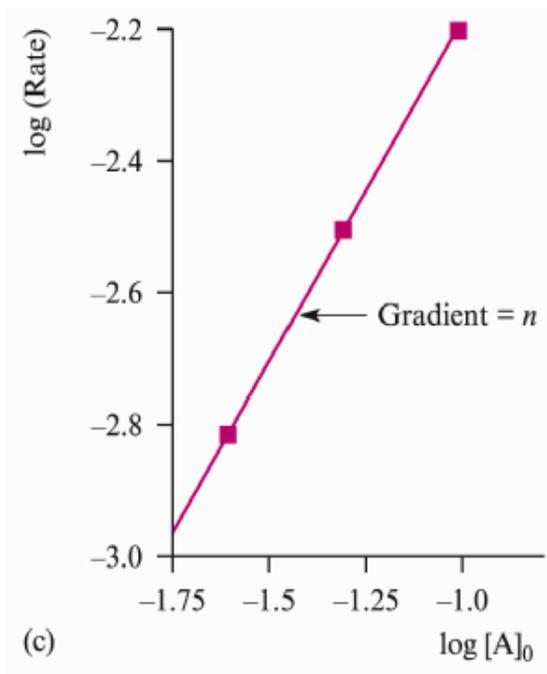
By taking the logarithms of both sides of

$$(\text{Initial Rate}) = k[A]_0^n[B]_0^m$$

we obtain\*\*

$$\log(\text{Initial Rate}) = \log k + n \log[A]_0 + m \log[B]_0$$

Therefore, the rate constant  $k$  and order  $n$  can be determined from a plot of  $\log(\text{Initial Rate})$  against  $\log[A]_0$ . Note that  $[B]_0$  should be kept to the same value in this analysis. By exchanging A and B, we can determine the order  $m$  from another set of experiments.



\*\* Remember that  $\log XY = \log X + \log Y$  and  $\log X^n = n \log X$ . Here the base can be anything, so we can use either  $\log_{10}$  or  $\ln$  depending on our particular conveniences.

## 4 Simple Reactions

### 4.1 Reversible reaction approaching to equilibrium

Let us consider a reversible reaction between A and B



If we start with pure A, i.e.,  $[A]_0 \neq 0$  and  $[B]_0 = 0$ , part of A will be converted to B until they reach the equilibrium state in which the concentrations are  $[A]_\infty$  and  $[B]_\infty$ . (These are  $[A]_t$  and  $[B]_t$  at time  $t = \infty$ . Although we use the symbol for infinity,  $\infty$ , this practically means a sufficiently long time compared to the time scale of the reaction.) The ratio between these two is the equilibrium constant of this reaction.

$$K = \frac{[B]_\infty}{[A]_\infty} \quad (37)$$

Note the difference from the reactions treated in the previous section



with no backward reaction. In this case,  $[A]$  will decay to zero, i.e.,  $[A]_\infty = 0$ . This is in contrast with the reversible reaction (36), in which finite amount of A will be restored due to the existence of the backward reaction and hence  $[A]_\infty \neq 0$  and the equilibrium constant  $K$  is finite.

We will assume that both the forward and backward rate constants  $k_f$  and  $k_b$  are first order. Therefore, the forward reaction contributes to the loss of A and gain of B as

$$-\frac{d[A]}{dt} = +\frac{d[B]}{dt} = k_f[A] \quad (38)$$

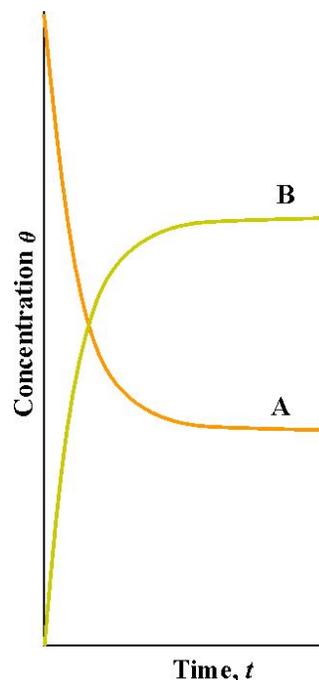
Similarly, the backward reaction contributes to the gain of A and loss of B as

$$+\frac{d[A]}{dt} = -\frac{d[B]}{dt} = k_b[B] \quad (39)$$

Overall, the rate of the change of  $[A]$  is a combination of these two contributions such as

$$\frac{d[A]}{dt} = -k_f[A] + k_b[B] \quad (40)$$

In sufficiently long time  $t = \infty$ , the system will relax to the equilibrium state in which the concentrations do not change any more. That is,  $d[A]/dt = 0$  at  $t = \infty$ .



