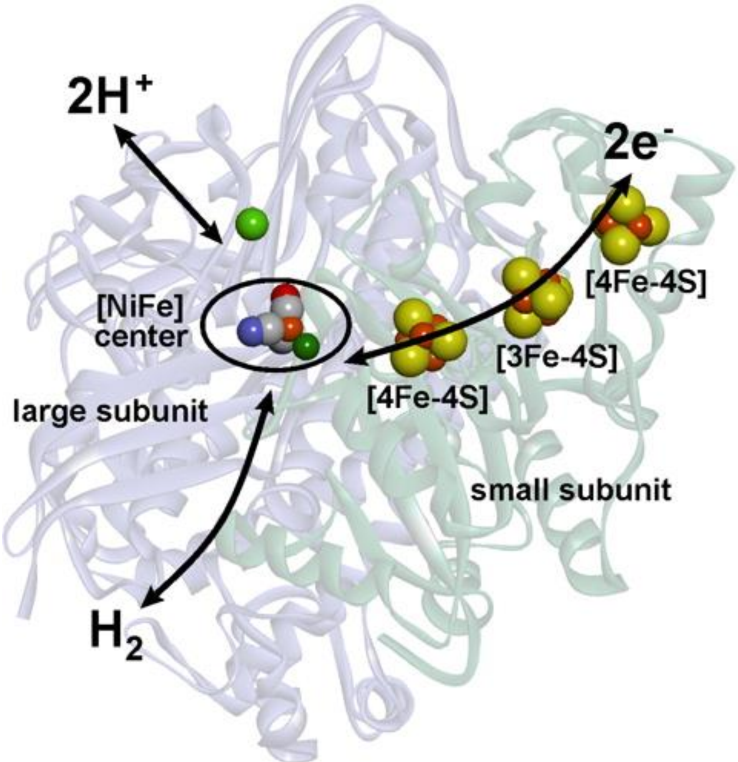
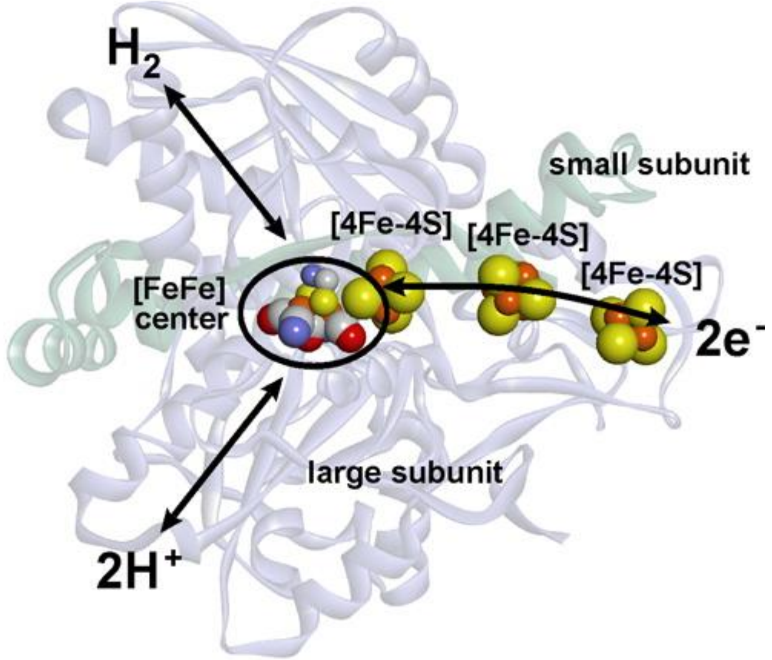
Redox balance $H_2 \leftrightarrows 2H^+ + 2e^-$ Energy production

