Freezing Time – in a Femtosecond

IN FEMTOSCIENCE MICROSCOPIC MOTION IS FILMED IN A MILLIONTH OF A BILLIONTH OF A SECOND

BY J. SPENCER BASKIN AND AHMED H. ZEWAIL

In the history of human civilization, the measurement of time and recording of the order and duration of events in the natural world are among the earliest activities that might be classified as science. The development of calendars permitting the tracking of yearly flooding of the Nile valley in ancient Egypt and of the seasons for planting and harvesting in Mesopotamia can be traced to the dawn of written language, and time has been an important concept in many areas of science ever since. As early as 1500 BCE, sun clocks were in use in Egypt for timing daily and seasonal events (Figure 1a). Until the 1800s, the ability to record the timing of individual steps in any process under investigation was essentially limited to time scales amenable to direct sensory perception — for example, the eye seeing the movement of a clock or the ear recognizing a tone. Anything more fleeting than the blink of an eye (~0.1 second) or the response of the ear (~0.1 millisecond) was simply beyond the realm of inquiry.

With ultrashort pulses of laser light, it has become possible to observe physical, chemical and biological changes with a resolution of femtoseconds, 15 orders of magnitude faster than the human heart beat, reaching the scale of atomic motion, spatial and temporal. As overviewed by Dr. Spencer Baskin and Professor Ahmed Zewail of Caltech, this freezing of time opens new fields of study in the microscopic world.

Consider, for example, the sequence of motions described by the legs of a running horse. In 1872, railroad magnate Leland Stanford wagered $25,000 that a galloping horse, at some point in its stride, lifts all four hooves off the ground simultaneously. To prove it, Stanford employed English photographer Eadweard Muybridge. After many attempts, Muybridge developed a camera with a shutter that remained open for only two-thousandths of a second. He used a line of 12 or 24 cameras along a track, with their shutters triggered by the horse's legs breaking equally spaced trip-wires (Figure 1b). In a series of photographs, some published in 1878 in a *Scientific American* article, he captured the detailed leg movement of a horse in full stride, thereby confirming Stanford's assertion. Since then, scientific disciplines from aeronautics to zoology have exploited high-speed photography to revolutionize understanding of mechanical and animal motions that are quicker than the eye can follow.

Molecules are about one billionth the size of a horse and their constituent atomic nuclei move 100 or more times faster than a horse. For Muybridge, whose objects of study moved with speeds of the order of 10 meters per second (m/s) and had minimum dimensions of ~ 0.1 m — the diameter of the horse's legs — a shutter speed on the order of milliseconds was essential to freeze the motion. Since the natural length scale of molecular bonds is the Ångstrom (Å, 1 Å = 10^{-10} m), discerning changes in atomic position to a fraction of an Å is required to establish a true map of any molecular transformation. With typical nuclear speeds of the order of 1000 m/s, time resolution of ~ 10 femtoseconds (fs, 1 fs = 10^{-15} s), or a shutter speed 100 billion times faster than Muybridge's, would be required to "photograph" the details of molecular motion.

ULTRAFAST LASER STROBOSCOPE

A shutter speed of such awesome rapidity is beyond the reach of any mechanical device. However, over the last 15 years, the advent of ultrafast pulsed laser techniques has made direct exploration of this temporal realm a reality. Laser pulses as short as a few femtoseconds are now possible, and ultrafast laser spectroscopy, mass spectrometry and diffraction techniques play the role of high-speed photography in the investigation of molecular processes.

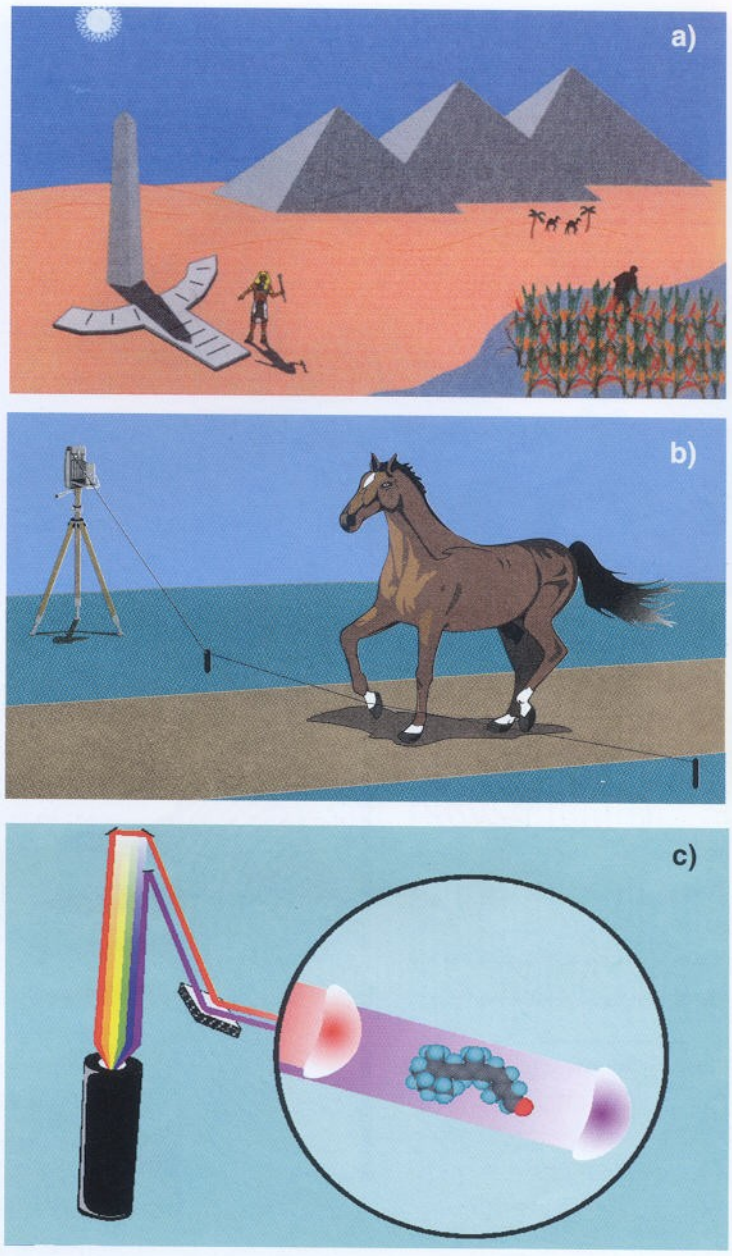
The laser pulse provides the shutter speed for freezing nuclear motion with the necessary spatial resolution. But in order to record in detail the full sequence of steps in the process, a well-defined series of measurements must be made, with relative timing also accurate to tens of femtoseconds. Furthermore, Muybridge's concern was with a single horse, while millions of molecules are typically used in the recording of molecular motion — their motion must be synchronized by a starting gun.

