Spectroscopic and Computation Studies of Ni-Containing Enzymes: Application to Acetyl-CoA Synthase/Carbon Monoxide Dehydrogenase and Methyl-Coenzyme M Reductase

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The enzyme acetyl-CoA synthase/carbon monoxide dehydrogenase (ACS/CODH) from Clostridium thermoacetica is a tetramer of the form α₂β₂. The A-cluster, which resides in the α-subunit, is responsible for the methylation of CoA to produce acetyl-CoA and consists of an [Fe₄S₄] cluster bound to a bimetallic center. Our density functional theory (DFT) computations, evaluated on the basis of electron paramagnetic resonance (EPR), Mössbauer, and magnetic circular dichroism (MCD) spectroscopic data, reveal that the active form of ACS contains two Ni centers in the A-cluster in addition to the [Fe₄S₄] cubane. Questions concerning the catalytic cycle of the A-cluster were also addressed using DFT; these studies support a mechanism involving [Fe₄S₄]⁺⁻Ni⁺⁻Ni⁺²⁺ over [Fe₄S₄]⁺²⁻Ni⁺⁻Ni⁺²⁺, thus implying that the catalytic mechanism does not proceed through a Ni⁺₀ intermediate.

Similar computational and spectroscopic studies were conducted on the Ni-containing hydrocorphin cofactor, F₄₃₀, found in methyl-CoM reductase (MCR). MCR catalyzes the synthesis of methane from methyl-CoM and CoB. QM/MM techniques were used for the first time to develop detailed geometric and electronic descriptions of both the Ni(I) and Ni (II) forms of F₄₃₀.