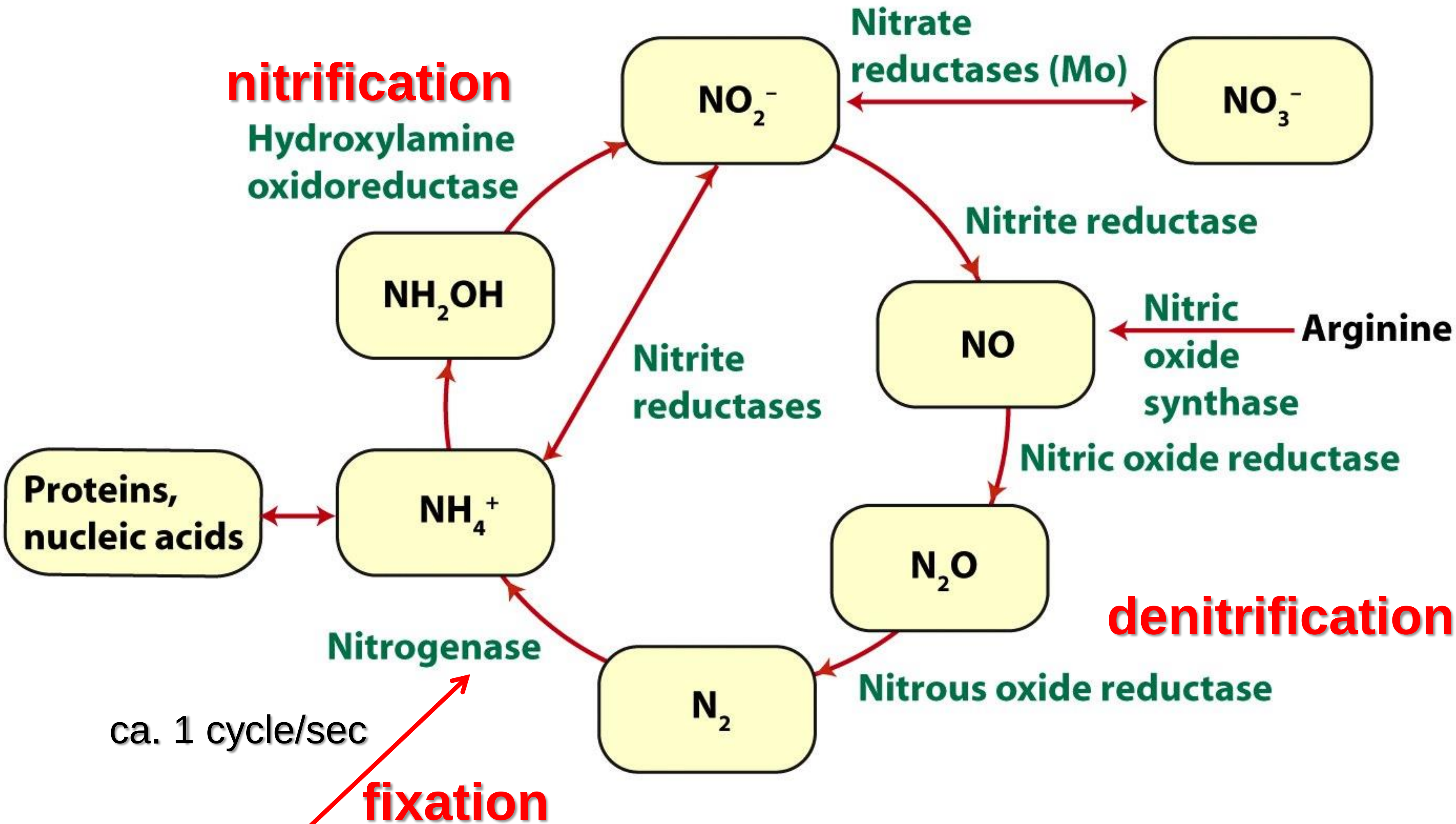
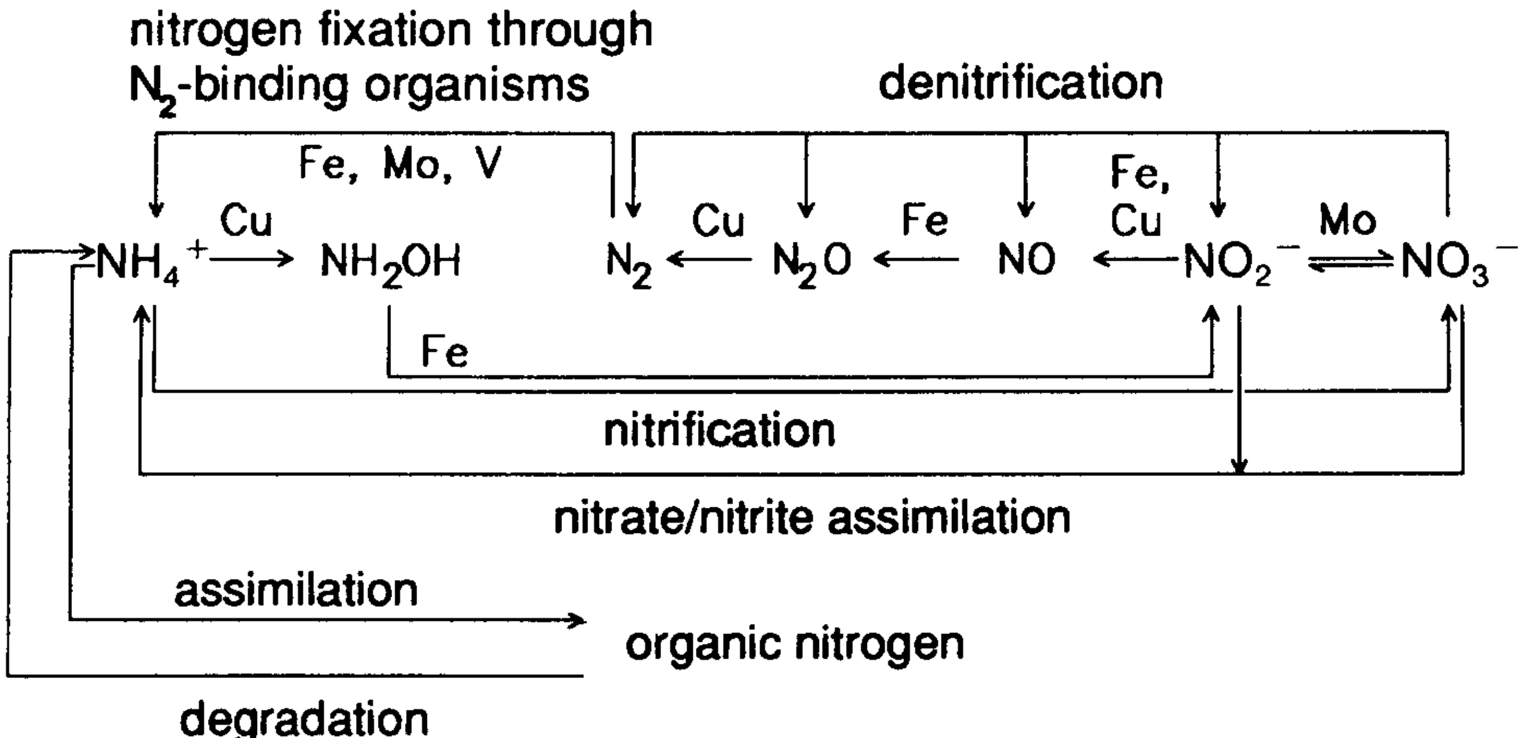
Early transition metals

Molybdenum is the only element of the second transition period (4d) that has a biological function. It is bioavailable in the form of molybdate MnO_4^{2-}

Nitrogen cycle



diazotropic prokaryote bacteria (leguminous plants): 10^8 ton N_2/y



$$N_2 + 10\,H^+ + 8e^- \xrightarrow[\textit{nitrogenase}]{\text{fixation}} 2NH_4^+ + H_2$$

$$NH_4^+ + 2O_2 \xrightarrow{\text{nitrification}} NO_3^- + H_2O + 2H^+$$

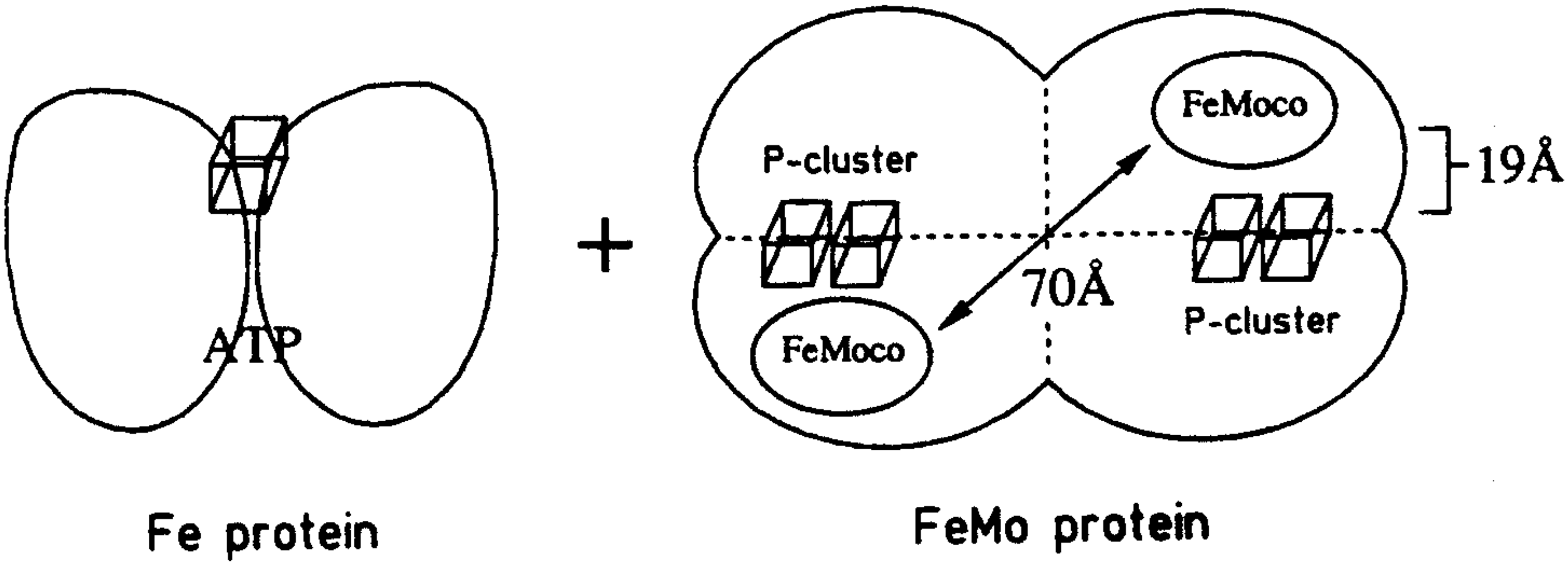
$$2NO_3^- + 12H^+ + 10e^- \xrightarrow{\text{denitrification}} N_2 + 6\,H_2O$$

Nitrogenase

$$N_2 + 10H^+ + 8e^- + 16MgATP \rightarrow 2NH_4^+ + H_2 + 16MgADP + 16PO_4^{3-}$$