Figure 1: Methods of time measurement through the ages — from years to femtoseconds.

(a) Sun clock measured hours (semicircular scale) and seasons (linear scale) with the obelisk's shadow — an artist's conception of a 1500 BCE experiment.

(b) Photographic clock measured a horse's motion with millisecond time resolution — 1878.

(c) Femtosecond clock uses pulsed lasers and pulse-pulse coincidence technique to measure events and motions with atomic-scale resolution — present.



Both requirements are satisfied by using two laser pulses, in what is referred to as a pump-probe configuration.

With this methodology, the process to be studied is clocked from the instant that the substance under investigation absorbs radiation from one of the pulses, the pump pulse. This satisfies the requirement of synchronization and defines the zero of time. Passage of a second pulse, the probe pulse, through the sample at some later point in time provides a snapshot of the status of the system at that time. The use of optically-delayed pulses to record fast events began in the last century and has been advancing throughout this century with ever shorter duration and ever higher intensity of the pulses.

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 μm corresponds to 3.3 fs. Thus measurements can be made which represent the state of the system at well-defined points of time in the ongoing process, frozen with femtosecond resolution (Figure 1c). This use of the speed of light to choose a series of points in time is analogous to Muybridge's use of the horse's speed in galloping between the spaced trip-wires of his series of cameras to establish the relative timing. In both cases, the individual snapshots combine to produce a complete record of the continuous time evolution — a motion picture, or a movie.

With these real-time femtosecond techniques, studies of fundamental, elementary phenomena define the fields of femtosecond science, such as femtochemistry and femtobiology. For example, chemistry deals with the bonding and spatial arrangement of atoms to form molecules. Rearrangements of nuclei to form new structures — the making and breaking of chemical bonds — constitute the essential steps of chemical processes, and femtochemistry has made it possible to observe in real time these steps from reactants to products. Similarly, with femtosecond resolution, physical and biological changes involving nuclear motion also reach their fundamental limit, namely the vibrational time scale. In this sense, femtoscience represents the end of a race against time (Figure 2).

ATOMIC-SCALE RESOLUTION OF DYNAMICS

We have spoken about the motions of nuclei as if they were billiard balls on a pool table. At the scale of atomic masses and energies, however, the quantum mechanical wave/particle duality of matter comes into play, and the notions of position and velocity common to everyday life must be applied cautiously and in accord with the uncertainty principle, which places limits on the precision of simultaneous measurements. In fact, the state of any material system is defined in quantum mechanics by a spatially varying "wave function" with many similarities to light waves. Since the wave nature of light is a much more familiar

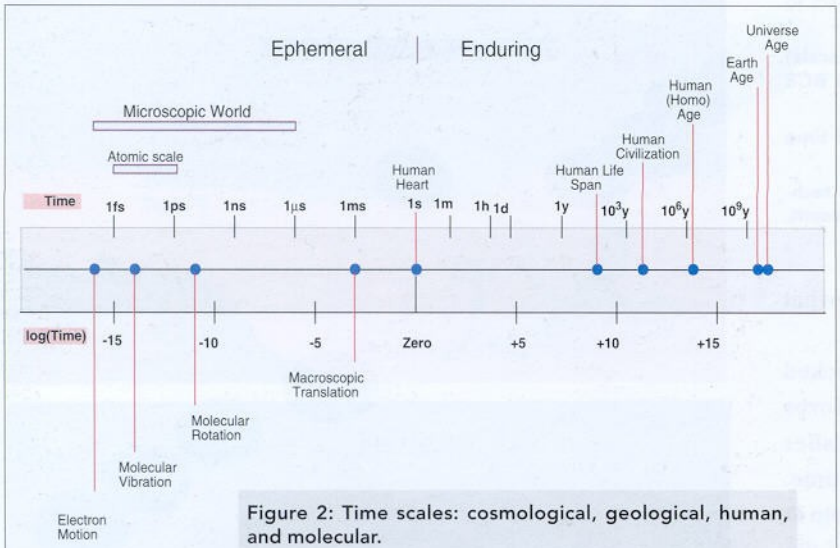


Figure 2: Time scales: cosmological, geological, human, and molecular.

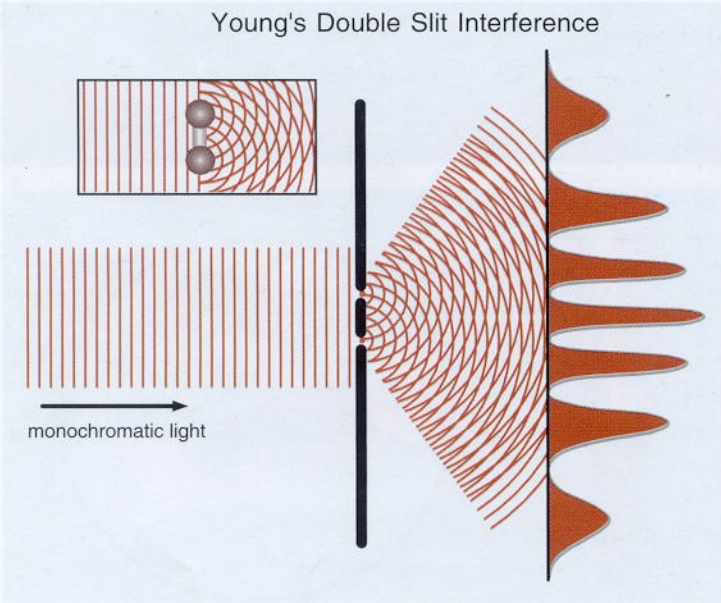


Figure 3: Thomas Young's experiment of 1800 on the interference of light waves. Waves passing coherently through two slits (or scattered from two atoms of a diatomic molecule, as in the inset) combine to produce an interference pattern of bright and dark fringes on a screen to the right.

concept than that of matter, we will use light to introduce the idea of wave superposition and interference, which plays an important role in atomic motion.

