Femtochemistry. Past, present, and future*,†

Ahmed H. Zewail

Arthur Amos Noyes Laboratory of Chemical Physics, California Institute of Technology, Pasadena, CA 91125 USA

Abstract: This review highlights, with a historical perspective, the development of the field, with focus on the evolution since its birth in 1987, the scope of applications in present-time research, and some future developments in femtochemistry and the sibling field, femtobiology.

INTRODUCTION

The actual atomic motions involved in chemical reactions had never been observed in real time despite the rich history of chemistry over two millennia. Chemical bonds break, form, or geometrically change with awesome rapidity. Whether in isolation or in any other phase, this ultrafast transformation is a dynamic process involving the mechanical motion of electrons and atomic nuclei. The speed of atomic motion is ~1 km/second and, hence, to record atomic-scale dynamics over a distance of an angström, the average time required is ~100 femtoseconds (fs). The very act of such atomic motions as reactions unfold and pass through their transition states is the focus of the field of femtochemistry. With fs time resolution we can "freeze" structures far from equilibrium and prior to their vibrational and rotational motions, or reactivity.

In over a century of development, ultrafast pulsed-laser techniques have made direct exploration of this temporal realm a reality (see next section). Spectroscopy, mass spectrometry, and diffraction play the role of "ultra-high-speed photography" in the investigation of molecular processes. A femtosecond laser *probe* pulse provides the shutter speed for freezing nuclear motion with the necessary spatial resolution. The pulse probes the motion by stroboscopy, i.e., by pulsed illumination of the molecule in motion and recording the particular snapshot. A full sequence of the motion is achieved by using an accurately timed series of these probe pulses, defining the number of frames per second.

For molecules, there exist three additional requirements in order to study the motion. First, we need to *clock* the motion by defining its zero of time, also accurate to tens of femtoseconds. Second, the motion must be *synchronized* since millions of molecules are typically used in the recording of molecular motion. Third, molecular *coherence* (see below) must be induced to localize the nuclei. These requirements are satisfied by using a femtosecond *pump* (*initiating*) laser pulse, in what is referred to as a *pump-probe* configuration. For femtosecond studies, where femtosecond control of relative timing is needed, the laser pump and probe pulses are produced in synchrony, then the probe pulse is diverted through an adjustable optical path length. The finite speed of light translates the difference in path length into a difference in arrival time of the two pulses at the sample; 1 micron corresponds to 3.3 fs. The individual snapshots combine to produce a complete record of the continuous time evolution—a motion picture, or a movie—in what may be termed femtoscopy.

In femtochemistry, studies of physical, chemical, or biological changes are at the fundamental timescale of molecular vibrations: the actual nuclear motions (Fig. 1). The ephemeral transition states, denoted in the past by a bracket [TS]‡ for their elusiveness, can now be clocked as a molecular species

TS‡. Moreover, the fs timescale is unique for the creation of coherent molecular wave packets on the atomic scale of length, a basic problem rooted in the development of quantum mechanics and the duality of matter. Molecular wave functions are spatially diffuse and exhibit no motion. Superposition of a number of separate wave functions of appropriately chosen phases can produce the spatially localized and moving coherent wave packet. The packet has a well-defined (group) velocity and position which now makes it analogous to a moving classical marble, but at atomic resolution, and without violation of the uncertainty principle. As long as the wave packet (typical width ~0.05 Å) is sufficiently localized on the scale of all accessible space (~0.5 Å or more), a description in terms of the classical concepts of particle position and momentum is entirely appropriate. In this way, localization in time and in space are simultaneously achievable for reactive and nonreactive systems, as discussed below.

