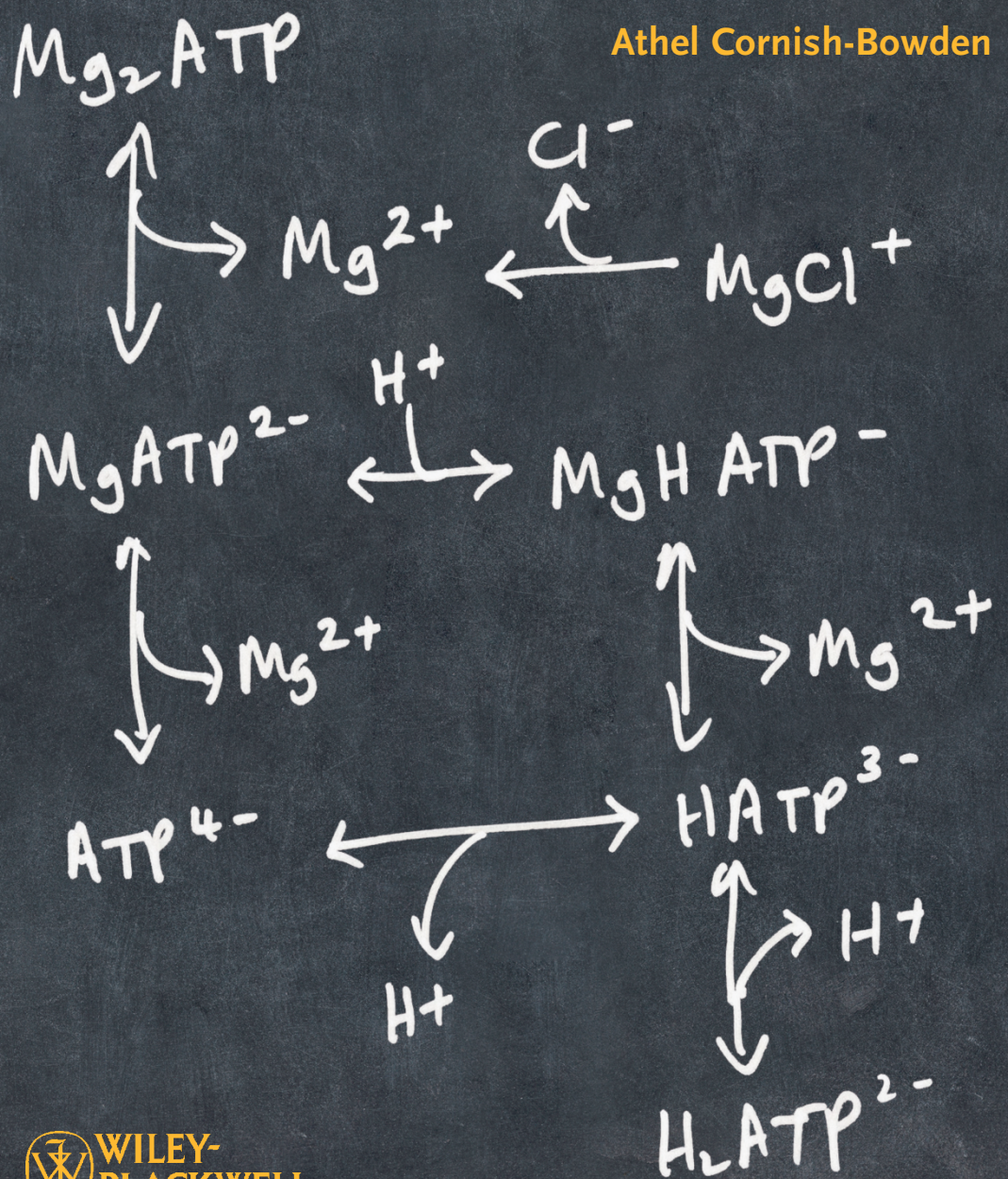
Fundamentals of Enzyme Kinetics

Fourth Edition

Athel Cornish-Bowden



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Fundamentals of Enzyme Kinetics

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Contents

Preface to the Fourth Edition

It was said of the great statistician R. A. Fisher that whenever he introduced a result with the words "it can easily be shown that . . . " one could be sure that two or three hours of hard work would be in store for anyone wishing to verify it. As a student I thought that many authors used this formula as a way to avoid explaining things that they could not explain. I hasten to add that in Fisher's case I am sure there was no lack of ability, though there may have been a lack of appreciation of the difficulties that his readers had. When I was writing the earliest version of this book, therefore, I resolved never to claim that anything was easy unless I was quite sure that it was. In the 35 years that have passed since then I believe I have kept this resolution, though I have often had to revise my views about what was simple enough to be left unexplained. Above all I have striven for clarity, being guided by a slogan from Keith Laidler: "Correctness, cogency, clarity: these three, but the greatest of these is clarity". Errors can be corrected, weak arguments can be strengthened, but lack of clarity leaves a fog that may take years to dispel.