Light is a traveling wave of electric and magnetic fields which change at a regular interval, the wavelength, from positive to negative to positive along the direction of propagation. When light from two or more sources overlaps in space, the instantaneous field amplitudes (not intensities) from each source must be added together to produce the resultant light field. A well known example is Young's two-slit experiment, in which light from a single source passes through two parallel slits in a screen to produce, in the space beyond, two phase-coherent fields of equal wavelength and amplitude (Figure 3). At points for which the distances to the two slits differ by $n + 1/2$ wavelengths (for integer n) the two waves add to zero at all time, and no light is detected. Elsewhere, the amplitudes do not cancel. Thus, a stationary pattern of light and dark interference fringes is produced. Knowledge of the wavelength of light and the spacing of fringes projected on a screen provide a measurement of the separation of the slits. In X-ray diffraction such interferences, with coherence between phases, make it possible to obtain molecular structures with atomic resolution — the positions of the atoms replace the slits (Figure 3, inset).

In studies of motion, we have exploited the concept of coherence among molecular wave functions to achieve atomic-scale resolution of dynamics — the change of molecular structures with time. Superposition of a number of separate matter waves of different wavelengths and appropriately chosen phases can produce a spatially localized and moving coherent superposition state, referred to as a wave packet (see sidebar). The packet has a well-defined (group) velocity and position which now makes it analogous to a moving classical billiard ball, but at atomic resolution. The femtosecond light induces the coherence and makes it possible to reach atomic-scale spatial and temporal resolution, without violation of the uncertainty principle.

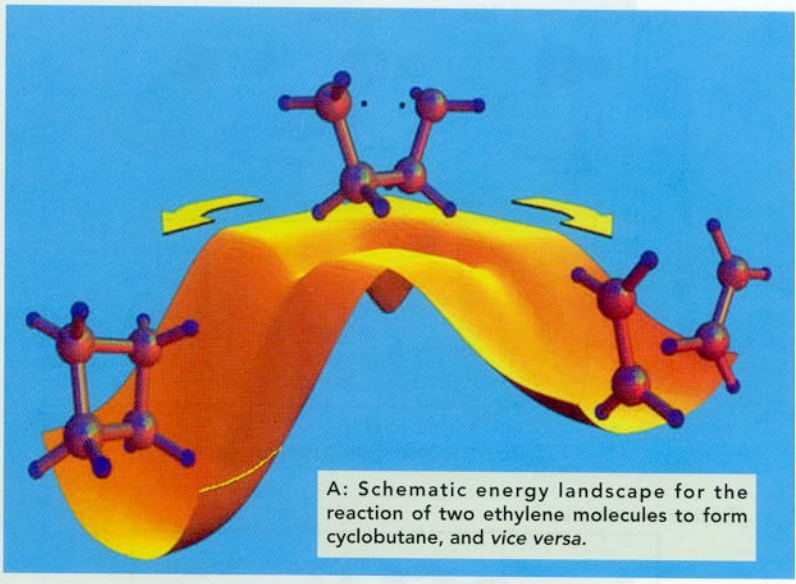
FEMTOSCOPY OF ATOMS IN MOTION

The alkali halide reactions turned out to be perfect prototypes demonstrating the concept of wave packet localization and motion. These reactions involve two potential energy surfaces (see sidebar), corresponding to covalent (electron sharing) and ionic electronic states, for nuclear motion along the reaction coordinate to bond breaking (Figure 4, top).

In the experiment, a laser pulse is first sent to excite molecules of sodium iodide (an analog of table salt, sodium chloride) from their ionic ground state to the covalent potential with sufficient energy to break the covalent bond. The atoms, sodium (Na) and iodine (I), begin to separate, but at a distance of ~7 Å the potentials cross, and the molecule can either continue to separate in the covalent state (small red wave packet in Fig 4), or jump to the ionic curve with the sodium atom giving an electron to the iodine atom. On the ionic potential, the electrostatic attraction of

Energy Landscapes and Wave Packets

Two important concepts in the discussion of atomic-scale motion are the potential energy surface and the wave packet. The potential energy surface (PES), or energy landscape, represents all the forces which act to induce atomic motion, and these change as the separations between nuclei change. Thus, the PES could have "mountains" and "valleys," depending on the nature of these forces, and configurations are classically inaccessible when the potential is higher than the total energy. Any assembly of atoms can be described by a global potential energy surface. The motion of nuclei during a reaction follows a trajectory on this surface from a region representing reactants to another region representing products. Along the way, there exist critical configurations called transition states, and there may also be separate energy valleys representing the existence of reaction "intermediates." In Figure A is shown a multidimensional PES for the reaction between two ethylenes to form cyclobutane discussed in the text.

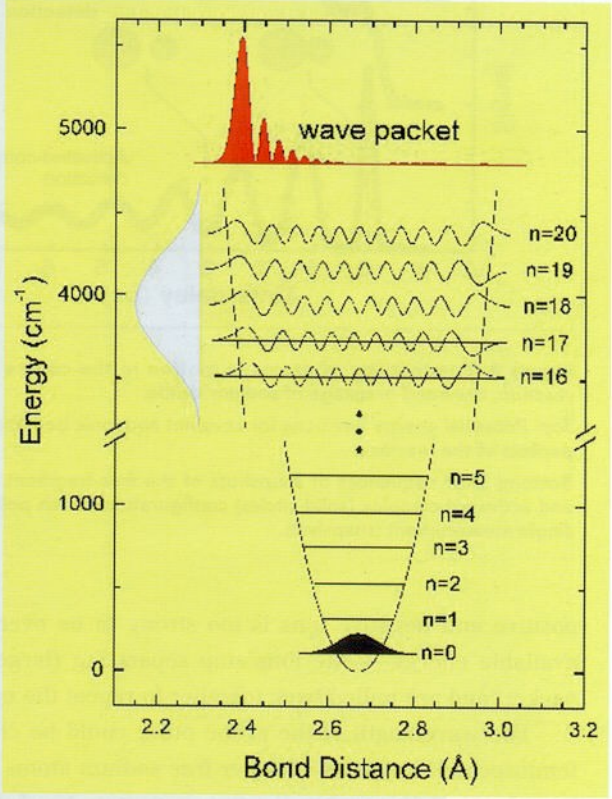


A: Schematic energy landscape for the reaction of two ethylene molecules to form cyclobutane, and *vice versa*.

For the case of a diatomic molecule, the PES takes a simple form, as shown in Figure B for a vibrating molecule similar to iodine, where the horizontal axis represents the separation of atomic nuclei. In this case, the possible energy values of the system and some of the associated wave functions are labeled by the quantum number *n*. The position probability of a molecule represented by any one of these wave functions is not localized and does not change with time.

