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Electrostatic Interaction of the Electrostatic-Embedding and Mechanical-Embedding Schemes for QM/MM Calculations

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Abstract: The geometries of the system including two waters have been optimized by the full quantum calculations with the constraints of the O—O distance. The HF and B3LYP density function levels with STO-3G, 6-31G, 6-31G*, and 6-31++G** four basis sets were used in the optimizations. At the optimized geometries, the QM/MM single point interaction energies of the electrostatic-embedding and mechanical-embedding schemes were calculated. The QM/MM interaction energies were compared with the full quantum calculations. The results reveal that the basis sets could be important in the QM/MM calculations. The QM/MM method of the two schemes could not accurately describe the energy of the structure. The electrostatic and VDW interaction energy between QM and MM regions of the electrostatic-embedding scheme is better than that of the mechanical-embedding scheme at the 6-31G and 6-31G* levels. At the 6-31++G** level, the energies of the two schemes are in good agreement with the full quantum calculations. Present investigation suggests that the electrostatic-embedding scheme could be more suitable in the QM/MM simulations of very large systems, e.g. emzyme reaction. The cutoff radius of the electrostatic-embedding scheme is at least 25a_0.

AMS subject classifications: 80A50, 92C40

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Combined quantum-mechanical and molecular-mechanical (QM/MM) method has been widely applied in the investigations of the complex large systems over the past decade [1-5]. In the method, the full system is partitioned into the reactive region which is treated at the quantum mechanical (QM) level and the region of surrounding environment which is treated at the molecular mechanics (MM) level. In principal, the approach combines the QM accuracy with the MM low computational cost. The total QM/MM energy of the full system can be given by the sum of the QM energy, the MM energy, and the QM/MM interaction energy between the QM and MM regions [5].

$$E(\text{QM/MM}) = E(\text{QM}) + E(\text{MM}) + E_{int}(\text{QM–MM}), \quad (1)$$

E(QM), E(MM) and E_{int}(QM–MM) correspond to QM region energy, MM region energy, and inteaction energy between QM and MM regions, respectively. E(QM) can be obtained by the the calculations of electronic-structure program. E(MM) is given by the compuations of MM force fields. The calculation of E_{int}(QM–MM) is more complex and a center of the QM/MM methodology. The interaction energy includes the bonding interactions, van der Waals (VDW) interactions, and electrostatic interactions. As the QM/MM boundary cutting the covalent bond, the special treating models (e.g. link atom [6-9], localized orbital [10-13], pseudo-atom model [14-16] *etc*) are required to saturate the dangling bond. In general, the van der Waals interactions are evaluated by the MM calculations. The treatment of electrostatic interactions has the different schemes in various QM/MM calculations. The schemes have been classified by Bakowies and Thiel into two general types which refer to the mechanical-embedding (ME) and electrostatic-embedding (EE) [17].

In ME scheme, QM energy is calculated in the gas phase. The electrostatic interactions between the QM and MM regions are computed by Coulomb's law of the MM level using atomic charges on the QM and MM atoms. In EE scheme, the point charges on the MM atoms are involved in QM Hamiltonian operators. It means that the electrostatic interaction of the scheme between the QM and MM regions is calculated at QM level. In the treatment, QM region is polarized by MM region, but MM region is not polarized by QM region. Recently, several mutual polarized embedding schemes were developed to allow the polarization of QM and MM regions with each other [18-23]. Theoretically, the electrostatic interaction computed by the EE scheme is more accurate than that of the ME scheme. Nevertheless, the MM partial atomic charges are generally used in the QM/MM schemes to describe the MM atomic charge density because most MM force fields contain the charge parameters to compute the electrostatic interactions at the MM level. The MM partial atomic charges are a part of the parameters for a whole MM force field which also includes the van der Waals parameters etc. It suggests that the charge parameters are fitted to calculate the