TCI SEMINAR

Understanding and exploiting proteins' alter egos

Monday,
3:00 p.m.

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Room 8335

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Basic principles of physical chemistry establish that all proteins adopt a distribution of different conformations but what do these structural ensembles look like? Answering this question would revolutionize our understanding of biology and create exciting new opportunities for treating diseases. For example, proteins' structural heterogeneity is the basis for allostery—the mysterious process by which perturbing one site on a protein alters the behavior of a distant site in the protein. Understanding allostery would help explain many regulatory mechanisms and potentially uncover new target sites for drug design. Unfortunately, it is extremely difficult to watch allostery in action experimentally. To overcome this limitation, my lab is developing Markov state model (MSM) methods for building atomically-detailed maps of proteins' conformational ensembles, employing these tools to both understand known allosteric effects and to discover new cases of allostery, and testing our predictions experimentally. I will explain our tools for integrating information from thousands of atomically-detailed molecular dynamics simulations to build maps of proteins' conformational ensembles, introduce the insights we've gained into the mechanisms of allosteric communication, and present our computational and experimental evidence for new allosteric sites that we've discovered.

Theoretical Chemistry Institute Seminar Series