We see motion in femtosecond experiments only when the system is in a superposition state, which is a coherent sum of stationary wave functions for different energies — the wave packet. Constructive and destructive interference (as in the interference of light waves) results in a total wave function with a large amplitude only in a restricted area of the available space at any given time: a localized wave packet. At the top of Figure B is shown a snapshot of the position probability (in red) of such a wave packet, formed from wave functions n = 16 to 20 with weighting according to the distribution curve at the left of the figure. As time advances, the wave packet moves back and forth across the potential well. As long as the wave packet is sufficiently localized on the scale of all accessible space, as in the figure (~0.04 Å vs. 0.6 Å), 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.

The observation of motion in a real system 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 observed evolution will then be that of a classical single-molecule trajectory. The key to achieving this condition is generally provided by the well-defined initial, equilibrium configuration of the studied molecules before excitation. This spatial confinement establishes the phase relations between the excited wave functions which produce and define the localized wave packets, so the entire sample of molecules is launched from essentially the same starting point.



B: Matter waves: wave functions and wave packet of a harmonic oscillator. The parabolic potential is an approximation to the internuclear potential of a vibrating iodine molecule. The horizontal lines indicate the allowed energy levels, and wave functions are shown for the energy levels with n = 16 to 20; when these wave functions are added in phase (coherently) according to the gray energy distribution at left, the wave packet shown in red at the top is formed.

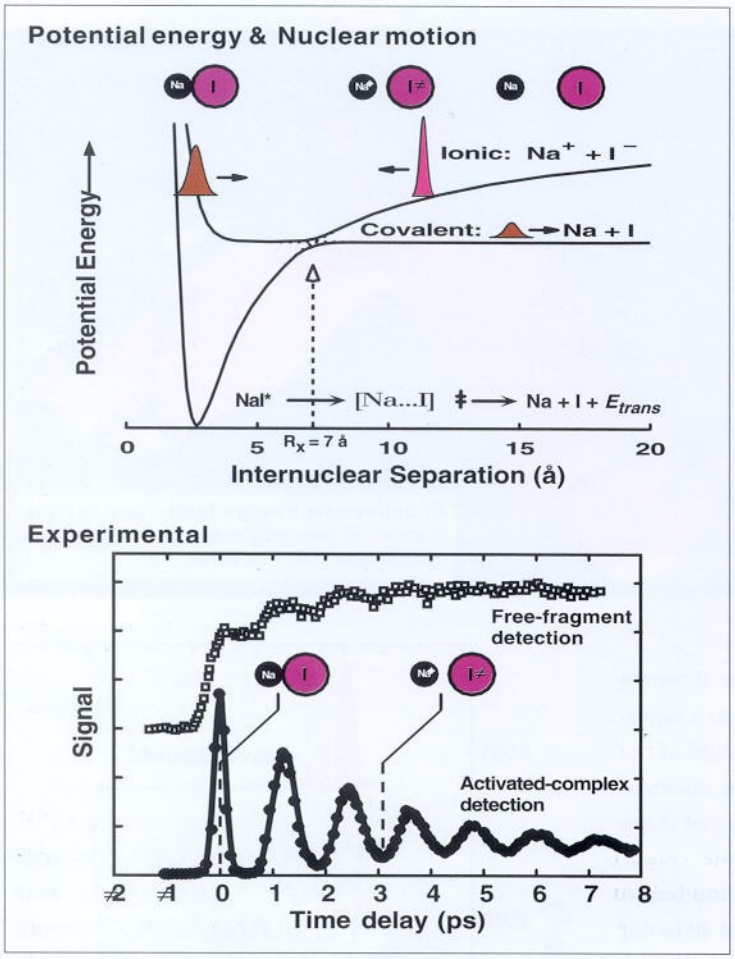


Figure 4: Femtoscopy of atoms in motion in the course of a chemical reaction, the bond breakage of sodium iodide.

Top: Potential energy functions for covalent and ionic bonding and the wave packets of the reaction.

Bottom: Time sequences of snapshots of the free-fragment (open squares) and activated-complex (solid circles) configurations. Each point represents a single measurement (snapshot).

positive and negative ions is too strong to be overcome by the available energy — the ions stop separating (large violet wave packet) and are pulled back together to repeat the cycle.

The wavelength of the probe pulse could be chosen to take femtosecond snapshots of either free sodium atoms or the quasi-bound activated complex, the transition state Na···I (Figure 4, bottom). In the first case, the total free sodium population was seen to build up in steps as each round trip of the residual molecular wave packet brought it back to the crossing point in the outward-bound direction, and some fraction escaped on the covalent surface. In activated complex detection, the diminishing bound population was observed in periodic glimpses each time the wave packet passed through the specific configuration accessed by the probe wavelength. The results show the motion of the molecule during the breaking of the chemical bond and give the microscopic details of the potential energy curves governing the motion.

This paradigm case shifted our thinking about the dynamics of the chemical bond. The NaI case was the first to demonstrate the resonance behavior, in real time, of a bond converting from being covalent to being ionic in nature. We could show experimentally that the wave packet was localized in space to better than 0.5 Å, with minimal spreading up to several picoseconds (ps, 1 ps = 10^{-12} s), and that an intuitive classical mechanical trajectory of a single molecule could be used to describe the dynamics, from reactants, to transition states, and then to final products. Coherence was observed throughout the entire course of the reaction, and quantum effects did not prevent the observations. This is fundamental and particularly important because prior understanding envisioned quite an opposite behavior of localization; most theories dealt with delocalized states of matter.

