

Kinetic mechanism of acetyl-CoA synthesis catalyzed by CO dehydrogenase / acetyl-CoA synthase: preliminary evidence for a molecular tunnel

Ernest L. Maynard, Paul A. Lindahl

Department of Chemistry, Texas A&M University, College Station, Texas 77843

Ernie@tamu.edu

CO dehydrogenase / acetyl-CoA synthase (CODH/ACS) catalyzes the reversible reduction of CO₂ to CO and the assembly of acetyl-CoA from a methyl-bound corrinoid protein, CO, and CoA. These reactions are catalyzed at two separate and structurally distinct NiFeS clusters named C and A. The enzyme has a $\alpha_2\beta_2$ quaternary structure and a molecular weight of 310 kDa. The A- and C-clusters are located in different subunits and do not magnetically interact suggesting that a substantial distance separates them. CODH/ACS is found in the bacterium *Clostridium thermoaceticum*. The enzyme allows this organism to grow autotrophically utilizing CO₂ and H₂ as its sole source of cellular carbon and energy. Although the synthesis of acetyl-CoA is a key reaction in the metabolism of CO₂, its mechanism is not well understood. Steady-state kinetic experiments have been carried out to elucidate the roles of the two active sites in this reaction. We will present preliminary evidence that in the presence of CO₂ a molecular tunnel connecting the two active sites of CODH/ACS is formed. This tunnel allows CO generated at the C-cluster to migrate to the A-cluster without equilibrating with the bulk solvent. The characteristics and mechanistic implications of the molecular tunnel will be discussed.