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New implementation of the generalized hybrid orbital method for accurate energetics in biological molecules

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We develop novel QM/MM methods based on a frozen orbital treatment named the generalized hybrid orbitals (GHO)^{1,2}. In the GHO method, sp^3 hybridized orbitals are generated for each boundary atom. One of them is used as an active orbital quantum mechanically and the rest three are used as frozen auxiliary orbitals. The original GHO method parameterizes the occupation numbers

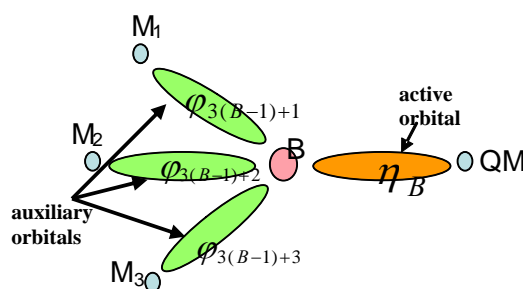


Figure 1

of auxiliary orbitals only from the partial charges of boundary atoms. The occupation number assigned to each auxiliary orbital is chosen to be $1 - \frac{q_B}{3}$, where q_B is the MM partial charge of the boundary atom, so that the charge is equally distributed over the three auxiliary orbitals.

In our new implementation³, we introduce a novel technique which makes use of the charge equalization scheme to assign the occupation numbers of the auxiliary orbitals. The occupation number of the auxiliary orbital α pointing to the MM atom M connected to the boundary is

$$n_\alpha = 1 + \frac{EN_{C_{sp^3}} - EN_M}{2(H_{C_{sp^3}} + H_M)}, \quad (1)$$

where EN and H are the electronegativity and hardness, respectively⁴. The occupation numbers are scaled in each domain such that the neutrality of the system is satisfied. We also develop an orthogonalization procedure for the auxiliary orbitals of different boundary atoms.

The analytic gradient method based on the new GHO energy expression has been implemented. The modified Fock equation is

$$\sum_q F_{pq} C_{qi} = \varepsilon_i \sum_q S_{pq} C_{qi} + \sum_{\alpha} \sum_q^{aux.} S_{pq} A_{q\alpha} \omega_{\alpha i} . \quad (2)$$

The gradient with respect to the coordinate of an atom is

$$\frac{\partial E}{\partial R_a} = \sum_{pq} P_{pq} \frac{\partial h_{pq}}{\partial R_a} + \frac{1}{2} \sum_{pqrs} P_{pq} P_{rs} \frac{\partial}{\partial R_a} [(pq | rs) - \frac{1}{2} (pr | qs)] + \sum_{pq} \frac{\partial P_{pq}}{\partial R_a} F_{pq} \quad (3)$$

where the last term of Eq. (3) is given by

$$\sum_{pq} \frac{\partial P_{pq}}{\partial R_a} F_{pq} = - \sum_{pq} W_{pq} \frac{\partial S_{pq}}{\partial R_a} - 4 \sum_i \sum_{\alpha}^{d.o.} \sum_{pq} C_{pi} S_{pq} \frac{\partial A_{q\alpha}}{\partial R_a} \omega_{\alpha i} + 2 \sum_{pq} \sum_{\alpha}^{aux.} n'_{\alpha} \frac{\partial A_{p\alpha}}{\partial R_a} F_{pq} A_{q\alpha} , \quad (4)$$

and the energy-weighted density is

$$W_{pq} = 2 \sum_i \sum_i^{d.o.} C_{pi} C_{qi} \varepsilon_i + 4 \sum_i \sum_{\alpha}^{d.o.} C_{pi} A_{q\alpha} \omega_{\alpha i} . \quad (5)$$

The new implementation improves the accuracy of the interaction energy between polar molecules. Figure 2 shows that our new method MGHO³ reproduces the full QM result better than GHO for the interaction between the alanine dipeptide and water molecules.

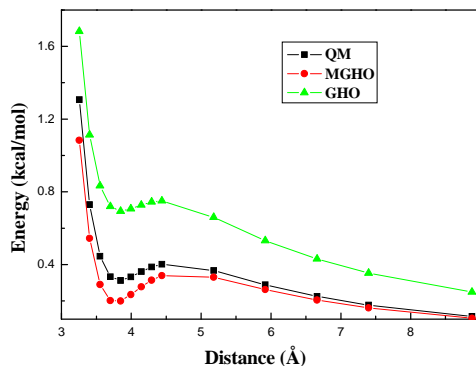


Figure 2

We carry out calculations of the new GHO scheme on the catalytic subunit of cAMP-dependent protein kinase (PKA). PKA is known to catalyze the phosphorylation reaction which plays a critical role in cellular regulation and signal transduction. From the geometry optimization and specific energy calculations, we investigate the effects of the enzyme in detail.

Reference

1. J. Gao, P. Amara, C. Alhambra, and M. J. Field, *J. Phys. Chem. A* **102**, 4714 (1998).
2. J. Pu, J. Gao, and D. G. Truhlar, *J. Phys. Chem. A* **108**, 632 (2004).
3. J. Jung, C. H. Cheol, Y. Sugita, and S. Ten-no, *J. Chem. Phys.* to appear (2007).
4. D. Bergmann and J. Hinze, *Angew. Chem. Int. Ed. Engl.* **35**, 150 (1996).