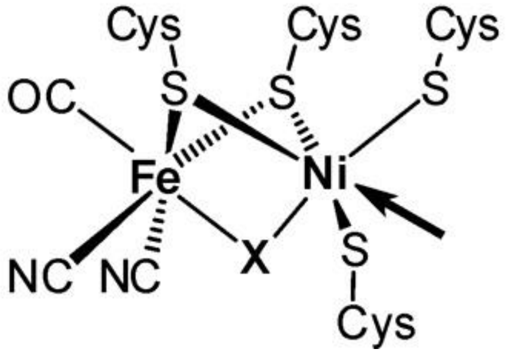
[NiFe] Hydrogenase

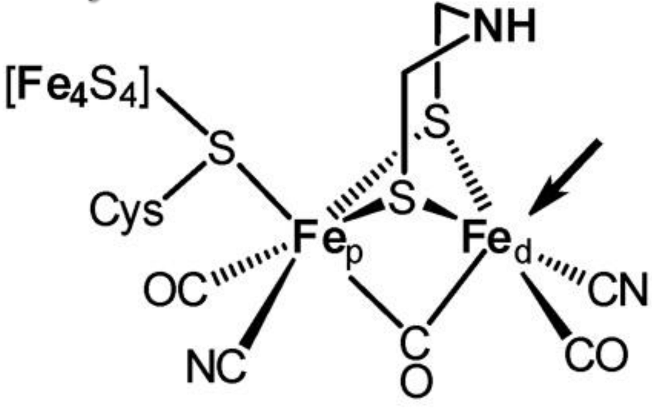


[FeFe] Hydrogenase

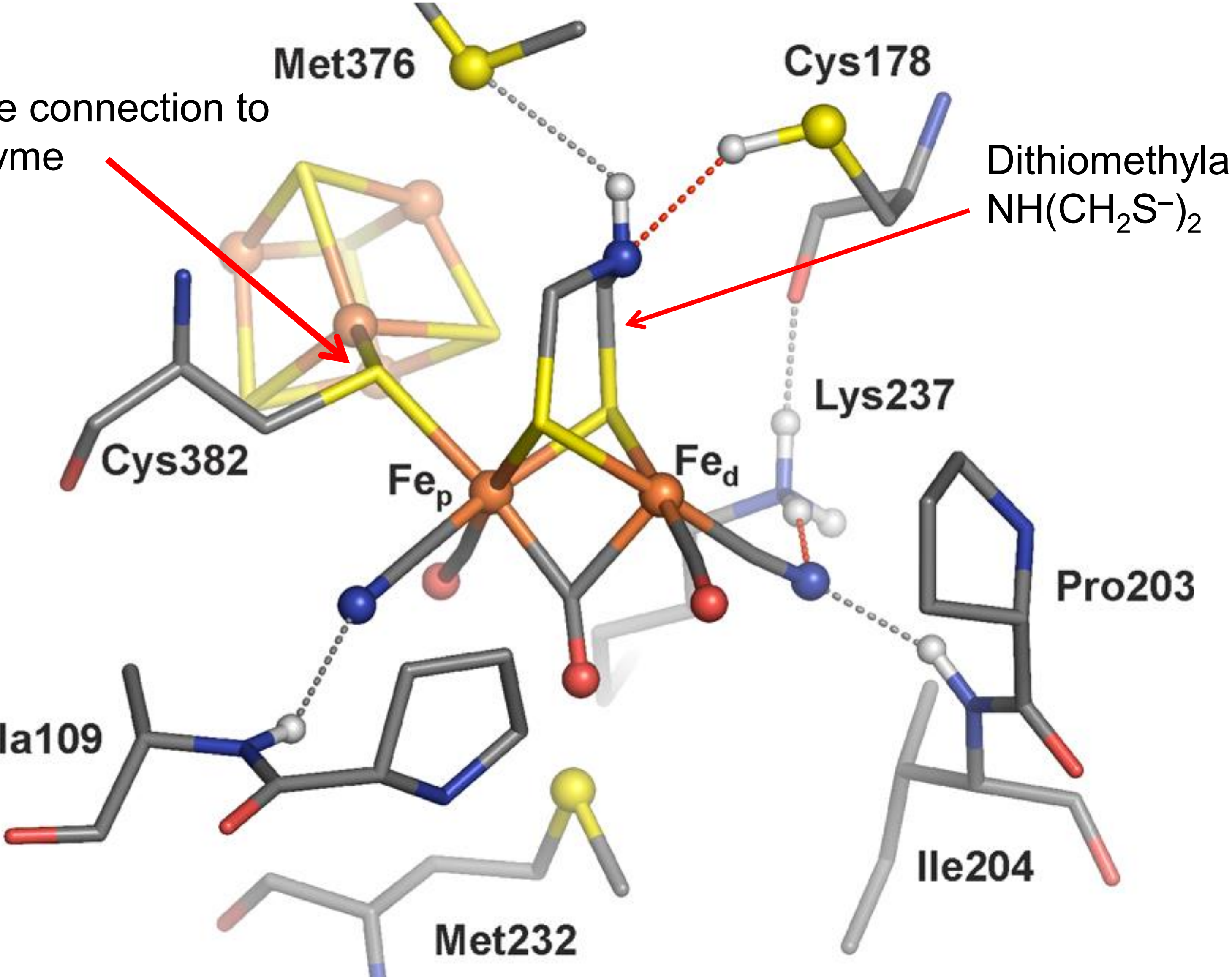


Turnover up to 10^4 cycles/second



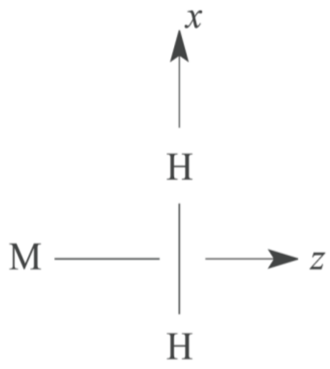


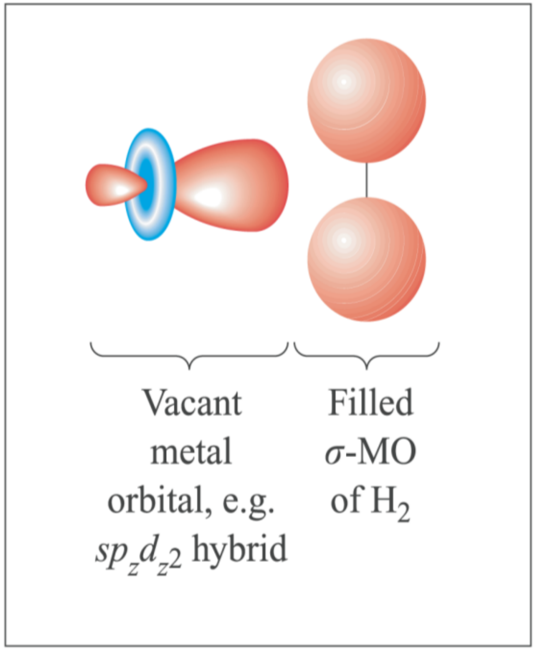
[FeFe] hydrogenase



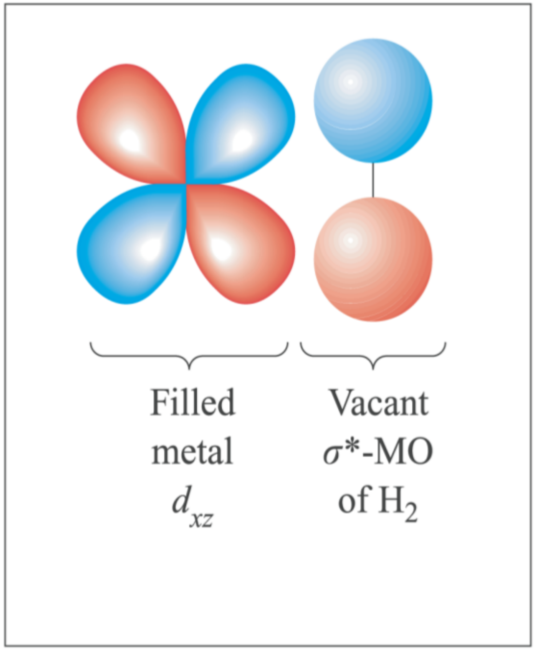
Only one connection to the enzyme

Dithiomethylamine, $NH(CH_2S^-)_2$



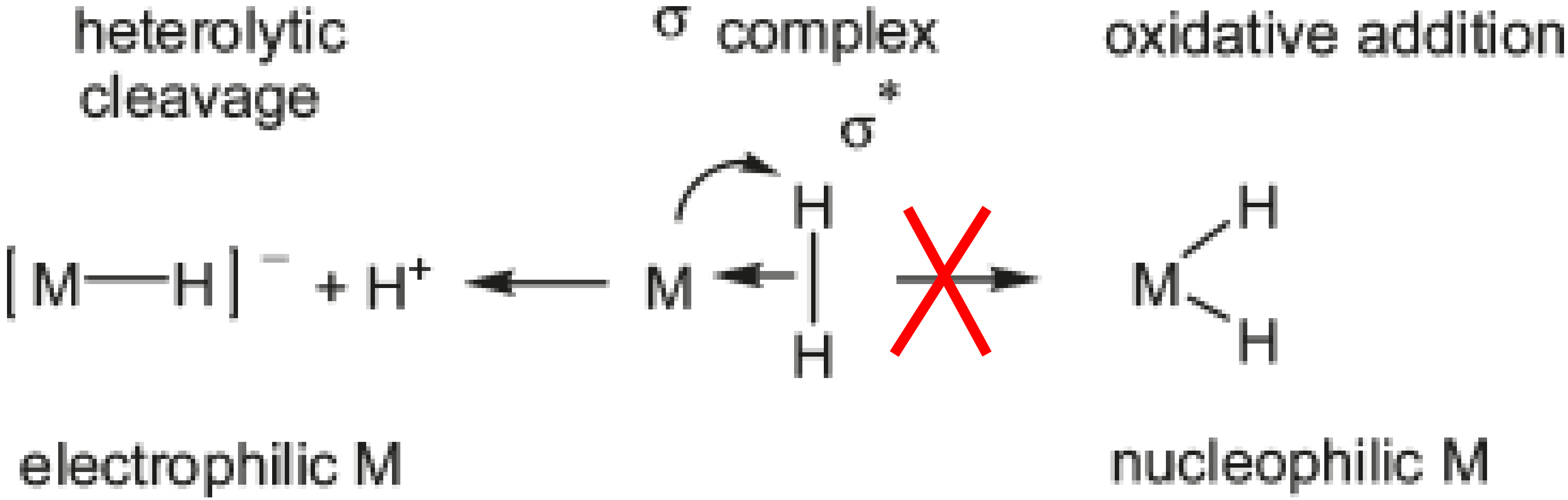


