CHAPTER 1

TOOLS AND TECHNIQUES OF KINETIC ANALYSIS

1.1 GENERALITIES

Chemists are concerned with the laws of chemical interactions. The theories that have been expounded to explain such interactions are based largely on experimental results. Two main approaches have been used to explain chemical reactivity: *thermodynamic* and *kinetic*. In thermodynamics, conclusions are reached on the basis of changes in energy and entropy that accompany a particular chemical change in a system. From the magnitude and sign of the free-energy change of a reaction, it is possible to predict the direction in which a chemical change will take place. Thermodynamic quantities do not, however, provide any information on the rate or mechanism of a chemical reaction. Theoretical analysis of the kinetics, or time course, of processes can provide valuable information concerning the underlying mechanisms responsible for these processes. For this purpose it is necessary to construct a mathematical model that embodies the hypothesized mechanisms. Whether or not the solutions of the resulting equations are consistent with the experimental data will either prove or disprove the hypothesis.

Consider the simple reaction $A + B \rightleftharpoons C$. The *law of mass action* states that the rate at which the reactant A is converted to product C is proportional to the number of molecules of A available to participate in the chemical reaction. Doubling the concentration of either A or B will double the number of collisions between molecules that lead to product formation.

The *stoichiometry* of a reaction is the simplest ratio of the number of reactant molecules to the number of product molecules. It should not be mistaken for the mechanism of the reaction. For example, three molecules of hydrogen react with one molecule of nitrogen to form ammonia: $N_2 + 3H_2 \rightleftharpoons 2NH_3$.

The *molecularity* of a reaction is the number of reactant molecules participating in a simple reaction consisting of a single elementary step. Reactions can be unimolecular, bimolecular, and trimolecular. *Unimolecular reactions* can include isomerizations ($A \rightarrow B$) and decompositions ($A \rightarrow B + C$). *Bimolecular reactions* include association ($A + B \rightarrow AB$; $2A \rightarrow A_2$) and exchange reactions ($A + B \rightarrow C + D$ or $2A \rightarrow C + D$). The less common *termolecular reactions* can also take place ($A + B + C \rightarrow P$).

The task of a kineticist is to predict the rate of any reaction under a given set of experimental conditions. At best, a mechanism is proposed that is in qualitative and quantitative agreement with the known experimental kinetic measurements. The criteria used to propose a mechanism are (1) consistency with experimental results, (2) energetic feasibility, (3) microscopic reversibility, and (4) consistency with analogous reactions. For example, an exothermic, or least endothermic, step is most likely to be an important step in the reaction. *Microscopic reversibility* refers to the fact that for an elementary reaction, the reverse reaction must proceed in the opposite direction by exactly the same route. Consequently, it is not possible to include in a reaction mechanism any step that could not take place if the reaction were reversed.

1.2 ELEMENTARY RATE LAWS

1.2.1 Rate Equation

The *rate equation* is a quantitative expression of the change in concentration of reactant or product molecules in time. For example, consider the reaction $A + 3B \rightarrow 2C$. The rate of this reaction could be expressed as the disappearance of reactant, or the formation of product:

$$\text{rate} = -\frac{d[\mathrm{A}]}{dt} = -\frac{1}{3}\frac{d[\mathrm{B}]}{dt} = \frac{1}{2}\frac{d[\mathrm{C}]}{dt} \tag{1.1}$$

Experimentally, one also finds that the rate of a reaction is proportional to the amount of reactant present, raised to an exponent n:

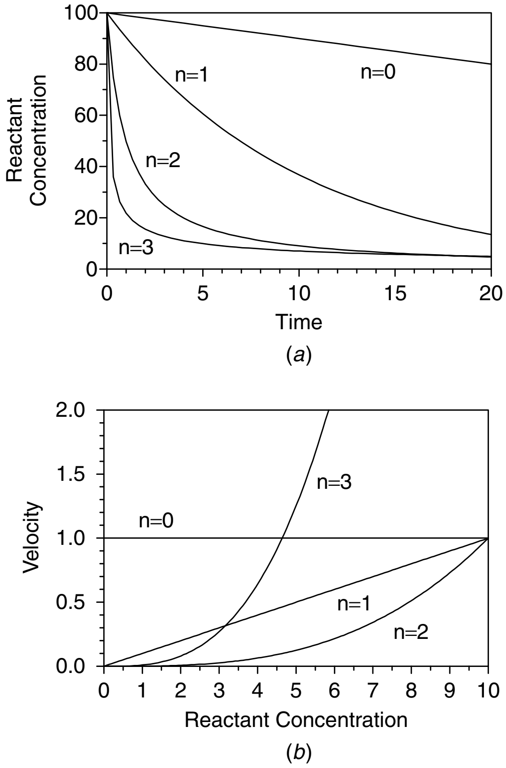
$$\text{rate} \propto [\mathrm{A}]^n \tag{1.2}$$

where n is the order of the reaction. Thus, the rate equation for this reaction can be expressed as

$$-\frac{d[\mathrm{A}]}{dt} = k_r[\mathrm{A}]^n \tag{1.3}$$

where k_r is the rate constant of the reaction.

As stated implicitly above, the rate of a reaction can be obtained from the slope of the *concentration–time curve* for disappearance of reactant(s) or appearance of product(s). Typical reactant concentration–time curves for zero-, first-, second-, and third-order reactions are shown in Fig. 1.1(*a*). The dependence of the rates of these reactions on reactant concentration is shown in Fig. 1.1(*b*).



(*a*)

(*b*)

Figure 1.1. (*a*) Changes in reactant concentration as a function of time for zero-, first-, second-, and third-order reactions. (*b*) Changes in reaction velocity as a function of reactant concentration for zero-, first-, second-, and third-order reactions.

1.2.2 Order of a Reaction

If the rate of a reaction is *independent* of a particular reactant concentration, the reaction is considered to be zero order with respect to the concentration of that reactant ($n = 0$). If the rate of a reaction is *directly proportional* to a particular reactant concentration, the reaction is considered to be *first-order* with respect to the concentration of that reactant ($n = 1$). If the rate of a reaction is proportional to the square of a particular reactant concentration, the reaction is considered to be *second-order* with respect to the concentration of that reactant ($n = 2$). In general, for any reaction $\mathrm{A} + \mathrm{B} + \mathrm{C} + \cdots \rightarrow \mathrm{P}$, the rate equation can be generalized as

$$\text{rate} = k_r[\mathrm{A}]^a[\mathrm{B}]^b[\mathrm{C}]^c \cdots \tag{1.4}$$

where the exponents a, b, c correspond, respectively, to the order of the reaction with respect to reactants A, B, and C.

1.2.3 Rate Constant

The *rate constant* (k_r) of a reaction is a concentration-independent measure of the velocity of a reaction. For a first-order reaction, k_r has units of (time)$^{-1}$; for a second-order reaction, k_r has units of (concentration)$^{-1}$ (time)$^{-1}$. In general, the rate constant of an nth-order reaction has units of (concentration)$^{-(n-1)}$(time)$^{-1}$.

1.2.4 Integrated Rate Equations

By integration of the rate equations, it is possible to obtain expressions that describe changes in the concentration of reactants or products as a function of time. As described below, integrated rate equations are extremely useful in the experimental determination of rate constants and reaction order.

1.2.4.1 Zero-Order Integrated Rate Equation

The reactant concentration–time curve for a typical zero-order reaction, A → products, is shown in Fig. 1.1(a). The rate equation for a zero-order reaction can be expressed as

$$\frac{d[\mathrm{A}]}{dt} = -k_r[\mathrm{A}]^0 \tag{1.5}$$

Since $[\mathrm{A}]^0 = 1$, integration of Eq. (1.5) for the boundary conditions $\mathrm{A} = \mathrm{A}_0$ at $t = 0$ and $\mathrm{A} = \mathrm{A}_t$ at time t,

$$\int_{\mathrm{A}_0}^{\mathrm{A}_t} d[\mathrm{A}] = -k_r \int_0^t dt \tag{1.6}$$

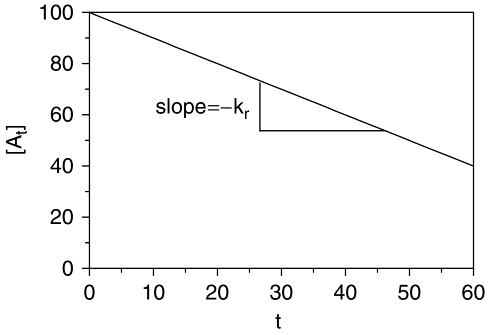


Figure 1.2. Changes in reactant concentration as a function of time for a zero-order reaction used in the determination of the reaction rate constant (k_r).

yields the integrated rate equation for a zero-order reaction:

$$[\mathrm{A}_t] = [\mathrm{A}_0] - k_r t \tag{1.7}$$

where $[\mathrm{A}_t]$ is the concentration of reactant A at time t and $[\mathrm{A}_0]$ is the initial concentration of reactant A at $t = 0$. For a zero-order reaction, a plot of $[\mathrm{A}_t]$ versus time yields a straight line with negative slope $-k_r$ (Fig. 1.2).

1.2.4.2 First-Order Integrated Rate Equation

The reactant concentration–time curve for a typical first-order reaction, A → products, is shown in Fig. 1.1(*a*). The rate equation for a first-order reaction can be expressed as

$$\frac{d[\mathrm{A}]}{dt} = -k_r[\mathrm{A}] \tag{1.8}$$

Integration of Eq. (1.8) for the boundary conditions $\mathrm{A} = \mathrm{A}_0$ at $t = 0$ and $\mathrm{A} = \mathrm{A}_t$ at time t,

$$\int_{\mathrm{A}_0}^{\mathrm{A}_t} \frac{d[\mathrm{A}]}{[\mathrm{A}]} = -k_r \int_0^t dt \tag{1.9}$$

yields the integrated rate equation for a first-order reaction:

$$\ln \frac{[\mathrm{A}_t]}{[\mathrm{A}_0]} = -k_r t \tag{1.10}$$

or

$$[\mathrm{A}_t] = [\mathrm{A}_0]\, e^{-k_r t} \tag{1.11}$$

For a first-order reaction, a plot of $\ln([A_t]/[A_0])$ versus time yields a straight line with negative slope $-k_r$ (Fig. 1.3).

A special application of the first-order integrated rate equation is in the determination of *decimal reduction times*, or D values, the time required for a one-$\log_{10}$ reduction in the concentration of reacting species (i.e., a 90% reduction in the concentration of reactant). Decimal reduction times are determined from the slope of $\log_{10}([A_t]/[A_0])$ versus time plots (Fig. 1.4). The modified integrated first-order integrated rate equation can be expressed as

$$\log_{10}\frac{[A_t]}{[A_0]} = -\frac{t}{D} \tag{1.12}$$

or

$$[A_t] = [A_0]\cdot 10^{-(t/D)} \tag{1.13}$$

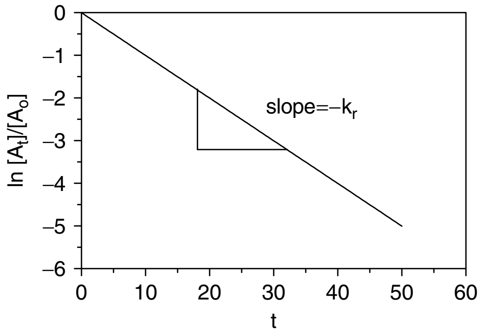


Figure 1.3. Semilogarithmic plot of changes in reactant concentration as a function of time for a first-order reaction used in determination of the reaction rate constant (k_r).

