

Decrypting Photoinduced Electron Transfer in Cryptochromes: First-Principles Study

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Predictive and quantitative simulation of the photoinduced electron transfer (PET) in biological systems remains a challenge for modern computational chemistry. Proper characterization of ET requires (i) identifying the active players and establishing the efficient channels in the cascade of ET processes, and (ii) quantifying thermodynamics and dynamics of ET events. Here, we present the results of multi-level computational study of PET in cryptochromes, involved in circadian rhythms, growth and development processes in plants, and magnetosensory mechanism in migratory birds and insects [1]. We exploit multiple computational chemistry methods targeting various aspects of ET process at different levels from empirical coarse-grained description to atomistic QM/MM simulations. Specifically, we first use our recently developed web application [2] to identify all existing chains of aromatic amino acid side chains, cofactors and metabolites that can serve for efficient electron/hole hopping [3]. We then employ the accurate first-principles electronic structure methods to compute model parameters of sites of interest for an ensemble of local minima sampled with the classical MD and locally optimized at QM level in the presence of MM environment. The energetic parameters are extracted from QM/MM simulations using density functional theory, post-Hartree-Fock methods, and a recently developed extension of effective fragment potential approach to macromolecules (mEFP/BioEFP) [4, 5], which takes into account the effects of environment polarization, crucial in redox [5, 6] and charge transfer/separation processes. The computed from the first-principles parameters are utilized for evaluating efficiency of the first ultrafast step of competing conventional and alternative ET pathways [7, 8] by calculating the time scales and quantum yield from the population dynamics, using semiclassical path integral methods in combination with the accurate approach to describe relevant electronic-nuclear interactions [9]. The obtained results indicate that photoexcitation can initiate several competing ET channels, and contribute to understanding of complex PET processes accompanying formation of photoactivated state of the protein *in vivo* and *in vitro* in diverse systems including cryptochromes in plants, birds, and humans.

References

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