Copper enzymes

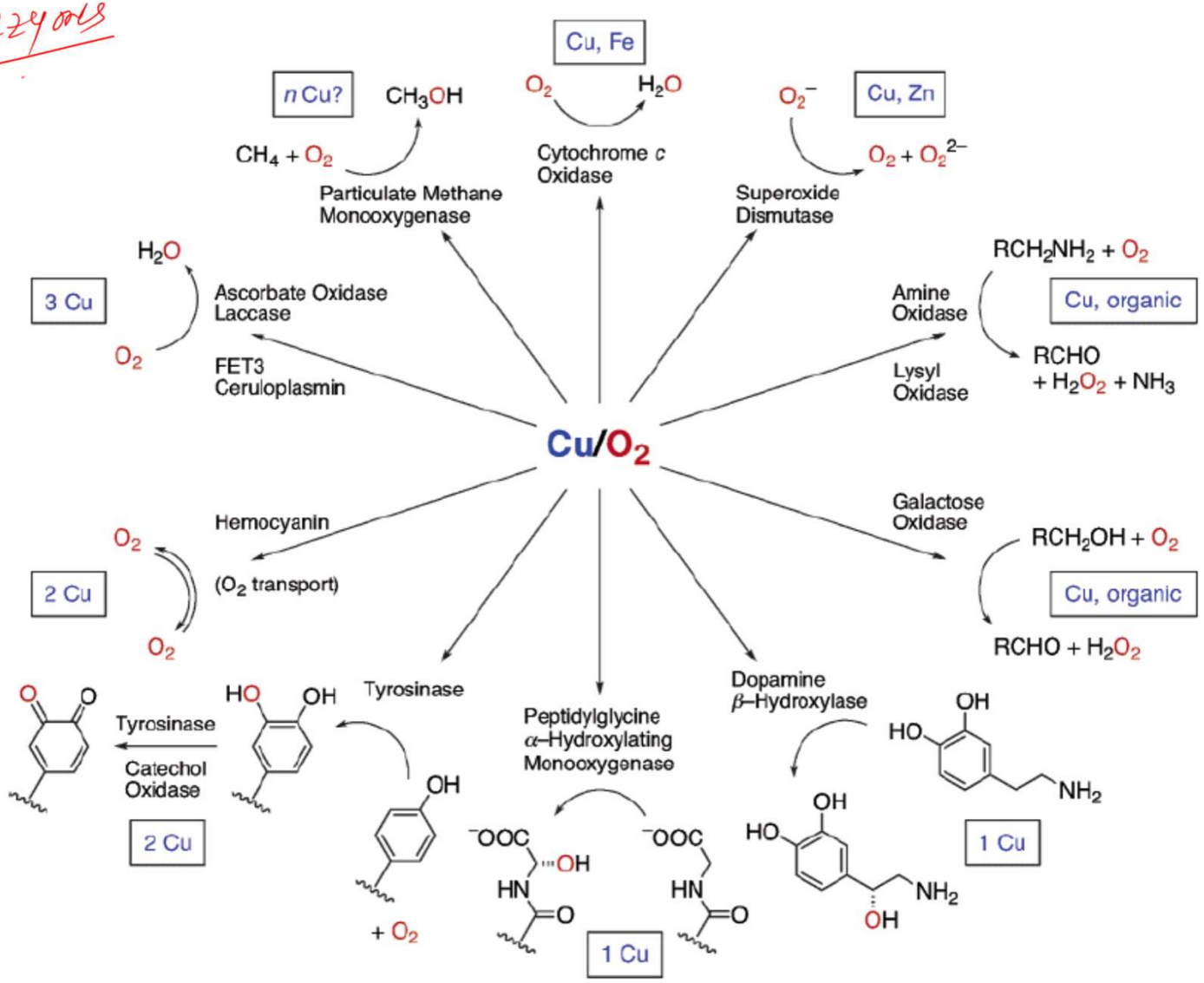
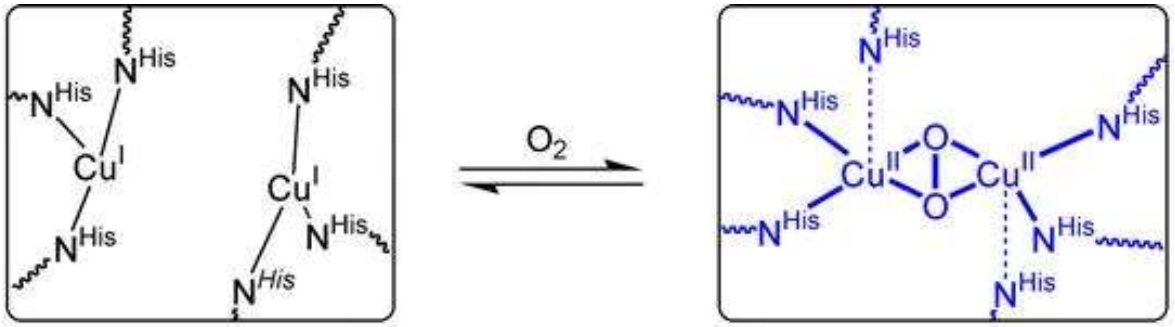