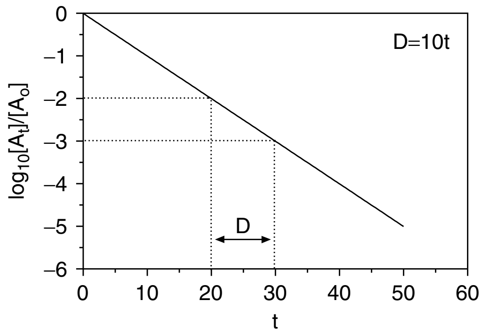


Figure 1.4. Semilogarithmic plot of changes in reactant concentration as a function of time for a first-order reaction used in determination of the decimal reduction time (D value).

The decimal reduction time (D) is related to the first-order rate constant (k_r) in a straightforward fashion:

$$D = \frac{2.303}{k_r} \tag{1.14}$$

1.2.4.3 Second-Order Integrated Rate Equation

The concentration–time curve for a typical second-order reaction, 2A → products, is shown in Fig. 1.1(*a*). The rate equation for a second-order reaction can be expressed as

$$\frac{d[\mathrm{A}]}{dt} = -k_r[\mathrm{A}]^2 \tag{1.15}$$

Integration of Eq. (1.15) for the boundary conditions $\mathrm{A} = \mathrm{A}_0$ at $t = 0$ and $\mathrm{A} = \mathrm{A}_t$ at time t,

$$\int_{\mathrm{A}_0}^{\mathrm{A}_t} \frac{d[\mathrm{A}]}{[\mathrm{A}]^2} = -k_r \int_0^t dt \tag{1.16}$$

yields the integrated rate equation for a second-order reaction:

$$\frac{1}{[\mathrm{A}_t]} = \frac{1}{[\mathrm{A}_0]} + k_r t \tag{1.17}$$

or

$$[\mathrm{A}_t] = \frac{[\mathrm{A}_0]}{1 + [\mathrm{A}_0]k_r t} \tag{1.18}$$

For a second-order reaction, a plot of $1/\mathrm{A}_t$ against time yields a straight line with positive slope k_r (Fig. 1.5).

For a second-order reaction of the type A + B → products, it is possible to express the rate of the reaction in terms of the amount of reactant that is converted to product (P) in time:

$$\frac{d[\mathrm{P}]}{dt} = k_r[\mathrm{A}_0 - \mathrm{P}][\mathrm{B}_0 - \mathrm{P}] \tag{1.19}$$

Integration of Eq. (1.19) using the method of partial fractions for the boundary conditions $\mathrm{A} = \mathrm{A}_0$ and $\mathrm{B} = \mathrm{B}_0$ at $t = 0$, and $\mathrm{A} = \mathrm{A}_t$ and $\mathrm{B} = \mathrm{B}_t$ at time t,

$$\frac{1}{[\mathrm{A}_0] - [\mathrm{B}_0]} \int_0^{\mathrm{P}_t} \left(\frac{d\mathrm{P}}{[\mathrm{B}_0 - \mathrm{P}]} - \frac{d\mathrm{P}}{[\mathrm{A}_0 - \mathrm{P}]} \right) = -k_r \int_0^t dt \tag{1.20}$$

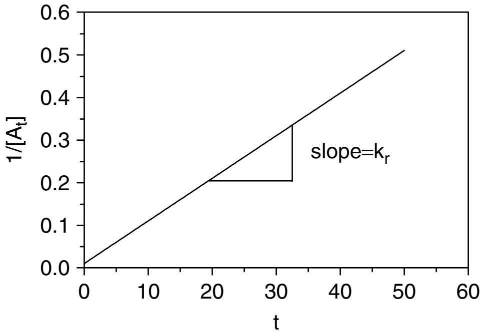


Figure 1.5. Linear plot of changes in reactant concentration as a function of time for a second-order reaction used in determination of the reaction rate constant (k_r).

yields the integrated rate equation for a second-order reaction in which two different reactants participate:

$$\frac{1}{[A_0 - B_0]} \ln \frac{[B_0][A_t]}{[A_0][B_t]} = k_r t \tag{1.21}$$

where $[A_t] = [A_0 - P_t]$ and $[B_t] = [B_0 - P_t]$. For this type of second-order reaction, a plot of $(1/[A_0 - B_0]) \ln([B_0][A_t]/[A_0][B_t])$ versus time yields a straight line with positive slope k_r.

1.2.4.4 Third-Order Integrated Rate Equation

The reactant concentration–time curve for a typical second-order reaction, 3A → products, is shown in Fig. 1.1(a). The rate equation for a third-order reaction can be expressed as

$$\frac{d[A]}{dt} = -k_r[A]^3 \tag{1.22}$$

Integration of Eq. (1.22) for the boundary conditions $A = A_0$ at $t = 0$ and $A = A_t$ at time t,

$$\int_{A_0}^{A_t} \frac{d[A]}{[A]^3} = -k_r \int_0^t dt \tag{1.23}$$

yields the integrated rate equation for a third-order reaction:

$$\frac{1}{2[A_t]^2} = \frac{1}{2[A_0]^2} + k_r t \tag{1.24}$$

or

$$[\mathrm{A}_t] = \frac{[\mathrm{A}_0]}{\sqrt{1 + 2[\mathrm{A}_0]^2 k_r t}} \tag{1.25}$$

For a third-order reaction, a plot of $1/(2[\mathrm{A}_t]^2)$ versus time yields a straight line with positive slope k_r (Fig. 1.6).

1.2.4.5 *Higher-Order Reactions*

For any reaction of the type $n\mathrm{A} \rightarrow$ products, where $n > 1$, the integrated rate equation has the general form

$$\frac{1}{(n-1)[\mathrm{A}_t]^{n-1}} = \frac{1}{(n-1)[\mathrm{A}_0]^{n-1}} + k_r t \tag{1.26}$$

or

$$[\mathrm{A}_t] = \frac{[\mathrm{A}_0]}{\sqrt[n-1]{1 + (n-1)[\mathrm{A}_0]^{n-1} k_r t}} \tag{1.27}$$

For an nth-order reaction, a plot of $1/[(n-1)[\mathrm{A}_t]^{n-1}]$ versus time yields a straight line with positive slope k_r.

1.2.4.6 *Opposing Reactions*

For the simplest case of an opposing reaction $\mathrm{A} \rightleftharpoons \mathrm{B}$,

$$\frac{d[\mathrm{A}]}{dt} = -k_1[\mathrm{A}] + k_{-1}[\mathrm{B}] \tag{1.28}$$

where k_1 and k_{-1} represent, respectively, the rate constants for the forward ($\mathrm{A} \rightarrow \mathrm{B}$) and reverse ($\mathrm{B} \rightarrow \mathrm{A}$) reactions. It is possible to express the rate

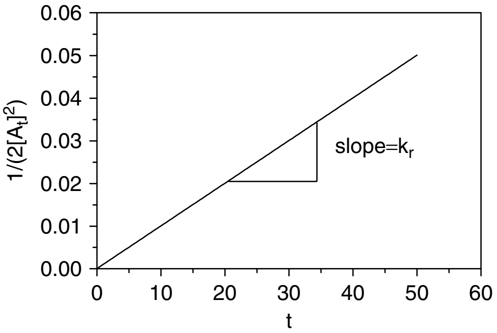


Figure 1.6. Linear plot of changes in reactant concentration as a function of time for a third-order reaction used in determination of the reaction rate constant (k_r).

of the reaction in terms of the amount of reactant that is converted to product (B) in time (Fig. 1.7*a*):

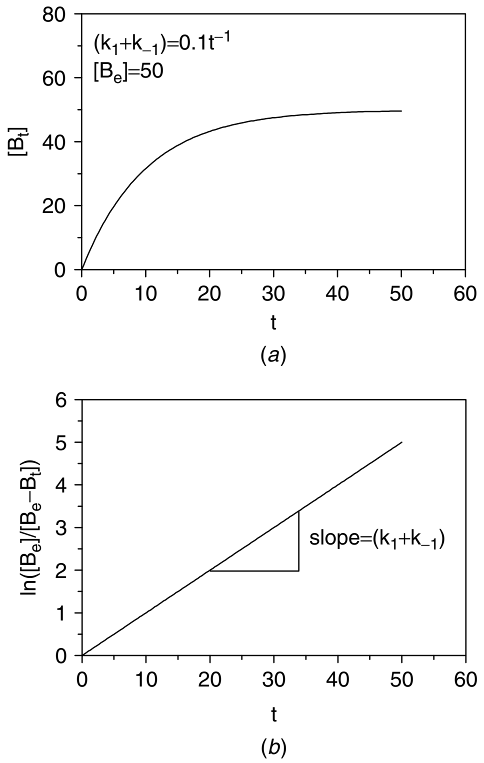
$$\frac{d[\mathrm{B}]}{dt} = k_1[\mathrm{A}_0 - \mathrm{B}] - k_{-1}[\mathrm{B}] \tag{1.29}$$

At equilibrium, $d[\mathrm{B}]/dt = 0$ and $[\mathrm{B}] = [\mathrm{B}_e]$, and it is therefore possible to obtain expressions for k_{-1} and $k_1[\mathrm{A}_0]$:

$$k_{-1} = \frac{k_1[\mathrm{A}_0 - \mathrm{B}_e]}{[\mathrm{B}_e]} \quad \text{and} \quad k_1[\mathrm{A}_0] = (k_{-1} + k_1)[\mathrm{B}_e] \tag{1.30}$$

Substituting the $k_1[\mathrm{A}_0 - \mathrm{B}_e]/[\mathrm{B}_e]$ for k_{-1} into the rate equation, we obtain

$$\frac{d[\mathrm{B}]}{dt} = k_1[\mathrm{A}_0 - \mathrm{B}] - \frac{k_1[\mathrm{A}_0 - \mathrm{B}_e][\mathrm{B}]}{\mathrm{B}_e} \tag{1.31}$$



(*a*)

(*b*)

Figure 1.7. (*a*) Changes in product concentration as a function of time for a reversible reaction of the form $\mathrm{A} \rightleftharpoons \mathrm{B}$. (*b*) Linear plot of changes in product concentration as a function of time used in the determination of forward (k_1) and reverse (k_{-1}) reaction rate constants.

Summing together the terms on the right-hand side of the equation, substituting $(k_{-1} + k_1)[\mathrm{B}_e]$ for $k_1[\mathrm{A}_0]$, and integrating for the boundary conditions $\mathrm{B} = 0$ at $t = 0$ and $\mathrm{B} = \mathrm{B}_t$ at time t,

$$\int_0^{\mathrm{B}_t} \frac{d\mathrm{B}}{[\mathrm{B}_e - \mathrm{B}]/[\mathrm{B}_e]} = (k_1 + k_{-1}) \int_0^t dt \tag{1.32}$$

yields the integrated rate equation for the opposing reaction $\mathrm{A} \rightleftharpoons \mathrm{B}$:

$$\ln \frac{[\mathrm{B}_e]}{[\mathrm{B}_e - \mathrm{B}_t]} = (k_1 + k_{-1})t \tag{1.33}$$

or

$$[\mathrm{B}_t] = [\mathrm{B}_e] - [\mathrm{B}_e]\, e^{-(k_1+k_{-1})t} \tag{1.34}$$

A plot of $\ln([\mathrm{B}_e]/[\mathrm{B}_e - \mathrm{B}])$ versus time results in a straight line with positive slope $(k_1 + k_{-1})$ (Fig. 1.7*b*).