1992

ca. 1 cycle/sec



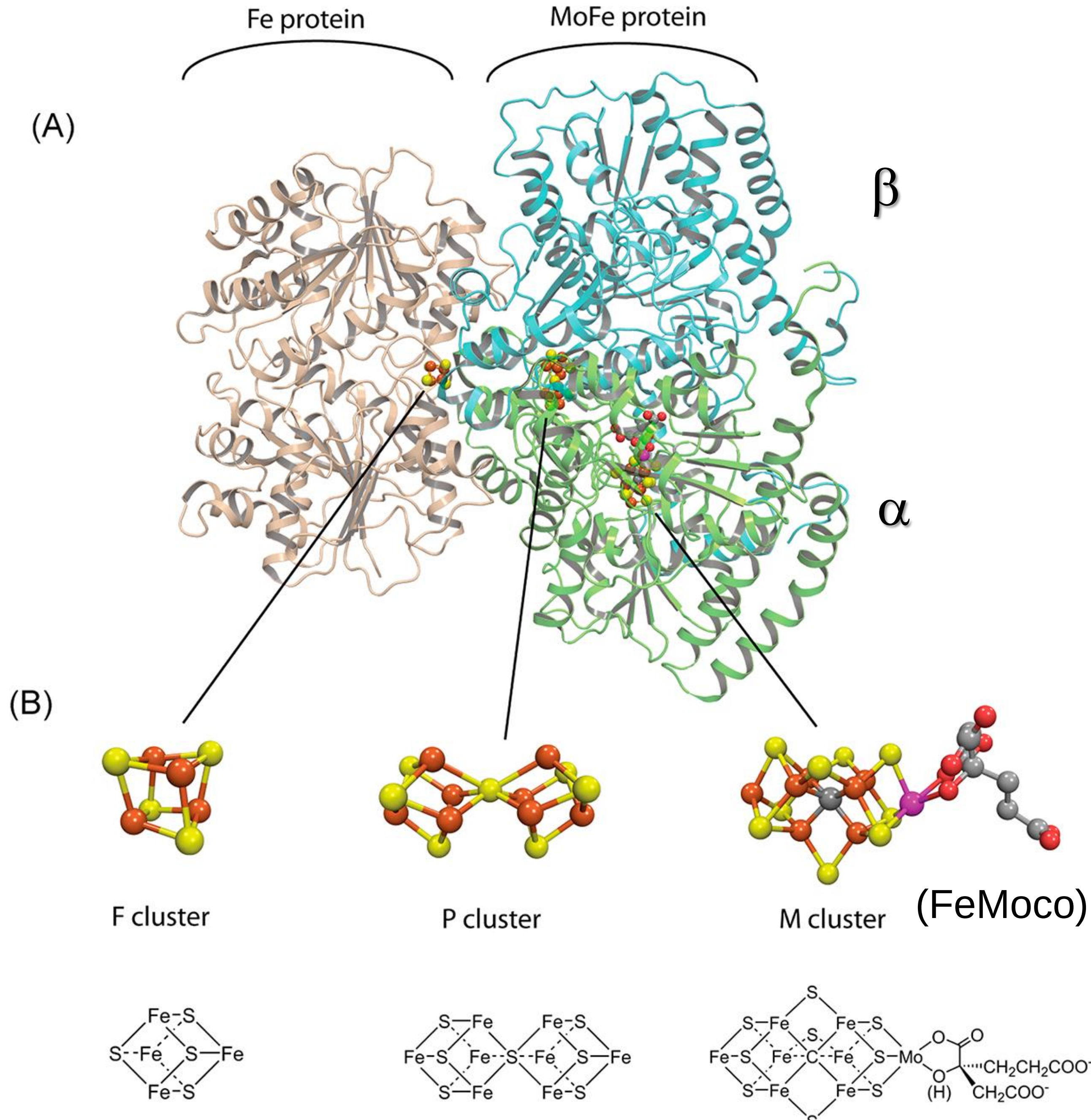
γ_2

60 kDa

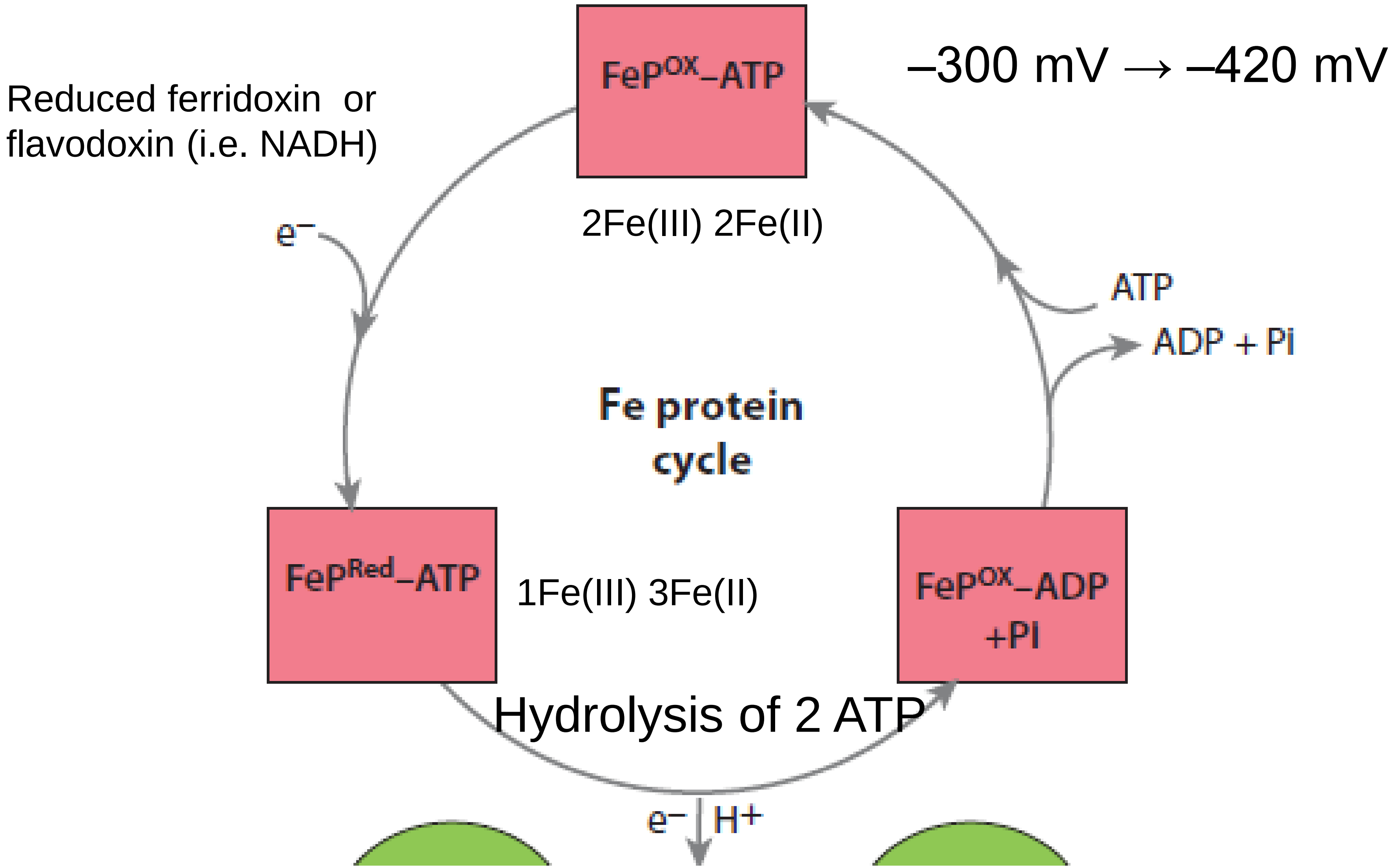
$\alpha_2\beta_2$

220 kDa

Nitrogenase

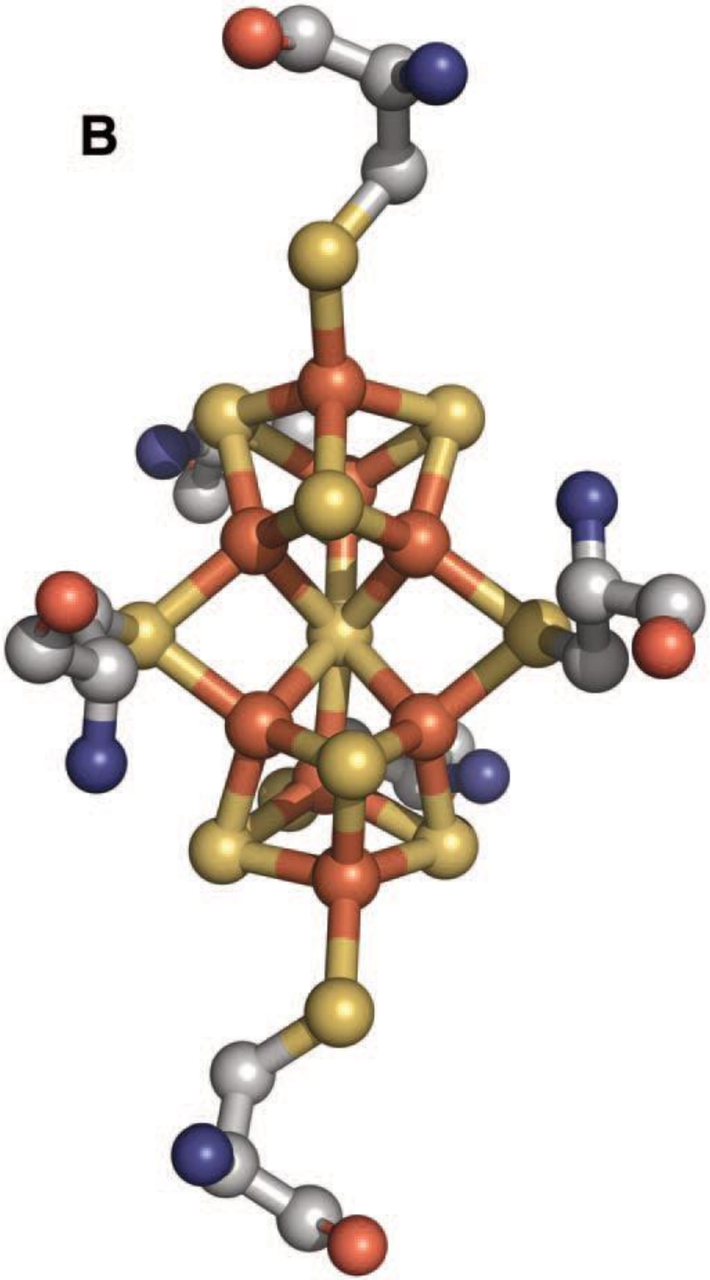


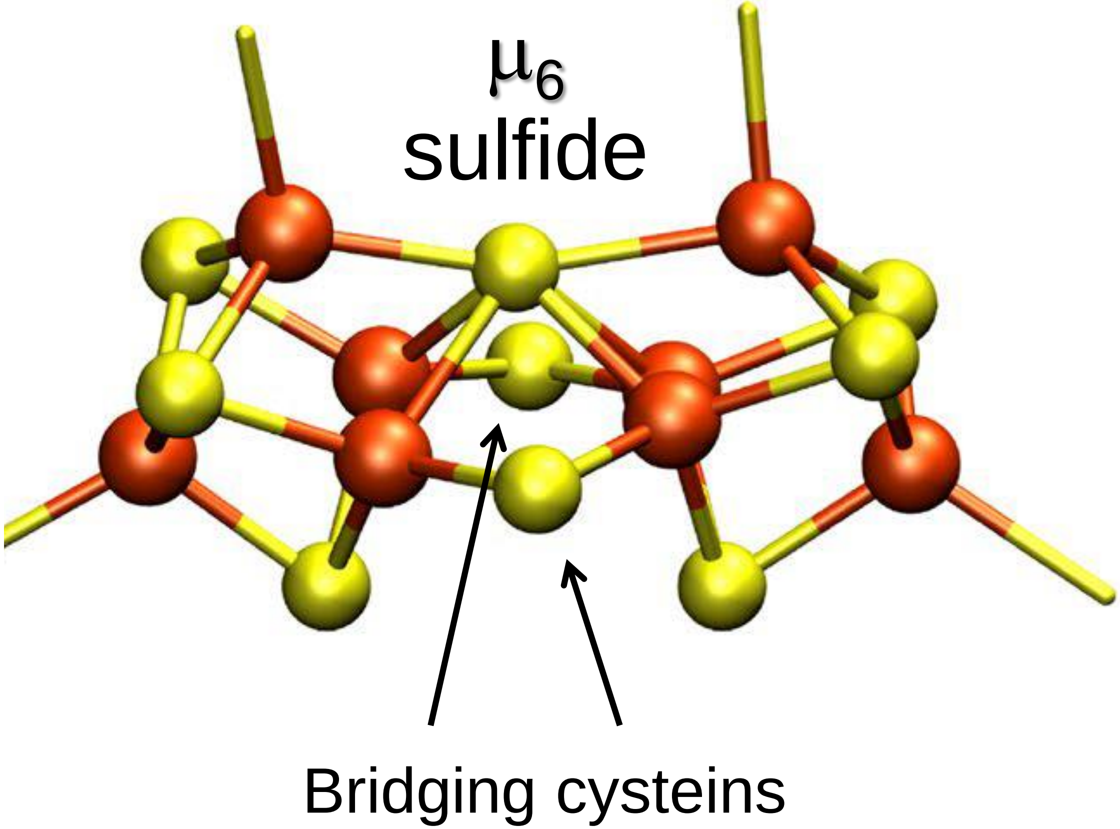
Fe-protein



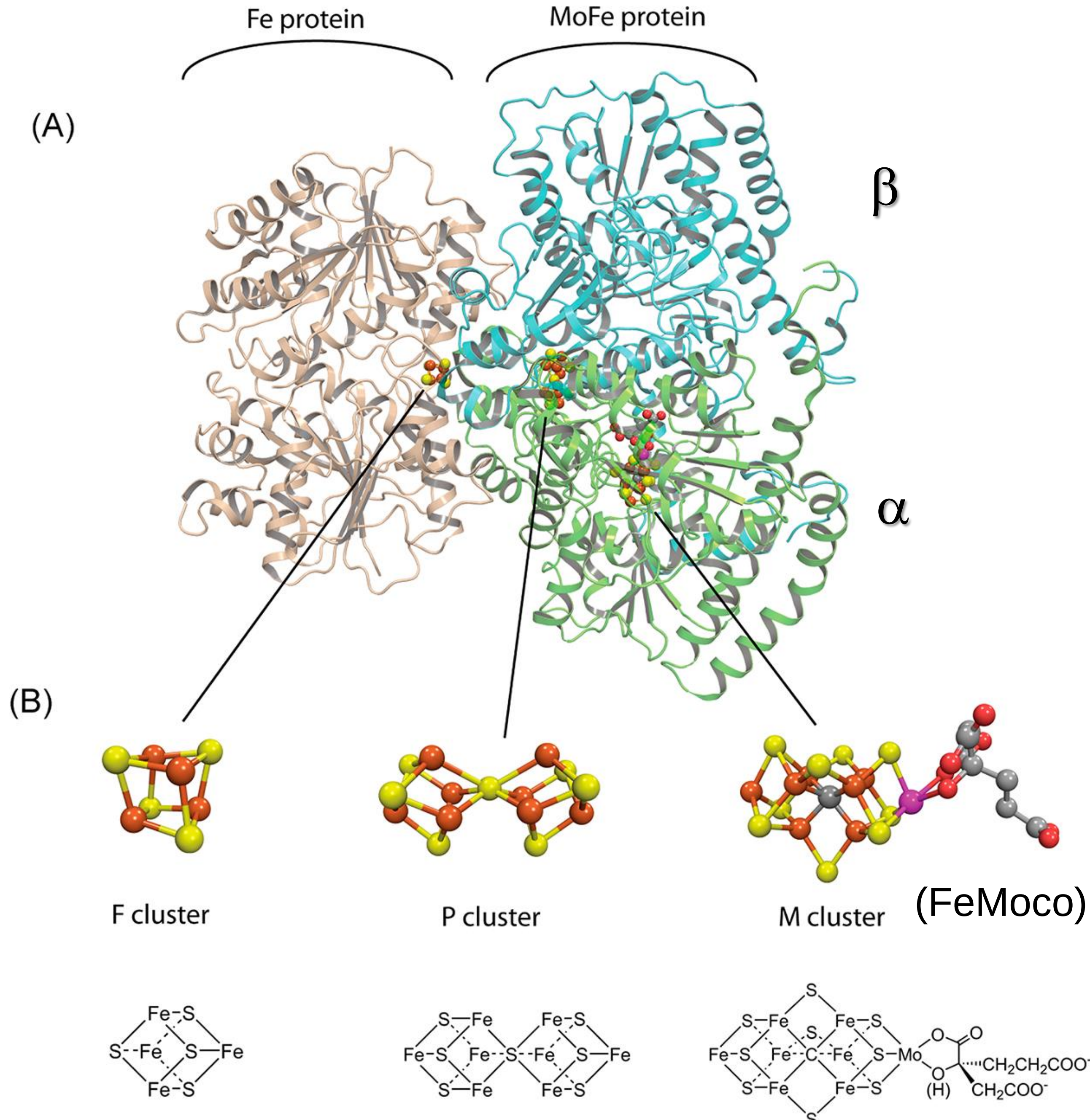
–300 mV → –420 mV
Reduced ferridoxin or flavodoxin (i.e. NADH)
FeP^OX–ATP
2Fe(III) 2Fe(II)
e⁻
ATP
ADP + Pi
Fe protein cycle
FeP^Red–ATP
1Fe(III) 3Fe(II)
FeP^OX–ADP +PI
Hydrolysis of 2 ATP
e⁻
H+

