

Techniques and Applications of Fast Reactions in Solution

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Techniques and Applications of Fast Reactions in Solution

THE STUDY OF FAST REACTIONS IN SOLUTION

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1. Introduction.
2. Methods and techniques.
3. Characteristics of some fast-reaction techniques.
4. The choice of method and technique.
5. Fields of application.

1. INTRODUCTION

The study of reaction kinetics is our main way of investigating reaction mechanisms and the energetics of the actual path. Its data are measurements on the kinetic effects of systematically varying the concentration, temperature, pressure, solvent, and (where possible) the substituents and isotopic composition of the reactants. Accurate determinations of rate constants are therefore fundamental. Many familiar reactions, however, are too fast to be followed by conventional means, such as mixing the reactant solutions by hand and following the reaction by an ordinary spectrophotometer. Such reactions used to be written off as 'instantaneous' and their kinetics could not be investigated. This was unfortunate, since fast reactions (i.e. those with half-lives less than a few seconds) have widely varying rate constants, distributed over a range covering as many powers of ten as the range of conventional rates. The development of special methods has now made possible the study of even the fastest reactions.

Fast reactions in solution are the subject of a number of books (1-11) and innumerable papers. The early experiments of Hartridge and Roughton which laid the foundation for modern flow

methods were published in 1923 (12), and up to 1940 it was mainly flow methods that were developed (13), apart from some work on fluorescence quenching and photochemical methods, and on the use of low temperatures. When the Faraday Society held a discussion on fast reactions (14) in 1954, however, not only had the stopped-flow technique reached essentially its present form but relaxation methods, flash photolysis, and the use of n.m.r. and e.s.r. had been developed. A conference in Germany in 1959 (15) showed that all these methods were in full and systematic use. In 1967 the fifth Nobel Symposium (3) was devoted to fast reactions, and the Nobel Prize for chemistry was awarded to Professors Eigen, Norrish and Porter jointly for their pioneer work on the newer methods. From being the concern largely of biochemists and a few physical chemists, fast-reaction techniques have become major tools for the mechanistic investigation of organic and inorganic reactions, and have begun to generate chemical information of new types. From being difficult techniques requiring special experimental skill, some of them have developed into almost routine methods, not much more difficult to learn than conventional spectrophotometry.

In this introductory lecture we consider the use of fast-reaction methods in the measurement of the effects on reaction rates of variations in the concentration, temperature, pressure, and solvent, as required for the purposes of reaction kinetics. The aim is to show the characteristic virtues and defects of the various methods and techniques, so that an informed choice may be made for a given investigation.

2. METHODS AND TECHNIQUES

Four Basic Methods

In conventional methods, where the reactant solutions are mixed by shaking together and the progress of the reaction is subsequently followed by chemical or physical means, the time for mixing is short compared with the much longer time required for observing the course of the reaction. For fast reactions, ordinary mixing methods are too slow. There are various ways of overcoming the difficulty; they may be classified according to four basic principles which lead to four possible types of procedure, as follows.

1. Bring the rate down to the conventional range, by the use of low concentrations, or low temperatures.
2. Mix the solutions rapidly, by flow methods, as in the continuous-flow and stopped-flow methods.
3. Disturb a system at equilibrium, and follow the subsequent chemical change. There are two variants:-

3(a) Flash photolysis and pulse radiolysis produce large changes, e.g. formation of excited states or free radicals.

3(b) Small perturbations are brought about by the temperature-jump and other 'relaxation' methods; the rate of the shift of a chemical equilibrium to its new position is observed.

4. Make the reaction compete with some other fast process. In fluorescence quenching, for example, the reaction between the fluorescent molecule and some added reagent competes with the fluorescence of the molecule, which takes about 10^{-8} seconds. In nuclear magnetic resonance and electron-spin resonance methods, the reaction competes with spin relaxation. In the various electrochemical methods, reaction competes with diffusion towards an electrode.

Some representative techniques based on these four basic principles are summarised in Table 1. For descriptions of these and other techniques the reader should consult references 1-11. We now consider their applicability to the objectives of chemical kinetics, and their advantages and limitations from various points of view. The kineticist's concern is to select the technique which best suits his problem, as defined by the nature of the reactants, the solvent, temperature, rate constant, etc.

3. CHARACTERISTICS OF SOME FAST REACTION TECHNIQUES

(a) What is the maximum rate constant that can be measured?

Most of the methods, if pushed, allow the determination of second-order rate constants approaching $10^{10} \text{ M}^{-1} \text{ s}^{-1}$, which is about the diffusion-controlled limit in ordinary solvents. Such high rate constants are relatively easy to determine by temperature-jump, electric-field jump, ultrasonic absorption, dielectric absorption, flash, fluorescence-quenching, and e.s.r. methods. The stopped-flow method is not commonly used to determine rate constants above about $10^5 \text{ M}^{-1} \text{ s}^{-1}$.