K. J. Laidler (1998) *To Light such a Candle*, Oxford University Press, Oxford

The emphasis throughout is on *understanding* enzyme kinetics, not on covering every aspect of the subject in an encyclopedic style. So I have preferred to describe the principles that will allow readers to proceed as far as they want in any direction. In the words of Kuan-tzu (as quoted by Parzen): "If you give a man a fish, he will have a single meal; if you teach him how to fish, he will eat all his life".

E. Parzen (1980) "Comment" *American Statistician* ***34***, *78–79*

I make no apology for continuing to illustrate concepts with abundant graphs, including the straight-line graphs that biochemists have used for three-quarters of a century, although it is sometimes argued that the appearance of com-

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puters on every desk has made graphical methods obsolete. Professional statisticians who really know and understand data analysis think differently; for example, Chambers and co-workers wrote

> There is no statistical tool that is as powerful as a well-chosen graph. Our eye–brain system is the most sophisticated information processor ever developed, and through graphical displays we can put this system to good use to obtain deep insight into the structure of data.

J. M. Chambers, W. S. Cleveland, B. Klein and P. A. Tukey (1983) *Graphical Methods for Data Analysis*, Wadsworth, Belmont, California

There is little to "see" in a biochemical experiment and almost all our information comes at second hand from instruments, so it is essential to convert it into something visible. At the same time judicious use of the computer is equally necessary—not just graphs, not just computation, but both, in partnership—and in this spirit I have not only retained but have expanded the final chapter of the book, which has been a well received feature of the earlier editions.

Enzyme kinetics is not a topic that changes greatly from year to year, so why is a new edition needed? The text has of course been updated, with greater recognition of the importance of enzyme kinetics for biotechnology and drug development, and many recent literature references have been added. The major and most obvious change, however, is in the manner of presenting the information. There are more than three times as many figures as there were in the third edition, and the need for page-flipping has been virtually eliminated: not only figures and tables, but also references and notes, all appear as close as possible to the context in which they are mentioned; any that cannot appear on the same page opening where they are mentioned are never more than a page away. Here it is a pleasure to acknowledge the willingness of Wiley–VCH to allow the book to be laid out exactly as I wanted.

The original ancestor of this book was called *Principles of Enzyme Kinetics*, and appeared in 1976. Later I decided that the treatment needed to be made more elementary, and in 1979 the first edition of *Fundamentals of Enzyme Kinetics* had a new title to reflect the different emphasis. Over the years, however, much of the text that was dropped in 1979 has been put back, together with a significant amount of new material that is not particularly elementary. A case could be made, however, for reinstating the original title, or just calling it

Enzyme Kinetics, but I have discarded this course in order not to give the impression that it is more different than it is from the third edition.

In this edition I have added numerous brief biographies of some of the scientists who created enzymology. Why? Will it help students to be better biochemists if they know that Maud Menten was a woman, that James Sumner was left-handed but had lost the use of his left hand in a childhood accident, or that Emil Fischer's father considered him too stupid to be a businessman? Obviously not, but it will help them to understand that enzymology did not spring from nowhere, but was developed by real people with the same difficulties and hardships that people face today.

Acknowledgments

This edition has benefited greatly from the comments of many people who have read it all or in part: Dan Beard, Keith Brocklehurst, Marilú Cárdenas, Gilles Curien, Roy Daniel, Michael Danson, David Fell, Herbert Friedmann, Bob Goldberg, Brigitte Gontero, Jannie Hofmeyr, Peter Hughes, Marc Jamin, Carsten Kettner, Ana Ponces, Valdur Saks, Marius Schmidt, Keith Tipton, Chris Wharton. I have not followed all of their suggestions, and they are anyway not responsible for any faults that remain, but I have followed most of them, and I am extremely grateful for all of their comments.

I acknowledge with gratitude the *Centre National de la Recherche Scientifique* for giving me the possibility of continuing working as *Directeur de Recherche Émérite*. It is likewise a pleasure also to acknowledge Dr. Bruno Guigliarelli, Director of the Laboratory of *Ingénierie et Bioénergétique des Protéines* of the *Centre National de la Recherche Scientifique*, and Dr. Marie-Thérèse Giudici-Orticoni, head of the group that I have joined since becoming Emeritus, both of them for their general support and for their success in creating a congenial working environment.

