Chapter 2
Solving Rate Equations

The rate equation gives the rates of concentration change as a function of the concentrations themselves. A rate equation is said to be solved if a suitable function is found that satisfies the equation and gives the concentrations for each reaction time. It is trivial but not always clearly recognized that time can be the only independent variable in this solution: the time-dependent concentrations of other species cannot appear in it. The parameters of this function are usually the rate constants and initial concentrations. A common, but more confusing convention calls the rate equation **differential rate equation**, whilst the solution is termed **integrated rate equation**. Although the rate equation is certainly a differential equation and integration is typically needed to solve it, this wording does not do justice to the mathematical efforts needed to find the solution. In addition, this alternative convention also confuses equations with function definitions, which are usually separate concepts in mathematics and computation science.

The rate equation is always a **first order differential equation**, i.e., only first derivatives of the functions appear in it. It also has the important property of being **autonomous**: the independent variable (time) never appears directly in the rate equation, it exerts its effects exclusively through the concentrations. This is usually a favorable property from a mathematical point of view but also a very obvious one in a physical sense as it basically expresses the fact that the laws governing concentration changes (similarly to other laws of nature) do not depend on time. A further characteristic of the structure of the rate equation is that it gives the derivatives as an explicit function of the concentrations. Finally, a rate equation is typically nonlinear because the functions $f_i([A_1], [A_2], \dots, [A_n])$ are nonlinear.

An **analytical solution** is a function that satisfies the rate equation and the initial conditions, which are given by the concentration values at $t = 0$. In contrast, a **numerical solution** is usually a huge collection of discreet time-concentration points that is estimated based on the rate equation. It is not uncommon to speak of **approximate analytical solutions** for cases when a function is found that is not the

solution of the rate equation, but is close to it in some sort of measure. To avoid confusion, it would be best to drop the word "analytical" in this case and stick to the term approximate solution.

An analytical solution can typically be found only for relatively simple cases. However, when such an analytical solution is found, it clearly takes precedence over any numerical solution. This is why the following sections devote a lot of space to known analytical solutions.

2.1 Analytical Possibilities

2.1.1 Single-Concentration Rate Equations

The simplest possible class of rate equations only contains the concentration of a single species. In this case, function $f_1([A_1])$ also only has one independent variable. There is quite a good chance that a rate equation in this class can be solved analytically. At first sight, this class might seem utterly insignificant as no chemical process can be imagined that only contains a single species. Yet, a surprisingly high number of more complicated (and, of course, more realistic) rate equations can be transformed into a single-concentration variant using the law of mass conservation. As a consequence, single-concentration rate equations have a dominant role in classical chemical kinetics.

A general method to solve the differential equations in this class is called **separation of variables**. Variables in this phrase mean concentration (dependent) and time (independent). Separation is particularly easily achieved as time does not even appear in the equation explicitly: all that needs to be done is to divide both sides of the rate equation by $f_1([A_1])$. Subsequent integration of both sides gives rise to a form of the solution[1]:

$$\int_{[A_1]_0}^{[A_1]_t} \frac{1}{f_1([A_1])} d[A_1] = t \qquad (2.1)$$

To calculate $[A_1]_t$ from this equation, one first needs to find the definite integral on the left-hand side, then rearrange the resulting equation so that it gives an explicit formula for the concentration (in mathematics, this is called function **inversion**).

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[1]In a common description of this technique, the equation is said to be "multiplied" by the term *dt* and then "integrated." This method is often ridiculed by mathematicians, who point out that *dt* is part of a symbol on the left side, which does not have anything to do with division. Instead of joining the laughter, it is probably better to think a little bit about the fact that the method always gives the correct solution of the problem. In fact, this method also has rigorous mathematical background. It is called **nonstandard analysis** [16], where derivatives can be defined as a ratio of two infinitesimal quantities. But it is true that those who practice this method rarely have any ideas of the existence on nonstandard analysis.

If the first step (integration) cannot be completed, the rate equation cannot be solved analytically. However, failure to accomplish the second step means only that the solution found is implicit. In this case, as Eq. (2.1) is already explicit for t, **swapping the independent and dependent variables** is a useful trick. If concentration and time are swapped, the time passed to achieve a predetermined concentration can be calculated instead of determining the concentration at a given time.

The simplest member of the simplest class of rate equations is the **power law rate equation with a single concentration**:

$$\frac{d[A_1]}{dt} = -k[A_1]^\alpha \tag{2.2}$$

Because of traditions, some confusion may arise about the values of k for positive integer values of α. The source of this confusion is that such α values make it possible to give this rate equation in a kinetic mass action form:

$$\alpha A_1 \xrightarrow{k_1} \cdots \tag{2.3}$$

In this case, a consistent use of the conventions results in the appearance of α as a stoichiometric coefficient in the rate, so that $k = \alpha k_1$. Yet, this convention is often forgotten. Therefore, when reading the literature, it is imperative to check the definition of the rate constant, especially for $\alpha = 2$.

It must not be left without notice that this rate equation does not give a zero rate at $[A_1] = 0$ for non-positive orders of reaction (i.e., $\alpha \leq 0$). This should be kept in mind when using the general solution of Eq. (2.2), which is given as follows:

$$[A_1] = \left([A_1]_0^{1-\alpha} + (\alpha - 1)kt\right)^{\frac{1}{1-\alpha}} \quad \text{for} \quad \alpha \neq 1 \tag{2.4}$$

For $\alpha = 1$, the solution has a different form:

$$[A_1]_t = [A_1]_0 e^{-k_1 t} \quad \text{for} \quad \alpha = 1 \tag{2.5}$$

For $\alpha \geq 1$, the solutions tend to 0 asymptotically, so they decrease monotonously without ever reaching 0. For $\alpha < 1$, however, the concentrations reach the value of 0 at finite time, which gives rise to a **critical time**:

$$t_{\text{crit}} = \frac{[A_1]_0^{1-\alpha}}{(1-\alpha)k} \tag{2.6}$$

The source of this criticality is the fact the derivation of Eq. (2.1) involved a division by $f_1([A_1])$, which takes the value of 0 at the critical time. At this point, the function $[A_1]_t$ does not have a second derivative if $0 < \alpha < 1$ (break point occurs on the first derivative of the kinetic trace). For $\alpha = 0$, the curve does not have a first

derivative (break point on the kinetic trace) at this point. For $\alpha < 0$, the critical time represents a point of **singularity** at which the derivative is undefined.

Among the possible values of α, 1 is the most common by far. The curve itself is called a **first order curve** or **exponential curve**, its equation is given separately in Eq. (2.5). A further case of high importance is the **second order trace** at $\alpha = 2$:

$$[A_1]_t = \frac{[A_1]_0}{1 + [A_1]_0 kt} \tag{2.7}$$

Furthermore, **zeroth order traces** with $\alpha = 0$ are sometimes found:

$$[A_1]_t = 0.5|[A_1]_0 - kt| + 0.5([A_1]_0 - kt) \tag{2.8}$$

The reader may be surprised to see **absolute value** signs (|) appear in this equation: it is some resourceful use of mathematics to ensure that the formula can be used for any value of t including those after t_{crit}.

Finally, **half-order traces** with $\alpha = 0.5$ might have occasional significance, and can be written using the trick with absolute values again:

$$[A_1]_t = \left(0.5|\sqrt{[A_1]_0} - 0.5kt| + 0.5(\sqrt{[A_1]_0} - 0.5kt)\right)^2 \tag{2.9}$$

The kinetic curves given in Eq. (2.4) have two parameters, k and $[A_1]_0$. Both of these are **scaling parameters**, which define the concentration and time scales, but do not influence the shapes of the kinetic curves. So, all exponential curves have the same shape, the only difference is the scaling. The same is true for any other single-concentration power law kinetic curve. Figure 2.1 shows the shapes of these kinetic
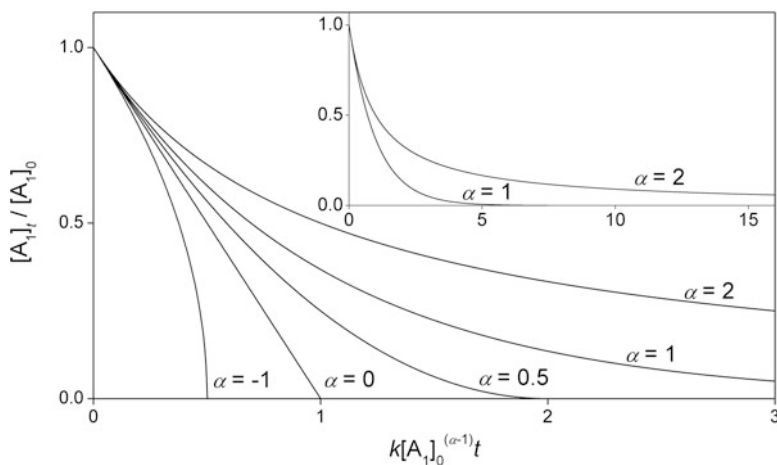
Fig. 2.1 Scaled kinetic traces of power-law rate equations in Eq. (2.2) with various values of the order of reaction α

curves for five different values of α. The characteristic shapes of these traces can be recognized by just looking at them. Scaling could be done in many different ways. Figure 2.1 uses what could be considered natural: the concentration unit is $[A_1]_0$, whereas the time unit is $k^{-1}([A_1]_0)^{1-\alpha}$. This scaling ensures that all the different curves shown have identical initial rates. This is a useful convention for preparing such comparative graphs, and can always be attained by setting the time unit to $[A_1]_0/f_1([A_1]_0)$ in single-concentration rate equations.

The natural time unit does not depend on the initial concentrations for $\alpha = 1$. Knowledge of the initial concentration is not necessary to determine the rate constant k in this case, the reciprocal of which is also called **lifetime**. Moreover, a **shift in time** (for example $t = t' + \Delta$) does not influence the determination of the rate constant, it merely gives a different value for the initial concentration ($= [A_1]_0 e^{-k\Delta}$). Therefore, the rate constant can be determined for an exponential curve for which neither the initial concentration nor the initial time is known precisely.

It is usually advisable to fit the measured signal directly rather than calculating concentrations first from the signal. If a signal Y is a linear combination of the concentrations, then the exponential curve for the observed signal is as follows:

$$Y_t = Xe^{-kt} + E \tag{2.10}$$

In this equation, X is termed the **amplitude**, k is the first order rate constant, whereas E is called the **endpoint**. The initial reading is simply $A + E$.

Furthermore, exponential curves are also easily handled for cases when the observed signal is integrated in time or space (or both). Integration in time (in interval τ) is often a key question when the response time of the monitoring method is not much faster than the process studied. The **integrated observation** is described as:

$$Y_t^\tau = \frac{1}{\tau} \int_t^{t+\tau} (Xe^{-ks} + E)ds = \frac{1 - e^{-k\tau}}{k\tau} Xe^{-kt} + E \tag{2.11}$$

Despite some apparent complexity, it must be recognized that Eq. (2.11) is still an exponential curve with rate constant k and endpoint E, it is only the amplitude that is influenced by the integration in time.

These facts make the kinetic methods based on exponential curve fitting highly **robust**. This robustness is the primary reason why kineticists, whenever possible, prefer finding conditions under which (pseudo-)first order kinetic curves are detected. Unfortunately, this strong preference is sometimes even driven to absurdity: a great many published works attempt to evaluate obviously non-exponential kinetic curves using first order fitting. Needless to say, no valid conclusions can be drawn from force-fitting first order rate constants to a non-exponential experimental trace.

Turning to a bit more complicated, but still single-concentration rate equations now, the following one, in which the rate is described by a rational function of the concentration, has high practical importance:

$$\frac{d[A_1]}{dt} = -\frac{k_a[A_1]}{k_b + [A_1]} \tag{2.12}$$

This is called the **Michaelis–Menten rate equation** and is often used in describing catalysis, especially in the field of enzyme kinetics [13]. The rate constants k_a and k_b are both positive (if $k_b = 0$, the equation would reduce to a zeroth order rate equation). The exact solution is surprisingly seldom used in the literature:

$$[A_1]_t = k_b W \left(\frac{[A_1]_0}{k_b} e^{([A_1]_0 - k_a t)/k_b} \right) \tag{2.13}$$

The solution uses the **Lambert W function** (denoted W), which is the inverse of the xe^x function. This is a three-parameter curve $(k_a, k_b, [A_1]_0)$, so even when scaling is taken into account, curves may look different. A convenient scaling is $[A_1]_0$ as the concentration is unit and $(k_b + [A_1]_0)/k_a$ as the time unit. A third, dimensionless parameter combination $[A_1]_0/k_b$ characterizes the shapes of the curves. Figure 2.2 gives examples of the kinetic curves with different shape parameters.

