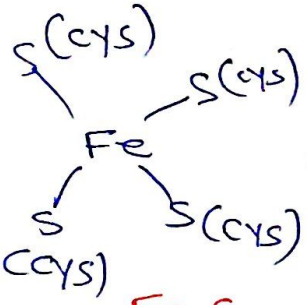
Iron - Sulfur Proteins

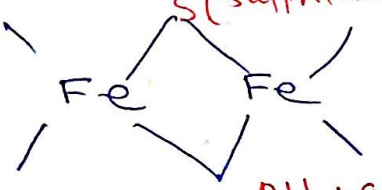
1) Relatively low mol. wt. compounds
2) Non-heme iron proteins, consisting of peptide chain bound through cysteine (Amino acid) sulfur atom to redox iron centre.
3) Present in anaerobic and aerobic bacteria, algae and higher plants and animals ⇒ present in all forms of life.
4) (a) → In plants act as electron carrier for redn of N_2 in Nitrogenase activity.
   (b) and in photosynthesis electron transfer from PSI to PS II.
   (b) In the animals, they assist electron transfer process in the mitochondria. (Respiration)
5) Similar to cytochromes → one electron transfer process in the $Fe(III) \rightleftharpoons Fe(II)$ couple.
6) classified two types (a) Rubredoxin one prosthetic centre
   (b) Ferredoxins $(Fe-S)_n$

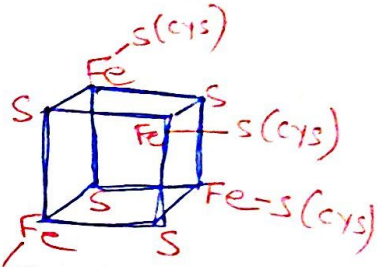
7) Iron-sulfur Proteins show wide range of Redox Potentials

   i.e $+0.35$ to -0.6 V

Name of the protein	Source	M.M.
1) Rubredoxin (1Fe)	Clostridium Pasturianum (anaerobic bacteria 1st observed)	6000
2) Ferredoxins		
(a) (2Fe-2S)	Spinach	10,000
	Pig Adrenals	13000
	Mitochondria	30000
(3Fe-3S) ⟶	Beef heart & Nitrogen fixing bacteria Azotobacter	
(b) (4Fe-4S)	Some bacteria content	8000 – 12500
(c) (8Fe-8S)	chromatium clostridium etc	6000-9000







Fe_1S_0

$Fe_0(S\text{-}cys)_4$

$HS-CH_2-\underset{NH_2}{CH}-COOH$

Cysteine

$RH + O_2 \xrightarrow{\text{oxo process}} ROH + H_2O$

Fe_2S_2

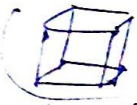
$Fe_2(S\text{-}cys)_4^{3+}$

$2Fe^{2+}$

Fe_4S_4

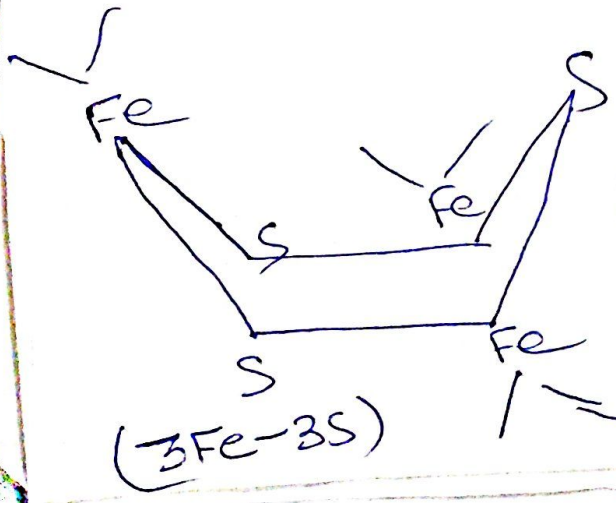
$Fe_4S_4(S\text{-}cys)_4$

$2Fe(III) + 2Fe(II)$



spin coupling $Fe(III)-Fe(III)$

$Fe(II)-Fe(II)$



on red^n resultant structure

$1Fe(III) + 3Fe(II)$

$Fe(III)-Fe(II)$ } one e^- red^n

$Fe(II)-Fe(II)$

⟹ easily converted to Fe_4S_4

(27)