Then, Eq (40) will be<sup>††</sup>

$$0 = -k_f[A]_\infty + k_b[B]_\infty \Rightarrow \frac{[B]_\infty}{[A]_\infty} = \frac{k_f}{k_b} \quad (41)$$

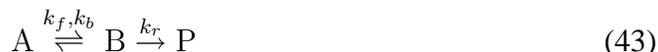
As seen in Eq (37), the left hand side of the last equation is equal to the equilibrium constant  $K$ . We therefore find a relation

$$K = \frac{[B]_\infty}{[A]_\infty} = \frac{k_f}{k_b} \quad (42)$$

Although this might appear a simple equation, it is conceptually remarkable because it finds a relation between the **equilibrium** property  $K$  and the **kinetic** quantities  $k_f$  and  $k_b$ .

## 4.2 Pre-equilibrium

Now we introduce, in addition to the reversible process  $A \rightleftharpoons B$  just considered, a reactive process from B to a final product P.



This last process will disturb, or even destroy, the equilibrium between A and B. However, we will assume that this process is very slow such that the equilibrium between A and B is well maintained. In other words, we will consider situations where the ratio  $[B]/[A]$  is approximately kept constant. Let us denote this constant by  $K$ .

$$\frac{[B]}{[A]} \simeq K = \frac{k_f}{k_b} \quad (44)$$

The last equality has been found in the previous section in Eq (42). We call this the ‘**pre-equilibrium**’ assumption: the equilibrium  $A \rightleftharpoons B$  prior to the reactive process  $B \rightarrow P$  is approximately well maintained throughout the reaction.

**Question:** Sketch (roughly) the changes of  $[A]$ ,  $[B]$  and  $[P]$  along time  $t$ . (Hint: Look at the graph in the previous page for  $A \rightleftharpoons B$ , and consider what will happen by introducing the reactive step  $B \rightarrow P$ .)

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<sup>††</sup> We can also derive Eq (41) by the following consideration. In equilibrium at  $t = \infty$ , the forward Eq (38) and backward Eq (39) processes will balance, such that

$$k_f[A]_\infty = k_b[B]_\infty$$

We further assume that the reactive step  $B \rightarrow P$  is a 1st order process:

$$\frac{d[P]}{dt} = k_r[B]$$

The overall reaction rate is given by this rate of the product formation.

$$\text{Rate} = \frac{d[P]}{dt}$$

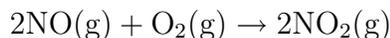
With the pre-equilibrium assumption, Eq (44), this is rewritten as

$$\text{Rate} = \frac{d[P]}{dt} = k_r[B] \simeq k_r K[A] = \frac{k_r k_f}{k_b} [A] \propto [A] \quad (45)$$

Therefore, the overall rate law turns out to be 1st order with respect to A.

Now, a question arises: How can we distinguish this from the straightforward 1st order reaction  $A \rightarrow P$  when we have no way to detect the intermediate specie B? Sometimes, though not always, we can get some clue to this question by looking at the **temperature dependence** of the reaction rate. To this end, it is useful to look at the following specific example.

**Example:** Oxidation of nitrogen oxide



Experimental facts are:

1. Rate law is given by;  $\text{Rate} = k [\text{NO}]^2[\text{O}_2]$  (overall 3rd order)
2. Reaction rate decreases as the temperature increases.

These observations cannot be explained by the simple bimolecular collision mechanism (which predicts a 2nd order rate law  $k [\text{NO}][\text{O}_2]$ ). In particular, the second observation is unusual in view of the ordinary temperature dependence described by the Arrhenius equation (Section 2.3).

Let us assume a pre-equilibrium mechanism for this reaction:



From the pre-equilibrium assumption we get

$$\frac{[\text{N}_2\text{O}_2]}{[\text{NO}]^2} \simeq K = \frac{k_f}{k_b} \Rightarrow [\text{N}_2\text{O}_2] \simeq K[\text{NO}]^2$$

Putting this into the rate expression derived from the reactive step EQ (47),

$$\text{Rate} = \frac{d[\text{NO}_2]}{dt} = k_r[\text{N}_2\text{O}_2][\text{O}_2]$$

we obtain

$$\text{Rate} = k_r K[\text{NO}]^2[\text{O}_2] \quad (48)$$

This immediately explains the first fact, the overall 3rd order rate law.