Figure 1. Selected Cu enzymes and proteins that activate O_2.[18]

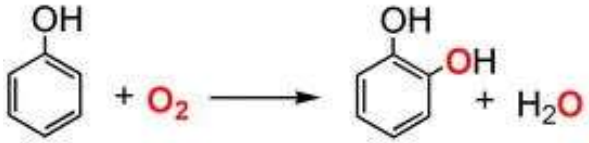
Active site structures and reactions of hemocyanin, tyrosinase, and catechol oxidase



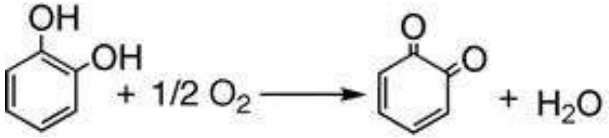
***deoxy*-Hemocyanin**
Limulus II (horseshoe crab)
Cu...Cu = 4.6 Å
Trigonal-planar copper(I)

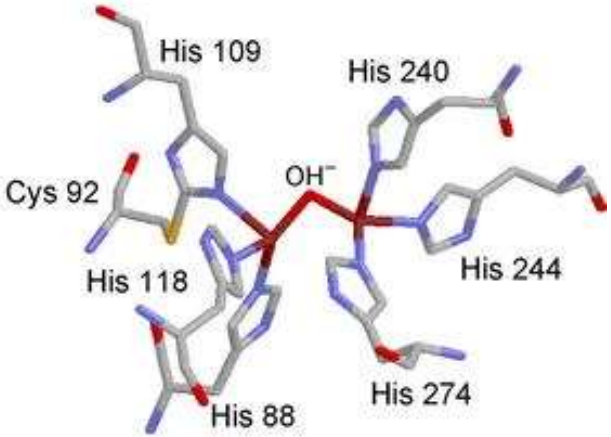
***oxy*-Hemocyanin**
Limulus II (horseshoe crab)
Cu...Cu = 3.6 Å; pyramidal Cu(II)
λ_{max} = 350 nm (ε ~ 20,000)
$\nu_{(O\text{-}O)}$ ~ 750 cm^{-1}

Cresolase (Tyr) reaction:



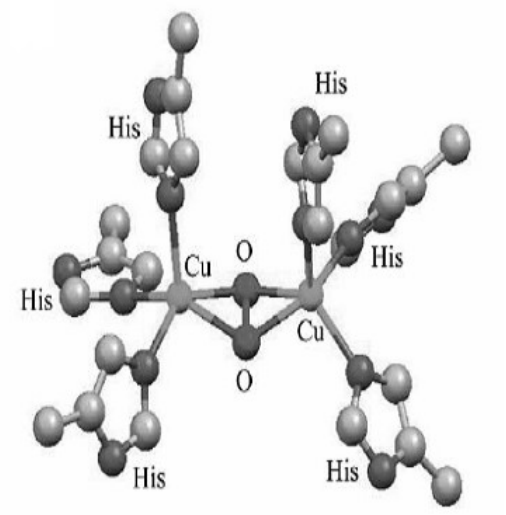
Catechol Oxidase (Tyr & CO) reaction:



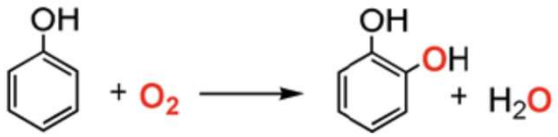


***met* Catechol Oxidase (CO)**
Cu...Cu = 2.9 Å

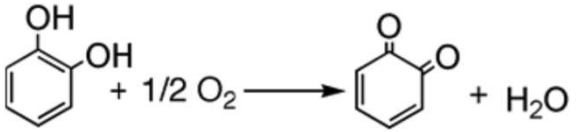
Tyrosinase



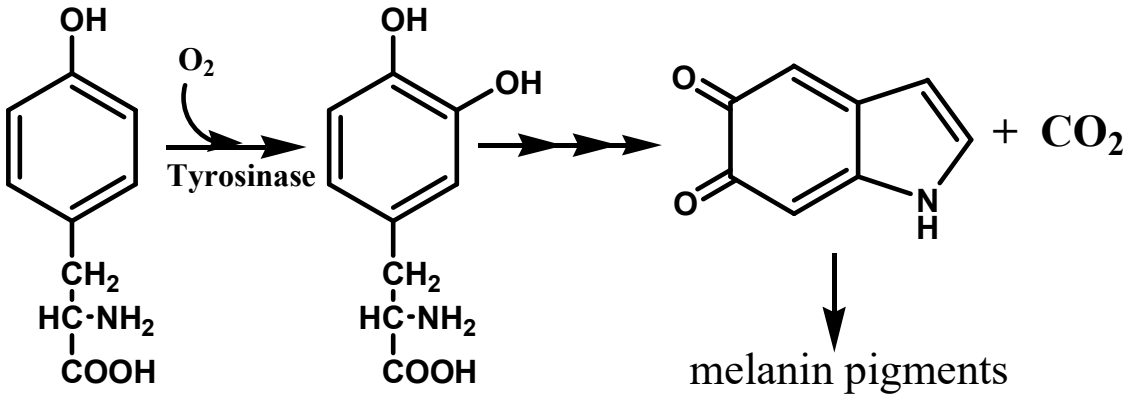
Cresolase (Tyr) reaction:



Catechol Oxidase (Tyr & CO) reaction:



❖ *Tyrosinase* (Tyr), a monooxygenase which hydroxylates monophenols (tyrosine) – *o*-hydroxylation of phenols: monophenolase activity - and further oxidizes the *o*-diphenols (catechols – like DOPA) to an *o*-quinone – catecholsae activity. The enzymesTyr and *Catechol Oxidase* are responsible for melanin formation and browning of fruits:



Catechol Oxidase

❖ It catalyzes exclusively the oxidation of catechols to the corresponding *o*-quinone, without acting on monophenols. The resulting highly reactive quinones auto-polymerize to form brown polyphenolic catechol melanins, a process thought to protect the damaged plant from pathogens or insects

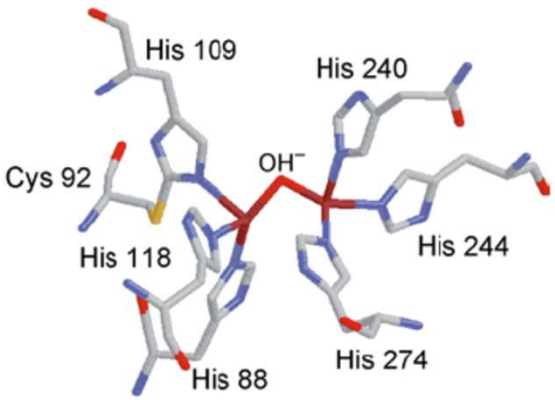
❖Both copper centers have three histidine ligands

