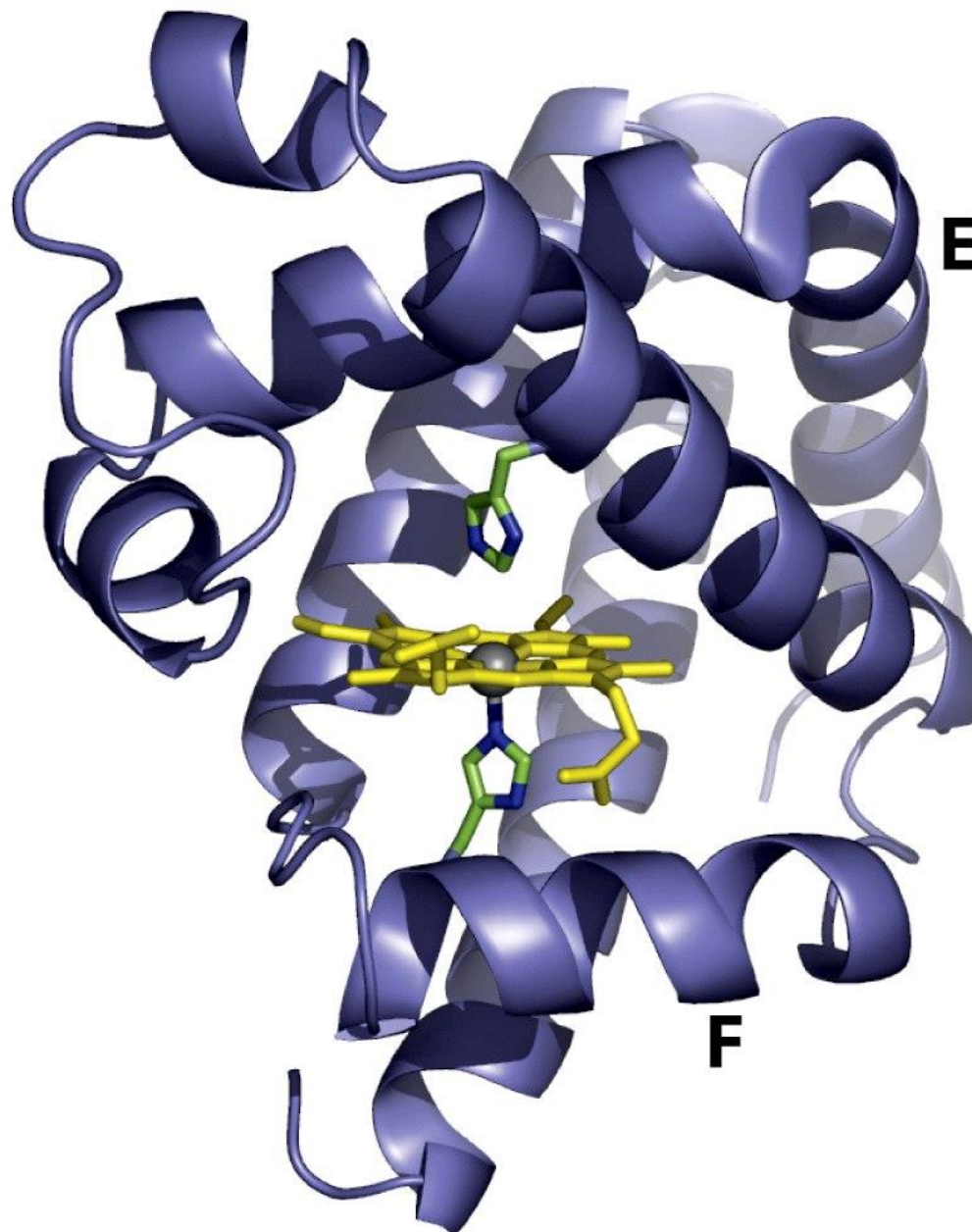


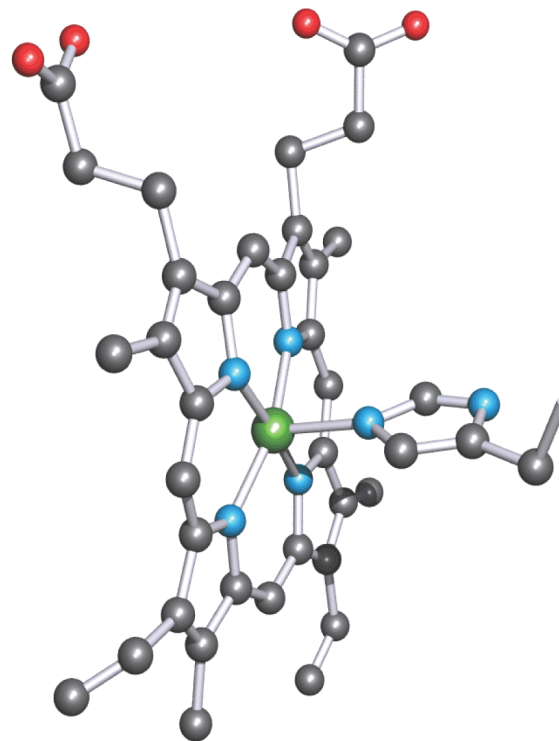
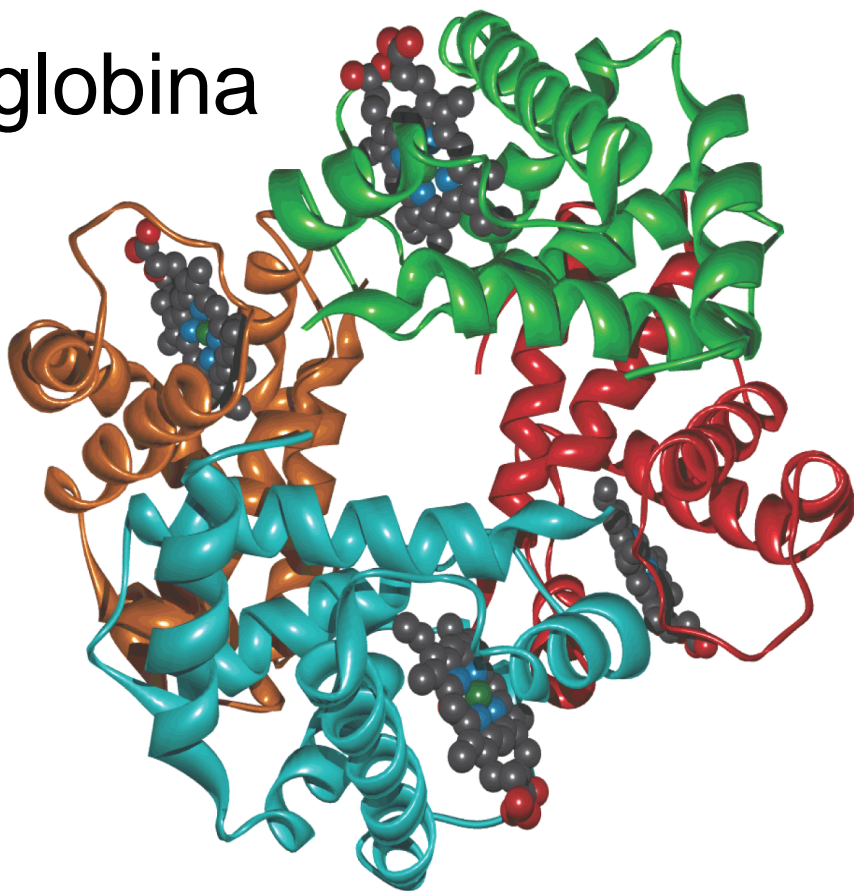
Mioglobina

17.8 kDa



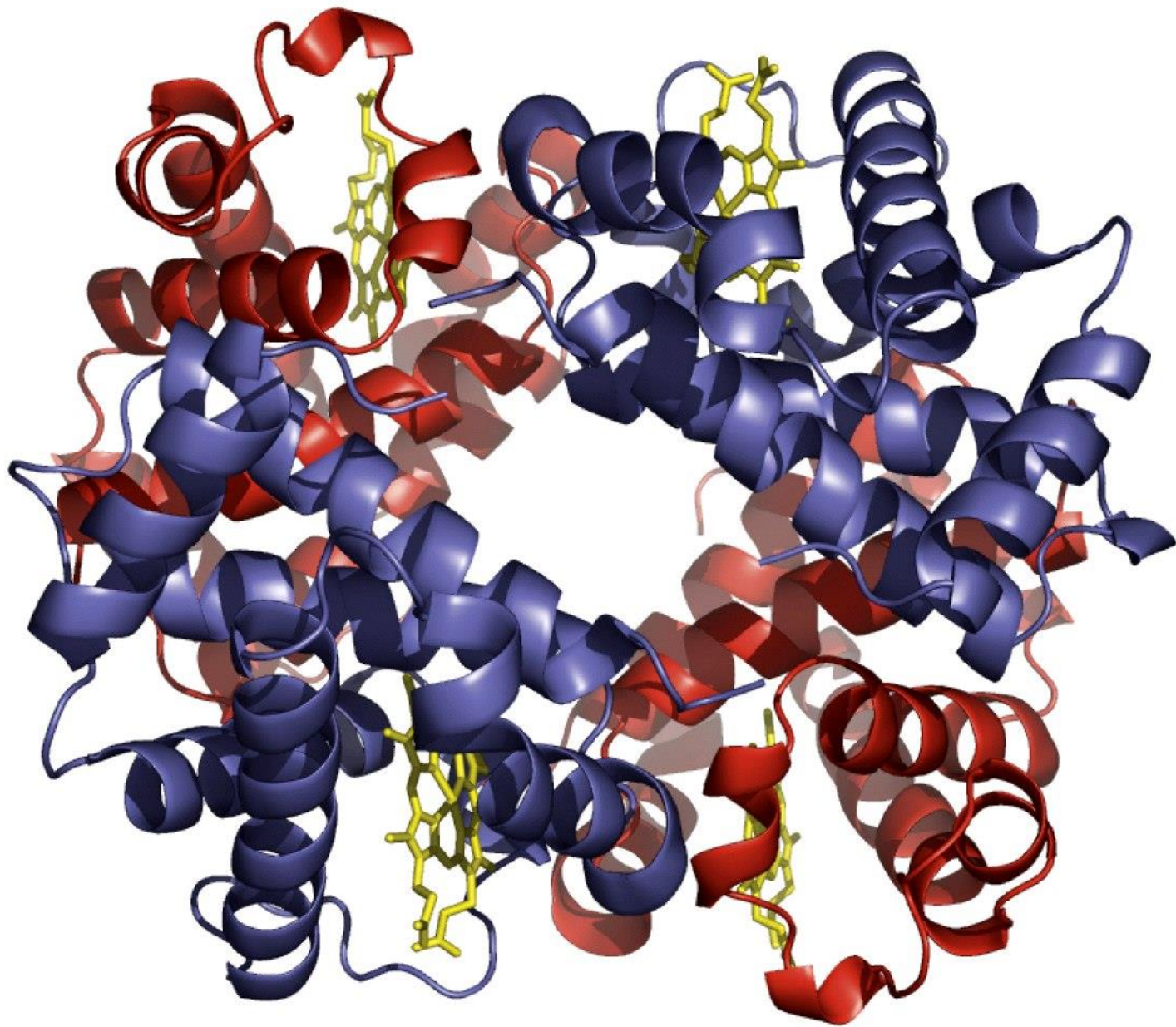
ca. 6%  $\text{Fe}_{\text{tot}}$

# Emoglobina



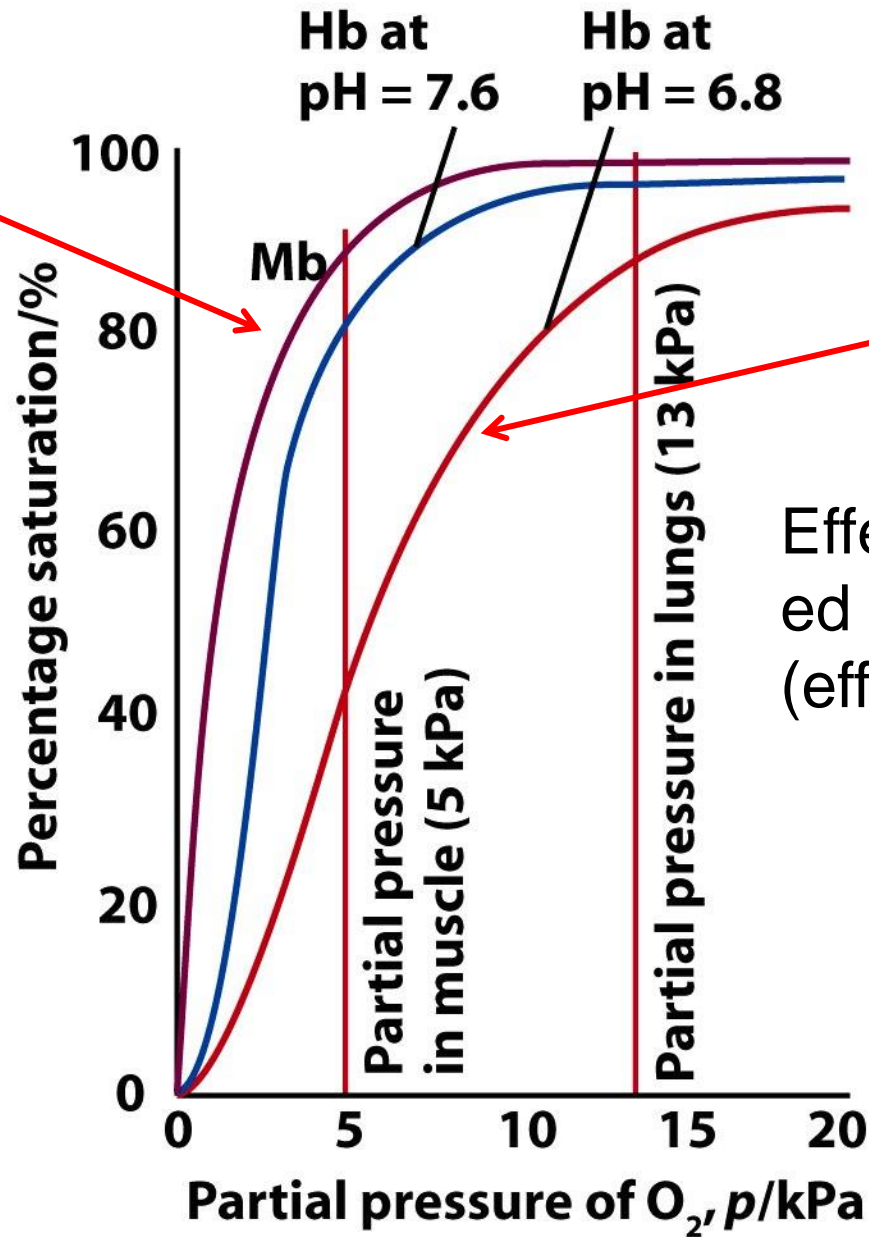
tetramero  $\alpha_2\beta_2$       141 e 146 a.a.    64.5 kDa