A different sort of acknowledgment is needed for Bob Alberty, still active at the age of 90 in the subject that he helped revolutionize in the 1950s. He first wrote to me in 1977, and I was delighted that my first effort to write a book about enzyme kinetics had found favor with a giant in the subject; subsequently he has given me much encouragement.

As mentioned already, the publishers were very cooperative in allowing a layout that would achieve my aim of

making it as easy as possible to find insertions referred to in the text.

Marilú Cárdenas read all of the book in proof with me, and allowed numerous errors to be corrected. However, I owe her far more than that: as my wife as well as my collaborator (and originally my competitor in the field of hexokinase research), she has contributed in innumerable ways to my life during the past 30 years.

Corrections

It would be nice to think that there were no typographical or other errors in this book. Nice, yes, but if past experience is any guide, not very realistic, so a list of corrections will be maintained at http://bip.cnrs-mrs.fr/bip10/fek.htm.

Athel Cornish-Bowden
Marseilles, July 2011

Chapter 1

Basic Principles of Chemical Kinetics

1.1 Symbols, terminology and abbreviations

This book follows as far as possible the recommendations of the International Union of Biochemistry and Molecular Biology. However, as these allow some latitude and in any case do not cover all of the cases that we shall need, it is useful to begin by noting some points that apply generally in the book. First of all, it is important to recognize that a chemical substance and its concentration are two different entities and need to be represented by different symbols. The recommendations allow square brackets around the chemical name to be used without definition for its concentration, so [glucose] is the concentration of glucose, [A] is the concentration of a substance A, and so on. In this book I shall use this convention for names that consist of more than a single letter, but it has the disadvantage that the profusion of square brackets can lead to forbiddingly complicated equations in enzyme kinetics (see some of the equations in Chapter 8, for example, and imagine how they would look with square brackets). Two simple alternatives are possible: one is just to put the name in italics, so the concentration of A is A, for example, and this accords well with the standard convention that chemical names are written in roman (upright) type and algebraic symbols are written in italics. However, experience

International Union of Biochemistry (1982) "Symbolism and terminology in enzyme kinetics" *European Journal of Biochemistry* **128**, 281–291

Chapter 8, pages 189–226

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shows that many readers barely notice whether a particular symbol is roman or italic, and so it discriminates less well than one would hope between the two kinds of entity. For this reason I shall use the lower-case italic letter that corresponds to the symbol for the chemical entity, so a is the concentration of A, for example. If the chemical symbol has any subscripts, these apply unchanged to the concentration symbol, so a_0 is the concentration of A_0, for example. Both of these systems (and others) are permitted by the recommendations as long as each symbol is defined when first used. This provision is satisfied in this book, and it is good to follow it in general, because almost nothing that authors consider obvious is perceived as obvious by all their readers. In the problems at the ends of the chapters, incidentally, the symbols may not be the same as those used in the corresponding chapters: this is intentional, because in the real world one cannot always expect the questions that one has to answer to be presented in familiar terms.

As we shall see, an enzyme-catalyzed reaction virtually always consists of two or more steps, and as we shall need symbols to refer to the different steps it is necessary to have some convenient indexing system to show which symbol refers to which step. The recommendations do not impose any particular system, but, most important, they do require the system in use to be stated. Because of the different ways in which, for example, the symbol k_2 has been used in the biochemical literature one should never assume in the absence of a clear definition what is intended. In this book I use the system preferred by the recommendations: for a reaction of n steps, these are numbered 1, 2 ... n; lower-case italic k with a positive subscript refers to the kinetic properties of the forward step corresponding to the subscript, for example, k_2 refers to the forward direction of the second step; the same with a negative subscript refers to the corresponding reverse reaction, for example, k_{-2} for the second step; a capital italic K with a subscript refers to the thermodynamic (equilibrium) properties of the whole step and is typically the ratio of the two kinetic constants, for example, $K_2 = k_2/k_{-2}$.

The policy regarding the use of abbreviations in this book can be stated very simply: *there are no abbreviations in this book* (other than in verbatim quotations and the index, which needs to include the entries readers expect to find). Much of the modern literature is rendered virtually unintelligible to nonspecialist readers by a profusion of unnecessary abbreviations. They save little space, and little work (because with

modern word-processing equipment it takes no more than a few seconds to expand all of the abbreviations that one may have found it convenient to use during preparation), but the barrier to comprehension that they represent is formidable. A few apparent exceptions (like "ATP") are better regarded as standardized symbols than as abbreviations, especially because they are more easily understood by most biochemists than the words they stand for.

