Molecular Dynamics Studies of Metal-Bound and Apo Forms of the Nickel Regulatory Protein: NikR

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NikR is a homotetrameric Nickel regulatory protein whose binding to free Ni^{2+} increases its affinity for a Nickel transporter gene. It is comprised of a tetrameric Nickel-binding domain, surrounded by two wing-like dimeric DNA-binding domains. Though x-ray crystallography data reveal many forms and conformations of NikR, the dynamics of the conformational changes between Nickel-bound, DNA-bound, and apo-forms have never been observed. We have run molecular dynamics simulations of three forms of the Pyrococcus Horikoshii species of NikR including two apo-forms and one Nickel-bound form. Though all 552 residues of this species are natural, quantum-mechanics-based force field parameterization was required to accurately represent the four nickel centers in the holo-form. Analysis of the three 80-ns-long simulations indicates slow-conformational kinetics, structure-dependent and binding-dependent fluctuations, and independent wing-motion. Due to the slow-kinetics, a much longer simulation would be required to achieve conformational equilibrium.