H_2-to-M donation

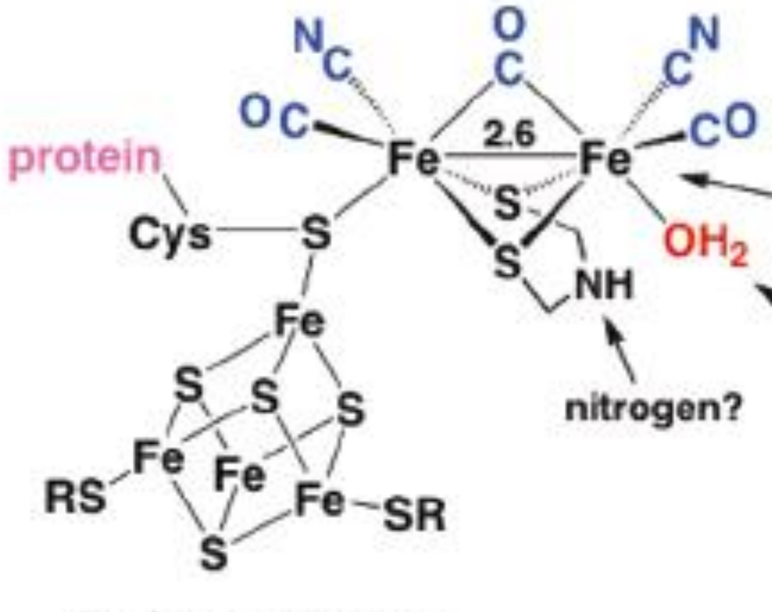


M-to-H_2 back-donation

The CO ligand favors the heterolytic cleavage of H_2



Fe–Fe hydrogenase



Fe–S cubane cluster for electron transfer

- Active site attached at only one point
- CO and CN ligands on low-spin Fe^{II}
- Metal-metal bonds
- Intramolecular heterolysis of H_2 ostensibly at this site

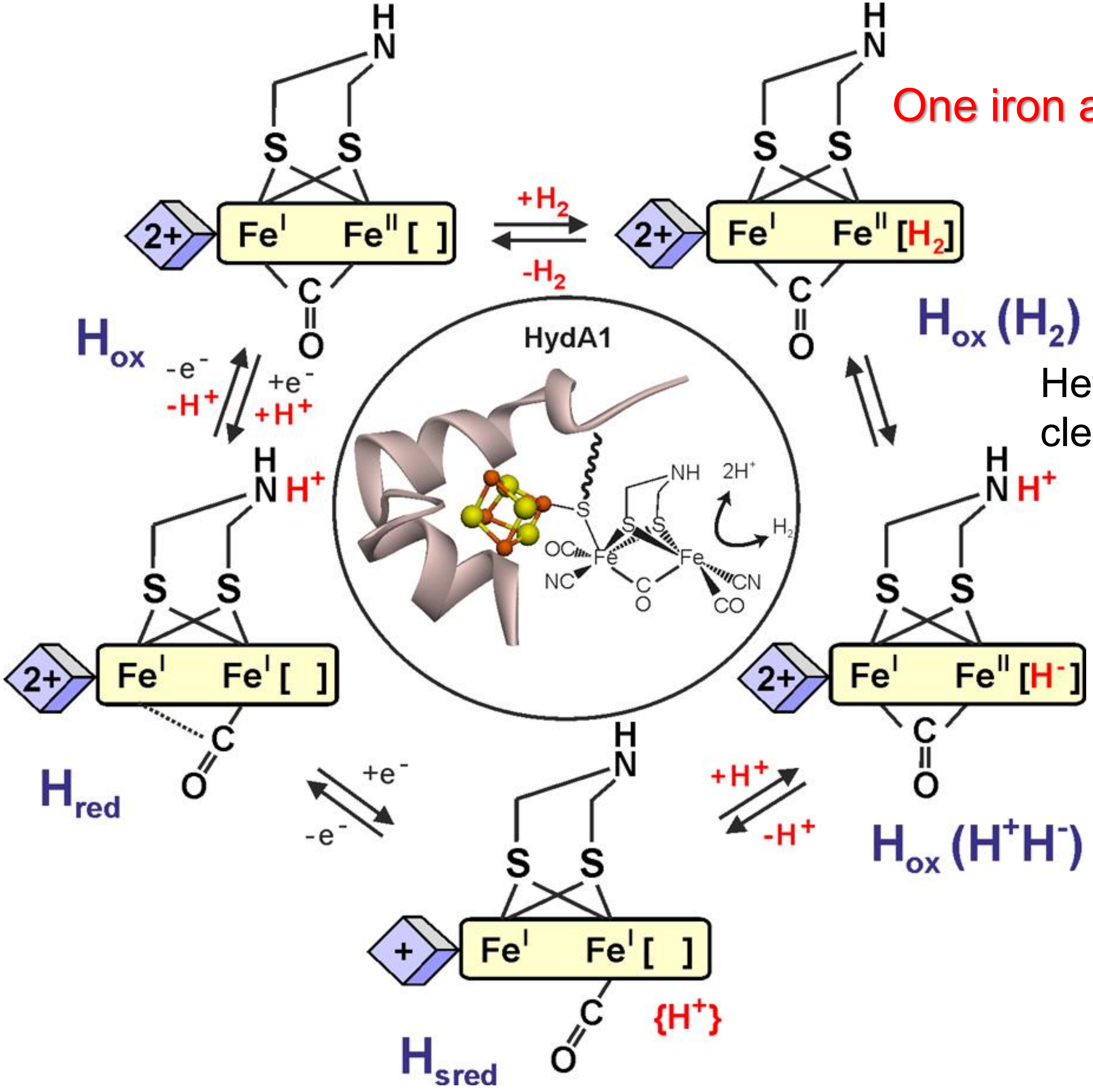
  CO can displace H_2O; can H_2?

