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Review

The competition between chemistry and biology in assembling iron–sulfur derivatives. Molecular structures and electrochemistry. Part I. $\{Fe(S^{\gamma}_{Cys})_4\}$ proteins

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ABSTRACT

In the present review, we focus on the relationships between molecular geometry and electron transfer ability of the different classes of proteins bearing the $\{Fe(S^{\gamma}_{Cys})_4\}$ core as active site. We will highlight the role played by the amino acid composition in determining the redox activity of rubredoxins, flavorubredoxins, rubrerythrins, nigerythrins, desulfoferrodoxins and desulforedoxins, including, when available, their mutants. We will conclude with the electrochemical and structural aspects of synthetic FeS_4 derivatives able to mimic the above cited proteins (usually the rubredoxins).

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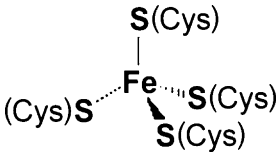
1. Introduction

The surprising structural analogies between biological iron–sulfur complexes and their synthetic analogues constitute an evergreen topic in bioinorganic chemistry dating at least from the last 40/50 years [1]. Iron–sulfur proteins play a crucial role in biological processes such as dinitrogen fixation, photosynthesis and respiration. Since most biological iron–sulfur complexes act as electron transfer mediators, a number of papers have been devoted to their redox properties [1n,2], as well as to those of their synthetic models [1n,3]. In fact, electron transfer processes not only trigger the transformation of solar into chemical energy for living organisms, but in biological processes such as photosynthesis, respiration, and nitrogen fixation the priority and the intensity of electron flows is finely controlled by the redox potential of the proteins designed for such processes.

The commonest iron–sulfur wild-type assemblies can be classified as [4]:

- single $\{Fe(S^{\gamma}_{Cys})_4\}$ (in rubredoxins and flavorubredoxins) and double $\{Fe(S^{\gamma}_{Cys})_4\}$ (in rubrerythrins, nigerythrins, desulfoferrodoxins and desulforedoxins);



- binuclear $\{[Fe_2S_2](S^{\gamma}_{Cys})_4\}$ in 2Fe ferredoxins;
- binuclear $\{[Fe_2S_2](S^{\gamma}_{Cys})_2(N^{\delta}_{His})_2\}$ in Rieske ferredoxins;
- trinuclear $\{[Fe_3S_4](S^{\gamma}_{Cys})_3\}$ in 3Fe ferredoxins;
- tetranuclear $\{[Fe_4S_4](S^{\gamma}_{Cys})_4\}$ in 4Fe ferredoxins and high potential iron–sulfur proteins (HIPIPs);
- heptanuclear $\{[Fe_3S_4](S^{\gamma}_{Cys})_3 + [Fe_4S_4](S^{\gamma}_{Cys})_4\}$ in 7Fe ferredoxins;
- octanuclear 2 $\{[Fe_4S_4](S^{\gamma}_{Cys})_4\}$ in 8Fe ferredoxins;
- octanuclear $\{[Fe_8S_7](S^{\gamma}_{Cys})_6\}$ in P cluster of nitrogenase FeMo-protein;
- octanuclear $\{([MoFe_7S_9]$ homocitrate$)S^{\gamma}_{Cys}\ N^{\delta}_{His}\}$ in nitrogenase FeMo-cofactor.

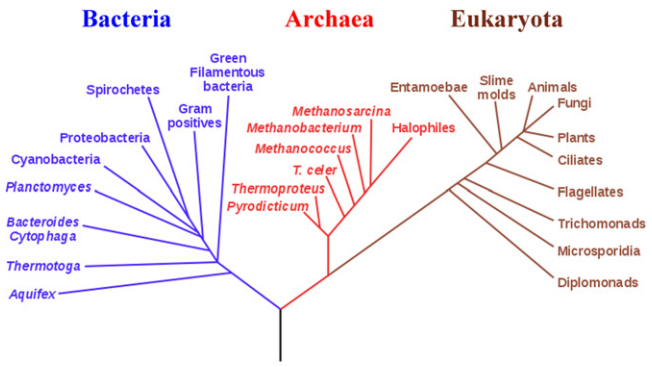


Fig. 1. The Woese phylogenetic tree of life for living organisms (NASA image).

As imaginable from the presentation, the present review is devoted to proteins containing $\{Fe(S^{\gamma}_{Cys})_4\}$ core(s), in particular to those of known molecular structure.

2. Single-$\{Fe(S^{\gamma}_{Cys})_4\}$ proteins

2.1. Rubredoxins

Rubredoxins are small proteins of molar mass about 6000 Da which contain an iron atom tetrahedrally coordinated to the sulfur atoms of four cysteine residues. Their biological role is still unclear, but it is widely accepted that they participate in electron transfer processes. In fact they are involved in a number of important biochemical reactions [5].

Rubredoxins are located in the protein components of several microorganisms. In this connection, in order to account for the (not always familiar to chemists) nomenclature of some biological species which will appear in the text, it may be useful to consider the recent classification of the three domains which characterize the living organisms, Fig. 1 [6].

2.1.1. Bacteria rubredoxins

The first *rubredoxin* was isolated from the dinitrogen-fixing anaerobic bacterium *Clostridium pasteurianum* (from hereafter *Cp*Rd) by Lovenberg and Sobel in 1965, who also assigned the name

Table 1
Amino acid sequence of *Cp*Rd.

Residue	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Amino acid	Met	Lys	Lys	Tyr	Thr	**Cys**	Thr	Val	**Cys**	Gly	Tyr	Ile	Tyr	Asp	Pro
Residue	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
Amino acid	Glu	Asp	Gly	Asp	Pro	Asp	Asp	Gly	Val	Asn	Pro	Gly	Thr	Asp	Phe
Residue	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45
Amino acid	Lys	Asp	Ile	Pro	Asp	Asp	Trp	Val	**Cys**	Pro	Leu	**Cys**	Gly	Val	Gly
Residue	46	47	48	49	50	51	52	53	54						
Amino acid	Lys	Asp	Glu	Phe	Glu	Glu	Val	Glu	Glu						

Source: [9].

Table 2
Bond distances (Å; rounded off to the second decimal figure) and selected bond angles (°) for *Cp*Rd in different oxidation states.

Rubredoxin	Bond lengths				Bond angles		Reference
	Fe—S6	Fe—S9	Fe—S39	Fe—S42	S9FeS42	S6FeS39	
Oxidized form							
*Cp*Rd (wild-type)	2.24	2.30	2.26	2.24	114.7	112.1	[10e]
*Cp*Rd (recombinant)	2.28	2.24	2.28	2.22	112.7	110.1	[10d]
Reduced form							
*Cp*Rd (wild-type)	2.38	2.36	2.39	2.30	110.1	112.8	[10e]