Now, let's see how this explains the second fact, the unusual temperature dependence of the rate. As seen in Eq (48), the overall rate constant is a product of two factors,  $k = k_r K$ . We can naturally assume that the rate constant of the reactive step  $k_r$  has a normal temperature dependence such that it increases in higher temperatures. However, the behaviour of the equilibrium constant  $K$  can be different. It may increase or decrease in higher temperatures depending on the sign <sup>‡‡</sup> of the free energy change  $\Delta G^\circ$ . For example,  $\Delta G^\circ < 0$  means that the product state has lower  $G$  than the reactant. Generally, by raising the temperature we increase the populations of the higher energy state. This means that, when  $\Delta G^\circ < 0$ , increase of the temperature will result in an increase of the reactant concentrations and hence a decrease of  $K$ .

In this way, the overall rate constant  $k = k_r K$  may contain competing positive and negative factors of the temperature dependence. The observed fact for this particular reaction suggests that the decrease of  $K$  is the dominant factor to determine the overall temperature dependence.

### 4.3 Consecutive reaction

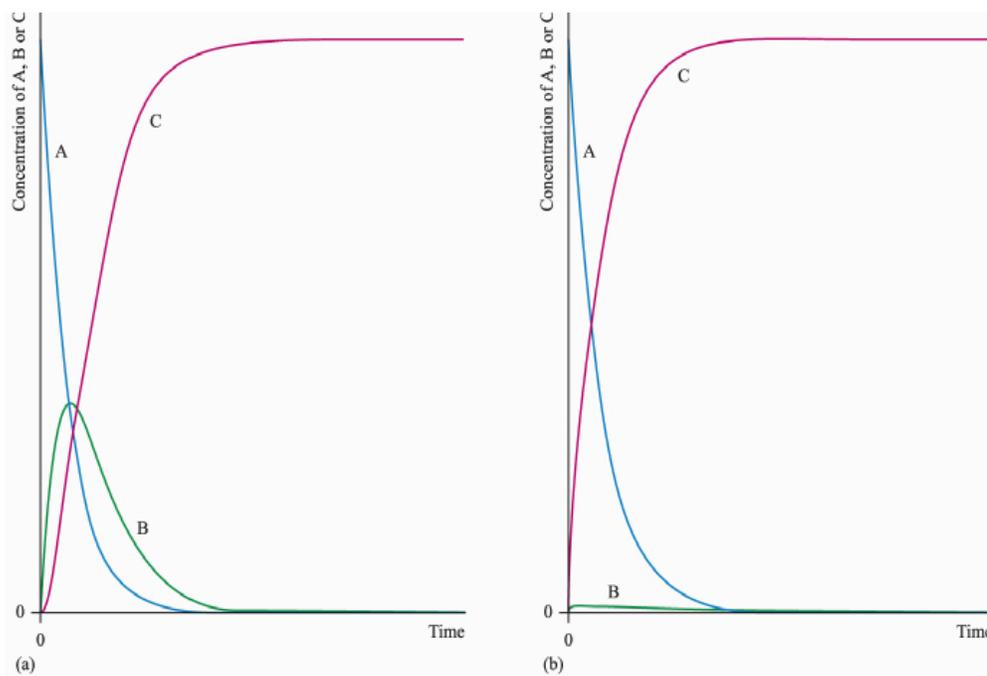
Let us next consider the following consecutive reaction



The behaviour of the intermediate [B] will depend on the difference between  $k_a$  and  $k_b$ .

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<sup>‡‡</sup> This can be described more quantitatively by  $K = e^{-\Delta G^\circ/RT}$ .



**Question:** State, with explanation, which diagram corresponds to  $k_a \gg k_b$ .

Assuming 1st order reactions for both of the two steps, it is possible to solve the rate equations analytically,\* which gives

$$\begin{cases} [A]_t = [A]_0 e^{-k_a t} \\ [B]_t = \frac{k_a}{k_a - k_b} (-e^{-k_a t} + e^{-k_b t}) [A]_0 \\ [C]_t = \left( 1 + \frac{1}{k_a - k_b} (k_b e^{-k_a t} - k_a e^{-k_b t}) \right) [A]_0 \end{cases}$$

The mathematical derivation is far beyond the assumed level of this course. The reason for showing these equations is because the formula for  $[C]_t$  is useful to demonstrate the

\* The rate equations for this scheme are:

$$\frac{dA}{dt} = -k_a A, \quad \frac{dB}{dt} = k_a A - k_b B, \quad \frac{dC}{dt} = k_b B$$

The first equation for  $A(t)$  is the same as what we have seen previously in Sec 3.1.2. We put the solution  $A(t) = A(0)e^{-k_a t}$  in the second equation. This yields an ordinary differential equation for  $B(t)$ , for which the solution method is well established (though we have no space to expand it here).  $C(t)$  can be obtained from a relation  $A(t) + B(t) + C(t) = \text{constant} = A(0)$ , which describes the conservation of gross materials.

concept of **rate-determining step**, as will be discussed next.

