Calculation of Redox Potentials in Iron-Sulfur Proteins

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There are many redox proteins having the same redox-active cofactor bound, but differing in redox potential. How the protein modulates the redox potential of the cofactor is not well understood.

We developed a procedure to compute redox potentials in proteins accurately by first principle methods. Our approach is to combine quantum mechanical calculations on the DFT level with continuum electrostatic methods. Our results on the iron-sulfur protein Ferredoxin show excellent agreement with experiments.

By x-ray crystallography it was observed, that a peptide bond can be in two conformations in the reduced state, but only one conformation in the oxidized state. Our calculations provide insights into the energtics of this structural change in Ferredoxin and how it influences the redox potential. Paramagnetic NMR studies determined the iron of the 2Fe2S center which changes its redox state. Our calculations are in agreement with experiments, but the two reduced states only differ in energy, when polarization effects of the surrounding are included properly. Thus, a sufficiently large quantum region or a Self-Consistent Reaction Field method need to be considered. The redox potential can be decomposed into its contributions to judge their relative importance.

Taking into account the experimental difficulties in measuring an “absolute” redox potential accurately and the theoretical challenge in computing it, the agreement obtained with both methods is promissing.