P-cluster: 8Fe-7S + 6cys bridges α and β proteins



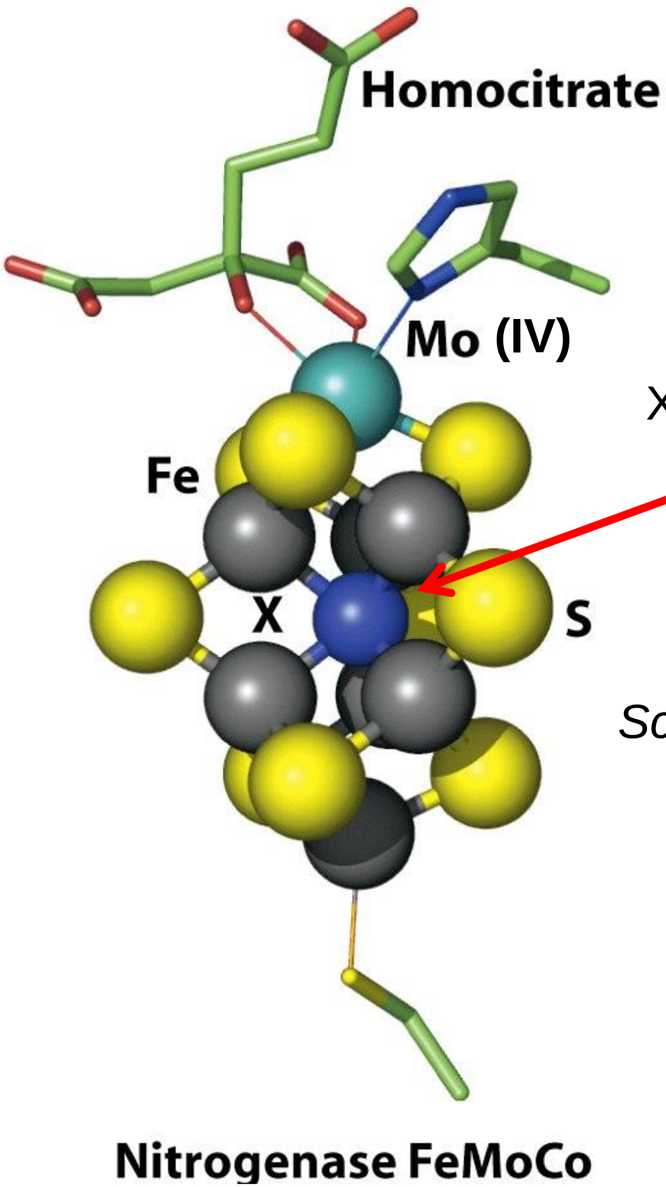


Nitrogenase



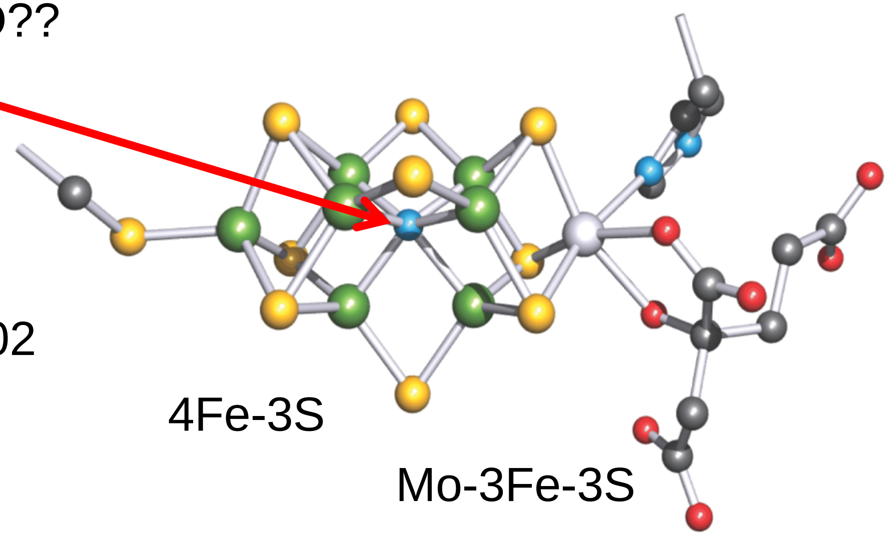
FeMo cofactor

7Fe-9S-Mo-homocitrate

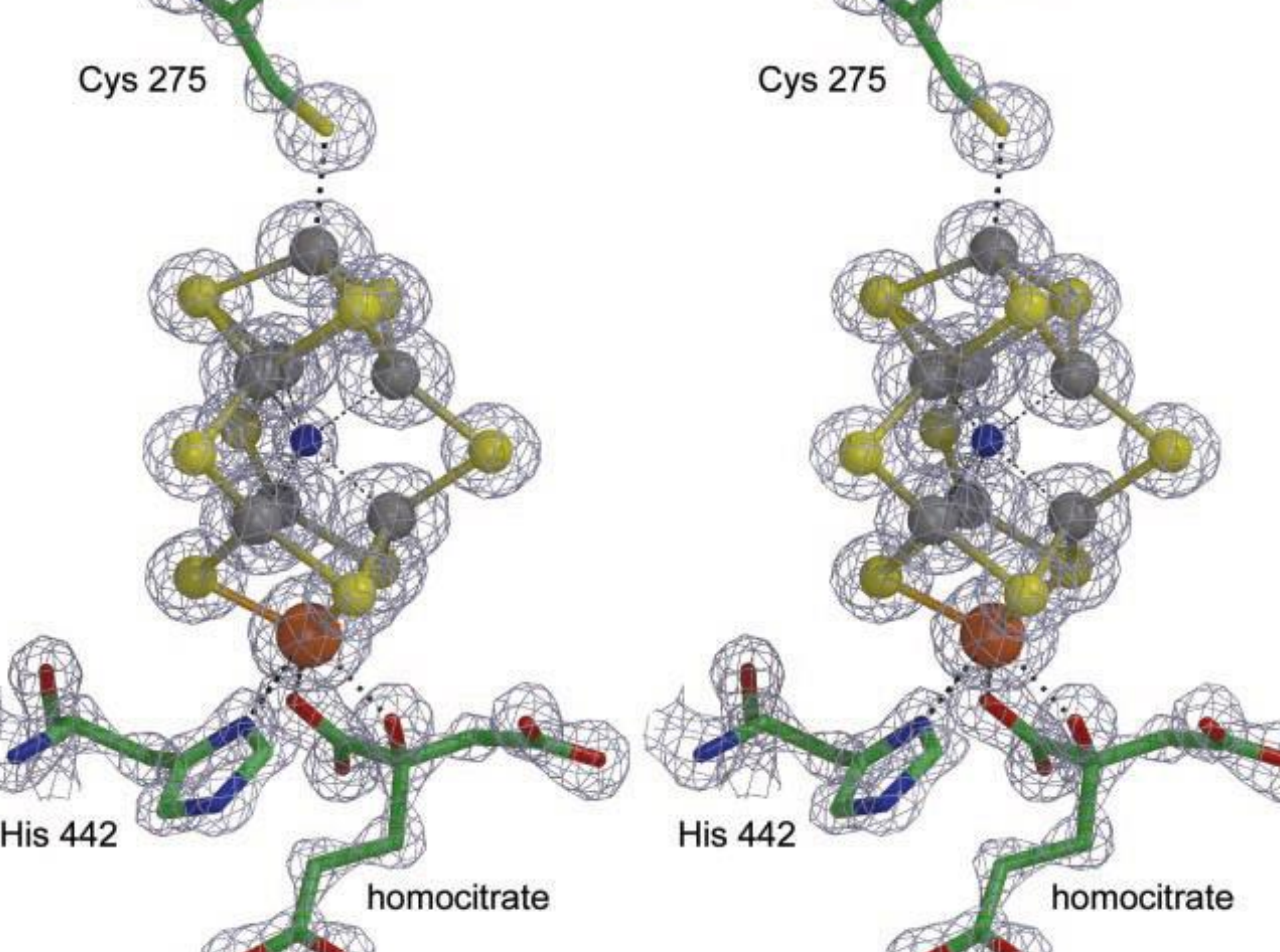


X = C, N, O??

