Example of Technical Highlight

Toward Probing Intermediates in Protein Folding: Ultrafast Two-dimensional Infrared Spectroscopy Distinguishes between Different Helical Structures

Nien-Hui Ge, University of California at Irvine

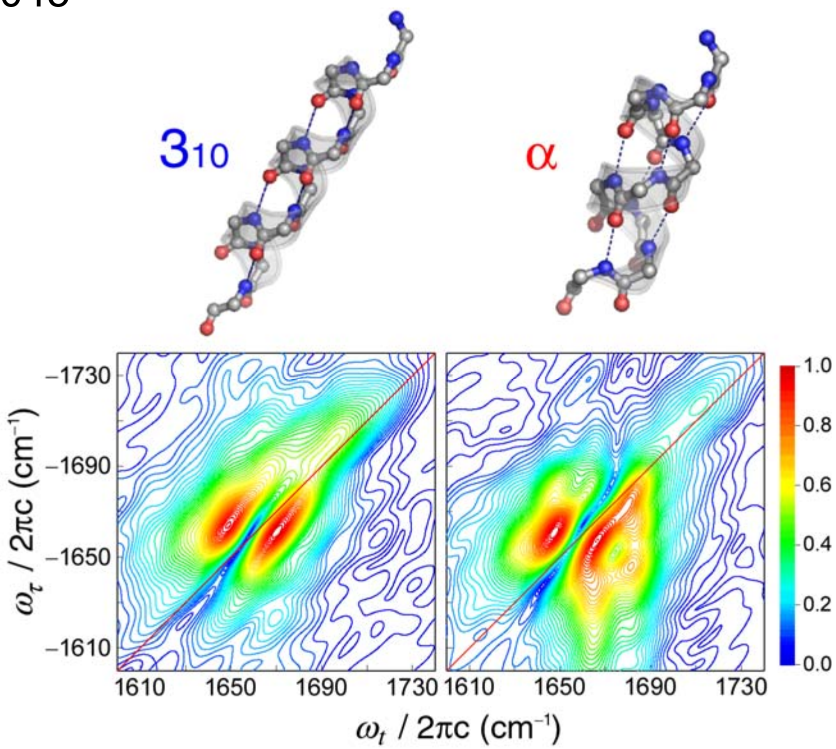
CHE-0450045

Understanding how proteins fold into their unique and highly organized functional three-dimensional structure has significant consequences for basic biology and biomedicine. Although immense progress has been made in this field, the earliest steps of protein folding still are poorly understood.

For example, simulations predict that the 3_{10}-helix secondary protein structure is a transient intermediate in the folding of secondary protein α-helices. However, experimental verification is lacking because conventional spectroscopic techniques do not have sufficient temporal and structural resolution to capture the two helical structures in real time.

Professor Ge has demonstrated experimentally, for the first time, that the relatively new method of ultrafast two-dimensional infrared (2D IR) spectroscopy can distinguish between 3_{10}- and α-helices. The figure shows that the two helices exhibit distinct cross-peak spectral patterns. Connection between the spectra and the structures was made through calculations based on a vibrational exciton model, which treats the system as a network of coupled oscillators.

The result is a key step toward developing experimental approaches that will open avenues for elucidating the role of the 3_{10}-helix in early protein folding events.



Ultrafast 2D IR spectroscopy reveals distinct cross-peak spectral patterns when an octapeptide adopts different secondary structures: a doublet pattern for the 3_{10}-helix and a multiple-peak pattern for the α-helix. Figure provided by Hiroaki Maekawa and Nien-Hui Ge, Department of Chemistry, University of California at Irvine.

Hiroaki Maekawa, Claudio Toniolo, Quirinus Broxterman, and Nien-Hui Ge, “Two-Dimensional Infrared Spectral Signatures of 3_{10}- and α-Helical Peptides,” *Journal of Physical Chemistry B*, vol. 111, p. 3222 (2007).

Hiroaki Maekawa, Claudio Toniolo, Alessandro Moretto, Quirinus B. Broxterman, and Nien-Hui Ge, "Different Spectral Signatures of Octapeptide 3_{10}- and alpha-Helices Revealed by Two-Dimensional Infrared Spectroscopy,“ *Journal of Physical Chemistry B*, vol. 110, p. 5834 (2006).

