KINETIC MEASUREMENTS

1. Introduction

Kinetic measurements are studies of the rates at which chemical reactions occur. Generally, they involve preparing a chemical system with reagent concentrations different from their equilibrium values and then monitoring concentration changes as the system approaches equilibrium. Chemical kinetic data play a dominant role in testing models of chemical reactivity, and are used also throughout materials science, biochemistry and molecular biology, earth and atmospheric science, and many branches of engineering. Kinetic measurements are undertaken to elucidate basic mechanisms of chemical change, to understand how substances change throughout the physical world. The ultimate goal may be control of reactions for practical purposes, but the immediate significance lies in the patterns of kinetic behavior and their interpretation in terms of microscopic models of chemical reactivity of quite broad import. Data obtained in chemical kinetic studies are useful for modeling applications that extend far beyond chemical theory to interpret such natural phenomena as the observed depletion of stratospheric ozone (qv) (see also ATMOSPHERIC MODELING; ENGINEERING, CHEMICAL DATA CORRELATION). Finally, data are essential in the design of efficient, practical industrial processes. Compilations of measured rate constants are published in the United States by the National Institute of Standards and Technology, NIST, as well as many others. Compilations are not as well integrated nor as easy to find as those dealing with equilibrium thermodynamic quantities. It is often possible to find useful compilations for a given purpose using search engines on the Internet, so long as one can evaluate the credentials of the author.

2. Macroscopic Behavior and the Rate Law

2.1. Chemical Equations. Chemical changes are discussed with the aid of the same equations used to treat equilibrium. The reaction of reactants A, B, C, and so on, to produce products P, Q, etc, is described as

$$a\mathrm{A} + b\mathrm{B} + c\mathrm{C} + \cdots \rightleftharpoons p\mathrm{P} + q\mathrm{Q} + \cdots \quad (1)$$

The components A, B, P, Q, ... may be atoms, molecules, or ions. Species to the left are called reactants; those on the right are products. Most often, a kinetic change is written so that there is an initial excess of reactants that decreases over time. Kinetic rates are sensitive to a host of factors that must be specified or inferred, such as temperature or pressure and the involvement of solvents or catalysts.

The essential information implied by the chemical equation is the stoichiometry at the macroscopic level: If a mol of A react, then b mol of B do also, p mol of P are formed, etc. No inference can be made about behavior at the atomic level, eg, there is no implication that p molecules of P appear simultaneously. There may also be intermediates that appear and disappear in the course of the reaction but are not shown in the overall equation.

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Chemical kinetics is simplest when all components are gases or all components are solutes in a liquid solvent. In such cases of homogeneous reactions, molar concentrations are represented by brackets and the reaction quotient Z is defined as

$$Z = [\mathrm{P}]^p[Q]^q \cdots [\mathrm{A}]^a[\mathrm{B}]^b[\mathrm{C}]^c \cdots \tag{2}$$

The reaction quotient Z may, in principle, be measured at any time. If Z is observed not to change, the system is at equilibrium or at least may be treated as such for some purposes. In informal work, a time-independent Z is identified directly with the equilibrium constant K_c. Note that with this definition, K_c has units, unless they fortuitously cancel. See below for a more formal definition. For work with gases, concentrations are often expressed as partial pressures and a K_p is defined. For ideal gases, $p_x = [\mathrm{X}](RT)$. So it is possible to convert between K_c and K_p if ideal conditions apply or if the proper relationship is known.

A kinetic study typically prepares some initial Z_i not equal to K_c and describes the subsequent evolution of each of the concentrations. A basic assumption is that each component evolves according to some differential equation,

$$d[\mathrm{P}]/dt = f\ ([\mathrm{A}], [\mathrm{B}], \ldots, [\mathrm{P}], \ldots, \text{other conditions}) \tag{3}$$

Establishing precisely the conditions necessary to justify such a macroscopic differential equation starting from a microscopic, quantum description is an interesting question in theoretical physics that raises issues well beyond the macroscopic–microscopic relations derived by the usual treatments of rigorous statistical mechanics. The more abstruse aspects have been treated in considerable detail (1) but have little practical import. More practical treatments that connect statistical dynamics with macroscopic rate laws are mentioned briefly later in this article.

Formal treatments of equilibrium, eg, when relating equilibrium to a change in free energy, require specific conventions. The equilibrium constant should be defined only after standard states are specified. The factors in the equilibrium constant should be ratios of concentrations to those of the standard states, so that the equilibrium constant is dimensionless.

All references to pressures or concentrations should be to fugacities or activities. The activity corrections typically become important for ionic species at concentrations above $\sim$1 mM and fugacities may be useful for gas pressures $>$1–10 MPa, depending on molecular size. In some situations, eg, reactions on a surface, measures of chemical activity other than volumetric concentrations must be introduced. Such cases may often be treated with straightforward modifications of the basic approach described herein.

The focus here is a survey of contemporary experimental approaches to determining the form of equation 3 and quantifying rate parameters, followed by a brief consideration of microscopic models that offer a molecular interpretation of kinetic equations. In general, the differential equations could be very complicated. Experiments are designed to ensure that simplified equations apply, eg, to eliminate any spatial variation in concentrations.

2.2. The Well-Stirred Mixture. A key assumption of most laboratory kinetic measurements on homogeneous systems is that of a well-mixed solution of reactants. Then any component can be characterized by a single space-independent, but time-dependent, concentration applicable to the entire system. This simplifies the interpretation of experiments and the extraction of rate constants. The assumption is usually valid for gases or low viscosity liquids in volumes of laboratory dimensions over times that are not too short, typically 1 ms for mixing experiments, but sometimes as little as 1 ns or less for the perturbation methods described below. Mixing may be accomplished by relying on passive diffusion of components or by actively stirring the mixture (see MIXING AND BLENDING). The assumption, however, fails in many contexts outside the laboratory. Engineers must combine chemical kinetic data with the description of mass transport to design practical reactors (see MASS TRANSFER; REACTOR TECHNOLOGY). Geologists, atmospheric chemists, and biologists also need to confront mass transport along with chemical changes.

2.3. The Rate Law. The goal of chemical kinetic measurements for well-stirred mixtures is to validate a particular functional form of the rate law and determine numerical values for one or more rate constants that appear in the rate law. Frequently, but certainly not always, reactant concentrations appear in the rate equation raised to some power:

$$d[\mathrm{P}]/dt = k[\mathrm{A}]^x[\mathrm{B}]^y \ldots [\mathrm{P}]^w \ldots \tag{4}$$

This rate law, or rate equation, is in differential form. The exponents describe the order of the reaction. It is said to be x order in [A], y order in [B], and $(x+y+\cdots+w+\cdots)$-order overall. The exponents may be positive, negative, or zero. A reaction that is zero order with respect to a component proceeds at the same rate regardless of the amount of that component present. For example, if a reaction goes to completion, with equilibrium lying far to the right, then the rate law may well be independent of the amount of any products, and therefore zero order in all products. In practice, the products would simply be omitted from the rate law. The orders are usually integers, but may be simple fractions like three-halves or one-third. Some rate laws do not allow specifying reaction orders, but may show apparent reaction orders over limited ranges of concentrations, for eg,

$$d[\mathrm{P}]/dt = k_1[\mathrm{A}]^x/(k_2 + [\mathrm{B}]^y) \tag{5}$$

The rate law draws attention to the role of component concentrations. All other influences are lumped into coefficients k_i. The k_i are often referred to as rate constants, since they are not supposed to change as concentrations vary during the course of the reaction. They do, however, change with temperature, solvent, and other reaction conditions.