The observation of motion in real systems requires not only the formation of localized wave packets in each molecule, but also a small spread in position among wave packets formed in the typically millions of molecules on which the measurement is performed. The key to achieving this condition is generally provided by (a) the well-defined *initial*, equilibrium configuration of the studied molecules before excitation and (b) by the *"instantaneous"* femtosecond launching of the packet. The spatial confinement (in this case ~0.05 Å) of the initial ground state of the system ensures that all molecules, each with its own coherence among the states which form its wave packet, begin their motion in a bond-distance range much smaller than that executed by the motion. The femtosecond launching ensures that this narrow range of bond distance is maintained during the entire process of preparation, as discussed below. Unless molecular and ensemble coherences are destroyed by intra- and/or intermolecular perturbations, the motion is that of a *single-molecule trajectory*.
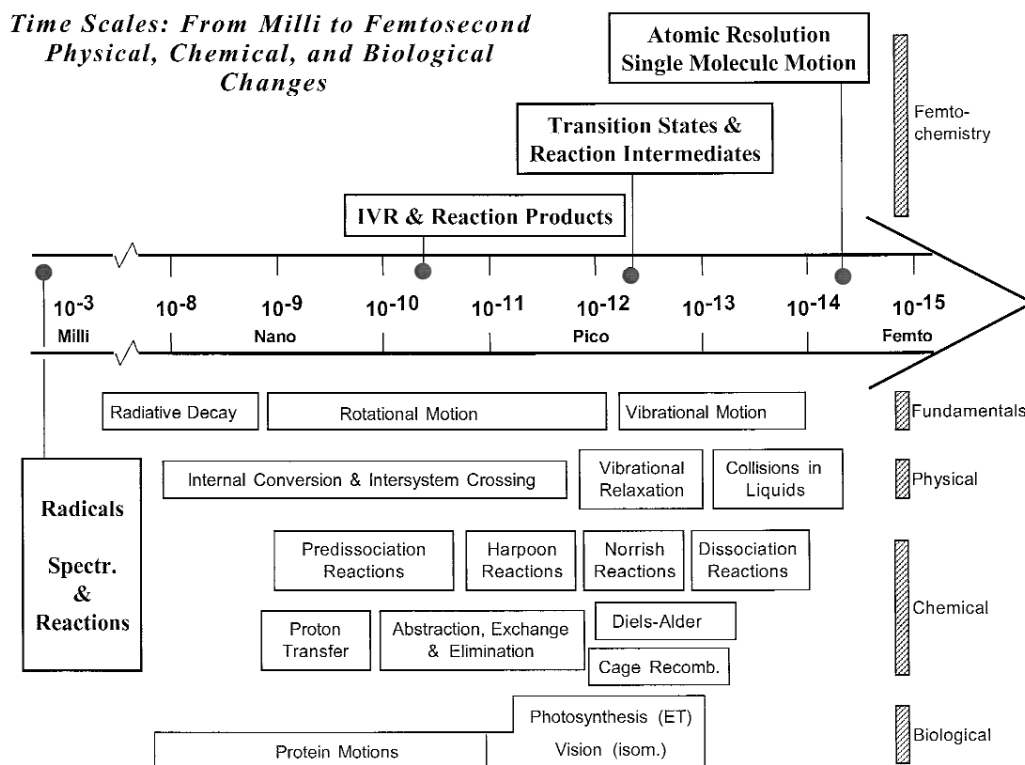

Fig. 1 Timescales. The relevance to physical, chemical, and biological changes. The fundamental limit of the vibrational motion defines the regime for femtochemistry. Examples are given for each change and scale.

This powerful concept of *coherence* lies at the core of femtochemistry and was a key advance in observing the dynamics. The realization of its importance and its detection by selectivity in both preparation and probing were essential in all studies, initially of states and orientations, and culminating in atomic motions in reactions. With these concepts in mind, the marriage of ultrafast lasers with molecular beams proved to be essential for the initial development. Laser-induced fluorescence was the first probe used, but later we invoked mass spectrometry and nonlinear optical techniques. Now, numerous methods of probing are known and used in laboratories around the world; Coulomb explosion is the most recent powerful probe developed by Will Castleman for arresting reactive intermediates.

Applications of femtochemistry have spanned the different types of chemical bonds—covalent, ionic, dative and metallic, and the weaker ones, hydrogen and van der Waals bonds. The studies have continued to address the varying complexity of molecular systems, from diatomics to proteins and DNA. Studies have also been made in the different phases of matter: gases and molecular beams; mesoscopic phases of clusters, nanostructures, particles, and droplets; condensed phases of dense fluids, liquids, solids, surfaces and interfaces; and in sibling fields of femtoscience such as femtobiology (Fig. 2).
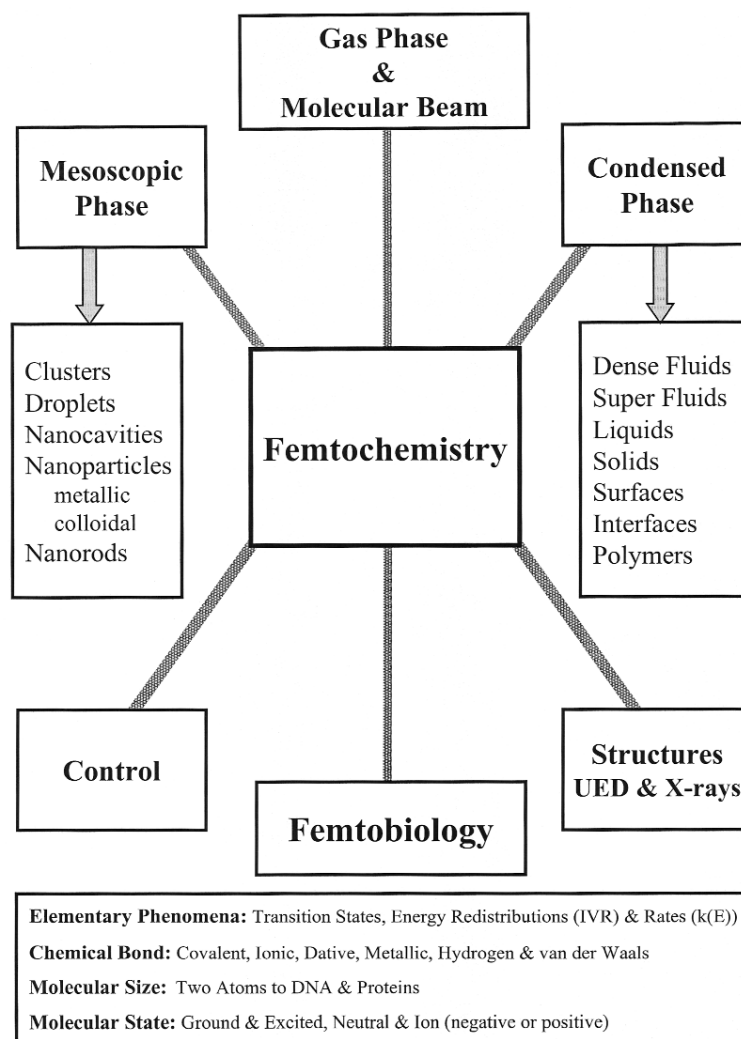

Fig. 2 Areas of study in femtochemistry.