  H_2 is slightly stronger ligand than H_2O on $W(CO)_3(PR_3)_2$

Trans CO ligand favors H_2 coordination and heterolysis

High ligand-field strength of CN may be needed to help maintain a *low-spin state* for Fe that is critical for strong CO binding. High-spin Fe^{II}-CO complexes are rare

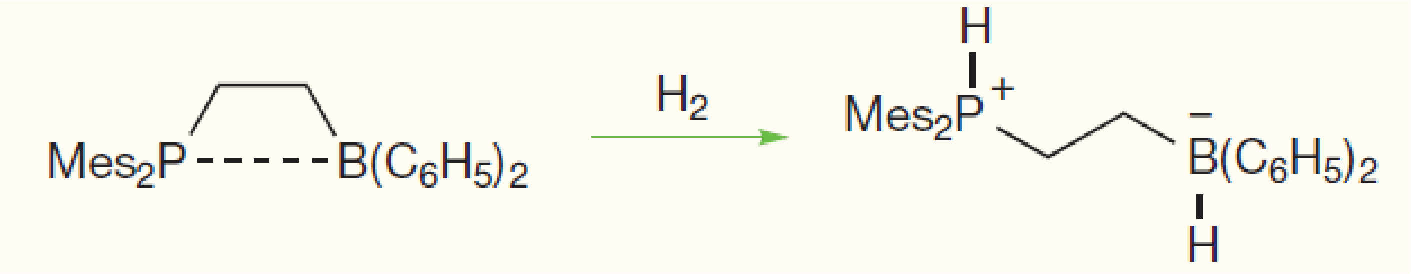
[FeFe] mechanism hypothesis



One iron always Fe(I)

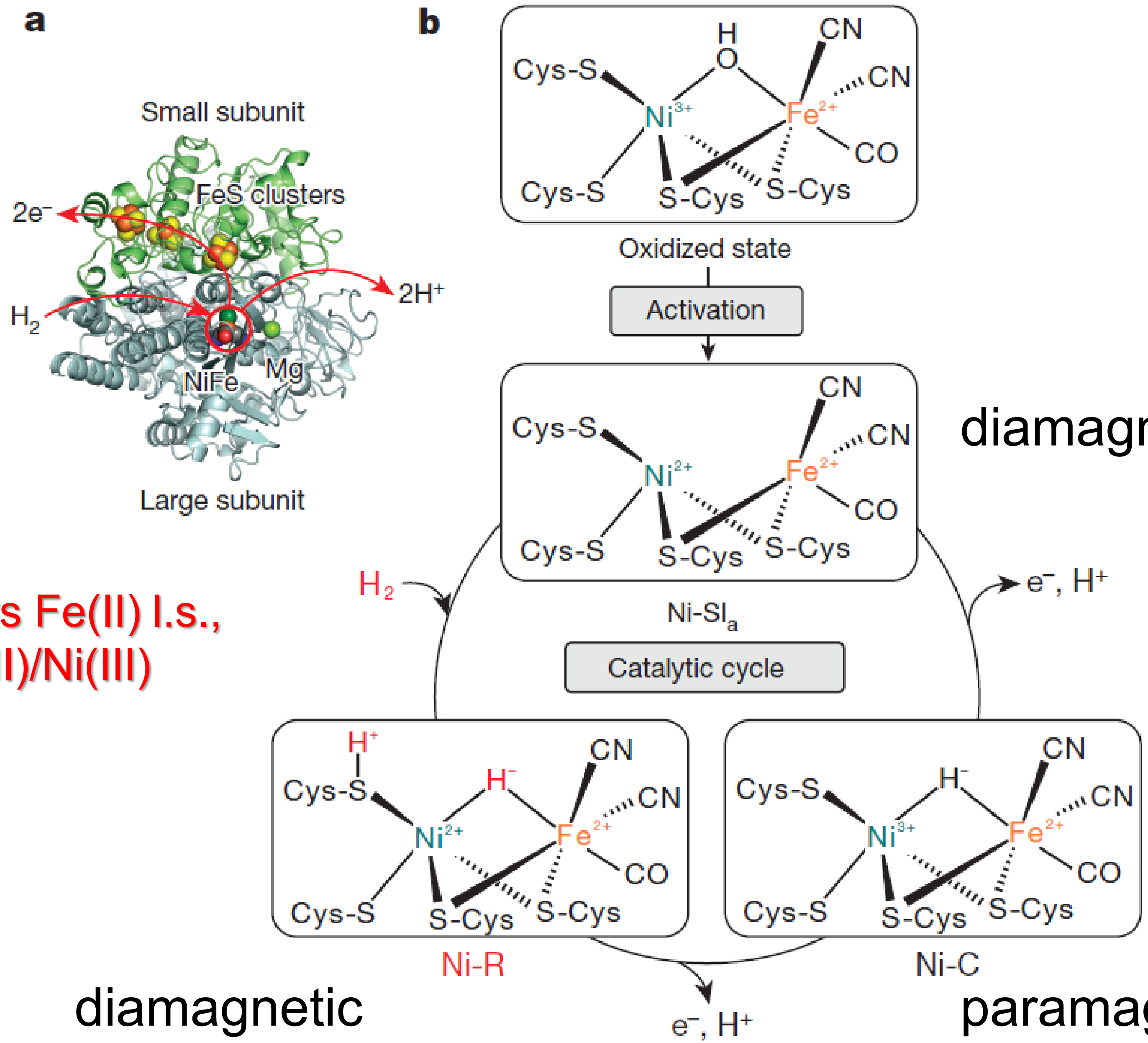
Heterolytic cleavage

The acidic Fe(II) atom and the basic NH group of the bridging dithiomethylamine behave as a *frustrated Lewis pair*, FLP, leading to the heterolytic cleavage of the H−H bond.



FLP (*frustrated Lewis pair*)