(b) What concentration range can be used? With most methods there is no problem. Fluorescence quenching and e.s.r. methods allow the use of exceptionally low concentrations. Relatively high concentrations are needed for n.m.r. and ultrasonics measurements as commonly practised.

(c) Can the temperature be varied, and can low temperatures be used? Temperature-control over a range sufficient for the determination of activation parameters presents no problem with most of the techniques; it is of course less precise where it is done by circulation of fluid rather than by immersion in a bath. Low-temperature work (to -100°C or below) is not difficult for n.m.r., e.s.r., fluorescence quenching, and stopped-flow measurements.

Method	Time resolution, sec	Comments
1. Reduce rate to conventional.		
Low concentrations	-	Accurate estimation needed.
Low temperatures	-	Non-aqueous solvent needed
2. Rapid mixing by flow.		
Continuous flow	10^{-3}	Large volume needed.
Stopped flow	10^{-3}	Any solvent; versatile.
3. Disturb equilibrium.		
Flash photolysis	$<10^{-8}$	(Any solvent.
Pulse radiolysis	$<10^{-8}$	(Free radicals.
Photostationary methods	10^{-2}	(Excited states.
Temperature-jump, etc	$<10^{-5}$	Versatile. Equilibrium needed.
Ultrasonic absorption	10^{-9}	Solvent restricted.
5. Competition with fast process.		
Fluorescence quenching	10^{-8}	Reagents restricted.
Electrochemical methods	10^{-4}	Ionising solvent, etc.
N.m.r. and e.s.r. methods	$<10^{-4}$	Inf. on particular atoms.

Table 1

Some Techniques for Fast Reactions in Solution

(d) Can high pressure be used? High-pressure forms of temperature-jump (16-19), pressure-jump (20), n.m.r. (21), and ultrasonic-absorption apparatus have been constructed. These can be pressurised to several kilobars. A stopped-flow apparatus working at pressures up to 1 kilobar has been constructed (22). Components for high-pressure work are available commercially, and these techniques seem likely to come into wider use (23).

(e) Can the solvent be varied? The choice of solvent is unrestricted for several of the techniques, including stopped-flow. Some techniques require an electrolyte solution, notably the commonest form of temperature-jump apparatus, which uses joule heating. With ultrasonic relaxation the solvent must be one which does not itself have a high absorption. With n.m.r. methods the signals due to the solvent must be considered; they may indeed be the important ones.

Characteristics of the most-used techniques. Some special benefits and restrictions of some of the most popular techniques are as follows (see Table 2). The use of low concentrations or low temperatures avoids expense but requires some time and ingenuity. The stopped-flow method is very adaptable to a variety of reactions (whether or not they go to completion; whether or not the product is stable; whether or not they involve ions or radicals) and to a range of solvents, detection methods, and temperatures; commercial apparatus is available relatively cheaply; but the fastest reactions are not accessible. The temperature-jump method is suitable for a wide variety of reactions in aqueous solution, and can handle very fast reactions; small volumes of solutions are enough, since the reactant solution is not lost but reverts to its original state; and commercial apparatus is available, which gives good results with aqueous solutions, though not with non-electrolyte or non-aqueous solutions, which require specially built laser or microwave apparatus (24). Flash-photolysis machines are commercially available and are especially useful for the study of excited states and of radical reactions; the reaction must of course be capable of photochemical initiation. Fluorescence quenching is perhaps the easiest method of studying very fast (diffusion-controlled) reactions, in any solvent, down to low temperatures; the main limitation is that one at least of the molecules taking part in the reaction must be fluorescent. The n.m.r. line-broadening technique can be used with good commercial apparatus, and gives uniquely detailed information, especially about the participation of the solvent (25); low temperatures are easily obtained; but the concentrations normally required are relatively high.

Principle	Method	Method requires:			Method permits:				Apparatus can be bought
		Fast mixing	Fast obsn	Equilm.	Small volume	Low temp	High pressure	Very fast reactions	
1	Low concentrations					*			
	Low temperatures					*			
2	Stopped flow	*	*			*	*		*
3	T-jump		*	*	*	*	*	*	*
	P-jump		*	*	*	*	*		*
	Ultrasonics			*	*	*	*	*	*
	Flash		*		*	*		*	*
	Pulse radiolysis		*			*		*	
4	Fluorescence				*	*		*	*
	Electrochemical			*				*	
	N.m.r.			*	*	*	*	*	*

* Those with second-order rate constants approaching $10^{10} \text{ M}^{-1} \text{ s}^{-1}$.