ARROW OF TIME

In over a century of development, time resolution in chemistry and biology has witnessed major strides. The famous Arrhenius equation (1889) for the speed of a chemical reaction gave information about the timescale of rates, and Eyring and Michael Polanyi's (1931) microscopic theoretical description made chemists think of the atomic motions through the transition state and on the vibrational timescale. But the focus naturally had to be on what could be measured in those days, namely the slow rates of reactions. Systematic studies of reaction velocities were hardly undertaken before the middle of the 19th century; in 1850 Ludwig Wilhelmy reported the first quantitative rate measurement, the hydrolysis of a solution of sucrose to glucose and fructose. In 1901, the first Nobel Prize for chemistry was awarded to van't Hoff for, among other contributions, the theoretical expressions (chemical dynamics) which were precursors to the important work of Arrhenius on rates. Arrhenius, too, received the Nobel Prize in 1903 for his work on electrolytic theory of dissociation.

A major advance in experiments involving sub-second time resolution was made with flow tubes in 1923 by H. Hartridge and F. J. W. Roughton for solution reactions. Two reactants were mixed in a flow tube, and the reaction products were observed at different distances. Knowing the speed of the flow, one could translate this into time, on a scale of tens of milliseconds. Such measurements of non-radiative processes were a real advance in view of the fact that they were probing the "invisible", in contrast with radiative glows which were seen by the naked eye and measured using phosphoroscopes. Then came the stopped-flow method (B. Chance, 1940) that reached the millisecond scale. The stopped-flow method is still used today in biological kinetics.

Around 1950, a stride forward for time resolution in chemistry came about when Manfred Eigen in Germany and R. G. W. Norrish and George Porter in England developed techniques reaching the microsecond timescale. For this contribution, Eigen and Norrish & Porter shared the 1967 Nobel Prize. The method of flash photolysis was developed by Norrish and Porter a few years after World War II, using electronics developed at the time. They produced an intense burst of light and created radicals in the sample, and, using other light, they recorded the spectra of these radicals. They achieved kinetics on this timescale and observed some relatively stable intermediates.

Before the turn of the 20th century, it was known that electrical sparks and Kerr cell shutters could have response times as short as 10 ns. In an ingenious experiment, Abraham and Lemoine (1899) in France demonstrated that the Kerr response of carbon disulfide was faster than 10 ns; it has now been measured to be about 2 picoseconds (with fs response). They used an electrical pulse which produced a spark and simultaneously activated a Kerr shutter. Light from the spark was collimated through a variable-delay path and through the Kerr cell (polarizer, CS_2 cell, and analyzer). The rotation of the analyzer indicated the presence of birefringence in the cell for short optical delays; this birefringence disappeared for path lengths greater than several meters, reflecting the total optical/electrical response time of 2.5 ns. They demonstrated in 1899 the importance of synchronization in a pump-probe configuration. The setting of time delays was achieved by varying the light path. Flash photolysis utilized the above approach, but one of the flashes was made very strong to generate high concentrations of free radicals and hence their utility in chemical and spectroscopic applications.

Eigen developed "the relaxation method", which reached the microsecond and close to the nanosecond scale. By disturbing the equilibrium of a solution by either a heat jump, a pressure jump, or an electric field, the system shifts from equilibrium. This is the point of time zero. Then the system equilibrates, and its kinetics can be followed. (At about the same time, shock-tube methods were used to provide kinetics on similar timescales.) Eigen called these reactions "immeasurably fast" in his Nobel lecture. There was a feeling that this time resolution was the fastest that could be measured or that needed to be measured for relevance to chemistry, as discussed below. The invention of the laser has changed the picture.

Shortly after the realization of the first (ruby) laser by Maiman (1960), the generation of giant and short pulses became possible: nanoseconds by Q-switching (Hellwarth, 1961) and picoseconds (De

Maria *et al.,* 1966) by mode-locking (1964). Sub-picosecond pulses from dye lasers (Schäfer and Sorokin, 1966) were obtained in 1974 by Chuck Shank and Eric Ippen at Bell Labs, and in 1987 a 6 fs pulse was achieved. In 1991, with the generation of fs pulses from solid-state Ti-sapphire lasers by Sibbett and colleagues, dye lasers were rapidly replaced, and fs pulse generation became a standard laboratory tool; the state of the art, once 8 fs, is currently ~4 fs and made it into the *Guinness Book of World Records* (Douwe Wiersma's group). The tunability is mastered using continuum generation (Alfano and Shapiro) and optical parametric amplification.