Example of Non-technical Highlight:

Toward Understanding How Proteins Fold: New Laser Method Distinguishes between Different Protein Structures

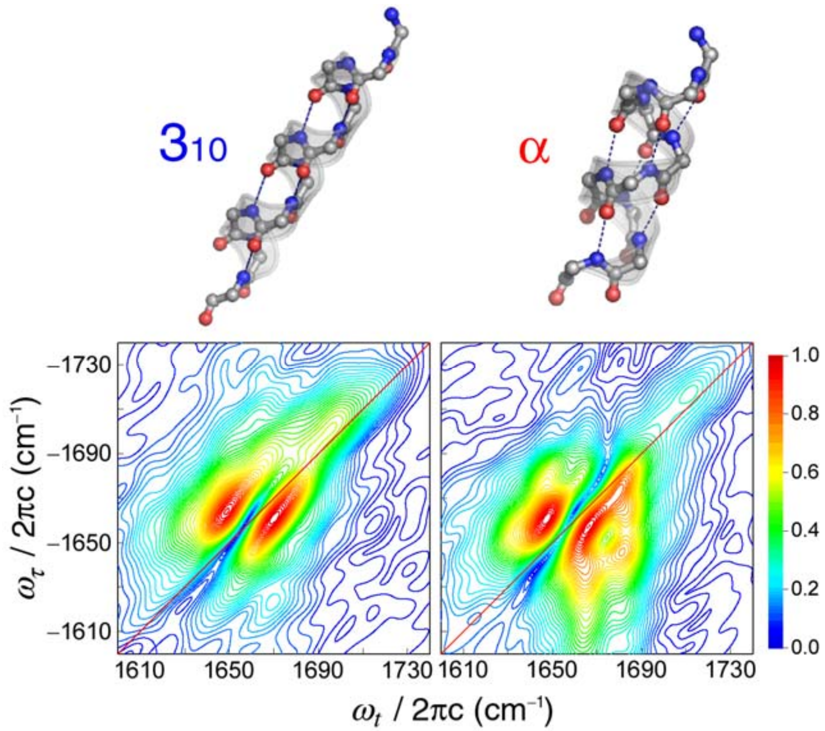
Nien-Hui Ge, University of California at Irvine

CHE-0450045

Since their invention more than 50 years ago, lasers have revolutionized the way chemists understand the molecular world. Through new developments in producing short pulses of laser light, chemists have been able to capture glimpses of very short-lived chemical compounds and structures. The goal is to make “movies” showing how molecules move and react in order to better understand how chemistry and biology work.

Proteins are structures consisting of chains of amino acids. How these structures fold into their characteristic shapes is still not understood, but the shapes are important. For example, misfolding can cause disease.

Development of new ultrafast laser techniques in the Ge laboratory has enabled the researchers to distinguishing a so-called 3_{10}-helix from an alpha (α) helix (see diagram). Using computer simulations, the 3_{10}-helix was predicted to exist as an intermediate on the way to folding an α-helix. No one knows for sure whether this is the case because it exists for only a tiny fraction of a second, and it is difficult to distinguish it from other structures. The colored diagrams resulting from the laser experiments show that the “signature” of each type of helix is distinct. Professor Ge’s experiments are exciting for two reasons: they show that the new laser method is highly structure-sensitive and that it can be used as a high-speed molecular camera to take snapshots of protein folding.



New laser method provides signatures that distinguish proteins of subtly different shapes. Figure provided by Hiroaki Maekawa and Nien-Hui Ge, Department of Chemistry, University of California at Irvine.

Hiroaki Maekawa, Claudio Toniolo, Quirinus Broxterman, and Nien-Hui Ge, “Two-Dimensional Infrared Spectral Signatures of 3_{10}- and α-Helical Peptides,” *Journal of Physical Chemistry B*, vol. 111, p. 3222 (2007).

Hiroaki Maekawa, Claudio Toniolo, Alessandro Moretto, Quirinus B. Broxterman, and Nien-Hui Ge, "Different Spectral Signatures of Octapeptide 3_{10}- and alpha-Helices Revealed by Two-Dimensional Infrared Spectroscopy,“ *Journal of Physical Chemistry B*, vol. 110, p. 5834 (2006).

Example of Broader Impact Highlight:

Toward Understanding How Proteins Fold: New Laser Method Distinguishes between Different Protein Structures

Nien-Hui Ge, University of California at Irvine

CHE-0450045

The development of new physical methods for studying biochemical phenomena is key to answering many unsolved problems in biology and medicine. The Ge laboratory is contributing to this pursuit by developing new methods based on ultrafast lasers. The method is a general approach that can be applied not only to the problem of how proteins fold but also to answer many questions in chemistry and biology.

To bring her research to the broader community, Professor Ge contributed lectures and experiments to the California State Summer School for Mathematics and Science at the University of California, Irvine (COSMOS-UCI) program in July 2006 and 2007. These lectures introduced high school students to the interdisciplinary area of the physical chemistry of macromolecules. Impact of her work is further broadened through international collaborations in Italy and the Netherlands.

High school students attending lectures, conducting experiments, and working on projects in the California State Summer School for Mathematics and Science at the University of California, Irvine (COSMOS-UCI) program. Photos provided by Nien-Hui Ge, Department of Chemistry, University of California at Irvine. Photos taken by Tescha Thayer, a teacher fellow from COSMOS-UCI, 2006.