Spatial distribution of QM based interaction energy between amino-acids and probe molecules

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Quantum chemical calculation and molecular dynamics simulation are used for prediction of the protein-ligand binding affinity [1]. First one is used as QM based single point calculation, which can deal with the molecular interactions accurately but have the problems in sampling. Second one is performed with MM force field, which has the problem in accuracy of interactions. Thus we have to use both QM based and MM based methods and select better one for adjusting the situation. For this purpose, we have to know how different between QM and MM for each situation. Current comparative studies between QM and MM, are limited on the potential minimum or along few directions. Thus, in this study, we evaluated interaction energies between amino acid residues and probe molecules with spatially comprehensive arrangement. We employed B97D/aug-cc-pVDZ method [2] because we confirmed this method provides only small deviation from higher level quantum chemical calculation (CCSD(T)/CBS) [3]. We compared QM based interaction energy and MM force field energy (MMFF94x) for each amino acid and different types of probe molecules. Figure 2 represents example of calculation for interaction energy PHE side chain and cation probe (NH_4^+). QM calculation provides spatially larger attractive region and deeper potential minimum. Comparison between various types of interaction will be discussed.

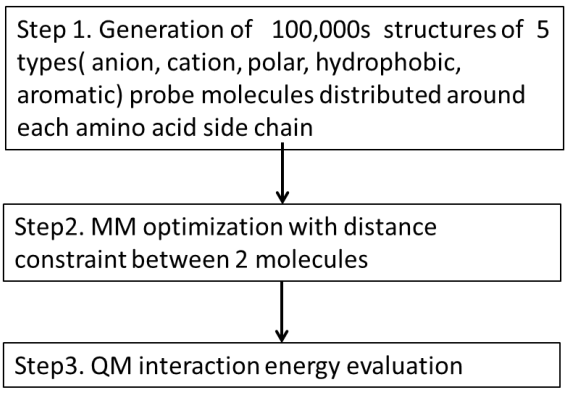

Figure1. Evaluation scheme of spatial distribution of QM based interation energy.

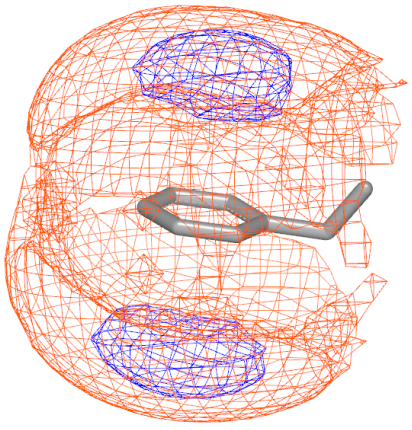

Figure2. Contour plot of interaction energy (Phe-NH_4^+) with QM(B97D:red) and MM(MMFF94x:blue).

[1] H. Watanabe et al. CBI Journal 10 (2010) 32-45.
[2] S. Grimme, J. Comput. Chem. 27, (2006), 1787-1799.
[3] The Benchmark Energy & Geometry Database (http://www.begdb.com/)