School of Molecular Sciences
Arizona State University

SMS 2023 P&T Seminar

Friday Aug 25 | 1pm | Biodesign Auditorium

Translating Anharmonic Molecular Vibrations into Information:

Molecular vibrations are commonly associated with covalent bonds and functional groups probed spectroscopically at mid-infrared frequencies. However, in absence of photons with sufficient energy to excite them, such vibrations are confined to their ground state at room temperature and essentially void of information.

This changes at low frequencies in the far-infrared ($\nu < 6$ THz; $\tilde{\nu} < 200$ cm-1; $E < 25$ meV) where molecular vibrations are easily excited by molecular collisions and the number of populated states increases exponentially with decreasing frequency. This is the regime of the often-quoted "jiggling and wiggling of atoms" that enables dynamic processes ranging from molecular transport to conformational transitions in biomolecules.

We develop tools to extract the information contained in low-frequency molecular vibrations from all-atom computer simulations on timescales suitable for high throughput applications. This allows us to predict collective dynamics in proteins that form the basis of conformational transitions and are essential for the design of efficient artificial enzymes and the discovery of allosteric modulation mechanisms. Further, our tools enable us to investigate solvent-mediated interactions in protein conformational transitions, complex formation, and aggregation. In parallel, we use our methods to identify unexplored driving forces in protein dielectrophoresis, a promising technique to manipulate and separate proteins in solution.

Notably, we extract information from vibrations and fluctuations on picosecond timescales that are often ignored in applications of molecular dynamics simulations, because their analysis cannot rely on standard analytical models and approximations: Thermally excited low-frequency vibrations violate every condition required to justify harmonic approximations and require new approaches that fully capture their highly anharmonic nature.

We developed the FREquency-SElective ANharmonic (FRESEAN) mode analysis, which uses an efficient time-correlation formalism and eliminates the need of harmonic or quasi-harmonic approximations. The FRESEAN mode analysis is the first method capable to isolate the lowest-frequency vibrations of anharmonic molecular systems, which we successfully exploit to sample conformational transitions in proteins. My group further developed 3D-2PT (3D two-phase thermodynamics), which generates spatially resolved maps of local solvation free energy contributions in the solvent environment of proteins, protein complexes, small molecules and ions. This enables us to explore water-mediated interactions in a variety of contexts and to formulate computational models for biomolecular crowding in living cells.

Matthias Heyden, PhD

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School of Molecular Sciences

Dr. Matthias Heyden joined ASU's School of Molecular Sciences as an Assistant Professor in October 2017. He obtained his undergraduate degree in Biochemistry (2004) and his PhD (Dr. rer. Nat., 2020) in Chemistry from the Ruhr-University Bochum in Germany, where his research combined experimental spectroscopy with molecular dynamics simulations in the group of Martina Havenith. He then performed postdoctoral research at the University of California, Irvine, with Douglas Tobias (2010-2013), where he used molecular simulations to study membrane protein dynamics, protein aggregation and hydration dynamics. Prior to moving to ASU (2013-2017), Dr. Heyden led a junior research group at the Max Planck Institute for Coal Research (Kohlenforschung) in Mülheim an der Ruhr, Germany, where he developed computational tools to study biomolecular solvation and molecular crowding.

*ZOOM option available: https://asu.zoom.us/j/84890997395