Table 2

Characteristics of Some Fast-Reaction Techniques

3. THE CHOICE OF METHOD AND TECHNIQUE

The experimental kineticist's choice between various courses of action, when confronted with a particular kinetic problem, will depend on several factors. He will first choose a method that seems appropriate to the nature of the reaction, - according to whether it involves ions, or free radicals, for example; whether it goes to completion or to a balanced equilibrium; whether the product is stable or not - bearing in mind the expected rate of the reaction. He will then choose one of the particular techniques, depending on such factors as the type of solvent (ionising, polar, non-polar), the possible ways of monitoring the reaction (spectrophotometric, conductimetric, etc), the expected rate of the reaction, and whether variation of concentration and temperature will suffice or whether variation of solvent or pressure is also desirable. The scheme in Table 3 (which is not exhaustive) may serve to summarise some of the points that have to be considered.

Considerations of cost and of workshop facilities are also important. Commercial instruments are well developed for stopped-flow, pressure-jump, temperature-jump (by joule heating), fluorescence, flash photolysis, pulse radiolysis, n.m.r. and e.s.r. Apparatus can also be built for most of these, given the necessary man-hours and workshops.

The techniques that appear to be most popular at present among kineticists in general are stopped-flow, temperature-jump, flash photolysis, and n.m.r. The stopped-flow apparatus is the most generally useful for times down to a few milliseconds, and spectrophotometric detection allows the use of concentrations down to about $10^{-5}M$ or below; several hundred such machines are now in existence. Temperature-jump and flash-photolysis apparatus extend the time-range down to microseconds or below; the former is used when a well-characterised equilibrium is to be studied, the latter when free radicals or excited states are to be generated. N.m.r. methods give more detailed information than others, for instance on the role of hydroxylic solvents in proton-transfer reactions (25).

5. FIELDS OF APPLICATION

The widespread use of fast-reaction methods has opened up the study of new types of reaction and new chemical species, and has raised new questions about physical aspects of mechanisms. Examples of types of reaction which could not be studied without fast-reaction techniques include the following: among reactions of labile metal ions, ligand substitution, solvent exchange, and electron-transfer; among organic reactions, many proton-transfer

Reactants	Is an equilm. set up?	Methods available	Techniques available
Molecules or ions	no	Flow	(Stopped-flow (Continuous flow
	yes	Relaxation Single pulse Periodic disturbance	(T-jump: Joule heating; (laser; microwave (P-jump: E-jump. (Ultrasonic absorption: (Pulse; resonance etc.
Free radicals or excited states		Above methods plus:-	
		Flash photolysis	(Flashlamp (Laser
		Pulse radiolysis	(Accelerator (Radiation
		Photostationary methods	(Rotating sector etc.

Table 3Factors in the Choice of Method and Technique

reactions (26, 27), hydrogen bonding, radical reactions, and fast steps in polymerisation reactions; among reactions of biological importance, those of haemoglobin with oxygen, helix-coil transitions in macromolecules, and fast steps in enzyme reactions, photosynthesis and reactions in micelles. Among new chemical species studied by these methods are short-lived free radicals, excited states and the solvated electron. Examples will be found in this volume and in references 1-11. Among new questions about physical aspects of mechanisms are the role of hydroxylic solvents as bridge molecules in proton transfer²⁵, the question whether solvent motions accompany or precede or follow changes of bonding, and problems about diffusion effects which are important when the activation energy is small.

CONCLUSION

Fast-reaction methods have developed rapidly and continuously over the last 25 years and are still being improved. Their applications have likewise proliferated. They are indispensable in the study of the kinetics and mechanisms of the numerous reactions which, though not essentially different from more familiar reactions, are too fast for conventional methods. They permit investigation of the reactions of short-lived species - free radicals and excited states - which would otherwise be inaccessible. They throw light on physical phenomena such as diffusion control of very fast reactions, the role of the solvent, and solvation changes. They are valuable both in the more intensive study of familiar types of reaction and in the exploration of new ones such as helix-coil transitions and enzyme reactions, which are of great biological importance. They appeal alike to chemists who, being romantic by temperament, are attracted to novel or complex situations, and those whose more classical bent leads them to enquire more deeply into subjects where there is already a modicum of understanding. The kinetics and mechanisms of fast reactions do not constitute a subject; they form part of the general subject of kinetics and mechanisms, and cannot be isolated. The techniques and methods, however, do have sufficient unity to constitute a recognisable field, as has been shown by successive meetings of the Fast Reactions in Solution discussion group of the Chemical Society; there is a degree of common approach that encourages cooperation and emulation. This unity of approach, coupled with the diversity of chemical problems, is the reason and justification for a book such as the present one.

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