1.2 Order of a reaction

1.2.1 Order and molecularity

Chemical kinetics as a science began in the middle of the 19th century, when Wilhelmy was apparently the first to recognize that the rate at which a chemical reaction proceeds follows definite laws, but although his work paved the way for the law of mass action of Waage and Guldberg, it attracted little attention until it was taken up by Ostwald towards the end of the century, as discussed by Laidler. Wilhelmy realized that chemical rates depended on the concentrations of the reactants, but before considering some examples we need to examine how chemical reactions can be classified.

L. F. Wilhelmy (1850) "Über das Gesetz, nach welchem die Einwirkung der Säuren auf Rohrzucker stattfindet" *Poggendorff's Annalen der Physik und Chemie* **81,** 413–433, 499–526

P. Waage and C. M. Guldberg (1864) "Studier over Affiniteten" *Forhandlinger: Videnskabs-Selskabet i Christiana*, 35–40, 111-120. There is an English translation by H. I. Abrash at `http://tinyurl.com/3levsgl`

K. J. Laidler (1993) *The World of Physical Chemistry*, pages 232–289, Oxford University Press, Oxford

One way is according to the *molecularity*, which defines the number of molecules that are altered in a reaction: a reaction $A \rightarrow P$ is *unimolecular* (sometimes called *monomolecular*), and a reaction $A + B \rightarrow P$ is *bimolecular*. One-step reactions of higher molecularity are extremely rare, if they occur at all, but a reaction $A + B + C \rightarrow P$ would be *trimolecular* (or *termolecular*). Alternatively one can classify a reaction according to its *order*, a description of its kinetics that defines how many concentration terms must be multiplied together to get an expression for the rate of reaction. Hence, in a *first-order reaction* the rate is proportional to one concentration; in a *second-order reaction* it is proportional to the product of two concentrations or to the square of one concentration; and so on.

For a simple reaction that consists of a single step, or for each step in a complex reaction, the order is usually the same as the molecularity (though this may not be apparent if one concentration, for example that of the solvent if it is also a reactant, is so large that it is effectively constant). However, many reactions consist of sequences of unimolecular and bimolecular steps, and the molecularity of the complete reaction need not be the same as its order. Indeed, a complex reaction often has no meaningful order, as the overall rate often cannot

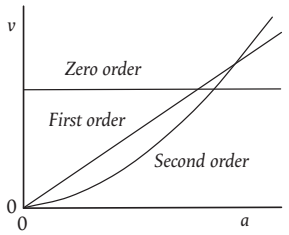

Figure 1.1. Order of reaction. When a reaction is of first order with respect to a reactant A the rate is proportional to its concentration a. If it is of second order the rate is proportional to a^2; if it is of zero order it does not vary with a.

be expressed as a product of concentration terms. As we shall see in later chapters, this is almost universal in enzyme kinetics, where not even the simplest enzyme-catalyzed reactions have simple orders. Nonetheless, the individual steps in enzyme-catalyzed reactions nearly always do have simple orders, usually first or second order, and the concept of order is important for understanding enzyme kinetics. The binding of a substrate molecule to an enzyme molecule is a typical example of a second-order bimolecular reaction in enzyme kinetics, whereas conversion of an enzyme–substrate complex into products or into another intermediate is a typical example of a first-order unimolecular reaction.

1.2.2 First-order kinetics

The rate v of a first-order reaction A $\rightarrow$ P can be expressed as

$$v = \frac{\mathrm{d}p}{\mathrm{d}t} = -\frac{\mathrm{d}a}{\mathrm{d}t} = ka = k(a_0 - p) \qquad (1.1)$$

in which a and p are the concentrations of A and P respectively at any time t, k is a *first-order rate constant* and a_0 is a constant. As we shall see throughout this book, the idea of a *rate constant*[1] is fundamental in all varieties of chemical kinetics. The first two equality signs in the equation represent alternative definitions of the rate v: because every molecule of A that is consumed becomes a molecule of P, it makes no difference to the mathematics whether the rate is defined in terms of the appearance of product or disappearance of reactant. It may make a difference experimentally, however, because experiments are not done with perfect accuracy, and in the early stages of a reaction the relative changes in p are much larger than those in a (Figure 1.2). For this reason it will usually be more accurate to measure increases in p than decreases in a.

