Three-Iron Clusters in Iron-Sulfur Proteins

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The existence of [3Fe-xS] clusters [1] was first postulated in late 1979/early 1980 based on a combined EPR and Mössbauer study of the Azotobacter vinelandii ferredoxin I (A.v. Fd) [2] and an x-ray crystallographic study of A.v. Fd I [3]. Shortly thereafter, this rather convincing evidence for a novel Fe/S cluster type was corroborated by the results of EPR and Mössbauer studies on Desulfovibrio gigas Fd II (D. gigas Fd II) [4] and beef heart mitochondrial aconitase [5]. At the present time, at least a dozen "native" proteins (i.e., obtained upon ordinary aerobic purification) have been shown to contain 3Fe clusters with an additional dozen displaying some of the characteristic features of this cluster type.

Mössbauer spectroscopy provides convincing evidence for the presence of 3Fe clusters [6]. Other spectroscopic probes that exhibit signals characteristic of [3Fe-xS] sites are low temperature magnetic circular dichroism [7], low temperature resonance raman [8] and the linear field effect in EPR [9].

The subject of 3Fe cluster containing proteins has had more than its share of controversy. By late 1981/1982, it had been demonstrated that, in a number of cases, 3Fe clusters are definitely man-made artifacts. For example, oxidation of certain native [4Fe-4S]²⁺,⁺ ferredoxins with Fe(CN)₆³⁻ yields not the expected [4Fe-4S]³⁺ oxidized HiPIP state, but rather, a [3Fe-xS] species [10,11]. In other systems, 3Fe clusters can be converted, under appropriate conditions, into [4Fe-4S] clusters with or without the addition of Fe²⁺ or S⁰ [5,12,13,14].

Another area of some controversy concerns the structure(s) of 3Fe clusters. Stout's 2.5 Å resolution x-ray crystallographic analysis of A.v. Fd (a 7Fe protein) showed, in addition to a conventional [4Fe-4S] site, a planar, twist-boat six-membered ring [3Fe-3S] structure with d₃Fe-Fe = 4.1 Å [3,15]. In contrast, Fe EXAFS studies on D. gigas Fd II [16] and aconitase [12] clearly indicate a much more closed cluster structure with d₃Fe-Fe = 2.7 Å.
Earlier studies on the activation of inactive "native" aconitase suggested a [3Fe-4S] cluster for aconitase [5,12,13]. This has been confirmed by a recent high-precision determination of the Fe/S stoichiometry showing that "native" aconitase contains 2.9 ± 0.2 Fe/molecule and 3.9 ± 0.2 S/molecule [17]. Very recently, it has been shown that the Fe EXAFS of [4Fe-4S] depleted A.v. Fd (i.e., containing only the 3Fe cluster) is virtually identical to that of "native" aconitase [18].

On the basis of the above, as well as on the strong similarity of the RR spectra for all studied [3Fe-xS] proteins and the results of normal mode calculations for various 3Fe cluster geometries [19], it has been suggested that all 3Fe clusters are of a "closed" (i.e., dFe-Fe = 2.7 Å) [3Fe-4S] form.

References

1. For a review current through Jan. 1983:


18. a) Stephens, P. J., personal communication.
    b) Scott, R. A., personal communication.