Additionally, the following points are important: (*1*) There is no guaranteed relation between the exponents $x, y, w, \ldots$ and the stoichiometric coefficients $a, b, p, \ldots$ (*2*) There is no assurance that the same rate law will apply over any range of conditions beyond what is measured. It is not unusual for different rate laws to be needed at different temperatures or concentrations, even when the same

stoichiometric chemical equation applies. (*3*) Reactions may depend on the strength of surrounding electromagnetic fields, such as visible light. (*4*) The effect of a catalyst maybe either an increase in some rate constant or a change of the form of the rate law itself. (*5*) A rate law may be written for each component. Relations among these are determined by the stoichiometric coefficients:

$$\text{Rate} = v = \frac{1}{p}\frac{d[\text{P}]}{dt} = \frac{1}{q}\frac{d[\text{Q}]}{dt} = -\frac{1}{a}\frac{d[\text{A}]}{dt} = -\frac{1}{b}\frac{d[\text{B}]}{dt} = \cdots \tag{6}$$

Before using any rate constant, one should be sure to know the stoichiometric equation assumed and the exact definition assumed for the rate constant. The rate of a reaction is also termed the reaction velocity v.

Integrated Forms of Rate Laws. Given a rate law valid over the time range considered, and a set of initial conditions, integration of the differential equation yields concentrations expressed explicitly as functions of time. Of course, sometimes there is no simple, analytical form available. In the past, considerable effort was devoted to cataloging integral solutions and training students in their use in conjunction with graphical means of plotting experimental data. With computers able to perform numerical integrations very quickly and display time courses as graphical output, it is now possible, if one prefers, to work directly with the differential forms and avoid writing analytical solutions for the integrated forms. In any case, rate constants are now typically obtained using linear or nonlinear regression analysis and not from graphical analysis of hand-drawn plots.

3. Experimental Verification of a Rate Law

3.1. The Method of Initial Rates. The method of initial rates verifies a rate law directly from its differential form and extracts a value for the rate constant. A system is prepared with some initial concentration for each component and then allowed to react. A small change in the concentration of one component, $\Delta[\text{P}]$, eg, is measured over a small interval of time Δt. The velocity $v = \Delta[\text{P}]/p\Delta t$ and the concentrations (which change only negligibly during the measurement) can be substituted into the proposed rate law, along with postulated values for the exponents x, y,... to determine an observed rate constant k_{obs}. This is repeated for a range of initial concentrations, and if the postulated rate law with the same exponents always yields the same k_{obs}, then one asserts that the rate law has been verified and the rate constant have been determined. This approach is a reasonable strategy for an initial survey of a totally unknown system. In some cases, it can be the only practical approach. It is, however, tedious and it extracts relatively little data from each set of initial conditions. It is often more efficient to fit the integrated form of the rate law to concentration measurements recorded at successive times following each set of initial conditions. Observing the postulated time dependence both verifies the order assumed and extracts a more precise value for the rate constant.

3.2. Flooding and Pseudo-First-Order Conditions. For a simple example, assume that it is known that the reaction is independent of product

concentrations and there are three reagents. The experimenter uses a large excess of B_i, C_i, and measures the initial change in a much smaller amount of A_i. Such flooding of the system with all components but A permits the rate law to be integrated with the assumption that all concentrations are constant except [A] to obtain simple expressions for the time variation of [A]. Assume that is suspected that the reaction is first order in [A]. With flooding of [B] and [C], the following equation

$$d[\mathrm{A}]/dt = -k_3[\mathrm{A}]^1\mathrm{B}_i^y\mathrm{C}_i^z \tag{7}$$

may be integrated to express an exponential decrease in [A] from its initial value $[A]_i$ to its final equilibrium value, or endpoint, A_∞, as follows:

$$[\mathrm{A}(t)] - \mathrm{A}_\infty = (\mathrm{A}_i - \mathrm{A}_\infty)\ \exp\ (-k_{\mathrm{obs}}t) \tag{8}$$

The conditions chosen make the reaction appear not only first order in [A], but also first-order overall. This is termed a pseudo-first-order situation. The pseudo-first-order rate constant k_{obs} isrelated to the k_3 in the original rate law 7 by

$$k_{\mathrm{obs}} = k_3\mathrm{B}_i^y\mathrm{C}_i^z \tag{9}$$

If the same measurement is repeated for different B_i, it should be possible to extract y by plotting log k_{obs} versus log B_i. This should yield a straight line with slope y, if the assumed rate law is valid. In a similar manner, z can be obtained by varying C_i. Alternatively, one could flood with [A] and [C] to determine the order b with respect to [B]. Even if the order with respect to [A] is not 1, and the integrated rate equation is not a simple exponential, a useful simplification still results from flooding all components except one.

The equilibrium value for any component, such as A_∞ above, sometimes referred to as the infinity point, is extremely important in the data analysis, particularly when the order of the reaction is not certain. The obvious way to determine it, allowing the reaction to proceed for a long time, is frequently useful; but sometimes it is not reliable. It is possible for secondary reactions to interfere. it is better in some cases to calculate the endpoint from a knowledge of the equilibrium properties of the system.

Two very different strategies are employed to produce the initial, nonequilibrium concentrations of reactants: mixing reagents or perturbing a system previously at equilibrium. Each of these basic strategies has many variations.

4. Mixing Methods

The most obvious procedure for measuring reaction rates is simply to mix reactants together and then monitor either the disappearance of a reactant or the appearance of a product. For reactions that are slow enough, mixing can be as simple as pouring liquid solutions into a flask or admitting gases into a reaction bulb. Since reaction rates are usually very sensitive to temperature, a stable, well-calibrated thermal bath is essential. For monitoring concentration changes,

two general strategies are possible. The first method relies upon sampling. Aliquots are removed from the mixture at time intervals, quenched to stop further reaction, and the concentrations measured by any method useful for static concentration measurements. Quenching is accomplished by quickly plunging the aliquot into a low temperature bath or by diluting it with excess solvent. Concentrations of one or more components of the aliquots may be determined by volumetric titration, a classical method that is usually precise and accurate, or by a host of other methods (see ANALYTICAL METHODS, SURVEY; THERMAL, GRAVIMETRIC, AND VOLUMETRIC METHODS).

The second approach to making many concentration measurements over a period of time relies on *in situ* methods, which requires an appropriately selective procedure. Spectrophotometry in the visible (vis) or ultraviolet (uv) is very common, especially for liquid solutions, although almost any spectroscopic method may be used (ses SPECTROSCOPY OPTICAL; INFRARED AND RAMAN SPECTROSCOPY; MAGNETIC SPIN RESONANCE). It has the advantage of easily distinguishing among multiple species. Conductivity measurements are useful when ions are involved. Potentiometric and amperometric measurements are also employed (See ELECTROANALYTICAL TECHNIQUES). For gas phase kinetics involving simple reactions in which the mole numbers change between reactants and products, it sometimes suffices simply to measure the total pressure. In addition, a large variety of techniques depending on mass spectroscopy (qv) are very attractive, particularly for gas-phase reactions and for studies that focus on the behavior of isolated molecules, free from environmental influences.

Simple manual mixing is applicable to a rather narrow range of times. A few seconds are required for thorough mixing, so reactions that are over in much less than a minute cannot be studied, and reactions requiring even a thousand minutes become tedious. There is not much that can be done about slow reactions, except to change conditions to increase the rate, eg, by raising temperatures or increasing reactant concentrations. The problem with fast reactions occasionally lies with difficulty in making the concentration measurements rapidly, but with today's fast electronic methods, the greater problem usually involves shortening the mixing time. There are two general strategies for solving this mixing problem.

