

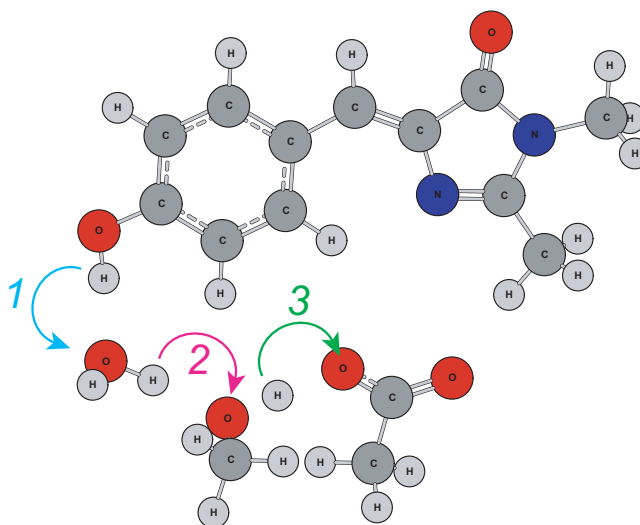
Quantum Mechanical Investigations of Proton Transfer Dynamics in Green Fluorescent Protein (GFP)

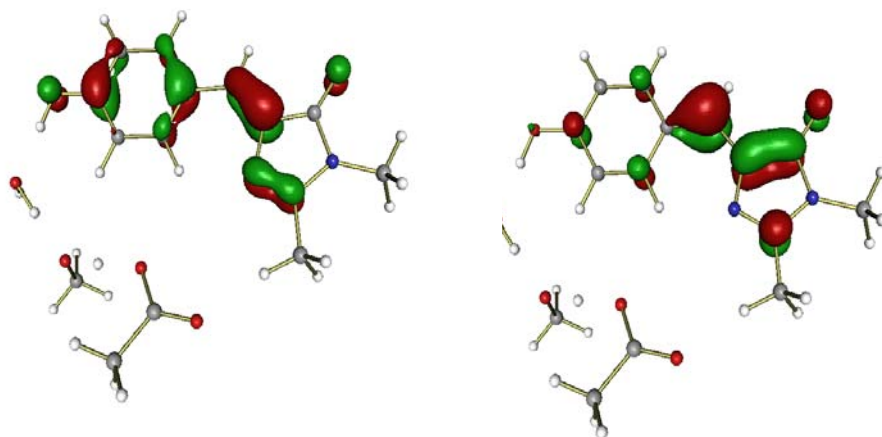
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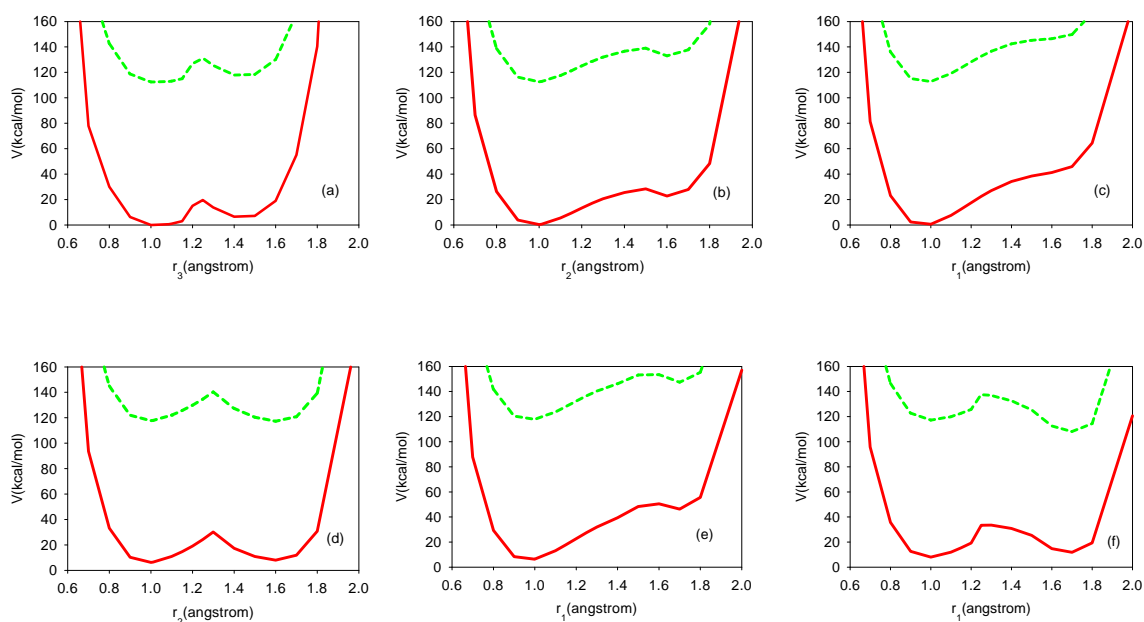
The green fluorescent protein (GFP) has emerged as a unique fluorescent label and has evolved into an extraordinarily important platform for biotechnological and cell biology applications. In GFP, the most important processes are the photo-absorption, the proton-transfers in the excited and ground state and the green fluorescence, which involve enormous photo-dynamics. Among them the proton transfers play a central role because *the photophysical properties of GFP are closely related to the mechanism of these proton transfers!* Given the lightness of proton and the corresponding quantum effects involved, these dynamics have to be considered within the framework of quantum mechanics. In this work we first characterize the excited and ground state potential energy surfaces (PESs) for the three proton transfers in a model GFP system based upon the chromophore, one water molecule and the surrounding residues Ser 205 and Glu 222. Based upon these PESs, we will then perform exact nuclear quantum dynamics simulations to explore the true pictures of the proton transfer dynamics in GFP.

Specifically we firstly optimize the ground and the first excited state structures for the neutral and anionic chromophore cases (four states labeled as A, A*, I and I*, respectively) using either density functional theory (DFT) or complete active space perturbation theory (CASPT2). The right figure shows one such optimized structure for ground state A with neutral chromophore. In this figure the three transferring protons are labeled as 1, 2, and 3. Based on these optimized structures, we then perform high level complete active space self-consistent field (CASSCF) and multi-reference configuration interaction (MRCI) calculations to generate three-dimensional potential energy surfaces for the three proton transfers. The following figure shows the two selected CASSCF molecular orbitals, i.e., the highest occupied molecular orbital HOMO (87a) and the lowest unoccupied molecular orbital LUMO (88a) for the state A case. The active space consists of six MOs: 83a to 88a. Analysis of the molecular orbitals indicate that the first excited state is of $^1\pi\pi^*$ character, which is the photoactive state. If further excitations (e.g., $^1\pi\sigma^*$) are of interests, we will need to include more MOs in our calculations.





In the following plots we show recent calculated potential energy curves for the three proton transfers right after the initial Franck-Condon excitation (keeping all other atom coordinates fixed at ground state A structure). Comparing (a)-(c) we can see that



on the excited state (the green dashed lines) the third proton will transfer first, and from (d) and (e) it is clear that the second one will then move, and finally the first proton moves after the third and the second ones have been transferred to their equilibrium positions in I^* state. The full three dimensional potential energy surface calculations and quantum dynamics simulations are under way.

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