Structure and function of the iron–sulfur protein Rubredoxin, studied by QM/MM methods

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Abstract

Iron–Sulfur proteins are an important class of electron transfer protein acting as electron sinks for many biological reactions. One such iron–sulfur protein is Rubredoxin (Rd) which has a high spin iron centre, tetrahedrally coordinated to four cysteine sulfurs. We have explored the redox chemistry of Rd using both density functional theory (DFT) and semi–empirical methods. These latter methods require quite modest computing resources, but their accuracy is often suspect, particularly when the molecule contains a transition metal atom. However, a possible way forward is to develop parameters for use in semi–empirical MO studies that are tailored for a particular chemical situation, the so–called specific reaction parameters SRP [1]. We first describe a possible strategy to extend this approach to transition metal complexes [2]. Based on fitting to DFT data for redox site analogue, a PM3 parameter set for iron has been developed, which is appropriate for the active site of iron sulfur proteins having a single iron atom, and further tested on similar molecules. The use of these parameters within a two layer ONIOM treatment of the protein Rd, yields accurate predictions of the effect of the protein on both Fe–S bond lengths and inner sphere reorganization energies [3]. We also describe calculations on similar proteins in which the central metal atom or the cysteine ligands are mutated

References

[1] Rossi, I., and Truhlar, D.G. *Chem. Phys. Lett*. **1995**, 233, 231–236.

[2] Mohr, M., McNamara, J.P., Wang, H., Rajeev, S.A., Ge, J., Morgado, C.A., and Hillier, I.H. *Faraday Discuss*. **2003**, 124, 413–428.

[3] Sundararajan, M., McNamara, J.P., Hillier, I.H., Wang, H., and Burton, N.A. *Chem. Phys. Lett.* **2005**, 404, 9–12.