ca. 65%  $Fe_{tot}$



tetramero  $\alpha_2\beta_2$

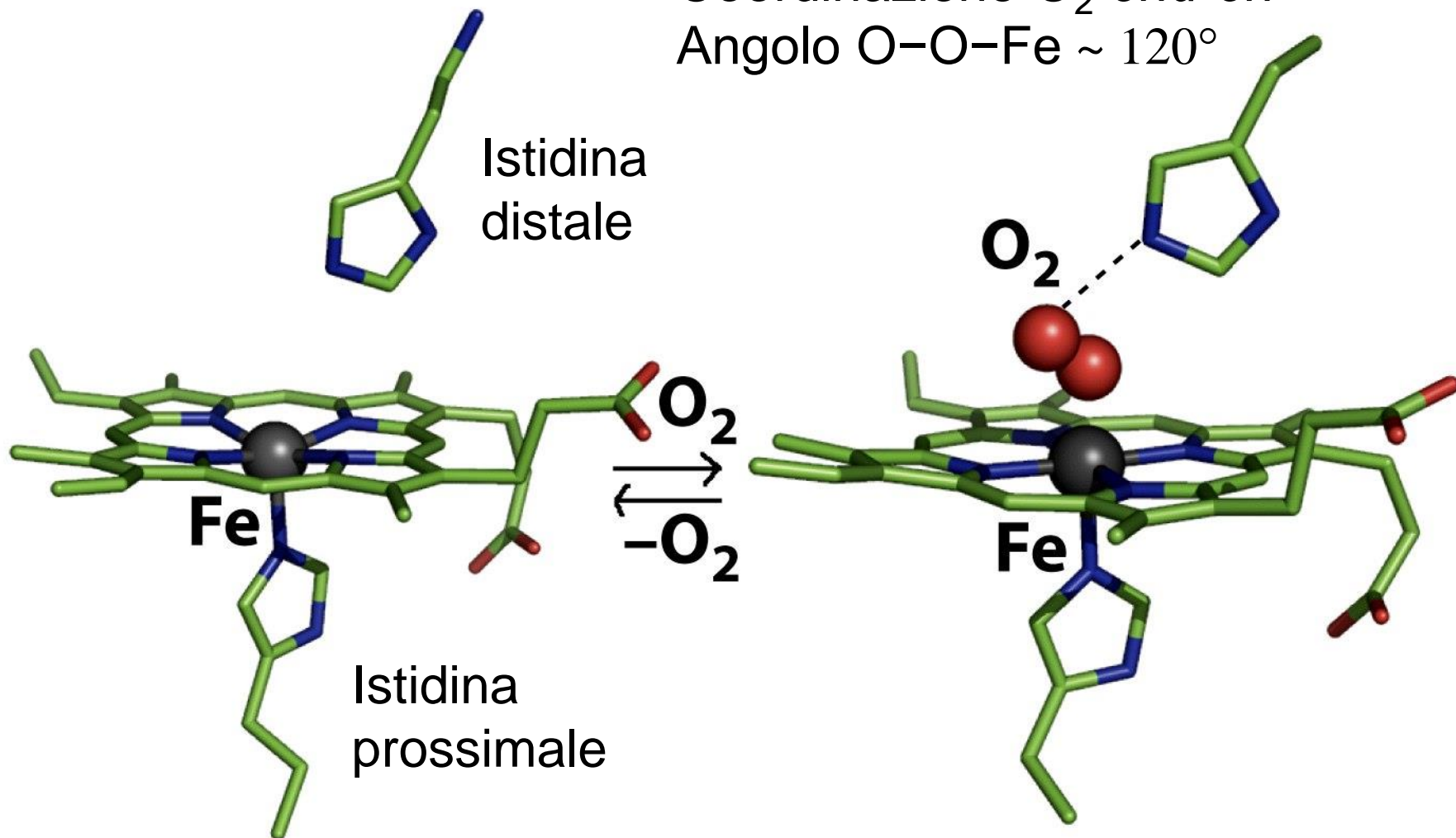
Curva di saturazione iperbolica



Curva di saturazione sigmoideale, pH dipendente

Effetto cooperativo ed effetto Bohr (effetto allosterico)

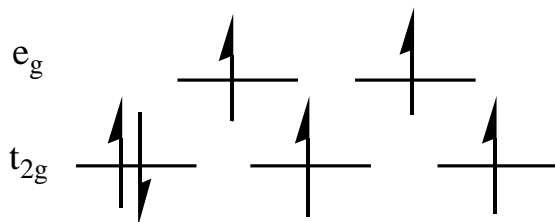
Coordinazione  $O_2$  *end-on*  
Angolo O-O-Fe  $\sim 120^\circ$



**desossi:**

$S = 2$

paramagnetica



Fe(II),  $d^6$  paramagnetico

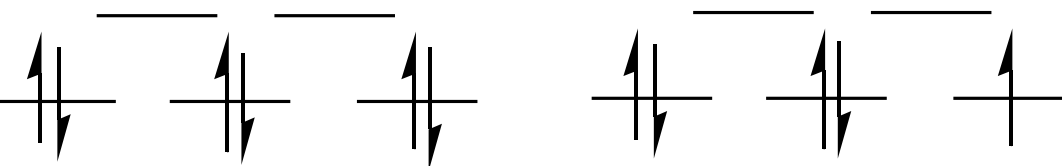
Pauling

Weiss

**ossi:**

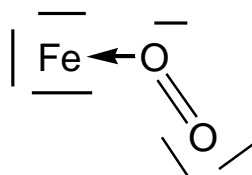
$S = 0$

diamagnetica



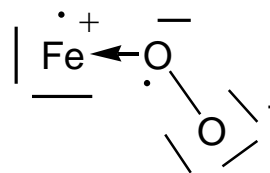
Fe(II)  $d^6$  basso spin

+  $^1\text{O}_2$  legato



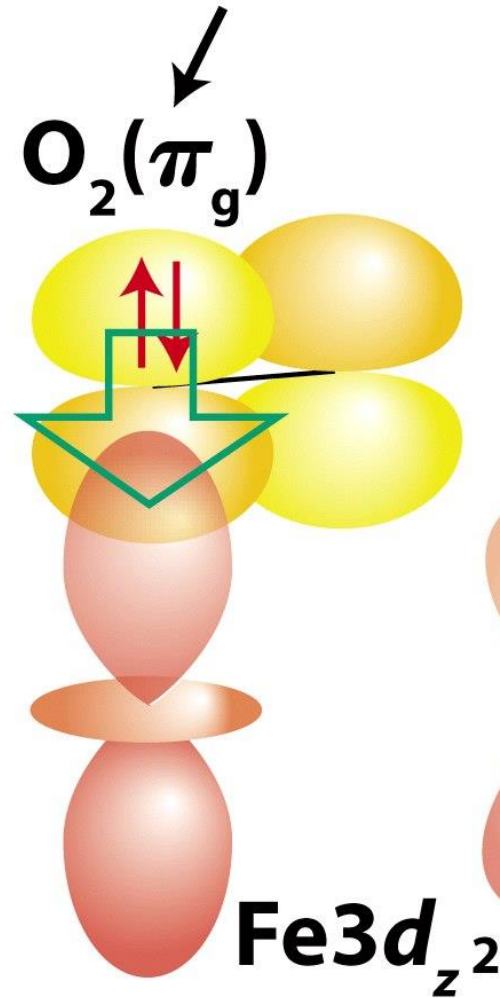
Fe(III)  $d^5$  basso spin

+  $^2\text{O}_2^{\cdot-}$  legato

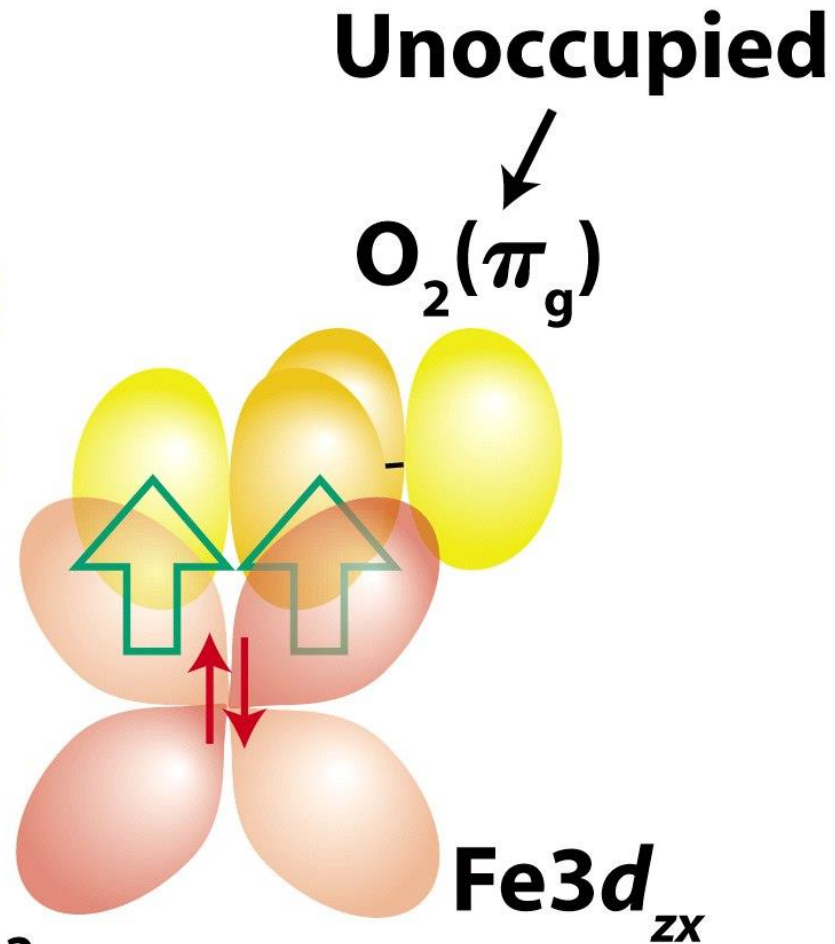


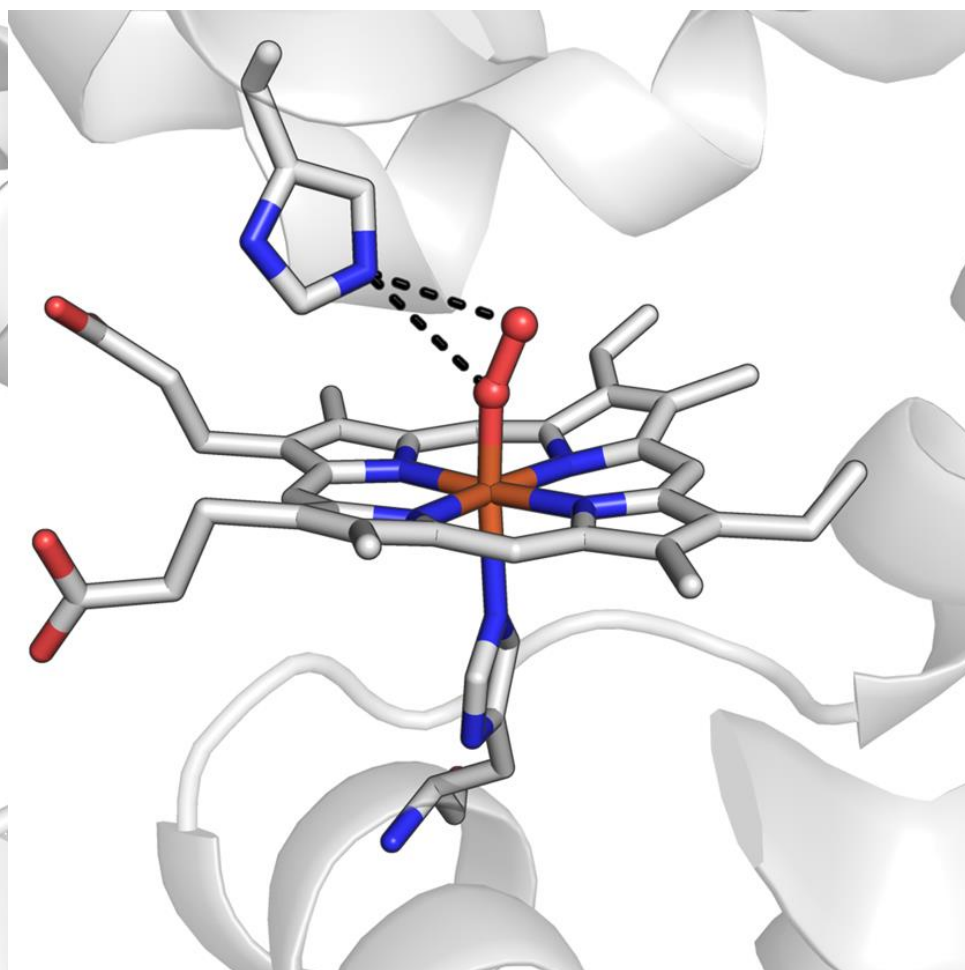
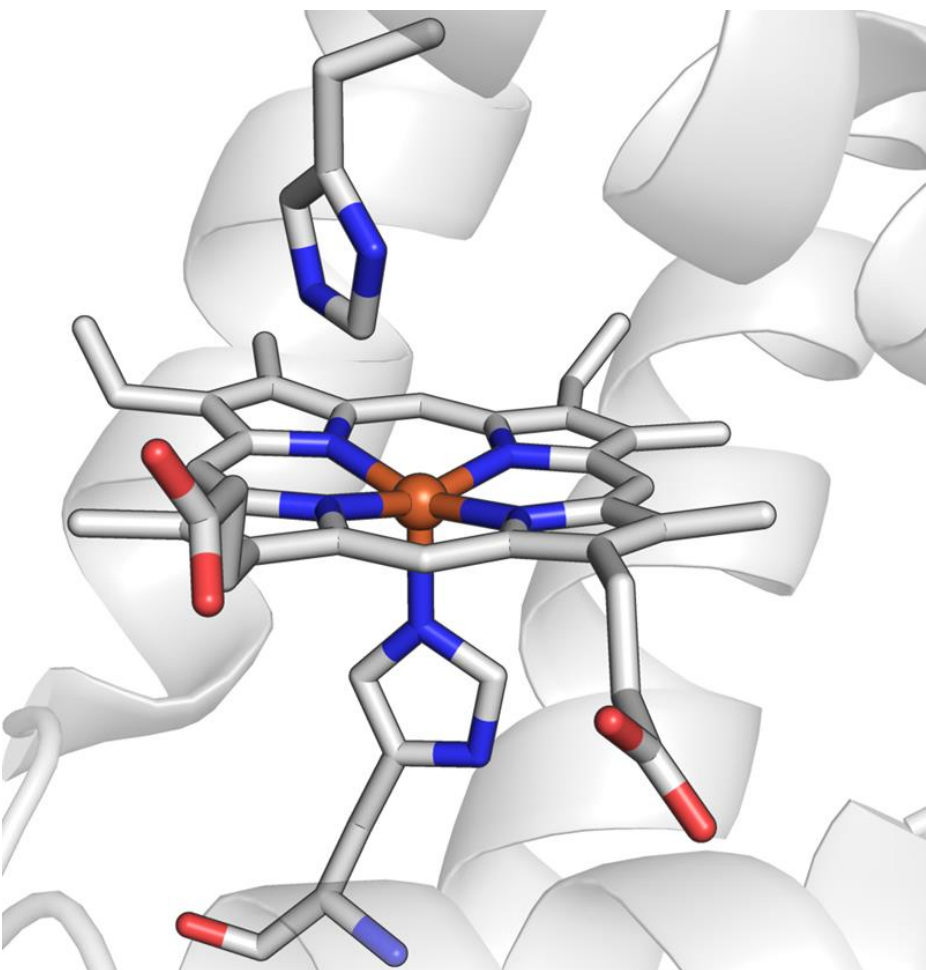
# Modello di Pauling: Fe(II) I.s. + $^1\text{O}_2$