Rubredoxins (1962)

Source
↓
Clostridium pasturianum

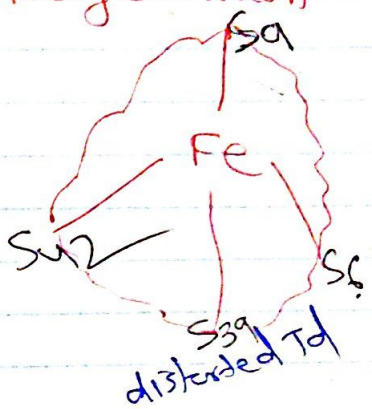
→ Participate in Redox Reactions (1 electron transfer agent)

→ MM = 6000

→ Surrounded by 4 S-atom from cysteine which is linked into protein chain

→ Fe_1S_0 | $Fe(S-cyst)_4$ S-inorganic sulfur
cyst-6, 9, 39, 42 in the sequential chain
CN = 4

Fe — S Distance = 2.24 — 2.33 Å, Averge = 2.26 Å
S — Fe — S Angle = 104 — 114°



→ usually No. of AA in the protein chain
54 = 54 (varies 50 — 60)

→ Fe at the centre of the distorted Td. (sp^3 hybridisation)

→ Redox Couple $Fe^{II} \rightleftharpoons Fe^{III}$ (0.05 Å radius changes)

→ Fe^{II} (reduced) H.S — d^6 → $eg^3 t_{2g}^3$ ⟷ $eg^2 t_{2g}^4$ (d-d transition 625 nm)

4 unpaired electrons, 5.05 BM, Distorted Td
Supported by spectral mag. moment.
Expected to experience Jahn-Teller Distortion imposed by the ligands.

→ Fe^{III} (Oxidised) H.S — d^5 — $eg^2 t_{2g}^3$ (No J.T. distortion)

5-unpaired electrons, 5.8 BM, Distorted Td.

→ Fe^{II} (H.S) $eg^3 t_{2g}^3$ ⇌ Fe^{III} (H.S) $(eg^2 t_{2g}^3)$ = Couple.

Redox Couple (Rubredoxin)

$Fe^{II}_{HS}(eg^3 t_{2g}^3) \rightleftharpoons (eg^2 t_{2g}^3) Fe^{III}_{HS}$

↓ red

$Fe^{II}(eg^2 t_{2g}^4)$

Self electron Exchange rate

$= 10^9$ ET | Sec · in case of Rubiredoxin

compared with aqua complex

$[Fe(OH_2)_6]^{2+} \rightleftharpoons [Fe(OH_2)_6]^{3+}$

→ M.B shows very very small quadrupole splitting as the charge distribution is spherical

→ Red colour due to $\bar{S} \longrightarrow Fe(III)$ charge transfer.

→ The distortion is extremely important for rapid electron transfer through an outer-sphere mechanism.

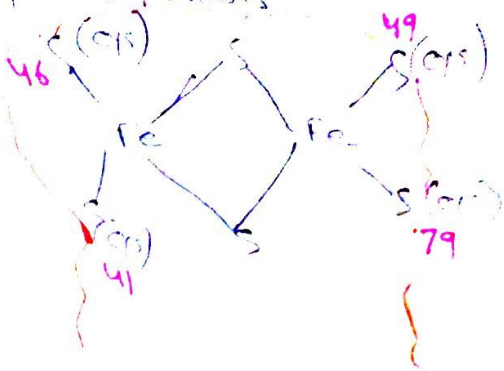
[redacted]

Role on the presence of acrobic bacteria

$CH_4 + O_2 \xrightarrow{2H^+ + 2e} CH_3OH + H_2O$

2Fe-2S

→ Mainly found in plants called plant ferredoxin (blue green algae)
→ Involved electron transfer process in photosynthesis
→ Prosthetic centre Fe_2S_2



On oxidised form 2Fe(III)
M.M - 11,000
Two bridged sulfur
Each Fe is distorted Tetrahedron