These curves are often described to change their order of reaction from 0 in the beginning to 1 at the end. The rationale in this characterization is that at high values of concentration $[A_1]$, the rate does not depend on this concentration, whereas the
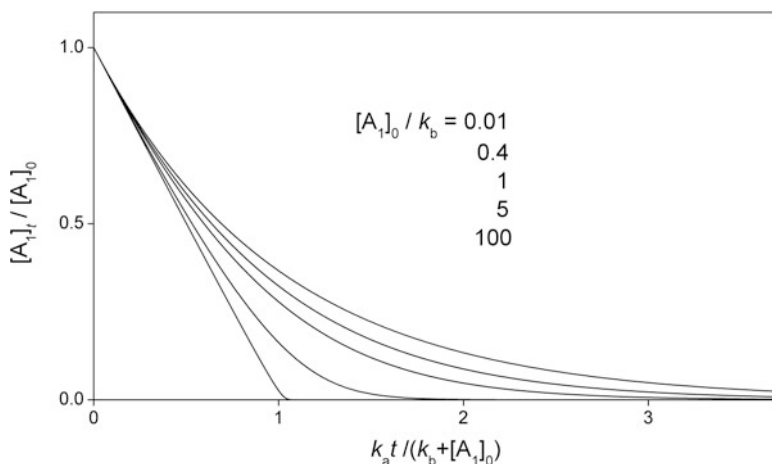
Fig. 2.2 Scaled kinetic traces based on Michaelis–Menten rate equation in (2.12) with different shape parameters, whose values are shown within the graph

rate is directly proportional to $[A_1]$ if its value is close to zero. The Lambert W function is not very commonly implemented in scientific softwares. In its absence, the trick of swapping time and concentration can still be used:

$$t = \frac{[A_1]_0 - [A_1]_t}{k_a} + \frac{k_b}{k_a} \ln \frac{[A_1]_0}{[A_1]_t} \tag{2.14}$$

In a similar, and sometimes significant rate equation, the order of reaction changes from 0.5 in the beginning to 1 at the end:

$$\frac{d[A_1]}{dt} = -\frac{k_a[A_1]}{k_b + \sqrt{[A_1]}} \tag{2.15}$$

The solution of this rate equation also uses the Lambert W function:

$$[A_1]_t = \left[k_b W \left(\frac{\sqrt{[A_1]_0}}{k_b} e^{(\sqrt{([A_1]_0} - k_a t/2)/k_b)} \right) \right]^2 \tag{2.16}$$

Further notable rate equations arise if terms of different power rate laws are summed. These are often called processes with parallel reaction paths, but their significance goes way beyond that, as will be shown later. A common and important case is when a first order and a second order term is summed:

$$\frac{d[A_1]}{dt} = -k_a[A_1] - k_b[A_1]^2 \tag{2.17}$$

As usual, separation of variables gives a straightforward solution:

$$[A_1]_t = \frac{k_a[A_1]_0 e^{-k_a t}}{k_a + k_b[A_1]_0 - k_b[A_1]_0 e^{-k_a t}} \tag{2.18}$$

This is a three-parameter curve, similarly to Eq. (2.16). The scaling parameters are best selected to be $[A_1]_0$ as the concentration unit and $|1/(k_a + k_b[A_1]_0)|$ as the time unit. The dimensionless shape parameter is $k_b[A_1]_0/k_a$. This formula reduces to a first order reaction by setting $k_b = 0$. However, $k_a = 0$ and $k_2[A_1]_0 = -k_a$ are not possible. Figure 2.3 gives 12 characteristic curve shapes.

The traces with positive shape parameters in Fig. 2.3 are straightforward, they are cases when both k_a and k_b are positive. Interestingly enough, one of the two rate constants can be negative without rendering the rate equation physically meaningless. Furthermore, the absolute value sign in the convenient time scale is not accidental, as $(k_a + k_b[A_1]_0)$ may also be negative. The condition $-1 < k_b[A_1]_0/k_a < 0$ and $(k_a + k_b[A_1]_0) > 0$ gives rise to curves that are often called autocatalytic: these curves are denoted by a + sign in the superscript after the parameter value in Fig. 2.3. For $-1 < k_b[A_1]_0/k_a < -0.5$, the traces have accelerating time intervals. If $(k_a + k_b[A_1]_0) < 0$, any negative value for the
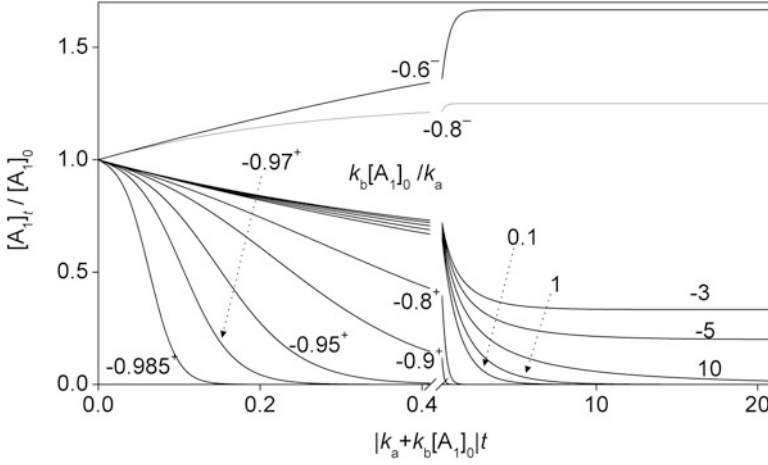
Fig. 2.3 Scaled kinetic traces based on rate Eq. (2.17) with different shape parameters, whose values are shown within the graph

shape parameter is meaningful. The solutions in this case do not tend to 0 final concentration values. The curves with $-1 < k_b[A_1]_0/k_a < 0$ describe an increase in concentration and are denoted by a – sign in the superscript after the parameter value in Fig. 2.3.

A logical extension of the rate equation (2.17) is the addition of a third, zeroth order term:

$$\frac{d[A_1]}{dt} = -k_a[A_1] - k_b[A_1]^2 - k_c \tag{2.19}$$

The solution breaks down to several different possibilities depending on the values of the parameters. If $4k_bk_c > k_a^2$, the solution is:

$$[A_1]_t = \frac{\sqrt{4k_bk_c - k_a^2}}{2k_b}\text{tg}\left(-\frac{\sqrt{4k_bk_c - k_a^2}}{2}t + \text{arctg}\frac{2k_b[A_1]_0 + k_a}{2}\right) - \frac{k_a}{2k_b} \tag{2.20}$$

On the other hand, if $4k_bk_c < k_a^2$, the solution takes the following form:

$$[A_1]_t = \frac{k_a(Xe^{-t\sqrt{k_a^2-4k_bk_c}} - 1) + \sqrt{k_a^2 - 4k_bk_c}(Xe^{-t\sqrt{k_a^2-4k_bk_c}} + 1)}{2k_b(Xe^{-t\sqrt{k_a^2-4k_bk_c}} - 1)} \tag{2.21}$$

In this equation, X is an auxiliary variable defined as:

$$X = \frac{k_b[A_1]_0 + k_a - \sqrt{k_a^2 - 4k_b k_c}}{k_b[A_1]_0 + k_a + \sqrt{k_a^2 - 4k_b k_c}} \tag{2.22}$$

Finally, if $4k_b k_c = k_a^2$ (or $k_c = k_a^2/(4k_b)$), the solution assumes a simpler form:

$$[A_1]_t = \frac{[A_1]_0 + k_a/(2k_b)}{k_b[A_1]_0 t + k_a t/2 + 1} - \frac{k_a}{2k_b} \tag{2.23}$$

These curves generally have four parameters, but the individual combinations that could serve as two scaling and two shape parameters are not obvious. If $k_a = 0$, the given solution is still useful, but the same is not true for $k_b = 0$. The solution of the case with $k_c = 0$ is already given in Eq. (2.18). The two-term rate equation that combines a zeroth and a first order term is handled separately:

$$\frac{d[A_1]}{dt} = -k_a[A_1] - k_c \tag{2.24}$$

The solution is stated in a relatively simple form:

$$[A_1]_t = \left([A_1]_0 + \frac{k_c}{k_a}\right) e^{-k_a t} - \frac{k_c}{k_a} \tag{2.25}$$

A closer look at this formula will reveal to the reader that this is actually an exponential curve that is shifted along the concentration axis. Negative values of k_c also make sense in this case, especially for describing reversible reactions. There is also a critical time for positive values of k_c when the concentration assumes 0, $t_{\text{crit}} = (1/k_a)\ln(k_a[A_1]_0/k_c + 1)$.

Notably, some rate equations containing more than one concentration can be rewritten into single-concentration equations. A prime example is the so-called mixed second order equation:

$$A_1 + A_2 \xrightarrow{k_1} A_3(+\cdots) \tag{2.26}$$

The rate equation is:

$$\frac{d[A_1]}{dt} = \frac{d[A_2]}{dt} = -k_1[A_1][A_2] \tag{2.27}$$

Mass conservation ensures that $[A_2]_t = [A_1]_t - [A_1]_0 + [A_2]_0$ holds. Therefore, the rate equation can be rewritten into a single concentration form:

$$\frac{d[A_1]}{dt} = \frac{d[A_2]}{dt} = -k_1[A_1]^2 + k_1([A_2]_0 - [A_1]_0)[A_1] \tag{2.28}$$

This is the same rate equation as shown in Eq. (2.17) with $k_b = k_1$ and $k_a = k_1([A_1]_0 - [A_0]_0)$. Yet, as the mixed second order rate equation is very important, some further considerations will be presented about it. If it also involves a stoichiometric ratio different from 1:1, the process itself is usually represented as follows:

$$\nu_1 A_1 + \nu_2 A_2 \longrightarrow A_3(+\cdots) \tag{2.29}$$
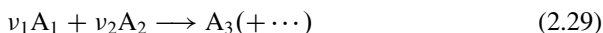
The rate equation corresponding to this process is then given as:

$$\frac{1}{\nu_1}\frac{d[A_1]}{dt} = \frac{1}{\nu_2}\frac{d[A_2]}{dt} = -k_1[A_1][A_2] \tag{2.30}$$

Combining the general strategy outlined above and the solution already given in Eq. (2.18) yields the following final formula for the concentration of A_1:

$$[A_1]_t = \frac{(\nu_1[A_2]_0 - \nu_2[A_1]_0)[A_1]_0 e^{-k_1(\nu_1[A_2]_0 - \nu_2[A_1]_0)t}}{\nu_1[A_2]_0 - \nu_2[A_1]_0 e^{-k_1(\nu_1[A_2]_0 - \nu_2[A_1]_0)t}} \tag{2.31}$$

A notable exception is the case $\nu_2[A_1]_0 = \nu_1[A_2]_0$. This is fully analogous to the $\alpha = 2$ case in Eq. (2.2), and the corresponding solution is very similar to the one given in Eq. (2.7) except the presence of the stoichiometric coefficient:

$$[A_1]_t = \frac{[A_1]_0}{1 + \nu_2[A_1]_0 k_1 t} \tag{2.32}$$

The reader can test her or his own understanding of the kinetic background of this formula by thinking about the question why the stoichiometric coefficient ν_1 does not appear in it.