#### 4.4 Rate-determining process

The above formula for  $[C]_t$  can be simplified in two limiting cases where one of the rate constants is much larger than the other. For example, when  $k_a \gg k_b$ , we find  $e^{-k_a t} \ll e^{-k_b t}$  and  $1/(k_a - k_b) \simeq 1/k_a$ . Therefore,  $[C]_t$  can be simplified as

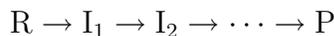
$$[C]_t \simeq (1 - e^{-k_b t})[A]_0$$

This means that the behaviour of  $[C]_t$  is determined by the rate constant of the slower step  $k_b$ .

**Question:** Show that when  $k_a \ll k_b$ ,

$$[C]_t \simeq (1 - e^{-k_a t})[A]_0$$

In this way, the slower step determines the overall rate of the product formation. This is called the **Rate-determining** or **Rate-limiting** step. The idea is straightforwardly generalized for reactions involving more than two steps, i.e., more than one intermediates  $I_1, I_2, \dots$ , involved between the reactant R and product P:



## 5 Steady-state approximation

It is seen in the right panel of the previous diagram that the concentration of B does not change much but stays low and nearly constant, and therefore  $d[B]/dt \simeq 0$ , when  $k_b \gg k_a$ , i.e., when this intermediate specie is highly reactive. This suggests a very useful and powerful method called the **steady-state approximation**.

### Recipe of the Steady-State Approximation

1. Identify reactive intermediates,  $I_1, I_2, \dots$ , in the mechanism
2. Write down  $\frac{d[I_i]}{dt}$  from the assumed mechanism.
3. Set  $\frac{d[I_i]}{dt} = 0$  and solve for  $[I_i]$ . (The solution will be denoted by  $[I_i]_{ss}$ .)
4. Deduce, and simplify if possible, the rate law by using  $[I_i]_{ss}$ .

## 5.1 Application

Let us see how the steady-state approximation works for the following scheme



which has been examined previously by invoking the pre-equilibrium approximation. The critical assumption there was the reaction from B to P is very slow such that it does not disturb very much the equilibrium between A and B. We will now relax this assumption. To this end, let us follow the recipe of the steady-state approximation. As before, we will assume that all the steps  $k_f$ ,  $k_b$  and  $k_r$  are 1st order.

1. We identify B as the reactive intermediate.
2. Noting that B is gained by  $k_f$  and lost by  $k_b$  and  $k_r$  steps,

$$\frac{d[B]}{dt} = k_f[A] - k_b[B] - k_r[B]$$

3. Set the above to be equal to zero, and solve for [B].

$$k_f[A] - k_b[B] - k_r[B] \simeq 0 \Rightarrow [B]_{ss} = \frac{k_f}{k_b + k_r}[A]$$

4. The overall reaction rate is that of the product formation described by the  $k_r$  step. We write down this equation and then replace [B] by  $[B]_{ss}$ .

$$\text{Rate} = \frac{d[P]}{dt} = k_r[B] \simeq k_r[B]_{ss} = \frac{k_r k_f}{k_b + k_r}[A] \quad (50)$$

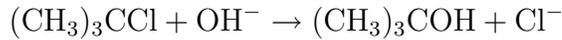
Compare this with the result from the pre-equilibrium assumption, Eq (45):

$$\text{Rate (pre-Eq)} \simeq k_r K[A] = \frac{k_r k_f}{k_b}[A]$$

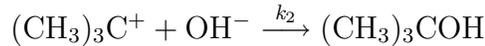
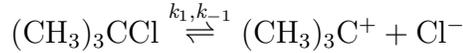
The difference is in the denominator of the rate factor. Remember that the fundamental assumption in the pre-equilibrium case was  $k_r \ll k_b$ . This means that the denominator in Eq (50) may be approximated as  $k_b + k_r \simeq k_b$ . We therefore find that the pre-equilibrium approximation Eq (45) is reproduced as a limiting case of the steady-state approximation Eq (50). In other words, the steady-state approximation generalizes, and therefore covers broader applicability than, the pre-equilibrium approximation.

