The Average Solvent Electrostatic Configuration QM/MM Approach for Flavoproteins

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Abstract

Flavins are versatile molecules that may exist in one of multiple redox and protonation states at physiological conditions. Flavins also have a rich photochemistry, and are capable of photoreduction, fluorescence, intersystem crossing, or internal conversion with relative efficiencies that depend on the protein hosting the flavin. The rich chemistry and photophysics of flavin underlies the wide array of catalytic and biological processes carried out by flavoproteins. QM/MM simulations have played and will continue to play an important role in improving our understanding of how proteins exert control over the properties and behavior of flavin. However, the investigation of chemical or excited-state processes in a dynamic protein environment is a challenge to QM/MM methods. The Average Solvent Electrostatic Configuration (ASEC) approach computes the structure and electronic properties of a QM subsystem self-consistently in a superposition of protein and solvent configurations obtained from molecular dynamics. Effectively, ASEC captures the potential imposed by a dynamic protein using a static model. In this presentation, we describe the ASEC approach and some of its applications to flavoproteins.