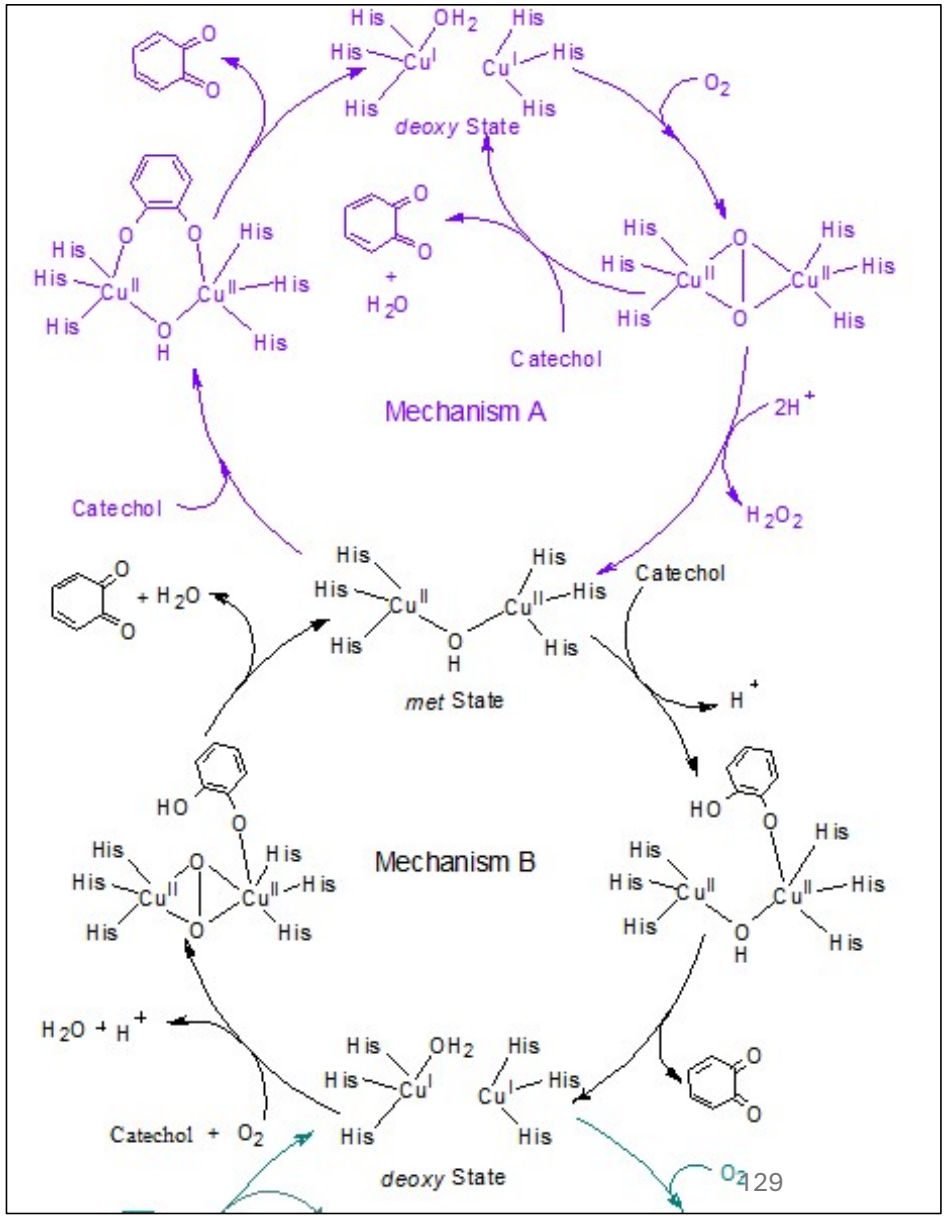
❖ Cu-Cu: 2.89 Å

❖ Antiferromagnetic coupling

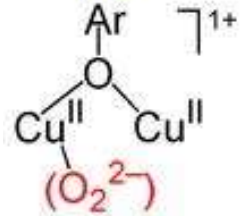
❖ A μ-hydroxo bridge between the two Cu(II) ions --- met form

