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FMO 法と DFTB 法と PCM 法の組み合わせ（FMO-DFTB/PCM）

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The Fragment Molecular Orbital Method Combined with Density-Functional Tight-Binding and the Polarizable Continuum Model

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Most biochemical processes occur in solution, and an appropriate treatment of solvent effects in simulations is essential. In this study,[1] the energy and its analytic gradient are formulated for the fragment molecular orbital (FMO) method[2] combined with the density-functional tight-binding (DFTB)[3] and the polarizable continuum model (PCM).

The total energy in FMO2/PCM method is

$$E^{\mathrm{FMO/PCM}} = \sum_{I}^{N} E_I'' + \sum_{I>J}^{N} (E_I'' - E_I'' - E_J'') + \sum_{I>J}^{N} \Delta E_{IJ}^{V} + G^{\mathrm{cdr}} + G\,,$$

where *N* is the number of fragments, and is the internal solute energy of fragment *X*. The fourth term is the non-electrostatic term computed as a sum of the cavitation, dispersion, and repulsion free energies. The fifth term is the electrostatic solute-solvent interaction energy,

$$G = \frac{1}{2}\mathbf{V}^{\mathrm{T}}\bar{\mathbf{q}}\,,$$

where $\bar{\mathbf{q}}$ is apparent surface charges (ASCs) and they are obtained by

$$\bar{\mathbf{q}} = \mathbf{C}^{-1}\mathbf{V}\,,$$

where **C** is a square matrix that depends on the tessera positions and the choice of a PCM model, and **V** is the electrostatic potential on tesserae.

The analytic gradient of FMO-DFTB/PCM<1> is obtained by differentiating the above total energy expression:

$$\frac{\partial E}{\partial a} = E^{a} + G^{a} + \frac{\partial G^{\mathrm{cdr}}}{\partial a} + \widetilde{R^{a}}\,,$$

where the first and second terms are the integral derivative contributions of *E* and *G*, and the last term represents the sum of orbital response contributions from *E* and *G*, and they are obtained by solving the self-consistent Z-vector equation.[4] The method outlined here, FMO-DFTB/PCM, was implemented in a development version of GAMESS-US.

The accuracy of FMO-DFTB/PCM is demonstrated in comparison with unfragmented

calculations and numerical gradients. The instability in the description of proteins (PDB: 1UAO) using density functional theory (DFT) and DFTB is analyzed for both unfragmented and FMO methods. In the gas phase, GGA functionals could not reach SCF convergence because of small gap between occupied and virtual orbitals. Adding solvent effects considerably increases the gap between occupied and virtual orbitals and stabilizes convergence.

The cause of the instability is shown to be charged residues from an analysis using the FMO approach. The structure of molecular orbital levels in monomer calculations highlights the problem of, what we call, charge transfer states in dimers. Consider two highest occupied orbitals in fragments *I* and *J* (Fig. 1A), which happen to have the HOMO in *J* above the LUMO in *I*. This electronic structure represents a ‘‘negative gap’’ in FMO. When the initial set of dimer orbitals is constructed by taking occupied monomer orbitals (Fig. 1B), according to the Aufbau principle in the dimer the HOMO of *J* is unoccupied, and instead, the LUMO of *I* is occupied. This means that two electrons are transferred from *J* to *I* (Fig. 1C). This problem is particularly severe in the gas phase when long-range functionals are not used.

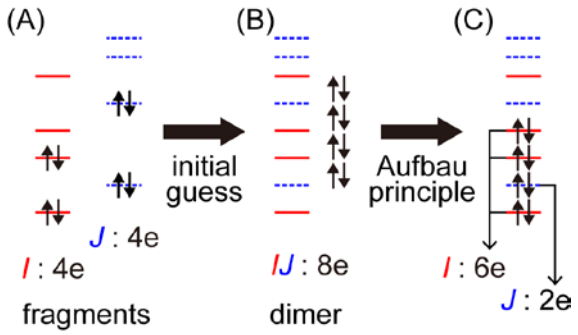

Fig 1 Origin of the problem of charge transfer states in dimers. (A) Orbital energies in monomers *I* (red solid lines) and *J* (blue dashed lines). (B) Initial levels in dimer *IJ*. (C) Population of initial levels in dimer *IJ*.

The pair interaction energies calculated using FMO-DFT and FMO-DFTB in solution are shown to be correlate, whereas the latter method is 4840 times faster than the former for a protein consisting of 1961 atoms. The structures of five proteins (containing up to 3578 atoms (PDB: 2CGA)) optimized using FMO-DFTB/PCM agree reasonably well with experiment. A single point energy + gradient evaluation for the 2CGA protein took 195 seconds on a single PC (six cores).

References

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