

Mechanism of color tuning in retinal protein: SAC-CI and QM/MM study

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Received 10 February 2005; in final form 11 April 2005

Available online 16 September 2005

Abstract

The SAC-CI and QM/MM methods were applied to calculations of the absorption peaks of the five retinal proteins, bovine rhodopsin (Rh), bacteriorhodopsin (bR) in BR, K, and KL states, and sensory rhodopsin II (sRII). The results nicely agree with the experimental excitation energies and provided an insight into the mechanism of the large blue shifts in Rh and sRII from BR: geometric distortion in Rh and protein electrostatic effect in sRII. These results indicate that the present approach is useful for studying the excitation spectra and the mechanism of the color tuning in the retinal proteins.

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Photo-absorption is the initial event of vision, photo-sensing, and ion-pumps in retinal proteins [1,2]. The absorption maxima of the retinal proteins are well regulated in wide spectral range to furnish the photo-receptors with color sensitivity, whereas the proteins include a common identical chromophore, retinal. The electronic excitation energy of retinal is, therefore, controlled by interaction with the apoprotein, opsin [1]. In order to physically characterize the electronic excitation of retinal, several theoretical studies have been carried out using modern quantum chemistry methodologies [3–8]. These studies, however, have not yet succeeded in definitive elucidation of the color tuning mechanism due to a lack of sufficient methodological accuracy for evaluation of the excitation energy. In a very recent report, the CASPT2 method was applied to one of the retinal proteins, and the result has been significantly improved [9]. Theoretical approaches that make it

possible to accurately predict the excitation energy would open the door toward the rational protein design for the color tuning.

In this study, we applied the symmetry-adapted cluster-configuration interaction (SAC-CI) method [10–13] to the ground and excited states of retinal proteins: bovine rhodopsin (Rh), bacteriorhodopsin (bR) and its early intermediate states, K and KL, and sensory rhodopsin II (sRII), which possess varied absorption maxima and protein structures. The SAC-CI method treats sufficiently and consistently electron correlations for both the ground and excited states, and thus has been established as a reliable tool for calculating the excitation energy and excited state properties [13]. The computational program of the SAC-CI method is now available in GAUSSIAN03 package [14]. In order to obtain chemically reliable protein structures, we refined the X-ray crystallographic structures [15–17] through geometry optimization with an ab initio quantum mechanical/molecular mechanical (QM/MM) method [6–8] at the Hartree–Fock/AMBER94 [18] level of theory (see, [6–8]). Fig. 1 shows the optimized structure of the

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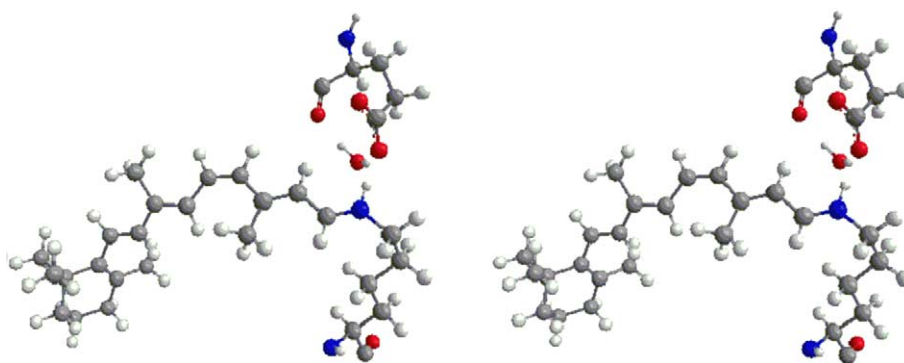


Fig. 1. The QM/MM optimized structure of retinal, Glu13, and Wat2b in Rh (stereo view).

chromophore-Lys296 moiety with the counter-ion group Glu13 and one water molecule, (Wat2b) [15,19], in Rh. In the SAC-CI calculations, the excitation energies were computed for the entire protonated Schiff base retinal chromophore with the side chain of lysine shown in Fig. 2 under the electrostatic (ES) field of protein represented by the point charges of AMBER94 [18]. The double- ζ plus polarization basis sets (D95(d)) were used for the C and N atoms in the π -system, and the double- ζ sets (D95) for the other atoms.

Table 1 summarizes the SAC-CI theoretical excitation energies and compares them with experimental values [1,2,20–25] and theoretical ones reported previously [3,6,9]. The SAC-CI calculations assign the first absorption peaks of all the proteins to the first excited states which exhibit large oscillator strengths (0.53–1.18). The main character of the first excited states is π – π^* excitation from HOMO to LUMO. The computed *absolute* values nicely agree with the experimentally observed absorption energies for *all* the systems studied, and are significantly improved compared to the previous theoretical ones [3,6]. The root mean square error is around 0.07 eV, and the maximum error is 0.14 eV for the K-state of bR. Recently, CASPT2 excitation energies for bovine rhodopsin have been reported and the result reproduced the experimental value

with the deviation of 0.1 eV [9]. However, our results would be the first report that the absorption energies of the retinal proteins are systematically reproduced. The results also support the reliability of the QM/MM optimized structures [6–8].

The highly accurate SAC-CI method now allows us to identify the molecular factors determining the spectral shifts between the proteins. The spectral shifts are analyzed in terms of geometric distortion of the chromophore itself due to protein confinement and ES interaction of the chromophore with the surrounding protein. Excitation energy difference for the isolated chromophores in the absence of the protein ES interaction (in vacuo) determines contribution of the geometric distortion and the rest of the overall shift is defined as the ES contribution.

Excitation energies of Rh (2.55 eV) and sRII (2.53 eV) exhibit similar large shifts from that of BR (2.22 eV), but the underlying mechanisms are completely different. In Rh, the geometric distortion gives rise to a blue shift by 0.21 eV, about two third of the overall blue shift, 0.33 eV. In fact, the geometries of chromophore are largely different from each other. The chromophore is in almost planar all-*trans* conformation in bR, whereas it is in strongly distorted 11-*cis* one in Rh. Strong torsion around a single bond C₆–C₇ appearing in Rh breaking a conjugation

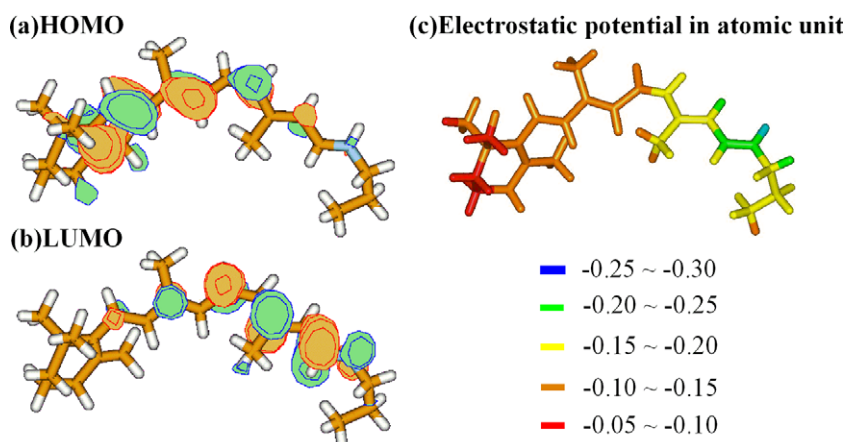


Fig. 2. (a) HOMO and (b) LUMO of retinal in Rh, and (c) the electrostatic potential by the protein environment of Rh.

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