**(a) Occupied**



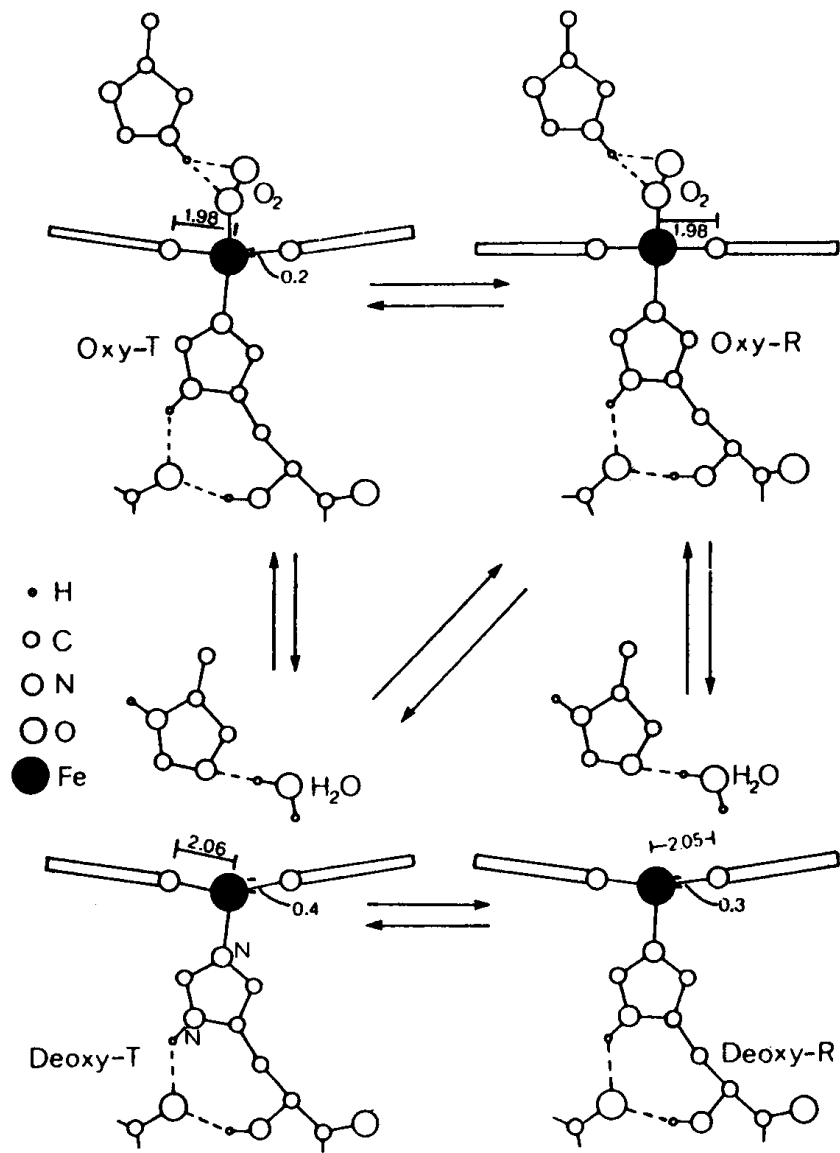
**(b)**

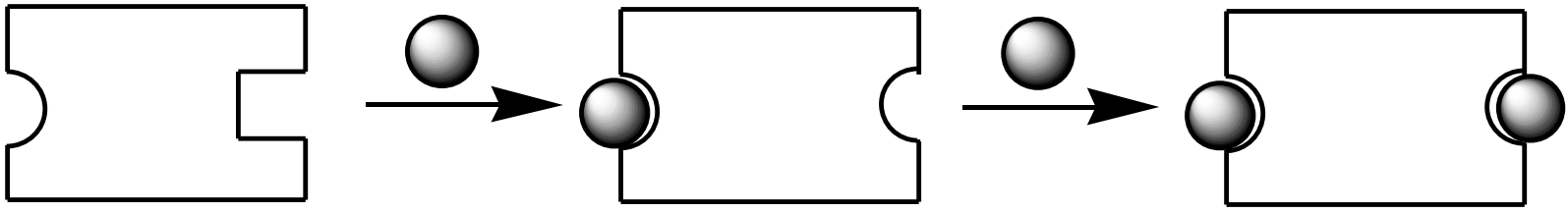




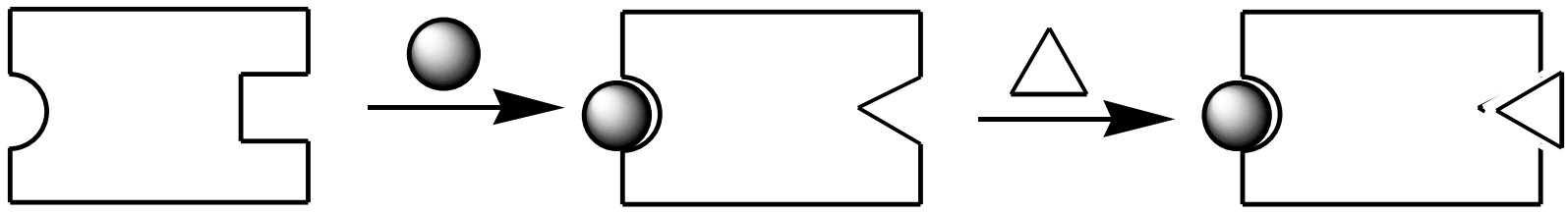
Fe(II) h.s.: 0.92 Å  
Fe(II) l.s.: 0.75 Å  
Fe(III) l.s.: 0.55 Å





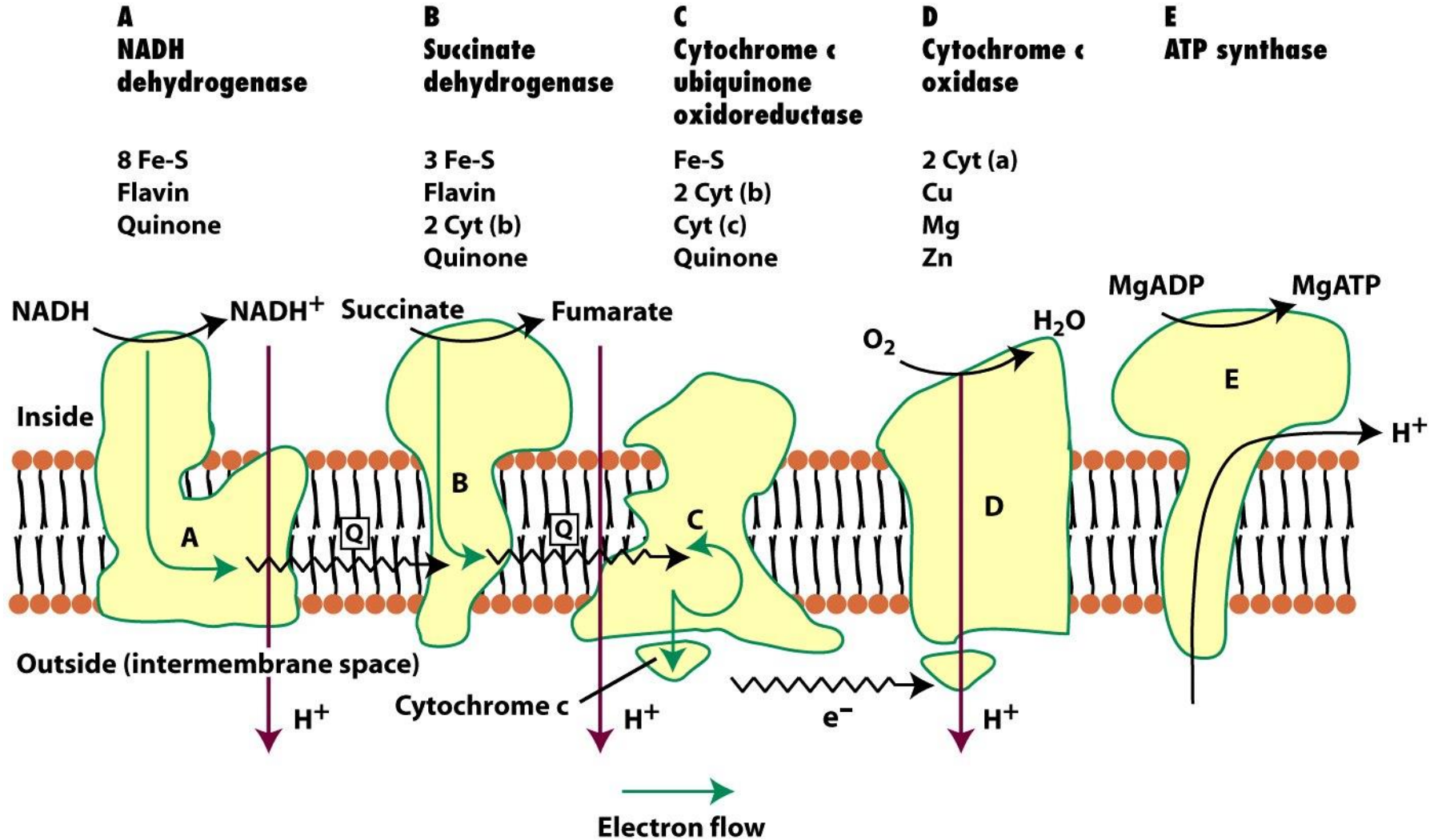


Allosterismo Omotropico



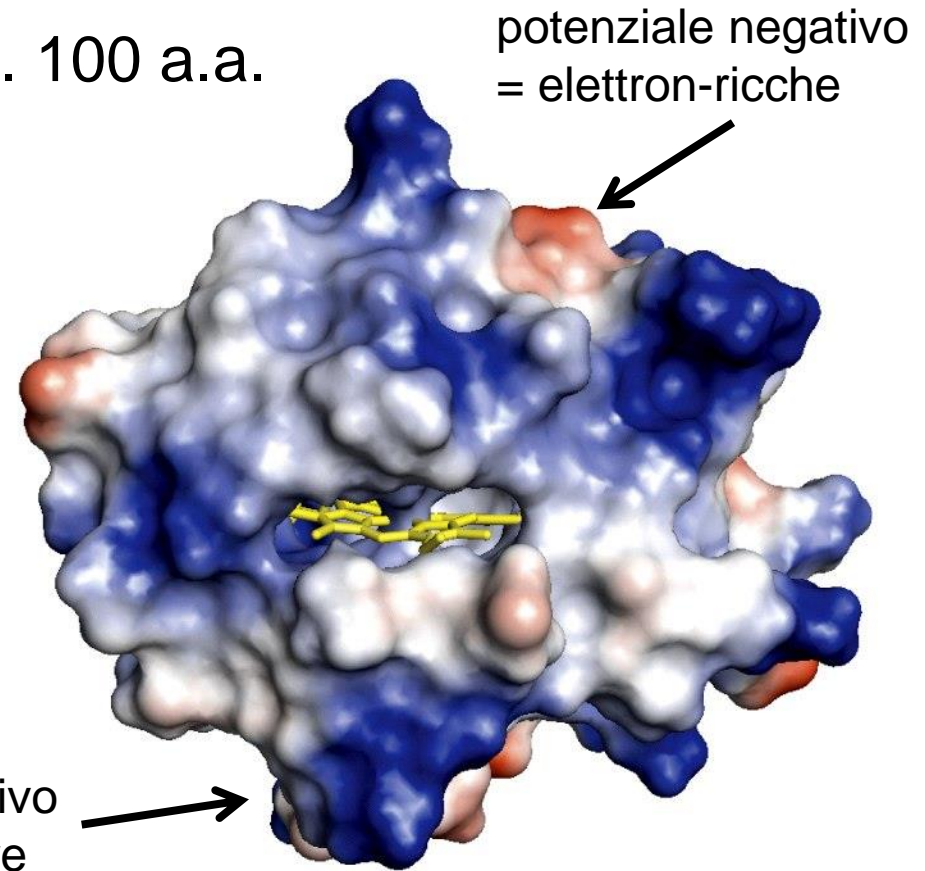
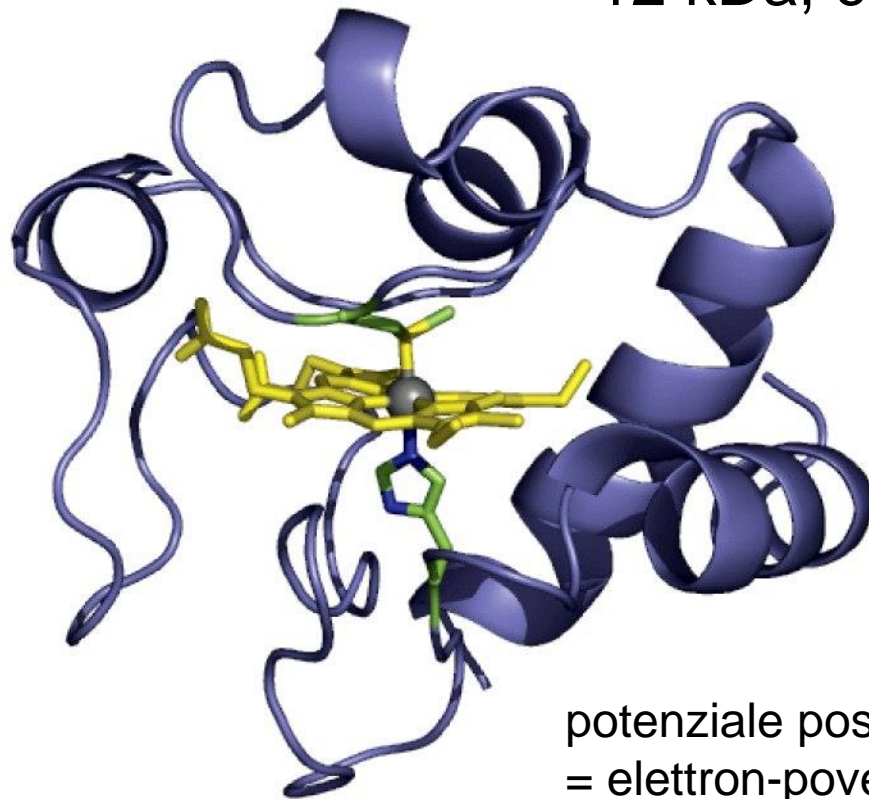
Allosterismo Eterotropico

# Catena della respirazione cellulare



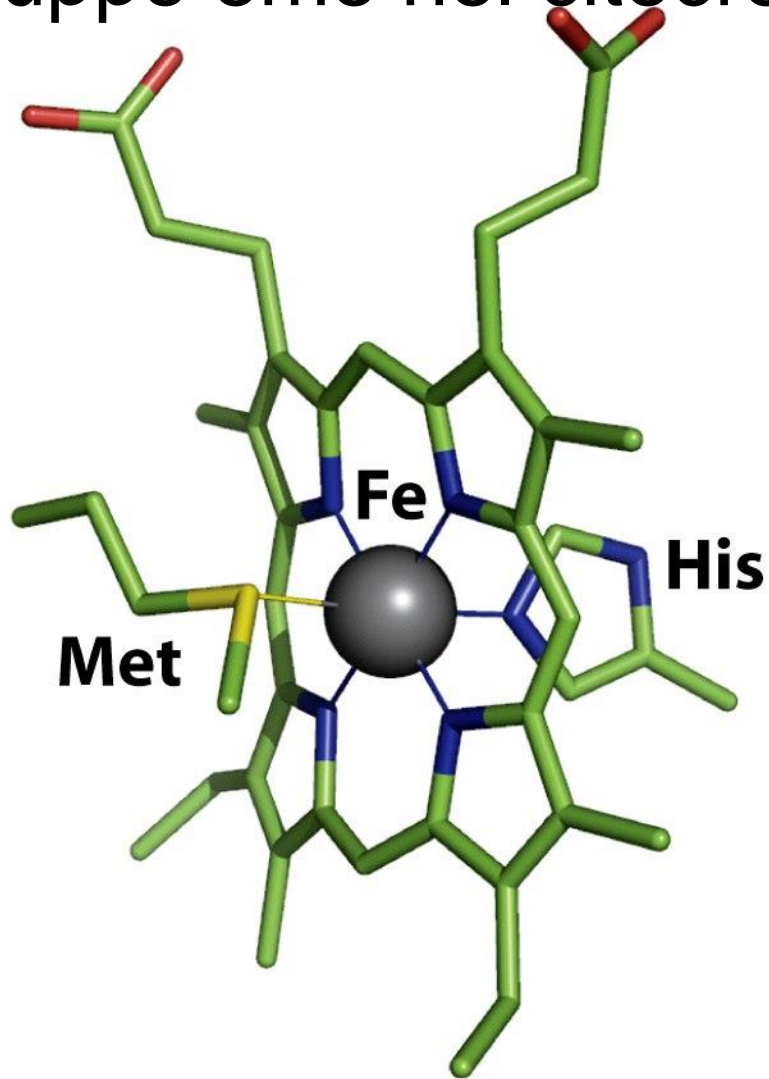
# Citocromo c da cuore di cavallo

12 kDa, ca. 100 a.a.