[FeNi] mechanism hypothesis



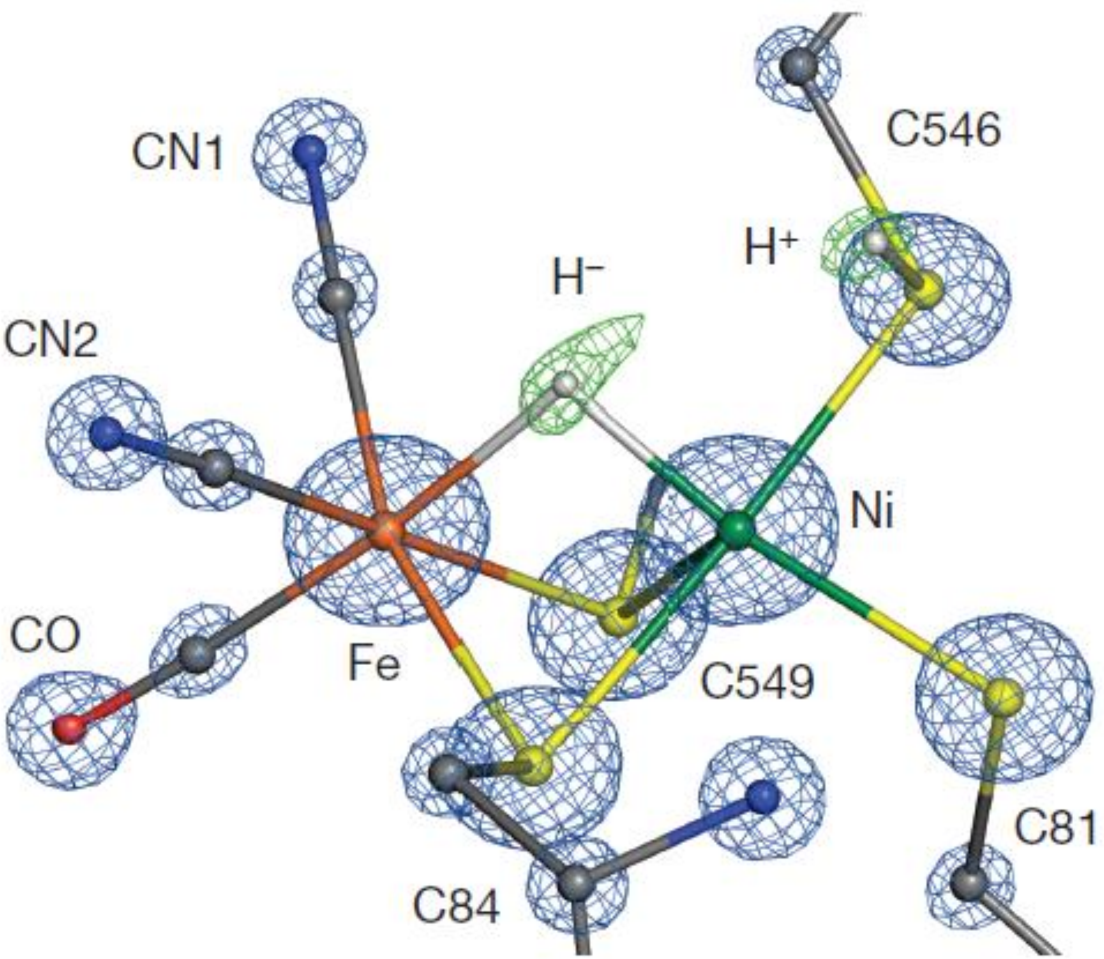
diamagnetic

Iron always Fe(II) l.s.,
Nichel Ni(II)/Ni(III)

diamagnetic

paramagnetic

Fe–Ni hydrogenase



Ultra-high resolution X-ray structure allowed to position also the H atoms.

Nature, **2015**

28
Ni
Nickel
58.693

Nickel enzymes play crucial roles in bacteria, *archaea*, fungi, algae and plants. There are currently no known Ni-enzymes in mammals, and nickel is classified as a “possibly essential element” for animals and humans (estimated need: 25 – 35 μg/day).

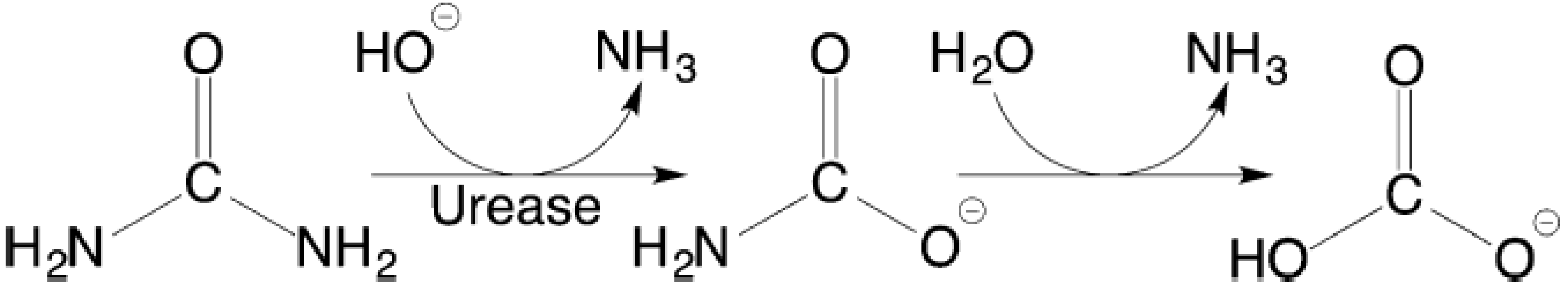
Redox Ni-enzymes

- Anionic sulfur ligands (Cys$^-$ e S^{2-})
- Redox pair Ni(II)/Ni(III)
- Coordinatively unsaturated
- Low spin

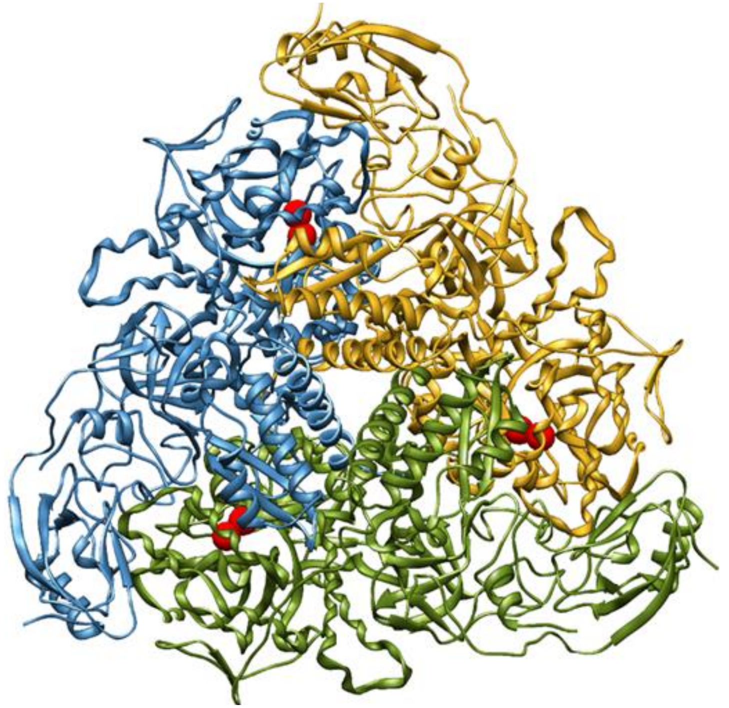
Non-redox Ni-enzymes

- O/N ligands
- Always as Ni(II), Lewis acid behavior
- Six-coordinate
- High spin

Urease (non-redox enzyme)