Science, 2002

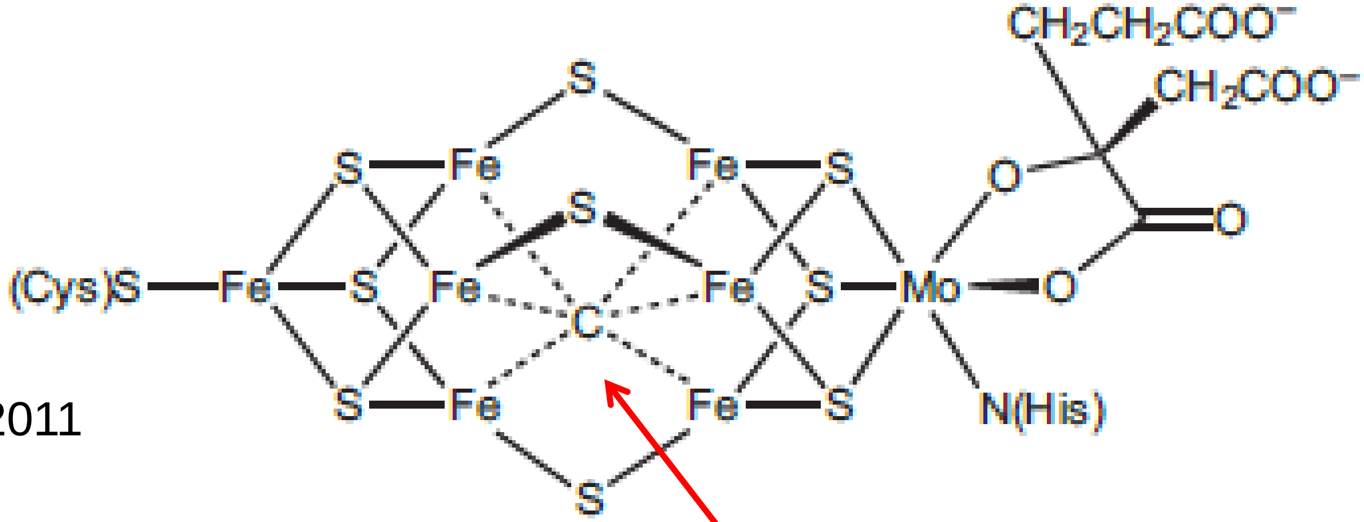


All in protein α

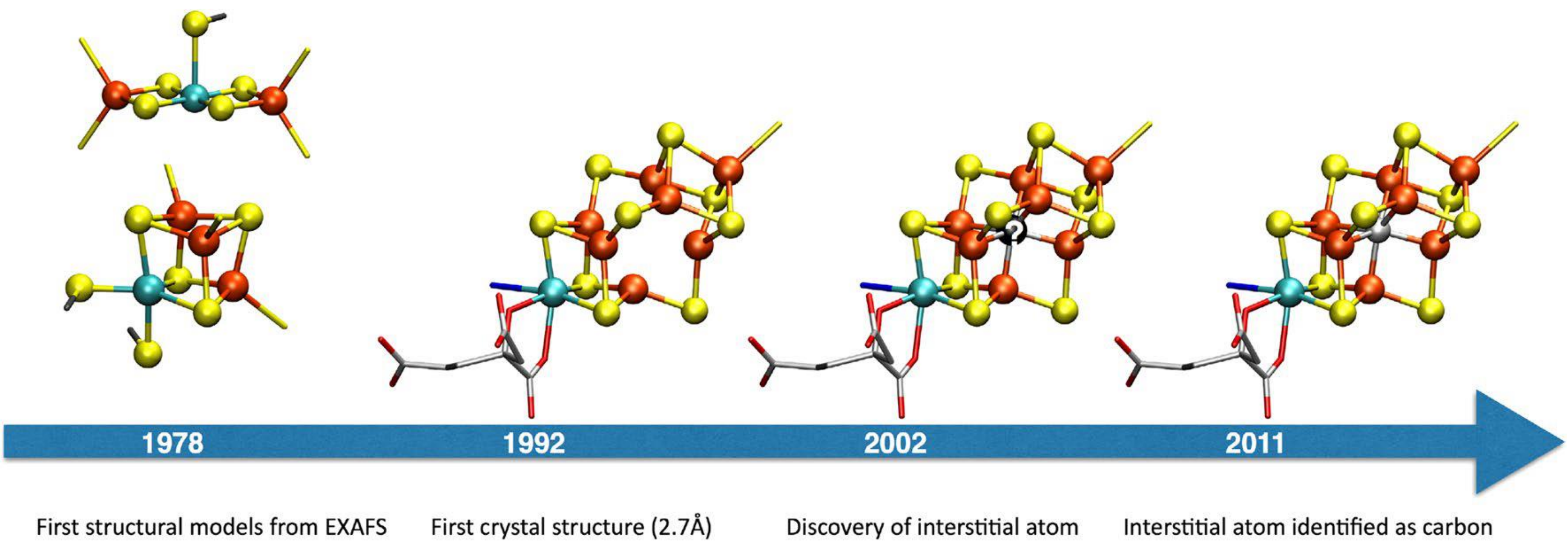

Cys 275
His 442
homocitrate
Cys 275
His 442
homocitrate

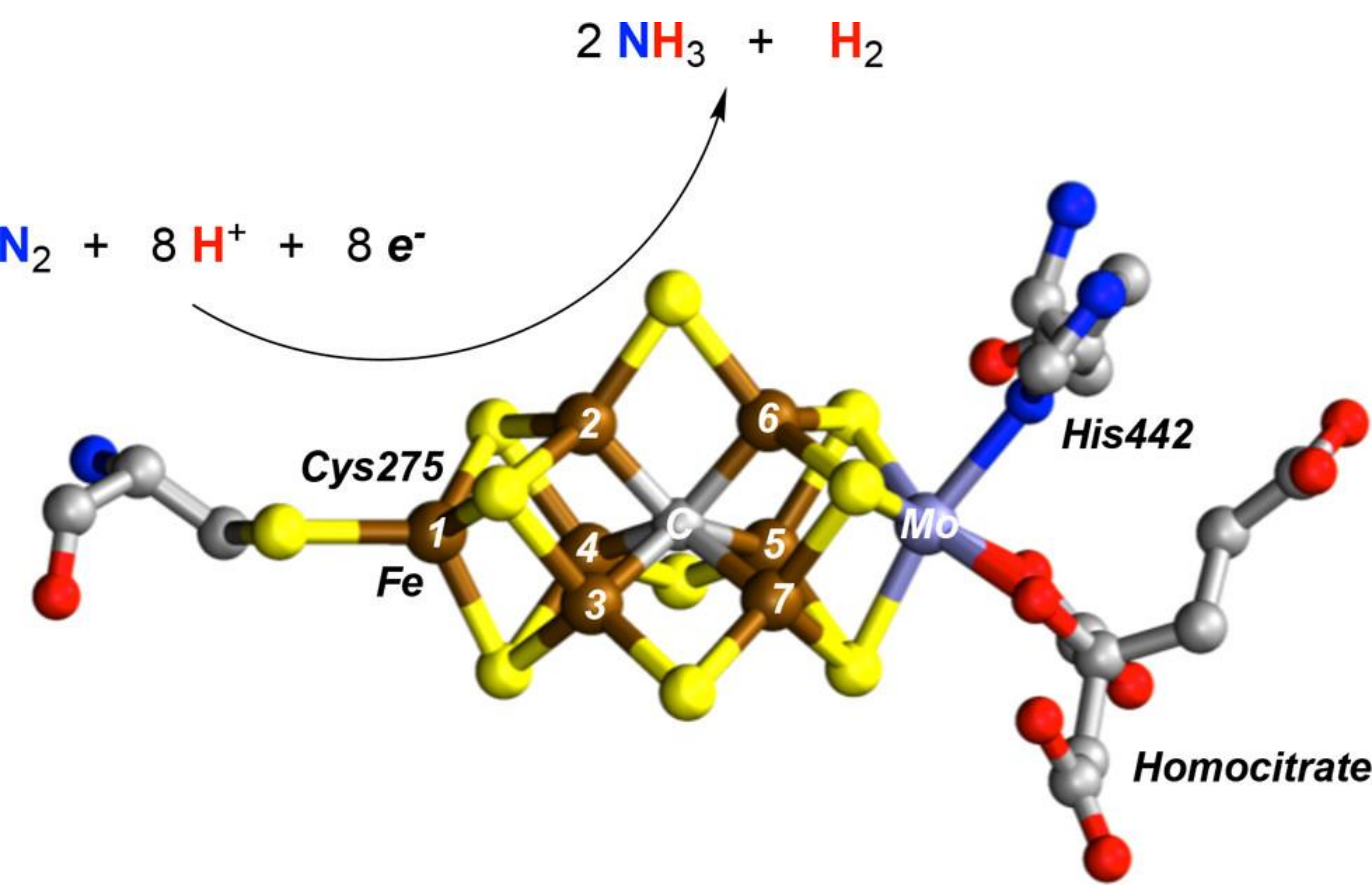
X = C

Science, 2011



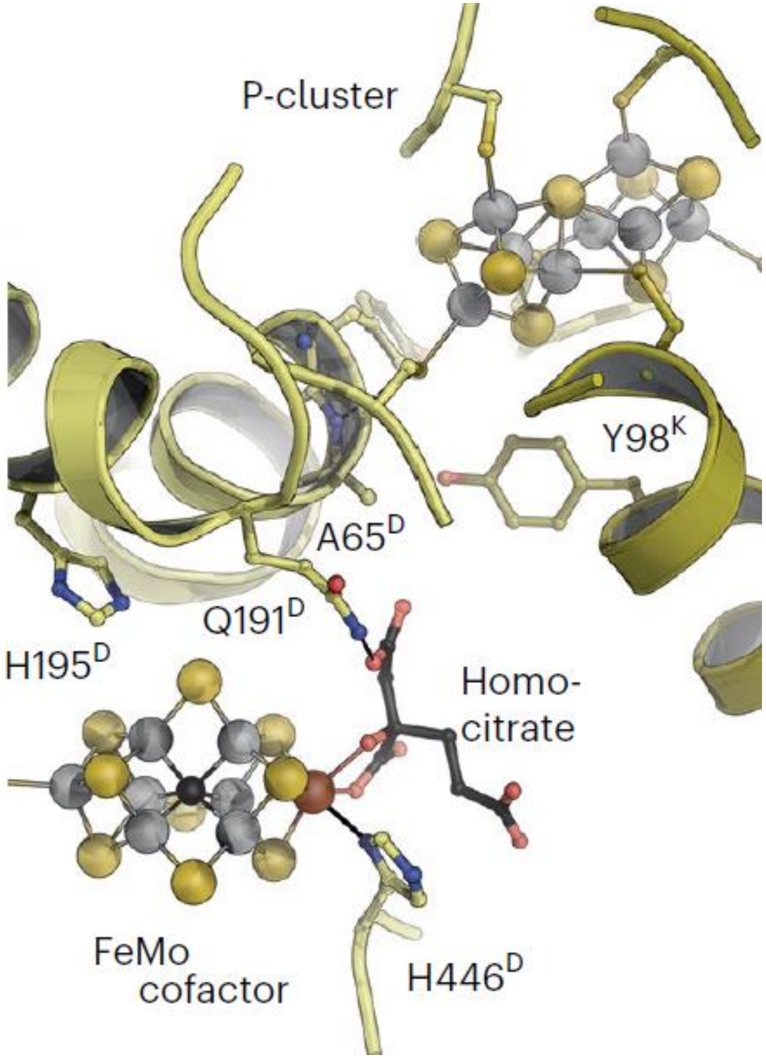
Carbide, C^{4-}



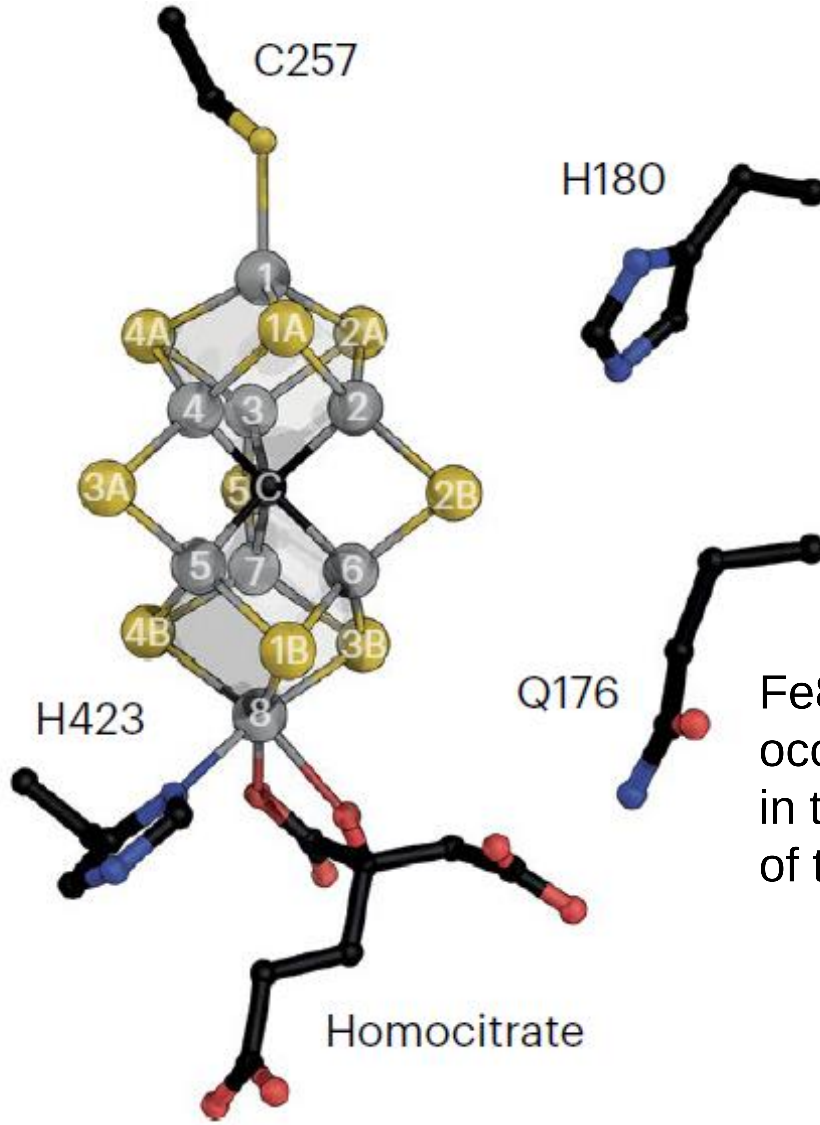


2 NH3 + H2
N2 + 8 H+ + 8 e-
Cys275
Fe
1
2
3
4
5
6
7
C
Mo
His442
Homocitrate

Presumed electron transfer pathway between P-cluster and FeMo cofactor



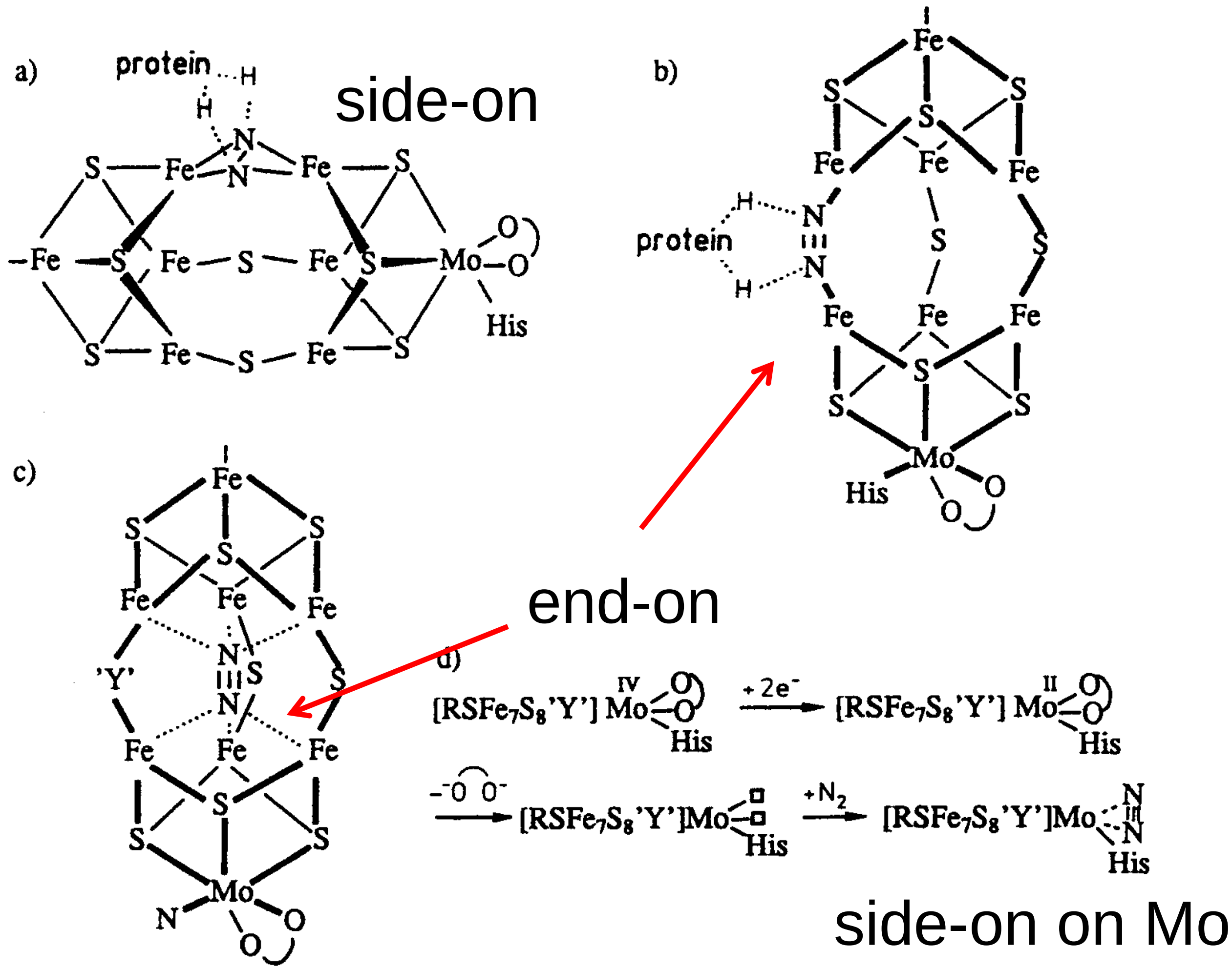
Structure of the FeFe cofactor



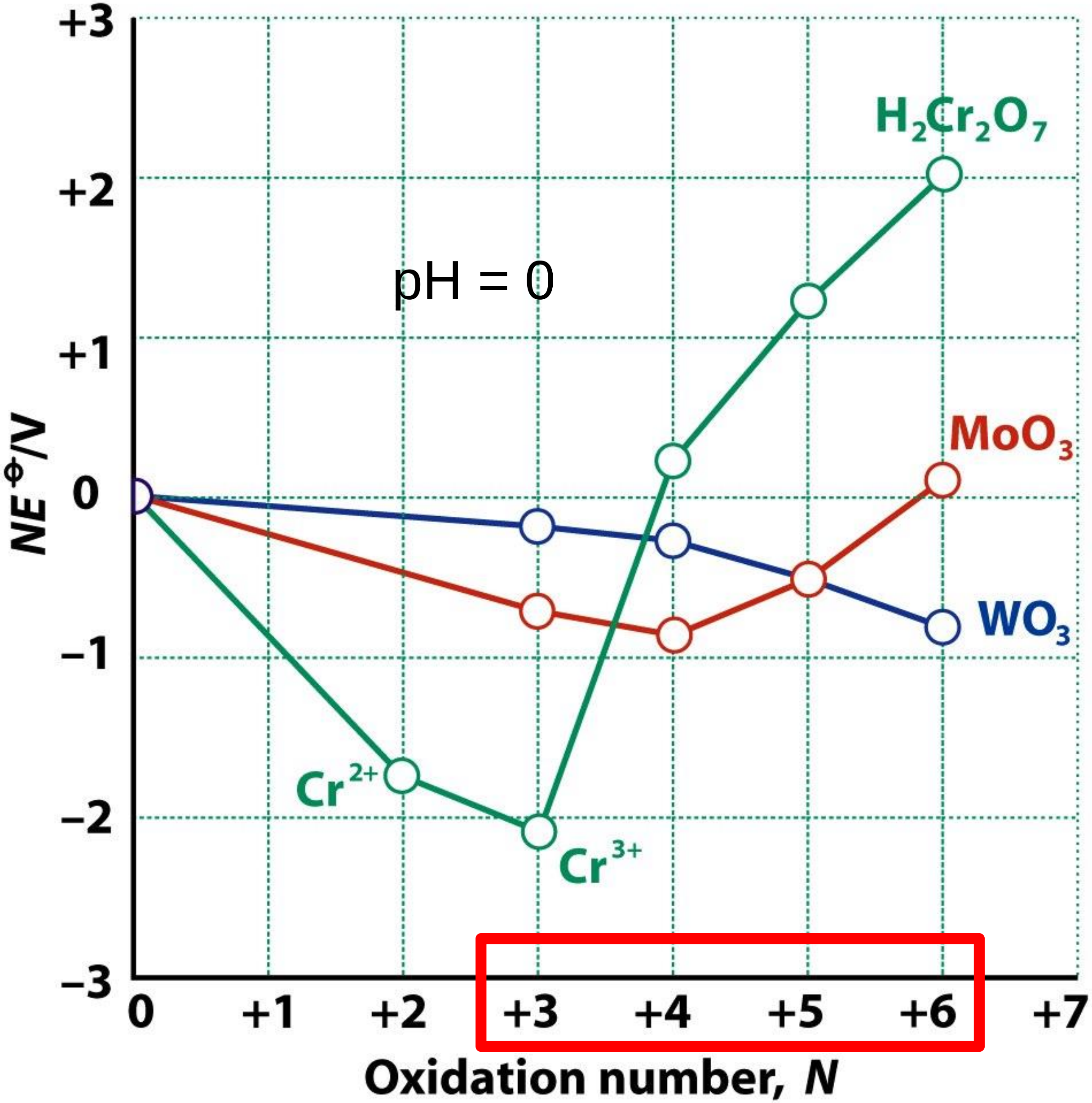
Fe8 takes the place occupied by Mo or V in the other isoforms of the enzyme

Nature Catalysis, 2023

Possible coordination modes of N_2 to FeMoco

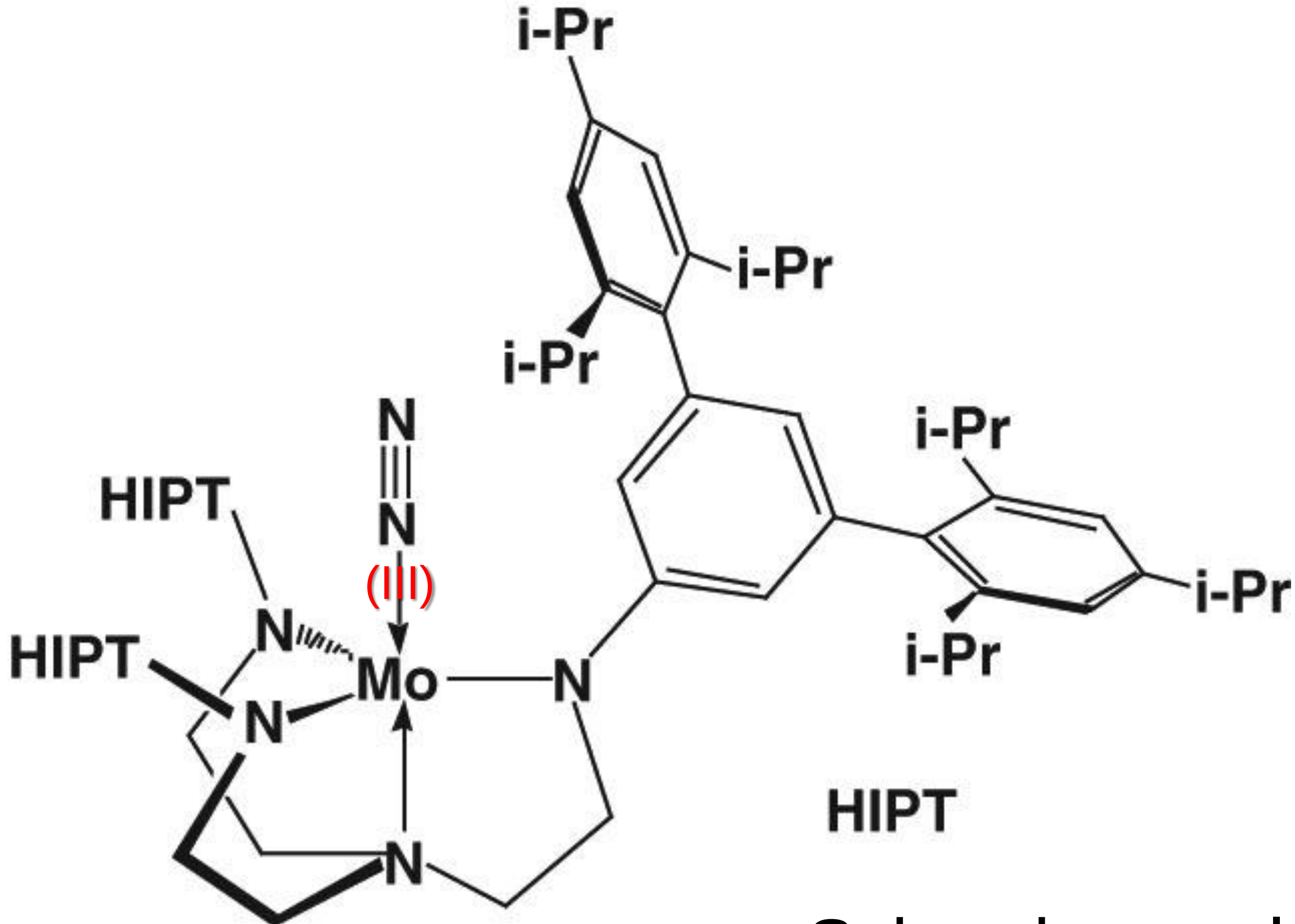


FeMoco binds N_2 only after having been reduced by 4 electrons



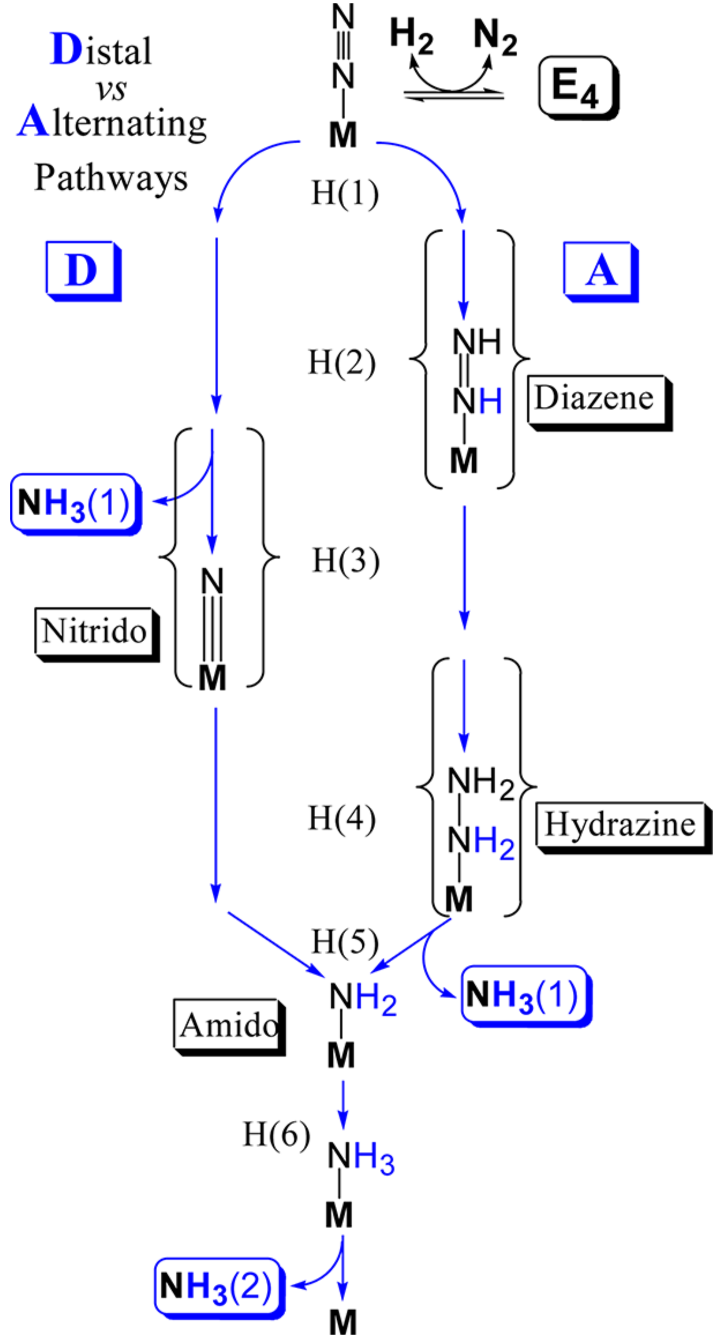
+3
+2
+1
0
−1
−2
−3
$NE^{\ominus}/V$
$H_2Cr_2O_7$
pH = 0
MoO_3
WO_3
Cr^{2+}
Cr^{3+}
0
+1
+2
+3
+4
+5
+6
+7
Oxidation number, N