It is not very trivial to see, but Eq. (2.31) actually describes curves with three essential parameters. Two of these are scaling parameters: initial concentration $[A_1]_0$ serves as the concentration unit, whereas the reciprocal of the composite parameter $k_1(\nu_1[A_2]_0 - \nu_2[A_1]_0)$ is a time unit. The third parameter, which is best selected as the dimension-free ratio $\nu_1[A_2]_0/(\nu_2[A_1]_0)$ is a shape parameter. Figure 2.4 displays a few examples of curves with different shape parameters (Fig. 2.3 already shows some relevant curves, but the rate equation there is more general and the scaling is somewhat different). From a practical point of view, it is also sufficient to limit the considerations to $\nu_1[A_2]_0/(\nu_2[A_1]_0) \geq 1$ so that A_1 is the limiting reagent that is completely used up, and the concentration of A_2 can be calculated form mass balance. In the opposite case, swapping A_1 and A_2 would lead back to this mathematical description.
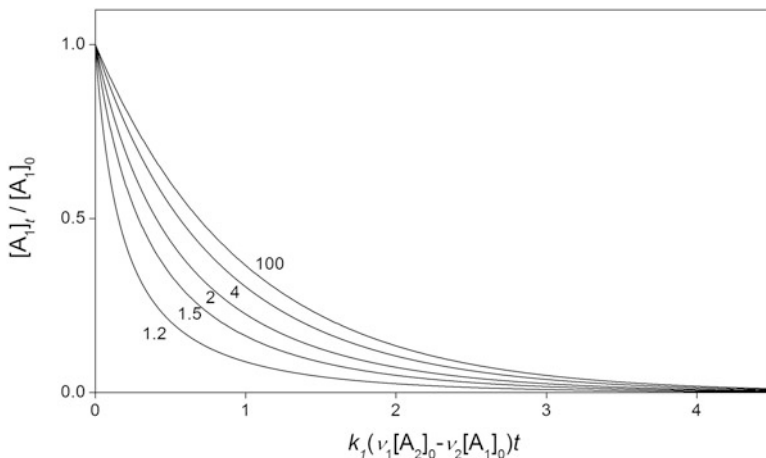
Fig. 2.4 Scaled kinetic traces based on Eq. (2.31) with different shape parameters

Another example in which a multiple-concentration rate equation can be simplified using mass balance is provided by the simplest autocatalytic rate equation including a direct term:

$$A_1 \longrightarrow A_2 \tag{2.33}$$

The rate equation of this process is given as:

$$\frac{d[A_1]}{dt} = -\frac{d[A_2]}{dt} = -k_1[A_1] - k_2[A_1][A_2] \tag{2.34}$$

Mass conservation ensures that $[A_2]_t = [A_1]_0 + [A_2]_0 - [A_1]_t$. Therefore, the rate equation can be rearranged into the following form:

$$\frac{d[A_1]}{dt} = -(k_1 + k_2[A_1]_0 + k_2[A_2]_0)[A_1] + k_2[A_1]^2 \tag{2.35}$$

Again, this is the same as the rate equation shown in Eq. (2.17) with $k_b = -k_2$ and $k_a = k_1 + k_2[A_1]_0 + k_2[A_2]_0$. Some sample solutions are given in Fig. 2.3.

The following rate equation is the simplest photochemical rate equation, but receives very little attention in practice:

$$\frac{d[A_1]}{dt} = -k_a(1 - e^{-k_b[A_1]}) \tag{2.36}$$

This describes a purely photochemical process for a case when the reaction is induced by monochromatic irradiation at which only the photoactive component absorbs light. These conditions are not uncommon in photochemistry. The term

showing the concentration in the exponential function stems from Beer's law, which generally describes light absorption (see Eq. (1.21)). An analytical solution can be found for this case as well:

$$[A_1]_t = \frac{1}{k_b} \ln \left[1 + e^{-k_a k_b t} e^{k_b [A_1]_0} \left(1 - e^{-k_b [A_1]_0} \right) \right] \tag{2.37}$$

This is again a three-parameter curve, where $k_a k_b$ and $[A_1]_0$ are scaling parameters, whereas $k_b [A_1]_0$ is a shape parameter. More complicated cases are also frequently encountered in photochemistry, but analytical solutions are typically very difficult, if not impossible to find because the concentration appears simultaneously in the exponential functions and their multiplication terms.

All the rate equations dealt with thus far were valid for irreversible reactions, although allowing negative values for the formal rate constant values also accommodates reversible cases, as will be shown later in this section. In reversible reactions, the initial substance A_1 can also be formed, and not only consumed.

Before dwelling on truly reversible chemical reactions, exchange reactions will be discussed at some length. An exchange process is commonly represented in the form of the following chemical scheme:

$$A_1^* + A_2 \rightleftharpoons A_1 + A_2^* \tag{2.38}$$

The sign * indicates some sort of a label, which is usually assumed not to interfere with any of the reactions of the chemical species. In the case of isotopes, a modifying influence of the label is usually called isotope effect (see Sect. 4.4), and it is negligible except when hydrogen isotopes are substituted. Because of the negligible effect of the label, R_{ex}, the rate of exchange, can be interpreted as a single, time-independent quantity in such an experiment as the rate itself does not differentiate between A_1^* and A_1. It is usually useful to work with isotopic abundances x_1 and x_2 in molecules in this scheme, which can be defined as:

$$x_1 = \frac{[A_1^*]}{[A_1^*] + [A_1]} = \frac{[A_1^*]}{[A_1]_T} \qquad x_2 = \frac{[A_2^*]}{[A_2^*] + [A_2]} = \frac{[A_2^*]}{[A_2]_T} \tag{2.39}$$

Concentrations $[A_1]_T$ and $[A_2]_T$ are the total concentration of species A_1 and A_2, which remain unchanged in time. The differential equation governing the time evolution of isotopic abundance x_1 is:

$$\frac{dx_1}{dt} [A_1]_T = -R_{ex} x_1 (1 - x_2) + R_{ex} x_2 (1 - x_1) = -R_{ex} x_1 + R_{ex} x_2 \tag{2.40}$$

A similar equation for x_2 is:

$$\frac{dx_2}{dt}[A_2]_T = -R_{ex}x_2(1-x_1) + R_{ex}x_1(1-x_2) = R_{ex}x_1 - R_{ex}x_2 \qquad (2.41)$$

Surprising as it may be, this is not a true rate equation as the exchange rate R_{ex} appears in it without giving the concentration dependence. The rationale in this formulation is that the quantity R_{ex} does not change during the course of a single kinetic experiment.

Adding Eqs. (2.40) and (2.41) shows that $x_1[A_1]_T + x_2[A_2]_T$ is independent of time, which is actually mass conservation for the label. This enables calculation of x_2 from the value of x_1:

$$x_2 = \frac{[A_1]_T}{[A_2]_T}(x_{1,0} - x_1) + x_{2,0} \qquad (2.42)$$

The equation can thus be restated with a single dependent variable, and then the equation is solved to yield:

$$x_{1,t} = (x_{1,0} - x_\infty)\exp\left(-\frac{[A_1]_T + [A_2]_T}{[A_1]_T[A_2]_T}R_{ex}t\right) + x_\infty \qquad (2.43)$$

The final value of the isotopic abundance is common to the two species:

$$x_\infty = \frac{x_{1,0}[A_1]_T + x_{2,0}[A_2]_T}{[A_2]_T + [A_1]_T} \qquad (2.44)$$

A fully symmetric equation gives the solution for $x_{2,t}$. Equation (2.43) means that the time dependence of isotopic abundance is always described by an exponential curve, no matter what the rate equation of the exchange process is. The rate equation itself can be established by determining the first order rate constants of the exponential curves and studying their dependence on the concentration of the species. The approach presented here and specifically Eq. (2.43) are typically referred to as the McKay equation [11, 12].

This exchange example leads further to the discussion of single-step **reversible reactions**. The general strategy is to use the conservation of mass to give all concentrations as a function of a single selected concentration. The simplest example is a reaction that is first order in both directions:

$$A_1 \underset{k_2}{\overset{k_1}{\rightleftharpoons}} A_2 \qquad (2.45)$$

The rate equation of such a process is:

$$\frac{d[A_1]}{dt} = -\frac{d[A_2]}{dt} = -k_1[A_1] + k_2[A_2] \qquad (2.46)$$

Despite the fact that two concentrations appear in it, this is a single-concentration rate equation as $[A_1]$ and $[A_2]$ are connected through mass conservation: $[A_2]_t = [A_1]_0 + [A_2]_0 - [A_1]_t$. With this conservation equation, it is a matter of very simple algebra to derive the following form:

$$\frac{d[A_1]}{dt} = -(k_1 + k_2)[A_1] + k_2([A_1]_0 + [A_2]_0) \tag{2.47}$$

This rate equation is identical to the one given in Eq. (2.24) with $k_a = k_1 + k_2$ and $k_b = k_2([A_1]_0 + [A_2]_0)$. The solution is therefore an exponential function with a nonzero final value.

Another reversible process involves a first and a second order reaction:

$$A_1 \underset{k_2}{\overset{k_1}{\rightleftharpoons}} A_2 + A_3 \tag{2.48}$$

The rate equation describing this scheme is:

$$\frac{d[A_1]}{dt} = -\frac{d[A_2]}{dt} = -\frac{d[A_3]}{dt} = -k_1[A_1] + k_2[A_2][A_3] \tag{2.49}$$

The analytical solution of this equation is the same as given after Eq. (2.19) with $k_a = k_1 + k_2(2[A_1]_0 + [A_2]_0 + [A_3]_0)$, $k_b = -k_2$, and $k_c = -k_2([A_1]_0 + [A_2]_0)([A_1]_0 + [A_3]_0)$.

Another significant reversible process is when both the forward and reverse reactions are second order overall:

$$A_1 + A_2 \underset{k_2}{\overset{k_1}{\rightleftharpoons}} A_3 + A_4 \tag{2.50}$$

The rate equation is given as follows:

$$\frac{d[A_1]}{dt} = \frac{d[A_2]}{dt} = -\frac{d[A_3]}{dt} = -\frac{d[A_4]}{dt} = -k_1[A_1][A_2] + k_2[A_3][A_4] \tag{2.51}$$

Similarly to the previous reversible scheme, the analytical solution given after Eq. (2.19) can be used here with $k_a = k_1([A_2]_0 - [A_1]_0) + k_2(2[A_1]_0 + [A_3]_0 + [A_4]_0)$, $k_b = k_1 - k_2$, and $k_c = -k_2([A_1]_0 + [A_3]_0)([A_1]_0 + [A_4]_0)$.

One more trick should be introduced for reversible reactions at this point using the process shown in Eq. (2.50) as an example. Reversible processes lead to an equilibrium, in which all of the components reach a nonzero final concentration. It leads to considerably simplified algebra if the differential equation is stated using a new variable, which is the **distance from equilibrium**. In the example of Eq. (2.50), these equilibrium or final concentrations are designated $[A_1]_\infty$, $[A_2]_\infty$, $[A_3]_\infty$, and $[A_4]_\infty$. For these, $k_1[A_1]_\infty[A_2]_\infty = k_2[A_3]_\infty[A_4]_\infty$ holds. The distance

from the equilibrium is introduced as time dependent function x, and the individual concentrations can be given at any time with the following equation:

$$[A_1]_t = [A_1]_\infty + x_t \quad [A_2]_t = [A_2]_\infty + x_t$$
$$[A_3]_t = [A_3]_\infty - x_t \quad [A_4]_t = [A_4]_\infty - x_t$$
(2.52)

Substituting these functions into Eq. (2.51) and rearrangement yield the following differential equation for x:

$$\frac{dx}{dt} = -(k_1[A_1]_\infty + k_1[A_2]_\infty + k_2[A_3]_\infty + k_2[A_4]_\infty)x + (k_2 - k_1)x^2 \quad (2.53)$$

Therefore, the introduction of the distance form equilibrium (x) offers the advantage that the differential equation describing it, which is identical to Eq. (2.17) with $k_a = k_1[A_1]_\infty + k_1[A_2]_\infty + k_2[A_3]_\infty + k_2[A_4]_\infty$ and $k_b = k_2 - k_1$, is simpler. The price of this (relative) simplicity is that the equilibrium concentrations have to be obtained in independent equilibrium calculations. On a conceptual level, this method fully separates the equilibrium information and the kinetic information available from the concentration data.

An archetype of two parallel processes is the first order formation of two different products from the same initial substance. The scheme can be given as follows:

$$A_1 \xrightarrow{k_1} A_2$$
$$A_1 \xrightarrow{k_2} A_3$$
(2.54)

It may be surprising, but this scheme also belongs to the group of single-concentration rate equations as A_2 and A_3 are only involved in the reaction as products:

$$\frac{d[A_1]}{dt} = -(k_1 + k_2)[A_1]$$
$$\frac{d[A_2]}{dt} = k_1[A_1]$$
$$\frac{d[A_3]}{dt} = k_2[A_1]$$
(2.55)

The solution is quite straightforward:

$$[A_1]_t = [A_1]_0 e^{-(k_1+k_2)t}$$
$$[A_2]_t = \frac{k_1}{k_1 + k_2}[A_1]_0 e^{-(k_1+k_2)t}$$
$$[A_3]_t = \frac{k_2}{k_1 + k_2}[A_1]_0 e^{-(k_1+k_2)t}$$
(2.56)

2.1.2 Multiple-Concentration Rate Equations

Multiple-concentration rate equations are those which cannot be simplified to a differential equation using only a single concentration, so they remain systems of simultaneous, coupled equations.