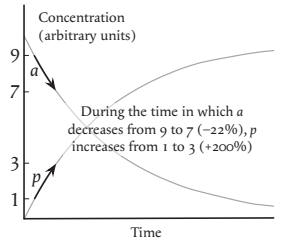

Figure 1.2. Relative changes in concentration. For a stoichiometric reaction A $\rightarrow$ P, any change in a is matched by an opposite change in p. However, in the early stages of a reaction the *relative* increases in p are much larger than the relative changes in a.

The third equality sign in the equation is the one that specifies that this is a first-order reaction, because it states that the rate is proportional to the concentration of reactant A.

[1] Some authors, especially those with a strong background in physics, object to the term "rate constant" (preferring "rate coefficient") for quantities like k in equation 1.1 and for many similar quantities that will occur in this book, on the perfectly valid grounds that they are not constant, because they vary with temperature and with many other conditions. However, the use of the word "constant" to refer to quantities that are constant only under highly restricted conditions is virtually universal in biochemical kinetics (and far from unknown in chemical kinetics), and it is hardly practical to abandon this usage in this book. See also the discussion at the end of Section 10.4.3.

§ 10.4.3, pages 264–265

Finally, if the time zero is defined in such a way that $a = a_0$ and $p = 0$ when $t = 0$, the stoichiometry allows the values of a and p at any time to be related according to the equation $a + p = a_0$, thereby allowing the last equality in the equation.

Equation 1.1 can readily be integrated by separating the two variables p and t, bringing all terms in p to the left-hand side and all terms in t to the right-hand side:

$$\int \frac{\mathrm{d}p}{a_0 - p} = \int k\,\mathrm{d}t$$

therefore

$$-\ln(a_0 - p) = kt + \alpha$$

in which α, the constant of integration, can be evaluated by noting that there is no product at the start of the reaction, so $p = 0$ when $t = 0$. Then $\alpha = -\ln(a_0)$, and so

$$\ln\left(\frac{a_0 - p}{a_0}\right) = -kt \tag{1.2}$$

Taking exponentials of both sides we have

$$\frac{a_0 - p}{a_0} = e^{-kt}$$

which can be rearranged to give

$$p = a_0(1 - e^{-kt}) \tag{1.3}$$

Notice that the constant of integration α was included in this derivation, evaluated and found to be nonzero. Constants of integration must always be included and evaluated when integrating kinetic equations; they are rarely found to be zero.

Inserting $p = 0.5a_0$ into equation 1.3 at a time $t = t_{0.5}$ known as the *half-time* allows us to calculate $kt_{0.5} = \ln 2 = 0.693$, so $t_{0.5} = 0.693/k$. This value is independent of the value of a_0, so the time required for the concentration of reactant to decrease by half is a constant, for a first-order process, as illustrated in Figure 1.3. The half-time is not a constant for other orders of reaction.

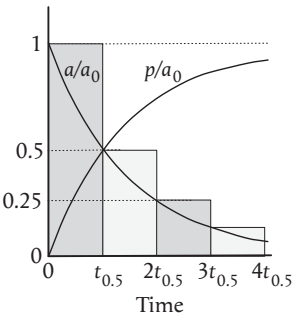

Figure 1.3. First-order decay. The *half-time* $t_{0.5}$ is the time taken for the reactant concentration to decrease by half from any starting point. For a first-order reaction, but not for other orders of reaction, it remains constant as the reaction proceeds.

1.2.3 Second-order kinetics

The commonest type of bimolecular reaction is one of the form A + B → P + Q, in which two different kinds of molecule

A and B react to give products. In this example the rate is likely to be given by a second-order expression of the form

$$v = \frac{\mathrm{d}p}{\mathrm{d}t} = kab = k(a_0 - p)(b_0 - p)$$

in which k is now a *second-order rate constant*.[2] Again, integration is readily achieved by separating the two variables p and t:

$$\int \frac{\mathrm{d}p}{(a_0 - p)(b_0 - p)} = \int k\,\mathrm{d}t$$

For readers with limited mathematical experience, the simplest and most reliable method for integrating the left-hand side of this equation is to look it up in a standard table of integrals.[3] It may also be done by multiplying both sides of the equation by $(b_0 - a_0)$ and separating the left-hand side into two simple integrals:

$$\int \frac{\mathrm{d}p}{a_0 - p} - \int \frac{\mathrm{d}p}{b_0 - p} = \int (b_0 - a_0)k\,\mathrm{d}t$$