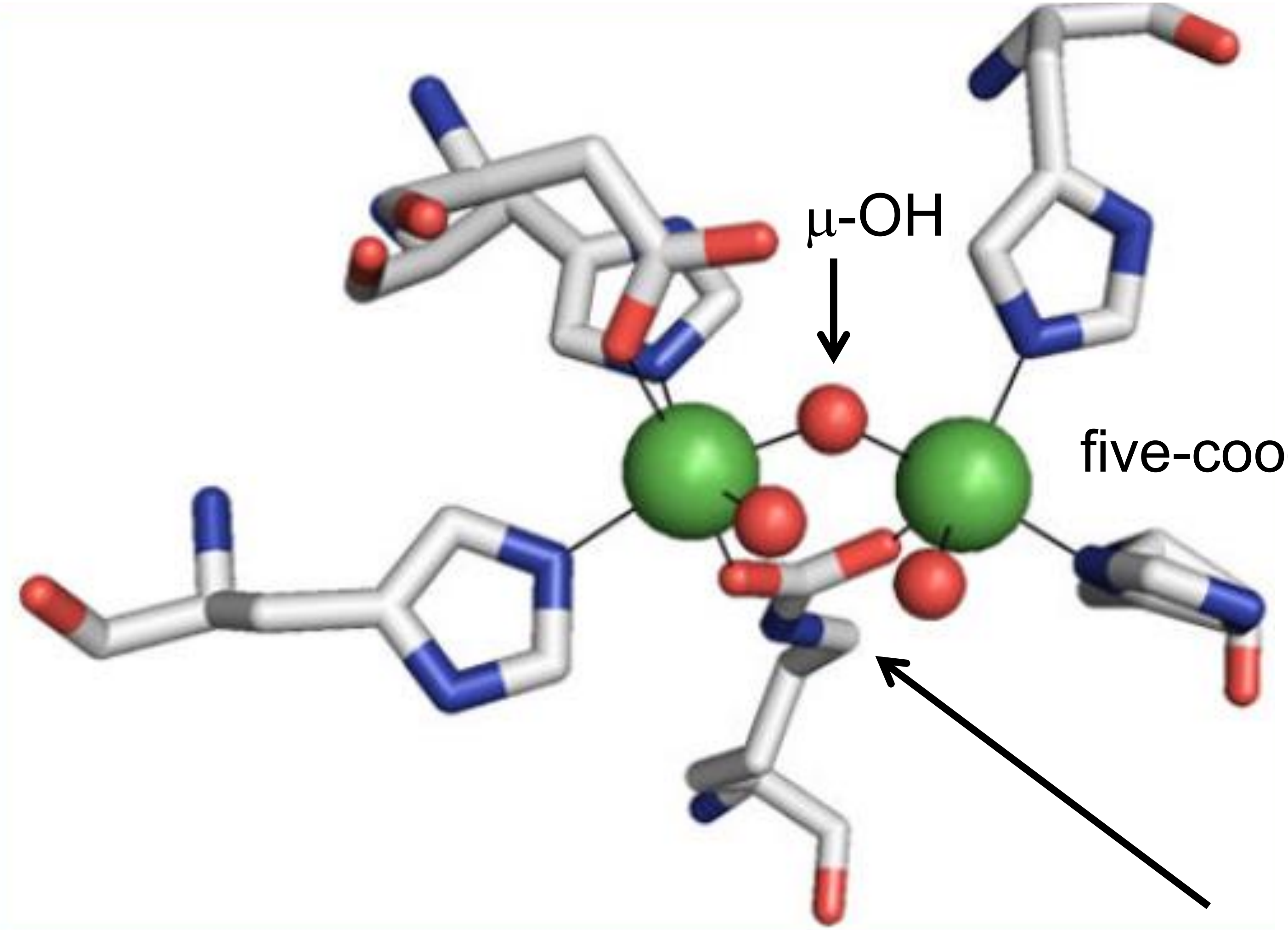


*urease is the most efficient of the known hydrolases, inducing a **3 × 10^{15} fold** increase in speed over the uncatalyzed reaction (from hundreds of years to microseconds)*