The end of the previous subsection showed that the simplest case of parallel processes, although involves two reactions with two rate constants, is in fact a single concentration rate equation as the reagent is common to the two irreversible processes. Therefore, the simplest multiple-concentration rate equations arise from consecutive processes.

A consecutive zeroth order process would be characterized by kinetic curves that are combinations of straight lines. Zeroth order kinetics is rare, so a case of two consecutive reactions both with zeroth order kinetics would be an extreme rarity, although still not without an experimental example. In some cases, the multistep oxidation reactions of the dithionate ion produce this unique phenomenon [8].

The class of first order reaction networks is among the few multiple-concentration rate equations for which the analytical solution can be given. The simplest such system is composed of two consecutive irreversible first order processes:

$$A_1 \xrightarrow{k_1} A_2 \xrightarrow{k_2} A_3 \tag{2.57}$$

The rate equation is:

$$\frac{d[A_1]}{dt} = -k_1[A_1]$$
$$\frac{d[A_2]}{dt} = k_1[A_1] - k_2[A_2] \tag{2.58}$$
$$\frac{d[A_3]}{dt} = k_2[A_2]$$

This scheme has two concentrations that should be handled in differential equations as $[A_3]$ can always be calculated from mass balance. The solution can be stated in terms of combinations of exponential functions. The formula for A_1 is a single exponential function, it is the solution of a single-concentration rate equation. The concentrations of A_2 and A_3, on the other hand, are described by functions called **biexponential** or **double exponential** functions:

$$[A_1]_t = [A_1]_0 e^{-k_1 t}$$
$$[A_2]_t = \frac{[A_1]_0 k_1}{k_1 - k_2}(e^{-k_2 t} - e^{-k_1 t}) + [A_2]_0 e^{-k_2 t} \tag{2.59}$$
$$[A_3]_t = [A_1]_0 + [A_2]_0 + [A_3]_0 + \frac{[A_1]_0 k_2}{k_1 - k_2}e^{-k_1 t} - \left(\frac{[A_1]_0 k_1}{k_1 - k_2} + [A_2]_0\right)e^{-k_2 t}$$

The formulas given for A_2 and A_3 cannot be used if $k_a = k_b(= k)$. In this case, the solutions take the following forms:

$$[A_2]_t = ([A_1]_0 k t + [A_2]_0)e^{-kt}$$
$$[A_3]_t = [A_1]_0 + [A_2]_0 + [A_3]_0 - ([A_1]_0 k t + [A_1]_0 + [A_2]_0)e^{-kt} \quad (2.60)$$

The concentration profile of A_2 shows a maximum in certain cases. The time at which this maximum occurs is given as:

$$t_{\max} = \frac{1}{k_a - k_b} \ln \frac{\frac{k_a[A_1]_0}{k_a - k_b} + [A_2]_0}{\frac{k_b[A_1]_0}{k_a - k_b}} \quad (2.61)$$

If this formula gives a negative value for $t_{\max}$, the concentration profile of A_2 decreases monotonously. In real experiments, typically $[A_2]_0 = [A_3]_0 = 0$ holds, which simplifies the solution somewhat. When the initial concentration of A_2 is zero, the concentration of this species is guaranteed to have a maximum and Eq. (2.61) is greatly simplified to assume the following form:

$$t_{\max} = \frac{\ln(k_a/k_b)}{k_a - k_b} \quad (2.62)$$

In this example, species A_2 is the archetype of an intermediate, and the whole reaction is understood as a transformation of A_1 into A_3 through intermediate A_2. This scheme is used very often, so it will be dealt with in some more detail. The kinetic curves have two scaling parameters: an advantageous time unit is k_b^{-1}, whereas $[A_1]_0$ is a suitable concentration unit. It is usually a good choice to select the dimensionless combination k_a/k_b as a shape parameter. Figure 2.1 shows how the kinetic traces for A_2 and A_3 depend on this shape parameter. A_1 is not displayed as its dependence is single exponential. In fact, it does not have a shape parameter and unlike for the other two species, selecting k_a^{-1} as the time unit is more advantageous.

Curves in Fig. 2.5 show that the maximum concentration of the intermediate decreases as k_a/k_b increases. This is understandable as the rate constant of the process consuming the intermediate becomes larger with the increase of this ratio.

Another phenomenon to be noted is that the concentration profile of species A_3 features a region where the rate of formation increases. This is often referred to as an **induction time** (or incubation time or even lag phase). Autocatalytic curves for the formation of a product often have similar features, but the induction period is also observed there in the concentration of initial substance A_1. Strictly speaking, the initial rate of the formation of A_3 is zero as A_2 is not present at $t = 0$.

The double exponential function is very commonly used in experimental kinetics. Its form for an instrumental reading is:

$$Y_t = X_1 e^{-k_1 t} + X_2 e^{-k_2 t} + E \quad (2.63)$$
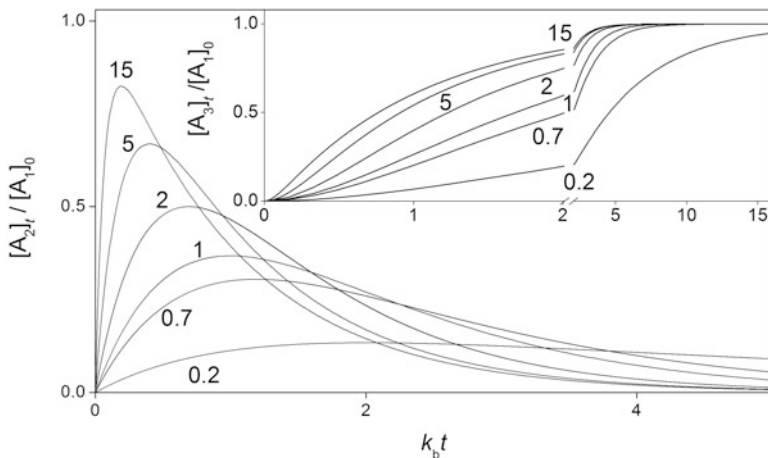
Fig. 2.5 Scaled kinetic traces based on Eq. (2.59) with different k_a/k_b shape parameters, the values of which are shown in the figure

In this equation, X_1 and X_2 are referred to as the first and second amplitudes (they can be positive or negative), k_1 and k_2 are the first and second rate constants, usually the higher given first (but that does not imply that the faster is always the first in the scheme!), whereas E is the endpoint. The initial reading is simply $X_1 + X_2 + E$.

A series of n irreversible first order reactions is represented by the following scheme:

$$A_1 \xrightarrow{k_1} A_2 \xrightarrow{k_2} \cdots \longrightarrow A_n \xrightarrow{k_n} A_{n+1} \tag{2.64}$$
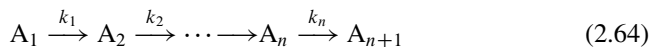
The concentration of A_i ($i \leq n$) in this scheme can usually be given as a combination of i exponential functions:

$$[A_i]_t = \sum_{j=1}^{i} C_{i,j} e^{-k_j t} \tag{2.65}$$

The coefficients $C_{i,j}$ can be calculated recursively in the following manner for any $i \leq n$:

$$C_{1,1} = [A_i]_0$$
$$C_{i,j} = \frac{k_{i-1}}{k_j - k_i} C_{i-1,j} \quad i > j \tag{2.66}$$
$$C_{i,i} = [A_i]_0 - \sum_{j=1}^{i-1} C_{i,j}$$

For the final product, species A_{n+1}, mass conservation gives a convenient way to calculate the concentration once the concentrations of the previous components are known:

$$[A_{n+1}]_t = [A_{n+1}]_0 + \sum_{j=0}^{n} ([A_j]_0 - [A_j]_t) \qquad (2.67)$$

As in the case of single concentration rate equations, allowing the processes to be reversible will not change the double exponential nature of the solution, but will make the calculations more laborious. The most general case is when two consecutive reversible first order reactions follow each other, this is represented by the following scheme:

$$A_1 \underset{k_2}{\overset{k_1}{\rightleftharpoons}} A_2 \underset{k_4}{\overset{k_3}{\rightleftharpoons}} A_3 \qquad (2.68)$$

The solution is given by double exponential functions:

$$[A_i]_t = [A_i]_\infty + C_{i,1}e^{-\lambda_1 t} + C_{i,2}e^{-\lambda_2 t} \qquad (2.69)$$

In this equation, λ_1 and λ_2 are the nonzero eigenvalues of a 3×3 matrix composed of the rate constants k_1, k_2, k_3, k_4 (see later paragraphs about compartmental processes) and are given as follows:

$$\lambda_1 = -\frac{k_1+k_2+k_3+k_4}{2} + \sqrt{\frac{(k_1+k_2+k_3+k_4)^2}{4} - k_1 k_3 - k_1 k_4 - k_2 k_4}$$

$$\lambda_2 = -\frac{k_1+k_2+k_3+k_4}{2} - \sqrt{\frac{(k_1+k_2+k_3+k_4)^2}{4} - k_1 k_3 - k_1 k_4 - k_2 k_4} \qquad (2.70)$$

The equilibrium values of the concentrations can be given independently of the solution of the differential equation:

$$[A_1]_\infty = \frac{([A_1]_0 + [A_2]_0 + [A_3]_0)k_2 k_4}{k_1 k_4 + k_2 k_4 + k_1 k_3} \qquad [A_2]_\infty = \frac{([A_1]_0 + [A_2]_0 + [A_3]_0)k_1 k_4}{k_1 k_4 + k_2 k_4 + k_1 k_3}$$

$$[A_3]_\infty = \frac{([A_1]_0 + [A_2]_0 + [A_3]_0)k_1 k_3}{k_1 k_4 + k_2 k_4 + k_1 k_3} \qquad (2.71)$$

The constants appearing in Eq. (2.68) (which are the amplitudes of the double exponential functions) are given as follows:

$$C_{1,1} = \frac{\lambda_2 + k_1}{\lambda_2 - \lambda_1}([A_1]_0 - [A_1]_\infty) + \frac{k_2}{\lambda_2 - \lambda_1}([A_2]_\infty - [A_1]_0)$$

$$C_{1,2} = \frac{\lambda_1 + k_1}{\lambda_1 - \lambda_2}([A_1]_0 - [A_1]_\infty) + \frac{k_2}{\lambda_1 - \lambda_2}([A_2]_\infty - [A_1]_0)$$

$$C_{3,1} = \frac{\lambda_2 + k_4}{\lambda_2 - \lambda_1}([A_3]_0 - [A_3]_\infty) + \frac{k_3}{\lambda_2 - \lambda_1}([A_2]_\infty - [A_1]_0) \qquad (2.72)$$

$$C_{3,2} = \frac{\lambda_1 + k_4}{\lambda_1 - \lambda_2}([A_3]_0 - [A_3]_\infty) + \frac{k_3}{\lambda_1 - \lambda_2}([A_2]_\infty - [A_1]_0)$$

$$C_{2,1} = -C_{1,1} - C_{3,1} \qquad C_{2,2} = -C_{1,2} - C_{3,2}$$

Compartmental processes [4, 9] are usually general networks of first order reactions in a closed system, which involve n different chemical species $(A_1, A_2, \ldots, A_n)$, every one of which can convert to any other, i.e., chemical reactions are possible for all pairs of species present:

$$A_i \xrightarrow{k_{i,j}} A_j \qquad (2.73)$$

This sort of reaction is sometimes termed **conversion** to distinguish it from other types of possible processes in compartmental systems. For easy symbolic handling, the rate constant of the "self-conversion" of species A_i is also defined but is set to zero ($k_{i,i} = 0$).

