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Colloquium
Dahlem Center for Complex Quantum Systems

DYNAMICS OF MOLECULES AND SPINS *IN SILICO*

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Abstract:

The functions of biological macromolecules (e.g., proteins, DNA) are dictated by the dynamics of these molecules as much as by their structures. In addition, the physical properties of molecular assemblies (e.g., lipid bilayers) depend on the dynamics of the solvent molecules surrounding them. Thus, one of the most ambitious aims in molecular biophysics—pursued both experimentally and computationally—is to understand these molecular dynamics in atomistic detail. Magnetic resonance spectroscopies, which exploit the presence of nuclear and/or electronic spins at the molecules of interest, are best suited to experimentally probe molecular dynamics under physiologically relevant conditions. In this talk, I focus on electron spin resonance (ESR) spectroscopy and dynamic nuclear polarization (DNP) in the liquid state. Continuous-wave ESR spectroscopy views the dynamics of proteins [1] and nucleic acids [2] through the eyes of local reporters carrying electron spins. The same electron spin "impurities" are employed in DNP to perturb the nuclear spins that are used as reporters. Consequently, DNP can probe the dynamics of water molecules at the surfaces of spin-labeled biological macromolecules [3] or lipid bilayers [4]. In spite of their unique utility, however, ESR and DNP experiments are oftentimes difficult to interpret unambiguously.

In this talk, I argue that the atomistic picture required for the conclusive interpretation of ESR and DNP data can be effectively obtained from molecular dynamics (MD) simulations. To support this claim, I first present a computational approach for calculating ESR spectra of spin-labeled biomolecules from MD simulations [5], and discuss applications to a protein [6] and a double-helical DNA. Then, I introduce a multiscale computational strategy for modeling the interactions between electron and nuclear spins on moving molecules, and show applications to DNP in simple liquids [7,8]. I discuss how the approach can be extended to DNP with spin labels on proteins and in lipid bilayers. Like any other model, MD simulations rely on approximations and have their own inherent limitations. Quantitative comparison with ESR and DNP experiments along the lines presented in the talk, therefore, offers a stringent validation of the simulations. Mechanistic understanding of how the dynamics of biological molecules affect their functions should ultimately emerge through such synergistic use of experiments and computations.

References

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