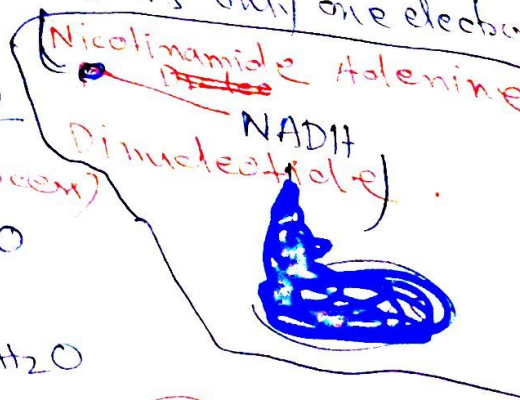
→ MB shows no quadrupole splitting
So Each $Fe^{III}_{H.S}$ — d^5 — 5 unpaired electron
→ but Protein is diamagnetic ⇒ strong super exchange between two Fe(III) thro' two bridging sulfides
→ Antiferromagnetic coupling between five unpaired electron on each of the two Fe(III) centres is very strong S = 0 EPR silent

→ On reduced form → Redox potential of the protein = −250 to −420 mv
⇒ reducing nature of the protein

1 Fe(III) → H.S (S = 5/2)
1 Fe(II) → H.S (S = 2)
⇒ 1 unpaired electron S = 1/2 ← EPR detectable electron
but not $Fe^{2.5}$ | $Fe^{2.5}$

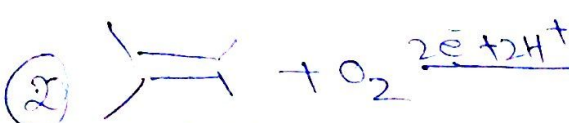
d^6 → $t_{2g}^4 e_g^2$

→ Two Fe centres present but it transfers only one electron same as Rubredoxin



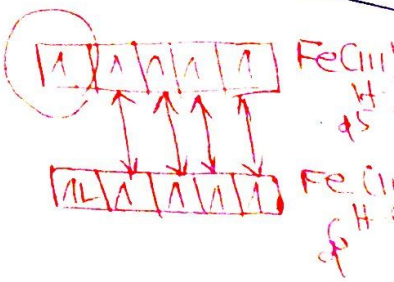
→ Activity of cytochrome P-450
1. e Oxygenase Activity (Oxo process)

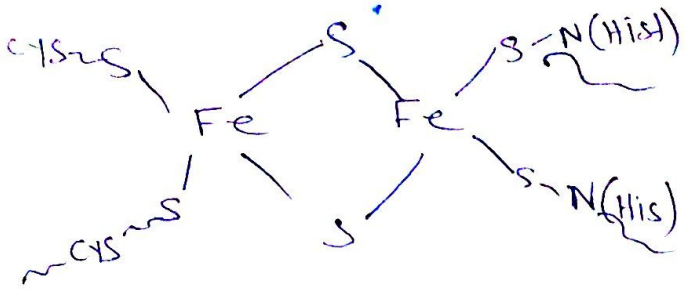
① $RH + O_2 \xrightarrow{2\bar{e}+2H^+} ROH + H_2O$