From a chemist's point of view, a reactor can be made open with inflow and outflow by including processes that produce or consume A_i molecules without consuming or producing any other molecules. The outflow process, sometimes termed **degradation**, is still within the general framework of first order reaction networks. The same is not true for the inflow process, which would be represented by a constant term that does not depend on any of the concentrations (see later). The degradation process is typically represented by the following notation:

$$A_i \xrightarrow{k_i^{out}} \emptyset \qquad (2.74)$$

The notation $\emptyset$ is used to mean the absence of species on the product side, or, more precisely, the fact that molecule A_i leaves the reactor. There is also a whole family of steps, termed **catalytic production from a source**, in which species A_j is produced with a rate that is proportional to number of A_i molecules:

$$\emptyset \xrightarrow{k_{i,j}^{cat}, A_i} A_j \qquad (2.75)$$

The notable case of $i = j$ here could be considered **self-reproduction** or autocatalytic formation. It should be noted that **catalytic degradation**, which would be a sort of equivalent of catalytic production, is not possible because a species cannot be degraded in a manner that is independent of its own presence.

Although the outflow process is often included in schemes as written in Eq. (2.74), this is not a conceptual necessity. In fact, in any system involving outflow, defining a $(n + 1)$th reservoir species, and including it as a common product of all outflow processes, will lead to a mathematically equivalent scheme.

In the absence of production steps, such an equivalent system will be closed. Open chemical reactors are sometimes conveniently formulated without the inflow or outflow processes described here in order to keep the number of molecules in the reactor finite. In this case, the **flow reactions** replace the contents of the reactor by the contents of the feed.

Another question arises about stoichiometry. All equations here are written with a set 1:1 stoichiometry for each process (meaning that for each molecule of reactant produced, there is one molecule of product formed) in the compartmental network. This is not necessarily the case in all examples and including stoichiometric coefficients may be needed. For 1:1 stoichiometry in a closed system without inflow and outflow, conservation of matter ensures that the sum of concentrations is always the same. With different stoichiometries but still in closed systems, a similar conservation relationship can be defined by using a suitable linear combination of concentrations.

A compartmental system is best characterized by matrix algebra and the rate constants are conveniently arranged in a form of a matrix, which is denoted $\underline{\underline{k}}$ here:

$$\underline{\underline{k}} = \begin{pmatrix} -k_1^{\text{out}} - \sum_{i=1}^n k_{1,i} & k_{2,1} + k_{2,1}^{\text{cat}} & \cdots & k_{n,1} + k_{n,1}^{\text{cat}} \\ k_{1,2} + k_{1,2}^{\text{cat}} & -k_2^{\text{out}} - \sum_{i=1}^n k_{2,i} & \cdots & k_{n,2} + k_{n,2}^{\text{cat}} \\ \vdots & \vdots & \ddots & \vdots \\ k_{1,n} + k_{1,n}^{\text{cat}} & k_{2,n} + k_{2,n}^{\text{cat}} & \cdots & -k_n^{\text{out}} - \sum_{i=1}^n k_{n,i} \end{pmatrix} \tag{2.76}$$

If the concentrations $[A_1], [A_2], \ldots, [A_n]$ are arranged into a vector ($\underline{c}$), the rate equation of a first order reaction network is simply given as follows:

$$\frac{d\underline{c}}{dt} = \underline{\underline{k}}\,\underline{c} \tag{2.77}$$

The solution of this equation is most conveniently given in a matrix form:

$$\underline{c}_t = \text{expm}(\underline{\underline{k}}t)\underline{c}_0 \tag{2.78}$$

In this formula, expm stands for the matrix exponential function, which is defined in a fashion that is fully analogous to the definition of the exponential function of real numbers. For any matrix $\underline{\underline{M}}$, its exponential is given as follows:

$$\text{expm}(\underline{\underline{M}}) = \sum_{i=0}^{\infty} \frac{1}{i!}\underline{\underline{M}}^i \tag{2.79}$$

In Eq. (2.78), $\underline{c}_0$ represents the initial conditions, i.e., the values of concentrations at $t = 0$. The individual $[A_i]$ functions can be given using the eigenvalues of matrix $\underline{\underline{k}}$. Let m be the number of different eigenvalues of matrix $\underline{\underline{k}}$, $\lambda_1, \lambda_2, \ldots, \lambda_m$ the

eigenvalues themselves, and $l_1, l_2, \ldots, l_m$ the multiplicities of these eigenvalues, in order. The following equation holds for the multiplicities:

$$n = \sum_{i=1}^{m} l_i \tag{2.80}$$

If the system is closed, the sums of all columns in matrix $\underline{\underline{k}}$ are zero, and the matrix itself is singular: at least one of its eigenvalues is zero. The solution can also be given without using the matrix exponential function, based on a combination of exponential functions and polynomials:

$$[\text{A}_i] = \sum_{j=1}^{m} \sum_{h=1}^{l_j} C_{i,j,h} t^{h-1} e^{\lambda_j t} \tag{2.81}$$

Complex numbers may arise as eigenvalues, but as all the elements of matrix $\underline{\underline{k}}$ are real, they can only appear in conjugate pairs. In this case, it is always possible to reformulate the solution using the real sine and cosine functions only, thus eliminating the need for using the complex exponential function. The values of constants $C_{i,j,h}$ can be given based on the initial conditions.

In the reactions representing the inflow, molecules are produced. These processes are sometimes termed **production from a source**:

$$\emptyset \xrightarrow{k_i^{\text{in}}} \text{A}_i \tag{2.82}$$

This will lead to a first order, inhomogeneous linear system of differential equations. The solution of this is relatively easily stated in a matrix form if the k_i^{in} values are arranged into a vector $\underline{k}^{\text{in}}$ as:

$$\underline{c}_t = \text{expm}(\underline{\underline{k}}t)(\underline{c}_0 - \underline{\underline{k}}^{-1}\underline{k}^{\text{in}}) + \underline{\underline{k}}^{-1}\underline{k}^{\text{in}} \tag{2.83}$$

Consecutive processes containing higher order reaction steps seldom have known analytical solutions. When the number of consecutive steps is only two, suitable analytical formulas can sometimes be found, but they often contain mathematical functions that are not generally preferred by chemists. Nevertheless, some of these analytical solutions will be given here.

A second order reaction followed by a first order process is described by the following scheme [10]:

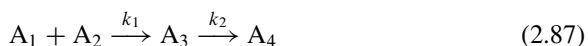$$2\text{A}_1 \xrightarrow{k_1} \text{A}_2 \xrightarrow{k_2} \text{A}_3 \tag{2.84}$$

The concentration of A_1 is obtained easily from a single-concentration rate law. The concentration of the intermediate is a more delicate matter:

$$[A_2]_t = \frac{4k_1[A_2]_0 + 2k_1[A_1]_0 - k_2 e^{-k_2/(2k_1[A_1]_0)} \mathrm{Ei}\left(\frac{k_2}{2k_1[A_1]_0}\right)}{4k_1} e^{-k_2 t}$$

$$+ \frac{-2k_1[A_1]_0 - k_2 e^{-k_2 t - k_2/(2k_1[A_1]_0)}(1 + 2k_1[A_1]_0)\mathrm{Ei}\left(k_2 t + \frac{k_2}{2k_1[A_1]_0}\right)}{4k_1(1 + 2k_1[A_1]_0)}$$

$$(2.85)$$

In this formula, $\mathrm{Ei}(x)$ is the exponential integral function, which is defined by the following integral:

$$\mathrm{Ei}(x) = -\int_{-x}^{\infty} \frac{e^{-z}}{z} dz \qquad (2.86)$$

The scheme involving a mixed second order reaction and a subsequent first order process can also be solved analytically [10]:

$$A_1 + A_2 \xrightarrow{k_1} A_3 \xrightarrow{k_2} A_4 \qquad (2.87)$$

The concentration of A_1 and A_2 is obtained readily from a single-concentration rate law and is given in Eq. (2.31). The general solution for intermediate A_3 is given as:

$$[A_3]_t = [A_3]_0 e^{-k_2 t} + [A_1]_0 e^{-k_2 t} - \frac{k_2[A_1]_0([A_2]_0 - [A_1]_0)H(0)}{[A_2]_0(k_1[A_1]_0 - k_1[A_2]_0 + k_2)} e^{-k_2 t}$$

$$+ \frac{[A_1]_0([A_2]_0 - [A_1]_0)e^{([A_1]_0 - [A_2]_0)k_1 t}}{([A_1]_0 e^{([A_1]_0 - [A_2]_0)k_1 t} - [A_2]_0)} + \frac{k_2[A_1]_0([A_2]_0 - [A_1]_0)e^{([A_1]_0 - [A_2]_0)k_1 t} H(t)}{[A_2]_0(k_1[A_1]_0 - k_1[A_2]_0 + k_2)} \qquad (2.88)$$

$$H(t) = {}_2F_1\left(1, 1 + \frac{k_2}{k_1([A_1]_0 - [A_2]_0)}, 2 + \frac{k_2}{k_1([A_1]_0 - [A_2]_0)}, \frac{[A_1]_0}{[A_2]_0} e^{([A_1]_0 - [A_2]_0)k_1 t}\right)$$

In this formula ${}_2F_1$ means the first hypergeometric function, which is defined as follows:

$${}_2F_1(a, b, c, x) = 1 + \sum_{n=1}^{\infty} \frac{a(a+1)\cdots(a+n-1)b(b+1)\cdots(b+n-1)}{c(c+1)\cdots(c+n-1)} \frac{x^v}{n!}$$

$$(2.89)$$

If $[A_1]_0 = [A_2]_0$, the solution can be obtained by the previously stated case of the second order-first order process (Eq. (2.85)). In the case where

$k_2 = jk_1([A_1]_0 - [A_2]_0)$ is true (where i is a positive integer), special solutions arise. For $j = 1$, the solution takes the following form:

$$[A_3]_t = [A_3]_0 e^{-k_2 t} + e^{-k_2 t}[A_1]_0 \left(1 - \tfrac{[A_1]_0}{[A_2]_0}\right) \ln \tfrac{[A_2]_0 e^{k_2 t} - [A_1]_0}{[A_2]_0 - [A_1]_0} +$$

$$\tfrac{[A_1]_0^2(1 - e^{k_2 t})}{[A_2]_0 e^{k_2 t} - [A_1]_0}$$

(2.90)

For $j > 1$, there are also special forms for the solution that can be obtained in an analogous manner.

A logical next possibility is a third order reaction followed by a first order process, which is represented as follows [10]:

$$3A_1 \xrightarrow{k_1} A_2 \xrightarrow{k_2} A_3 \tag{2.91}$$

The concentration of A_1 is obtained easily from a single-concentration rate law as in the previous cases, whereas the concentration of A_2 is given by the following expression:

$$[A_2]_t = [A_2]_0 e^{-k_2 t} + \frac{[A_1]_0}{3} e^{-k_2 t} + \frac{[A_1]_0}{3\sqrt{1 + 6k_1[A_1]_0^2 t}}$$

$$- \sqrt{\frac{\pi k_2}{54 k_1}} e^{-k_2 t - k_2/(6k_1[A_1]_0^2)} \mathrm{erfi}\left(\sqrt{\frac{k_2}{6k_1[A_1]_0^2}}\right)$$

$$+ \sqrt{\frac{\pi k_2}{54 k_1}} e^{-k_2 t - k_2/(6k_1[A_1]_0^2)} \mathrm{erfi}\left(\sqrt{\frac{k_2(1 + 6k_1[A_1]_0^2 t)}{6k_1[A_1]_0^2}}\right)$$

(2.92)

In this expression, $\mathrm{erfi}(x)$ refers to the imaginary error function, which is most easily defined through the complex error function $\mathrm{erf}(x)$, using the imaginary unit $i = \sqrt{-1}$ as follows:

$$\mathrm{erfi}(x) = -i \times \mathrm{erf}(i \times x) \tag{2.93}$$

The next consecutive process for which the analytical solution can be given is composed of a first order reaction followed by a second order process:

$$A_1 \xrightarrow{k_1} A_2$$
$$2A_2 \xrightarrow{k_2} A_3 \tag{2.94}$$

Again, the concentration of A_1 can be determined from a single-concentration rate law and follows single exponential decay. $[A_2]$ is given as:

$$[A_2]_t = \sqrt{\frac{k_1[A_1]_0 e^{-k_1 t}}{2k_2}} \frac{2K_1\left(\sqrt{8k_2[A_1]_0 e^{-k_1 t}/k_1}\right) - \omega I_1\left(\sqrt{8k_2[A_1]_0 e^{-k_1 t}/k_1}\right)}{2K_0\left(\sqrt{8k_2[A_1]_0 e^{-k_1 t}/k_1}\right) + \omega I_0\left(\sqrt{8k_2[A_1]_0 e^{-k_1 t}/k_1}\right)}$$

$$\omega = \frac{\sqrt{8k_1[A_1]_0/k_2}\, K_1\left(\sqrt{8k_2[A_1]_0/k_1}\right) - 4[A_2]_0 K_0\left(\sqrt{8k_2[A_1]_0/k_1}\right)}{\sqrt{2k_1[A_1]_0/k_2}\, I_1\left(\sqrt{8k_2[A_1]_0/k_1}\right) + 2[A_2]_0 I_0\left(\sqrt{8k_2[A_1]_0/k_1}\right)} \tag{2.95}$$