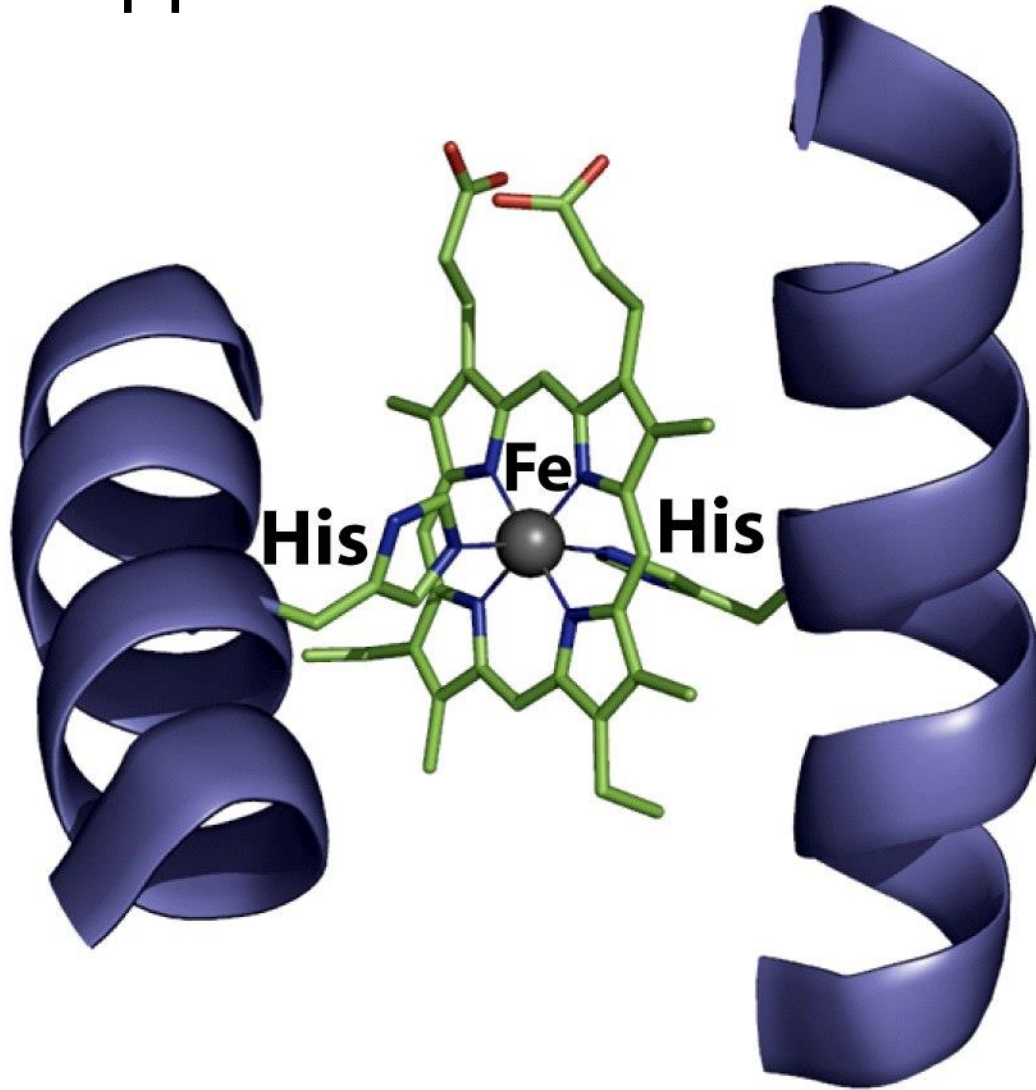
$$E_{\text{Fe(III)/Fe(II)}} = +260 \text{ mV}$$

# Gruppo eme nel citocromo c



$$E_{\text{Fe(III)/Fe(II)}} = +260 \text{ mV}$$

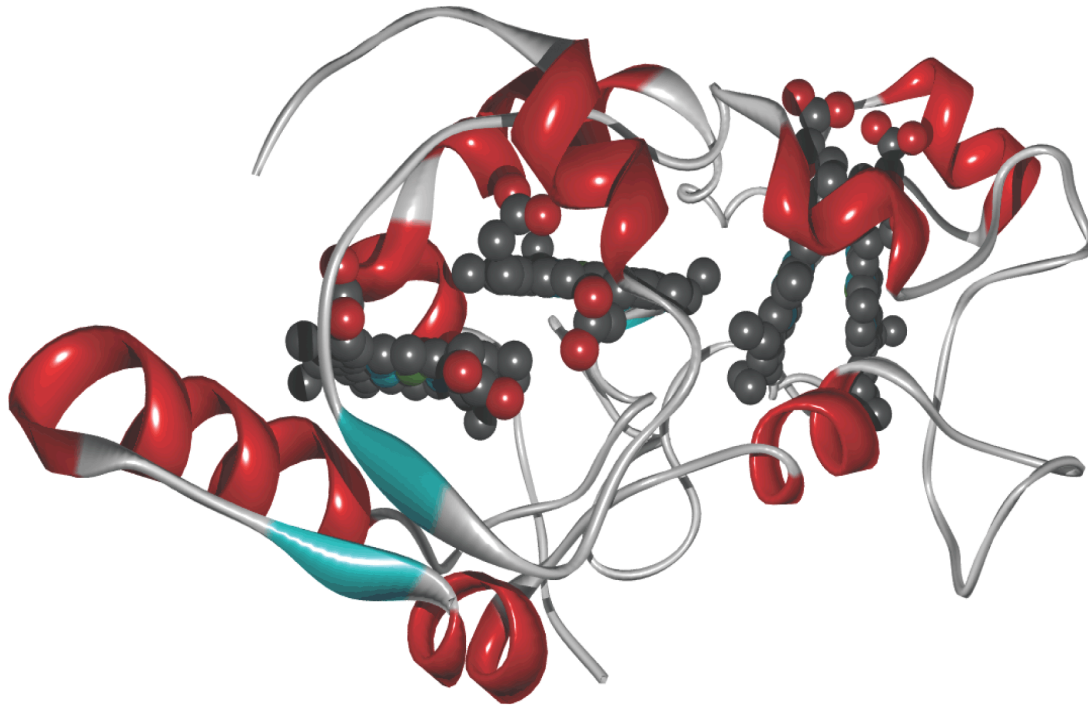
# Gruppo eme nel citocromo b



$$E_{\text{Fe(III)/Fe(II)}} = +20 \text{ mV}$$

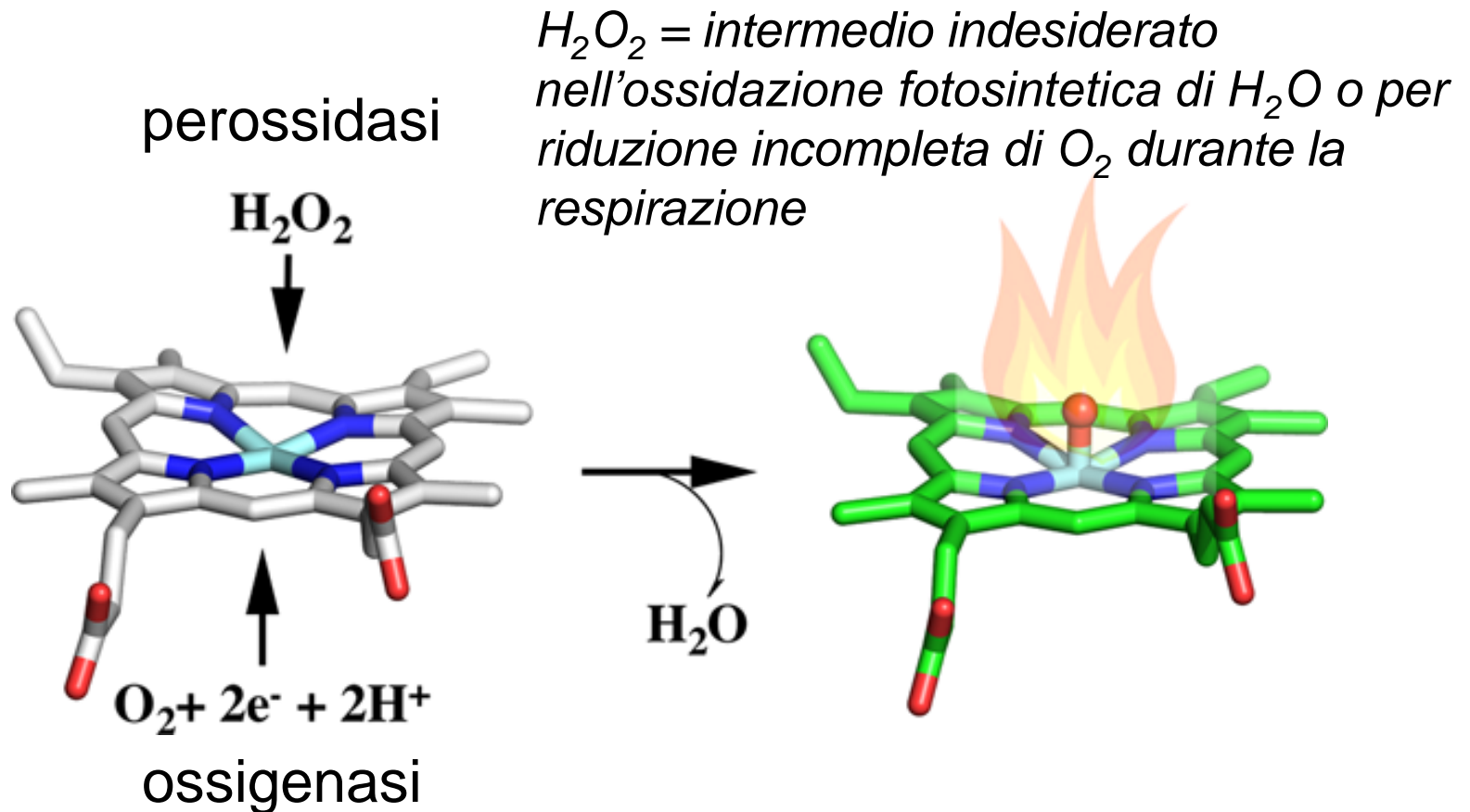
# Citocromo c554

(nitrificazione catalizzata da batteri)



Distanze Fe...Fe  $\approx$  950, 1220, 920 pm

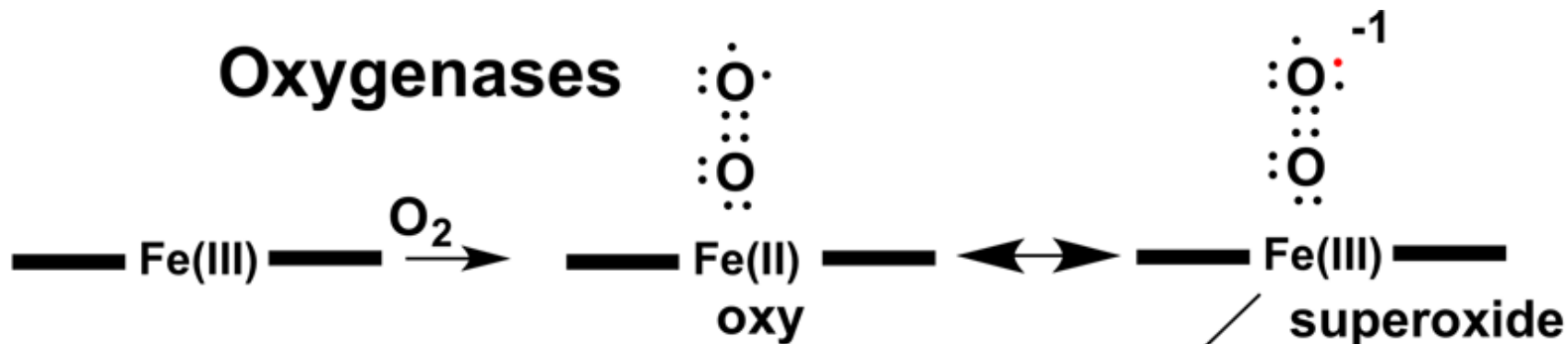
# Ossidazioni catalizzate da eme-proteine



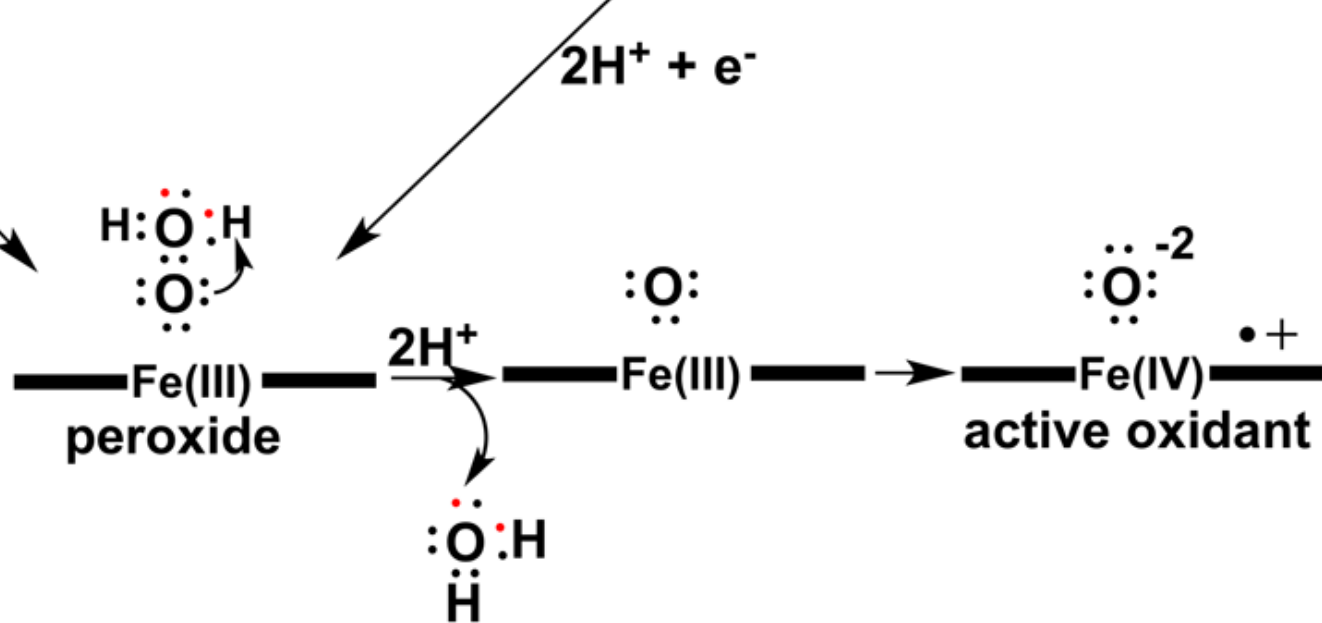
*ossidare non sempre implica anche ossigenare i substrati*