In the late 1960s and in the 1970s, ps resolution made it possible to study *nonradiative* processes, a major detour from the studies of conventional *radiative* processes to infer the nonradiative ones. As a beginning student, I recall the exciting reports of the photophysical rates of internal conversion and biological studies by Peter Rentzepis; the first ps study of chemical reactions (and orientational relaxations) in solutions by Ken Eisensthal; the direct measurement of the rates of intersystem crossing by Robin Hochstrasser; and the novel approach for measurement of ps vibrational relaxations (in the ground state of molecules) in liquids by Wolfgang Kaiser and colleagues. The groups of Shank and Ippen have made important contributions to the development of dye lasers and their applications in the ps and into the fs regime. Other studies of chemical and biological nonradiative processes followed on the ps timescale, the scale coined by G. N. Lewis as the "jiffy"—the time needed for a photon to travel 1 cm, or 33 ps.

At about the same time in the 1960s, molecular-beam studies of reactions were being developed; our group was not initially a member of this community, but later beams became part of our effort in femtochemistry. Molecular collisions occur on a shorter timescale than a ps and real time studies were not possible at the time. Crossed molecular beams and chemiluminescence techniques provided new approaches for examining the dynamics of single collisions using the post-attributes of the event, the reaction products. The contributions by Dudley Herschbach, Yuan Lee, and John Polanyi were acknowledged by the 1986 Nobel Prize. Crossed molecular beam-laser studies have probed dynamics via careful analyses of product internal energy (vibrational and rotational) distributions and steady-state alignment and orientation of products, as shown by Dick Zare, Dick Bernstein, and other colleagues.

THE BIRTH OF FEMTOCHEMISTRY

Stimulated by earlier work done at Caltech in the 1970s and early 1980s on coherence and intramolecular vibrational-energy redistribution (IVR), we designed in 1985 an experiment to monitor the process of bond breakage (ICN* $\rightarrow$ I + CN). The experimental resolution at the time was ~400 fs and we could only probe the formation of the CN fragment. We published a paper, ending with the following words: *"Since the recoil velocity is ~2×10^5 cm/s, the fragment separation is ~10Å on the timescale of the experiment (~500 fs). With this time resolution, we must, therefore, consider the proximity of fragments at the time of probing, i.e., the evolution of the transition state to final products."* This realization led, in two years time, to the study of the same reaction but with ~40 fs time resolution, resolving, for the first time, the elementary process of a chemical bond and observing its transition states.

One year later in 1988, we reported on the NaI discovery which represents a paradigm for the field of femtochemistry. There were two issues that needed to be established on firmer bases: the issue of the uncertainty principle and the influence of more complex potentials on the ability of the technique to probe reactions. The *alkali halide reactions* were thought of as perfect prototypes because they involve two potentials (covalent and ionic) along the reaction coordinate: the separation between Na and I. The resonance motion between covalent and ionic configurations is the key to the dynamics of bond breakage. *How could we probe such motion in real time?* We did the femtochemistry experiments on NaI and NaBr, and the results were thrilling and made us feel very confident of the ability to probe transition states and final fragments. The experiments established the foundation for the following reasons:

First, we could show experimentally that the wave packet was highly localized in space, ~ 0.1Å, thus establishing the concept of dynamics at *atomic-scale resolution*. Second, the spreading of the wave

packet was minimal up to a few picoseconds (ps), thus establishing the concept of *single-molecule trajectory*, i.e., the ensemble coherence is *induced* effectively, as if the molecules are glued together, even though we start with a random and noncoherent ensemble—dynamics, *not* kinetics. Third, vibrational (rotational) coherence was observed during the entire course of the reaction (detecting products or transition states), thus establishing the concept of *coherent trajectories in reactions*, from reactants to products. Fourth, on the fs timescale, the description of the dynamics follows an *intuitive classical picture* (marbles rolling on potential surfaces) since the spreading of the packet is minimal. Thus, a time-evolving profile of the reaction becomes parallel to our thinking of the evolution from reactants, to transition states, and then to products. The emerging picture is physically and chemically appealing.

The NaI case was the first to demonstrate the *resonance behavior*, in real time, of a bond converting from being covalent to being ionic along the reaction coordinate. From the results, we obtained the key parameters of the dynamics, such as the time of bond breakage, the covalent/ionic coupling strength, the branching of trajectories, etc. In the 1930s, Linus Pauling's description of this bond was static at equilibrium; now we can describe the dynamics in real time by preparing structures far from equilibrium. Numerous theoretical and experimental papers have been published by colleagues, and the system enjoys a central role in femtodynamics.

Following the studies of ICN and NaI elementary dynamics, we initiated a program to generalize the concepts of femtochemistry. First, we had to settle the issue of the uncertainty principle in a general way. At the time, some were raising a question about the "energy resolution" of the fs experiments: *How can a broad-energy pulse probe a sharp resonance*? In the conventional teaching on spectroscopy of "eigenstates", one thinks of stationary states and their populations, but now we must think of coherent states. All information pertinent to eigenstates is in the wave packet structure. This point was elucidated by our experiments on a *bound nonreactive* system—the iodine system. We observed the oscillations of the nuclear (vibration) motion and the recurrences of the molecular (rotation) motion, directly giving the change with time of the I-I separation and the rotation of I_2; the timescales were separated (fs vs. ps) and the vibrational (scalar) and rotational (vectorial) motions were clearly seen.

