Mapping EPR Spin Label Conformations by the Simulated Scaling Method

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- In order to efficiently simulate spin label behavior when attached to the protein backbone we developed a novel approach that enhances local conformational sampling. The simulated scaling (SS) approach couples the random walk of a potential scaling parameter and molecular dynamics in the framework of hybrid Monte Carlo. This approach allows efficient barrier crossings between conformations. The method retains the thermodynamic detailed balance allowing for determination of relative free energies between various conformations. The accuracy of our method was validated by comparison with the recently resolved X-ray crystal structure of a spin labeled T4 lysozyme in which the spin label was in the interior of the protein. The presented approach has great potential in the general strategy of describing the behavior of the spin label using molecular modeling and using this information in the interpretation of EPR measurements in terms of protein conformation and dynamics.

Fig.1: Comparison between the crystal structure of the labeled T4 lysozyme (Xtal) and the structure predicted by the simulated scaling (SS2).