

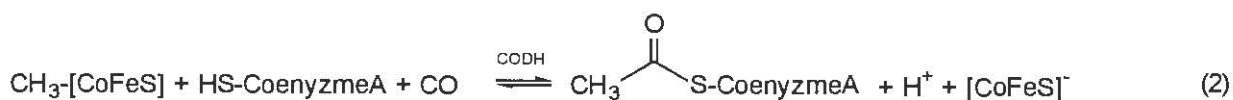
Structure and Function of the A-Cluster of Carbon Monoxide Dehydrogenase

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Carbon monoxide dehydrogenase (CODH) is an oxygen-sensitive nickel-containing enzyme that is known to catalyze two important reactions via the formation of proposed nickel-carbon bonds. This "bioorganometallic" enzyme catalyzes the oxidation of CO to CO₂ and the synthesis of acetyl Coenzyme-A from CO, Coenzyme-A, and a methyl group donated from a corrinoid iron-sulfur protein as shown in equations 1 and 2.^{1-3,14} Coenzyme-A is Nature's



carrier of acetyl and other acyl groups. CODH is a relatively large protein (310 kDa) that is a $\alpha_2\beta_2$ tetramer containing approximately 2 Ni and 12 Fe per $\alpha\beta$ dimer.³ CODH, which is isolated from the bacteria *Clostridium thermoaceticum*, contains both active and inactive Ni.^{7,11,15}

Carbon monoxide dehydrogenase contains three different transition metal clusters: A, B, and C, as shown in Figure 1.⁴ One of the most interesting and puzzling aspects of this

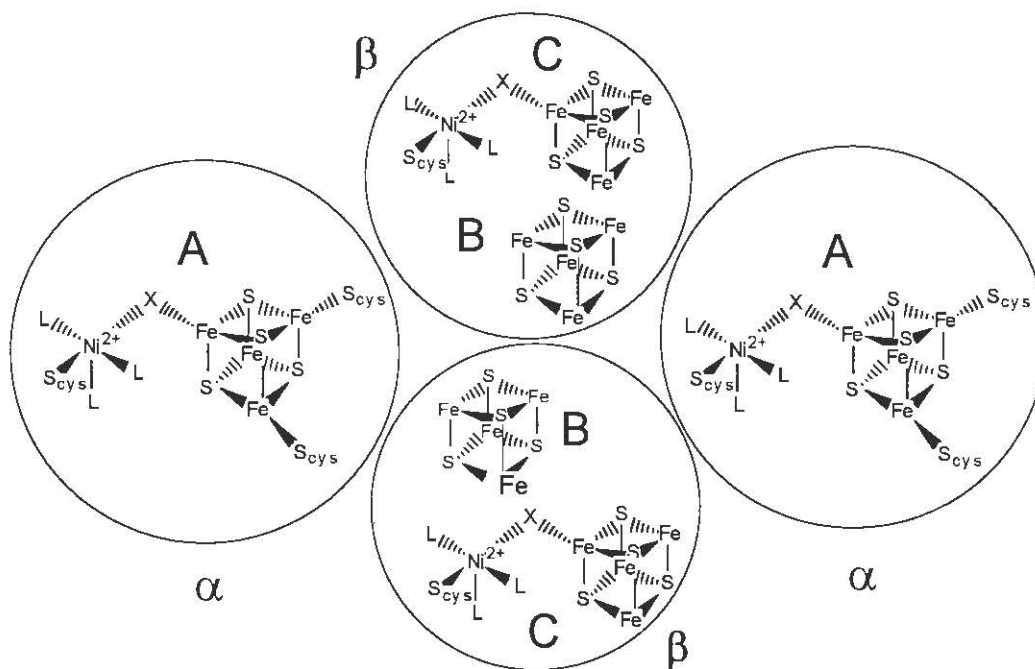


Figure 1

enzyme is that although the A and C-clusters are believed to have the same structure, they catalyze two different reactions. The C-cluster catalyzes the oxidation of CO, while the A-Cluster catalyzes acetyl coenzyme-A synthesis.^{6,7} The B-cluster is a $[\text{Fe}_4\text{S}_4]^{2+/1+}$ cluster, whose function is to transfer electrons between the C-cluster and external redox agents.⁵ Recently synthesized model complexes demonstrate that a single Ni compound can catalyze similar reactions shown in equations 1 and 2, mimicking the enzyme activity.⁷

The majority of published work focuses on the catalytic chemistry of the A-cluster. Both EPR and Mössbauer data suggest that the resting state is a pentacoordinate nickel bridged to a diamagnetic $[\text{Fe}_4\text{S}_4]$ cluster by an unknown ligand iXi .^{1-3,8,9,10,11,12} The first step in the enzymatic process is the addition of a methyl group from a B_{12} -like enzyme.^{13,14} Isotopic Labeling and metal removal studies provide evidence for this unique alkylation reaction.^{10,14} This step is followed by the addition of CO and its subsequent migratory insertion into the Ni-CH₃ bond, as indicated by stereochemical studies¹³. The final step is the formation of acetyl Coenzyme-A. Although more convincing evidence needs to be found before the presence of these complexes are widely accepted, the intermediates proposed here are consistent with all of the latest experimental evidence.

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