Here, I_1 and I_0 are the modified Bessel functions of the first kind, K_1 and K_0 are the modified Bessel functions of the second kind.

$$I_n(x) = \left(\frac{x}{2}\right)^n \sum_{j=0}^{\infty} \frac{1}{j!(n+j)!} \left(\frac{x}{2}\right)^j$$

$$K_n(x) = x^n \prod_{j=1}^{n}(2j-1) \int_0^{\infty} \frac{\cos w}{(w^2 + x^2)^{n+1/2}} dw \tag{2.96}$$

Finally, the case of a second order reaction followed by a second order process can also be handled in this way:

$$\begin{aligned} 2A_1 \xrightarrow{k_1} A_2 \\ 2A_2 \xrightarrow{k_2} A_3 \end{aligned} \tag{2.97}$$

The concentration of A_1 follows second order decay in this scheme. The concentration of A_2 is obtained as follows:

$$[A_2]_t = \frac{k_1[A_1]_0}{2k_2} \frac{(1+\xi)(\sqrt{1+2k_1[A_1]_0 t})^{-1+\xi} + \omega(1-\xi)(\sqrt{1+2k_1[A_1]_0 t})^{-1-\xi}}{(\sqrt{1+2k_1[A_1]_0 t})^{1+\xi} + \omega(\sqrt{1+2k_1[A_1]_0 t})^{1-\xi}}$$

$$\xi = \sqrt{1+2k_2/k_1} \qquad \omega = \frac{k_1(1+\xi) - 2k_2[A_2]_0/[A_1]_0}{2k_2[A_2]_0/[A_1]_0 + k_1(\xi - 1)} \tag{2.98}$$

Figure 2.6 displays some example curves for the concentration of the intermediate in the schemes discussed in the previous paragraphs. The parameters of all of the shown curves were selected so that the initial rate of the formation of A_2 is the same.

Among the single-concentration rate equations, the one describing isotope exchange in Eq. (2.38) might have been the most unusual. This process can be
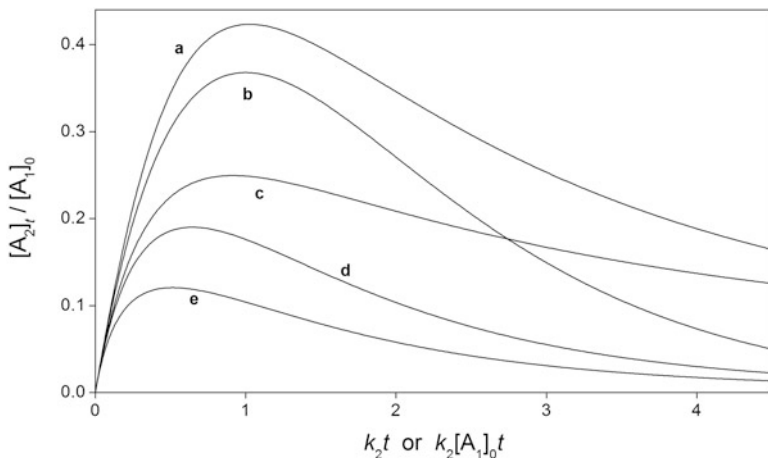
Fig. 2.6 Scaled kinetic traces for consecutive reactions. Formulas used: Eq. (2.95) $k_1/(k_2[A_1]_0) = 1$ (a), Eq. (2.98) $k_1/k_2 = 1$ (b), Eq. (2.60) $k_1/k_2 = 1$ (c), Eq. (2.85) $k_1[A_1]_0/k_2 = 1$ (d), Eq. (2.92) $k_1[A_1]_0^2/k_2 = 1$ (e)

coupled to first order decays in the number of labels, which gives rise to the following scheme:

$$A_1^* + A_2 \rightleftharpoons A_1 + A_2^*$$

$$A_1^* \xrightarrow{k_1} A_1 \tag{2.99}$$

$$A_2^* \xrightarrow{k_2} A_2$$
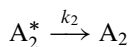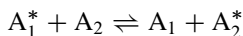
This seemingly artificial scheme actually has immense importance in the field of medical diagnostics, and it also forms the basis of measuring exchange rates in nuclear magnetic resonance spectroscopy. The labeling in these cases, rather than isotope substitution in Eq. (2.38), arises from the magnetization of nuclei. The quantities x_1 and x_2 are defined as given in Eq. (2.39) earlier. The differential equations describing the change in these abundances are as follows:

$$\frac{dx_1}{dt}[A_1]_T = -(R_{ex} + k_1[A_1]_T)x_1 + R_{ex}x_2$$

$$\frac{dx_2}{dt}[A_2]_T = -(R_{ex} + k_2[A_2]_T)x_2 + R_{ex}x_1 \tag{2.100}$$

The solution of this system of linear homogeneous differential equations is given by double exponential functions as follows:

$$x_{1,t} = \left(\frac{(x_{2,0}-x_{1,0})R_{ex}}{(\lambda_1-\lambda_2)[A_1]_T} + x_{1,0}\frac{\lambda_2+k_1}{\lambda_2-\lambda_1} \right) e^{\lambda_1 t}$$

$$+ \left(\frac{(x_{2,0}-x_{1,0})R_{ex}}{(\lambda_2-\lambda_1)[A_1]_T} + x_{1,0}\frac{\lambda_1+k_1}{\lambda_1-\lambda_2} \right) e^{\lambda_2 t} \tag{2.101}$$

$$x_{2,t} = \left(\frac{(x_{1,0}-x_{2,0})R_{ex}}{(\lambda_1-\lambda_2)[A_2]_T} + x_{2,0}\frac{\lambda_2+k_2}{\lambda_2-\lambda_1} \right) e^{\lambda_1 t}$$

$$+ \left(\frac{(x_{1,0}-x_{2,0})R_{ex}}{(\lambda_2-\lambda_1)[A_2]_T} + x_{2,0}\frac{\lambda_1+k_2}{\lambda_1-\lambda_2} \right) e^{\lambda_2 t} \tag{2.102}$$

The values λ_1 and λ_2 are the eigenvalues of a matrix similar to $\underline{\underline{k}}$ given in Eq. (2.76):

$$\lambda_1 = -\left(\frac{k_1}{2} + \frac{k_2}{2} + \frac{R_{ex}}{2[A_1]_T} + \frac{R_{ex}}{2[A_2]_T} \right)$$

$$+ \sqrt{ \left(\frac{k_1}{2} + \frac{k_2}{2} + \frac{R_{ex}}{2[A_1]_T} + \frac{R_{ex}}{2[A_2]_T} \right)^2 - k_1 k_2 - \frac{k_1 R_{ex}}{[A_2]_T} - \frac{k_2 R_{ex}}{[A_1]_T} }$$

$$\lambda_2 = -\left(\frac{k_1}{2} + \frac{k_2}{2} + \frac{R_{ex}}{2[A_1]_T} + \frac{R_{ex}}{2[A_2]_T} \right) \tag{2.103}$$

$$- \sqrt{ \left(\frac{k_1}{2} + \frac{k_2}{2} + \frac{R_{ex}}{2[A_1]_T} + \frac{R_{ex}}{2[A_2]_T} \right)^2 - k_1 k_2 - \frac{k_1 R_{ex}}{[A_2]_T} - \frac{k_2 R_{ex}}{[A_1]_T} }$$

The usual significance of these equations is that R_{ex} can be calculated from λ_1 and λ_2, which can be obtained directly from the detected kinetic curves.

As already pointed out, multiple-concentration rate equations often do not have known analytical solutions. Yet, it is difficult to predict the cases in which the solution can actually be given and some surprises may await the researchers. Usually, manual attempts at solving a rate equation are very time-consuming, but in all cases, trying to find the analytical solution using the differential equation solver of a symbolic software such as Mathematica is usually short, and may actually find the solution for most of the cases where it is available.

In multiple-concentration rate equations, it is possible that an explicit solution as a function of time cannot be given for the concentrations, yet an explicit formula connecting the concentrations to each other can be obtained. If concentration data are available for these components, this limited analytical formula provides some possibility to test adherence to the assumed rate equation. Two examples will be given in the following paragraphs.

The first example is the scheme where a reactant is transformed into a product in a first order step, then this product reacts with a second molecule of the reactant in a second order step. The scheme is given as follows:

$$A_1 \xrightarrow{k_1} A_2$$

$$A_1 + A_2 \xrightarrow{k_2} A_3$$

(2.104)

The corresponding rate equation is:

$$\frac{d[A_1]}{dt} = -k_1[A_1] - k_2[A_1][A_2]$$

$$\frac{d[A_2]}{dt} = k_1[A_1] - k_2[A_1][A_2]$$

(2.105)

As the concentration of component A_1 decreases monotonously, it makes sense to seek a function that describes the concentration of A_2 as function of the concentration of A_1 and not time. The concentration of A_2 changes monotonously: Eq. (2.105) shows that $[A_2] > k_1/k_2$ would be needed for a decrease, yet the initial concentration is zero, which guarantees that this state can never be reached. The mathematical background of the technique employed here is the derivation of composite functions, but an often useful shortcut is simply to think that two lines of Eq. (2.105) are "divided" by each other (see the footnote for the paragraph before Eq. (2.1)). The result is a differential equation without time derivatives:

$$\frac{d[A_1]}{d[A_2]} = \frac{k_1 + k_2[A_2]}{k_2[A_2] - k_1}$$

(2.106)

The concentration of component A_1 does not appear on the right-hand side of Eq. (2.106), so it is clearly a separable differential equation, which can be solved readily. The typical case is when $[A_2]_0 = 0$, for which the solution is:

$$[A_1]_t = [A_1]_0 + [A_2]_t + \frac{2k_1}{k_2} \ln\left(1 - \frac{k_2[A_2]_t}{k_1}\right)$$

(2.107)

This formula connects the concentrations of A_1 and A_2, which might be useful even without an analytical formula for the time dependence. This technique might also aid finding an analytical solution, as substitution of the formula gained here into the original rate equation will lead to a separable single concentration rate equation.

The second example is a competition reaction, where two reactants react with a common material in a pair of second order processes:

$$A_1 + A_3 \xrightarrow{k_1} A_4$$
$$A_2 + A_3 \xrightarrow{k_2} A_5$$

(2.108)

The rate equation is given as follows:

$$\frac{d[A_1]}{dt} = -k_1[A_1][A_3]$$

$$\frac{d[A_2]}{dt} = -k_2[A_2][A_3]$$

(2.109)

Although further equations would describe the rates of change for the other components, these two suffice for our present purposes. Both $[A_1]$ and $[A_2]$ decrease monotonously. Therefore, they can be described by changing the independent variable from time to a concentration. The resulting differential equation is:

$$\frac{d[A_2]}{d[A_1]} = \frac{k_2[A_2]}{k_1[A_1]}$$

(2.110)

Again, the solution this separable differential equation is readily obtained:

$$[A_2]_t = [A_2]_0 \left(\frac{[A_1]_t}{[A_1]_0}\right)^{\frac{k_2}{k_1}}$$

(2.111)

Curves in Fig. 2.7 show the two concentrations as a function of each other. The first model has one scaling parameter ($[A_1]_0$) and one shape parameter ($k_2[A_1]_0/k_1$) as the typical initial concentration of A_2 is zero. In fact, it could be shown with two scaling parameters and no shape parameters, but for this, $[A_1] - [A_2]$ would need
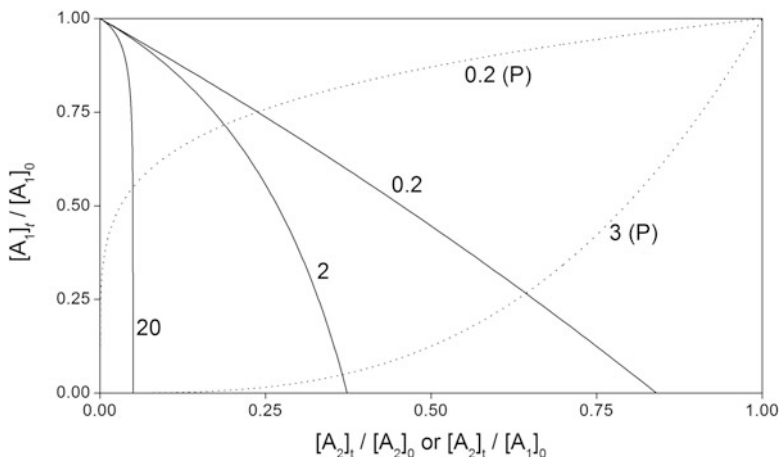
Fig. 2.7 Scaled concentrations as a function of each other in two mechanisms. *Solid lines*: Eq. (2.104) with $k_2[A_1]_0/k_1$ as the shape parameter. *Dotted lines* (also marked with P): Eq. (2.108) with k_1/k_2 as the shape parameter

to be plotted as function of $[A_2]$, which would make an unusual representation, the utility of which is not obvious. The second model has two scaling parameters ($[A_1]_0$ and $[A_0]_0$) and one shape parameter (k_1/k_2).

