[P9] Estimation of Non-covalent Interactions with a New Efficient Dispersion Corrected HF Approach

Tatsusada Yoshida, Akira Mashima, Katsunori Sasahara, Hiroshi Chuman

Laboratory of Theoretical Chemistry for Drug Discovery, Institute of Health Biosciences, The University of Tokushima, Graduate School, 770-8505, Tokushima, Japan

An accurate estimation of binding interaction energy of complex formation between a ligand and a 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 work, we examined our newly proposed dispersion correction for the Hartree–Fock method (HF-D_{tq}) [1] on several complexes of biologically relevant molecules.

We selected a set of 68 small non-covalently bonded complexes: 40 dispersion-dominated (DISP), 22 hydrogen-bonded (HB), and 6 other types of complexes (OTHERS). Some of the 68 complexes were taken from the S22 benchmark set [2] and a part of the S66 [3] one. The geometry of each complex was optimized with CCSD(T)/cc-pVTZ and MP2/(aug-)cc-pVTZ. We calculated complexation energies ($E_{complex}$) using HF-D_{tq}, and the counterpoise corrections were employed to reduce the basis set superposition errors (BSSE). In our HF-D_{tq} approach, the HF energy was corrected by introducing damped classical dispersion energy term using a sigmoid-type function; $E_{complex}(\text{HF-D}_{tq}) = E_{complex}(\text{HF}) - s_6 \Sigma [a_1 + (1 - a_1) / (1 + \exp(-\eta(R_0/R_{ij} - shift)))] c^{ij}_6 / R^6_{ij}$. The performance of HF-Ds and DFT(-D)s (HF-D_{tq}, HF-D_3, B3LYP-D_3, B3LYP-D_3(BJ), B2PLYP-D_3, B2PLYP-D_3(BJ), M06-2X, and M11) as to the 68 complexes was compared with higher level calculations (CCSD(T)/complete basis set (CBS) and CCSD(T)/aug-cc-pVTZ).

Figure 1 shows the mean absolute error (MAE) of $E_{complex}$ estimated from 'the golden standard' CCSD(T) values. The HF-D_{tq} nicely reproduces $E_{complex}$(CCSD(T)) for all three types of complexes. It should be noted that MAE of HF-D_{tq} shows significantly smaller than that of more computationally expensive MP2 in all complexes (MAE(ALL) = 0.32 and 1.20 kcal/mol, respectively). The MAE of HB is slightly lager than that of DISP, because $|E_{complex}|$ of HB is on avergae larger than that of DISP. Although B3LYP-D_3(BJ) and B2PLYP-D_3(BJ) give the most excellent performance (MAE(ALL) = 0.26 and 0.26 kcal/mol, respectively) among the tested methods, probably because of the additional D_3(BJ) correction. The performance of HF-D_{tq} is nearly competitive with those of B3LYP-D_3 and B2PLYP-D_3. The computational cost of the D_{tq} correction is negligible. HF-D_{tq} approach is simple, but probably effective and practical compared with time-consuming post-HF and DFT methods in evaluating quantitatively the interaction energy of large molecular systems such as complex of a ligand with protein. We will also discuss the introduction of HF-D_{tq} to the LERE-QSAR analysis [4].

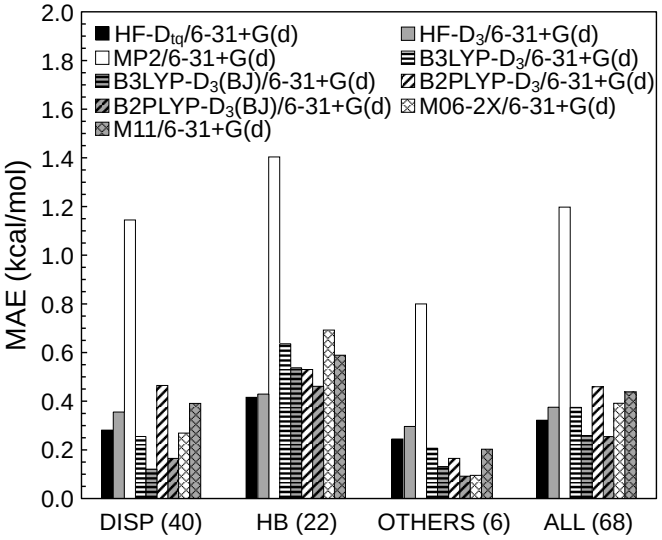

Figure 1. Performance of HF-D_{tq} for 68 non-covalent complexes.

Bibliography:

[1] Yoshida. T; Mashima. A; Sasahara. K; Chuman. H. Bioorg. Med. Che. Lett. 24 (2014) 1037–1042.
[2] Jurečka. P; Šponer. J; Černý. J; Hobza. P. Phys. Chem. Chem. Phys. 8 (2006) 1985–1993.
[3] Řezáč. J; Riley. K. E; Hobza. P. J. Chem. Theory Comput. 7 (2011) 2427–2438.
[4] Hitaoka. S; Chuman. H. Pestic. Sci. 38 (2013) 60–67.