A QM/MM-MD study on protein electronic properties: Circular dichroism spectra of oxytocin and insulin

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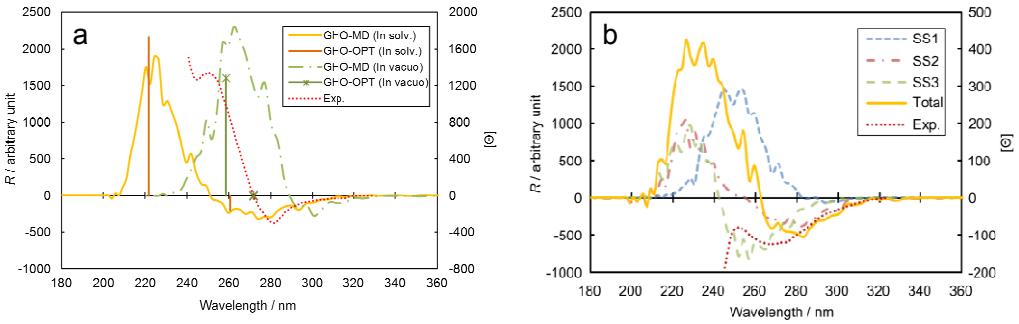
Molecular simulation is becoming more and more important method in the field of molecular biology. QM/MM (quantum-mechanical/molecular-mechanical) methods have been applied widely to analysis of electronic property of various biological molecules.

In this study, we carry out QM/MM molecular dynamics (MD) simulations for circular dichroism (CD) spectra based on the generalized hybrid-orbital (GHO) method [1-4]. The analytic energy gradient method for GHO-MP2 is employed for QM/MM MD trajectories, and the GHO-based second-order approximate coupled-cluster (GHO-CC2) model is used to calculate the CD spectra subject to the conformational changes of a protein.

CD spectra originating from chiral disulfide bridges are computed for oxytocin and insulin molecules in aqueous at room temperature. Appling the thermal fluctuation to the oxytocin molecule shifts the lowest CD peak to red. The protein environments in an oxytocin molecule have significant electrostatic effects on the chiral center, albeit it is compensated by solvent induced charges. These results give reasonable explanations of experimental observations [5].



CD spectra of (a) oxytocin and (b) insulin obtained by means of GHO and experiment.

[1] J. Jung, C.H. Choi, Y. Sugita, S. Ten-no, *J. Chem. Phys.* **127** 204102 (2007).

[2] J. Jung, Y. Sugita, S. Ten-no, *J. Chem. Phys.* **132** 084106 (2010).

[3] Y. Kawashima, H. Nakano, J. Jung, S. Ten-no, *Phys. Chem. Chem. Phys.* **13** 11731 (2011).

[4] Y. Akinaga, J. Jung, S. Ten-no, *Phys. Chem. Chem. Phys.* **13** 14490 (2011).

[5] Y. Kitagawa, Y. Akinaga, Y. Kawashima, J. Jung, S. Ten-no, *Chem. Phys.* in press.