2.2   Numerical Methods

A **numerical solution** of a rate equation usually gives a collection of numbers rather than functions. The process is also called **numerical integration**, which generates approximate values of concentrations at predetermined time intervals.

The simplest numerical integration method is called the **Euler method**, in which the product of a preselected small time step (τ) and the derivative given in the rate equation is simply added to the concentration of A_i to obtain the new concentration value at the later time:

$$[A_i]_{t+\tau} = [A_i]_t + f_i([A_1]_t, [A_2]_t, \ldots, [A_n]_t)\tau \tag{2.112}$$

The additive term $f_i([A_1]_t, [A_2]_t, \ldots, [A_n]_t)\tau$ on the right is called a **concentration increment**. This method is applied in a progressive manner, giving approximate concentrations at gradually increasing times.

A more advanced method is called the fourth order **Runge–Kutta method** [7, 17]. The term "fourth order" refers to the fact that four different approximations of the concentration increment are estimated with the following formulas:

$$\begin{aligned}
h_{i,1} &= f_i([A_1]_t, [A_2]_t, \ldots, [A_n]_t) \\
h_{i,2} &= f_i([A_1]_t + h_{1,1}\tau/2, [A_2]_t + h_{2,1}\tau/2, \ldots, [A_n]_t + h_{n,1}\tau/2) \\
h_{i,3} &= f_i([A_1]_t + h_{1,2}\tau/2, [A_2]_t + h_{2,2}\tau/2, \ldots, [A_n]_t + h_{n,2}\tau/2) \\
h_{i,4} &= f_i([A_1]_t + h_{1,3}\tau, [A_2]_t + h_{2,3}\tau, \ldots, [A_n]_t + h_{n,3}\tau)
\end{aligned} \tag{2.113}$$

Finally, the concentration increment actually used for a given species is calculated as the weighted average of the four different approximated terms.

$$[A_i]_{t+\tau} = [A_i]_t + \frac{h_{i,1} + 2h_{i,2} + 2h_{i,3} + h_{i,4}}{6}\tau \tag{2.114}$$

A still more advanced method is dependent of the use of Taylor series. According to the Taylor theorem, the concentration $[A_i]_{t+\tau}$ can be calculated from concentration $[A_i]_t$ using the derivatives at time t by the following infinite sum:

$$[A_i]_{t+\tau} = [A_i]_t + \sum_{j=1}^{\infty} \frac{1}{j!} \frac{d^j[A_i]}{dt^j} \tau^j \tag{2.115}$$

The first derivative ($j = 1$) is already known from the rate equation to be $f_i([A_1], [A_2], \ldots, [A_n])$. The higher order derivatives can be calculated from the rate equation by successive differentiation:

$$\frac{d^j[A_i]}{dt^j} = \sum_{k=1}^{n} \frac{\partial \frac{d[A_k]^{j-1}}{dt^{j-1}}}{\partial [A_k]} \frac{d[A_k]}{dt} = \sum_{k=1}^{n} \frac{\partial \frac{d[A_k]^{j-1}}{dt^{j-1}}}{\partial [A_k]} f_k([A_1], [A_2], \ldots, [A_n])$$

(2.116)

The sum is calculated to a finite number of terms in the series. The higher the number of terms considered, the better the approximation becomes. It should be noted that the Euler method is the same as the Taylor series method truncated to a single additive term (i.e., stopping at the first derivative).

The Taylor series method can sometimes provide analytical solutions as well if the resulting infinite sum is recognized as the exact Taylor series of a particular function. For the simple first order rate equation, this is a very spectacular way of proving that the solution is the exponential function. In this case, $f_1([A_1]) = -k[A_1]$, and the derivatives at $t = 0$ can all be calculated quite simply:

$$\left(\frac{d^j[A_1]}{dt^j}\right)_0 = (-k)^j[A_1]_0$$

(2.117)

Substituting these derivatives into Eq. (2.115) with $t = 0$ gives the following formula:

$$[A_i]_\tau = [A_i]_0 + \sum_{j=1}^{\infty} \frac{1}{j!}(-k)^j[A_1]_0\tau^j = [A_1]_0 \sum_{j=0}^{\infty} \frac{(-k\tau)^j}{j!}$$

(2.118)

The infinite sum on the right of this equation is exactly the value of e^{-kt} by the definition of the exponential function.[2]

The key question in using numerical integration is the selection of suitable τ time step values. Too small a value requires a lot of computational power, whereas the numerical calculations do not approximate the solution well if τ is too high. In addition, it often happens that at the beginning of the process, very low values of τ are needed, but later on, the time steps can be increased significantly without any loss in accuracy. A numerical instability arising from this sort of sensitivity to the time step is called **stiffness** [2]. When stiff differential equations are solved numerically, it is imperative to use variable time steps. The **Gear algorithm**, also called **predictor-corrector method** [5] provides a common way of solving stiff systems in chemical kinetics.

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[2]Hungarian-born mathematician Pál Erdős often told his audience that God has a book for recording the most elegant proofs of all theorems. As he used to say, mathematicians need not believe in God, but all of them must believe in the book. The author is sure this proof is from God's book.

In all of these numerical methods, there are two conceptually different sources of error, which cause the differences between the results of the numerical calculations and the actual solution. The first is called **formula error**, which originates from the approximate nature of the formulas used to calculate the concentration increment. The second kind of error is called **propagating error**, which is caused by the fact that the value $[A_i]_t$ used in calculating the next value $[A_i]_{t+\tau}$ is imprecise except in the case of $t = 0$.

There are a number of different softwares that can solve almost any rate equation numerically. Here is a list of softwares this author has some familiarity with: COPASI [1], KINSIM [6], Pro-Kineticist [15], Scientist [14], SPECFIT [18], ZiTa [19]. All of these softwares can solve kinetic differential equations numerically, some of them even contain a least squares minimizing algorithm that is suitable for finding the combination of parameters that best fit a set of experimentally measured data.

2.3   Fitting to Measured Data

Fitting to measured data is a very common problem in chemical kinetics. It serves two different purposes, the more important of which is to test whether detected data follow some sort of theoretical function or not. The second purpose is to determine the values of the parameters appearing in the theoretical function, which are often used to draw further conclusions. It should be emphasized that checking the quality of the fit takes precedence over determining the parameter values. The usual mathematical procedures used in fitting yield parameter values even if the measured data do not resemble the theoretical function at all. However, if the quality of the fit is not sufficient, the determined parameters do not contain any physical information. Unfortunately, this sort of **force fitting**, i.e., using theoretical functions that do not describe the measured data well is very common today's science (e.g., exponential curves are used to fit kinetic traces even if the curves are spectacularly far away from being exponential). This is often caused by an insufficient knowledge of possible theoretical functions describing the phenomenon and the belief that one of a very narrow selection of functions must describe the results for theoretical reasons. It cannot be emphasized strongly enough that no scientific conclusion can be drawn from the values of such force-fitted parameters. The primary objective of fitting is to learn whether the theoretical function describes the data well, and the determined parameter values only make sense if this first question is answered positively.

There are a huge number of scientific softwares that use built-in algorithms to carry out fitting and statistical analysis. These algorithms could even be used as a black box (without any knowledge of the principles on which they are based), but for scientific users, it is highly advisable to get familiar at least with the basics of

the mathematical background. It is also a good idea to test computer softwares used for such statistical analysis before first use and compare their results against some sort of standard, well-known data set.

The most common mathematical method used in fitting is called least squares fitting. The term "least squares" refers to the fact that those parameter values are determined for which the square of the difference between the measured points and the theoretical function is minimal. The procedure is also often called nonlinear, which should be interpreted not in the context of the independent variable, but with respect to the parameters. For example, consider the following second order polynomial:

$$g(t) = C_1 t^2 + C_2 t + C_3 \qquad\qquad (2.119)$$

This is a nonlinear function with respect to the independent variable t, but it is linear for the parameters C_1, C_2, and C_3.

Let $g(t)$ be the theoretical function of interest, N the number of measured points, $g_1, g_2, \ldots, g_N$ the values of the dependent variable experimentally determined for the independent variables $t_1, t_2, \ldots, t_N$. Some of the values $t_1, t_2, \ldots, t_N$ may be equal to each other, this means that the dependent variable was measured multiple times at a certain independent variable.

The difference $g_i - g(t_i)$ is called a **residual**. The sum of the squares of the residuals is calculated and minimized in the fitting procedure. This sum is handled as a function of the parameter values that must be determined. If function $g(t)$ has m different parameters, the sum of squares is defined as follows:

$$S(C_1, C_2, \ldots, C_m) = \sum_{i=0}^{N} (g_i - g(t_i))^2 \qquad\qquad (2.120)$$

In the process of fitting, those parameter values are sought for which the function $S(C_1, C_2, \ldots, C_m)$ is at minimum. The process is also called **optimization**. From time to time, the physically meaningful values of the parameters may be limited, these limitations can be built into the optimization procedure.

In real-life applications, the different measured points may not be equally important or not equally reliable (these concepts are usually connected). These differences can be taken into account in the fitting procedure by defining weights $(w_1, w_2, \ldots, w_N)$ for each measured point. In this case, the function to be minimized involves multiplication of each residual with its individual weight.

$$S(C_1, C_2, \ldots, C_m) = \sum_{i=0}^{N} w_i \, (g_i - g(t_i))^2 \qquad\qquad (2.121)$$

If all weights are equal, that will lead to the same result as no weighting at all $(w_1 = w_2 = \cdots = w_N = 1)$ as given for the function in Eq. (2.120). This is

called **uniform weighting**. Uniform weighting assumes that the absolute errors of the measured points are constant, so their reliability is independent of their value.

Another common case is when the relative errors of measured points are constant, i.e., their reliability is directly proportional to their value. The weights for this case, called **proportional weighting**, are the squares of the reciprocals of the measured values ($w_i = 1/g_i^2$).

If the individual standard deviations of all measured points ($\sigma_1, \sigma_2, \ldots, \sigma_N$) are known, the squares of their inverse reciprocals are best used as weights ($w_i = 1/\sigma_i^2$). This basically means that each point is weighted according to their reliability. However, it is not typical to measure experimental points together with their standard deviations.

Kinetic and rate data are often determined from light absorption measurements. Absorbance is defined as the logarithm of the ratio of two light intensities (one measured in the sample and a reference value). The detectors used in instruments used for measurements (spectrophotometers) typically have an error in the measurement of light intensity that is close to independent of the light intensity. High absorbance values mean low intensity, which is not measured reliably. One solution of this problem is to exclude the use of absorbance values above a cut-off limit (most often absorbance 2, which means that 99 % of the incoming light is absorbed, so 1 % reaches the detector), and use uniform weighting for lower values. Another possibility, which is by no means in widespread use, is to employ special weights based on the assumption of uniform error in intensity measurements. This might be referred to as **absorbance weighting** and takes the following mathematical following form:

$$w_i = 10^{-2g_i} \tag{2.122}$$

Whatever procedure is used, the weights in such a procedure should be defined independently of the results of the fitting. The reliability or importance of the individual data points should not be assessed based on how well they fit to the theoretical equation. Unfortunately, weighting in a way that gives the best fit to the theoretical equation is not unknown in practice. However, this is a highly prejudiced procedure that is a mere mathematical trick to make fitting statistics look good. In fact, this sort of weighting is equivalent to gradually erasing the experimental points that do not fit the theory.

