QnAs with Shaul Mukamel

Farooq Ahmed, *Science Writer*

Since the invention of the laser in the 1960s, researchers have recognized that the device could be used to investigate atomic structure and nuclear motions. Over the course of his career, Shaul Mukamel, a professor of chemistry, physics, and astronomy at the University of California, Irvine, has advanced theories underlying nonlinear laser spectroscopy and imaging. Mukamel has shed light on the many uses of short laser pulses in medicine, in studies of electron and energy transfer, and in solar energy harvesting. Generations of scientists and engineers consider his 1995 book, *Principles of Nonlinear Optical Spectroscopy* (1), essential reading. Mukamel's research focuses on the design of experiments that leverage light sources, such as X-ray free-electron lasers, that operate at femtosecond timescales. His Inaugural Article (2) demonstrates how short X-ray pulses can probe conical intersections, which are molecular geometries where electronic-state energies and vibrational energies become comparable. Based on the principle of quantum superposition, molecules exist simultaneously in both the ground and the excited state, an effect also known as the Schrodinger's cat paradox. PNAS recently spoke to Mukamel, who was elected to the National Academy of Sciences in 2015.

Shaul Mukamel. Image courtesy of Shaul Mukamel.

PNAS: In your Inaugural Article (2), you describe using a femtosecond, X-ray free-electron laser for time-resolved diffraction of a small molecule, NaF. How has this technique advanced molecular imaging?

Mukamel: Scientists typically perform X-ray diffraction on crystals to resolve a molecule's structure. This technique in its stationary or time-independent form has been around for a century. Time-resolved X-ray diffraction is a more recent development and makes use of short pulses to record snapshots of evolving charge density, which is the placement of electrons within a molecule.

Free-electron lasers, which were first predicted in the 1970s, create short, intense X-ray pulses so that researchers can perform diffraction quickly and more efficiently. They are intense enough to detect diffraction from nanocrystals and possibly even from single molecules. We no longer need to grow large crystals, which is time consuming and often difficult for complex biological molecules.

However, the analysis of time-resolved diffraction in excited molecules becomes more complex. Normally in molecules, the electrons move much faster than the nuclei, so we can separate the description of the molecule into the electronic and the nuclear parts. In excited states, the electrons and the nuclei are often strongly coupled so that they move on the same timeframe, creating conical intersections. Ultrafast diffraction can monitor this strongly coupled motion that is crucial for many elementary processes.

PNAS: If you are investigating a small or single molecule with a high-energy pulse, how can you be certain that you are not altering the molecular structure with the laser?

Mukamel: The duration of the pulse is so short—the laser is so fast—that no significant structural changes occur in that timeframe. It's rather like taking a snapshot, or really a series of snapshots, in that the pulse occurs quickly at different times. Of course, once the "image" has been taken, the molecule is free to ionize, dissociate, or react.

PNAS: How might this technique be used to view molecular reactions?

Mukamel: A major motivation for constructing a femtosecond, X-ray free-electron laser, which is a huge investment, was the desire to film reactions as they happened. The potential of the technology is enormous because we can now monitor in real time how bonds form and break and how nuclei move and oscillate. In biological and chemical processes, the applications are unbounded, whether its capturing the

This is a QnAs with a member of the National Academy of Sciences to accompany the member's Inaugural Article on page 6538 in issue 26 of volume 115.
Published online July 2, 2018.

isomerization of rhodopsin, which is the main pigment involved in light-sensing, or seeing photosynthesis occur at the electronic level.

PNAS: How do you anticipate using free-electron lasers beyond diffraction?

Mukamel: They can be used for spectroscopic purposes as well. Whereas diffraction measures charge density without exciting the molecule, spectroscopy views the emission or absorption spectra of atoms probed with light of a certain wavelength. Multidimensional spectroscopy with short pulses originated in NMR spectroscopy (NMR), which deploys bursts of radio waves to excite the nuclei in a sample. Biologists and chemists routinely use NMR [for structure analysis]. In the 1990s, the technique was extended to use visible and infrared lasers to study electron and nuclear motion. Down the road, the extension to X-rays will allow us to study core electrons at much faster, attosecond timescales. This will allow us to probe not just global molecular structures but also specific atoms within a structure or in a protein and view the chemistry of various reactants. With multiple laser pulses, we will be able to produce movies of these changes over short periods of time.

PNAS: How do you see this technology developing in the future?

Mukamel: Femtosecond lasers in the visible light range are now commercially available. However, the duration of these lasers is limited down to about 5 femtoseconds, which is adequate for studying the motion of nuclei. X-ray free-electron lasers can produce pulses down to attoseconds, and these faster pulses can capture molecular dynamics with a much higher resolution. The period of the electron in the hydrogen atom is about 150 attoseconds, so we should be able to view the movement of electrons themselves. This is ideal because for chemical processes and condensed matter physics applications, we don't need to get any faster. Certainly, we can vary the intensity or the number of pulses to produce a robust amount of information. If we wanted to look inside the nucleus, then perhaps we'd switch to even faster and higher-energy gamma rays.

PNAS: As a theorist, how do you see your role developing in the future?

Mukamel: My mission is really to push and inspire the experimentalists: to anticipate how the technology will evolve in the near future and propose new, more sophisticated, and challenging experiments. Ultrafast X-ray spectroscopy is still in its infancy, and many possible applications are on the horizon. I look forward to continue developing the theoretical framework for the design, computation, and interpretation of the upcoming experiments.

1 Mukamel S (1995) *Principles of Nonlinear Optical Spectroscopy* (Oxford Univ Press, New York).

2 Bennett K, Kowalewski M, Rouxel JR, Mukamel S (2018) Monitoring molecular nonadiabatic dynamics with femtosecond X-ray diffraction. *Proc Natl Acad Sci USA* 115:6538–6547.