4.1. Continuous-Flow Mixing. Flow mixing provided the first general solution to the study of the kinetics of fast reactions. Reactants are injected continuously into a flowing stream, where they mix quickly to achieve the well-stirred condition. The reacting mixture then moves along a tube or, occasionally, in a free jet. The concentration of products grows with time, and therefore with position along the flow tube. Time delay after mixing becomes encoded into spatial position along the tube. Concentrations at one or more observation points remain constant and can be measured with slow analytic instruments. This was very important before the invention of fast electronic methods and was used for both liquids and gases. Flow mixing, however, can be somewhat unwieldy for liquid solutions and, worse, it often requires large volumes of reactants. It has been replaced for most studies of 1iquid-phase reactions by stopped-flow mixing. Flow mixing, of course, is still useful in special circumstances, particularly in chemical engineering in the design of industrial reactors, where not just the chemical kinetics but also the mass transport and mixing are essential parts of the

study. For gas-phase reactions, flow mixing has remained an important technique. It is particularly prominent when ions are among the reagents. In flow-discharge methods, ions are created by an electrical discharge in a flow, perhaps in a sidearm that merges with another flow. Examples are numerous among investigations of reactions important in atmospheric science (2). Flows with or without discharges are also convenient for low pressure, isolated molecule studies using mass spectrometry or other highly sensitive and selective methods, such as high resolution laser excitation of luminescence.

4.2. Stopped-Flow Mixing. Reactants that are low viscosity liquids may be placed in separate syringes and then expelled rapidly through a mixing orifice into a chamber in which the reaction occurs and in which concentrations are measured by one of the *in situ* methods. With some attention to detail, mixing times of <1 ms can be achieved. Figure 1 shows a schematic diagram of the essential elements of such a stopped-flow apparatus. Such instruments are available commercially from several sources. The syringe plungers are pushed forward very quickly, usually by means of high pressure air discharge. A catching syringe is provided to recover the sample and provide a controllable means of halting the high speed flow. Most often concentrations are measured using absorption spectrophotometry or, less often, spectrofluorimetry. Measurements may be made of absorption changes using a single wavelength, but it is also possible to measure complete spectra at successive intervals, many times per second. This allows more certain identification of intermediates in a reaction. Analysis of time-resolved spectra by singular value decomposition using matrix methods is a powerful technique (3). Since the apparatus is quite compact, the sample can be thermostatted easily over a reasonable temperature range near ambient, and with more effort can be adapted for extreme conditions. Analogous methods for gas-phase reactions use pulsed valves connected to high-pressure reservoirs.

Stopped-flow methods are a simple extension of familiar manual methods of kinetic analysis and have the advantage of using a minimum amount of reagents. This is especially desirable for biochemical investigations. Modern electronic digitizers can capture thousands of sequential data points for concentration measurements for each mixing cycle. Stopped-flow instruments usually include a two-way valve for each reactant syringe, so they may be refilled easily from a reservoir to allow signal-averaging 5 or 10 measurements. Stopped-flow devices have become the standard kinetic procedure for biochemistry and bench-scale organic and inorganic solution chemistry, for all reactions occurring over times longer than a few milliseconds.

5. Measurement Strategies Based on Perturbations

At times much less than a millisecond, it becomes impossible to achieve good mixing. Instead, one must start with a thoroughly mixed system and make some uniform change simultaneously throughout the entire sample to produce initial conditions that are displaced from equilibrium. Two different strategies to this end were introduced in the 1950s and led to Nobel awards for their discoverers.

5.1. Perturbation of External Thermodynamic Variables. In Germany, Manfred Eigen and his collaborators demonstrated how to carry out kinetic measurements by perturbing an external thermodynamic parameter, such as temperature, T (4). In a T-jump experiment, the temperature of the sample, usually a liquid solution, is increased suddenly by $\sim 5^{\circ}C$ and maintained at the new temperature, while the response of the mixture is measured. Usually, the time required to make the kinetic measurement is short enough that maintaining the new temperature is not an issue; but some investigations have incorporated active stabilization at the new, higher T. This approach works because changing T often has a large effect on the equilibrium constant, K_c. The original set of concentrations existing before the T-jump is not the set of equilibrium concentrations appropriate to the new T. The kinetic measurement involves observing the relaxation of the concentrations toward the values appropriate to the new temperature, so perturbation methods are frequently called relaxation methods. The reaction must not go to completion toward either reactants or products (because in that case even a large change in K_c would still not have any measurable significance for concentrations) and K_c must vary with T, but otherwise the method is quite general.

For the simple, prototypical reaction

$$A + B \underset{k_r}{\overset{k_f}{\rightleftharpoons}} P \tag{10}$$

define the equilibrium concentrations at the new temperature to be A_∞, B_∞, and P_∞. Assume that raising T drives the equilibrium toward the left, encouraging dissociation. Then immediately after the T-jump, before relaxation to the new equilibrium, the concentrations may be expressed as $[A] = A_\infty - \Delta A$, $[B] = B_\infty - \Delta B$, and $[P] = P_\infty + \Delta P$, with all $\Delta X > 0$. The kinetic measurement involves the time evolution of $\Delta A(t)$, $\Delta B(t)$, and $\Delta P(t)$. The governing differential equation for [P] might be assumed to be

$$d[P]/dt = k_f[A][B] - k_r[P] \tag{11}$$

or, equivalently,

$$d[P_\infty + \Delta P]/dt = k_f[A_\infty - \Delta A]\ [B_\infty - \Delta B] - k_r[P + \Delta P] \tag{12}$$

Three simplifications may be invoked: $dP_\infty/dt = 0$ and $k_f A_\infty B_\infty - k_r P_\infty = 0$, both from the definition of equilibrium; and $k_f[\Delta A][\Delta B] \approx 0$ because it is the product of small factors. Consequently, a simple, linearized equation results:

$$d[\Delta P]/dt = -k_f(A_\infty \Delta B + B_\infty \Delta A) - k_r \Delta P \tag{13}$$

From the stoichiometry of equation 10, the initial deviations have equal magnitudes, $[\Delta A] = [\Delta B] = [\Delta P]$, and consequently

$$d[\Delta A]/dt = d[\Delta B]/dt = -d[\Delta P]/dt = \{k_f(A_\infty + B_\infty) + k_r\}\Delta P \tag{14}$$

The solution of equation 14 for ΔP is a decreasing exponential with $k_{obs} = k_f([A_\infty] + [B_\infty]) + k_r$. The perturbation approach usually generates small deviations in concentrations that permit use of the linearized differential equation and is another example of pseudo-first-order behavior. A plot of k_{obs} versus $[A_\infty + B_\infty]$ for a range of $[A_\infty + B_\infty]$ yields k_f from the slope and k_r from the intercept.

A number of approaches have been demonstrated for producing a T-jump. The most common, compact, and inexpensive strategy uses Joule heating by an electrical discharge through a conducting salt solution, as illustrated in Figure 2. The energy stored in the capacitor is $E = CV^2/2$.

If the resistance of the solution is R and the resistance and inductance of the rest of the discharge circuit is negligible, then almost all of the stored energy should be deposited in the salt solution in a time $\tau = RC$ after the switch is closed. A 0.1 μF capacitor charged to 20 kV stores 40 J, enough to raise the temperature of 1 mL of water solution almost 10°C. If $R = 20\ \Omega$, then the discharge time is $\tau = 2\ \mu s$, a considerable improvement over dead time in a mixing experiment. The capacitor may be recharged over several seconds through the high value resistor shown. Reactions investigated using T-jumps are usually reversible, and measurements may be repeated on the same sample after it has cooled down again to the initial temperature. Both C and R must be small in order to minimize the discharge time. Small C implies that voltage V must be large to store enough energy. Small R implies large salt concentrations, which limits the choice of solvents. In practice, water is used almost exclusively. The method is attractive for proton transfer, ie, acid–base, reactions and for some biochemical reactions. Concentration changes are often monitored using absorption spectrophotometry. Short discharge times encounter a problem, however. When the temperature is increased, the solution normally expands. Density variations lead to acoustic waves and cavitation, which have very deleterious effects on light transmission. The problem can be minimized by working near a temperature at which the coefficient of expansion of the solution is zero, which occurs for aqueous solutions near 4°C. Unfortunately, this precludes investigation of the temperature dependence of rates, which ordinarily is an important part of a kinetic study. Pressurizing the solution also helps.