The rate equation for a more complex case of an opposing reaction, $\mathrm{A} + \mathrm{B} \rightleftharpoons \mathrm{P}$, assuming that $[\mathrm{A}_0] = [\mathrm{B}_0]$, and $[\mathrm{P}] = 0$ at $t = 0$, is

$$\frac{[\mathrm{P}_e]}{[\mathrm{A}_0]^2 - [\mathrm{P}_e]^2} \ln \frac{[\mathrm{P}_e][\mathrm{A}_0^2 - \mathrm{P}_e]}{[\mathrm{A}_0]^2[\mathrm{P}_e - \mathrm{P}_t]} = k_1 t \tag{1.35}$$

The rate equation for an even more complex case of an opposing reaction, $\mathrm{A} + \mathrm{B} \rightleftharpoons \mathrm{P} + \mathrm{Q}$, assuming that $[\mathrm{A}_0] = [\mathrm{B}_0]$, $[\mathrm{P}] = [\mathrm{Q}]$, and $[\mathrm{P}] = 0$ at $t = 0$, is

$$\frac{[\mathrm{P}_e]}{2[\mathrm{A}_0][\mathrm{A}_0 - \mathrm{P}_e]} \ln \frac{[\mathrm{P}_t][\mathrm{A}_0 - 2\mathrm{P}_e] + [\mathrm{A}_0][\mathrm{P}_e]}{[\mathrm{A}_0][\mathrm{P}_e - \mathrm{P}_t]} = k_1 t \tag{1.36}$$

1.2.4.7 Reaction Half-Life

The half-life is another useful measure of the rate of a reaction. A reaction half-life is the time required for the initial reactant(s) concentration to decrease by $\frac{1}{2}$. Useful relationships between the rate constant and the half-life can be derived using the integrated rate equations by substituting $\frac{1}{2}\mathrm{A}_0$ for A_t.

The resulting expressions for the half-life of reactions of different orders (n) are as follows:

$$n = 0 \cdots t_{1/2} = \frac{0.5[\mathrm{A}_0]}{k_r} \tag{1.37}$$

$$n = 1 \cdots t_{1/2} = \frac{\ln 2}{k_r} \tag{1.38}$$

$$n = 2 \cdots t_{1/2} = \frac{1}{k_r[\mathrm{A}_0]} \tag{1.39}$$

$$n = 3 \cdots t_{1/2} = \frac{3}{2k_r[\mathrm{A}_0]^2} \tag{1.40}$$

The half-life of an nth-order reaction, where $n > 1$, can be calculated from the expression

$$t_{1/2} = \frac{1 - (0.5)^{n-1}}{(n-1)k_r[\mathrm{A}_0]^{n-1}} \tag{1.41}$$

1.2.5 Experimental Determination of Reaction Order and Rate Constants

1.2.5.1 Differential Method (Initial Rate Method)

Knowledge of the value of the rate of the reaction at different reactant concentrations would allow for determination of the rate and order of a chemical reaction. For the reaction $\mathrm{A} \rightarrow \mathrm{B}$, for example, reactant or product concentration–time curves are determined at different initial reactant concentrations. The absolute value of slope of the curve at $t = 0$, $|d[\mathrm{A}]/dt)_0|$ or $|d[\mathrm{B}]/dt)_0|$, corresponds to the initial rate or initial velocity of the reaction (Fig. 1.8).

As shown before, the reaction velocity (v_A) is related to reactant concentration,

$$v_\mathrm{A} = \left|\frac{d[\mathrm{A}]}{dt}\right| = k_r[\mathrm{A}]^n \tag{1.42}$$

Taking logarithms on both sides of Eq. (1.42) results in the expression

$$\log v_\mathrm{A} = \log k_r + n \log [\mathrm{A}] \tag{1.43}$$

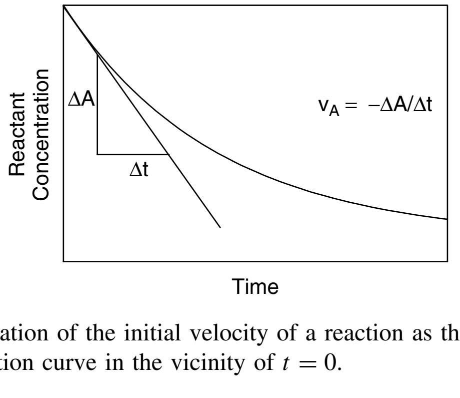


Figure 1.8. Determination of the initial velocity of a reaction as the instantaneous slope of the substrate depletion curve in the vicinity of $t = 0$.

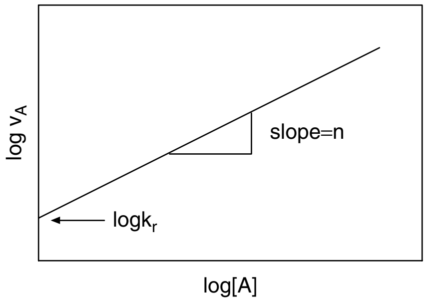


Figure 1.9. Log-log plot of initial velocity versus initial substrate concentration used in determination of the reaction rate constant (k_r) and the order of the reaction.

A plot of the logarithm of the initial rate against the logarithm of the initial reactant concentration yields a straight line with a y-intercept corresponding to log k_r and a slope corresponding to n (Fig. 1.9). For more accurate determinations of the initial rate, changes in reactant concentration are measured over a small time period, where less than 1% conversion of reactant to product has taken place.

1.2.5.2 Integral Method

In the integral method, the rate constant and order of a reaction are determined from least-squares fits of the integrated rate equations to reactant depletion or product accumulation concentration–time data. At this point, knowledge of the reaction order is required. If the order of the reaction is not known, one is assumed or guessed at: for example, $n = 1$. If necessary, data are transformed accordingly [e.g., $\ln([A_t]/[A_0])$] if a linear first-order model is to be used. The model is then fitted to the data using standard least-squares error minimization protocols (i.e., linear or nonlinear regression). From this exercise, a best-fit slope, y-intercept, their corresponding standard errors, as well as a coefficient of determination (CD) for the fit, are determined. The r-squared statistic is sometimes used instead of the CD; however, the CD statistic is the true measure of the fraction of the total variance accounted for by the model. The closer the values of $|r^2|$ or |CD| to 1, the better the fit of the model to the data.

This procedure is repeated assuming a different reaction order (e.g., $n = 2$). The order of the reaction would thus be determined by comparing the coefficients of determination for the different fits of the kinetic models to the transformed data. The model that fits the data best defines the order of that reaction. The rate constant for the reaction, and its corresponding standard error, is then determined using the appropriate model. If coefficients of determination are similar, further experimentation may be required to determine the order of the reaction. The advantage of the differential method over the integral method is that no reaction order needs to be assumed. The reaction order is determined directly from the data analysis. On the other hand, determination of initial rates can be rather inaccurate.

To use integrated rate equations, knowledge of reactant or product concentrations is not an absolute requirement. Any parameter *proportional* to reactant or product concentration can be used in the integrated rate equations (e.g., absorbance or transmittance, turbidity, conductivity, pressure, volume, among many others). However, certain modifications may have to be introduced into the rate equations, since reactant concentration, or related parameters, may not decrease to zero—a minimum, nonzero value (A_{min}) might be reached. For product concentration and related parameters, a maximum value (P_{max}) may be reached, which does not correspond to 100% conversion of reactant to product. A certain amount of product may even be present at $t = 0$ (P_0). The modifications introduced into the rate equations are straightforward. For reactant (A) concentration,

$$[A_t] \Longrightarrow [A_t - A_{min}] \quad \text{and} \quad [A_0] \Longrightarrow [A_0 - A_{min}] \tag{1.44}$$

For product (P) concentration,

$$[P_t] \Longrightarrow [P_t - P_0] \quad \text{and} \quad [P_0] \Longrightarrow [P_{max} - P_0] \tag{1.45}$$

These modified rate equations are discussed extensively in Chapter 12, and the reader is directed there if a more-in-depth discussion of this topic is required at this stage.

1.3 DEPENDENCE OF REACTION RATES ON TEMPERATURE

1.3.1 Theoretical Considerations

The rates of chemical reactions are highly dependent on temperature. Temperature affects the rate constant of a reaction but not the order of the reaction. Classic thermodynamic arguments are used to derive an expression for the relationship between the reaction rate and temperature.

The molar standard-state free-energy change of a reaction (ΔG°) is a function of the equilibrium constant (K) and is related to changes in the molar standard-state enthalpy (ΔH°) and entropy (ΔS°), as described by the Gibbs–Helmholtz equation:

$$\Delta G^\circ = -RT \ln K = \Delta H^\circ - T\Delta S^\circ \tag{1.46}$$

Rearrangement of Eq. (1.46) yields the well-known van't Hoff equation:

$$\ln K = -\frac{\Delta H^\circ}{RT} + \frac{\Delta S^\circ}{R} \tag{1.47}$$

The change in ΔS° due to a temperature change from T_1 to T_2 is given by

$$\Delta S^\circ_{T_2} = \Delta S^\circ_{T_1} + \Delta C_p \ln \frac{T_2}{T_1} \tag{1.48}$$

and the change in ΔH° due to a temperature change from T_1 to T_2 is given by

$$\Delta H^\circ_{T_2} = \Delta H^\circ_{T_1} + \Delta C_p (T_2 - T_1) \tag{1.49}$$

If the heat capacities of reactants and products are the same (i.e., $\Delta C_p = 0$) ΔS° and ΔH° are independent of temperature. Subject to the condition that the difference in the heat capacities between reactants and products is zero, differentiation of Eq. (1.47) with respect to temperature yields a more familiar form of the van't Hoff equation:

$$\frac{d \ln K}{dT} = \frac{\Delta H^\circ}{RT^2} \tag{1.50}$$

For an endothermic reaction, ΔH° is positive, whereas for an exothermic reaction, ΔH° is negative. The van't Hoff equation predicts that the ΔH° of a reaction defines the effect of temperature on the equilibrium constant. For an endothermic reaction, K increases as T increases; for an exothermic reaction, K decreases as T increases. These predictions are in agreement with Le Chatelier's principle, which states that increasing the temperature of an equilibrium reaction mixture causes the reaction to proceed in the direction that absorbs heat. The van't Hoff equation is used for the determination of the ΔH° of a reaction by plotting $\ln K$ against $1/T$. The slope of the resulting line corresponds to $-\Delta H^\circ/R$ (Fig. 1.10). It is also possible to determine the ΔS° of the reaction from the y-intercept, which corresponds to $\Delta S^\circ/R$. It is important to reiterate that this treatment applies only for cases where the heat capacities of the reactants and products are equal and temperature independent.