②  $+ O_2 \xrightarrow{2\bar{e}+2H^+}$ $+ H_2O$

insoluble

③ Hydroxylation of steroids





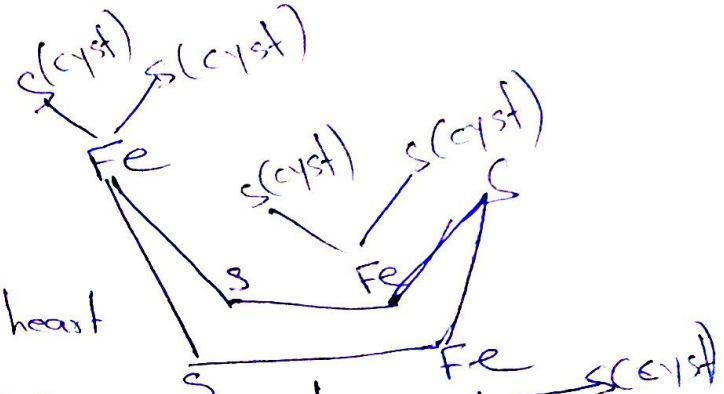
Two side
→ Rieske Protein

→ or one CN occupied by N(Hist) also called Rieske Protein

→ Red^n Potential +0.35 to −0.15 V

→ for plant −0.25 to −0.45 V

3Fe − 3S



→ $Fe_3S_3(S\text{-cyst})_6$

→ Recently discoved from beef heart

→ Present in Nitrogen fixing bacteria Azotobactor called Vinclandii (AvFdI)

→ 3Fe are Fe(III) Equivalent

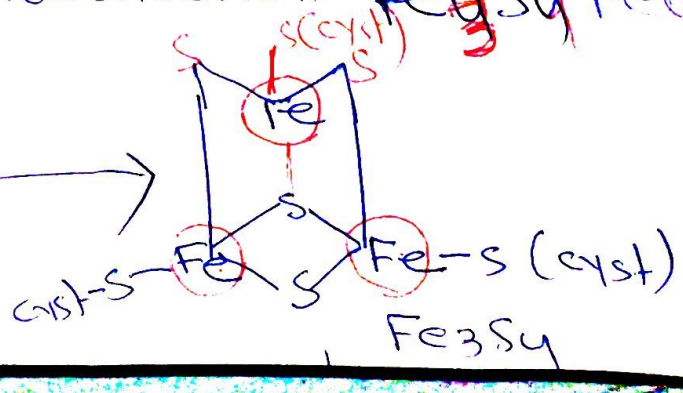
→ Undergoes $1\bar{e}$ reduction

i.e $3Fe(III) + 1\bar{e} \longrightarrow 2Fe(III) + 1Fe(II)$

→ Easily converted to Fe_3S_4

→ It is the intermediate for biosynthetic route of the formation Fe_3S_4 Fe_4S_4

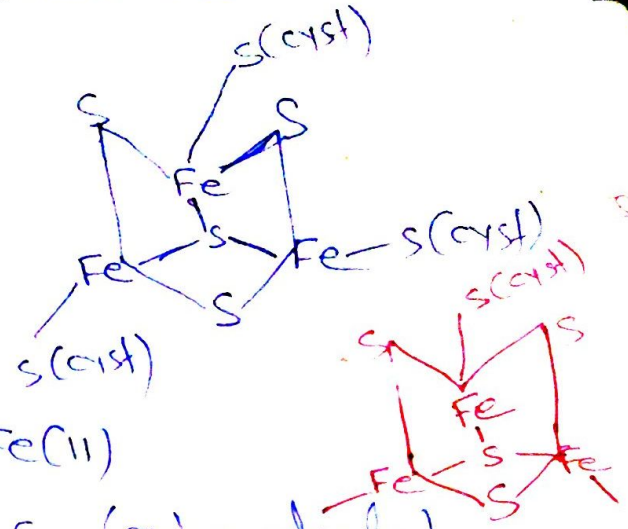
Fe_3S_3



Fe_3S_4

(3)

$Fe_3S_4(S\text{-cyst})_3$



→ 3Fe(III) 8 equivalent
EPR active

$3Fe(III) \underset{-1e^-}{\overset{+1e^-}{\rightleftharpoons}} 2Fe(III) + 1Fe(II)$

→ Easily converted to Fe_4S_4 (intermediate)

[8Fe-8S] → 2[Fe_4S_4] situated at a distance 12A° linked through the protein

One Fe_4S_4 binds → S of cyst(8), (11), (14), (47)

another " " → S " 18, 35, 38 and 42

Each [Fe_4S_4] contain 2Fe(III) and 2Fe(II) and undergoes $1\bar{e}$ reduction as Fd.

⇒ whole protein act as $2\bar{e}$ acceptor

→ when one [Fe_4S_4] accepts electron there is a change in the ~~tertiary~~ protein chain. This prompts to accept another electron.