Models

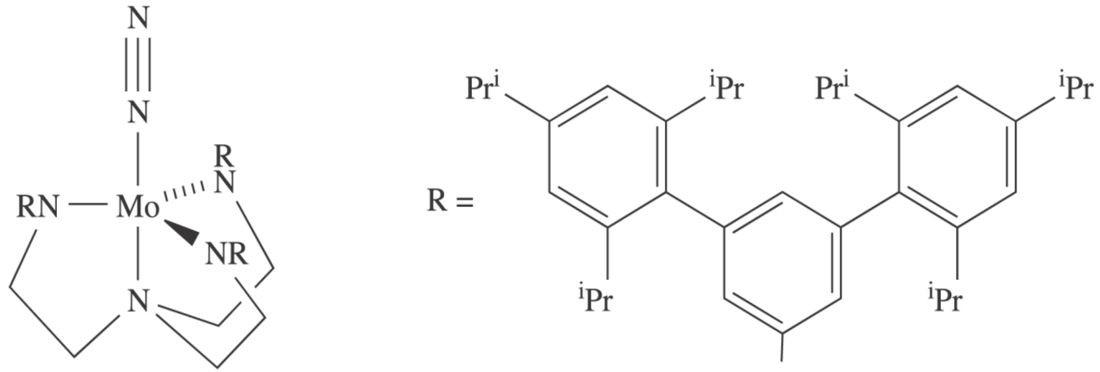


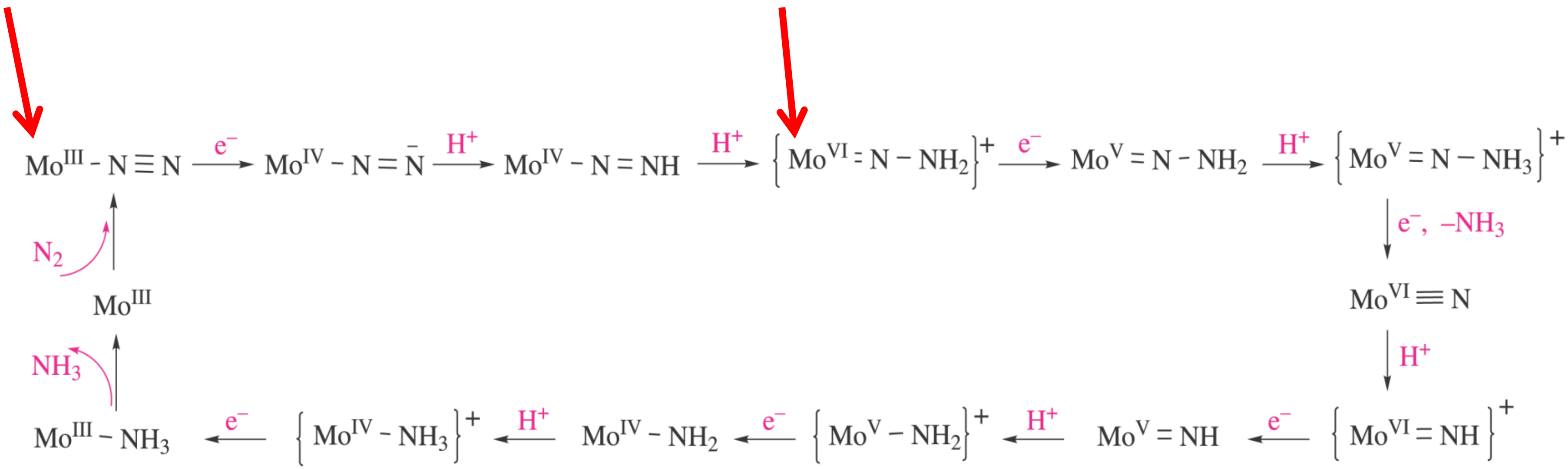
Schrock complex
(*Science* 2003)

Distal and Alternating hypotetical catalytic cycles



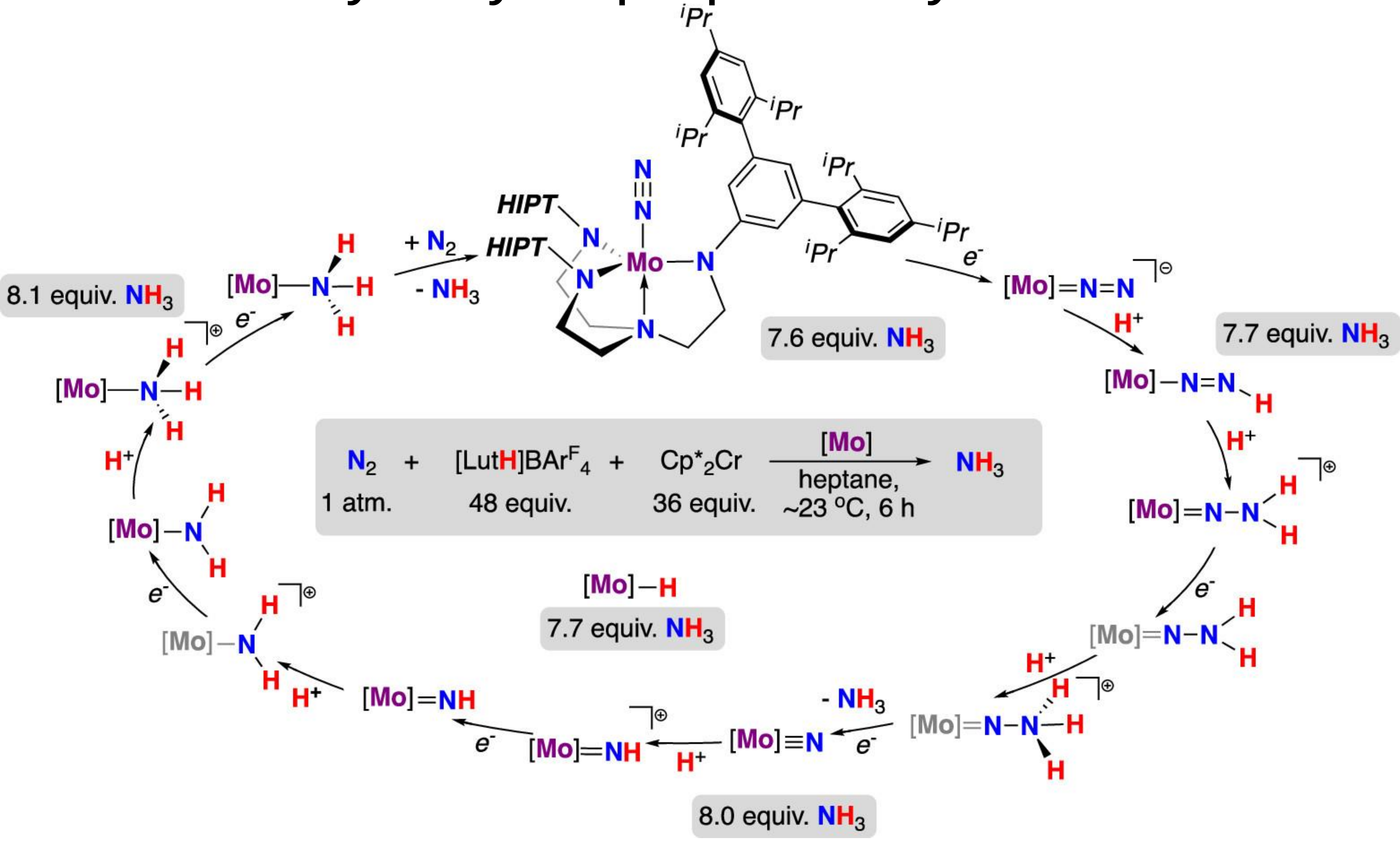
Scheme of the N_2 to NH_3 "catalytic" reduction on Mo





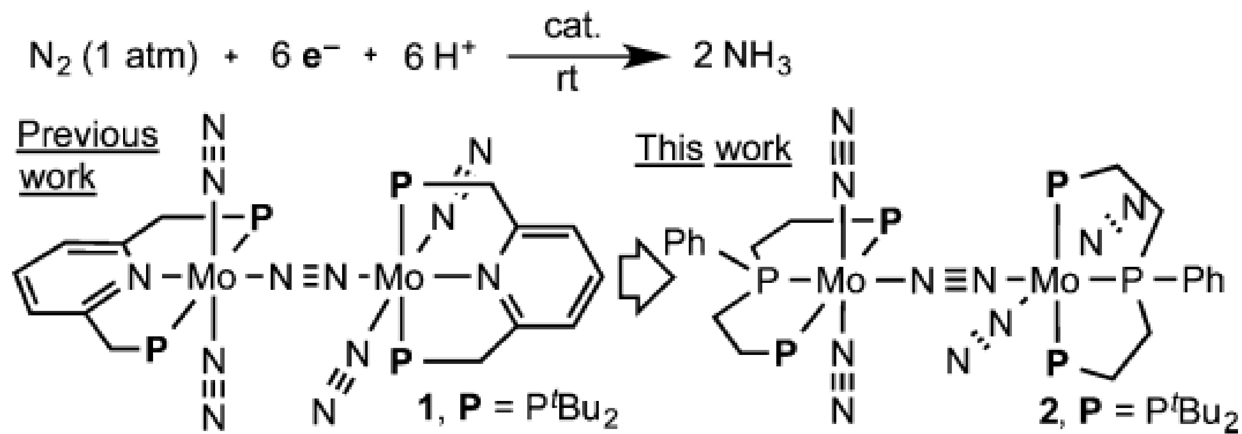
8 catalytic cycles, *distal* mechanism

Catalytic cycle proposed by Schrock

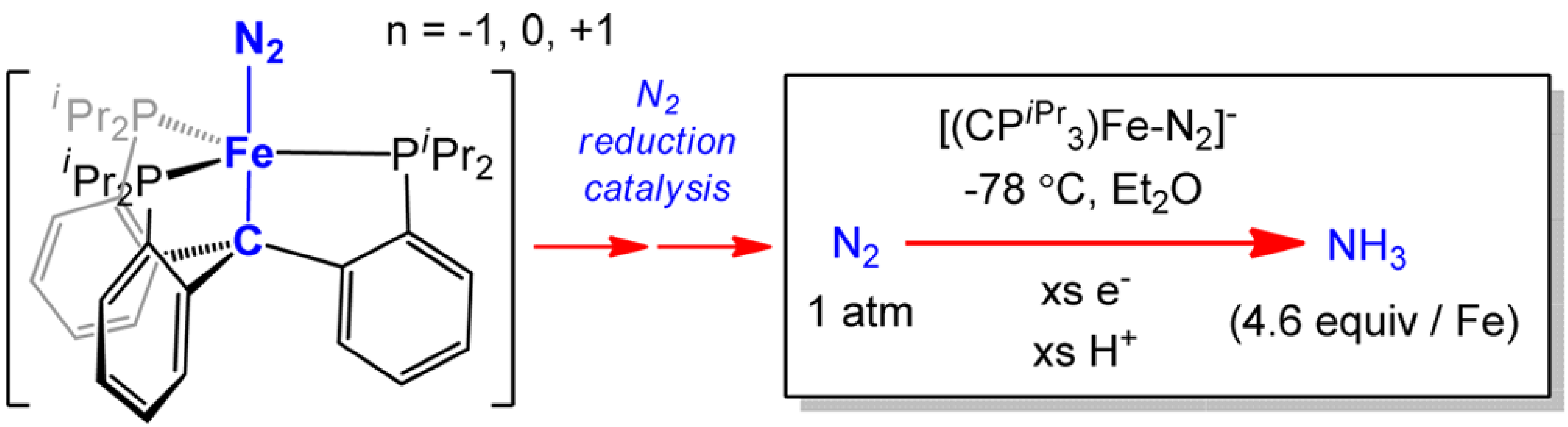


Characterized species are in purple, those hypothesized are in grey

Nishibayashi complexes (2011 e 2015)
26 catalytic cycles, reductant $CoCp^*_2$

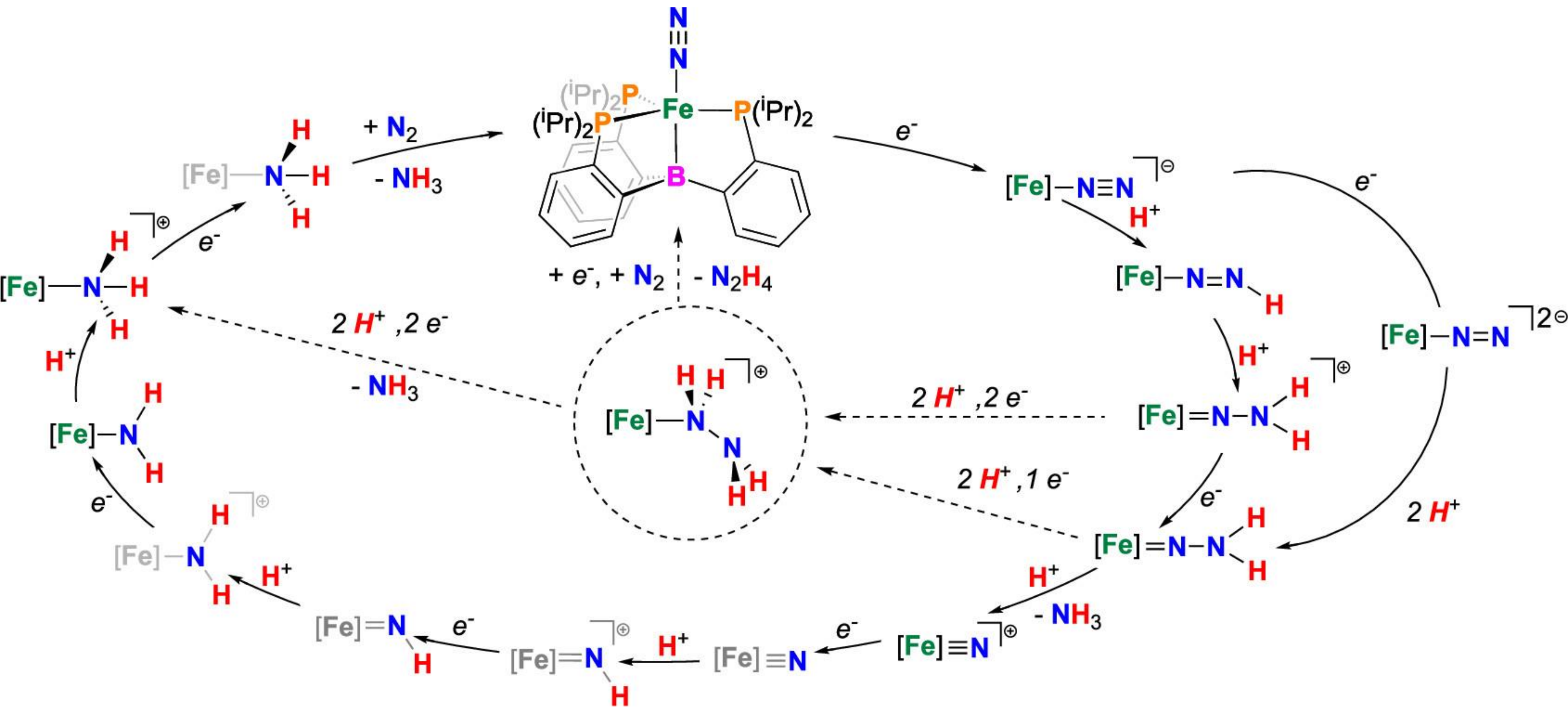


Peters complex (2014)
4.6 catalytic cycles, reductant K(crown)

