A benchmark for the size of the QM system required for accurate hybrid QM/MM calculations on the metal site of the protein copper, zinc superoxide dismutase

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The protein superoxide dismutase 1 (SOD1) is a copper and zinc-binding protein that has been implicated in the pathogenesis of amyotrophic lateral sclerosis (ALS). The Zn(II) binding to SOD1 is critical for the stability of the protein, and has been by itself implicated in ALS pathogenesis. Hence, the quantum mechanical (QM) study of the Zn(II)-site of SOD1 is relevant for understanding ALS. The hybrid QM-molecular mechanics (QM/MM) approach commonly employed for the QM study of proteins is highly dependent on the size of the sub-system treated quantum-mechanically. The size of the QM system also determines the computational feasibility of a given method. In the present work, we compare optimized geometries for the metal site and Zn(II) dissociation energies obtained with a QM/MM methodology employing different sizes for the QM sub-system. We find that geometries converge rapidly to RMSDs of around 0.3 Å, and fails to converge further, while a QM system of 480 atoms was required for converging the Zn(II) interaction energy of SOD1 to within 5 kcal*mol?1, and a 611-atoms QM system for a 1 kcal*mol?1 convergence with respect to our reference, 1280 QM-atoms system. [Figure not available: see fulltext.].

QM-system size

QMMM

SOD1

copper zinc superoxide dismutase

zinc

copper

protein binding

superoxide dismutase

Article

dissociation

energy

geometry

priority journal

quantum mechanics

chemistry

conformation

molecular dynamics

quantum theory

Copper

Molecular Conformation

Molecular Dynamics Simulation

Protein Binding

Quantum Theory

Superoxide Dismutase

Zinc