❖ μ-η^2:η^2 binding mode for the peroxide --- active form



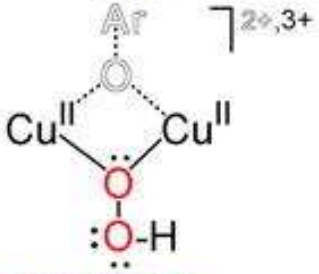


peroxo (A)



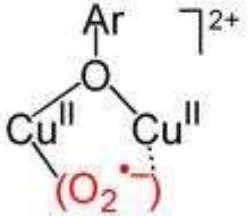
nucleophilic

hydroperoxo (B)



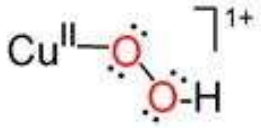
electrophilic

superoxo (C)



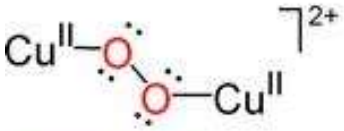
?

end-on, η^1 hydroperoxo (D)



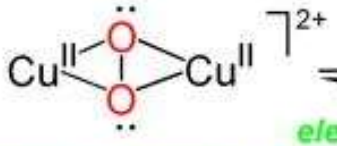
electrophilic ?

μ-1,2-peroxo (E)



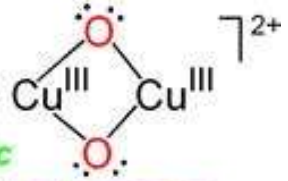
nucleophilic

μ-η^2:η^2-peroxo (F)



aromatic hydroxylation

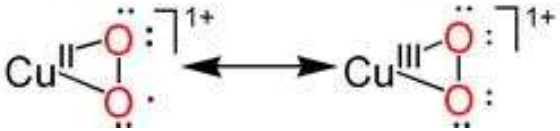
bis-μ-oxo (G)



electrophilic

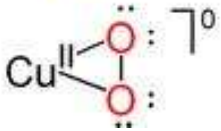
H• abstraction

side-on, η^2 superoxo (H)

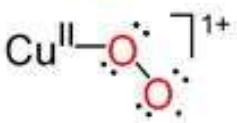


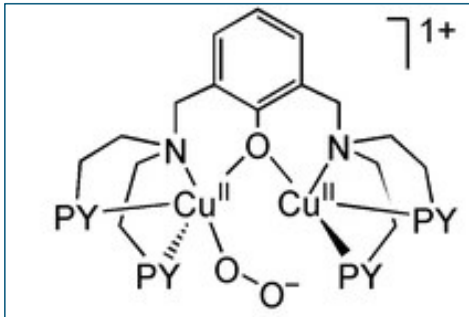
side-on, η^2 peroxo-Cu^{III} (I)

side-on, η^2 peroxo-Cu^{II} (J)



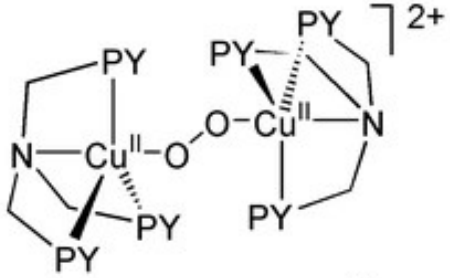
end-on, η^1 superoxo (K)





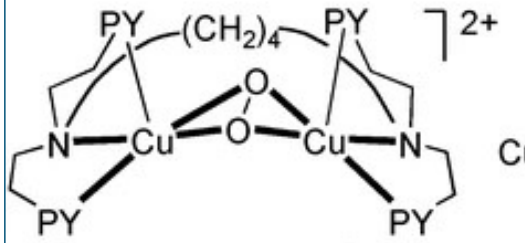
$[Cu_2(XYLO^-)(O_2)]^+$

λ_{max} = 505 nm
Cu...Cu = 3.31 Å (EXAFS)
$\nu_{(O-O)}$ = 803 cm^{-1}
$\Delta H_{on}°$ = –66 kJ/mol