Hence

$$-\ln(a_0 - p) + \ln(b_0 - p) = (b_0 - a_0)kt + \alpha$$

Putting $p = 0$ when $t = 0$ we find $\alpha = \ln(b_0/a_0)$, and so

$$\ln\left[\frac{a_0(b_0 - p)}{b_0(a_0 - p)}\right] = (b_0 - a_0)kt$$

or

$$\frac{a_0(b_0 - p)}{b_0(a_0 - p)} = e^{(b_0 - a_0)kt} \tag{1.4}$$

A special case of this result is important: if a_0 is negligible compared with b_0, then $(b_0 - a_0) \approx b_0$; p can never exceed a_0, on account of the stoichiometry of the reaction, and so $(b_0 - p) \approx b_0$. Introducing both approximations, equation 1.4 can be simplified as follows:

$$\frac{a_0 \cancel{b_0}}{\cancel{b_0}(a_0 - p)} = e^{kb_0 t}$$

Table 1.1. Standard integrals

$\int a\mathrm{d}x = ax$
$\int a \cdot f(x)\mathrm{d}x = a\int f(x)\mathrm{d}x$
$\int x\mathrm{d}x = \frac{1}{2}x^2$
$\int x^2\mathrm{d}x = \frac{1}{3}x^3$
$\int x^n\mathrm{d}x = \frac{x^{n+1}}{n+1}$ for $n \neq -1$
$\int \frac{1}{x}\mathrm{d}x = \ln x$
$\int e^x\mathrm{d}x = e^x$
$\int \frac{\mathrm{d}x}{a+bx} = \frac{1}{b}\ln(a+bx)$
$\int \frac{x\mathrm{d}x}{a+bx} = \frac{a+bx-a\ln(a+bx)}{b^2}$

1. In all examples, x is variable; a, b and n are constants and $f(x)$ is a function of x.

2. Standard tables usually omit the constant of integration (assuming that users know that it must be added).

3. Tables intended primarily for the use of mathematicians often write $\log x$ where a biochemist would expect $\ln x$.

Chapter 7, pages 169–188

[2] Conventional symbolism does not indicate the order of a rate constant. For example, it is common practice to illustrate simple enzyme kinetics with a mechanism in which k_1 is a second-order rate constant and k_2 is a first-order rate constant: there is no way to know this from the symbols alone, it is important to define each rate constant when it is first used.

[3] The integrals listed in Table 1.1 are sufficient for the purposes of this chapter (and the last one will not be needed until Chapter 7).

and, remembering that $1/e^{kb_0t} \equiv e^{-kb_0t}$, this can be rearranged to read

$$p = a_0(1 - e^{-kb_0t})$$

which has exactly the same form as equation 1.3, the equation for a first-order reaction. This type of reaction is known as a *pseudo-first-order reaction*, and kb_0 is a *pseudo-first-order rate constant*. Pseudo-first-order conditions occur naturally when one of the reactants is the solvent, as in most hydrolysis reactions, but it is also advantageous to create them deliberately, to simplify evaluation of the rate constant (Section 1.5).

§1.5, pages 11–13

1.2.4 Third-order kinetics

A trimolecular reaction, such as A + B + C → P + ..., does not normally consist of a single trimolecular step involving a three-body collision, which would be inherently unlikely; consequently it is not usually third-order. Instead it is likely to consist of two or more *elementary steps*, such as A + B ⇌ X followed by X + C → P. In some reactions the kinetic behavior as a whole is largely determined by the rate constant of the step with the smaller rate constant, accordingly known as the *rate-limiting step* (or, more objectionably, as the *rate-determining step*).[4] When there is no clearly defined rate-limiting step the rate equation is typically complex, with no integral order. Some trimolecular reactions do display third-order kinetics, however, with $v = kabc$, where k is now a *third-order rate constant*, but it is not necessary to assume a three-body collision to account for third-order kinetics. Instead, we can assume a two-step mechanism, as before but with the first step rapidly reversible, so that the concentration of X is given by $x = Kab$, where K is the equilibrium constant for binding of A to B, the association constant of X (Figure 1.4). The rate of reaction is then the rate of the slow second step:

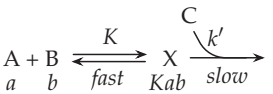

Figure 1.4. Third-order kinetics. A reaction can be third-order overall without requiring any third-order step in the mechanism, if a rapid equilibrium maintains an intermediate X at a concentration Kab and this reacts slowly with the third reactant C in a second-order reaction with rate constant k'.

$$v = k'xc = k'Kabc$$

where k' is the second-order rate constant for the second step. Hence the observed third-order rate constant is actually the product of a second-order rate constant and an equilibrium constant.

[4] These terms are widespread in chemistry, but they involve some conceptual confusion, as discussed in Section 14.1.3, and as far as possible are best avoided.