Enthalpy changes are related to changes in internal energy:

$$\Delta H^\circ = \Delta E^\circ + \Delta(PV) = \Delta E^\circ + P_1V_1 - P_2V_2 \tag{1.51}$$

Hence, ΔH° and ΔE° differ only by the difference in the PV products of the final and initial states. For a chemical reaction at constant pressure

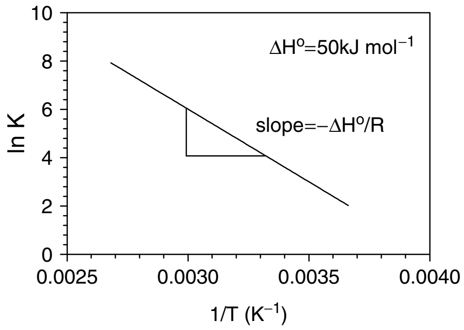


Figure 1.10. van't Hoff plot used in the determination of the standard-state enthalpy ΔH° of a reaction.

in which only solids and liquids are involved, $\Delta(PV) \approx 0$, and therefore ΔH° and ΔE° are nearly equal. For gas-phase reactions, $\Delta(PV) \neq 0$, unless the number of moles of reactants and products remains the same. For ideal gases it can easily be shown that $\Delta(PV) = (\Delta n)RT$. Thus, for gas-phase reactions, if $\Delta n = 0$, $\Delta H^\circ = \Delta E^\circ$.

At equilibrium, the rate of the forward reaction (v_1) is equal to the rate of the reverse reaction (v_{-1}), $v_1 = v_{-1}$. Therefore, for the reaction A $\rightleftharpoons$ B at equilibrium,

$$k_1[\mathrm{A}_e] = k_{-1}[\mathrm{B}_e] \tag{1.52}$$

and therefore

$$K = \frac{[\text{products}]}{[\text{reactants}]} = \frac{[\mathrm{B}_e]}{[\mathrm{A}_e]} = \frac{k_1}{k_{-1}} \tag{1.53}$$

Considering the above, the van't Hoff Eq. (1.50) can therefore be rewritten as

$$\frac{d\ln k_1}{dT} - \frac{d\ln k_{-1}}{dT} = \frac{\Delta E^\circ}{RT^2} \tag{1.54}$$

The change in the standard-state internal energy of a system undergoing a chemical reaction from reactants to products (ΔE°) is equal to the energy required for reactants to be converted to products minus the energy required for products to be converted to reactants (Fig. 1.11). Moreover, the energy required for reactants to be converted to products is equal to the difference in energy between the ground and transition states of the reactants ($\Delta E_1^\ddagger$), while the energy required for products to be converted to reactants is equal to the difference in energy between the ground and

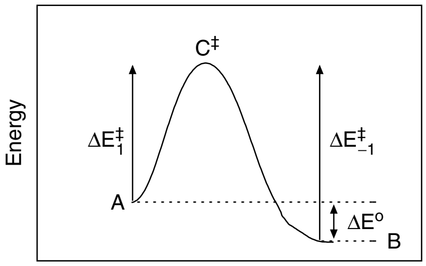


Figure 1.11. Changes in the internal energy of a system undergoing a chemical reaction from substrate A to product B. $\Delta E^{\ddagger}$ corresponds to the energy barrier (energy of activation) for the forward (1) and reverse (−1) reactions, $C^{\ddagger}$ corresponds to the putative transition state structure, and ΔE° corresponds to the standard-state difference in the internal energy between products and reactants.

transition states of the products ($\Delta E^{\ddagger}_{-1}$). Therefore, the change in the internal energy of a system undergoing a chemical reaction from reactants to products can be expressed as

$$\Delta E^{\circ} = E_{\text{products}} - E_{\text{reactants}} = \Delta E_1^{\ddagger} - \Delta E^{\ddagger}_{-1} \tag{1.55}$$

Equation (1.54) can therefore be expressed as two separate differential equations corresponding to the forward and reverse reactions:

$$\frac{d \ln k_1}{dT} = \frac{\Delta E_1^{\ddagger}}{RT^2} + C \quad \text{and} \quad \frac{d \ln k_{-1}}{dT} = \frac{\Delta E^{\ddagger}_{-1}}{RT^2} + C \tag{1.56}$$

Arrhenius determined that for many reactions, $C = 0$, and thus stated his law as:

$$\frac{d \ln k_r}{dT} = \frac{\Delta E^{\ddagger}}{RT^2} \tag{1.57}$$

The Arrhenius law can also be expressed in the more familiar integrated form:

$$\ln k_r = \ln A - \frac{\Delta E^{\ddagger}}{RT} \quad \text{or} \quad k_r = Ae^{-(\Delta E^{\ddagger}/RT)} \tag{1.58}$$

$\Delta E^{\ddagger}$, or E_a as Arrhenius defined this term, is the energy of activation for a chemical reaction, and A is the *frequency factor*. The frequency factor has the same dimensions as the rate constant and is related to the frequency of collisions between reactant molecules.

1.3.2 Energy of Activation

Figure 1.11 depicts a potential energy reaction coordinate for a hypothetical reaction $A \rightleftharpoons B$. For A molecules to be converted to B (forward reaction), or for B molecules to be converted to A (reverse reaction), they must acquire energy to form an activated complex $C^{\ddagger}$. This potential energy barrier is therefore called the *energy of activation* of the reaction. For the reaction to take place, this energy of activation is the minimum energy that must be acquired by the system's molecules. Only a small fraction of the molecules may possess sufficient energy to react. The rate of the forward reaction depends on $\Delta E_1^{\ddagger}$, while the rate of the reverse reaction depends on $\Delta E_{-1}^{\ddagger}$ (Fig. 1.11). As will be shown later, the rate constant is inversely proportional to the energy of activation.

To determine the energy of activation of a reaction, it is necessary to measure the rate constant of a particular reaction at different temperatures. A plot of $\ln k_r$ versus $1/T$ yields a straight line with slope $-\Delta E^{\ddagger}/R$ (Fig. 1.12). Alternatively, integration of Eq. (1.58) as a definite integral with appropriate boundary conditions,

$$\int_{k_1}^{k_2} d \ln k_r = \int_{T_1}^{T_2} \frac{dT}{T^2} \tag{1.59}$$

yields the following expression:

$$\ln \frac{k_2}{k_1} = \frac{\Delta E^{\ddagger}}{R} \frac{T_2 - T_1}{T_2 T_1} \tag{1.60}$$

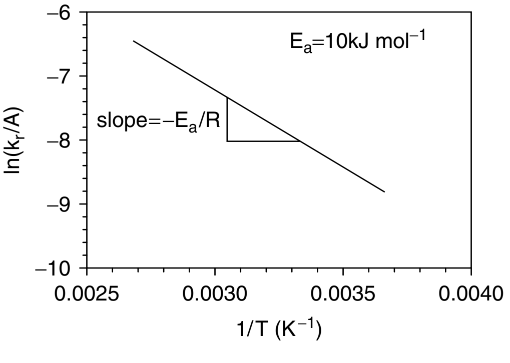


Figure 1.12. Arrhenius plot used in determination of the energy of activation (E_a) of a reaction.

This equation can be used to obtain the energy of activation, or predict the value of the rate constant at T_2 from knowledge of the value of the rate constant at T_1, and of $\Delta E^{\ddagger}$.

A parameter closely related to the energy of activation is the Z *value*, the temperature dependence of the decimal reduction time, or D *value*. The Z value is the temperature increase required for a one-$\log_{10}$ reduction (90% decrease) in the D value, expressed as

$$\log_{10} D = \log_{10} C - \frac{T}{Z} \tag{1.61}$$

or

$$D = C \cdot 10^{-T/Z} \tag{1.62}$$

where C is a constant related to the frequency factor A in the Arrhenius equation.

The Z value can be determined from a plot of $\log_{10} D$ versus temperature (Fig. 1.13). Alternatively, if D values are known only at two temperatures, the Z value can be determined using the equation

$$\log_{10} \frac{D_2}{D_1} = -\frac{T_2 - T_1}{Z} \tag{1.63}$$

It can easily be shown that the Z value is inversely related to the energy of activation:

$$Z = \frac{2.303 R T_1 T_2}{\Delta E^{\ddagger}} \tag{1.64}$$

where T_1 and T_2 are the two temperatures used in the determination of $\Delta E^{\ddagger}$.

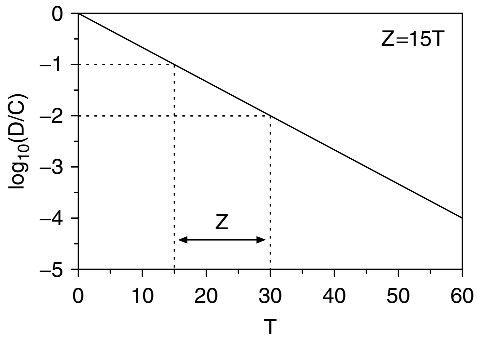


Figure 1.13. Semilogarithmic plot of the decimal reduction time (D) as a function of temperature used in the determination of the Z value.

1.4 ACID–BASE CHEMICAL CATALYSIS

Many homogeneous reactions in solution are catalyzed by acids and bases. A Brönsted acid is a proton donor,

$$\mathrm{HA} + \mathrm{H_2O} \longleftrightarrow \mathrm{H_3O^+} + \mathrm{A^-} \tag{1.65}$$

while a Brönsted base is a proton acceptor,

$$\mathrm{A^-} + \mathrm{H_2O} \longleftrightarrow \mathrm{HA} + \mathrm{OH^-} \tag{1.66}$$

The equilibrium ionization constants for the weak acid (K_{HA}) and its conjugate base ($K_{\mathrm{A^-}}$) are, respectively,

$$K_{\mathrm{HA}} = \frac{[\mathrm{H_3O^+}][\mathrm{A^-}]}{[\mathrm{HA}][\mathrm{H_2O}]} \tag{1.67}$$

and

$$K_{\mathrm{A^-}} = \frac{[\mathrm{HA}][\mathrm{OH^-}]}{[\mathrm{A^-}][\mathrm{H_2O}]} \tag{1.68}$$

The concentration of water can be considered to remain constant ($\sim$55.3 M) in dilute solutions and can thus be incorporated into K_{HA} and $K_{\mathrm{A^-}}$. In this fashion, expressions for the acidity constant (K_a), and the basicity, or hydrolysis, constant (K_b) are obtained:

$$K_a = K_{\mathrm{HA}}[\mathrm{H_2O}] = \frac{[\mathrm{H_3O^+}][\mathrm{A^-}]}{[\mathrm{HA}]} \tag{1.69}$$

$$K_b = K_{\mathrm{A^-}}[\mathrm{H_2O}] = \frac{[\mathrm{HA}][\mathrm{OH^-}]}{[\mathrm{A^-}]} \tag{1.70}$$

These two constants are related by the self-ionization or autoprotolysis constant of water. Consider the ionization of water:

$$2\mathrm{H_2O} \longleftrightarrow \mathrm{H_3O^+} + \mathrm{OH^-} \tag{1.71}$$

where

$$K_{\mathrm{H_2O}} = \frac{[\mathrm{H_3O^+}][\mathrm{OH^-}]}{[\mathrm{H_2O}]^2} \tag{1.72}$$

The concentration of water can be considered to remain constant ($\sim$55.3 M) in dilute solutions and can thus be incorporated into $K_{\mathrm{H_2O}}$.