# Oxygenases

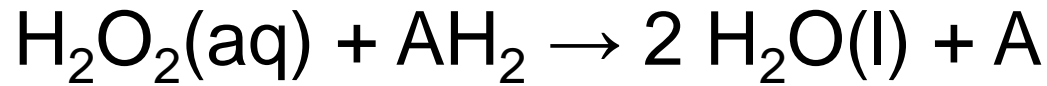


# Peroxidases



# Perossidasi e Catalasi

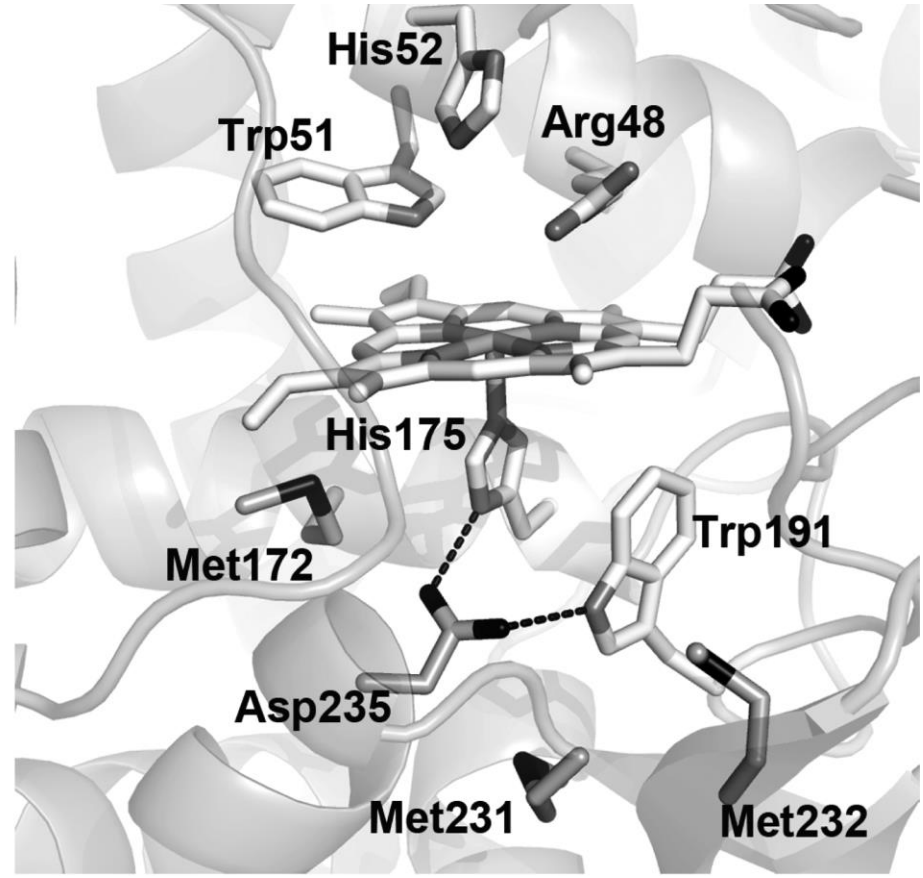
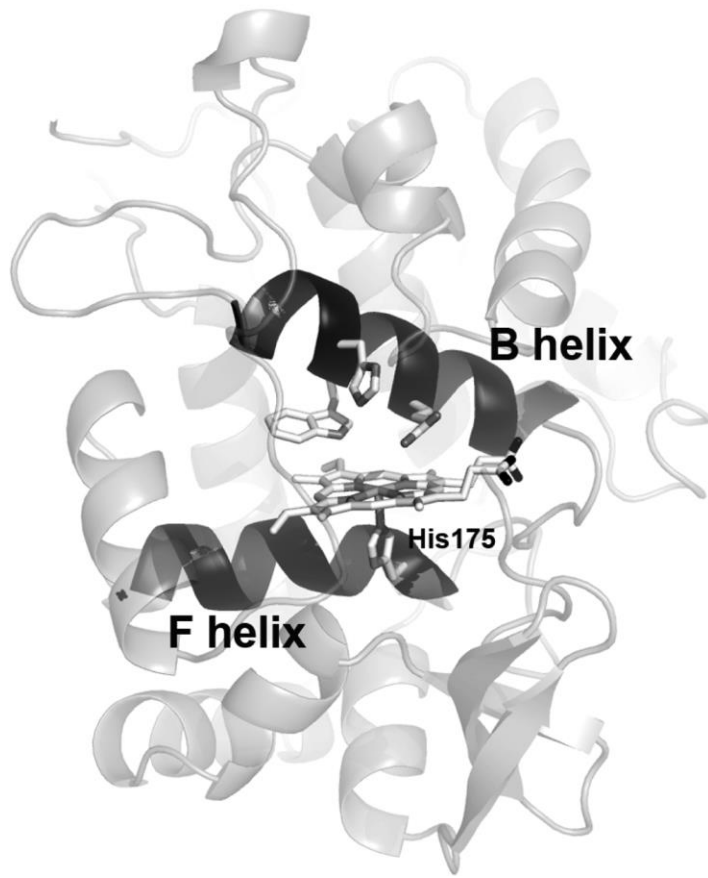
e.g. *lignina perossidasi*, *horse-radish perossidasi (HRP)*,  
*Citocromo c perossidasi*, *ascorbato perossidasi...*



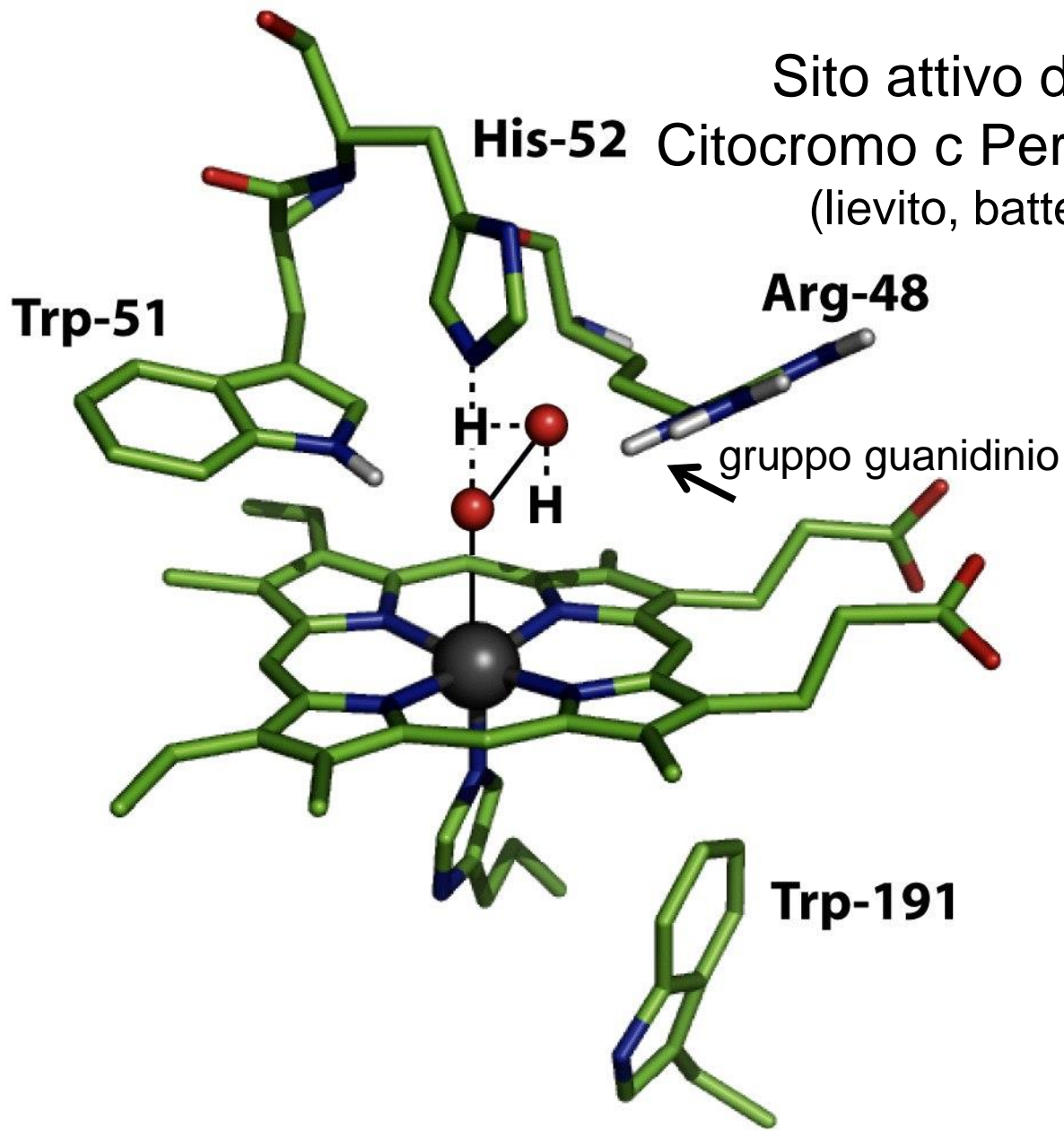
Substrati: acidi grassi, ammine, fenoli, tossine xenobiotiche,....

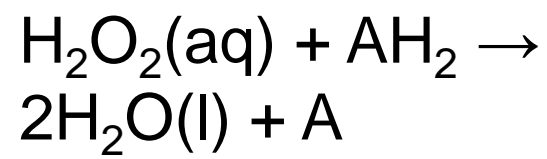
# Citocromo c Perossidasi

(lievito, batteri)

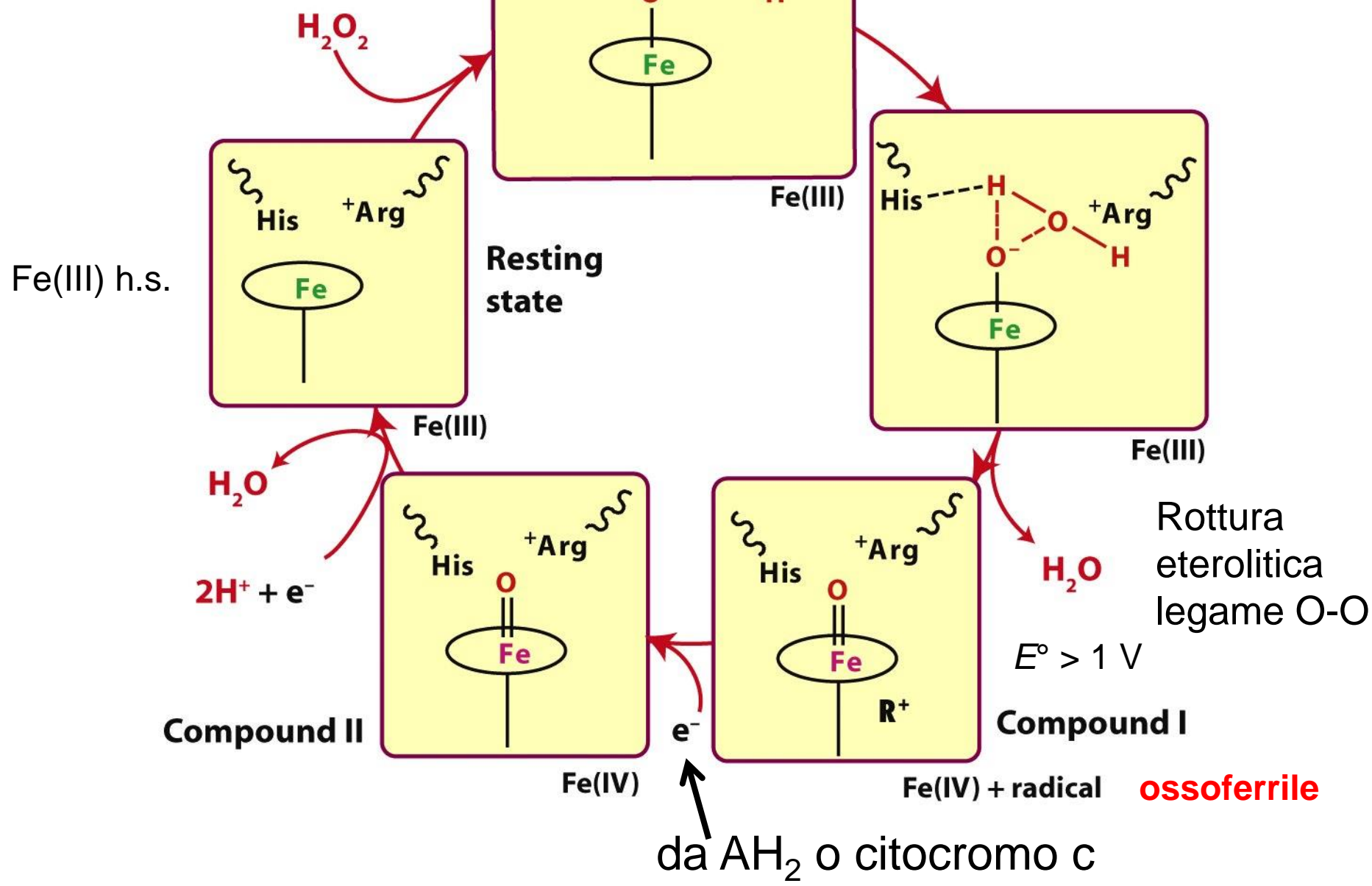


Sito attivo della  
Citocromo c Perossidasi  
(lievito, batteri)