§14.1.3, pages 383–385

1.2.5 Zero-order kinetics

Some reactions are observed to be of *zero order*, with a constant rate, independent of the concentration of reactant. If a reaction is zero order with respect to only one reactant, this may simply mean that the reactant enters the reaction after the rate-limiting step. However, some reactions are zero-order overall, which means that they are independent of all reactant concentrations. These are invariably catalyzed reactions and occur if every reactant is present in such large excess that the full potential of the catalyst is realized. Enzyme-catalyzed reactions commonly approach zero-order kinetics at very high reactant concentrations.

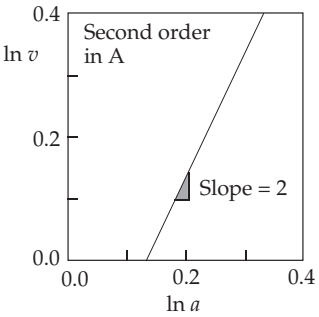

Figure 1.5. Determination of the order of reaction. The line is drawn for a reaction that is second-order in a reactant A (and first-order in another reactant B, but this is not evident from the plot) so the slope of the line is 2. The appearance of the plot (though not the numerical values) would be the same if logarithms to base 10 or any other base were used instead of natural logarithms, provided that the same changes were made in both coordinates.

1.2.6 Determination of the order of a reaction

The simplest means of determining the order of a reaction is to measure the rate v at different concentrations a of the reactants. A plot of $\ln v$ against $\ln a$ is then a straight line with slope equal to the order. As well as the *overall order* it is useful to know the order with respect to each reactant, which can be found by altering the concentration of each reactant separately, keeping the other concentrations constant. The slope of the line is then equal to the order with respect to the variable reactant. For example, if the reaction is second-order in A and first-order in B,

$$v = ka^2b$$

then

$$\ln v = \ln k + 2\ln a + \ln b$$

Hence a plot of $\ln v$ against $\ln a$ (with b held constant) has a slope of 2 (Figure 1.5), and a plot of $\ln v$ against $\ln b$ (with a held constant) has a slope of 1 (Figure 1.6). If the plots are drawn with the slopes measured from the *progress curve* (a plot of concentration against time), the concentrations of all the reactants change with time. Therefore, if valid results are to be obtained, either the initial concentrations of the reactants must be in stoichiometric ratio, in which event the overall order is found, or (more usually) the "constant" reactants must be in large excess at the start of the reaction, so that the changes in their concentrations are insignificant. If neither of these alternatives is possible or convenient, the rates must be obtained from a set of measurements of the slope at zero time, that is to say measurements of initial rates. This method

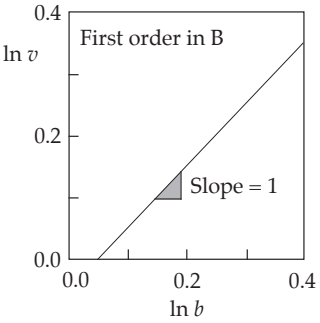

Figure 1.6. Determination of the order of reaction for a reaction that is first-order in a reactant B. The slope of the line is 1.

is usually preferable for kinetic measurements of enzyme-catalyzed reactions, because the progress curves of enzyme-catalyzed reactions often do not rigorously obey simple rate equations for extended periods of time. The progress curve of an enzyme-catalyzed reaction (Section 2.9) often requires a more complicated equation than the integrated form of the rate equation derived for the initial rate, because of progressive loss of enzyme activity, inhibition by accumulating products and other effects.

§2.9, pages 63–71

1.3 Dimensions of rate constants

Dimensional analysis provides a quick and versatile technique for detecting algebraic mistakes and checking results. It depends on the existence of a few simple rules governing the permissible ways of combining quantities of different dimensions, and on the frequency with which algebraic errors result in dimensionally inconsistent expressions. Concentrations can be expressed in M (or $\mathrm{mol} \cdot \mathrm{l}^{-1}$), and reaction rates in $\mathrm{M} \cdot \mathrm{s}^{-1}$. In an equation that expresses a rate v in terms of a concentration a as $v = ka$, therefore, the rate constant k must be expressed in s^{-1} if the left- and right-hand sides of the equation are to have the same dimensions. All first-order rate constants have the dimensions of time^{-1}, and by a similar argument second-order rate constants have the dimensions of $\mathrm{concentration}^{-1} \times \mathrm{time}^{-1}$ (Figure 1.7), third-order rate constants have the dimensions of $\mathrm{concentration}^{-2} \times \mathrm{time}^{-1}$, and zero-order rate constants have the dimensions of $\mathrm{concentration} \times \mathrm{time}^{-1}$.