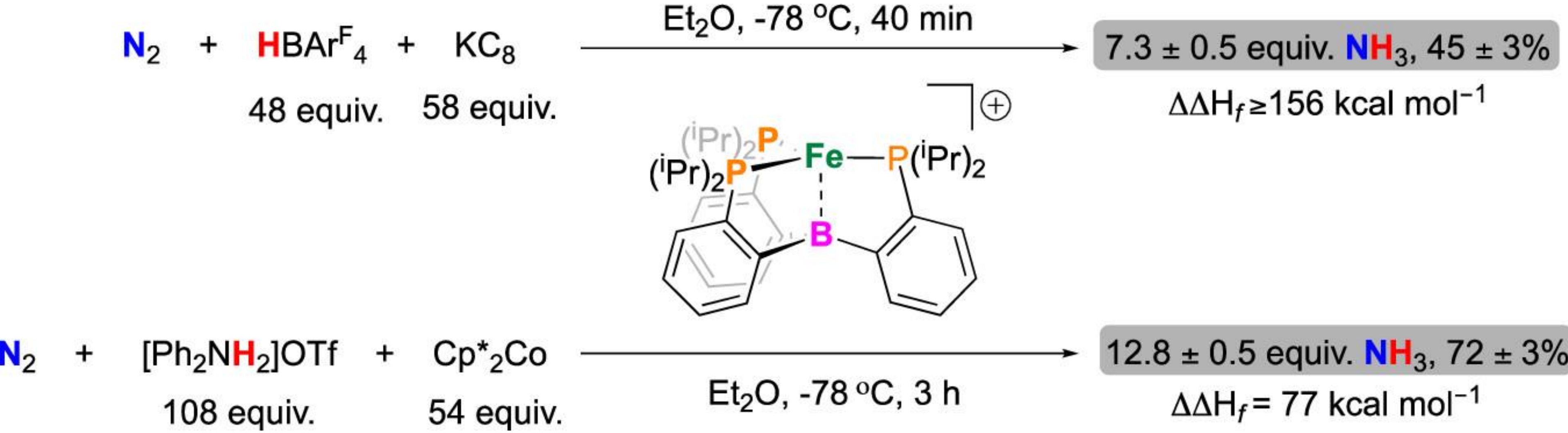


$(CP^{iPr}_3)Fe-N_2$

Catalytic cycle proposed by Peters



Characterized species are in green, those hypothesized are in grey


N2 + HBArF4 + KC8
48 equiv. 58 equiv.
Et2O, -78 oC, 40 min
7.3 ± 0.5 equiv. NH3, 45 ± 3%
ΔΔHf ≥156 kcal mol−1
(iPr)2P
(iPr)2P
Fe
P(iPr)2
B
N2 + [Ph2NH2]OTf + Cp*2Co
108 equiv. 54 equiv.
Et2O, -78 oC, 3 h
12.8 ± 0.5 equiv. NH3, 72 ± 3%
ΔΔHf = 77 kcal mol−1

electronic and spin structure of FeMoco

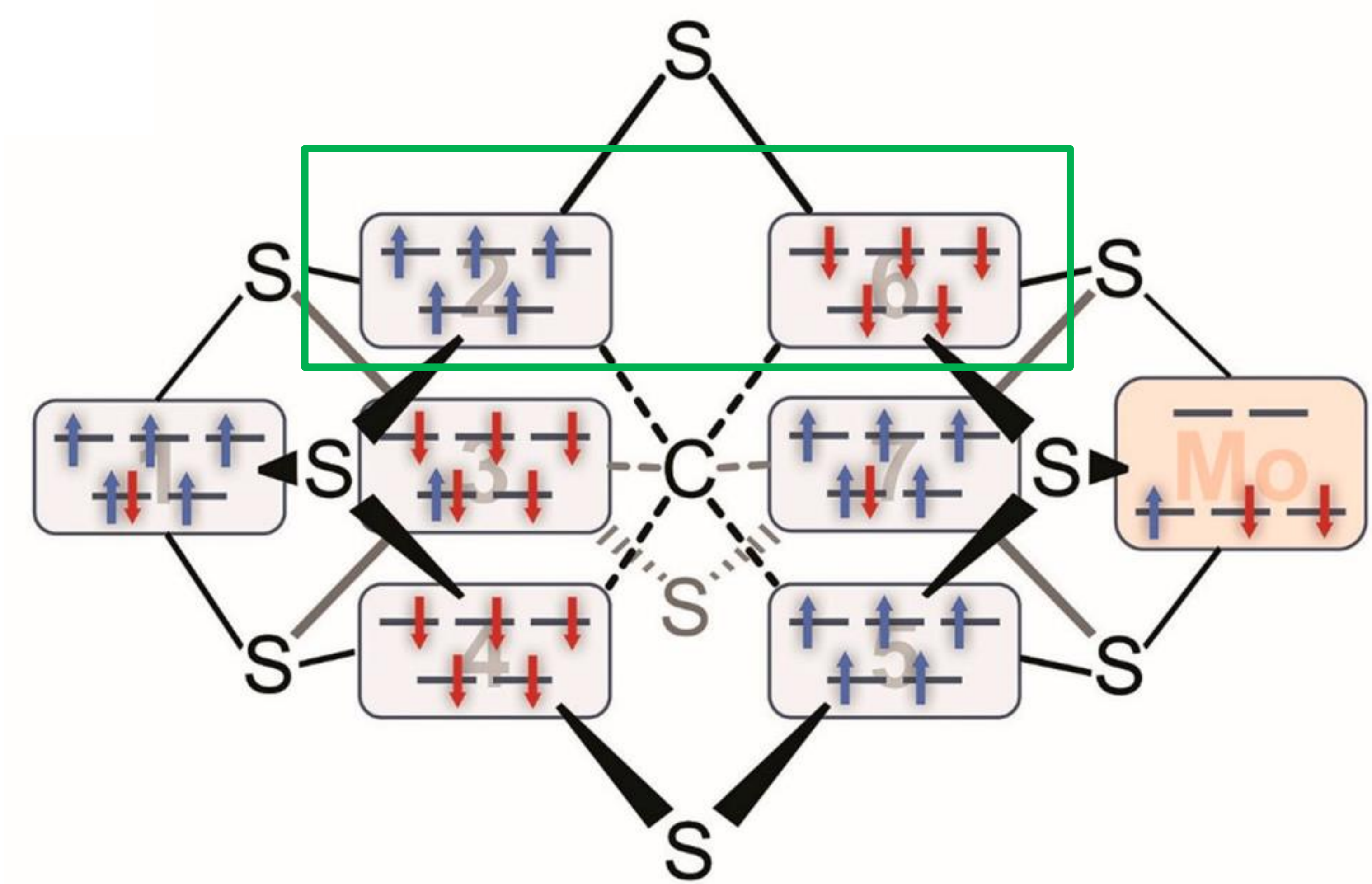
Resting state: S = 3/2

1) $[MoFe_7S_9C]^{3-}$ 6Fe(II)1Fe(III)Mo(IV)
2) $[MoFe_7S_9C]^{1-}$ 4Fe(II)3Fe(III)Mo(IV) Mo(IV), d^2 $S = 0$
3) $[MoFe_7S_9C]^{1+}$ 2Fe(II)5Fe(III)Mo(IV)

2014: Mo(III), d^3 low spin (↑↑↓)? (violation of Hund's rule)

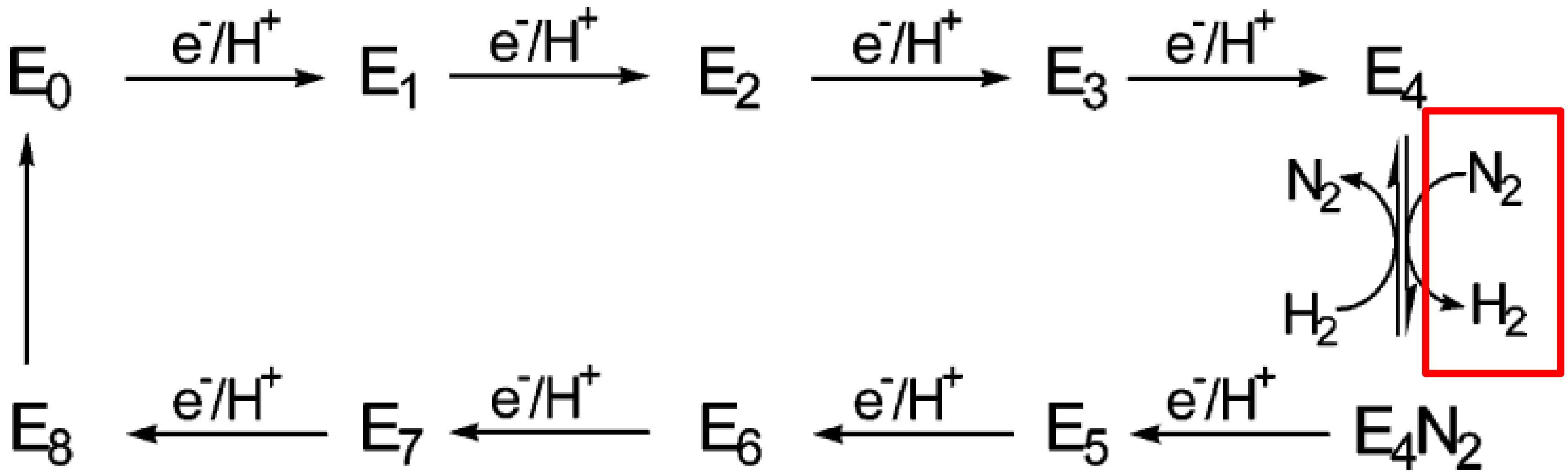
6Fe(II)1FeIII)Mo(IV) → 5Fe(II)2Fe(III)Mo(III)
4Fe(II)3Fe(III)Mo(IV) → 3Fe(II)4Fe(III)Mo(III)
2Fe(II)5Fe(III)Mo(IV) → 1Fe(II)6Fe(III)Mo(III)

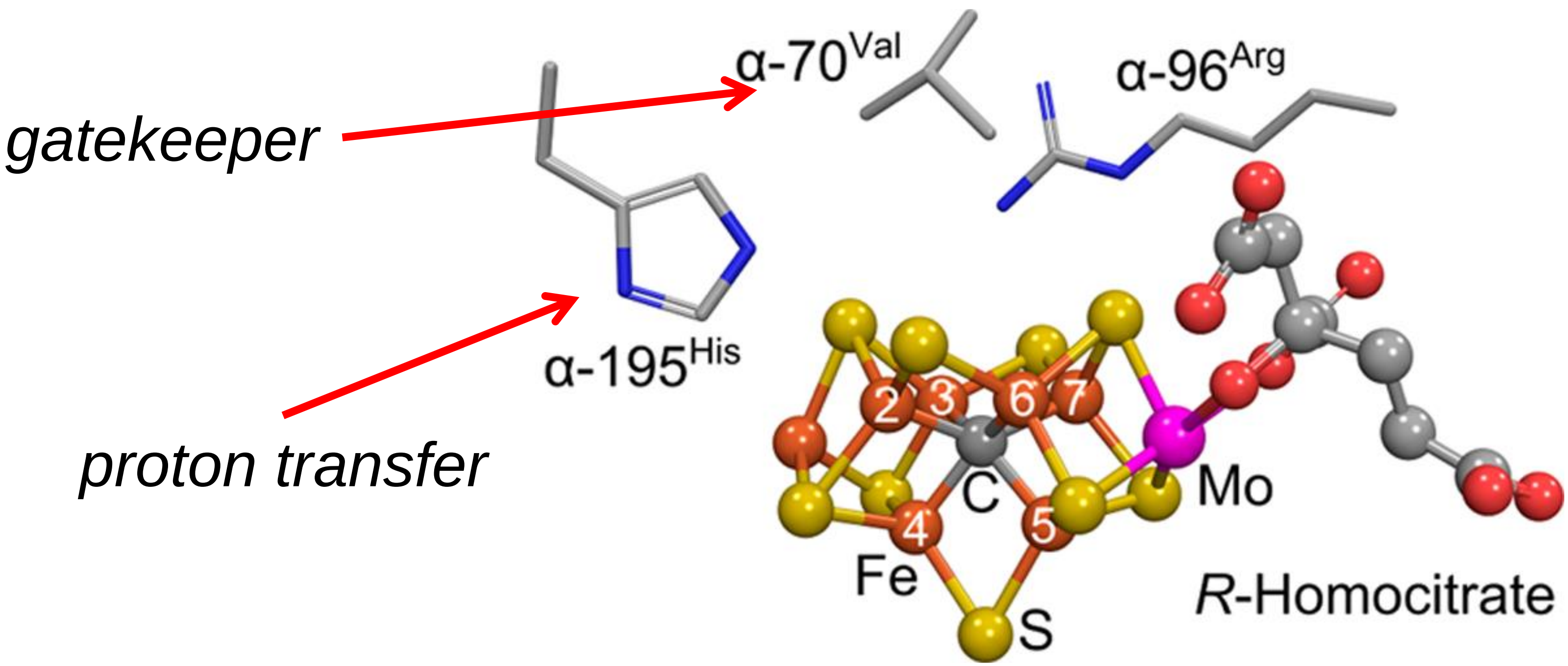
Currently most accepted electronic and spin structure of FeMoco



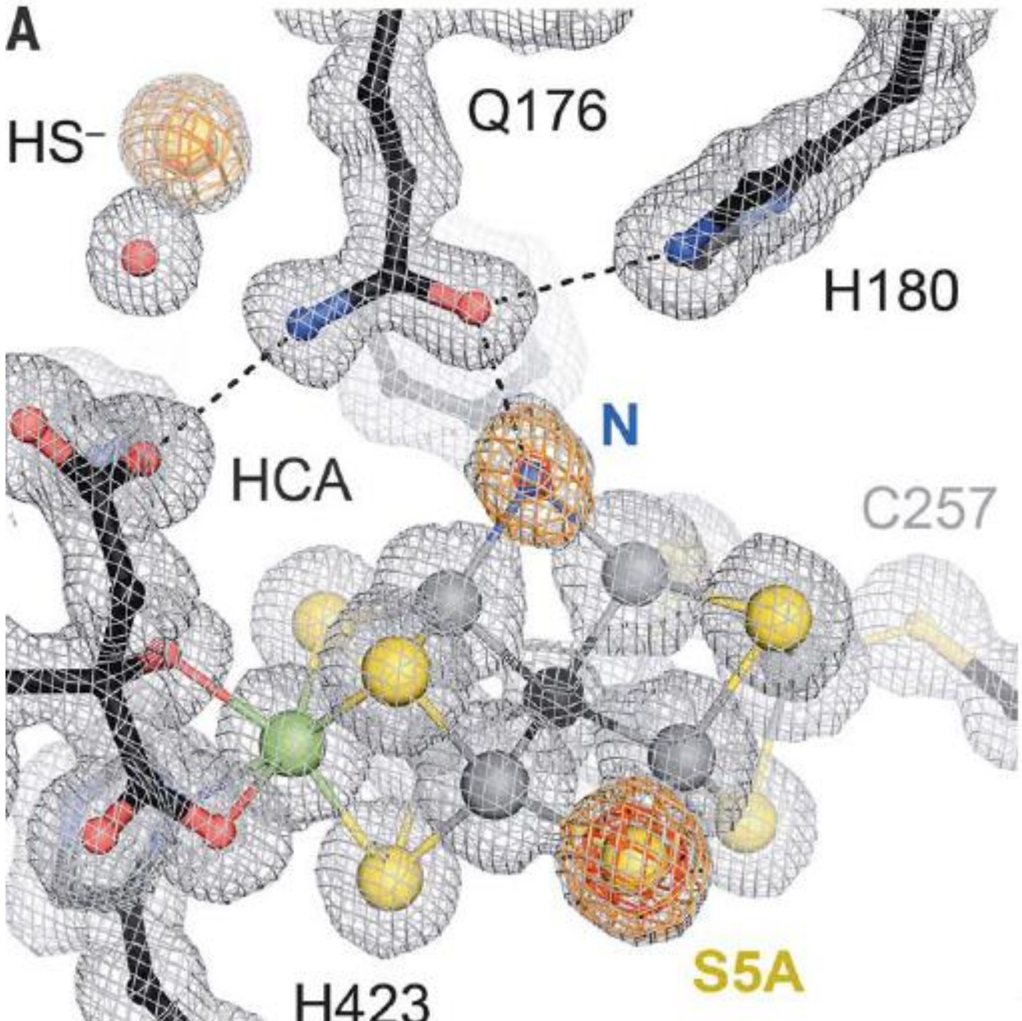
4Fe(III) + 3Fe(II)