Equation (1.72) can then be expressed as

$$K_w = K_{H_2O}[H_2O]^2 = [H_3O^+][OH^-] \tag{1.73}$$

where K_w is the self-ionization or autoprotolysis constant of water. The product of K_a and K_b corresponds to this self-ionization constant:

$$K_w = K_a K_b = \frac{[H_3O^+][A^-]}{[HA]} \cdot \frac{[HA][OH^-]}{[A^-]} = [H_3O^+][OH^-] \tag{1.74}$$

Consider a substrate S that undergoes an elementary reaction with an undissociated weak acid (HA), its conjugate conjugate base (A^-), hydronium ions (H_3O^+), and hydroxyl ions (OH^-). The reactions that take place in solution include

$$\begin{gathered}
S \xrightarrow{k_0} P \\
S + H_3O^+ \xrightarrow{k_{H^+}} P + H_3O^+ \\
S + OH^- \xrightarrow{k_{OH^-}} P + OH^- \\
S + HA \xrightarrow{k_{HA}} P + HA \\
S + A^- \xrightarrow{k_{A^-}} P + A^-
\end{gathered} \tag{1.75}$$

The rate of each of the reactions above can be written as

$$\begin{aligned}
v_0 &= k_0[S] \\
v_{H^+} &= k_{H^+}[H_3O^+][S] \\
v_{OH^-} &= k_{OH^-}[OH^-][S] \\
v_{HA} &= k_{HA}[HA][S] \\
v_{A^-} &= k_{A^-}[A^-][S]
\end{aligned} \tag{1.76}$$

where k_0 is the rate constant for the uncatalyzed reaction, k_{H^+} is the rate constant for the hydronium ion–catalyzed reaction, k_{OH^-} is the rate constant for the hydroxyl ion–catalyzed reaction, k_{HA} is the rate constant for the undissociated acid-catalyzed reaction, and k_{A^-} is the rate constant for the conjugate base–catalyzed reaction.

The overall rate of this acid/base-catalyzed reaction (v) corresponds to the summation of each of these individual reactions:

$$\begin{aligned} v &= v_0 + v_{\mathrm{H^+}} + v_{\mathrm{OH^-}} + v_{\mathrm{HA}} + v_{\mathrm{A^-}} \\ &= k_0[\mathrm{S}] + k_{\mathrm{H^+}}[\mathrm{H_3O^+}][\mathrm{S}] + k_{\mathrm{OH^-}}[\mathrm{OH^-}][\mathrm{S}] \\ &\quad + k_{\mathrm{HA}}[\mathrm{HA}][\mathrm{S}] + k_{\mathrm{A^-}}[\mathrm{A^-}][\mathrm{S}] \\ &= (k_0 + k_{\mathrm{H^+}}[\mathrm{H_3O^+}] + k_{\mathrm{OH^-}}[\mathrm{OH^-}] + k_{\mathrm{HA}}[\mathrm{HA}] + k_{\mathrm{A^-}}[\mathrm{A^-}])[\mathrm{S}] \\ &= k_c[\mathrm{S}] \end{aligned} \tag{1.77}$$

where k_c is the catalytic rate coefficient:

$$k_c = k_0 + k_{\mathrm{H^+}}[\mathrm{H_3O^+}] + k_{\mathrm{OH^-}}[\mathrm{OH^-}] + k_{\mathrm{HA}}[\mathrm{HA}] + k_{\mathrm{A^-}}[\mathrm{A^-}] \tag{1.78}$$

Two types of acid–base catalysis have been observed: general and specific. *General acid–base catalysis* refers to the case where a solution is buffered, so that the rate of a chemical reaction is not affected by the concentration of hydronium or hydroxyl ions. For these types of reactions, $k_{\mathrm{H^+}}$ and $k_{\mathrm{OH^-}}$ are negligible, and therefore

$$k_{\mathrm{HA}},\ k_{\mathrm{A^-}} \ggg k_{\mathrm{H^+}},\ k_{\mathrm{OH^-}} \tag{1.79}$$

For general acid–base catalysis, assuming a negligible contribution from the uncatalyzed reaction ($k_0 \lll k_{\mathrm{HA}},\ k_{\mathrm{A^-}}$), the catalytic rate coefficient is mainly dependent on the concentration of undissociated acid HA and conjugate base $\mathrm{A^-}$ at constant ionic strength. Thus, k_c reduces to

$$k_c = k_{\mathrm{HA}}[\mathrm{HA}] + k_{\mathrm{A^-}}[\mathrm{A^-}] \tag{1.80}$$

which can be expressed as

$$k_c = k_{\mathrm{HA}}[\mathrm{HA}] + k_{\mathrm{A^-}}\frac{K_a[\mathrm{HA}]}{[\mathrm{H^+}]} = \left(k_{\mathrm{HA}} + k_{\mathrm{A^-}}\frac{K_a}{[\mathrm{H^+}]}\right)[\mathrm{HA}] \tag{1.81}$$

Thus, a plot of k_c versus HA concentration at constant pH yields a straight line with

$$\text{slope} = k_{\mathrm{HA}} + k_{\mathrm{A^-}}\frac{K_a}{[\mathrm{H^+}]} \tag{1.82}$$

Since the value of K_a is known and the pH of the reaction mixture is fixed, carrying out this experiment at two values of pH allows for the determination of k_{HA} and $k_{\mathrm{A^-}}$.

Of greater relevance to our discussion is *specific acid–base catalysis*, which refers to the case where the rate of a chemical reaction is proportional only to the concentration of hydrogen and hydroxyl ions present. For these type of reactions, k_{HA} and k_{A^-} are negligible, and therefore

$$k_{\text{H}^+},\ k_{\text{OH}^-} \ggg k_{\text{HA}},\ k_{\text{A}^-} \tag{1.83}$$

Thus, k_c reduces to

$$k_c = k_0 + k_{\text{H}^+}[\text{H}^+] + k_{\text{OH}^-}[\text{OH}^-] \tag{1.84}$$

The catalytic rate coefficient can be determined by measuring the rate of the reaction at different pH values, at constant ionic strength, using appropriate buffers.

Furthermore, for acid-catalyzed reactions at high acid concentrations where k_0, $k_{\text{OH}^-} \lll k_{\text{H}^+}$,

$$k_c = k_{\text{H}^+}[\text{H}^+] \tag{1.85}$$

For base-catalyzed reactions at high alkali concentrations where k_0, $k_{\text{H}^+} \lll k_{\text{OH}^-}$,

$$k_c = k_{\text{OH}^-}[\text{OH}^-] = k_{\text{OH}^-}\frac{K_w}{[\text{H}^+]} \tag{1.86}$$

Taking base 10 logarithms on both sides of Eqs. (1.85) and (1.86) results, respectively, in the expressions

$$\log_{10} k_c = \log_{10} k_{\text{H}^+} + \log_{10}[\text{H}^+] = \log_{10} k_{\text{H}^+} - \text{pH} \tag{1.87}$$

for acid-catalyzed reactions and

$$\log_{10} k_c = \log_{10}(K_w k_{\text{OH}^-}) - \log_{10}[\text{H}^+] = \log_{10}(K_w k_{\text{OH}^-}) + \text{pH} \tag{1.88}$$

for base-catalyzed reactions.

Thus, a plot of $\log_{10} k_c$ versus pH is linear in both cases. For an acid-catalyzed reaction at low pH, the slope equals -1, and for a base-catalyzed reaction at high pH, the slope equals $+1$ (Fig. 1.14). In regions of intermediate pH, $\log_{10} k_c$ becomes independent of pH and therefore of hydroxyl and hydrogen ion concentrations. In this pH range, k_c depends solely on k_0.

1.5 THEORY OF REACTION RATES

Absolute reaction rate theory is discussed briefly in this section. Collision theory will not be developed explicitly since it is less applicable to

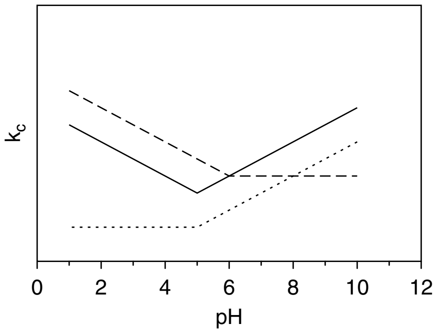


Figure 1.14. Changes in the reaction rate constant for an acid/base-catalyzed reaction as a function of pH. A negative sloping line (slope $= -1$) as a function of increasing pH is indicative of an acid-catalyzed reaction; a positive sloping line (slope $= +1$) is indicative of a base-catalyzed reaction. A slope of zero is indicative of pH independence of the reaction rate.

the complex systems studied. Absolute reaction rate theory is a collision theory which assumes that chemical activation occurs through collisions between molecules. The central postulate of this theory is that the rate of a chemical reaction is given by the rate of passage of the activated complex through the transition state.

This theory is based on two assumptions, a dynamical bottleneck assumption and an equilibrium assumption. The first asserts that the rate of a reaction is controlled by the decomposition of an activated transition-state complex, and the second asserts that an equilibrium exists between reactants (A and B) and the transition-state complex, $C^\ddagger$:

$$A + B \rightleftharpoons C^\ddagger \longrightarrow C + D \tag{1.89}$$

It is therefore possible to define an equilibrium constant for the conversion of reactants in the ground state into an activated complex in the transition state. For the reaction above,

$$K^\ddagger = \frac{[C^\ddagger]}{[A][B]} \tag{1.90}$$

As discussed previously, $\Delta G^\circ = -RT \ln K$ and $\ln K = \ln k_1 - \ln k_{-1}$. Thus, in an analogous treatment to the derivation of the Arrhenius equation (see above), it would be straightforward to show that

$$k_r = ce^{-(\Delta G^\ddagger/RT)} = cK^\ddagger \tag{1.91}$$

where $\Delta G^{\ddagger}$ is the free energy of activation for the conversion of reactants into activated complex. By using statistical thermodynamic arguments, it is possible to show that the constant c equals

$$c = \kappa \nu \tag{1.92}$$

where κ is the transmission coefficient and ν is the frequency of the normal-mode oscillation of the transition-state complex along the reaction coordinate—more rigorously, the average frequency of barrier crossing. The transmission coefficient, which can differ dramatically from unity, includes many correction factors, including tunneling, barrier recrossing correction, and solvent frictional effects. The rate of a chemical reaction depends on the equilibrium constant for the conversion of reactants into activated complex.

