Exploring Chemical Reactivity in Biological Systems with hybrid QM/MM Methods

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We present a hybrid Quantum Mechanics Molecular Mechanics (QM/MM) implementation developed to deal with large molecular complexes. It is particularly suited to study relatively large systems in which the environment effects are important, as in the case of an enzyme active site immersed in a protein matrix, or a solute in a condensed phase. In the QM/MM scheme, a region of the system receives a quantum-mechanical description, while the environment is treated at the molecular mechanics level using the biomolecules Amber force field. The QM calculations are performed with the SIESTA code, a DFT scheme based on finite basis sets and pseudopotentials, which makes the overall implementation very efficient. We will present results obtained with this scheme for the following problems:
(i) conversion of chorismate to prephenate catalyzed by the enzyme chorismate mutase of *Bacillus Subtilus*. (ii) modulation of oxygen affinity in heme proteins by proximal, distal and dynamical effects. (iii) detoxification of nitric oxide by the truncated hemoglobin N of *Mycobacterium Tuberculosis*.