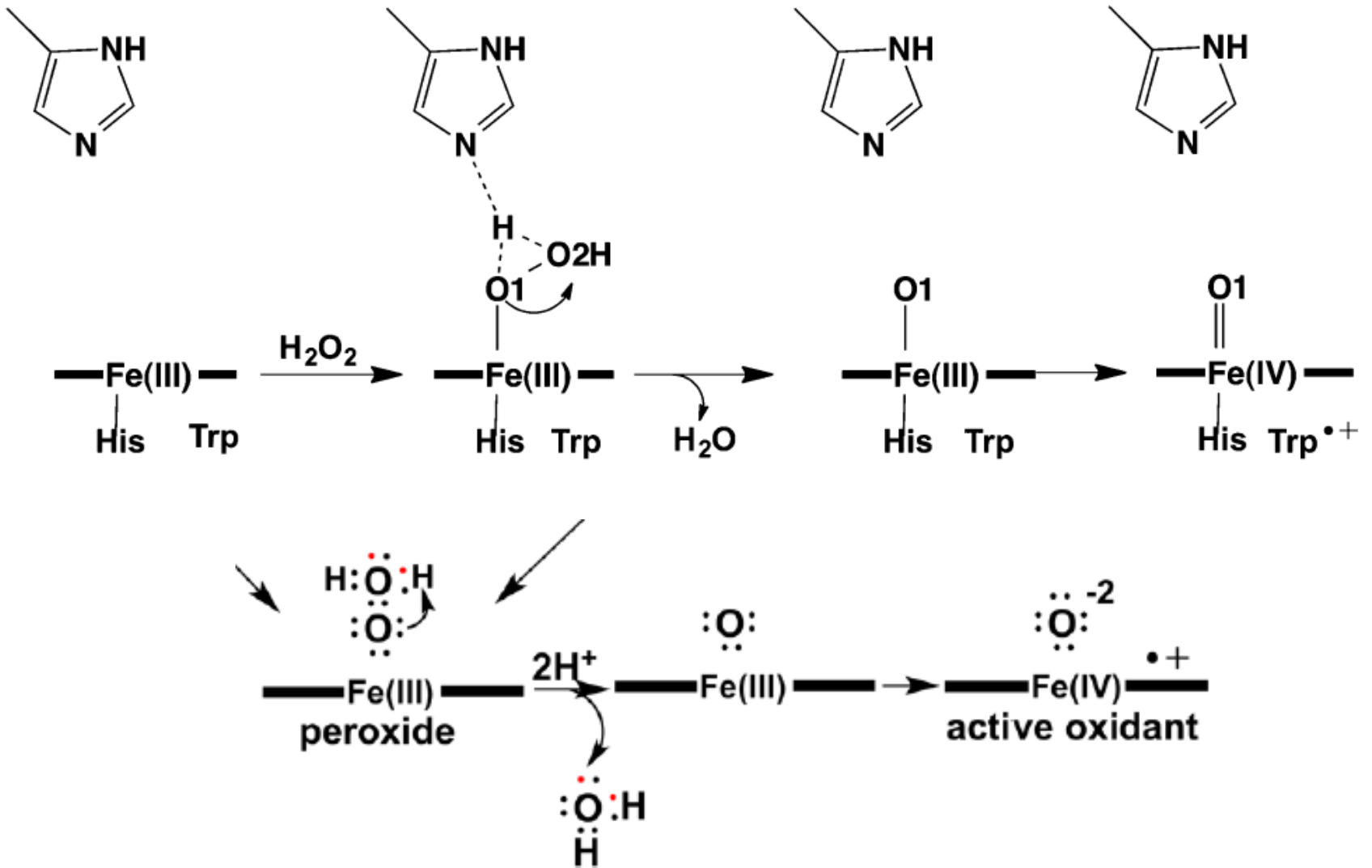


Ciclo catalitico di una perossidasi

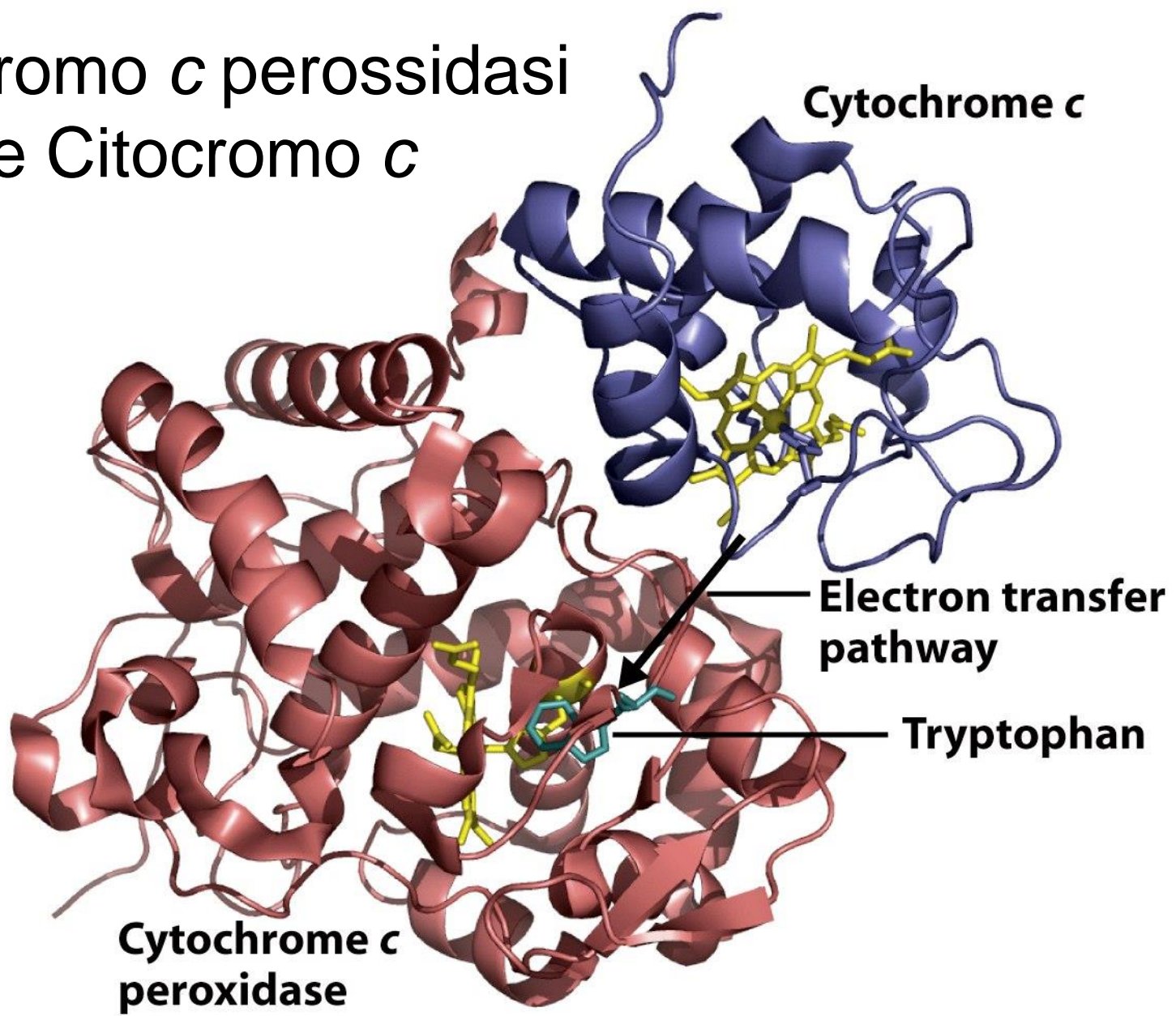


# Formazione dell'osso-ferrile

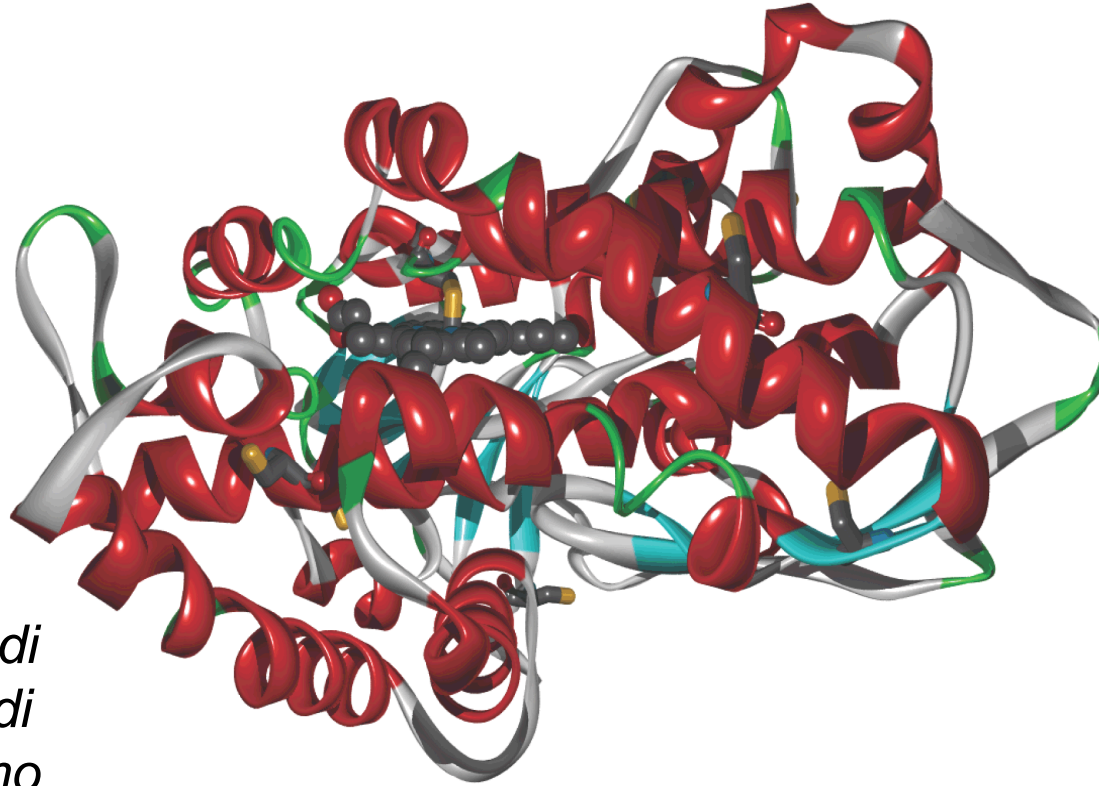
## Original Mechanism



# Citocromo c perossidasi e Citocromo c



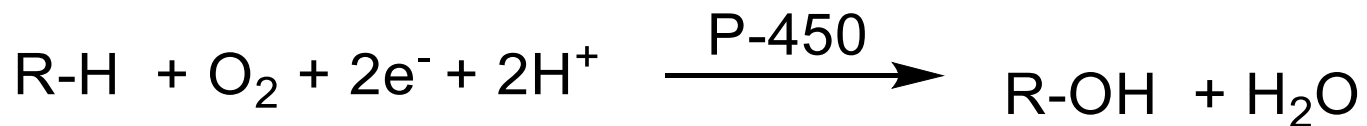
# Monoossigenasi



*individuati più di  
18.000 P450, di  
cui 57 nell'uomo*

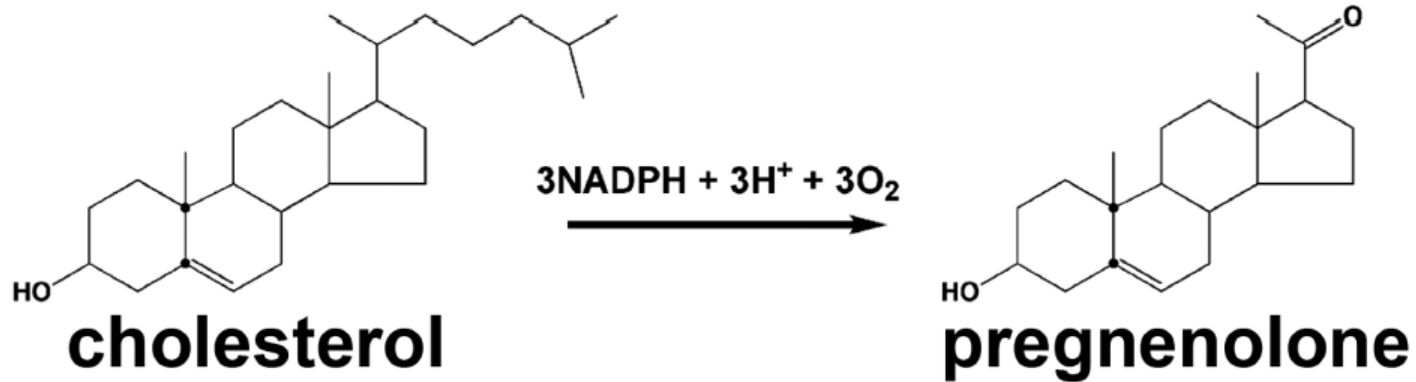
## Citocromo P-450

(da *Pseudomonas putida*) 50 kDa

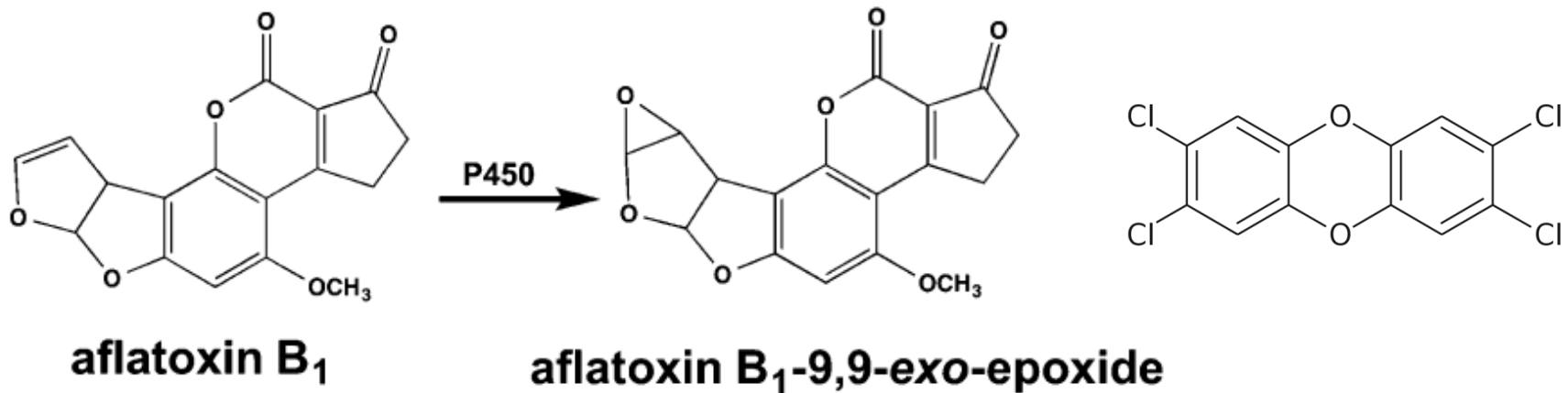




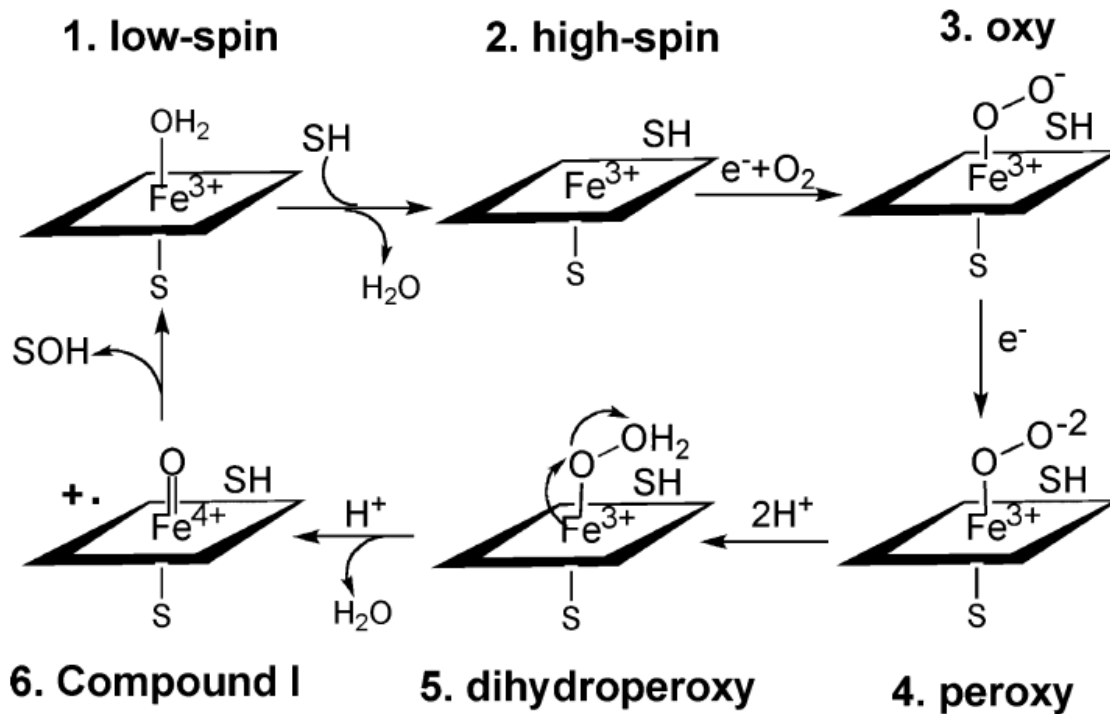
# Ossigenazione di substrati specifici da parte di P450



