A combined strategy based on the computation of absorption energies, using the ZINDO/S semiempirical method, for a statistically relevant number of thermally sampled configurations extracted from QM/MM trajectories is used to establish a one-to-one correspondence between the structures of the different early intermediates (dark, batho, BSI, lumi) involved in the initial steps of the rhodopsin photoactivation mechanism and their optical spectra. A systematic analysis of the results based on a correlation-based feature selection algorithm shows that the origin of the color shifts among these intermediates can be mainly ascribed to alterations in intrinsic properties of the chromophore structure, which are tuned by several residues located in the protein binding pocket. In addition to the expected electrostatic and dipolar effects caused by the charged residues (Glu113, Glu181) and to strong hydrogen bonding with Glu113, other interactions such as pi-stacking with Ala117 and Thr118 backbone atoms, van der Waals contacts with Gly114 and Ala292, and CH/pi weak interactions with Tyr268, Ala117, Thr118, and Ser186 side chains are found to make non-negligible contributions to the modulation of the color tuning among the different rhodopsin photointermediates.

P. Campomanes, M. Neri, B. Horta, U.F. Röhrig, S. Vanni, I. Tavernelli, and U. Rothlisberger