## 5.2 Exercise

Consider a nucleophilic substitution reaction:



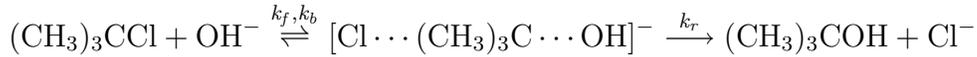
Let us first assume the following mechanism



**Q1.** Apply the steady-state approximation for the intermediate  $(\text{CH}_3)_3\text{C}^+$  and derive the rate law.

**Q2.** Show that the rate law is 1st-order when  $[\text{OH}^-]$  is in excess or when  $k_{-1} \ll k_2$

Let us next consider an alternative mechanism



**Q3.** Apply the steady-state approximation for the intermediate complex and show that this mechanism gives a 2nd-order rate law.

**Answers:**

1.

$$\text{Rate} = \frac{k_1 k_2 [(\text{CH}_3)_3\text{CCl}] [\text{OH}^-]}{k_{-1} [\text{Cl}^-] + k_2 [\text{OH}^-]}$$

2.

$$\text{Rate} \simeq k_1 [(\text{CH}_3)_3\text{CCl}] \text{ when } k_{-1} [\text{Cl}^-] \ll k_2 [\text{OH}^-]$$

3.

$$\text{Rate} = \frac{k_f k_r}{k_b + k_r} [(\text{CH}_3)_3\text{CCl}] [\text{OH}^-]$$

## 5.3 Michaelis-Menten equation

Let us consider an enzyme catalysis reaction in which the enzyme E and a substrate S form an intermediate complex ES and then the reaction occurs to release the product P:



This looks similar to the scheme in Eq (49), and hence the steady-state approximation will give

$$\text{Rate} = \frac{k_1 k_2}{k_2 + k_{-1}} [\text{E}][\text{S}]$$

(It will be a good exercise to derive and confirm this.) However, this looks very different from the famous Michaelis-Menten equation:

$$\text{Rate} = \frac{V_{\max}[\text{S}]}{[\text{S}] + K_M}$$

We notice that one of the major difference is that the enzyme concentration  $[\text{E}]$  is not involved in the latter. We therefore try to eliminate  $[\text{E}]$  in the course of the application of the steady-state approximation. To this end, it is essential to recognize that the enzyme is a catalyst. Therefore, it is not destroyed by the reaction and the total number of enzyme molecules is kept constant. This is described by

$$[\text{E}] + [\text{ES}] = \text{constant} = [\text{E}]_0 \quad (52)$$

in which  $[\text{E}]_0$  is the initially prepared concentration of the enzyme. Now we apply the recipe of the steady-state approximation. First we identify that the ES complex is the intermediate. Its change in the scheme (51) is written as

$$\frac{d[\text{ES}]}{dt} = k_1[\text{E}][\text{S}] - k_{-1}[\text{ES}] - k_2[\text{ES}]$$

The steady-state approximation sets the right hand side to be equal to zero. But before doing it, we will eliminate  $[\text{E}]$  by using Eq (52):

$$k_1([\text{E}]_0 - [\text{ES}])[\text{S}] - k_{-1}[\text{ES}] - k_2[\text{ES}] \simeq 0$$

$$\Rightarrow [\text{ES}]_{\text{ss}} = \frac{k_1[\text{E}]_0[\text{S}]}{k_1[\text{S}] + k_{-1} + k_2} \quad (53)$$

The overall rate is that of the product formation determined by the final step of the scheme (51):

$$\text{Rate} = \frac{d[\text{P}]}{dt} = k_2[\text{ES}]$$

We replace  $[\text{ES}]$  by Eq (53):

$$\text{Rate} = \frac{k_2 k_1 [\text{E}]_0 [\text{S}]}{k_1 [\text{S}] + k_{-1} + k_2} = \frac{k_2 [\text{E}]_0 [\text{S}]}{[\text{S}] + \frac{k_{-1} + k_2}{k_1}} = \frac{V_{\max} [\text{S}]}{[\text{S}] + K_M}$$

in which  $V_{\max} = k_2[\text{E}]_0$  is the maximum rate and  $K_M = (k_{-1} + k_2)/k_1$  is the Michaelis constant.

## Further Readings

Now there would be two ways for you to proceed. One is to review the basics again by reading the recommended textbooks. In particular, it would be a good idea to attempt the worked examples and problems in order to see how the theories work in more practical situations and to confirm your understanding of the theories. It is also useful to read explanations by different authors. This is because no one can explain things perfectly and you will have to build your own way of understanding by repeating reading and thinking.

Another way forward would be to read advanced books and research papers. One of recommendable books is:

- A Fersht, Structure and Mechanism in Protein Science, Freeman.  
(There are 8 long loan and 2 week loan copies in Barnes Library, Medical School, Shelfmark QP 551/F.)

I trust that this lecture course has provided sufficient background to get ready for this and other books and papers.