Evaluate the Shift of Redox Potential of [Fe_4S_4] Clusters in Protein Tuned by Environment Using S K-edge XAS

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A large family of metalloproteins contains [Fe_4S_4] clusters, which have different oxidation states and a wide range of redox potentials, thus each can have unique physiological functions. Our previous studies showed that the potential of the ironsulfur cluster had a good correlation with the Fe-S bond covalencies, which can be directly measured by S K-edge XAS. A series of perturbations, including lyophilization, unfolding the protein, and binding with DNA were made on ironsulfur proteins to understand how the protein environment can tune the redox potentials. In Ferredoxin (Fd), which has the [Fe_4S_4] cluster exposed at the surface, solvent water H-bonds weaken the Fe-S bond, thus stabilize the reduced state. While in HiPIP, which has the [Fe_4S_4] cluster buried, lacking of strong H-bonds can significantly increase the redox potential, and removing of solvent water can increase the H-bonds intensities from the protein backbones, which lead to an inverse solvent effect than Fd. Furthermore, binding with DNA can introduce negative charge next to the [Fe_4S_4] cluster, which stabilizes the oxidized state of the protein.