Towards the Computational Design of Highly Fluorescent Rhodopsins

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The search for rhodopsins featuring large fluorescence quantum yields is an important topic in optogenetics.[1] In this theoretical work we propose a novel method for designing a specific protein environment that blocks the ultrafast isomerization[2] of a microbial rhodopsin, increasing its fluorescence quantum yield.

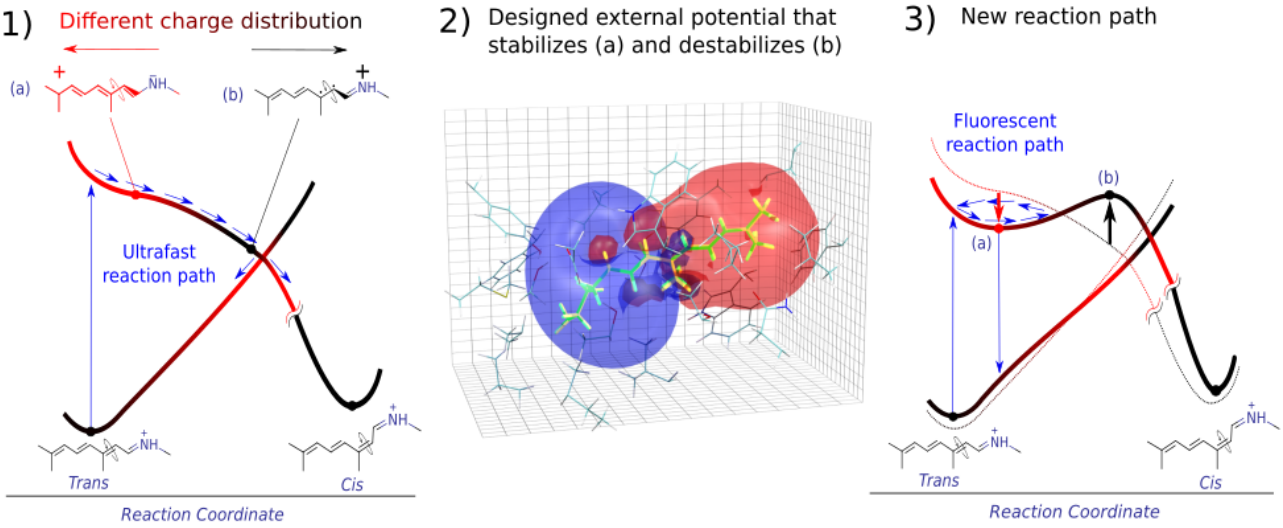

Figure 1: the ultrafast photoisomerization of rhodopsins occurs with a charge displacement in the chromophore along the reaction path (1). This feature is exploited to calculate an external potential (2) that can selectively stabilize/destabilize certain regions of the potential energy surface. Guided by the spatial topology of this potential, a new protein environment is imposed to the chromophore, effectively blocking the isomerization and creating a new fluorescent species (3).

The work has been performed employing high level QM/MM multiconfigurational models of Anabaena Sensory Rhodopsin with a simplified chromophore. First we present the application of the method on this minimal model and then we use the results as a guideline to propose a set of mutations for the full rhodopsin model.

We exploit a typical feature of these chromophores photoreaction paths:[3] the structures of an excited state intermediate have a different charge distribution with respect to the ones close to the conical intersection (1) and, as a consequece of this, they are affected differently by an external electrostatic potential. The method calculates the optimal charge distribution in space that stabilizes the structures of the Franck-Condon region and destabilizes the ones close to the conical intersection (2).

We study the effects and the consequences of this new potential applied on the system, via cavity sidechains polarization or full mutations. We show that it is possible to reshape the excited state potential energy surface (3), forming a new fluorescent species (a minimum) isolated from the conical intersection by a thermal transition state.

Funding: Scientifique PDR.T.0132.16 - FRFC. HFSP (RGP0049/2012) - USIAS Fellowship 2015, Universitè de Strasbourg.

Acknowledgements: A.V. thanks prof. Françoise Remacle for her kind support.

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