Liquid samples may be heated by other means, eg, microwave irradiation was used very early (see MICROWAVE TECHNOLOGY). The method giving the fastest heating times is irradiation with light from a giant pulse, Q-switched laser, which can deposit energy in ~10 ns. The laser energy may be absorbed by the solvent directly or by some inert species that absorbs the laser radiation but does not interfere with the reaction or the monitoring of concentration changes. The major difficulty is the limited energy available in a laser pulse. Depositing even 1 J uniformly throughout a solution requires a large, expensive laser system and still gives only a small temperature change, unless one is prepared to work with very small volumes.

Other perturbations besides T have been demonstrated. The pressure jump, p-jump, is similar to the T-jump, but is less convenient, because quite large pressure changes (10–100 MPa) are needed to perturb equilibrium constants. One approach for producing such a large change is to pressurize a liquid solution using an inert gas above the liquid, until a brass or steel membrane ruptures

and suddenly reduces the pressure to ambient. Electric field perturbations affect some reactions and have also been used (4), but only infrequently.

The perturbation methods described above introduce the change as a step function with the transition much faster than the kinetics to be measured. Other approaches are possible. If an oscillatory temperature or pressure variation can be applied to a sample, reactant concentrations will attempt to follow the oscillatory perturbation. If the perturbation oscillates slowly, the concentrations changes will reach maximum amplitude and remain in phase with the perturbation. If the perturbation is introduced at a higher frequency, there will be both a phase lag and a reduced amplitude for the oscillatory concentration changes (4). Methods based on this approach facilitate extensive signal averaging. Sinusoidal modulation is well suited to electric field perturbations. Oscillatory temperature changes are difficult to impose, unless they are very slow. One may, however, observe the lag of concentrations behind a monotonic increasing temperature change, which amounts to the same principle restricted to less than one cycle. A periodic pressure change is attractive compared with bursting membranes and a version competitive with the classic p-jump has been demonstrated (5). A very rapidly oscillating pressure wave is also a sound wave. Acoustic methods for fast reactions are used in conjunction with a different detection strategy. Instead of measuring concentrations, one measures the attenuation of ultrasound waves as a function of frequency (see ULTRASONICS) (4). Absorption is maximized at frequencies corresponding to chemical relaxation rates. An extreme case of pressure perturbation is shock wave propagation, which has a separate history in rather specialized kinetic studies of very fast reactions.

5.2. Perturbation by Flash Photolysis and Pulse Radiolysis. A quite different strategy for studying fast kinetics was introduced in England by Ronald Norrish and George Porter. This they named flash photolysis (6). Ideally, flash photolysis would leave the pressure and temperature unchanged, while using a flash of light to perturb reactant concentrations away from preexisting values. In practice, the energy deposited rarely causes significant alterations in T or p, but the possibility must be kept in mind. Both irreversible and reversible reactions may be studied. For irreversible reactions, the light flash is absorbed by a thermally unreactive precursor to generate active reagents, whose subsequent kinetic behavior is monitored. The precursor must be replaced before the measurement can be repeated. For reversible reactions, the perturbation produces an active species that starts the chemical change of interest, but ultimately the system relaxes back to the original equilibrium, from which it may again be perturbed. A short flash of vis or uv light is a very convenient excitation, easily introduced into glass or fused silica reaction vessels. Shorter wavelength radiation in the X-ray region is similar in principle, but is used only when there is specific interest in the effect of X-rays or gamma rays and not as a general means of starting chemical reactions. Closely related is pulse radiolysis, in which a particle beam, usually of electrons, is incident on the sample and starts the reaction. In all of these cases, a single quantum of excitation, either a photon or a particle, carries energy greatly in excess of characteristic thermal energies k_BT and sufficient to break a chemical bond or otherwise have a major influence on the molecule excited.

Flash photolysis is prominent in studies of photochemistry (See PHOTOCHEMICAL TECHNOLOGY SURVEY). Important examples of photochemical processes, both desirable and undesirable, occur in natural phenomena, such as photosynthesis or the induction of skin cancer. Over the past century, photochemical processes have assumed steadily increasing importance in applied technology, such as photography (qv) and optical data storage (See INFORMATION STORAGE MATERIALS, OPTICAL). Flash photolysis is used to study all these, but its convenience and its usefulness for studying the very fastest chemical reactions, even those $<10^{-12}$ s, has led to its extension into areas not generally considered a part of photochemistry. All that is necessary is to devise a photosensitive species that can initiate the thermal reaction of interest. For example, the bonding of oxygen to the iron in the hemoglobin of red blood cells happens to be photosensitive and has been studied extensively by flash photolysis, even though such photodissociation has little consequence in nature. A major early application of flash photolysis was the study of shortlived, reactive free radical species that were suspected to occur also in thermal reactions.

Figure 3**a** shows a simple arrangement for flash photolysis studies. The optical flash is introduced perpendicular to a spectrophotometric probe beam. For measurements down to millisecond times, the flashlamp excitation can be as simple as a common photographic flashgun. It is usually necessary to restrict the excitation flash to a limited spectral region and to isolate the detector from scattered photolysis radiation. Most often the probe is optical absorption, as shown, but any on-line analytic technique can be used. Many different analytic probes can achieve time resolution down to millisecond or microsecond time scales.

The unique virtue of flash photolysis, however, is the ease with which it can be extended to much shorter times. Photolysis pulses in the nanosecond range almost always rely on lasers. Several technologies, such as Q-switching, pulsed gas discharge lasers, including the important uv-emitting excimer lasers, pulsed dye lasers pumped by Q-switched or excimer lasers, cavity-dumped lasers, and even pulsed excitation of semiconductor lasers, all conveniently generate pulses with durations near or <10 ns. The first three methods can produce pulses with tens to hundreds of millijoules of energy at rates of $\sim$l–10^3 Hz; the last two generate smaller energy pulses at much higher repetition rates ranging from $\sim 10^3$–10^6 Hz. In addition to producing short pulses of spectrally well-defined light, lasers have the advantage that the optical energy can be delivered to the sample very efficiently and focused to illuminate a small volume. In order to produce the largest transmittance changes for given pulse energies, the excitation should be confined to a region that creates a long optical pathlength for the probe with as small a cross-sectional area as instrument design permits. The geometry of Figure 3**b** shows how this is accomplished using excitation collinear with the probe. In some cases, truly microscopic methods can be used. An energy of only 1 μJ deposited in a volume <0.01 mm^3, yields an energy density >0.1 J/cm^3, which can be sufficient to produce a millimolar concentration of chemical transients. Such modest energies are compatible with high repetition rates and extensive signal averaging to attain impressive sensitivity. Repeated excitation of a small volume, however, often leads to sample degradation, which must be

counteracted by using flow systems for gases or liquid solutions and spinning or translating samples for solids.