For bimolecular reactions, the problem was that the transit time for reactants to undergo a collision is generally nanoseconds to microseconds. By using van der Waals complexes, we could expand the reactants, HI and CO_2, in a single molecular beam. But now, with the two reagents within angstroms of each other, we could examine the dynamics of the single collision. We used the first pulse to liberate the H atom with a given translational energy and a second pulse to probe the nascent OH product— the *zero of time* became well-defined and the collision was that of a limited impact parameter. The results were exciting, and we termed this the "birth of OH from $H + CO_2$"—the "simultaneous" processes of bonds being broken and formed. The $H + CO_2$ *ground-state* reaction proved to be important for a number of reasons, among them the direct determination of the lifetime ($\tau \sim 1$ ps) of the intermediate complex HOCO‡. The reaction $OH + CO \rightarrow CO_2 + H$ is one of the key reactions in both combustion and atmospheric chemistry, and represents the most studied 4-atom reaction, both theoretically and experimentally.

These first femtochemistry experiments on elementary systems and later on complex systems (see below), elucidated the nature of the coherent packet with the atomic scale for the de Broglie wave length. Accordingly, we could invoke a simple classical picture of the motion. The first of such models we published after considering the theoretical treatment of absorption of fragments *during* reactions. We derived the following expression:

$$A(t;R) = C\left\{\delta^2 + W^2\left(t,t^{\ddagger}\right)\right\}^{-1} \tag{1}$$

where C is a constant and $W = V(t) - V(t^{\ddagger})$ is the potential (or more generally, the difference of the two potentials probed); δ is a half-width of the pulse (and damping). For exponential repulsion, with L

defining the length scale and v being the speed at the total energy E, the time for bond breakage can thus be related to observables:

$$\tau_{BB} = (L/v)\, ln\!\left(4E/\delta\right) \tag{2}$$

The model describes the reaction trajectory R(t) or τ(R) and provides a simple picture of the dynamics: The dissociation time (when V drops to δ), transition-state lifetime, and the acting forces. We extended the model to obtain the potential using an inversion approach. Next, we considered the treatment of the effect of alignment and orientation on femtochemical reaction dynamics. The time evolution of alignment and coherence were considered for a single rotational angular momentum and then averaged over the different trajectories to define the coherence time(τ_c). We applied this approach to reactions of simple and complex nature.

For complex systems, our theoretical effort has taken on the following approach. With the help of molecular dynamics (MD) simulations, we compare theory with experiments. Then we use the MD simulations as a tool and vary parameters until we reduce the problem to identify the important key forces of dynamics. At this point, we can provide a microscopic dynamical picture with focus on the relative vibrational coordinates, timescales or system parameters. Two examples illustrate the point. The first was our study of the dynamics of a guest molecule in dense fluids with focus on the density dependence of microscopic friction, T_1 and T_2, and of bond breaking/remaking dynamics. The second is the study of numerous organic reaction mechanisms. For the latter, we also use advanced computational methods, such as density functional theory (DFT), *ab initio* and CASSCF computations. For ground-state reactions, the theory can be compared in a critical way with experiment, while for excited states the situation is more challenging.

PRESENT APPLICATIONS: EXAMPLES FROM CALTECH

The range of applications to different systems and phases in many laboratories around the world is extensive and beyond the purpose of this report. In this section we limit ourselves to the examples studied by the Caltech group.

Elementary reactions and transition states

The focus here was on the studies of elementary reactions. Some of these have already been discussed above. The dynamics are generally of three classes:

- Dynamics of bond breakage
- Dynamics of the (saddle-point) transition state
- Dynamics of (bimolecular) bond breakage/bond formation

Organic chemistry

With the integration of mass spectrometry into femtochemistry experiments, the field of organic reaction mechanisms became open to investigations of *multiple* transition states and reaction intermediates. The technique of fs-resolved kinetic-energy-time-of-flight (KETOF) provided a new dimension to the experiment—correlations of *time, speed*, and *orientation* which elucidate the *scalar* and *vectorial* dynamics. The examples of reactions include:

- Isomerization reactions
- Pericyclic addition and cleavage reactions
- Diels–Alder/sigmatropic reactions
- Norrish-type I and II reactions

- Nucleophilic substitution (S_N) reactions
- Extrusion reactions
- β-Cleavage reactions
- Elimination reactions
- Valence structure isomerization
- Reactive intermediates

Electron and proton transfer

Here, we examined both bimolecular and intramolecular electron transfer reactions, and these studies were the first to be made under solvent-free conditions. We also studied the transfer in clusters and in solutions. For proton transfer, three classes of reactions were of interest, those of bimolecular and intramolecular reactions, and those involving double proton transfer (base-pair models):

- Bimolecular electron transfer reactions
- Intramolecular electron transfer and folding reactions
- Acid-base bimolecular reactions
- Intramolecular hydrogen-atom transfer
- Tautomerization reactions: DNA base-pair models

Inorganic and atmospheric chemistry

We extended the applications of femtochemistry to complex inorganic reactions of organometallics. Organometallic compounds have unique functions and properties which are determined by the dynamics of metal–metal (M–M) and metal–ligand (M–L) bonding. The timescales for cleavage of such bonds determine the product yield and the selectivity in product channels. They also establish the nature of the reactive surface: ground-state versus excited-state chemistry. Similarly, we studied the dynamics of chlorine atom production from OClO, a reaction of relevance to ozone depletion.