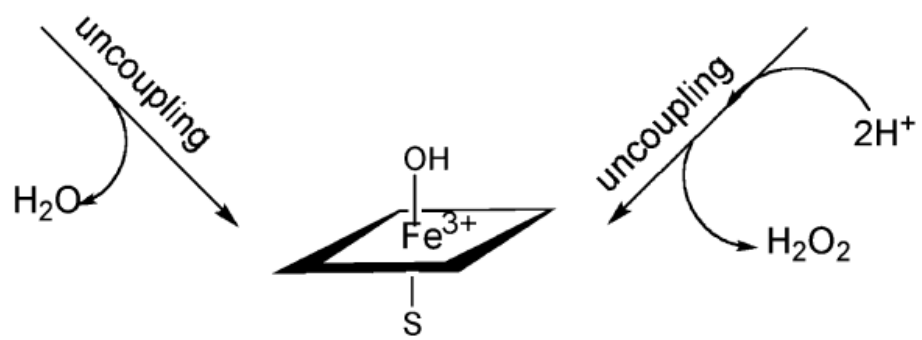
# Attivazione (involontaria) di substrati da parte di P450



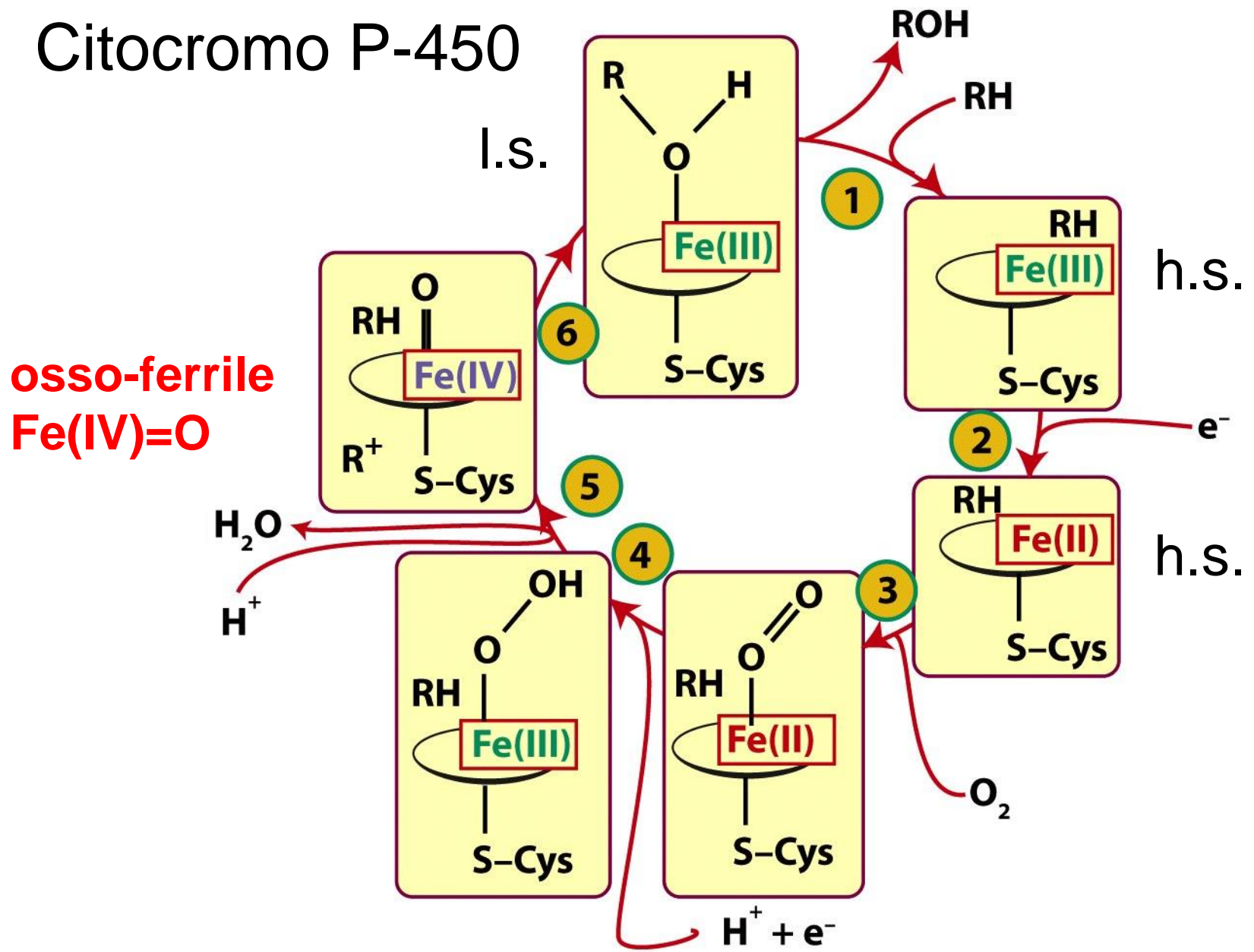
# Citocromo P-450



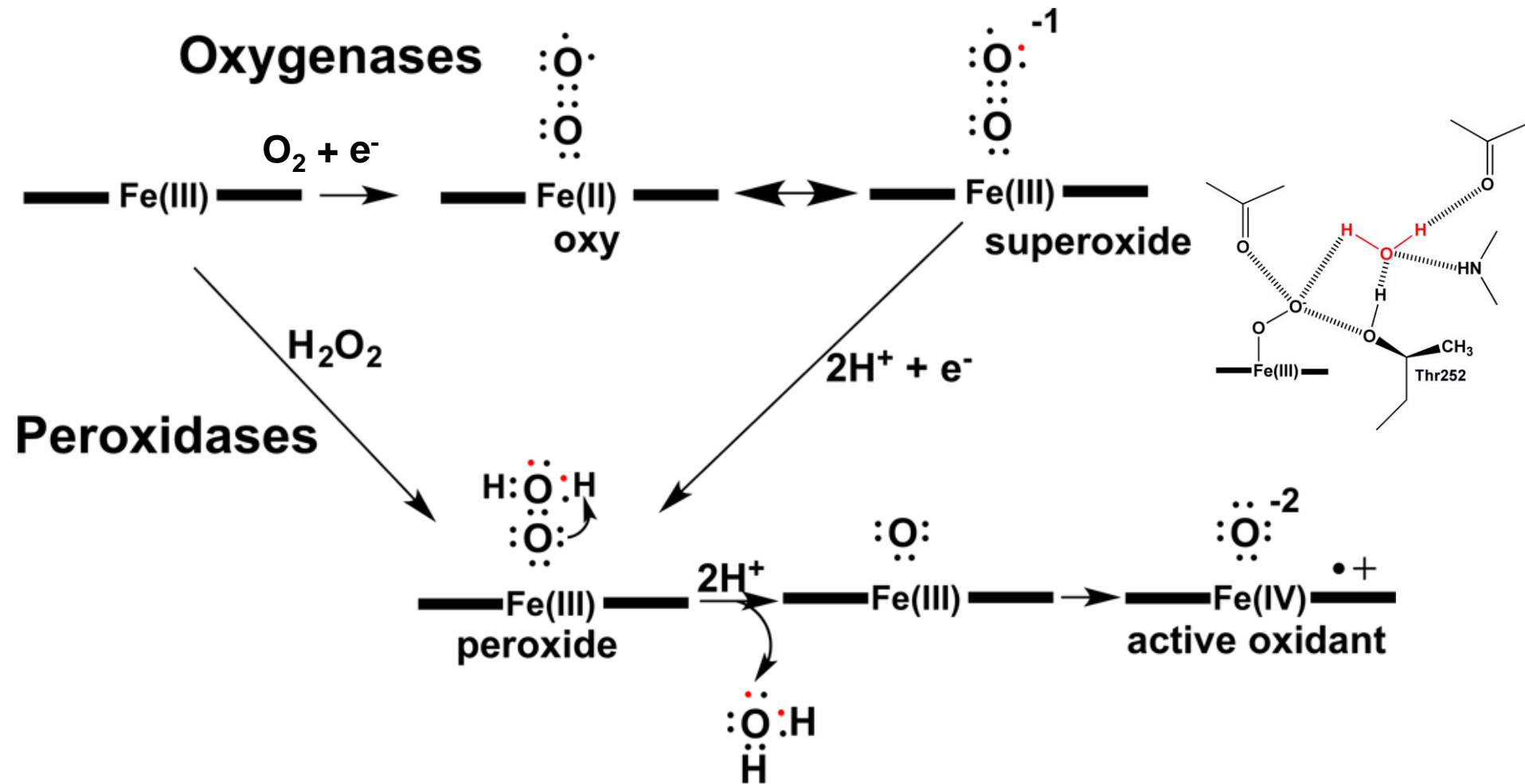
osso-ferrile  
Fe(IV)=O



# Citocromo P-450

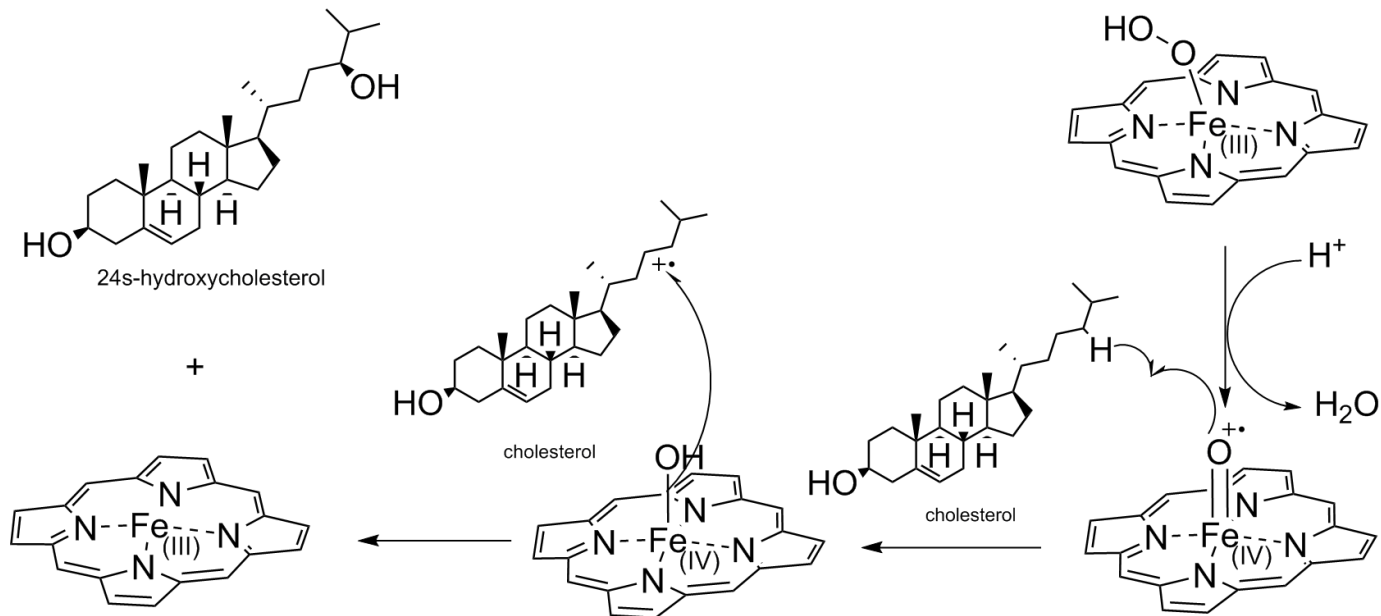
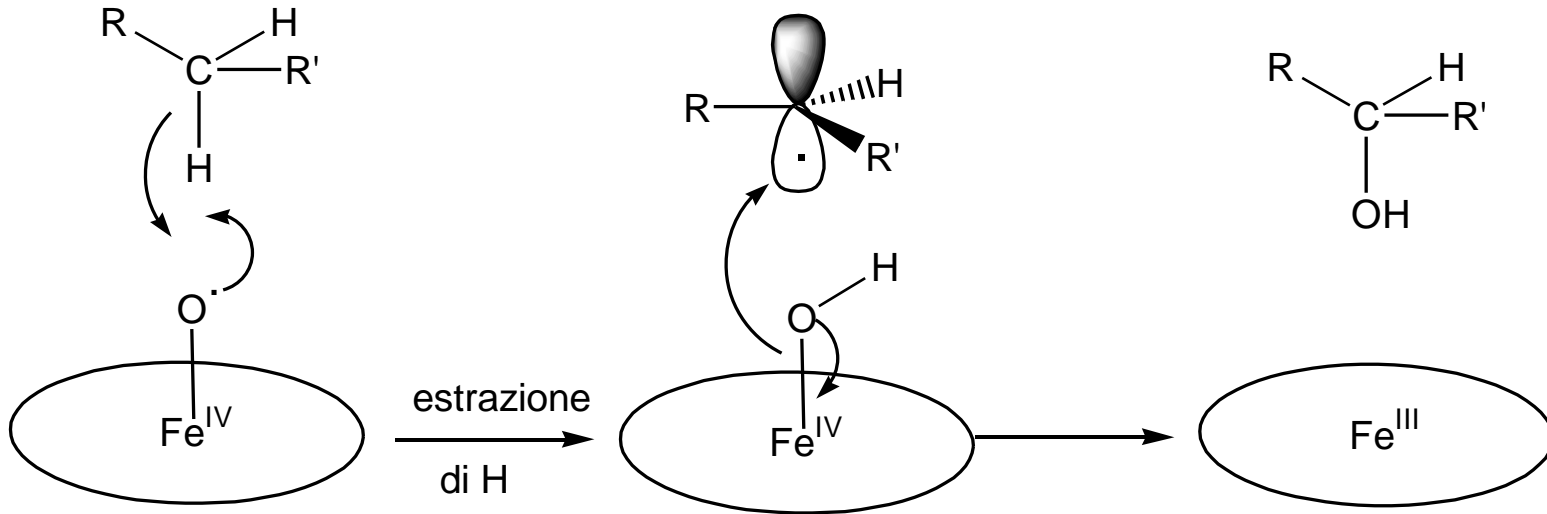