Catalytic cycle



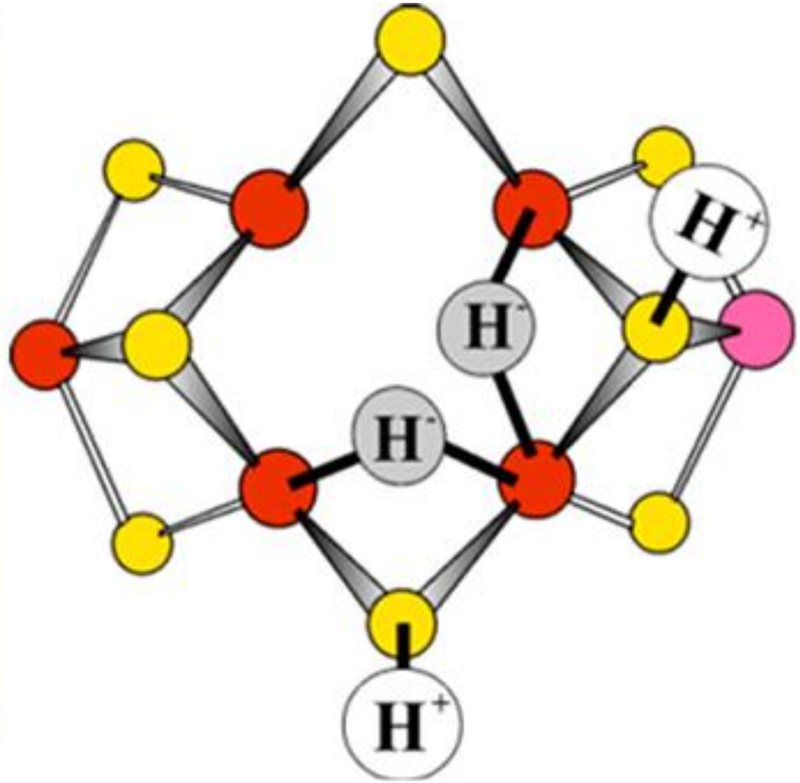


Intermediate in the FeV cofactor catalytic cycle with (presumably) a protonated NH in the active site bridging Fe2 and Fe6



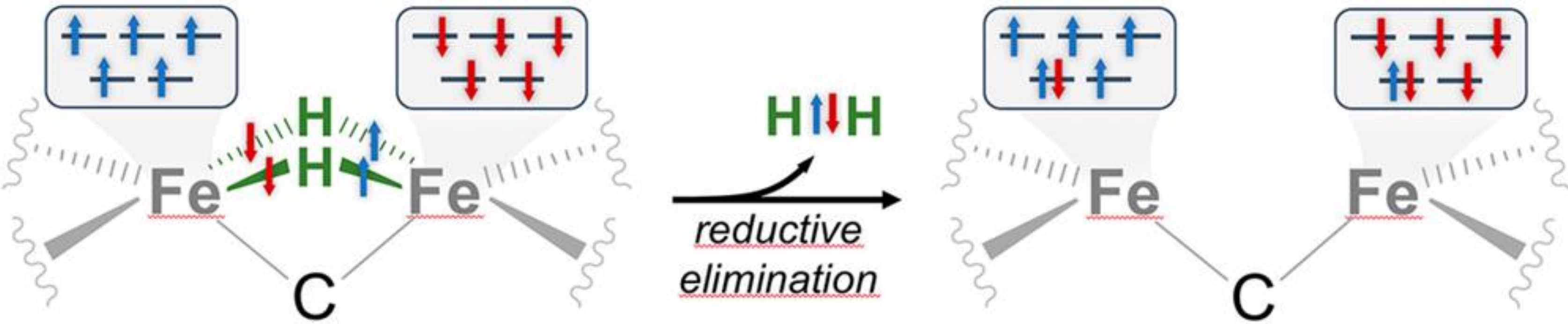
Science, 2018

«Old» model for E_4 based on spectroscopic evidence



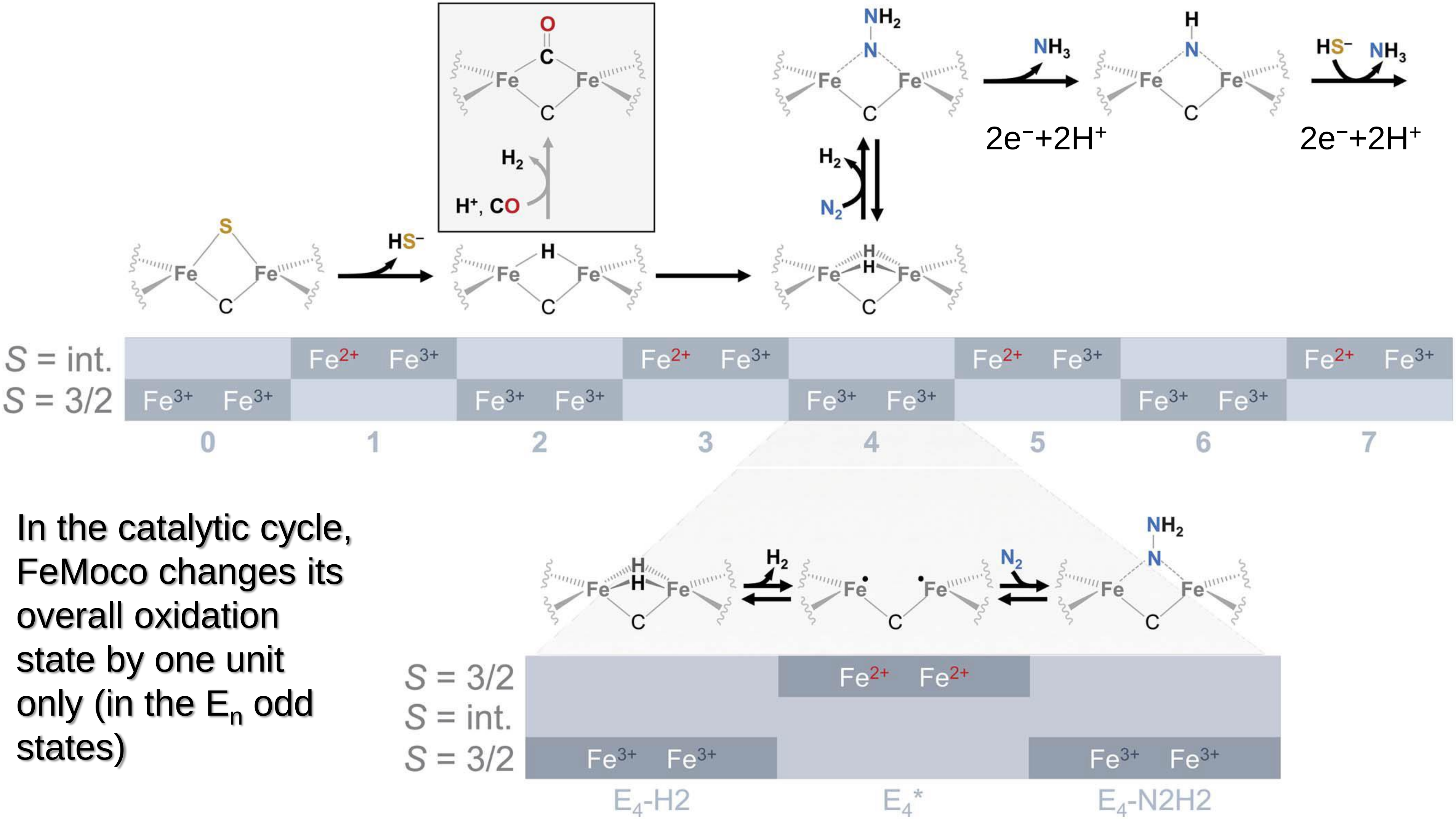
The first 4 electrons accumulate on hydrides and not on iron atoms

More recent model for E_4 based on spectroscopic evidence considering the SH displacement

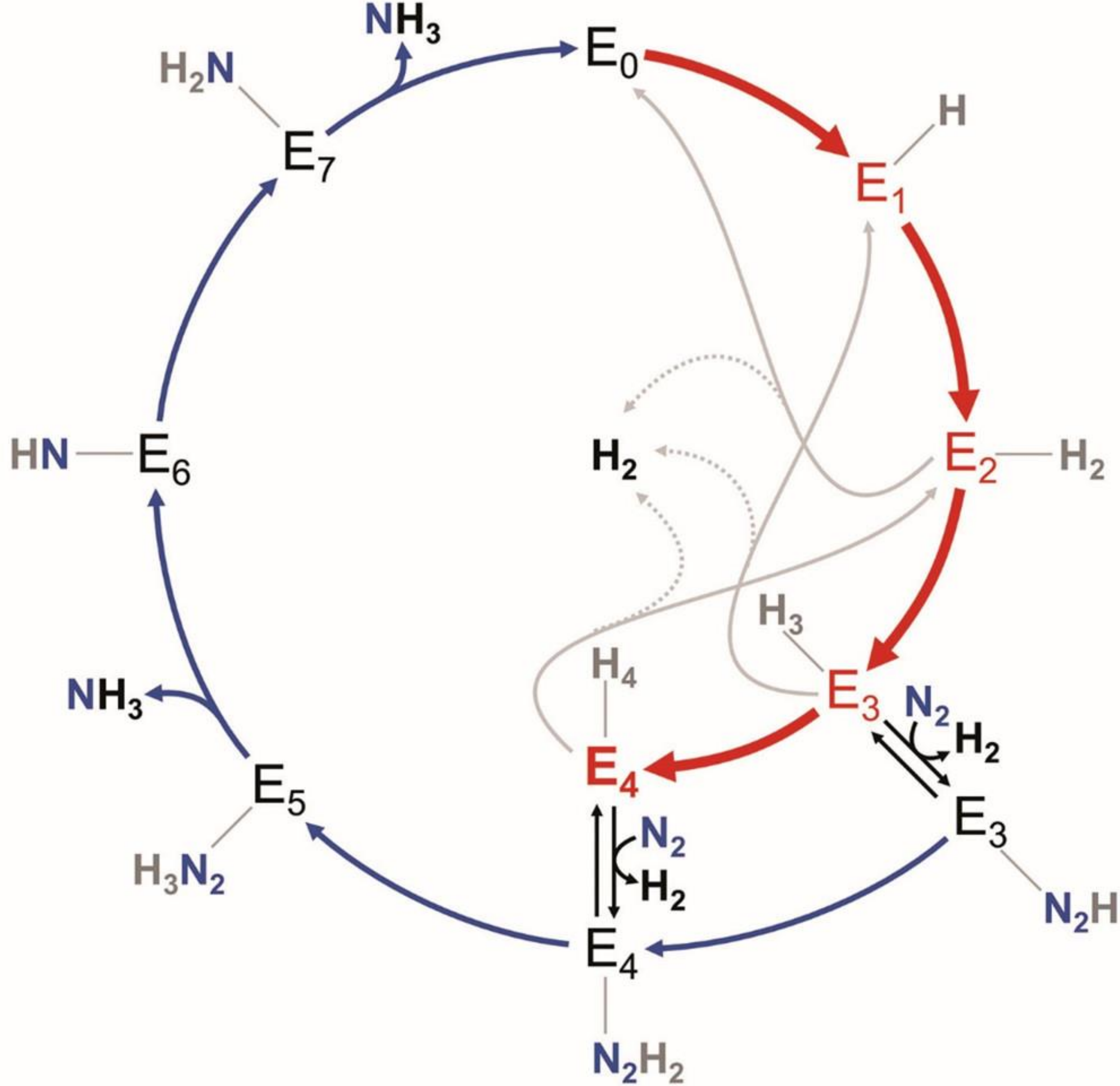


Spin-allowed process

Most recent hypothesis on catalytic cycle



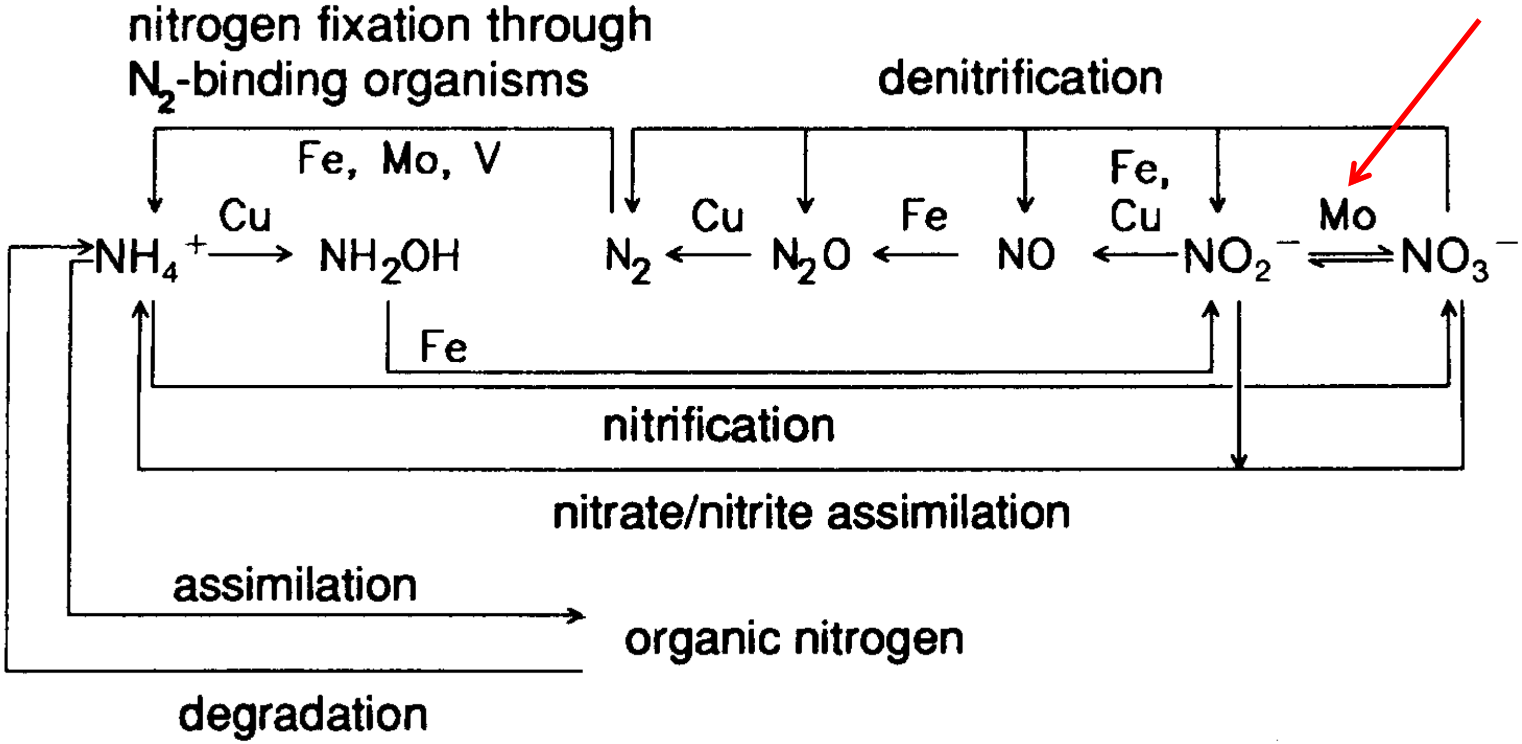
In the catalytic cycle, FeMoco changes its overall oxidation state by one unit only (in the E_n odd states)