Since $\Delta G = \Delta H - T\Delta S$, it is possible to rewrite Eq. (1.91) as

$$k_r = \kappa \nu e^{\Delta S^{\ddagger}/R} e^{-(\Delta H^{\ddagger}/RT)} \tag{1.93}$$

Consider $\Delta H = \Delta E + (\Delta n)RT$, where Δn equals the difference between the number of moles of activated complex (n_{ac}) and the moles of reactants (n_r). The term n_r also corresponds to the molecularity of the reaction (e.g., unimolecular, bimolecular). At any particular time, $n_r \ggg n_{\mathrm{ac}}$ and therefore $\Delta H \approx \Delta E - n_r RT$. Substituting this expression for the enthalpy change into Eq. (1.93) and rearranging, we obtain

$$k_r = \kappa \nu \, e^{(n_r + \Delta S^{\ddagger})/R} e^{-(\Delta E^{\ddagger}/RT)} \tag{1.94}$$

Comparison of this equation with the Arrhenius equation sheds light on the nature of the frequency factor:

$$A = \kappa \nu \, e^{(n_r + \Delta S^{\ddagger})/R} \tag{1.95}$$

The concept of entropy of activation ($\Delta S^{\ddagger}$) is of utmost importance for an understanding of reactivity. Two reactions with similar $\Delta E^{\ddagger}$ values at the same temperature can proceed at appreciably different rates. This effect is due to differences in their entropies of activation. The entropy of activation corresponds to the difference in entropy between the ground and transition states of the reactants. Recalling that entropy is a measure of the randomness of a system, a positive $\Delta S^{\ddagger}$ suggests that the transition state is more disordered (more degrees of freedom) than the ground state. Alternatively, a negative $\Delta S^{\ddagger}$ value suggests that the transition state is more ordered (less degrees of freedom) than the ground state. Freely diffusing, noninteracting molecules have many translational, vibrational and rotational degrees of freedom. When two molecules interact at the onset of a chemical reaction and pass into a more structured transition state, some of these degrees of freedom will be lost. For this reason, most entropies of activation for chemical reactions are negative. When the change in entropy for the formation of the activated complex is small ($\Delta S^{\ddagger} \approx 0$), the rate of the reaction is controlled solely by the energy of activation ($\Delta E^{\ddagger}$).

It is interesting to use the concept of entropy of activation to explain the failure of collision theory to explain reactivity. Consider that for a bimolecular reaction $\mathrm{A} + \mathrm{B} \rightarrow$ products, the frequency factor (A) equals the number of collisions per unit volume between reactant molecules (Z) times a steric, or probability factor (P):

$$A = PZ = \kappa \nu \, e^{2+\Delta S^{\ddagger}/R} \tag{1.96}$$

If only a fraction of the collisions result in conversion of reactants into products, then $P < 1$, implying a negative $\Delta S^{\ddagger}$. For this case, the rate of the reaction will be slower than predicted by collision theory. If a greater number of reactant molecules than predicted from the number of collisions are converted into products, $P > 1$, implying a positive $\Delta S^{\ddagger}$. For this case, the rate of the reaction will be faster than predicted by collision theory. On the other hand, when $P = 1$ and $\Delta S^{\ddagger} = 0$, predictions from collision theory and absolute rate theory agree.

1.6 COMPLEX REACTION PATHWAYS

In this section we discuss briefly strategies for tackling more complex reaction mechanisms. The first step in any kinetic modeling exercise is to write down the differential equations and mass balance that describe the process. Consider the reaction

$$\mathrm{A} \xrightarrow{k_1} \mathrm{B} \xrightarrow{k_2} \mathrm{C} \tag{1.97}$$

Typical concentration–time patterns for A, B, and C are shown in Fig. 1.15. The differential equations and mass balance that describe this reaction are

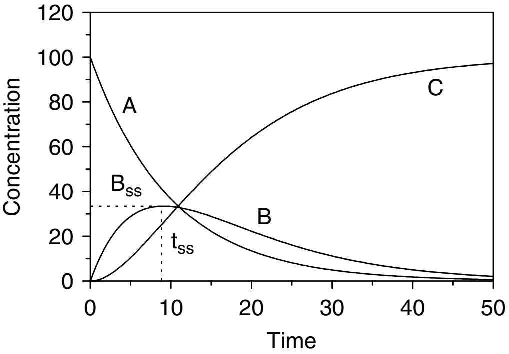


Figure 1.15. Changes in reactant, intermediate, and product concentrations as a function of time for a reaction of the form A → B → C. B_{ss} denotes the steady-state concentration in intermediate B at time t_{ss}.

$$\frac{d\mathrm{A}}{dt} = -k_1[\mathrm{A}] \tag{1.98}$$

$$\frac{d[\mathrm{B}]}{dt} = k_1[\mathrm{A}] - k_2[\mathrm{B}] \tag{1.99}$$

$$\frac{d[\mathrm{C}]}{dt} = k_2[\mathrm{B}] \tag{1.100}$$

$$[\mathrm{A}_0] + [\mathrm{B}_0] + [\mathrm{C}_0] = [\mathrm{A}_t] + [\mathrm{B}_t] + [\mathrm{C}_t] \tag{1.101}$$

Once the differential equations and mass balance have been written down, three approaches can be followed in order to model complex reaction schemes. These are (1) numerical integration of differential equations, (2) steady-state approximations to solve differential equations analytically, and (3) exact analytical solutions of the differential equations without using approximations.

It is important to remember that in this day and age of powerful computers, it is no longer necessary to find analytical solutions to differential equations. Many commercially available software packages will carry out numerical integration of differential equations followed by nonlinear regression to fit the model, in the form of differential equations, to the data. Estimates of the rate constants and their variability, as well as measures of the goodness of fit of the model to the data, can be obtained in this fashion. Eventually, all modeling exercises are carried out in this fashion since it is difficult, and sometimes impossible, to obtain analytical solutions for complex reaction schemes.

1.6.1 Numerical Integration and Regression

1.6.1.1 Numerical Integration

Finding the numerical solution of a system of first-order ordinary differential equations,

$$\frac{dY}{dx} = \mathrm{F}(x, Y(x)) \qquad Y(x_0) = Y_0 \tag{1.102}$$

entails finding the numerical approximations of the solution $Y(x)$ at discrete points $x_0, x_1, x_2 < \cdots < x_n < x_{n+1} < \cdots$ by $Y_0, Y_1, Y_2, \ldots, Y_n$, $Y_{n+1}, \ldots$. The distance between two consecutive points, $h_n = x_n - x_{n+1}$, is called the *step size*. Step sizes do not necessarily have to be constant between all grid points x_n. All numerical methods have one property in common: finding approximations of the solution $Y(x)$ at grid points one by one. Thus, if a formula can be given to calculate Y_{n+1} based on the information provided by the known values of $Y_n, Y_{n-1}, \cdots, Y_0$, the problem is solved. Many numerical methods have been developed to find solutions for ordinary differential equations, the simplest one being the Euler method. Even though the Euler method is seldom used in practice due to lack of accuracy, it serves as the basis for analysis in more accurate methods, such as the Runge–Kutta method, among many others.

For a small change in the dependent variable (Y) in time (x), the following approximation is used:

$$\frac{dY}{dx} \sim \frac{\Delta Y}{\Delta x} \tag{1.103}$$

Therefore, we can write

$$\frac{Y_{n+1} - Y_n}{x_{n+1} - x_n} = F(x_n, Y_n) \tag{1.104}$$

By rearranging Eq. (1.104), Euler obtained an expression for Y_{n+1} in terms of Y_n:

$$Y_{n+1} = Y_n + (x_{n+1} - x_n)F(x_n, Y_n) \quad \text{or} \quad Y_{n+1} = Y_n + hF(x_n, Y_n) \tag{1.105}$$

Consider the reaction A → B → C. As discussed before, the analytical solution for the differential equation that describes the first-order decay in [A] is $[\mathrm{A}_t] = [\mathrm{A}_0]\,e^{-kt}$. Hence, the differential equation that describes changes in [B] in time can be written as

$$\frac{d[\mathrm{B}]}{dt} = k_1[\mathrm{A}_0]\,e^{-k_1 t} - k_2[\mathrm{B}] \tag{1.106}$$

A numerical solution for the differential equation (1.106) is found using *the initial value* $[\mathrm{B}_0]$ at $t = 0$, and from knowledge of the values of k_1, k_2, and $[\mathrm{A}_0]$. Values for $[\mathrm{B}_t]$ are then calculated as follows:

$$\begin{aligned}
[\mathrm{B}_1] &= [\mathrm{B}_0] + h(k_1[\mathrm{A}_0] - k_2[\mathrm{B}_0]) \\
[\mathrm{B}_2] &= [\mathrm{B}_1] + h(k_1[\mathrm{A}_0]\,e^{-k_1t_1} - k_2[\mathrm{B}_1]) \\
&\vdots \\
[\mathrm{B}_{n+1}] &= [\mathrm{B}_n] + h(k_1[\mathrm{A}_0]\,e^{-k_1t_n} - k_2[\mathrm{B}_n])
\end{aligned} \tag{1.107}$$

It is therefore possible to generate a numerical solution (i.e., a set of numbers predicted by the differential equation) of the ordinary differential equation (1.106). Values obtained from the numerical integration (i.e., predicted data) can now be compared to experimental data values.

1.6.1.2 Least-Squares Minimization (Regression Analysis)

The most common way in which models are fitted to data is by using least-squares minimization procedures (regression analysis). All these procedures, linear or nonlinear, seek to find estimates of the equation parameters $(\alpha, \beta, \gamma, \ldots)$ by determining parameter values for which the sum of squared residuals is at a minimum, and therefore

$$\left[\frac{\partial \sum_1^n (y_i - \hat{y}_i)^2}{\partial \alpha}\right]_{\beta,\gamma,\delta,\ldots} = 0 \tag{1.108}$$

where y_i and $\hat{y}_i$ correspond, respectively, to the ith experimental and predicted points at x_i. If the variance $({s_i}^2)$ of each data point is known from experimental replication, a weighted least-squares minimization can be carried out, where the weights (w_i) correspond to $1/{s_i}^2$. In this fashion, data points that have greater error contribute less to the analysis. Estimates of equation parameters are found by determining parameter values for which the chi-squared (χ^2) value is at a minimum, and therefore

$$\left[\frac{\partial \sum_1^n w_i(y_i - \hat{y}_i)^2}{\partial \alpha}\right]_{\beta,\gamma,\delta,\ldots} = 0 \tag{1.109}$$

At this point it is necessary to discuss differences between uniresponse and multiresponse modeling. Take, for example, the reaction A → B → C. Usually, equations in differential or algebraic form are fitted to individual data sets, A, B, and C and a set of parameter estimates obtained.

However, if changes in the concentrations of A, B, and C as a function of time are determined, it is possible to use the entire data set (A, B, C) simultaneously to obtain parameter estimates. This procedure entails fitting the functions that describe changes in the concentration of A, B, and C to the experimental data *simultaneously*, thus obtaining one global estimate of the rate constants. This *multivariate response modeling* helps increase the precision of the parameter estimates by using all available information from the various responses.

A determinant criterion is used to obtain least-squares estimates of model parameters. This entails minimizing the determinant of the matrix of cross products of the various residuals. The maximum likelihood estimates of the model parameters are thus obtained without knowledge of the variance–covariance matrix. The residuals ϵ_{iu}, ϵ_{ju}, and ϵ_{ku} correspond to the difference between predicted and actual values of the dependent variables at the different values of the uth independent variable ($u = t_0$ to $u = t_n$), for the ith, jth, and kth experiments (A, B, and C), respectively. It is possible to construct an error covariance matrix with elements ν_{ij}:

$$\nu_{ij} = \sum_{u=1}^{n} \epsilon_{iu}\epsilon_{ju} \tag{1.110}$$

The determinant of this matrix needs to be minimized with respect to the parameters. The diagonal of this matrix corresponds to the sums of squares for each response (ν_{ii}, ν_{jj}, ν_{kk}).

