Calculating Free Energy Profiles and Rates for Thermal Isomerization in Retinal

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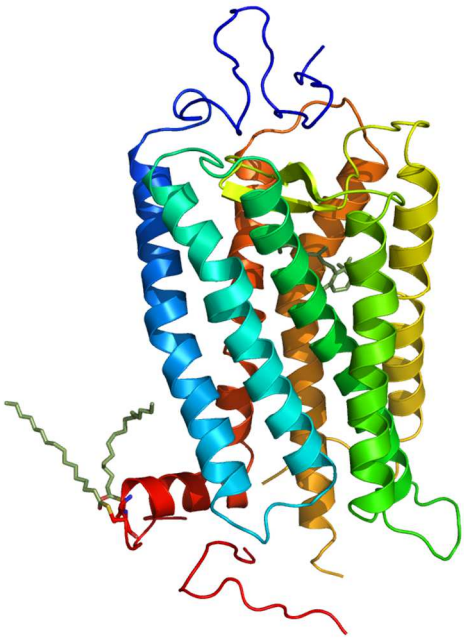

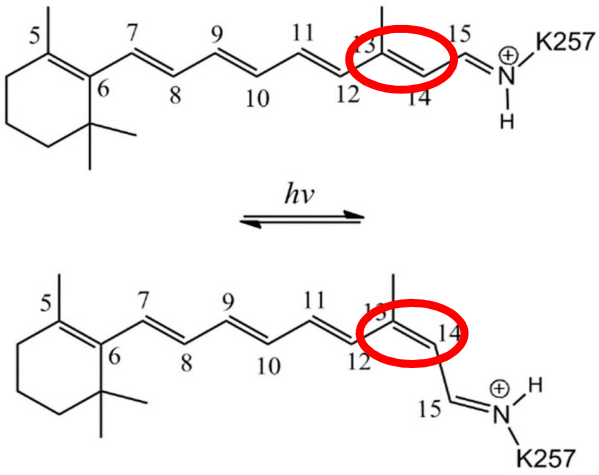

Rhodopsins are light-sensing membrane proteins ubiquitous in visual receptors of higher life forms, but also serving as antennas in light energy transformation and phototaxis of bacteria. Consisting of a protein molecule and a covalently bound cofactor called retinal, rhodopsins show an extremely wide adaptability of its spectral absorption characteristics and a precise selection of photoproducts steered by interaction of the retinal cofactor with the protein binding pocket[1].

While the photoactivation mechanism of retinal is a domain of intensive study in computational chemistry[2,3], less attention has gone to the thermal back-isomerization of the retinal cofactor in a later stage of the photocycle. To model this ground-state isomerization, ab-initio MD simulations have been carried out using the approximate quantum chemical method DFTB3[4]. In the initial part of the project, different state-of-the-art methods for calculation of free energy profiles and reaction rates are compared for the general case of the retinal cofactor, where both their computational feasibility as well as accuracy is considered.

[1] Schulten, Klaus, and Shigehiko Hayashi, *Cambridge University Press*, **2014**. 237-263.
[2] González-Luque, R., Garavelli, M., Bernardi, F., Merchán, M., Robb, M. A., & Olivucci, M. (2000) *Proceedings of the National Academy of Sciences*, 97(17), 9379-9384.
[3] Molnar, Ferenc, et al. *Journal of Molecular Structure:* THEOCHEM 506.1-3 (2000): 169-178.
[4] Gaus, Michael, Qiang Cui, and Marcus Elstner. *Journal of chemical theory and computation 7.4* (2011): 931-948.