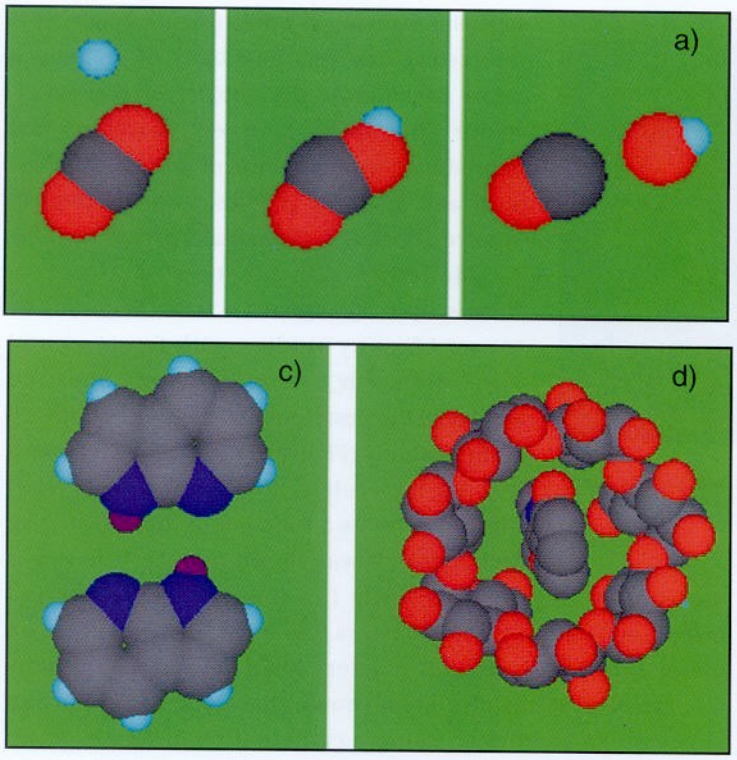
APPLICATIONS

Femtoscience is being advanced today by numerous research groups around the world and the efforts of many colleagues are represented in the following examples.

Chemistry

In the past decade, femtochemistry has been extended to all areas and in all phases of matter, from elementary to complex chemical reactions, from the gas phase to clusters to dense fluids and solutions and to solids, surfaces and interfaces. In retrospect, the femtosecond time scale was just right for seeing the fundamental dynamics of the chemical bond. Processes often appear complex because we look at them on an extended time scale during which there is integration over many steps in the process. On the femtosecond scale, the steps are resolved, and the process breaks down into a series of simpler events. A few examples will illustrate how such observations were critical to the way we think about the phenomena.

A reaction relevant in combustion and the upper atmosphere is that of a hydroxy group (HO) with carbon monoxide to produce carbon dioxide and a hydrogen atom, or the reverse. For the reverse reaction, the hydrogen atom approaches carbon dioxide to take away an oxygen (Figure 5a). The nature of transition states was unknown, and this raised many questions: How does an H-O bond form and a C-O bond break? Do they happen together, that is, in a concerted manner, or does an intermediate complex HOCO form and live long enough for energy redistribution to become a determining factor for product formation? How long does it take? Femtosecond measurements



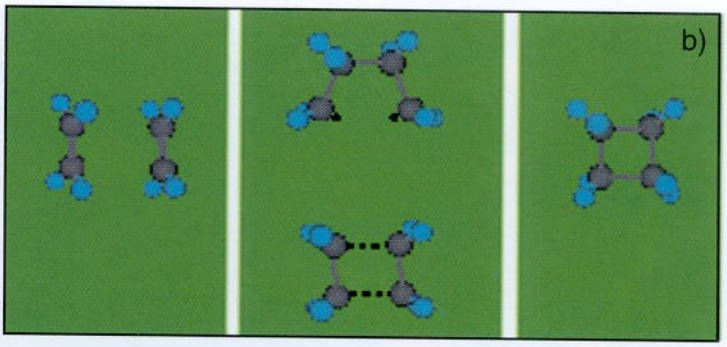


Figure 5: Femtochemistry. In these molecular structures, carbon atoms are represented in black, hydrogen in light blue, oxygen in red, and nitrogen in dark blue.

a) Atmospheric/combustion reaction between CO_2 and a hydrogen atom to form CO and OH. Passage through the intermediate complex HOCO was recorded in real time.

b) Organic reaction: the addition of two ethylenes ($H_2C{=}CH_2$, left) to form cyclobutane (right). The two possible pathways involving a transition state (bottom) or an intermediate complex (top) are indicated in the middle.

c) Proton transfer in a hydrogen-bonded dimer of two 7-azaindole molecules, a model for DNA base pairs (the two hydrogen atoms involved are shown in purple).

d) Nanocavity reaction: proton transfer and twisting in the basket-like sugar molecule cyclodextrine (hydrogen atoms are not shown).

on this isolated, single-collision reaction showed that the H-O bond-making and the C-O bond-breaking occur in a nonconcerted manner and that the intermediate HOCO lives for ~1 ps. By isolating the transition-state/intermediate in real time, we could establish the mechanism, and equally important, test theoretical predictions at the most fundamental level. Comparisons of the experiment with high quality calculations of the dynamics by theorists indicate that quantum resonances for trapping the energy must be considered.

The extension to complex organic reactions has been of central importance to questions that chemists have asked for more than half a century: What are the elementary steps and the overall mechanism? What is the nature of the transition state region? How do multiple chemical bonds form and break, concertedly or nonconcertedly? What is the time scale for the dynamics of different bonds: weak bonds, such as the hydrogen bond; and strong bonds, such as covalent, ionic, or metallic? For a variety of reactions, we have examined these and related questions.

Perhaps one archetypal case is that of the famous addition reaction of two ethylenes to form cyclobutane (Figure 5b and Figure A in the sidebar on p. 65). In this process, the transition state could be thought of as a symmetric cyclic structure (Figure 5b, lower center) as if the two ethylenes approach each other in perfect synchrony (concertedly). Experimentally, using a precursor to generate the transient species, we observed an intermediate (Figure 5b, upper center), which is a chain of four singly-bonded carbon atoms and two free electrons, a reactive diradical; it lives for 800 fs, many times more than the vibrational period, and then yields products of ethylene and cyclobutane. This indicates the nonconcerted nature of the mechanism and the existence of a quasi-bound species between reactants and products.

In the area of condensed phase chemistry, the concept of the solvent cage effect is of considerable importance, and has been discussed for over 60 years, but not directly observed. It is invoked when a chemical bond is broken in a solvent and there is a finite probability that the two fragments of the molecule will recombine. If this process is observed with picosecond or nanosecond resolution, one will be integrating over the time for the separation of the fragments, their interactions with the solvent, and their return to each other and re-establishment of the bond. Following recombination, the molecules are vibrationally hot, and the integration includes the cooling down period as well.