The mesoscopic phase: clusters and nanostructures

We have studied different types of reactions under microscopic solvation condition in clusters. These include:

- Reactions of van der Waals complexes
- Unimolecular reactions
- Bimolecular reactions
- Recombination, caging reactions
- Electron and proton transfer reactions
- Isomerization reactions

The condensed phase: dense fluids, liquids, and polymers

In this area of research, we have focused our efforts on the study of reactions in dense fluids and comparison with dynamics in liquids. By varying the solvent density, we could study the femtosecond dynamics from gas-phase conditions to the condensed phase of liquid-state density. Accordingly, we could observe the influence of solute-solvent collisions on reaction dynamics in real time. We also did studies in liquid solutions for some of the systems examined in the gas phase: bond breakage and caging; valence structure isomerization; and double proton transfer. Similarly, we studied systems of nanocavities and polymers. Some highlights include:

- Dynamics of the gas-to-liquid transition region (T_1 and T_2)
- Dynamics of bimolecular (one-atom) caging
- Dynamics of microscopic friction
- Dynamics in the liquid state
- Dynamics of energy flow in polymers
- Dynamics of small and large molecules in cyclodextrins

OPPORTUNITIES FOR THE FUTURE

Three areas of study are discussed here:

Transient structures from ultrafast electron diffraction (UED)

Electron diffraction of molecules in their ground state has been a powerful tool over the past 50 years, and both electron and X-ray methods are now being advanced in several laboratories for the studies of structural changes. We have reported the latest advance in UED, by which major challenges were surmounted: the very low number densities of gas samples; the absence of the long-range order that is present in crystals, which enhances coherent interference; and the daunting task of determining *in situ* the zero-of-time when diffraction changes are on the ps and sub-ps timescale.

With UED, we have been able to study molecular structures and branching ratios of final products on the ps timescale. The change in diffraction from before to after a chemical reaction was observed. However, the direct observation of transient structural changes in the course of a reaction was published only recently. Specifically, we observed the transient intermediate in the elimination reaction of 1,2-diiodotetrafluoroethane ($C_2F_4I_2$) to produce the corresponding ethylene derivative by the breakage of two carbon–iodine bonds. The evolution of the ground-state intermediate (C_2F_4I radical) was revealed in the population change of a single chemical bond, namely the second C–I bond. The elimination of two iodine atoms is nonconcerted, with the reaction time of the second C–I bond breakage being ~17 ps. The UED results for the short-lived C_2F_4I intermediate indicate its nature, the classical structure and not the bridged structure. *Ab initio* calculations were made to compare theory with experiments.

This leap in our ability to record structural changes on the ps and shorter timescales bodes well for many future applications to complex molecular systems, including biological systems. We have completed a new apparatus equipped with diffraction detection and also with mass spectrometry. This universal system is capable of studying complex systems in the gas and other phases. It holds great promise with opportunities for the future.

Reaction control

Our interest in this area goes back to the late 1970s when a number of research groups were reporting on the possibility of (vibrational) mode-selective chemistry with lasers. At the time, the thinking was directed along two avenues. One of these suggested that, by tuning a continuous-wave laser to a given state, it might be possible to induce selective chemistry. It turned out that its generalization could not be made without knowing and controlling the timescales of IVR in molecules. Moreover, state-selective chemistry is quite different from bond-selective chemistry. The second avenue was that of IR multiphoton chemistry. In this case, it was shown that the initial IR coherent pumping could be used for selective isotope separation. Such an approach has proven successful, even on the practical scale, and Letokhov has called the process "incoherent control".

Earlier, in 1980, I wrote a *Physics Today* article in a special issue on laser chemistry suggesting the use of ultrashort pulses (not CW or long-time lasers) to control the outcome of a chemical reaction. The title of the paper was "Laser selective chemistry—Is it possible?" The subtitle stated the message,

"With sufficiently brief and intense radiation, properly tuned to specific resonances, we may be able to fulfill a chemist's dream, to break particular selected bonds in large molecules." Ultrashort pulses should be used to control the system in the desired configuration by proper choice of the time duration and delay and the coherence time.

Experimentally, we had already developed methods for the control of the phase of the field of optical pulses with the idea of using the *phase* (*"pulse shaping"*) to control molecular processes—collisions, inhomogeneous broadenings, and even photon locking which could inhibit relaxation; the timescale was ns and for the control of IVR, fs pulses were needed. Prior to this work, the optical pulse field,

$$E(t) = E_o \, A(t) \cos\left[\omega t + \phi(t)\right],\tag{3}$$

was simply defined by the envelope A(t) and the frequency ω; the phase $\phi(t)$ was unknown. By controlling $\phi(t)$ we were able to make sequences of phase-coherent multiple pulses (optical analog of NMR) and to tailor a composite "single" pulse with a prescribed $\phi(t)$. For example, with composite shaped-pulses, a sequence of phase segments and tilt angles (in the rotating frame) of, e.g., $60(x) - 300(\overline{x}) - 60(x)$, we showed experimentally that the emission of a molecule can be made twice that as when a normal single pulse was used. Similarly, by choosing pulse sequences such as x-y-x(x) we experimentally locked the system and thus lengthened its relaxation time considerably.

