Abstract for an Invited Paper
for the MAR07 Meeting of
The American Physical Society

Modeling Enzymatic Reactions in Proteins.

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We will discuss application of our density functional (DFT)-based QM/MM methodology to modeling a variety of protein active sites, including methane monooxygenase, myoglobin, and cytochrome P450. In addition to the calculation of intermediates, transition states, and rate constants, we will discuss modeling of reactions requiring protein conformational changes. Our methodology reliably achieves small errors as a result of imposition of the QM/MM boundary. However, the accuracy of DFT methods can vary significantly with the type of system under study. We will discuss a novel approach to the reduction of errors in gradient corrected and hybrid DFT functionals, using empirical localized orbital corrections (DFT-LOC), which addresses this problem effectively. For example, the mean unsigned error in atomization energies for the G3 data set using the B3LYP-LOC model is 0.8 kcal/mole, as compared with 4.8 kcal/mole for B3LYP and 1.0 kcal/mole for G3 theory.