With femtosecond resolution we were able to time the different steps in studies in solvent clusters and in supercritical fluids from gas to liquid densities. We also investigated the necessity of the solvent cage. We found that even one solvent molecule is capable of "caging" the atoms in bimolecular solvent-solute encounters. The collision with the solvent particle takes

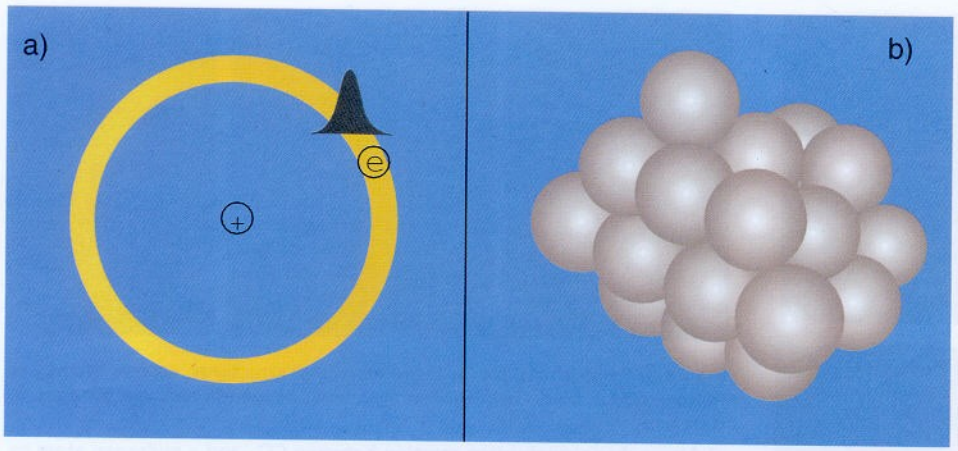


Figure 6: Femtophysics. a) Electron motion: formation of an electron wave packet in a high Rydberg orbit (n>>1). b) Cluster dynamics: a schematic of a cluster of sodium atoms.

most of the energy of the departing atom, and it is trapped within 100 fs of the initiation of the reaction, without reversing its outward motion. This mechanism, based on direct observations, is in sharp contrast to the image of the atoms separating completely, then bouncing back from a solvent cage wall.

In many areas of chemistry and biology, the weak interaction between hydrogen and nitrogen or oxygen, known as hydrogen bonding, and the related process of proton transfer, have been important for structural networks (supramolecular chemistry) and for molecular recognition. An example which has been studied in both gas phase and solution is proton transfer in a doubly hydrogen-bonded dimer of the molecule 7-azaindole (Figure 5c), a model for the DNA base pairs, and for its mutation dynamics. When the dimer is excited, proton transfer takes place at each bond, and the two steps were shown to be nonconcerted, and their rates measured on the femtosecond time scale. Charge separation is involved in the first step, a key (perhaps) for recognition of mutation. Similar studies for proton and electron transfer were made for acid-base reactions and reactions in nanocavities (Figure 5d).

Physics

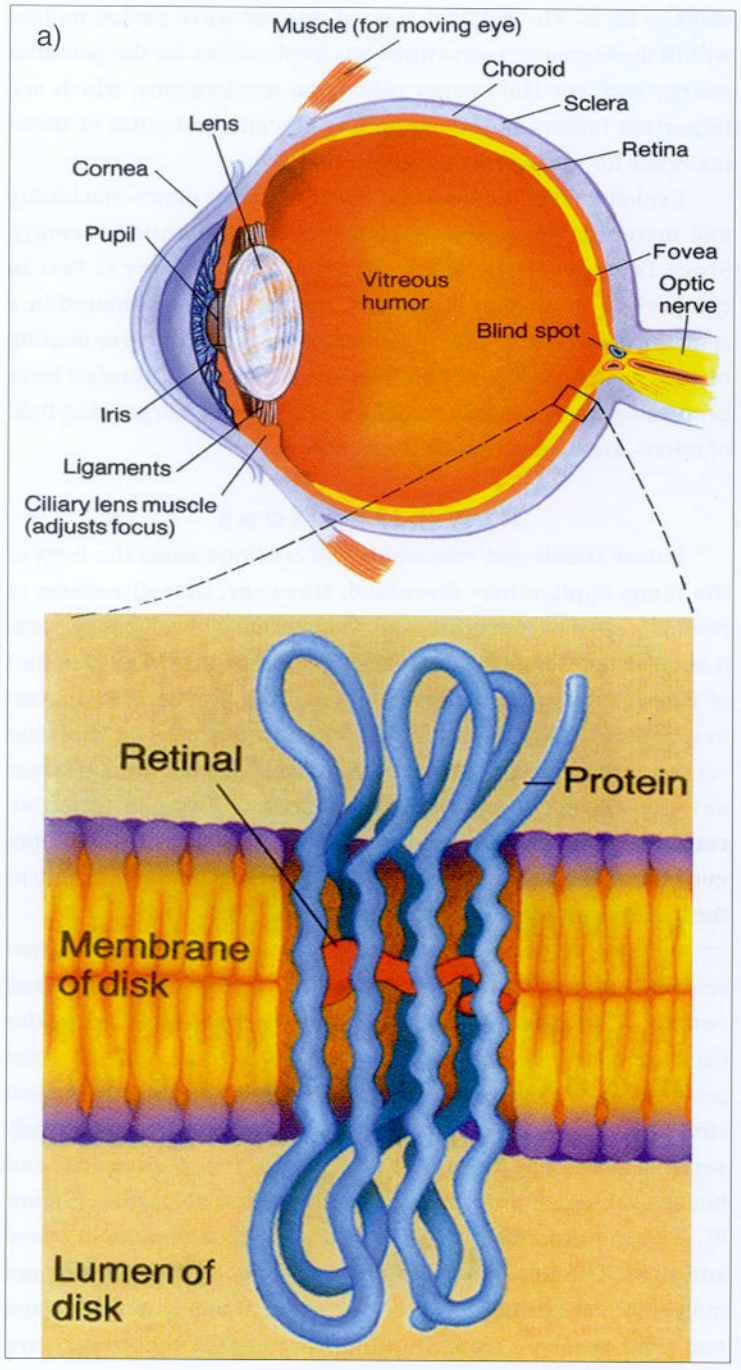
On the atomic level, the dynamics of electron motion in the hydrogen atom has been central to the development of quantum mechanics. Now, we may ask: Can we observe such dynamics? In Bohr's atom, the electron is considered as a classical particle. The time for making a circular motion in the lowest energy orbital (principal quantum number $n = 1$) of hydrogen is 0.15 fs. Actually, because of the uncertainty principle, this classical view is inappropriate for $n = 1$, but becomes valid for $n >> 1$. In recent time, wave packets have been synthesized in atomic systems (e.g. sodium) and shown to evolve on the ultrashort time scale, as classical particles evolving in orbits (Figure 6, left). It is interesting that this possibility of creating a wave packet was the subject of correspondence in 1926 between Lorentz and Schrödinger, two preeminent scientists of classical and quantum physics, in an attempt to resolve classical and quantal views of motion.

