Interactions of small molecules at isolated FeMoco : relic chemistry of an ancient enzyme ?

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There is a remarkable biology recently elucidated which has revealed the unusual association of cyanide and carbon monoxide as essential ligands at the active site of the iron-only and nickel-iron hydrogenases, hydrogen metabolising enzymes widespread in the Archaea and other microrganisms. Nitrogenase, the enzyme system which reduces dinitrogen to ammonia also catalyses hydrogen production and this occurs at the iron-molybdenum cluster of the enzyme (FeMoco). Intriguingly, under certain conditions this cluster also coordinates carbon monoxide and cyanide. Alone cyanide suppresses proton and substrate reduction but in the co-presence of carbon monoxide the production of dihydrogen is restored.

Cyanide, carbon monoxide and other small molecule interactions of nitrogenase may 'simply' reflect the extraordinary reactivity of sites on the FeMoco cluster which must bind, activate and reduce a relatively inert molecule, dinitrogen. However, it has been argued on the basis of phylogenetic evidence that the modern nitrogen fixing apparatus may have evolved from ancient cyanide metabolising or detoxifying iron-sulfur systems, with the later nitrogen reducing activity 'bolted – on' by molybdenum incorporation as fixed nitrogen became depleted in the biosphere. Thus interactions of the FeMoco cluster in the enzyme with cyanide, carbon monoxide, acetylene *etc* at the iron-sulfur core may reflect *relic chemistry* whereas their interactions at Mo may reflect the intrinsic reactivity of a dinitrogen binding and activating site. Here we report electrochemical and spectroelectrochemical studies of the isolated FeMo-cofactor which provides support for 'independent' binding sites together with a remarkable synergy in the co-binding of CO and CN to this cluster.