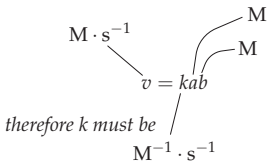

Figure 1.7. Units of rate constants. If a rate $v = kab$ is measured in $\mathrm{M} \cdot \mathrm{s}^{-1}$ and the two concentrations a and b are measured in M, then the left- and right-hand sides of the equation can only have the same units if the second-order rate constant k is measured in $\mathrm{M}^{-1} \cdot \mathrm{s}^{-1}$.

Knowledge of the dimensions of rate constants allows the correctness of derived equations to be checked easily: the left- and right-hand sides of any equation (or inequality) must have the same dimensions, and all terms in a summation must have the same dimensions. For example, if $(1 + t)$ occurs in an equation, where t has the dimensions of time, then the equation is incorrect, even if the "1" is intended to represent a time that happens to have the numerical value of 1. Rather than mixing dimensioned constants and variables in an expression in this way it is better to write the unit after the number, (1 s + t) for example, or to give the constant a symbol, $(t_0 + t)$ for example, with a note in the text defining t_0 as 1 s. Although both alternatives appear more clumsy than just writing $(1 + t)$ they avoid confusion. Section 9.6.1 contains an example, equation 9.12, where clarity requires inclusion of units inside an equation.

§9.6.1, pages 242–244

$$\frac{k_{1\mathrm{H}}}{k_{2\mathrm{H}}} = e^{4.8\,\mathrm{kJ\,mol^{-1}}/RT}$$

To include the value of a dimensioned quantity in an equation (4.8 kJ/mol in this example, which is simplified from equation 9.12 on page 243) one must include the units explicitly in the equation, or else introduce an algebraic symbol defined as having the value concerned.

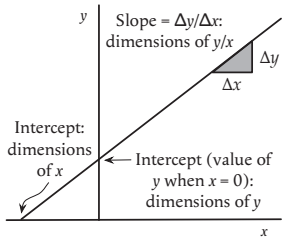

Figure 1.8. Application of dimensional analysis to graphs. The intercept on the ordinate is the value of y when $x = 0$, and has the same dimensions as y; The intercept on the abscissa is the value of x when $y = 0$, and has the same dimensions as x. The slope is an increment in y divided by the corresponding increment in x, and has the dimensions of y/x.

Quantities of different dimensions can be multiplied or divided, but must not be added or subtracted. Thus, if k_1 is a first-order rate constant and k_2 is a second-order rate constant, a statement such as $k_1 \gg k_2$ is meaningless, just as $5\,\mathrm{g} \gg 25\,^\circ\mathrm{C}$ is meaningless. However, a pseudo-first-order rate constant such as $k_2 a$ has the dimensions of concentration^{-1} × time^{-1} × concentration, which simplifies to time^{-1}; it therefore has the dimensions of a first-order rate constant, and *can* be compared with other first-order rate constants.

Another major principle of dimensional analysis is that one must not use a dimensioned quantity as an exponent or take its logarithm. For example, e^{-kt} is permissible, if k is a first-order rate constant, but e^{-t} is not. An apparent exception is that it is often convenient to take the logarithm of what appears to be a concentration, for example when pH is defined as $-\log[\mathrm{H^+}]$. The explanation is that the definition is not strictly accurate and to be dimensionally correct one should define pH as $-\log[\mathrm{H^+}]/[\mathrm{H^+}]_0$, where $[\mathrm{H^+}]_0$ is the value of $[\mathrm{H^+}]$ in the standard state, corresponding to pH = 0. As $[\mathrm{H^+}]_0$ has a numerical value of 1 it is usually omitted from the definition. Whenever one takes the logarithm of a dimensioned quantity in this way, a standard state is implied whether stated explicitly or not.

Dimensional analysis is particularly useful as an aid to remembering the slopes and intercepts of commonly used plots, and the rules are simple: any intercept must have the same dimensions as whatever variable is plotted along the corresponding axis, and a slope must have the dimensions of the ordinate (y) divided by those of the abscissa (x). These rules are illustrated in Figure 1.8.

1.4 Reversible reactions

All chemical reactions are reversible in principle, and for many the reverse reaction is readily observable in practice as well, and must be allowed for in the rate equation:

$$\underset{a_0 - p}{\mathrm{A}} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \underset{p}{\mathrm{P}} \qquad (1.5)$$

In this case,

$$v = \frac{\mathrm{d}p}{\mathrm{d}t} = k_1(a_0 - p) - k_{-1}p = k_1 a_0 - (k_1 + k_{-1})p$$