Why 11-*cis*-Retinal? Why Not 7-*cis*-, 9-*cis*-, or 13-*cis*-Retinal in the Eye?

Sivakumar Sekharan[†] *and Keiji Morokuma*[†‡]

[†]Cherry L. Emerson Center for Scientific Computation and Department of Chemistry, Emory University, Atlanta, Georgia 30322, United States. [‡]Fukui Institute for Fundamental Chemistry, Kyoto University, 34-4 Takano, Nishihiraki-cho, Kyoto 606-8103, Japan.

One of the basic and unresolved puzzles in the chemistry of vision concerns the natural selection of 11-*cis*-retinal as the light-sensing chromophore in visual pigments. A detailed computational examination of the structure, stability, energetics, and spectroscopy of 7-*cis*-, 9-*cis*-, 11-*cis*-, and 13-*cis*-retinal isomers in vertebrate (bovine, monkey) and invertebrate (squid) visual pigments was carried out using a hybrid quantum mechanics/molecular mechanics (QM/MM) method. The results show that the electrostatic interaction between retinal and opsin dominates the natural selection of 11-*cis*-retinal over other *cis* isomers in the dark state. In all of the pigments, 9-*cis*-retinal was found to be only slightly higher in energy than 11-*cis*-retinal, which provides strong evidence for the presence of 9-*cis*-rhodopsin in nature. Mechanism of molecular rearrangements, energy storage, and origin of the bathochromic shift accompanying the transformation of rhodopsin to bathorhodopsin are also presented. 7-*cis*-Retinal is suggested to be an "upside-down" version of the all-*trans*-isomer because the structural rearrangements observed for 7-*cis*-rhodopsin from squid were found to be very similar to those for squid bathorhodopsin. The progressive red shift in the calculated absorption wavelength (λ_{max}) (431, 456, 490, and 508 nm for the 7-*cis*-, 9-*cis*-, 11-*cis*-, and 13-*cis*-retinal isomers) is due to the decrease in bond length alternation of the retinal. By using dehydro and dihydro-retinal analogues we classify the binding site of vertebrate rhodopsin as *rigid and stiff* and that of invertebrate rhodopsin as *malleable and ductile*.

References

[1] Sekharan, S.; Morokuma, K. *J. Am. Chem. Soc.* **2011**, DOI: 10.1021/ja208789h
[2] Sekharan, S.; Morokuma, K. *J. Am. Chem. Soc.* **2011**, *133*, 4734-4737.
[3] Sekharan, S.; Altun A.; Morokuma, K. *Annu. Rev. Comp. Chem.* **2011**, 7, 215-231.
[4] Sekharan, S.; Altun A.; Morokuma, K. *J. Am. Chem. Soc.* **2010**, *132*, 15856-15869.
[5] Sekharan, S.; Morokuma, K. *J. Phys. Chem. Lett.* **2010**, *1*, 668-672.
[6] Sekharan, S.; Altun A.; Morokuma, K. *Chem. Eur. J.* **2010**, *16*, 1744-1749.
[7] Sekharan, S.; Yokoyama S.; Morokuma, K. *J. Phys. Chem. B.* **2011.** (Submitted).