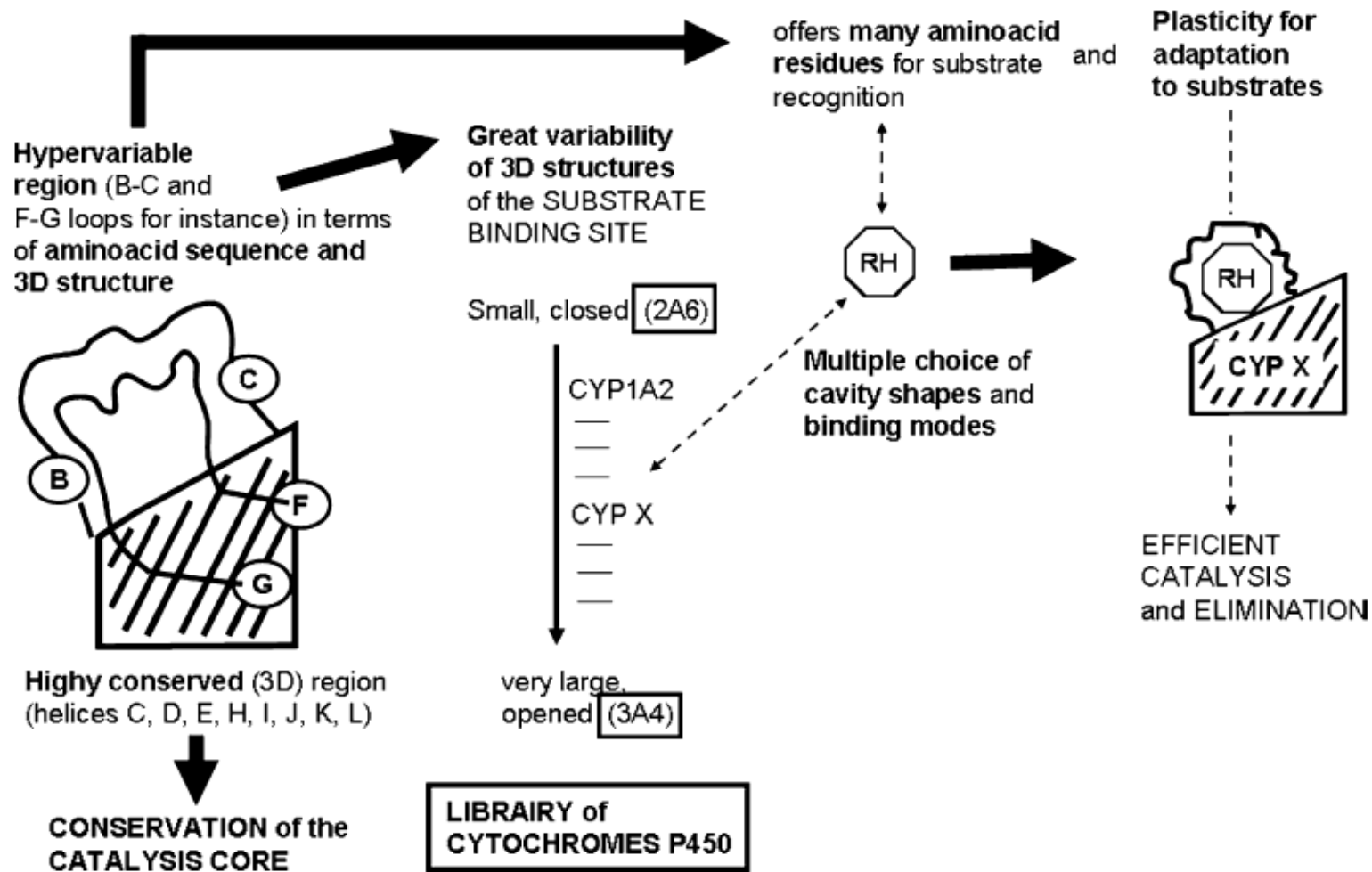
# Rottura eterolitica del legame O–O e protonazione dell'ossigeno distale



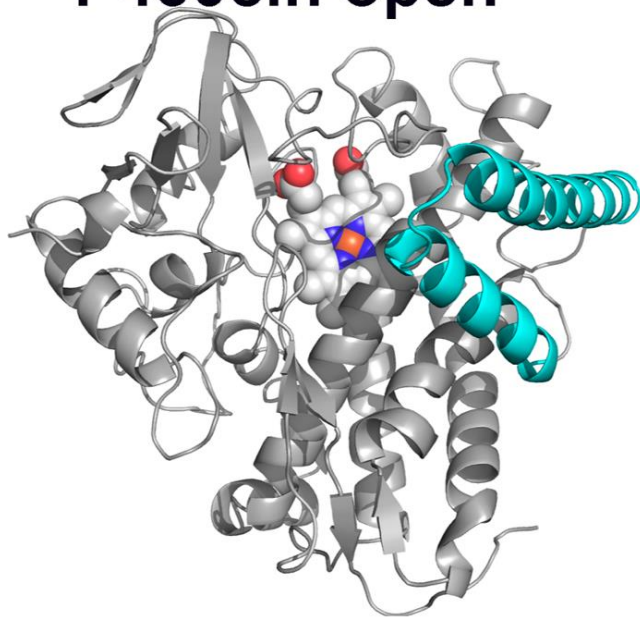
# Meccanismo di ossidazione del substrato

## Oxygen Rebound Mechanism

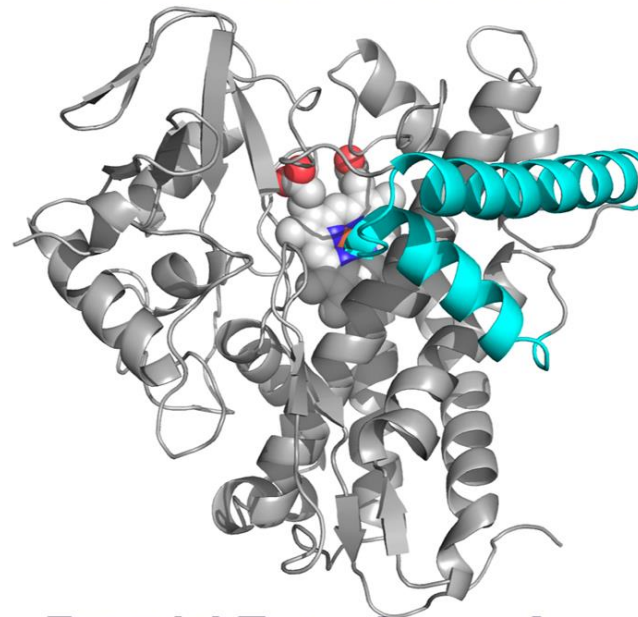




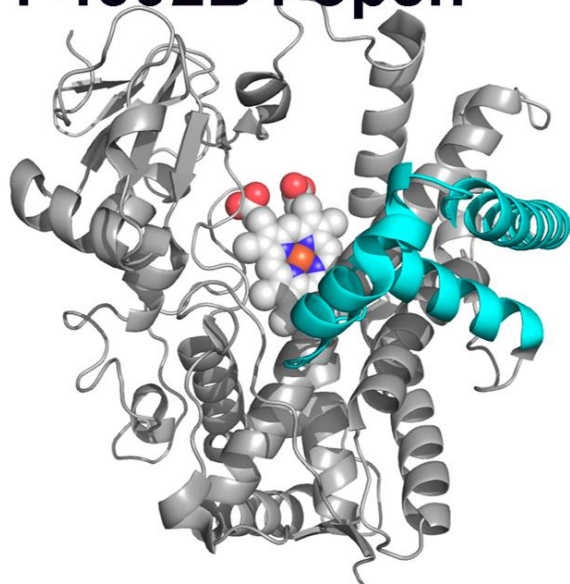
**P450cin open**



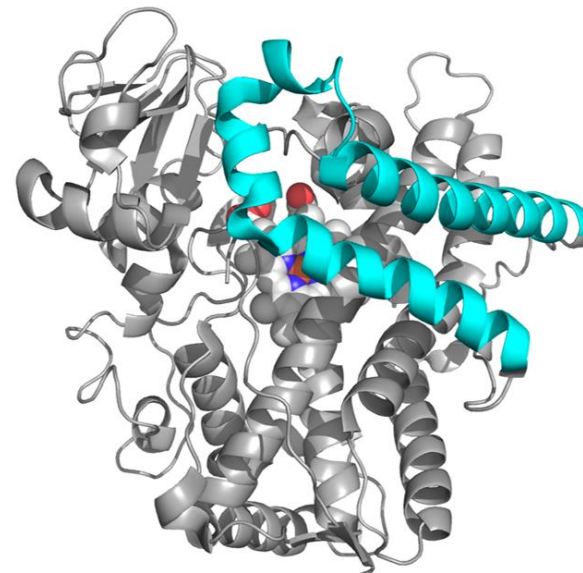
**P450cin closed**



**P4502B4 open**



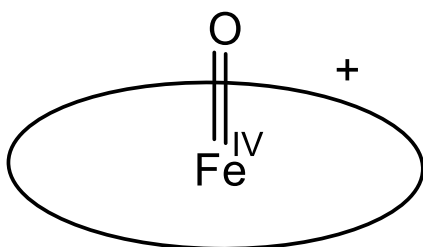
**P4502B4 closed**



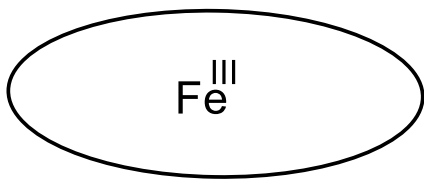
# P450

*cage*

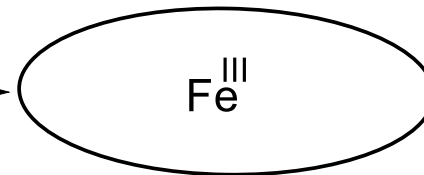
*escape*



+ Sub

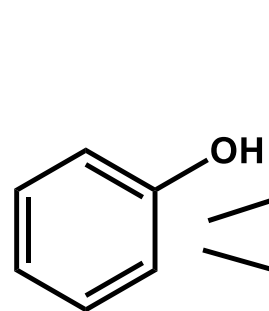
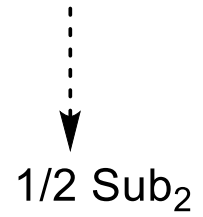


+ SubO



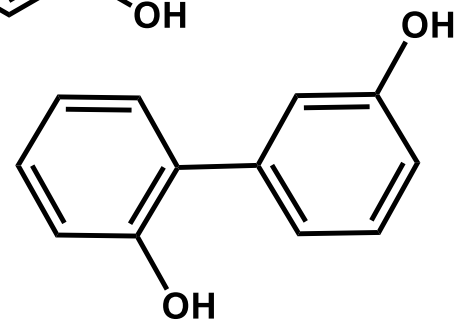
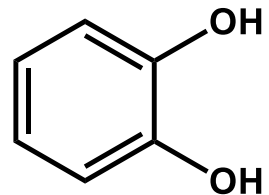
+ H<sub>2</sub>O + Sub<sup>••</sup>

perossidasi

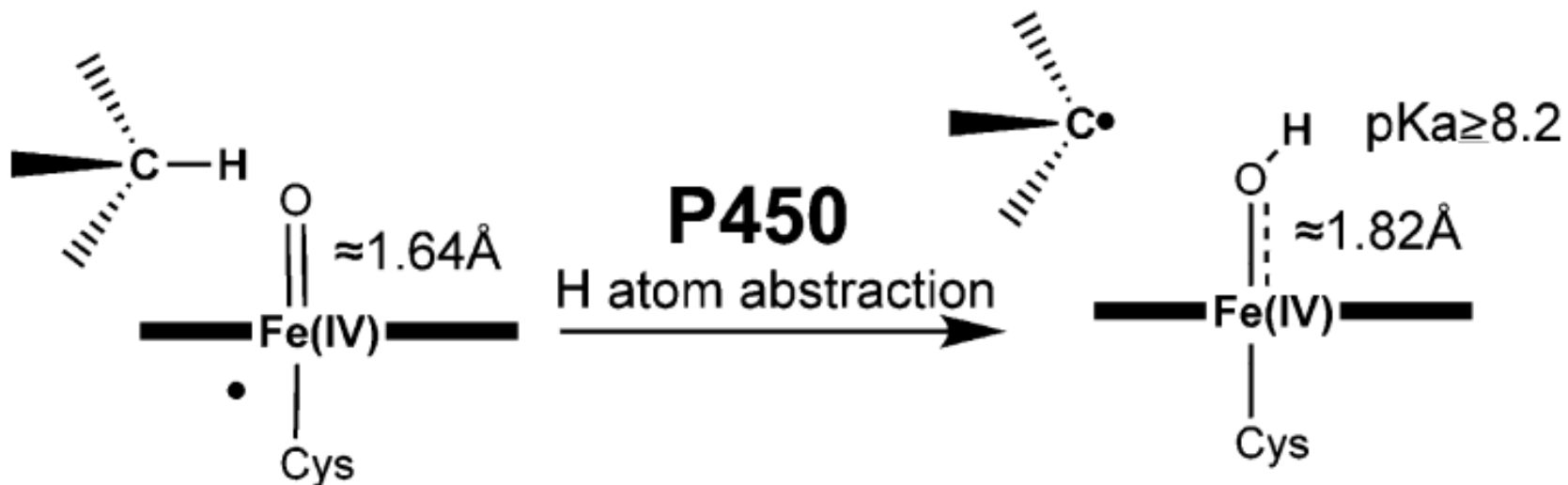


*cage*

*escape*



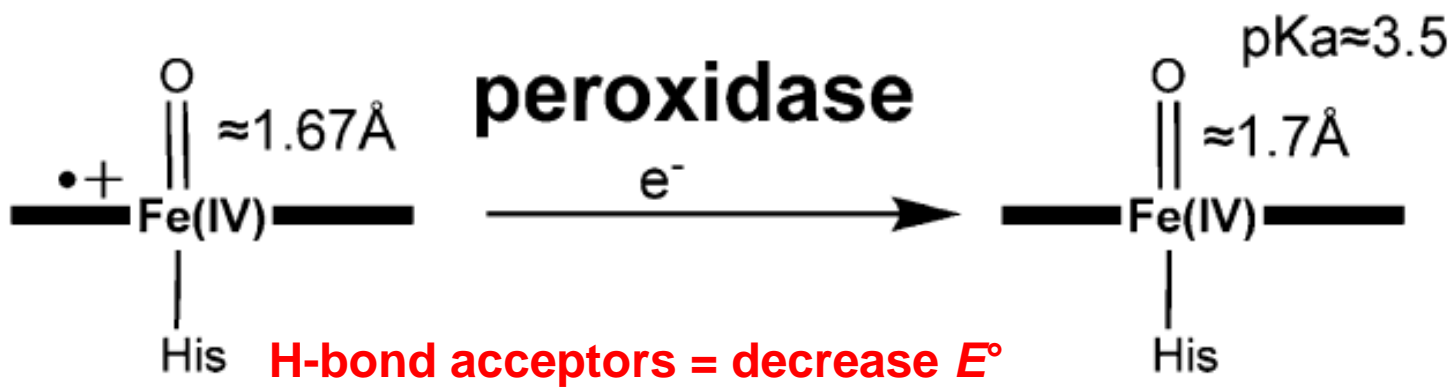




H-bond donors = increase  $E^\circ$

**Compound I**

**Compound II**



H-bond acceptors = decrease  $E^\circ$