On the fs timescale, we studied some elementary reactions (NaI, I_2, and Xe + I_2), and recently, we turned our attention to complex molecular systems to implement the 1980 idea. In a series of molecules of increasing complexity, but retaining the same reaction coordinate, we studied selectivity control (IVR and entering near the transition state); the rate of reaction was two to three orders of magnitude larger than the expected *statistical* limit. This work was published in *Science* and promises to be significant for achieving nonstatistical chemistry at high energies. The concept suggests that control at high energies (chemical energies) is more realistic, in contrast with the conventional wisdom that asserts the need for low energies—time is of the essence! Further studies should explore other systems.

In the future, there will be extensions and new directions in fs light-matter control based on the temporal coherence of light and its interference with matter waves. Applications of the Tannor–Rice–Kosloff scheme will continue in this area of control on the fs timescale. One area that holds promise is the use of fs pulses to induce selectivity by utilizing the three parameters of the pulse, the central frequency, the width and the chirp, in an iterative algorithm; the chirp is, in a way, similar to a composite pulse of the type described above. The technique of liquid-crystal-display developed by Andy Weiner for fs pulse shaping, combined with the evolutionary feedback idea of Herschel Rabitz, makes possible the generation of the desired complex E(t) field to achieve (combinatorial) control. This optimal control has been demonstrated for a targeted second harmonic generation or a yield of chemical reaction as reported by Gerber's group in Würzburg. Kent Wilson showed the importance of chirped pulses in focusing and reflecting wave packets and, in a more recent contribution, he, with Warren Warren, used the evolutionary feedback approach to optimize the fluorescence of a molecule in solution. It should be noted that all of the above schemes change the coherent composition of the initial packet and hence the evolution in different channels—but we have not changed the evolution dictated by the natural forces of the atoms! Intense fields may do so. We did not discuss here the CW control scheme advanced by Paul Brumer and Moshe Shapiro.

Biological dynamics

There have been important contributions to femtobiology, and these include: studies of the elementary steps of vision; photosynthesis; protein dynamics; and electron and proton transport in DNA. In proteins such as those of photosynthetic reaction centers and antennas, hemoglobins, cytochromes, and

rhodopsin, a femtosecond event, bond-breaking, twisting, or electron transfer occurs. There exist global and coherent nuclear motions, observed in these complex systems, and it is possible that the complexity is not as complicated as we think (see below).

Our efforts in this direction have so far focused on DNA twisting dynamics, electron transfer in DNA assemblies, DNA base-pair models, and on protein-ligand dynamics. The work on the torsional rigidity of DNA was published in 1980–1982, while that relating to proton transfer in model base pairs was reported in the last few years. With donors (D) and acceptors (A) covalently bonded to DNA, studies of ET on more well-defined assemblies were made possible, and the effect of distance could be addressed. With fs resolution, we obtained the actual timescale of ET and related the rates to the distance between D and A. In collaboration with Jackie Barton's group, we recently published this work. The timescale of orientational coherence and solvation was also examined, allowing us to elucidate the role of molecular motions, including the effect of DNA rigidity. The results reveal the nature of ultrafast ET and its mechanism: in DNA, ET cannot be described as in proteins simply by a phenomenological parameter, β. Instead, the local involvement of the base pairs controls the timescale and the degree of coherent transport. Molecular dynamics are critical to the description of the transport. The measured rates and the distance range of the transfer suggest that DNA is not an efficient molecular wire.

For proteins, our current interest is in the studies of the hydrophobic forces and ET, and oxygen reduction in models of metallo-enzymes. For the former, we have studied, with fs resolution, the protein Human Serum Albumin (HSA), probed with the small (ligand) molecule hydroxyphenyl methyloxazole (HPMO); this work is in collaboration with Abderrazzak Douhal. We also studied ET in hyperthermophilic proteins. For model enzymes, we examined novel picket-fence structures which bind oxygen to the central metal with ~85% efficiency at room temperature. In this system, we observed the release of O_2 in 1.9 ps and the recombination was found to occur on a much longer timescale. We published our first report recently in *Angewandte Chemie* in collaboration with Fred Anson's group at Caltech. These are fruitful areas for future research, especially in that they provide prototype systems for O_2 reduction in the transition state at room temperature.

FEMTOCHEMISTRY: A PERSPECTIVE

The key to the explosion of research can perhaps be traced to three pillars of femtochemistry.