The sum of squares shown in Eqs. (2.120) and (2.121) minimize the difference along the dependent variable and, taken literally, they assume that the values of the independent variable are known with high precision. Of course, this is a useful assumption when the error in the independent variable is at least an order of magnitude lower than the error in the dependent variables. Should this not be the case, different definitions of the sum of squares function may be employed. Statistical procedures based on this idea are often called **Deming regressions** [3]. A special case is **orthogonal fitting**, which minimizes the sum of squared perpendicular

distances from the data points to the theoretical function. In chemical kinetics, it is seldom necessary to use these techniques, but a careful experimenter should know about their existence and recognize the special cases when they are needed.

Function $S(C_1, C_2, \ldots, C_m)$, as defined in Eq. (2.121), cannot be negative as it involves summing the squares of real numbers. The minimum of this multivariable function is found where the partial derivatives are zero:

$$\frac{\partial S(C_1, C_2, \ldots, C_m)}{\partial C_i} = 0 \tag{2.123}$$

Solving these equations, which are nonlinear if the theoretical function $g(t)$ is nonlinear with respect to at least one of the parameters, gives the optimized values of the parameters. The number of equations in Eq. (2.123) is the same as the number parameters, so, at least in theory, all parameters can be determined from this equation. Quite often, Taylor series expansion is used to transform Eq. (2.123) into a set of linear equations called **normal equations** using the partial derivatives of function $g(t)$ with respect to the parameters. With this technique, Eq. (2.123) is not solved precisely, but the errors caused by the approximations are usually so small that they are without any consequence in experimental science.

An often neglected point is that when the values of the parameters are determined, the reliability of the values must also be assessed. This is done through estimating the standard deviations of the parameters. The usual course of calculations involves the definition of a matrix, $\underline{\underline{M}}$, based on the products of partial derivatives with respect to the parameters as follows:

$$\underline{\underline{M}} = \begin{pmatrix} \sum_{i=1}^{N} w_i \frac{\partial g(t_i)}{\partial C_1} \frac{\partial g(t_i)}{\partial C_1} & \sum_{i=1}^{N} w_i \frac{\partial g(t_i)}{\partial C_1} \frac{\partial g(t_i)}{\partial C_2} & \cdots & \sum_{i=1}^{N} w_i \frac{\partial g(t_i)}{\partial C_1} \frac{\partial g(t_i)}{\partial C_m} \\ \sum_{i=1}^{N} w_i \frac{\partial g(t_i)}{\partial C_2} \frac{\partial g(t_i)}{\partial C_1} & \sum_{i=1}^{N} w_i \frac{\partial g(t_i)}{\partial C_2} \frac{\partial g(t_i)}{\partial C_2} & \cdots & \sum_{i=1}^{N} w_i \frac{\partial g(t_i)}{\partial C_2} \frac{\partial g(t_i)}{\partial C_m} \\ \vdots & \vdots & \ddots & \vdots \\ \sum_{i=1}^{N} w_i \frac{\partial g(t_i)}{\partial C_m} \frac{\partial g(t_i)}{\partial C_1} & \sum_{i=1}^{N} w_i \frac{\partial g(t_i)}{\partial C_m} \frac{\partial g(t_i)}{\partial C_2} & \cdots & \sum_{i=1}^{N} w_i \frac{\partial g(t_i)}{\partial C_m} \frac{\partial g(t_i)}{\partial C_m} \end{pmatrix} \tag{2.124}$$

This matrix appears to involve a lot of calculations. This is indeed true, but these are highly routine and in a way simple as they only require the knowledge of the theoretical function and the values of t_i. Neither the experimentally measured values g_i nor the optimized values of the parameters are necessary.

As a next step, the inverse of matrix $\underline{\underline{M}}$ needs to be calculated. The elements of this inverse matrix, denoted $\langle \underline{\underline{M}}^{-1} \rangle_{i,j}$ for row i and column j, are essential in calculating further statistical descriptors. The standard deviation of parameter C_i is given as:

$$\sigma_{C_i} = \sqrt{\frac{\langle \underline{\underline{M}}^{-1} \rangle_{i,i} S(C_1, C_2, \ldots, C_m)}{N - m}} \tag{2.125}$$

Another highly significant statistical descriptor is the correlation coefficient between two parameters, which can be defined for any pairs of parameters as follows:

$$c_{C_i, C_j} = \frac{\langle \underline{\underline{M}}^{-1} \rangle_{i,j}}{\sqrt{\langle \underline{\underline{M}}^{-1} \rangle_{i,i} \langle \underline{\underline{M}}^{-1} \rangle_{j,j}}} \tag{2.126}$$

There are a number of other statistical descriptors (such as coefficient of determination, skewness, curtiosis, etc.) that can be used to characterize the quality of a fit. They rarely have major significance, but from time to time, they may be useful.

With this mathematical background, the following paragraphs will show specific examples of fitting through linear and exponential functions.

Fitting a straight line, which is also called **linear regression**, is identical to fitting a first order polynomial to measured data. This is a very common problem, and in earlier times, a ruler and some good judgment in eyesight were enough to obtain reasonably reliable data. The mathematics behind the fitting procedure was well known even then, and using the full statistical calculations became very easy after the personal computers became available for everyday use. The theoretical function in this case is a linear one with two parameters:

$$g(t) = C_1 t + C_2 \tag{2.127}$$

C_1 is commonly called slope and C_2 is called intercept, which is the value of the function at $t = 0$. Another sort of intercept is when $g(t) = 0$, which is not a direct parameter of the function but can be derived from the intercept and slope as $-C_2/C_1$. The equations that arise from setting the partial derivatives of $S(C_1, C_2, \ldots, C_m)$ to zero are as follows:

$$\frac{\partial \sum_{i=0}^{N} w_i (g_i - C_1 t_i - C_2)^2}{\partial C_1} = -2 \sum_{i=0}^{N} w_i (g_i - C_1 t_i - C_2) t_i = 0$$

$$\frac{\partial \sum_{i=0}^{N} w_i (g_i - C_1 t_i - C_2)^2}{\partial C_2} = -2 \sum_{i=0}^{N} w_i (g_i - C_1 t_i - C_2) = 0 \tag{2.128}$$

This is a system of two simultaneous linear equations. The solution yields the following parameter values:

$$C_1 = \frac{\left(\sum_{i=1}^{N} w_i g_i t_i \right) \left(\sum_{i=1}^{N} w_i \right) - \left(\sum_{i=1}^{N} w_i g_i \right) \left(\sum_{i=1}^{N} w_i t_i \right)}{\left(\sum_{i=1}^{N} w_i t_i^2 \right) \left(\sum_{i=1}^{N} w_i \right) - \left(\sum_{i=1}^{N} w_i t_i \right)^2}$$

$$C_2 = \frac{\left(\sum_{i=1}^{N} w_i t_i^2 \right) \left(\sum_{i=1}^{N} w_i g_i \right) - \left(\sum_{i=1}^{N} w_i t_i \right) \left(\sum_{i=1}^{N} w_i g_i t_i \right)}{\left(\sum_{i=1}^{N} w_i t_i^2 \right) \left(\sum_{i=1}^{N} w_i \right) - \left(\sum_{i=1}^{N} w_i t_i \right)^2} \tag{2.129}$$

The standard errors of the individual parameters are calculated as:

$$\sigma_{C_1} = \sqrt{\frac{\sum_{i=1}^{N} w_i}{\sum_{i=1}^{N} w_i \sum_{i=1}^{N} w_i t_i^2 - \left(\sum_{i=1}^{N} w_i t_i\right)^2}} \sqrt{\frac{\sum_{i=0}^{N} w_i (g_i - C_1 t_i - C_2)^2}{N-2}}$$

$$\sigma_{C_2} = \sqrt{\frac{\sum_{i=1}^{N} w_i t_i^2}{\sum_{i=1}^{N} w_i \sum_{i=1}^{N} w_i t_i^2 - (\sum_{i=1}^{N} w_i t_i)^2}} \sqrt{\frac{\sum_{i=0}^{N} w_i (g_i - C_1 t_i - C_2)^2}{N-2}}$$

(2.130)

The correlation between the slope and intercept is given as:

$$c_{C_1,C_2} = \frac{-\sum_{i=1}^{N} w_i t_i}{\sqrt{\sum_{i=1}^{N} w_i \sum_{i=1}^{N} w_i t_i^2}}$$

(2.131)

In chemical kinetics, the most common problem is fitting an exponential function to measured data. This is a clearly nonlinear problem as one of the three parameters appears in the exponent. The form already given in Eq. (2.10) is used:

$$g(t) = Xe^{-kt} + E$$

(2.132)

The optimized values for the linear parameters X and E are easily found as:

$$X = \frac{N \sum_{i=1}^{N} g_i e^{-kt_i} - (\sum_{i=1}^{N} e^{-kt_i})(\sum_{i=1}^{N} g_i)}{N \sum_{i=1}^{N} e^{-2kt_i} - (\sum_{i=1}^{N} e^{-kt_i})^2}$$

$$E = \frac{(\sum_{i=1}^{N} e^{-2kt_i})(\sum_{i=1}^{N} g_i) - (\sum_{i=1}^{N} e^{-kt_i})(\sum_{i=1}^{N} g_i e^{-kt_i})}{N \sum_{i=1}^{N} e^{-2kt_i} - (\sum_{i=1}^{N} e^{-kt_i})^2}$$

(2.133)

However, for the nonlinear parameter k, the equation remains implicit:

$$\left(N \sum_{i=1}^{N} e^{-2kt_i} - (\sum_{i=1}^{N} e^{-kt_i})^2\right) \sum_{i=1}^{N} g_i t_i e^{-kt_i}$$

$$= \left(N \sum_{i=1}^{N} g_i e^{-kt_i} - \sum_{i=1}^{N} e^{-kt_i} \sum_{i=1}^{N} g_i\right) \sum_{i=1}^{N} t_i e^{-2kt_i}$$

$$+ \left((\sum_{i=1}^{N} e^{-2kt_i})(\sum_{i=1}^{N} g_i) - (\sum_{i=1}^{N} e^{-kt_i})(\sum_{i=1}^{N} g_i e^{-kt_i})\right) \sum_{i=1}^{N} t_i e^{-kt_i}$$

(2.134)

This equation can be solved with a suitable numerical method. Alternatively, the Taylor series expansion can be used the set up a normal equation instead of Eq. (2.134). Then the standard deviations and the correlations of the parameters can be obtained from Eqs. (2.125) and (2.126).

The exponential function is well suited as a probe function to determine rates of concentration change. For this purpose, a relatively small portion of the experimentally detected trace is fitted. The selected portion should contain the time for which the derivative is sought and should be narrow enough so that the exponential function fits quite well. The rate is then calculated by the following formula:

$$\frac{dg(t)}{dt} = -kXe^{-kt} \tag{2.135}$$

If the initial rate of the process is determined by this technique, the probe function can be re-parametrized so that the initial rate v_0 (the derivative at $t = 0$) appears in it as parameter:

$$g(t) = \frac{v_0}{k}e^{-kt} + E \tag{2.136}$$

Finally, a further phenomenon related to parameter correlation should be mentioned here. Consider the following three-parameter equation:

$$g(t) = (C_1 + C_2)t + C_3 \tag{2.137}$$

In this equation, there is no way of determining C_1 and C_2 independently, only their sum $(C_1 + C_2)$ is available from the fitting. In the results of a fitting procedure, this would be apparent from a correlation coefficient of 1 between C_1 and C_2. The example shown here is quite an obvious one as the correlation is caused by the form of the function. In real life examples, such functions are easily recognized. A lot more difficult to recognize is the case when the parameter correlation is caused by the insufficient range of measured data, which cannot be avoided because of experimental limitations. The phenomenon is detected by large values of standard errors and correlations between the parameters close to 1.

Another reason why a particular parameter may have very large standard error as calculated in the fitting is that it does not influence the calculated values of the theoretical function in the range of independent variables covered by the data. In this case, the large standard error is only calculated for a single parameter rather than a pair of C_i values.

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