

7.11: Report on the Nitrogenase Crystal Structure

A significant breakthrough has occurred in the crystallographic analysis of the iron-molybdenum protein of nitrogenase. The overall distribution of the metal clusters in the protein is shown in Figure 7.40. The distance between the two FeMoco units is fully consistent with each cofactor acting as an independent active site. On the other hand, the closeness of the P cluster and FeMoco centers in each unit is indicative of their likely cooperation in the N_2 fixation reaction.

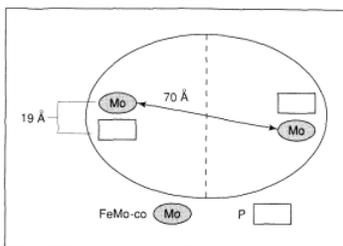


Figure 7.40 - A schematic representation of the spatial arrangement of the metal sulfur clusters bound to Cpl as determined by the x-ray anomalous scattering studies described in the text. The representation of the large, "8-Fe" cluster with a P symbol indicates only that it must contain the Fe atoms normally assigned to P-clusters.

The proposed structure of the P cluster, shown in Figure 7.41, involves a doubly bridged, double cubane unit consisting of one normally bound Fe_4S_4 cluster with all cysteine ligands and one Fe_4S_4 cluster that contains an unusual cysteine/serine (S/O) ligand pair on one of its two nonbridged Fe positions. Such five-coordinate iron in an Fe_4S_4 cluster is not unprecedented.¹³⁸ The two Fe_4S_4 clusters are disposed to produce a face-sharing arrangement with two cysteine ligands bridging the two sets of Fe atoms. An interesting feature of the structure is a disulfide unit linking the two clusters; this unit potentially could be redox-active during nitrogenase turnover.

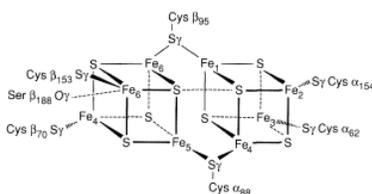


Figure 7.41 - Proposed P-cluster pair in *A. vinelandii* FeMo protein.

Most striking of the new results is the proposed structure of FeMoco shown in Figure 7.42. The cluster core of composition Fe_7MoS_8 can be viewed as two halves bridged by two S^{2-} ions and an unknown ligand (designated Y in the figure). The $MoFe_3S_3$ half of the core is in the shape of a thiocubane fragment missing one μ_3-S^{2-} ion. The Mo is six coordinate; the ligands are three μ_2-S^{2-} ions, which bridge to the three Fe ions, an α -His-442 nitrogen, and two oxygen donors (the hydroxyl and central carboxylate) of the homocitrate ligand. Interestingly, the second half of FeMoco is a similar thiocubane fragment, Fe_4S_3 , also missing a μ_3-S^{2-} ion. This unit has a single noncore ligand, α -Cys-275, which is bound to the terminal Fe atom of the cluster. The two thiocubane fragments ($MoFe_3S_3$ and Fe_4S_3) are bridged by three ligands in a face-sharing mode with the two Fe_3 faces eclipsed with respect to each other. The eight metal ions display a bis(end-capped) trigonal prismatic arrangement with three bridges on the edges of the prism, which connect the two thiocubane fragments. The two sulfide bridges between the thiocubane halves are clearly defined in the structure, but the third bridge is not, suggesting the possibility that this is in fact part of the N_2 -binding site. Interestingly, α -His-195, identified as essential for N_2 fixation by mutagenesis and ESEEM studies, does not appear to be covalently bound, although it is close to the FeMoco unit.

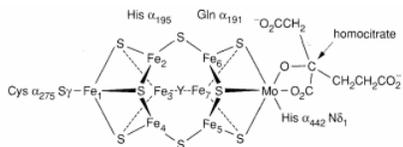


Figure 7.42 - Proposed cofactor cluster in *A. vinelandii* FeMo protein.

Clearly, this structure is not the same as any of those previously proposed (Figure 7.31), although it does possess many features that were identified in model studies. While it is tempting to speculate that the central bridge of the cluster (the Y ligand) is the site of N_2 reduction, this is in no way established at present. The structural definition of the nitrogenase proteins is now progressing at a

rapid rate. Many of the physical measurements will have to be reexamined in light of the new data. Through further experimentation involving physical methods, mutagenesis, and kinetic/mechanistic studies, much more information about the role of ATP, the activation of hydrogen, and the binding, activation, and reduction of N_2 and other nitrogenase substrates should be obtained.

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