Regression analysis involves several important assumptions about the function chosen and the error structure of the data:

1. The correct equation is used.
2. Only dependent variables are subject to error; while independent variables are known exactly.
3. Errors are normally distributed with zero mean, are the same for all responses (homoskedastic errors), and are uncorrelated (zero covariance).
4. The correct weighting is used.

For linear functions, single or multiple, it is possible to find analytical solutions of the error minimization partial differential. Therefore, exact mathematical expressions exist for the calculation of slopes and intercepts. It should be noted at this point that a linear function of parameters does not imply a straight line. A model is *linear* if the first partial derivative of the function with respect to the parameter(s) is independent of such parameter(s), therefore, higher-order derivatives would be zero.

For example, equations used to calculate the best-fit slope and y-intercept for a data set that fits the linear function $y = mx + b$ can easily be obtained by considering that the minimum sum-of-squared residuals (SS) corresponds to parameter values for which the partial differential of the function with respect to each parameter equals zero. The squared residuals to be minimized are

$$(\text{residual})^2 = (y_i - \hat{y}_i)^2 = [y_i - (mx_i + b)]^2 \tag{1.111}$$

The partial differential of the slope (m) for a constant y-intercept is therefore

$$\left(\frac{\partial \text{SS}}{\partial m}\right)_b = -2\sum_1^n x_i y_i + 2b\sum_1^n x_i + 2m\sum_1^n x_i^2 = 0 \tag{1.112}$$

and therefore

$$m = \frac{\sum_1^n x_i y_i - b\sum_1^n x_i}{\sum_1^n x_i^2} \tag{1.113}$$

The partial differential of the y-intercept for a constant slope is

$$\left(\frac{\partial \text{SS}}{\partial b}\right)_m = m\sum_1^n x_i - \sum_1^n y_i + nb = 0 \tag{1.114}$$

and therefore

$$b = \frac{\sum_1^n y_i - m\sum_1^n x_i}{n} = \overline{y} - m\overline{x} \tag{1.115}$$

where x and y correspond to the overall averages of all x and y data, respectively. Substituting b into m and rearranging, we obtain an equation for direct calculation of the best-fit slope of the line:

$$m = \frac{\sum_{i=1}^n x_i y_i - \left(\sum_{i=1}^n x_i \sum_{i=1}^n y_i / n\right)}{\sum_{i=1}^n x_i^2 - \left(\sum_{i=1}^n x_i\right)^2 / n} = \frac{\sum_{i=1}^n (x_i - \overline{x})(y_i - \overline{y})}{\sum_{i=1}^n (x_i - \overline{x})^2} \tag{1.116}$$

The best-fit y-intercept of the line is given by

$$b = \overline{y} - \frac{\sum_{i=1}^{n} (x_i - \overline{x})(y_i - \overline{y})}{\sum_{i=1}^{n} (x_i - \overline{x})^2} \overline{x} \tag{1.117}$$

These equations could have also been derived by considering the orthogonality of residuals using $\sum (y_i - \hat{y}_i)(x_i) = 0$.

Goodness-of-Fit Statistics

At this point it would be useful to mention goodness-of-fit statistics. A useful parameter for judging the goodness of fit of a model to experimental data is the reduced χ^2 value:

$$\chi_\nu^2 = \frac{\sum_1^n w_i (y_i - \hat{y}_i)^2}{\nu} \tag{1.118}$$

where w_i is the weight of the ith data point and ν corresponds to the degrees of freedom, defined as $\nu = (n - p - 1)$, where n is the total number of data values and p is the number of parameters that are estimated. The reduced χ^2 value should be roughly equal to the number of degrees of freedom if the model is correct (i.e., $\chi_\nu^2 \approx 1$). Another statistic most appropriately applied to linear regression, as an indication of how closely the dependent and independent variables approximate a linear relationship to each other is the *correlation coefficient* (CC):

$$\mathrm{CC} = \frac{\sum_{i=1}^{n} w_i (x_i - \overline{x})(y_i - \overline{y})}{\left[\sum_{i=1}^{n} w_i (x_i - \overline{x})^2\right]^{1/2} \left[\sum_{i=1}^{n} w_i (y_i - \overline{y})^2\right]^{1/2}} \tag{1.119}$$

Values for the correlation coefficient can range from -1 to $+1$. A CC value close to ± 1 is indicative of a strong correlation. The *coefficient of determination* (CD) is the fraction $(0 < \mathrm{CD} \leq 1)$ of the total variability accounted for by the model. This is a more appropriate measure of the goodness of fit of a model to data than the R-squared statistic. The CD has the general form

$$\mathrm{CD} = \frac{\sum_{i=1}^{n} w_i (y_i - \overline{y})^2 - \sum_{i=1}^{n} w_i (y_i - \hat{y}_i)^2}{\sum_{i=1}^{n} w_i (y_i - \overline{y})^2} \tag{1.120}$$

Finally, the r^2 statistic is similar to the CD. This statistic is often used erroneously when, strictly speaking, the CD should be used. The root of the r^2 statistic is sometimes erroneously reported to correspond to the CD. An r^2 value close to ± 1 is indicative that the model accounts for most of the variability in the data. The r^2 statistic has the general form

$$r^2 = \frac{\sum_{i=1}^{n} w_i y_i{}^2 - \sum_{i=1}^{n} w_i (y_i - \hat{y}_i)^2}{\sum_{i=1}^{n} w_i y_i{}^2} \tag{1.121}$$

Nonlinear Regression: Techniques and Philosophy

For nonlinear functions, however, the situation is more complex. Iterative methods are used instead, in which parameter values are changed simultaneously, or one at a time, in a prescribed fashion until a global minimum is found. The algorithms used include the Levenberg–Marquardt method, the Powell method, the Gauss–Newton method, the steepest-descent method, simplex minimization, and combinations thereof. It is beyond our scope in this chapter to discuss the intricacies of procedures used in nonlinear regression analysis. Suffice to say, most modern graphical software packages include nonlinear regression as a tool for curve fitting.

Having said this, however, some comments on curve fitting and nonlinear regression are required. There is no general method that guarantees obtaining the best global solution to a nonlinear least-squares minimization problem. Even for a single-parameter model, several minima may exist! A minimization algorithm will eventually succeed in find *a minimum*; however, there is no assurance that this corresponds to the *global minimum*. It is theoretically possible for one, and maybe two, parameter functions to search all parameter initial values exhaustively and find the global minimum. However, this approach is usually not practical even beyond a single parameter function.

There are, however, some guidelines that can be followed to increase the likelihood of finding the best fit to nonlinear models. All nonlinear regression algorithms require *initial estimates* of parameter values. These initial estimates should be as close as possible to their best-fit value so that the program can actually succeed in finding the global minimum. The development of good initial estimates comes primarily from the scientists' physical knowledge of the problem at hand as well as from intuition and experience. Curve fitting can sometimes be somewhat of an artform.

Generally, it is useful to carry out simulations varying initial estimates of parameter values in order to develop a feeling for how changes in initial estimate values will affect the nonlinear regression results obtained. Some programs offer simplex minimization algorithms that do not require the input of initial estimates. These secondary minimization procedures may provide values of initial estimates for the primary minimization procedures. Once a minimum is found, there is no assurance, however, that it corresponds to the global minimum. A standard procedure to test whether the global minimum has been reached is called *sensitivity analysis*. Sensitivity analysis refers to the variability in results (parameter estimates) obtained from nonlinear regression analysis due to changes in the values of initial estimates. In sensitivity analysis, least-squares minimizations are carried out for different starting values of initial parameter estimates to determine whether the convergence to the same solution is attained. If the same minimum is found for different values of initial estimates, the scientist can be fairly confident that the minimum proposed is the best answer. Another approach is to fit the model to the data using different weighting schemes, since it is possible that the largest or smallest values in the data set may have an undue influence on the final result. Very important as well is the visual inspection of the data and plotted curve(s), since a graph can provide clues that may aid in finding a better solution to the problem.

Strategies exist for systematically finding minima and hence finding the best minimum. In a multiparameter model, it is sometimes useful to vary one or two parameters at a time. This entails carrying out the least-squares minimization procedure floating one parameter at a time while fixing the value of the other parameters as constants and/or analyzing a subset of the data. This simplifies calculations enormously, since the greater the number of parameters to be estimated simultaneously, the more difficult it will be for the program to find the global minimum. For example, for the reaction $A \rightarrow B \rightarrow C$, k_1 can easily be estimated from the first-order decay of [A] in time. The parameter k_1 can therefore be fixed as a constant, and only k_2 and k_3 floated. After preliminary parameter estimates are obtained in this fashion, these parameters should be fixed as constants and the remaining parameters estimated. Only after estimates are obtained for all the parameters should the entire parameter set be fitted simultaneously. It is also possible to assign physical limits, or constraints, to the values of the parameters. The program will find a minimum that corresponds to parameter values within the permissible range.

Care should be exercised at the data-gathering stage as well. A common mistake is to gather all the experimental data without giving much thought as to how the data will be analyzed. It is extremely useful to use the model to simulate data sets and then try to fit the model to the simulated data. This exercise will promptly point out where more data would be useful to the model-building process. It is a good investment of time to simulate the experiment and data analysis to identify where problems may lie and identify regions of data that may be most important in determining the properties of the model. The data gathered must be amenable to analysis in such a way as to shed light on the model.

For difficult problems, the determination of best-fit parameters is a procedure that benefits greatly from experience, intuition, perseverance, skepticism, and scientific reasoning. A good answer requires good initial estimates. Start the minimization procedure with the best possible initial estimates for parameters, and if the parameters have physical limits, specify constraints on their value. For complicated models, begin model fitting by floating a single parameter and using a subset of the data that may be most sensitive to changes in the value of the particular parameter. Subsequently, add parameters and data until it is possible to fit the full model to the complete data set. After the minimization is accomplished, test the answers by carrying out sensitivity analysis. Perhaps run a simplex minimization procedure to determine if there are other minima nearby and whether or not the minimization wanders off in another direction. Finally, plot the data and calculated values and check visually for goodness of fit—the human eye is a powerful tool. Above all, care should be exercised; if curve fitting is approached blindly without understanding its inherent limitations and nuances, erroneous results will be obtained.

The F-test is the most common statistical tool used to judge whether a model fits the data better than another. The models to be compared are fitted to data and reduced χ^2 values (χ_ν^2) obtained. The ratio of the $\chi_\nu{}^2$ values obtained is the F-statistic:

$$F_{\mathrm{df}_n,\mathrm{df}_d} = \frac{\chi_\nu^2(a)}{\chi_\nu^2(b)} \tag{1.122}$$

where df stands for *degrees of freedom*, which are determined from

$$\mathrm{df} = n - p - 1 \tag{1.123}$$

where n and p correspond, respectively, to the total number of data points and the number of parameters in the model. Using standard statistical tables, it is possible to determine if the fits of the models to the data are significantly different from each other at a certain level of statistical significance.