Nanosecond excitation pulses are useful for the entire time range of bimolecular chemical kinetics, which depends on reagents diffusing until they meet and react. As the needed time resolution becomes shorter, however, fewer analytic probes remain practical. Optical or infrared (ir) absorption is most common. For times much <1 μs, it is difficult to make continuous lamps bright enough for transmittance measurements. Pulsed flashlamps are used instead, because they are bright while the measurement is made, but require less electrical input power, reduce cooling requirements, and minimize needless exposure of the (presumably photosensitive) sample to light. Lasers can be an attractive alternative for the probe, but continuous or long-pulse lasers are still not easily and inexpensively tunable in wavelength over wide ranges. Bright probe lamps require that attention be given to detectors (see PHOTODETECTORS). Photomultipliers can introduce subtle nonlinear distortions long before they fail in any obvious manner. Specially designed high current photomultipliers and associated electronic circuits remain linear to anode currents of many milliamps. Large-area, high current avalanche photodiodes are now available and have great potential. Electronic instruments must minimize stray capacitance and keep impedances suitably low. Analogue oscilloscopes with photographic recording, much used in the past, are tedious and no longer cost-effective for any time range. Also vanishing (for times longer than a nanosecond) are so-called electronic "sampling" methods. Although appropriate for repetitive electrical signals, sampling no longer has any significant cost advantage and is not a good general purpose strategy for chemical kinetics. Even if the excitation can be repeated, the chemical system may not tolerate so much photolysis. Electronic digitization of an entire oscilloscope trace is routine as of this writing ($\sim$2003) and offers time resolution to 1 ns or better.

Although most kinetic measurements by optical methods monitor changes at a single wavelength, there has always been an important role for measurements of time-resolved spectra in order to aid in determining the identity of transient intermediates. In the past, time-resolved spectra were recorded photographically or by piecing together transient spectra from electronic measurements made one wavelength at a time. The introduction of diode arrays and charge-coupled devices (CCDs) has revolutionized the design of spectrographs, combining the multiplex advantages of photographic emulsions with the convenience and superior linearity of electronic detection, while at the same time offering time resolution down to a few nanoseconds. The distinction between kinetic analysis and time-resolved spectroscopy blurs. The analysis of a complete, but often complicated, series of spectra taken at intervals over a long time range is aided by the mathematical methods of singular value decomposition using matrix algebra (3).

The most profound recent advance in fast and ultrafast kinetic studies may be progress in vibrational analyses, utilizing either time-resolved infrared absorption or time-resolved Raman scattering. These can be more selective and more diagnostic than traditional uv-vis measurements.

5.3. Very Fast Kinetics. One nanosecond is by no means the limit in time for kinetic measurements using optical or vibrational spectroscopies. The

state-of-the-art for direct, time-domain measurements now lies close to 10^{-14} s (l0 fs). At times shorter than a few nanoseconds, however (and sometimes much longer), there is usually not a well-stirred solution. Even using a homogeneous distribution of precursor molecules and a uniform excitation pulse, the reagent species created by photolysis retain the memory that they originated from precursors. Often times, the effect of photolysis (literally, "breaking apart by light") is to dissociate a molecule into two fragments. At short times the distribution of partners is not random; they are close together. Each might recombine with its partner fragment to reform the precursor in a process called geminate recombination (from *geminate*, meaning twin or born together). Another concern is orientational randomness. Photoexcitation typically creates a distribution of reactants that is partially aligned. Large molecules, such as proteins (qv), take a few nanoseconds to become rotationally randomized. Finally, at times of a few picoseconds in typical liquids and longer in special cases, thermal equilibration cannot be assumed even just among vibrational degrees of freedom.

Time-domain kinetic measurements in the picosecond and femtosecond regimes rely mainly on mode-locked lasers. Whereas other pulsed lasers generate microsecond or nanosecond pulses by, in some sense, turning the lasing action on and off, mode-locked lasers depend on a more subtle phenomenon. They use constructive and destructive interference of a superposition of light waves to produce short spikes of light, which repeat at intervals to produce a train of pulses that are typically spaced ~10 ns apart. Each individual pulse has a duration ranging from 50 ps down to 10 fs, depending on the lasing medium and details of the construction of the laser. The pulse train may be used directly, or some of the "picopulses" can be extracted and amplified to larger energies. Pulses of 1-mJ energy are routinely available at l-kHz repetition rates. The shortest pulses and highest average powers became possible with the development of a new types of solid-state lasers, particularly the titanium–sapphire laser.

Femtosecond lasers provide very short photolysis pulses. Detecting femtosecond or picosecond transients, however, is a challenge that can be met only with measurement strategies different from those used at longer times. Even the fastest electronic amplifiers, digitizers, and oscilloscopes are inadequate. One option is electronic streak cameras, the fastest of which provide time resolution from ~1 ps to many ns for both luminescent emission and vis or uv absorption. More commonly, a stroboscopic strategy is adopted. Short laser flashes are used not only to initiate the reaction, but also to probe concentrations at subsequent times. This is a sampling method, usually measuring one time delay per photolysis pulse. In compensation, it is often possible to measure a broad spectrum of wavelengths for each excitation cycle. The time delay between excitation and probe is determined by changing the position of mirrors to introduce a variable delay into the optical path, with the probe pulse following a longer path than the photolysis pulse. Since the reciprocal of the speed of light is ~3.3 ps/mm, micrometer adjustments readily give subpicosecond time delays, while a meter of delay extends measurements well into the nanosecond regime. Almost always the probe pulse is generated by extracting a fraction of the excitation pulse and, if necessary, using nonlinear optical processes to shift the wavelength (see NONLINEAR OPTICAL MATERIALS). The optical detection and electronic digitization

simply respond to the total light in the probe pulse and have nothing directly to do with timing or time resolution.

6. Other Measurement Strategies

6.1. Combined Methods for Unstable Reagents. Combinations of the above procedures are useful for the study of unstable compounds. Double stopped-flow is easily accomplished. Two reagents are mixed in a stopped-flow apparatus and allowed to incubate for some time, eg, 1 s, to produce the reactive but unstable reagent of interest. Then the mixture is combined in the measurement cell with the contents of a third syringe to initiate a reaction, which is studied in the usual way. Similarly, components may be combined using stopped-flow and the resulting mixture investigated by a *T*-jump timed to occur soon after mixing is complete. Flash photolysis could be done in the same manner; but since flash photolysis lends itself to signal averaging at high repetition rates and is often used for submillisecond measurements, a continuous flow mixer with a flash photolysis cell located downstream at the appropriate time delay works very well.

6.2. Frequency Domain Measurements. It is possible to measure the absorption of electromagnetic radiation as a function of frequency (or wavelength) and interpret the line shape to yield kinetic information. Until recently this was the only method available for picosecond and subpicosecond time scales, which could be extracted from line widths of visible and ir spectra. For gases, linewidths increase at higher pressures due to collision broadening. For isolated molecules, linewidths may be determined by predissociation, internal rearrangements, electron transfer, etc. More subtle effects occur in liquids. Slower processes are often measured by lineshape analysis in Mossbauer spectroscopy or by magnetic resonance. It is very common to use nmr to measure exchange rates, which are the inverse of the mean lifetime of some species before it is changed by some kinetic process, such as association or dissociation of an atom like H or a small ligand like H_2O. Such linewidths are now actually measured in the time domain using pulse sequences, thus confirming the time-frequency duality (see MAGNETIC SPIN RESONANCE).

To reinforce the connection with time-domain studies, linewidth studies can be understood as monitoring the spontaneous fluctuations in concentrations that occur when a chemical system is at equilibrium

$$AB + C \rightleftharpoons AC + B \tag{15}$$

All the concentrations, such as [AB], constantly experiences tiny fluctuations, the duration of which can determine line widths.

6.3. Measurements on One or a Few Molecules. It is possible to adopt the traditional kinetic viewpoint and measure the time course of the spontaneous fluctuations in equation 15 directly by monitoring time-varying concentrations in an extremely small sample (7). Such spontaneous fluctuations obey the same kinetics of return to equilibrium that describe a macroscopic perturbation. The relative amplitude of a fluctuation is inversely proportional to square

root of the number of entities being observed. Consequently, fluctuation analysis is important when concentrations are low and volumes tiny.