Trimer of trimers of the type $(\alpha\beta\gamma)_3$

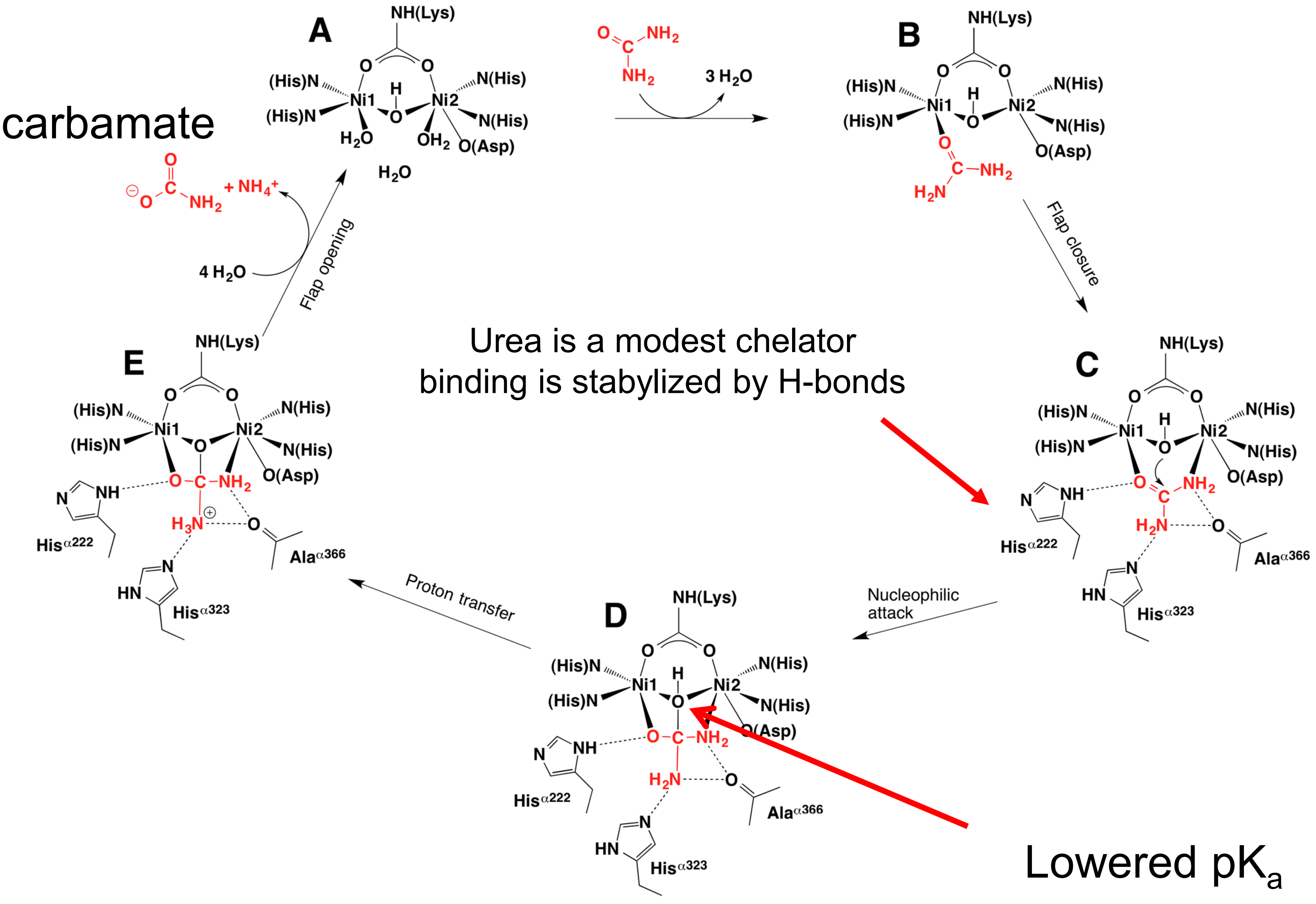
Dinuclear Ni(II) active site in urease



μ-OH

five-cooordinate

carbamylated lysine
CO_2 insertion as in
Rubisco

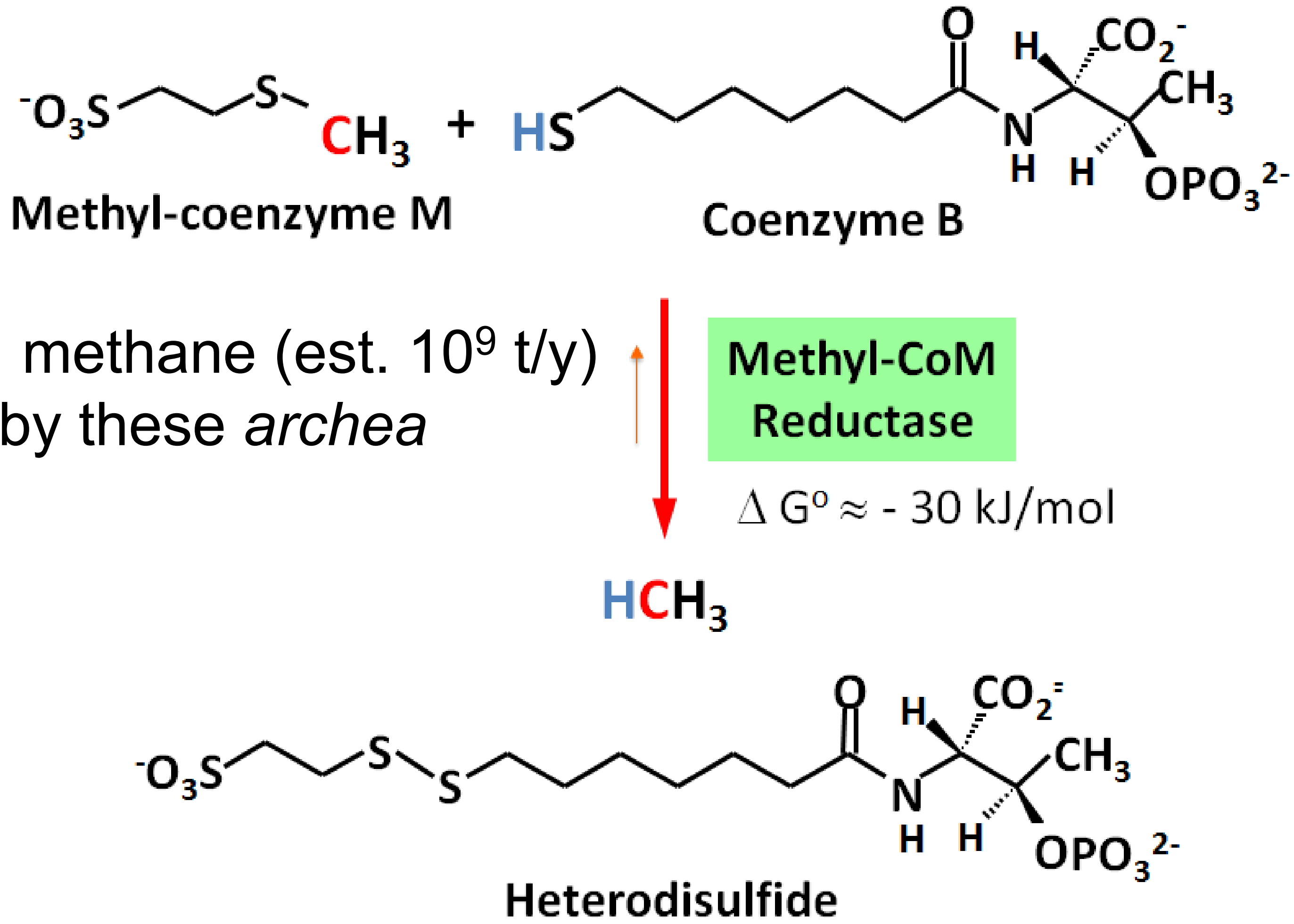


carbamate

Urea is a modest chelator
binding is stabylized by H-bonds

Lowered pK_a

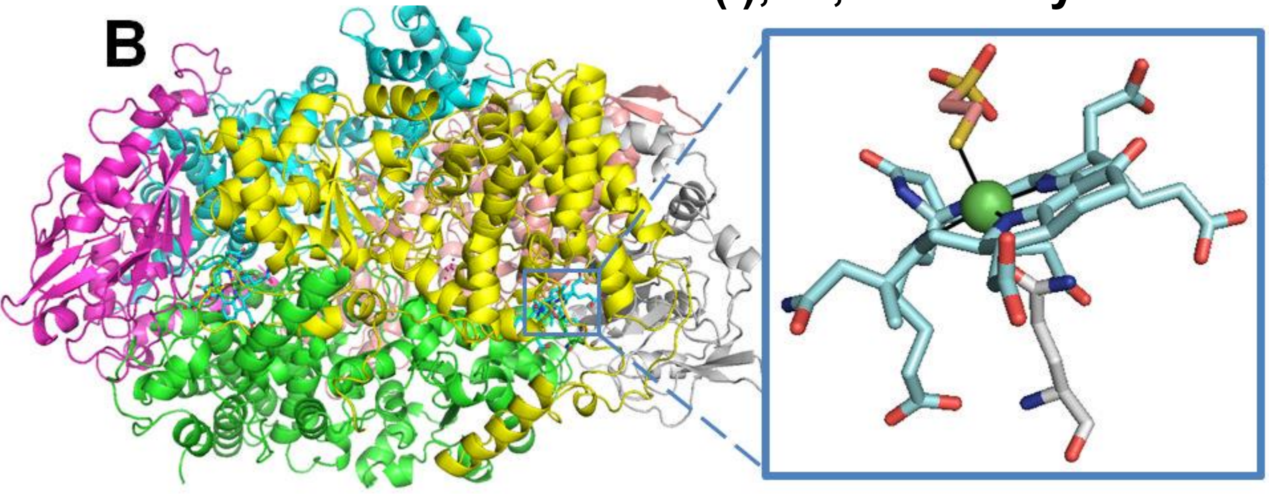
methyl-coenzyme M reductase redox enzyme in methanogenic *archei*

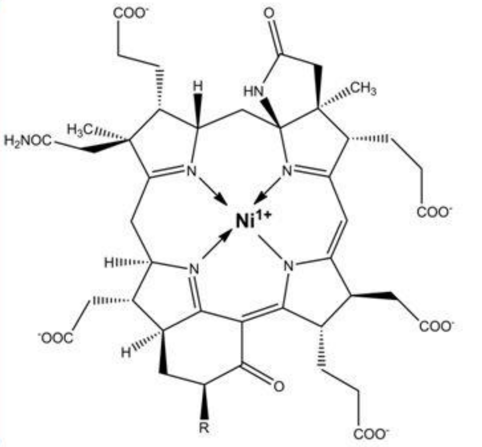


All biological methane (est. 10^9 t/y) is produced by these *archea*

Methanogenic *archea* utilize H_2 and CO_2 as unique sources for energy and carbon

