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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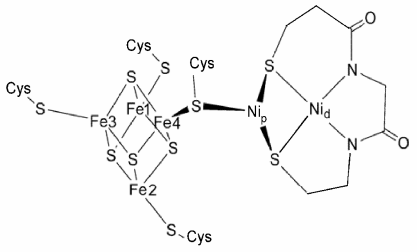
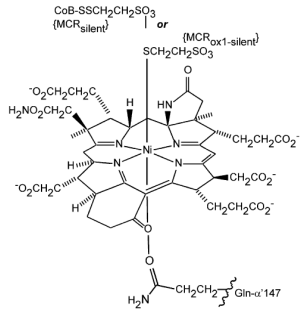
The enzyme acetyl-CoA synthase/carbon monoxide dehydrogenase (ACS/CODH) from *Clostridium thermoacetica* is a tetramer of the form $\alpha_2\beta_2$. The A-cluster, which resides in the α-subunit, is responsible for the methylation of CoA to produce acetyl-CoA and consists of an $[Fe_4S_4]$ cluster bound 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 $[Fe_4S_4]$ cubane. Questions concerning the catalytic cycle of the A-cluster were also addressed using DFT; these studies support a mechanism involving $[Fe_4S_4]^{+}$-Ni_p^{+}-Ni_d^{2+} over $[Fe_4S_4]^{2+}$-Ni_p^{0}-Ni_d^{2+}, thus implying that the catalytic mechanism does not proceed through a Ni_p^{0} intermediate.

Similar computational and spectroscopic studies were conducted on the Ni-containing hydrocorphin cofactor, F_{430}, 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 F_{430}.



Active form of the ACS A-cluster



Cofactor F_{430}