The ultimate in fluctuation analysis has now been achieved with the advent of methods that watch the behavior over time of single molecules. What is of most interest is not reproducing what can be learned more easily by studying ensembles of reactants but rather what is new when kinetics are carried out at the single molecule level. This topic has been addressed in a theoretical paper that also includes citations of a number of interesting experimental studies (8).

Even without resolving single molecules, there has been a revolution in applying optical microscopy to kinetic studies of processes within single biological cells or other nano-systems. Key to success is the design and synthesis of appropriate reagents. One powerful strategy utilizes a chemical precursor that can be infused into a cell, where it localizes to specific intracellular sites, but remains inert until a sudden flash of light modifies it to an active form. The kinetics of subsequent behavior can then be followed by traditional methods, usually fluorescence, or even by recording and analyzing a motion picture of structural changes.

Just as molecular structure determinations relying on physical methods were preceded by structure proofs based on chemical reasoning, the rapid *in situ* concentration measurements emphasized above supplanted an earlier tradition in some fields that relied on a more chemical strategy of measuring concentrations of reactants or intermediates by intercepting them with scavengers that react quickly to form stable products, which could be quantified later. Such methods remain useful because they can be designed to provide selective trapping and stabilization of important intermediates that are otherwise difficult to detect and identify.

7. Experimental Variation of Chemical Rates with Temperature and Pressure

The rates of chemical reactions vary with thermodynamic conditions such as temperature and pressure. This is accounted for by defining rate constants that depend on temperature and pressure. The temperature variation is often well described by the Arrhenius equation, at least over modest temperature ranges:

$$k_c = \mathrm{A}(T)\ \exp\left(-E_a/RT\right) \tag{16}$$

The preexponential factor A(T), has units of inverse seconds multiplied by reciprocals of concentrations as appropriate for the reaction order. It may have a weak dependence on temperature (some theoretical models predict a variation with $T^{1/2}$); but such variation is frequently ignored over limited temperature ranges and A is taken as constant. The parameter E_a is termed the activation energy and commonly ranges up to a few hundred kJ/mol, comparable to the energies of chemical bonds. The universal gas constant R must have appropriate units: for E_a in kilojoules/mole, R is 0.008314 kJ/mol · K. The temperature, T, is in kelvin. The crude, but oft-quoted, estimate that a 10°C increase in

temperature doubles a reaction rate is approximately correct near room temperature when E_a is ~54 kJ/mol (13 kcal/mol). With A assumed constant, the activation energy is determined from a plot of

$$d(\ln\,(k_c))/dT = -E_a/RT \tag{17}$$

The activation energy, E_a is almost always positive or zero, because increased temperatures almost always increase the rates of reactions, although there are rare exceptions.

Dependence of k_c on pressure, rarely measured until the 1980s, is now considered an important part of a comprehensive kinetic study. Gas-phase reactions, of course, depend strongly on pressure through the dependence of concentrations on the partial pressures of reagents. The variation of k_c with pressure is a different and much smaller effect. A factor of two change in rates for common liquid solutions might require an external pressure of as much as 100 MPa ($\approx$1000 atm). General procedures and precautions for working at high pressures apply to kinetic studies (See HIGH PRESSURE TECHNOLOGY). Almost all of the important kinetic methods, including stopped-flow mixing, T-jump, flash photolysis, and nmr methods, have been adapted for use at high pressures (9). The dependence on pressure is characterized by an activation volume V_a, defined by the relation

$$d(\ln\,(k_c))/dp = -V_a/RT \tag{18}$$

Activation volumes may be either positive or negative, corresponding to the fact that reactions may become either slower or faster at high pressures.

The failure of equation 17 or 18 to describe experimental data is most likely due to one of two circumstances: (*1*) There may be two entirely different reaction pathways, one of which has a small E_a and dominates at low T and the other of which has a larger E_a and dominates at high T. (*2*) The reaction pathway assumed may involve two or more sequential subsidiary reactions, each of which has its own E_a. This matter is explored in the next section.

8. Microscopic Models Used in Kinetic Studies

8.1. Reaction Schemes and Mechanisms. The macroscopic rate equations discussed above in most cases fall far short of describing what happens in a chemical reaction at the atomic level. In much of the older literature, any description that purported to give insight into the microscopic steps underlying some overall reaction was termed a mechanism. However, it has become common now (~2003) to distinguish a reaction scheme from a detailed mechanism. The reaction scheme is a set of chemical equations that identify any intermediate species that form and disappear in the course of the reaction as well the identities and numbers of the molecules that react in each step. In particular, a reaction scheme is sufficient to predict the macroscopic rate law of the reaction. It predicts the order with respect to each reagent and it identifies activation parameters that can be analyzed consistently and understood. The deduction is valid only in one direction, from reaction scheme to rate law, since an unlimited number

of different schemes are consistent with any measured rate law. A kinetic study, therefore, postulates a scheme, derives the rate law, and attempts to demonstrate that the rate law is sufficient to explain experimental data over some range of conditions. New data may be discovered later that prove inconsistent with the assumed rate law and require that a new scheme be postulated. Mechanisms for a reaction typically go a few steps further in providing a microscopic model of a reaction. A mechanism would not just assert that a large molecule reacts with an atom in one step of the reaction scheme, but would add the information that the atom reacts at a certain site in the large molecule and it would provide a rationalization for such site reactivity in terms thought to be applicable to a large number of related reactions. There are some general ideas used in mechanisms, such as an emphasis on regions of local excess or deficiency of electron density in a molecule, but the elaboration of mechanisms is more a matter to be developed by particular branches of chemistry, with at least somewhat different emphases in different branches, than a matter of general kinetic understanding. Evidence for a particular, detailed mechanism is not usually available solely from a single kinetic study, rather the ideas are postulated to help understand whole families of reactions whose kinetics have been previously elaborated.

Consider the following overall equation

$$\mathrm{A} + \mathrm{B} + \mathrm{C} \rightarrow \mathrm{P} \tag{19}$$

for which the following two-step reaction scheme might be postulated

$$\mathrm{A} + \mathrm{B} \underset{k_r}{\overset{k_f}{\rightleftharpoons}} \mathrm{I} \tag{20}$$

$$\mathrm{I} + \mathrm{C} \xrightarrow{k_2} \mathrm{P} \tag{21}$$

In this case, the single arrow is meant to specify that equilibrium lies far to the right. A source of confusion is that the steps of a reaction scheme and stoichiometric relations appear the same when written as equations, despite the very different connotations. A complete reaction scheme implies a set of differential equations. Assuming well-stirred conditions, the above pair of equations predicts, among other things

$$d[\mathrm{A}]/dt = -k_f[\mathrm{A}][\mathrm{B}] + k_r[\mathrm{I}] \tag{22}$$

$$d[\mathrm{P}]/dt = k_2[\mathrm{I}][\mathrm{C}] \tag{23}$$

Much of the language used for empirical rate laws can be applied to the differential equations associated with each step of a mechanism. For example, equation 20 in the forward direction is first order in A, and in B and second-order overall. The reverse reaction is first order in I. Additional language is used for these schemes and mechanisms that should never be applied to empirical rate laws. Equation 20 is said to describe a bimolecular mechanism or a bimolecular reaction in the forward direction and a unimolecular reaction in the reverse direction. A mechanism may be bimolecular in one component, eg,

$2A \rightarrow I$ or in two components, eg, $A + B \rightarrow I$. A bimolecular mechanism implies a second order differential equation; however, a second order empirical rate law does not necessarily guarantee a bimolecular mechanism, because the overall rate law by itself does not tell us whether the underlying reaction scheme involves just a single step or a whole set of steps.