Moderate size clusters of atoms — mesoscopic structures — have become the target of many studies with femtosecond resolution. For example, a basic question relates to the description of a cluster of, say, 20 sodium atoms (Figure 6, right): does it behave as a big molecule or as a small solid crystal? From studies as a function of the cluster size and energy, it was shown that the behavior is molecular, and the time scale for energy dissipation and fragmentation to smaller clusters was established. Studies on metal and semiconductor clusters have been done in many laboratories. It has also been shown that ionic reactions and clusters can be studied using a combination of femtosecond pulses. For example, by starting with a cluster of Ag_3^-, the negative ion of silver trimer, one can detach the electron in femtoseconds, creating neutral Ag_3 at a given nuclear configuration, and then use another pulse to ionize the neutral Ag_3 to Ag_3^+, the positive ion. In this way the nuclear dynamics of ground-state species can be directly studied in real time.

Other femtoscience applications include the use of femtosecond pulses to study the novel phenomenon of Coulomb explosion — blowup of an atomic or molecular system due to the presence of multiple like charges — and to study the first steps of electron solvation dynamics. Ultrahigh-intensity lasers (with petawatt powers; 1 pW = 10^{15} watts), can be used to study a variety of other phenomena including e.g. ultrafast phase transitions in electronic structure. Intense pulses are important for the generation of sub-femtosecond pulses and ultrafast electron and X-ray pulses.

Biology

A prime example of progress in femtobiology is the femtosecond study of the first step in vision. Seeing is the result of the conversion of light energy to an electrochemical impulse. The impulse is transmitted, through neurons, to the brain, where signals from all the visual receptors are interpreted. One of the initial receptors is called rhodopsin, a pigment located in the rods of the retina. The pigment consists of an organic molecule, retinal, in association with a protein named opsin (Figure 7a). The primary photochemical step in vision is the isomerization of the retinal backbone making the backbone more linear (Figure



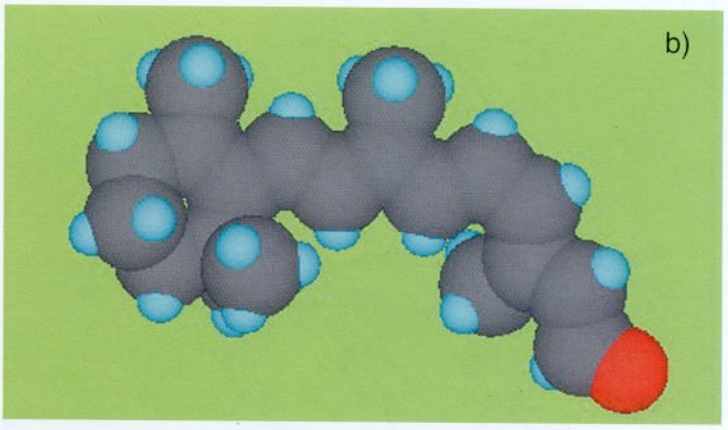


Figure 7: Femtobiology. The molecular basis of vision:

a) Within the light-sensitive rod and cone cells (not shown) covering the retina at the back of the eye are membranes (lower inset) in which are embedded photoreceptive molecules like rhodopsin, whose light absorbing part is retinal (figure adapted from *Biology*, by G. Brum, L. McKane, and G. Karp, Wiley, New York, 1995).

b) Molecular structure of retinal. The first step in vision is a coherent structural change in retinal — a twisting by 180° of the last five, downward-pointing carbon atoms at right which makes the backbone more linear; this takes place on a femtosecond time scale.

7b). The change of the retinal shape apparently gives opsin the signal to undergo a sequence of dark (thermal) reactions involved in triggering neural excitation.

Studies have shown that the primary process takes 200 fs and that coherent vibration of the reaction coordinate continues in the photoproduct after the reaction. The speed of the reaction and the product coherence indicate that the energy is not first absorbed, then redistributed to eventually find this particular bond, but, instead, the entire process proceeds in a coherent manner, that is, as a wave packet. This coherence is credited for making possible the high (~70 percent) efficiency of the twisting step, despite the large size of the rhodopsin molecule and the many channels for dissipation of energy. These dynamics are similar to those of sodium iodide discussed previously, even though the contrast in size is huge, from two atoms to a protein.

Another important area of research in femtobiology is the photosynthetic process of transforming light energy to chemical energy. The particular photosynthetic apparatus of purple bacteria has been thoroughly studied to unravel the complex sequence of events and to relate structure to function. The photosynthetic complex consists of two rings of pigment antenna molecules that absorb the light, and a reaction center protein to which the energy migrates over many pigments to be finally trapped by electron transfer reactions. Many of the individual steps occur on the femtosecond time scale, and femtosecond studies have revealed coherent nuclear vibrational motion in the antenna complexes and in the reaction center. As in vision, coherence appears to play an important role in the high efficiency (~95 percent) of the energy collection, with Nature having designed the process so that it is not using all the atoms of the protein and thus distributing and wasting the energy.

Material and polymer science

Polymers designed for use in electroluminescent displays must decay by emission of light after being excited by means of

