Bridging the gap between spectroscopic measurements and atomistic detail through simulations of biomolecular and spin dynamics

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Among the experimental methods that probe biomolecular dynamics, electron spin resonance (ESR) spectroscopy is extremely rich in information [1-3]. By monitoring the response of the electronic spins to perturbations from their immediate environment, the technique provides structural as well as dynamical information about the spin-bearing molecules. However, the interpretation of the obtained ESR spectra in terms of the underlying molecular properties is not always unambiguous.

In this talk I will argue that the atomistic picture required for the conclusive interpretation of ESR data can be effectively obtained from molecular dynamics (MD) simulations. One should keep in mind, however, that MD simulations, like any other model, rely on approximations and have their own inherent limitations. Therefore, it is essential to use the experimental data to validate the MD simulations while using the MD simulations to interpret the data. In my opinion, this can only be achieved by calculating the measured ESR spectra directly from the MD simulations. Naturally, such prediction of ESR spectra from "first principles" poses many challenges. Some of them, the successful solution of which will be illustrated for the spin-labeled protein T4 Lysozyme [4], include: efficient time-domain integrators for the quantal dynamics of the spins and for the global motions of the protein [5]; force field parameters for the nitroxide spin label [6]; a procedure for estimating a coarse-grained stochastic model from the MD trajectories, given the longer time scales required for the simulation of the ESR spectra [7].

In addition to probing the local dynamics of the biomolecule, spin labels attached to proteins can also be used to enhance the nuclear polarization of the nearby solvent molecules. This effect, known as dynamic nuclear polarization (DNP), has recently emerged as a way to study the dynamics of waters and lipids interacting with the protein surface. First applications of the proposed MD-ESR approach to DNP with free nitroxides in solution [8,9] will be presented, and the remaining challenges for its extension to DNP with spin-labeled biomolecules will be discussed.

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Biographical sketch

Deniz Sezer studied Electrical Engineering and Physics at Boğaziçi University, graduating in 1998. He obtained a Master's degree in Physics from the same university in 2000. Between 2000 and 2008 he was a graduate student in the Physics department at Cornell University, working successively at the following departments (institutions): Physics (Cornell University), Physiology and Biophysics (Graduate School of Medical Sciences of Cornell University), and Biochemistry and Molecular Biology (The University of Chicago). His PhD research was related to the calculation of electron spin resonance (ESR) spectra of spin-labeled proteins and lipids from molecular dynamics (MD) simulations. It was conducted in the group of Prof. Benoît Roux, who is mostly known for his computational work on potassium channels. The ESR part of the research was supervised by Prof. Jack Freed from the Dept. of Chemistry and Chemical Biology, Cornell University. Since 2008 Deniz is a postdoctoral researcher at the Institute for Physical and Theoretical Chemistry, University of Frankfurt. There, he continues to apply MD simulations to the quantitative and atomistic interpretation of ESR spectra. The results of his research have been published in *The Journal of Chemical Physics*, *Journal of Physical Chemistry B*, *The Journal of the American Chemical Society*, and *Physical Chemistry Chemical Physics*.