E0
NH3
H2N
E7
H
E1
E2
H2
H2
HN
E6
H3
E3
H4
E4
N2
H2
NH3
E5
E3
N2
H2
H3N2
N2H
E4
N2H2

Other molybdenum enzymes

They catalyze the oxidation or reduction of small molecules

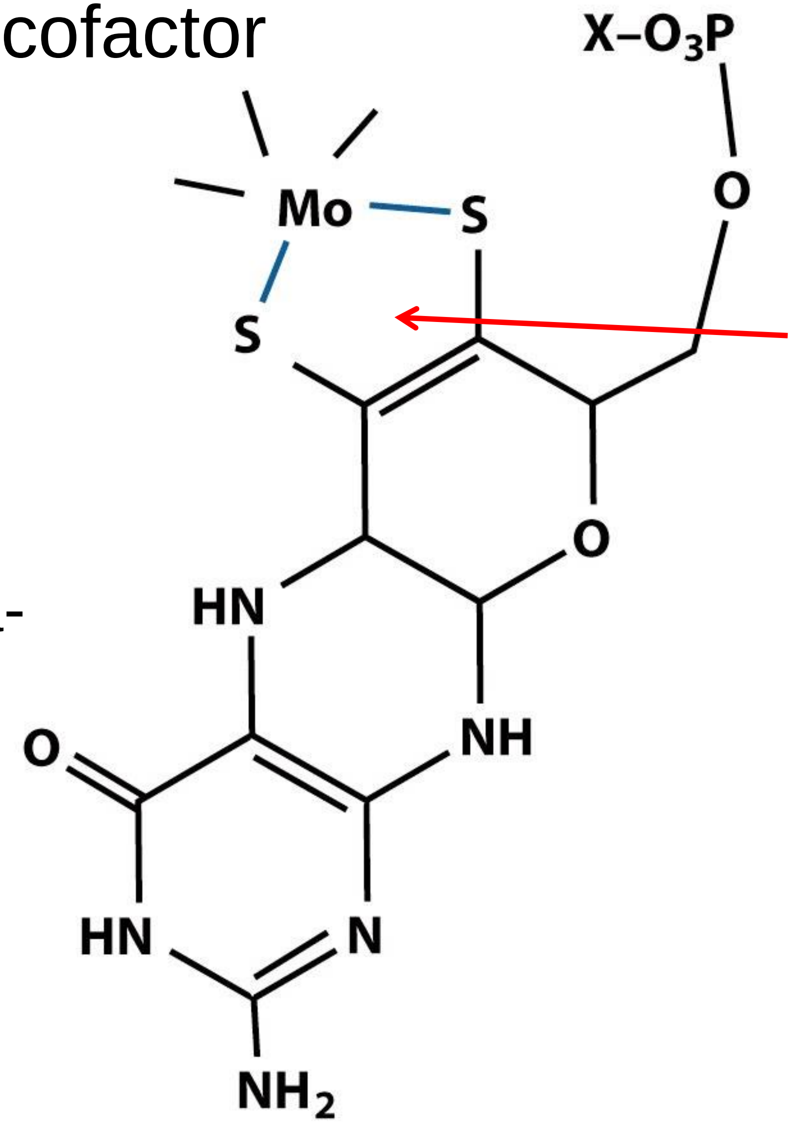


Three families of Mo enzymes (*oxotransferases*)

- xanthine-oxidase
- sulfite-oxidase
- DMSO-reductase

molybdenum cofactor

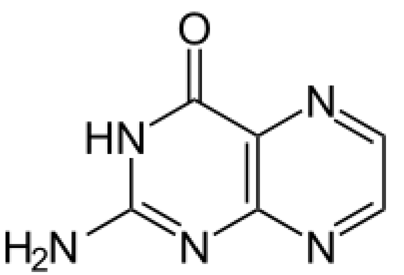
X can be a nucleobase



dithiolene

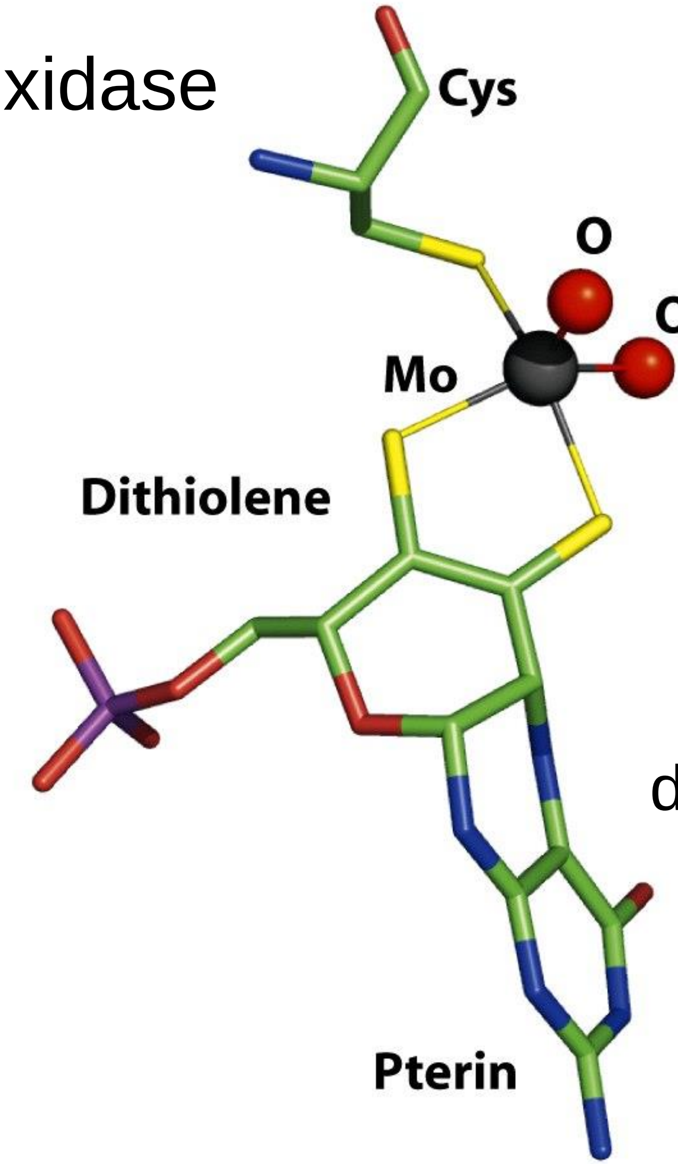
di-hydro or tetra-hydro pterin

Molybdopterin as ligand



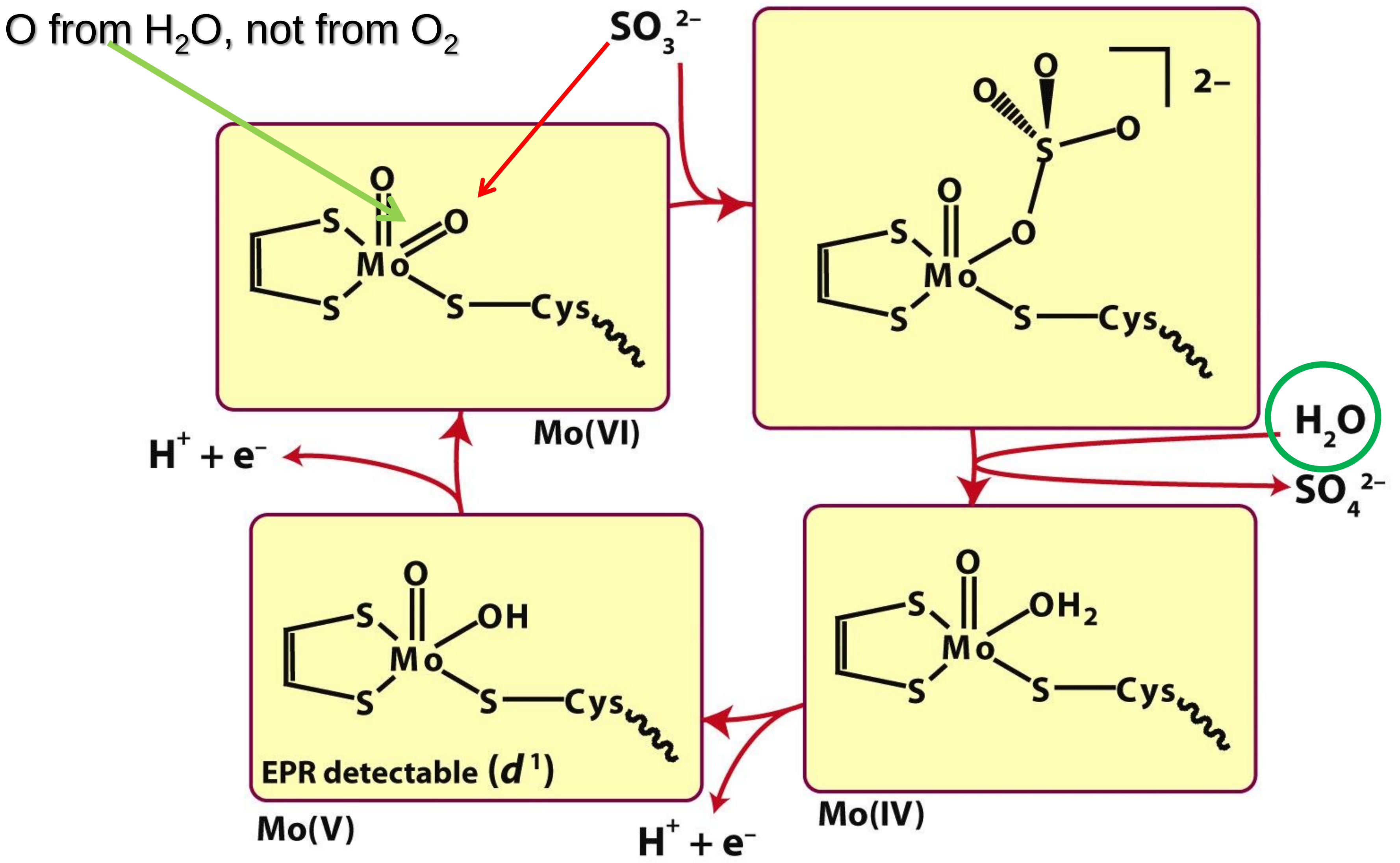
pterina

Site of sulfite-oxidase



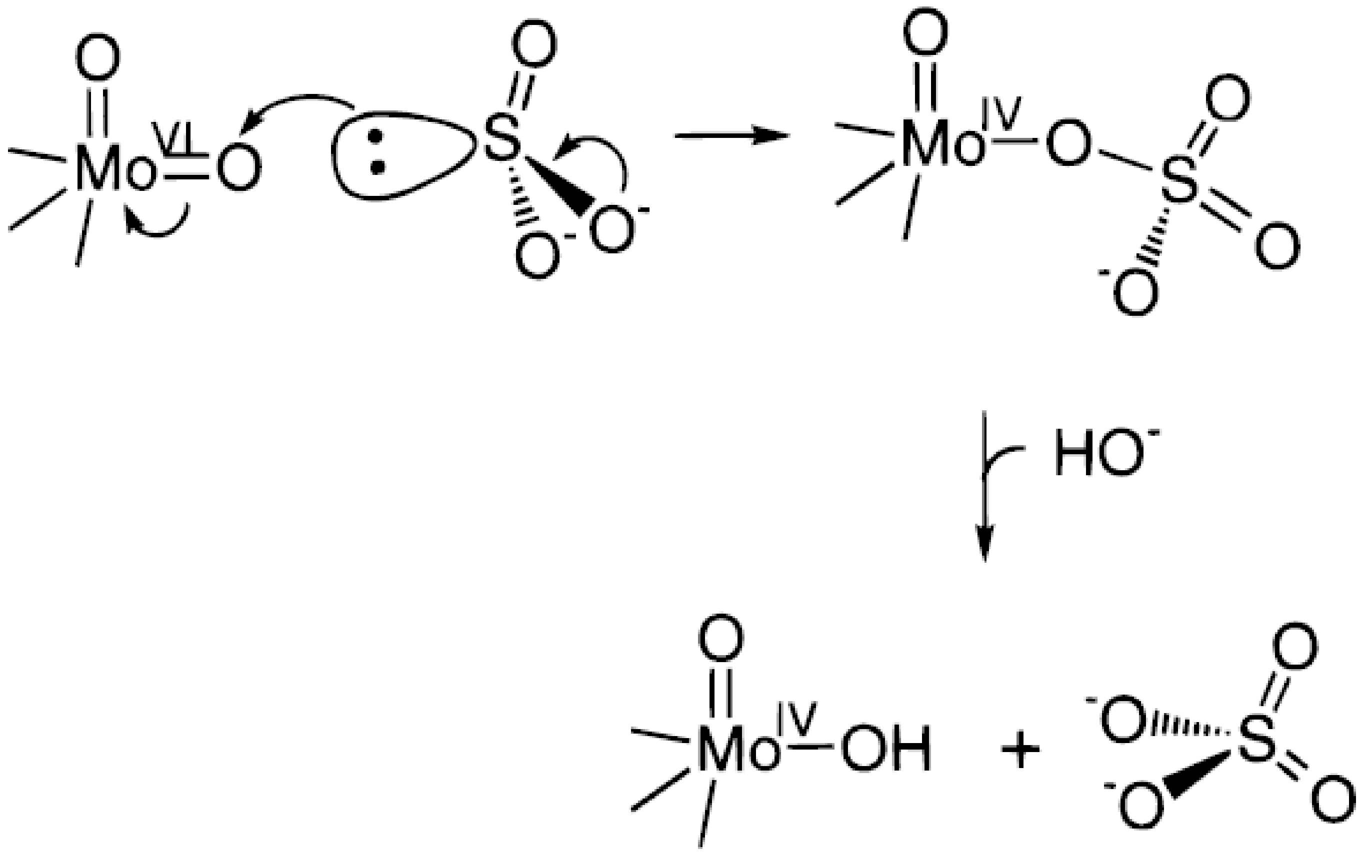
dihydro-pterin

Catalytic cycle of sulfite-oxidase

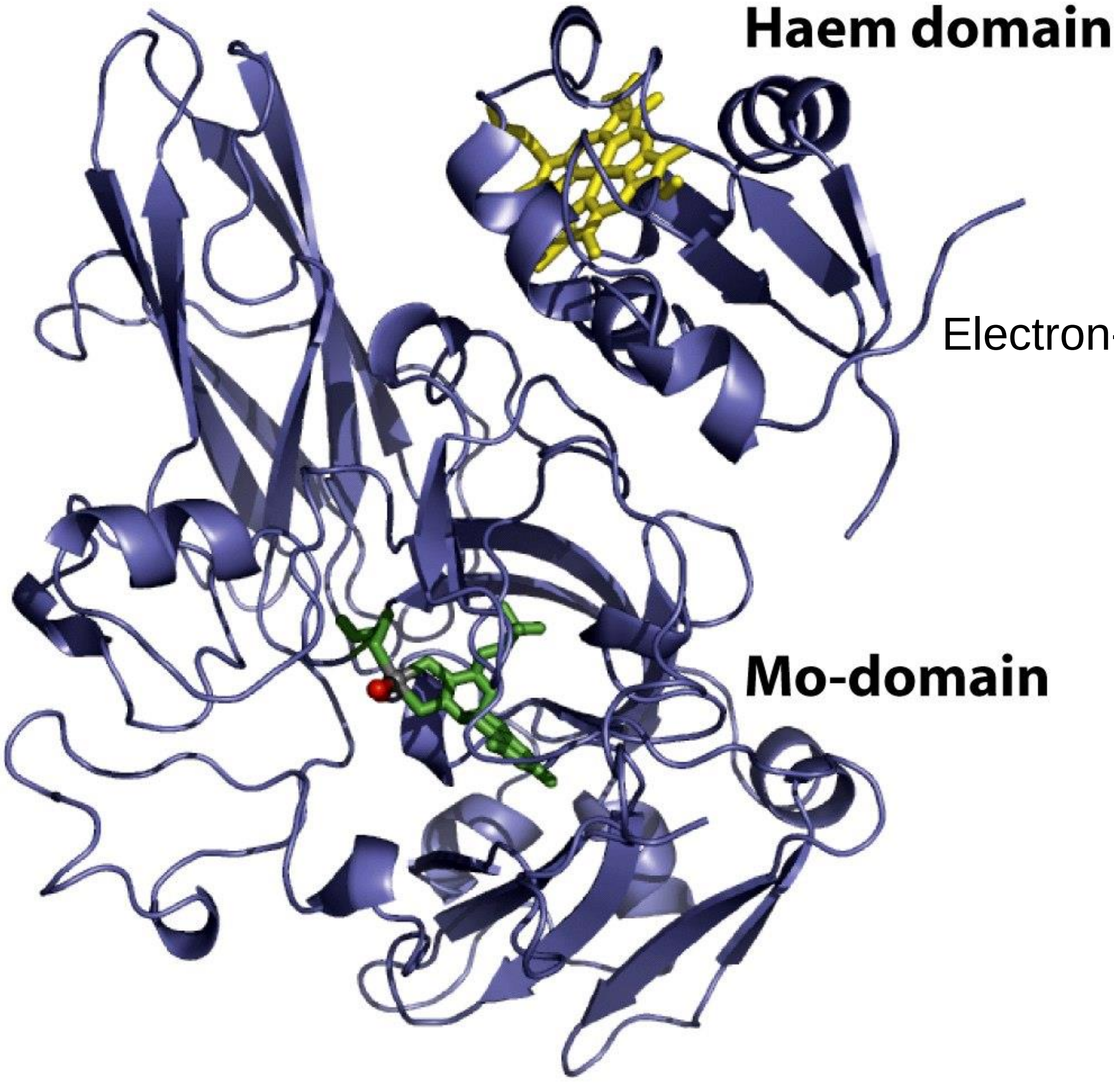


Mo has three stable oxidation states, Mo(IV), Mo(V) and Mo(VI)

Detail in the oxygen transfer mechanism



Structura of the sulfite-oxidase



(cytochrome)

Electron-acceptor from Mo

Enthalpy scale for oxygen atom transfer reactions