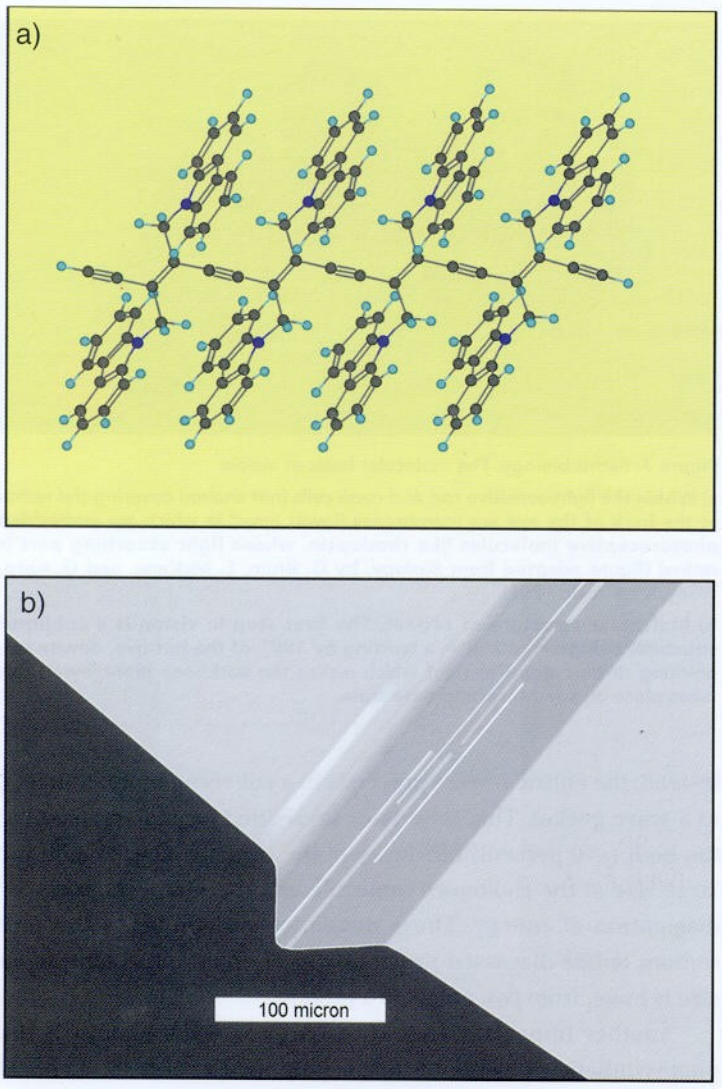


Figure 8: Polymer and material science.

a) A portion of a polymer chain, in which femtosecond stretching of triple and double carbon-carbon bonds in the polymer backbone has been studied.

b) Ultrafast micro-machining: an illustration of a micro-channel milled in fused silica by femtosecond light pulses, with residual roughness less than one micron.

an applied voltage. However, the desired result may be frustrated as the excitation travels from site to site along a polymer chain or between chains, leading to quenching by impurities or annihilation with another excitation. Femtosecond techniques have been applied to quantify the ultrafast movement of the excitation, which is an important parameter in modeling the performance of these materials.

In a similar vein, femtosecond time resolution has been used for direct monitoring of the coherent carbon-carbon stretching vibrations in polymeric materials (Figure 8a), with periods as short as 23 fs. The detailed view of nuclear wave packet motion within these complex structures has implications for the potential energy surfaces and energy relaxation mechanisms, which are important factors in understanding the rich potential of these materials for optoelectronic applications.

Exploitation of femtosecond laser pulses for micro-machining and materials processing has also received attention recently. Since the deposition of energy in a surface layer is fast in comparison to nuclear vibrations, material can be ablated in a spatially controlled manner, without melting or extensive heating of adjacent areas (Figure 8b). This unique aspect of ultrafast laser processing offers great potential for utility in the burgeoning field of micro- and nanostructure applications.

NEW DIRECTIONS

Future trends and extensions will continue along the lines of the many applications discussed. However, new directions of research are also emerging, and we mention a few. First, because it is clear that femtosecond resolution is 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 be pushed yet further? Attosecond (10^{-18} s) resolution may one day allow direct observation of the electron's motion. Since we made this point in a 1991 review, not much has been reported, but in coming decades we might view electron rearrangement, say, in the benzene molecule, in real time.

Second, major contributions will be made in biological science and medicine, with perhaps two focuses. The study and control of enzymatic reactions and the investigation of the catalytic nature of the transition state seem to be areas of great promise. Also, it may become possible to record a large biological structure changing with time and with atomic resolution. Already some success has been reported in studies of chemical and biological change utilizing X-ray and electron diffraction (Figure 9), with the ultimate goal of recording all coordinates in space and time. The impact on problems such as protein folding and molecular recognition is clear. For medical applications, pulsed and time-resolved transillumination imaging techniques are powerful methods; some have already been advanced for applications in tomography and time-resolved imaging of cancer tumors, currently with picosecond resolution. Femtosecond two-photon microscopy is now quite common.

Third is the area of reaction control. In 1980, we discussed the possibility of using ultrashort pulses to control the outcome of a chemical reaction and to perhaps fulfill the chemist's dream of selective chemistry by localized surgery using lasers. Many elegant theoretical proposals have been advanced and some

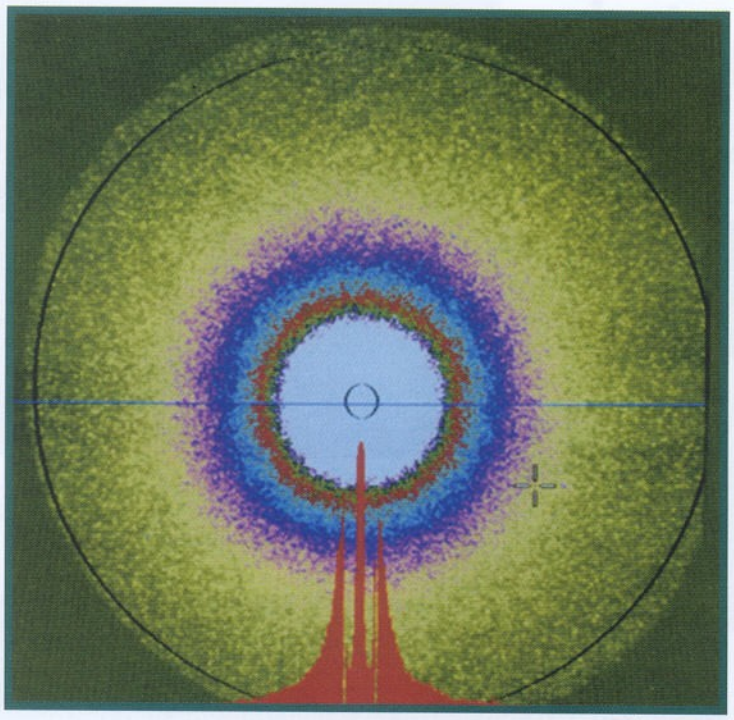


Figure 9: Molecular architecture: ultrafast electron diffraction. The diffraction pattern is that of a molecule, taken in the Caltech apparatus.

limited experimental progress has been achieved on small systems. The hope is to be able to extend the methodology to complex systems and to systems in different phases. Very recently we reported our first studies of femtosecond selective activation of complex reactions at high energies, and this effort is continuing for control of reactions.

As the ability to explore shorter and shorter time scales has progressed from milliseconds to the present stage of widely exploited femtosecond capabilities, each step along the way has provided surprising discoveries, new understanding of the basic operations of Nature, and new mysteries. We hope that we have given the reader some insight into the fruits of current research in the femtosecond domain, and conveyed some of our excitement about the bright future of femtoscience.

SUGGESTED READING

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