The solution of the simultaneous differential equations implied by the reaction scheme can always be expressed to give the time varying concentrations of reactants, products, and intermediates in terms of increasing and decreasing exponential functions (10). Expressions for each component become complicated very rapidly, but may be treated by matrix methods. Fortunately, in practical cases, approximations may often be made in solving the differential equations. In equations 20 and 21, the first reaction may reach equilibrium for [I] much more rapidly than I is converted to P. This is described as a case of preequilibrium. At equilibrium, $k_f[A][B] = k_r[I]$. Hence,

$$[I] = K[A][B] \tag{24}$$

where $K = k_f/k_r$, and

$$d[P]/dt = k_2K[A][B][C] \tag{25}$$

Empirical tests of this discover the reaction order with respect to each component and verify the molecularities assumed. They also measure a value for an observed rate constant for the formation of P, namely, $k_{obs} = k_2K$, but are unable to separate the factors k_2K or measure k_f and k_r as long as the assumption of prequilibrium remains valid. Improved time resolution in the experiment captures the initial stage of the reaction during which [I] approaches equilibrium and, consequently, violates that assumption of preequilibrium and permits the determination of all the kinetic parameters.

A second common approximation is the steady state condition. This arises in mechanism 20 and 21 if k_2 is fast compared with k_f, in which case [I] remains very small at all times. If [I] is small, then $d[I]/dt$ is approximately zero at all times, and this condition is commonly invoked as a mnemonic in deriving the differential rate equations. It cannot be literally correct, or no product could ever form. The necessary condition is actually somewhat weaker. For equations 20 and 21, the steady-state approximation leads, despite its different justification, to the same differential equations as the pre-equilibrium condition, namely, equations 24 and 25.

8.2. Michaelis-Menten Equation. Studies of enzyme-catalyzed reactions in biochemistry, molecular biology, and physiology, frequently invoke the Michaelis-Menten equation to describe the following model reaction scheme:

$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} I \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} E + P \tag{26}$$

where E is the enzyme catalyst that is typically a large protein molecule that remains unchanged after a full reaction cycle S is the substrate that is typically a smaller reactant molecule that is modified, P is the product derived from S

and I is the intermediate that is some complex between the enzyme and the substrate. The governing differential equation for [I] in equation 26 is

$$\frac{d[\mathrm{I}]}{dt} = k_1[\mathrm{E}][\mathrm{S}] - (k_{-1} + k_2)[\mathrm{I}] + k_{-2}[\mathrm{E}][\mathrm{P}] \tag{27}$$

By definition, a catalyst must facilitate any reaction in both directions, so k_{-2} must be nonzero.

However, k_{-2} is usually small. Furthermore, [P] is also usually small, even in nature and surely in the laboratory, where measurements can be made soon after adding S, before P accumulates. Consequently, the last term in equation 27 is normally neglected. As a further simplification, one usually assumes that for measurements of the initial reaction velocity, after a short induction period but before any reagents are depleted, a steady-state approximation may be invoked for I.

In that case,

$$[\mathrm{I}] = \left(\frac{k_1}{k_{-1} + k_2}\right)[\mathrm{E}][\mathrm{S}] \tag{28}$$

The enzyme catalyst can be assumed to be present in much smaller concentration than the substrate, so that $[\mathrm{E}] \ll [\mathrm{S}]$ and $[\mathrm{I}] \ll [\mathrm{S}]$. However, a large portion of E may be complexed as [I] and that fraction is unknown. Hence, the focus is placed on the quantity that the investigator can control by mixing reagents, namely, the total enzyme present, $[\mathrm{E}]_T = [\mathrm{E}] + [\mathrm{I}]$. In that case, equation 28 becomes

$$[\mathrm{I}] = \frac{k_1[\mathrm{S}][\mathrm{E}]_T}{k_1[\mathrm{S}] + k_{-1} + k_2} \tag{29}$$

The initial velocity v_0 for disappearance of substrate and formation of product is

$$v_0 = -\frac{d[\mathrm{S}]}{dt} = +\frac{d[\mathrm{P}]}{dt} = k_2[\mathrm{I}] = \frac{k_1 k_2[\mathrm{S}][\mathrm{E}]_T}{k_1[\mathrm{S}] + k_{-1} + k_2} \tag{30}$$

This equation is rearranged to

$$v_0 = \frac{k_2[\mathrm{E}]_T}{1 + \frac{k_{-1}+k_2}{k_1[\mathrm{S}]}} \tag{31}$$

and by defining $v_s = k_2[\mathrm{E}]_T$ and $K_\mathrm{M} = (k_{-1} + k_2) / k_1$, the Michaelis-Menten equation results

$$v_0 = \frac{v_s}{1 + K_\mathrm{M}/[\mathrm{S}]} \tag{32}$$

At high [S], when the system is saturated with substrate and the turnover rate to produce P reaches a maximum for a given amount of enzyme $[\mathrm{E}]_T$, then

the velocity is asymptotically equal to v_s. The rate constant k_2 is known as the turnover number as it determines the rate at which product is produced when the enzyme is operating at maximum efficiency with an unlimited supply of substrate. The Michaelis constant, K_M is equal to the concentration of S at which the reaction velocity reaches half its maximum value, v_s. Taking the reciprocals of both sides of equation 32 yields the Lineweaver-Burk equation:

$$\frac{1}{v_0} = \frac{1}{v_s} + \frac{K_m}{v_s[\mathrm{S}]} \tag{33}$$

Thus a double reciprocal plot of $1/v_o$ versus 1/[S] yields a straight line offering accurate values of the desired parameters, with y intercept $= 1/v_s$, x intercept $= -1/K_m$, and slope $= K_m/v_s$.

8.3. Interpreting Activation Parameters. Once an overall reaction and its k_{obs} have been successfully interpreted by a reaction scheme that elucidates all the steps involved and explains how rates depend on concentrations and the underlying rate constants have been extracted, then the activation parameters obtained from the temperature or pressure dependence are also given microscopic interpretations. Activation parameters should be associated only with elementary steps of a mechanism and not with overall empirical rate laws that involve two or more elementary steps. At the simplest level, a large E_a is interpreted by postulating a large potential barrier between reactants and products that must be overcome by kinetic energy available in the reactants, which increases at higher temperatures. Similarly, a positive V_a is interpreted by postulating that the reactants pass through some configuration that has a larger volume on their way to forming products. Increasing the pressure makes it more difficult to effect that expansion against the surrounding medium.

At more advanced levels of analysis, detailed atomic models are developed that define microscopic concepts that predict activation parameters. The simplest such model applied to bimolecular reactions of single atoms in low density gases predicts that the rate constant should be equal to the number of collisions multiplied by a probability that the translational kinetic energy due to the relative velocity difference between particles is greater than some threshold value, E^*. For the collision of two different atoms, A and B, this reproduces the result of the Arrhenius empirical law according to the following equation

$$k = \pi d^2 \left(\frac{8k_{\mathrm{B}}T}{\pi\mu}\right)^{1/2} e^{-E^*/k_{\mathrm{B}}T} \tag{34}$$

where d is the sum of the radii of A and B, k_{B} is the Boltzmann constant, and μ is the reduced mass of A and B. For multiatom molecules, the same equation can often be useful in providing insight, but the activation energy involves internal degrees of freedom as well as the relative velocity of reactants. A variety of other models exist that are grounded in statistical models rather than the kinetics of particles. These include activated complex theory, transition state theory, and so on. Probably the most successful and comprehensive of these statistical theories that do not include full, rigorous, quantum theoretical treatments (which are

impossible for most cases today) is RRKM theory, named for its originators, Rice, Ramsperger, Kassel, and Marcus. Note an important point in all these: the activation energy barriers and volumes are assigned to transition states, which are quite different from intermediates. The latter are real chemical species with a finite, albeit possibly short, lifetime, while the former have only the most fleeting existence at some set of atomic positions. With the development of femtosecond laser measurements, kineticists are being challenged to measure and characterize not only extremely short-lived intermediates, but even to measure some features of transition states more or less directly.