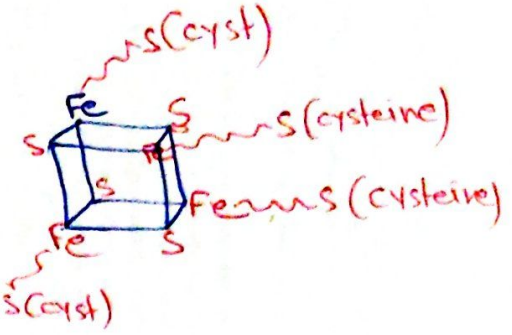
1

Fe_4S_4 system

→ Source → bacteria (chromatium clostridium), plants and animals etc.

→ Prosthetic group = Fe_4S_4

→ Structure : → This Cubane with four Fe and four S located at the corner with alternate. Each Fe is at the centre of Td



one S → from cysteine
three S → labile S.

X-ray crystallographic

$4Fe \rightarrow 1Fe(III) + 3Fe(II) \rightarrow [Fe_4S_4]^{+}$ — (1) $3+6 = 9-8 = 1+$

$2Fe(III) + 2Fe(II) \rightarrow [Fe_4S_4]^{2+}$ — (2) $6+4 = 10-8 = 2+$

$3Fe(III) + 1Fe(II) \rightarrow [Fe_4S_4]^{3+}$ — (3) $9+2 = 11-8 = 3+$

$$[Fe_4S_4]^{3+} \underset{-1e^-}{\overset{+1e^-}{\rightleftharpoons}} [Fe_4S_4]^{2+} \underset{-1e^-}{\overset{+1e^-}{\rightleftharpoons}} [Fe_4S_4]^{+}$$

(a) (b) (c)

(a) & (b) one redox couple = HiP/Ps (R.P = +350 mv)

(b) (&) (c) " " " = Fd (R.P = −600 mv)

→ Equ (1) & (3) oxidised form & reduced form both are paramagnetic with one unpaired electron.

Equ^{n} (1) $[Fe_4S_4]^{+} \rightarrow 1Fe(III) + 3Fe(II)$

$Fe(+1) \rightarrow d^6 \rightarrow$ ↑↓ | ↑ | ↑ | ↑ | ↑

$Fe(III) \rightarrow d^5 \rightarrow$ ↑ | ↑ | ↑ | ↑ | ↑

$Fe(II) \rightarrow d^6 \rightarrow$ ↑↓ | ↑ | ↑ | ↑ | ↑

$Fe(II) \rightarrow d^6 \rightarrow$ ↑↓ | ↑ | ↑ | ↑ | ↑

one unpaired electron.

EPR active.

Equⁿ (3) $[Fe_4S_4]^{3+} \longrightarrow 3Fe(III) + 1Fe(II)$

EPR active

Fe(III) — d^5 | Fe(III) — d^5
Fe(III) — d^5 | Fe(II) — d^6

one unpaired electron

Equⁿ (2) $[Fe_4S_4]^{2+} \longrightarrow 2Fe(III) + 2Fe(II)$

Fe(III) — d^5 | Fe(II) — d^6
Fe(III) — d^5 | Fe(II) — d^6

No unpaired electron

⇒ Complete quenching of paramagnetism (diamagnetic) super exchange through bridging sulfides.

⇒ In nature Equⁿ (2) present

⇒ No conversion from Equ(1) to Equ(2) then further Equⁿ(3) which causes partial breakdown and denaturing.

⇒ Redox behaviour due to the difference in protein structure. i.e cysteine s of proteins are hydrogen bonded to the backbone of protein. The redox behaviour of iron centre is controlled by the extent of H-bonding.

⇒ Incase of $[Fe_4S_4]^{2+}$ the O.S are not localised on specific Fe ions but incase Fe_2S_2 is specific. There is delocalisation over the Fe_4S_4 cluster ⇒ four Fe are equivalent and have the same averge O.S +2.5 and incase $[Fe_4S_4]^{3+}$. The O.S = +2.75 supported by MB spectrum.

⇒ Fe_4S_4(Protein) $+ 4L^- \longrightarrow [Fe_4S_4L_4]^{2-}$ + Apoprotein

Apoprotein losses its activity & regenerated on addition of [4Fe-4S]