Time resolution: Reaching the transition-state limit

Three points are relevant: (i) The improvement of nearly ten orders of magnitude in time resolution, from the (milli)microsecond timescale (Eigen, Norrish, and Porter) to present femtosecond resolution, opened the door to studies of new phenomena and to new discoveries; (ii) the transition state, the cornerstone of reactivity, could be clocked as a molecular species TS‡, providing a real foundation to the hypothesis of Arrhenius, Eyring, and Polanyi for ephemeral species [TS]‡, and leading the way to numerous new studies. Extensions will be made to study transition-state dynamics in complex systems, but the previous virtual status of the transition state has now given way to experimental reality; (iii) inferences deduced from "rotational periods" as clocks in uni- and bimolecular reactions can now be replaced by the actual clocking of the nuclear (vibrational) motion. This is particularly important when a chemical phenomenon such as "concertedness" is involved or the timescale of complexes or intermediates is many vibrational periods. In the 1960s, there was some thought that the relevant timescale for chemistry was the microsecond regime. Moreover, the uncertainty principle was thought to represent a severe limit of the utility of shorter time resolution; coherence was not part of the thinking in deciphering fs nuclear motion, as detailed above and summarized below.

Atomic-scale resolution

Two points are relevant: (i) The transition from *kinetics* to *dynamics*. On the femtosecond timescale, one can see the coherent nuclear motion of atoms—*oscillatory* or *quantized steps* instead of *exponential decays* or rises. This was proved to be the case for bound, quasi-bound, or unbound systems and in simple (diatomics) and in complex systems (proteins); (ii) the issue of *the uncertainty principle*. The thought was that the pulse was too short in time, thus broad in energy by the uncertainty principle $\Delta t \Delta E \sim \hbar$ but localization is consistent with the two uncertainty relationships, and coherence is the key. The energy uncertainty ΔE should be compared with bond energies: ΔE is 0.7 kcal/mol for a 60 fs pulse. At the 1972 Welch Conference, in a lively exchange between Eugene Wigner and Edward Teller, even picosecond time resolution was of concern because of the perceived fundamental limitation imposed on time and energy by Heisenberg's uncertainty principle.

Generality of the approach

Three points are relevant: (i) In retrospect, the femtosecond timescale was just right for observing the "earliest dynamics" at the actual vibrational timescale of the chemical bond. (ii) The time resolution offers unique opportunities when compared with other methods. Processes often appear complex because we look at them on an extended timescale, during which many steps in the process are integrated. (iii) The methodology is versatile and general, as evidenced by the scope of applications in different phases and of different systems. It is worth noting that both *excited* and *ground state* reactions can be studied. It has been known for some time that the use of multiple pulses can populate the ground state of the system and, therefore, the population and coherence of the system can be monitored. The use of Coherent Anti-Stokes Raman Spectroscopy (CARS), Degenerate Four-Wave Mixing (DFWM), simulated Raman scattering (SRS), π-pulses, or the use of direct IR excitation are some of the approaches possible. Two recent examples demonstrate this point: one invokes the use of IR fs pulses to study reactions involving hydrogen (bond) motions in liquid water, work done in France and Germany; and the other utilizes CARS for the study of polymers in their ground state, as discussed above. Ground-state dynamics have also been studied by novel fs photodetachment of negative ions, and the subfield of fs dynamics of ions is now active in a number of laboratories.

EPILOGUE

As the ability to explore shorter and shorter timescales has progressed from the millisecond to the present stage of widely exploited femtosecond capabilities, each step along the way has provided surprising discoveries, new understanding, and new mysteries. In their editorial on the 10th anniversary of Femtochemistry, Will Castleman and Villy Sundström put this advance in a historical perspective. The Nobel report addresses with details the field and its position in over a century of developments (see Further Readings). Figure 2 summarizes areas of study and the scope of applications. Developments will continue, and new directions of research will be pursued. Surely, studies of transition states and their structures in chemistry and biology will remain active for exploration in new directions, from simple systems to complex enzymes and proteins, and from probing to controlling of matter—femtochemistry, femtobiology, and femtophysics.

Since the current femtosecond lasers (4.5 fs) are now providing the limit of time resolution for phenomena involving nuclear motion, one may ask: Is there another domain in which the race against time can continue to be pushed? Sub-fs or attosecond resolution may one day allow for the direct observation of the coherent motion of electrons. I made this point in a 1991 *Faraday Discussion* review and, since then, not much has been reported except for some progress in the generation of sub-fs pulses. In the coming decades, this may change and we may view electron rearrangement, say, in the benzene molecule, in real time. Additionally, there will be studies involving the combination of the "three

scales", namely time, length, and number. We should see extensions to studies of the femtosecond dynamics of *single molecules* and of *molecules on surfaces* (e.g., using STM). Combined time/length resolution will provide unique opportunities for making the important transition from molecular structures to dynamics and to functions. We may also see that all of femtochemistry can be done at micro-to-nano Kelvin temperatures, utilizing lasers and other cooling techniques.

It seems that on the femtosecond to attosecond timescale we are reaching the "inverse" of the Big Bang time, with the human heartbeat "enjoying" the geometric average of the two limits. The language of molecular dynamics is even similar to that of cosmos dynamics. Cosmologists are speaking of energy landscapes and transition states for the Big Bang and universe inflation. Perhaps we are approaching a universal limit of time!

FURTHER READINGS

Reports and articles

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