Speaker: Simone Raugei (PNNL)

Redox Versatility of [4Fe-4S] Clusters: A Computational and Statistical Inquiry

Iron–sulfur clusters, particularly [4Fe–4S] cubanes, are central to biological redox chemistry, yet their reduction potentials span over 1 V despite high structural conservation. To rationalize this variability, I will begin with high-level correlated calculations that provide benchmarks for electronic structure, spin-state energetics, and redox behavior—highlighting the role of electron correlation and the limitations of approximate DFT treatments. Building on this foundation, I will examine how symmetry-resolved distortions and directional electrostatic perturbations modulate vertical electron affinities. Electrostatics emerge as the dominant drivers of redox tuning, with geometric distortions playing a secondary but quantifiable role. I will then present a large-scale statistical analysis of [4Fe–4S] clusters in protein structures, which reveals recurring electrostatic potential patterns linked to local environments and functional roles. Finally, I will discuss how fine-tuning of redox potentials via dynamical responses in the second coordination shell is exemplified in [FeFe] hydrogenase. Together, these multiscale insights offer a coherent framework for predicting and engineering redox properties in FeS proteins.