8.4. Reaction Dynamics. Mechanism is to chemical change as structure is to chemical identity. Throughout most of the twentieth century the goal of structural chemistry was to specify accurate spatial coordinates for all the atoms in a molecule or crystal. In contrast, the mechanisms that were the goal of kinetic studies were much less detailed. At the beginning of the twenty-first century there is progress toward a detailed atomic level description of simple chemical reactions. This is such a profound advance that practitioners do not describe what they do as kinetics. Instead they prefer the term reaction dynamics (11). In a crude sense, the goal is to specify atomic positions as a function of time, but the treatment is grounded in quantum mechanics, which places limits on such a classical description. Early progress was recognized with the award of the 1986 Nobel Prize to Dudley Herschbach and Yuan Lee of the United States and John Polanyi of Canada. More recent advances earned a Nobel award for Ahmed Zewail of the United States, originally from Egypt. For the simplest cases, such as the reaction of a small diatomic, eg, dihydrogen, with a single atom, eg, deuterium, there is now a detailed quantum mechanical treatment that calculates the entire potential energy surface by *ab initio* methods so that it is possible to characterize the initial and final states and everything in between to essentially any desired precision consistent with quantum uncertainty. For reactions involving somewhat larger molecules, including unusual compounds such as OOH, and for somewhat larger atoms such as Cl, calculating the entire *ab initio* potential energy surface for all atomic positions of all atoms in both reactants in reasonable time and at reasonable cost remains beyond the capability of current supercomputers. However, at this writing ($\sim$2003) direct dynamic calculations are making progress by calculating only the critical portions of potential surfaces along reaction paths that are deduced from more limited calculations (12). Since calculations do not rigorously consider all of parameter space, they do not prove with certainty that the minimum energy pathways have been found, and the path that is calculated is treated only to some level of approximation. However, the calculations are *ab initio* and will only improve as computers become faster and algorithms are refined. One reason for pursuing rigorous theoretical calculations is to obtain reliable rate constants for reactions that involve unusual molecules under conditions, eg, temperatures, that may be difficult to measure in the laboratory, including some of the processes that occur in atmospheric modeling.

Detailed reaction dynamic calculations require not only that reagents be fairly simple molecules but also that they be largely isolated from external perturbations that cannot yet be modeled accurately. Experiments designed to meet this objective employ one of three strategies. (*1*) Molecules in a gas at

low pressures may be taken to be isolated for the short time between collisions. In particular, unimolecular reactions such as photodissociation or isomerization induced by photon absorption can sometimes be studied between collisions. (*2*) Molecular beams can be produced so that motion is not random. Molecules have a fairly high velocity in one direction but almost zero velocity in perpendicular directions. Not only do beams reduce collisions, but by using two intersecting beams one may study bimolecular reactions with considerable control over initial conditions. Beams facilitate dozens of refined measurement techniques involving mass spectrometry and selective ionization. (*3*) It is possible to trap atoms or molecules in space using light beams, isolate them, and keep them almost motionless in space. Initial efforts have been directed toward manipulating the trapped particles and studying reactions with electromagnetic fields, but the future is bright for eventually exploiting the isolated molecules for dynamic studies.

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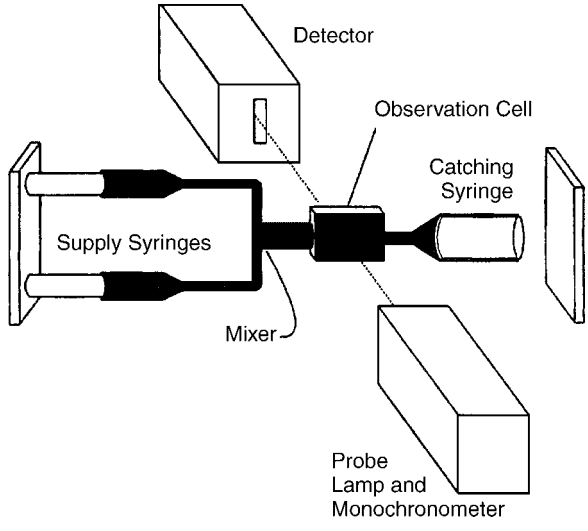

Fig. 1. Schematic of apparatus for stopped-flow measurements.

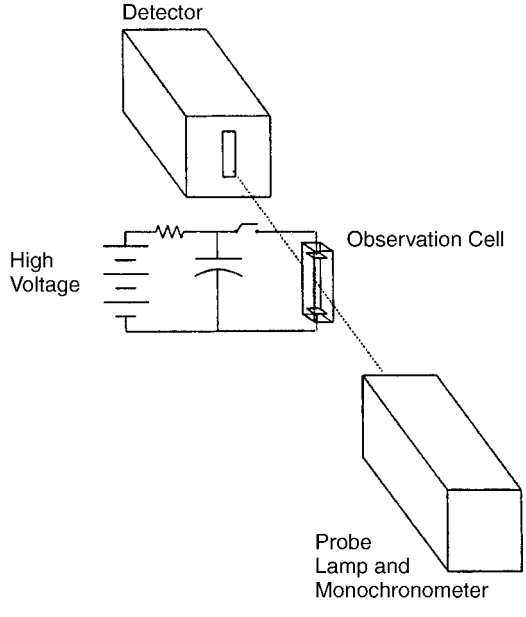

Fig. 2. Schematic of apparatus for temperature-jump (T-jump) measurements.

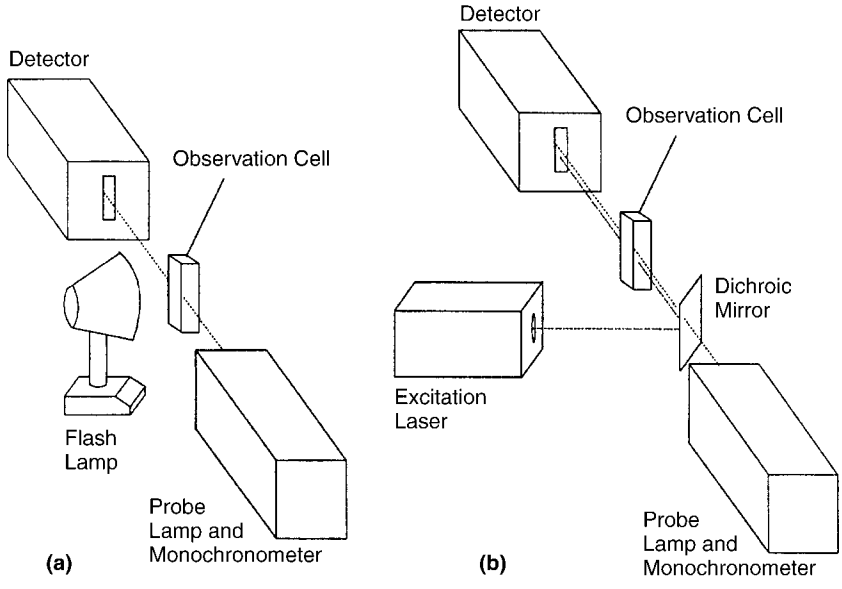

Fig. 3. Schematic of apparatuses for flash photolysis. (**a**) A simple instrument, and (**b**) a more sophisticated one using longitudinal excitation by a laser.