The analysis of residuals ($\hat{y}_i - y_i$), in the form of the *serial correlation coefficient* (SCC), provides a useful measure of how much the model deviates from the experimental data. Serial correlation is an indication of whether residuals tend to run in groups of positive or negative values or tend to be scattered randomly about zero. A large positive value of the SCC is indicative of a systematic deviation of the model from the data.

The SCC has the general form

$$\mathrm{SCC} = \sqrt{n-1}\frac{\sum_{i=1}^{n}\sqrt{w_i}(\hat{y}_i - y_i)\sqrt{w_{i-1}}(\hat{y}_{i-1} - y_{i-1})}{\sum_{i=1}^{n}[w_i(\hat{y}_i - y_i)]^2} \tag{1.124}$$

Weighting Scheme for Regression Analysis

As stated above, in regression analysis, a model is fitted to experimental data by minimizing the sum of the squared differences between experimental and predicted data, also known as the *chi-square* (χ^2) *statistic*:

$$\chi^2 = \sum_{i=1}^{n}\frac{(y_i - \hat{y}_i)^2}{s_i^2} = \sum_{i=1}^{n} w_i(y_i - \hat{y}_i)^2 \tag{1.125}$$

Consider a typical experiment where the value of a dependent variable is measured several times at a particular value of the independent variable. From these repeated determinations, a mean and variance of a sample of population values can be calculated. If the experiment itself is then replicated several times, a set of sample means ($\overline{y}_i$) and variances of *sample means* (s_i^2) can be obtained. This variance is a measure of the experimental variability (i.e., the experimental error, associated with $\overline{y}_i$). The central limit theorem clearly states that it is the means of population values, and not individual population values, that are distributed in a Gaussian fashion. This is an essential condition if parametric statistical analysis is to be carried out on the data set. The variance is defined as

$$s_i^2 = \frac{\sum_{i=1}^{n_i}(y_i - \overline{y}_i)^2}{n_i - 1} \tag{1.126}$$

A weight w_i is merely the inverse of this variance:

$$w_i = \frac{1}{s_i^2} \tag{1.127}$$

The two most basic assumptions made in regression analysis are that experimental errors are normally distributed with mean zero and that errors are the same for all data points (error homoskedasticity). Systematic trends in the experimental errors or the presence of outliers would invalidate these assumptions. Hence, the purpose of weighting residuals is to eliminate systematic error heteroskedasticity and excessively noisy data. The next challenge is to determine which error structure is present in the experimental data—not a trivial task by any means.

Ideally, each experiment would be replicated sufficiently so that individual data weights could be calculated directly from experimentally determined variances. However, replicating experiments to the extent that would be required to obtain accurate estimates of the errors is expensive, time consuming, and impractical. It is important to note that if insufficient data points are used to estimate individual errors of data points, incorrect estimates of weights will be obtained. The use of incorrect weights in regression analysis will make matters worse—if in doubt, do not weigh the data.

A useful technique for the determination of weights is described below. The relationship between the variance of a data point and the value of the point can be explored using the relationship

$$s_i^2 = K y_i^{\alpha} \tag{1.128}$$

A plot of $\ln s_i^2$ against $\ln y_i$ yields a straight line with slope $= \alpha$ and y-intercept $= \ln K$ (Fig. 1.16). The weight for the ith data point can then be calculated as

$$w_i = \frac{1}{s_i^2} \sim \frac{K}{s_i^2} = y_i^{-\alpha} \tag{1.129}$$

K is merely a constant that is not included in the calculations, since interest lies in the determination of the *relative* weighting scheme for a particular data set, not in the absolute values of the weights.

If $\alpha = 0$, s_i^2 is not dependent on the magnitude of the y values, and $w = 1/K$ for all data points. This is the case for an error that is constant throughout the data (homogeneous or constant error). Thus, if the error structure is homogeneous, weighting of the data is not required. A value

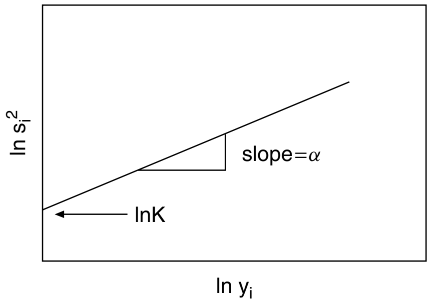


Figure 1.16. Log-log plot of changes in the variance (s_i^2) of the ith sample mean as a function of the value of the ith sample mean (y_i). This plot is used in determination of the type of error present in the experimental data set for the establishment of a weighting scheme to be used in regression analysis of the data.

of $\alpha > 0$ is indicative of a dependence of s_i^2 on the magnitude of the y value. This is referred to as *heterogeneous* or *relative error structure*. Classic heterogeneous error structure analysis usually places $\alpha = 2$ and therefore $w_i \sim 1/Ky_i^2$. However, all values between 0 and 2 and even greater than 2 are possible. The nature of the error structure in the data (homogeneous or heterogeneous) can be visualized in a plot of residual errors $(y_i - \overline{y}_i)$ (Figs. 1.17 and 1.18).

To determine an expression for the weights to be used, the following equation can be used:

$$w_i = y_i^{-\alpha} \tag{1.130}$$

The form of y_i will vary depending on the function used. It could correspond to the velocity of the reaction (v) or the reciprocal of the velocity of the reaction ($1/v$ or [S]/v). For example, for a classic heterogeneous

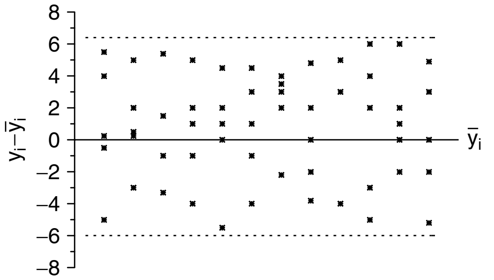


Figure 1.17. Mean residual pattern characteristic of a homogeneous, or constant, error structure in the experimental data.

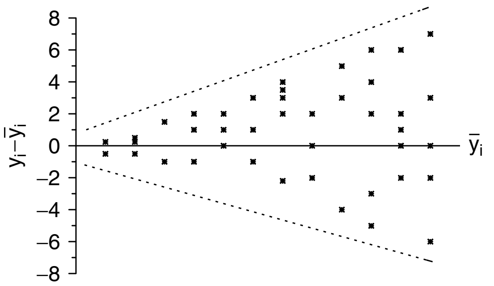


Figure 1.18. Mean residual pattern characteristic of a heterogeneous, or relative, error structure in the experimental data.

error with $\alpha = 2$, the weights for different functions would be

$$w_i(v_i) = \frac{1}{v_i^2} \qquad w_i\left(\frac{1}{v_1}\right) = v_i^2 \qquad w_i\left(\frac{[\mathrm{S}_i]}{v_i}\right) = \frac{v_i^2}{[S_i]^2} \tag{1.131}$$

It is a straightforward matter to obtain expressions for the slope and y-intercept of a weighted least-squares fit to a straight line by solving the partial differential of the χ^2 value. The resulting expression for the slope (m) is

$$\begin{aligned} m &= \frac{\sum_{i=1}^{n} w_i x_i y_i - \left(\sum_{i=1}^{n} w_i x_i \sum_{i=1}^{n} w_i y_i \Big/ \sum_{i=1}^{n} w_i\right)}{\sum_{i=1}^{n} w_i x_i^2 - \left(\sum_{i=1}^{n} w_i x_i\right)^2 \Big/ \sum_{i=1}^{n} w_i} \\ &= \frac{\sum_{i=1}^{n} w_i (x_i - \overline{x})(y_i - \overline{y})}{\sum_{i=1}^{n} w_i (x_i - \overline{x})^2} \end{aligned} \tag{1.132}$$

and the corresponding expression for the y-intercept (b) is

$$b = \frac{\sum_{i=1}^{n} w_i y_i}{\sum_{i=1}^{n} w_i} - \frac{\sum_{i=1}^{n} w_i (x_i - \overline{x})(y_i - \overline{y})}{\sum_{i=1}^{n} w_i (x_i - \overline{x})^2} \frac{\sum_{i=1}^{n} w_i y_i}{\sum_{i=1}^{n} w_i} \tag{1.133}$$

1.6.2 Exact Analytical Solution (Non-Steady-State Approximation)

Exact analytical solutions for the reaction A → B → C can be obtained by solving the differential equations using standard mathematical procedures. Exact solutions to the differential equations for the boundary conditions $[\mathrm{B}_0] = [\mathrm{C}_0] = 0$ at $t = 0$, and therefore $[\mathrm{A}_0] = [\mathrm{A}_t] + [\mathrm{B}_t] + [\mathrm{C}_t]$, are

$$[\mathrm{A}_t] = [\mathrm{A}_0]\, e^{-k_1 t} \tag{1.134}$$

$$[\mathrm{B}_t] = k_1 [\mathrm{A}_0] \frac{e^{-k_1 t} - e^{-k_2 t}}{k_2 - k_1} \tag{1.135}$$

$$[\mathrm{C}_t] = [\mathrm{A}_0]\left[1 + \frac{1}{k_1 - k_2}\left(k_2 e^{-k_1 t} - k_1 e^{-k_2 t}\right)\right] \tag{1.136}$$

Figure 1.15 shows the simulation of concentration changes in the system A → B → C. The models (equations) are fitted to the experimental data using nonlinear regression, as described previously, to obtain estimates of k_1 and k_2.

1.6.3 Exact Analytical Solution (Steady-State Approximation)

Steady-state approximations are useful and thus are used extensively in the development of mathematical models of kinetic processes. Take, for example, the reaction A → B → C (Fig. 1.15). If the rate at which A is converted to B equals the rate at which B is converted to C, the concentration of B remains constant, or in a steady state. It is important to remember that molecules of B are constantly being created and destroyed, but since these processes are occurring at the same rate, the net effect is that the concentration of B remains unchanged ($d[\mathrm{B}]/dt = 0$), thus:

$$\frac{d[\mathrm{B}]}{dt} = 0 = k_1[\mathrm{A}] - k_2[\mathrm{B}] \tag{1.137}$$

Decreases in [A] as a function of time are modeled as a first-order decay process:

$$[\mathrm{A}_t] = [\mathrm{A}_0]\, e^{-k_1 t} \tag{1.138}$$

The value of k_1 can be determined as discussed previously.

From Eqs. (1.137) and (1.138) we can deduce that

$$[\mathrm{B}] = \frac{k_1}{k_2}[\mathrm{A}] = \frac{k_1}{k_2}[\mathrm{A}_0]\, e^{-k_1 t} \tag{1.139}$$

If the steady state concentration of B $[\mathrm{B}_{\mathrm{ss}}]$, the value of k_1, and the time at which that steady state was reached (t_{ss}) are known, k_2 can be determined from

$$k_2 = \frac{k_1}{[\mathrm{B}_{\mathrm{ss}}]}[\mathrm{A}_0]\, e^{-k_1 t_{\mathrm{ss}}} \tag{1.140}$$

The steady state of B in the reaction A → B → C is short lived (see Fig. 1.15). However, for many reactions, such as enzyme-catalyzed reactions, the concentrations of important reaction intermediates are in a steady state. This allows for the use of steady-state approximations to obtain analytical solutions for the differential equations and thus enables estimation of the values of the rate constants.