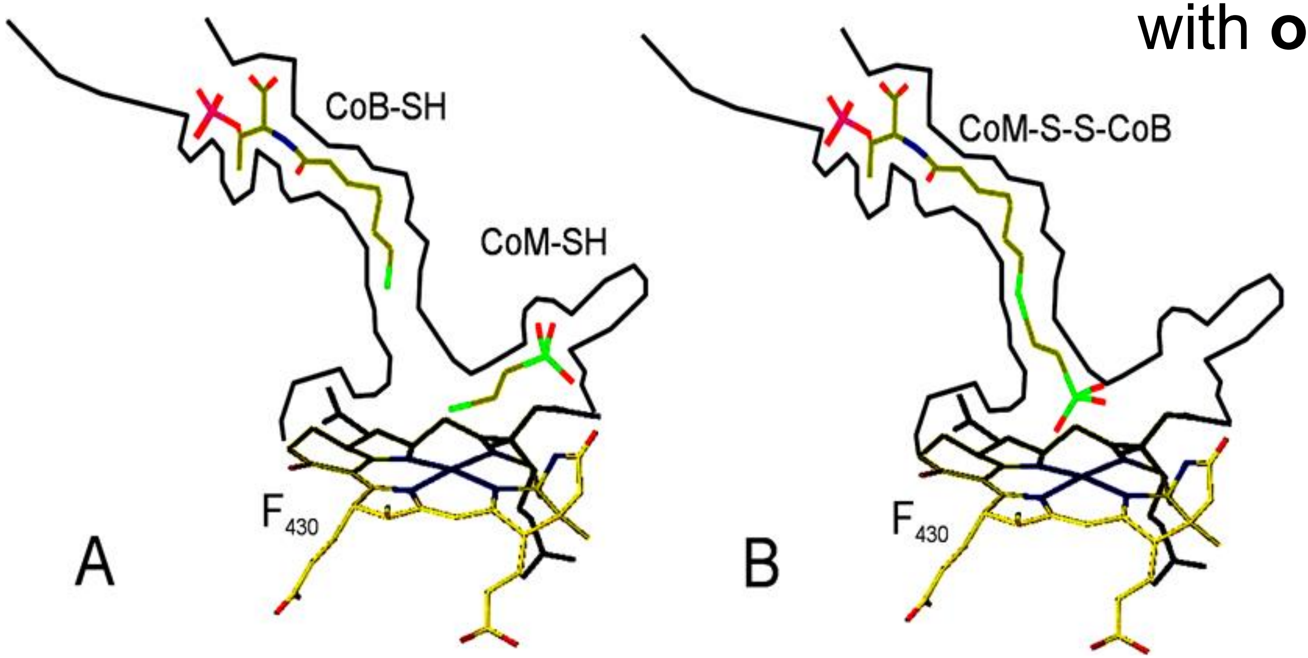
Ni(I), d^9, in coenzyme F-430

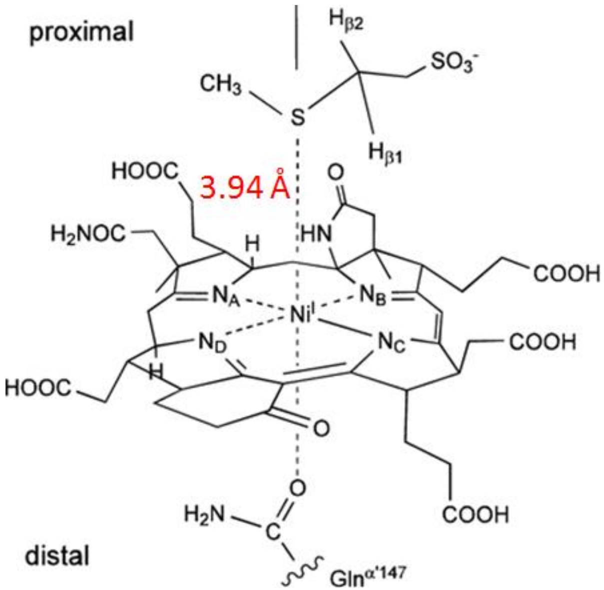




$\alpha_2\beta_2\gamma_2$

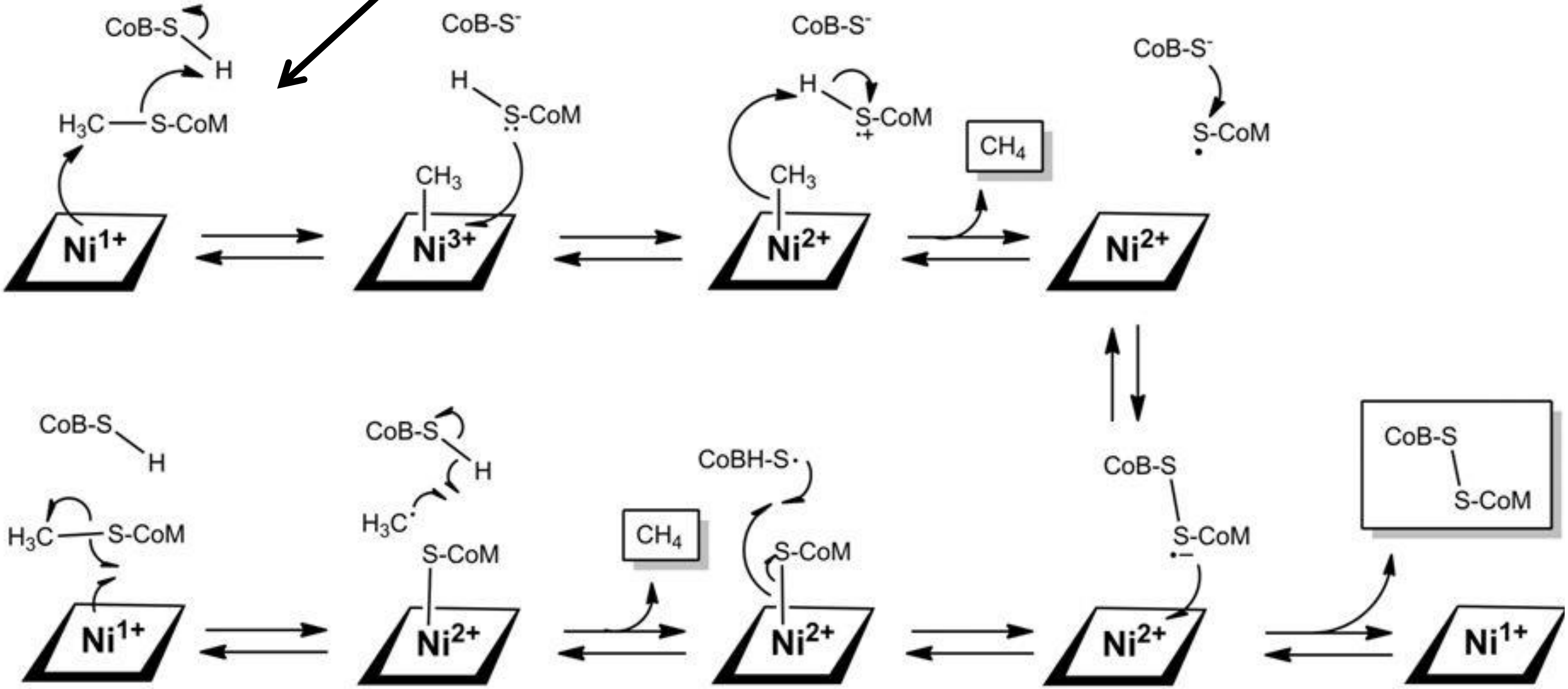
tetrapyrrole macrocycle with **only 5 double bonds**





glutamine

S_N2 mechanism, Ni(I)/Ni(II)/Ni(III)



$E°_{\text{Ni(II)F-430/Ni(I)F-430}} < -600$ mV

Radical mechanism, Ni(I)/Ni(II)