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Estimation of Non-covalent Interactions with a New Efficient Dispersion Corrected HF Approach

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An accurate estimation of binding interaction energy associated with complex formation of a ligand and protein is important for understanding the binding mechanism and rational drug design. Although the dispersion is one of the most important interaction as well as hydrogen-bonding and electrostatic ones, its evaluation based on molecular orbital methods is still not easy task. In this study, we examined our newly proposed dispersion correction for the Hartree–Fock method (HF-D) on several complexes of biologically relevant molecules.

We selected a set of eighteen small non-covalently bonded complexes: six dispersion-dominated (DISP), nine hydrogen-bonded (HB), and three other types of complexes (others). The geometry of each complex was fully optimized at the MP2/6-311++G(d,p) level. In our HF-D approach, the HF energy was corrected by introducing damped empirical dispersion energy term ($-f(R)C_6/R^6$) using a sigmoid-type function. We calculated interaction energies using HF-D and the counterpoise corrections were employed to reduce the basis set superposition errors (BSSE). The performance of HF-D were confirmed by comparing with post-HF methods (CCSD(T) and MP2) and several DFT based methods (M06-2X and Grimme's dispersion corrected B3LYP-D2 and B2PLYP-D).

Figure 1 shows the mean absolute error (MAE) of interaction energies estimated from the CCSD(T)/aug-cc-pVTZ reference values. The overall performance of HF-D is excellent; as expected, HF-D more accurately reproduces interaction energies for all three types of complexes than the conventional HF method. It should be noted that MAE of HF-D shows significantly smaller than that of more expensive MP2 in all complexes (MAE(overall) = 0.40 and 1.01 kcal/mol, respectively). Although M06-2X gives the best performance (MAE(overall) = 0.30) among the tested methods, HF-D is competitive with the M06-2X and other dispersion corrected B3LYP-D2 and B2PLYP-D. HF-D approach is probably effective and practical, compared with time-consuming post-HF and DFT methods to quantitatively evaluate the interaction energy of large molecular systems such as complex of a ligand with protein. We will also discuss the binding mechanism of a series of benzenesulfonamides with carbonic anhydrase using LERE-QSAR procedure [1] in which HF-D approach is introduced for estimation of binding interaction energy.

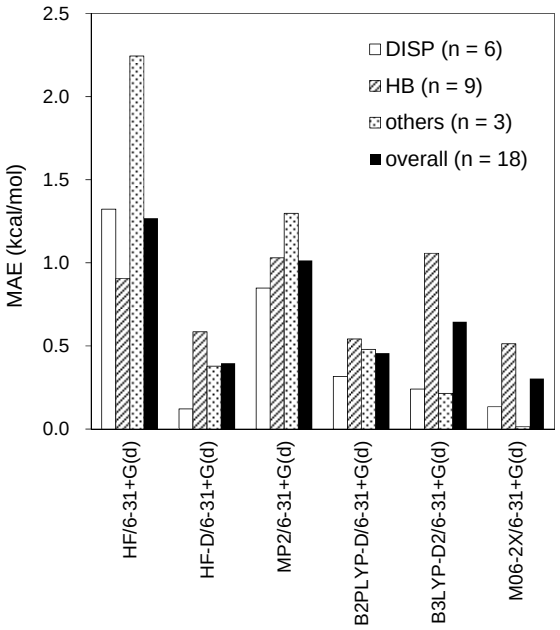

Figure 1. Comparison of the performance of HF-D and other methods for non-covalently bonded complexes.

[1] T. Yoshida, Y. Munei, S. Hitaoka, H. Chuman. *J. Chem. Inf. Model.*, **2010**, *50*, 850–860.