$[\{(TMPA)Cu\}_2(O_2)]^{2+}$

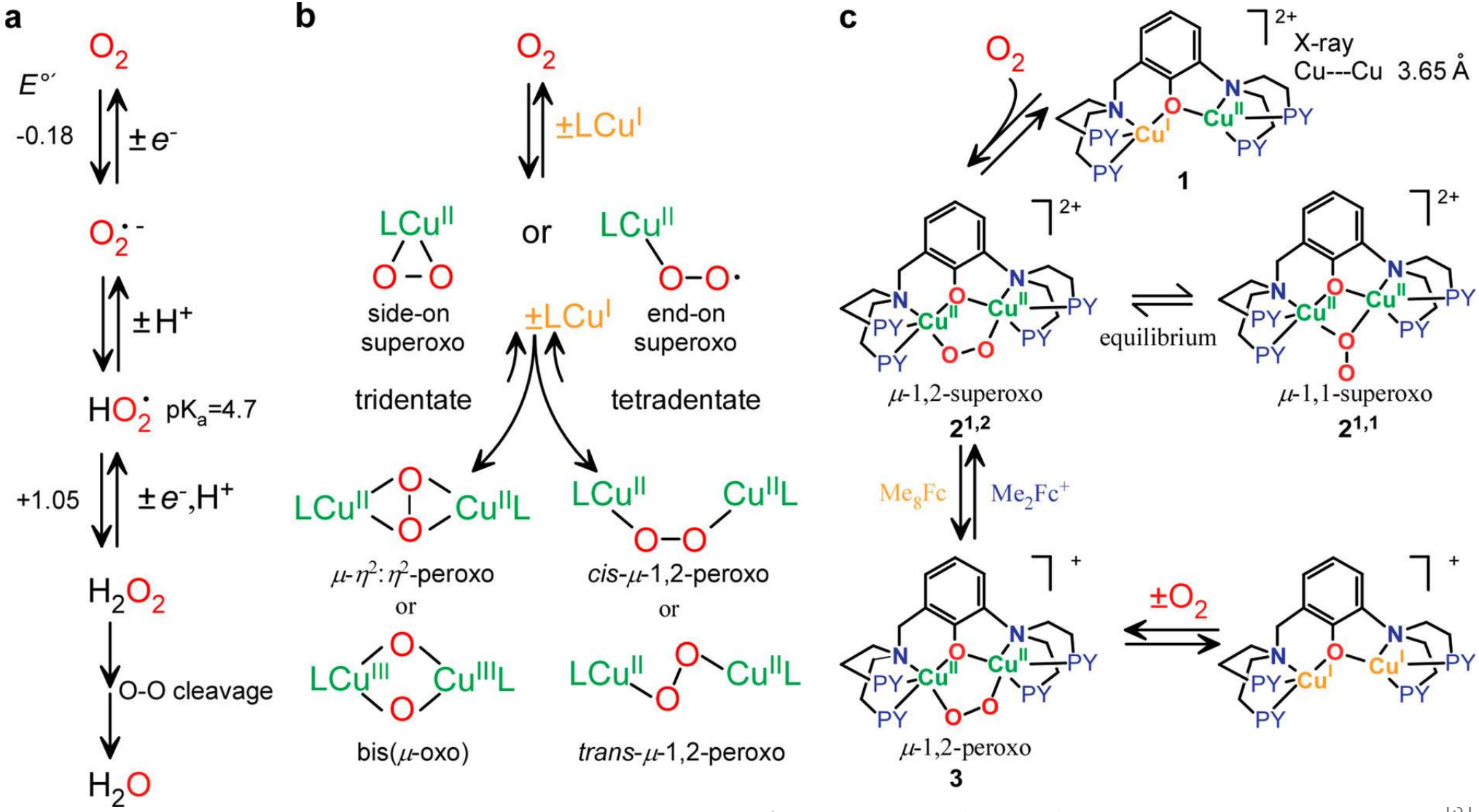
λ_{max} = 525, ~600 (sh) nm
Cu...Cu = 4.36 Å (X-ray)
$\nu_{(O-O)}$ = 834 cm^{-1}
$\Delta H_{on}°$ = –81 kJ/mol



$[Cu_2(N4)(O_2)]^{2+}$

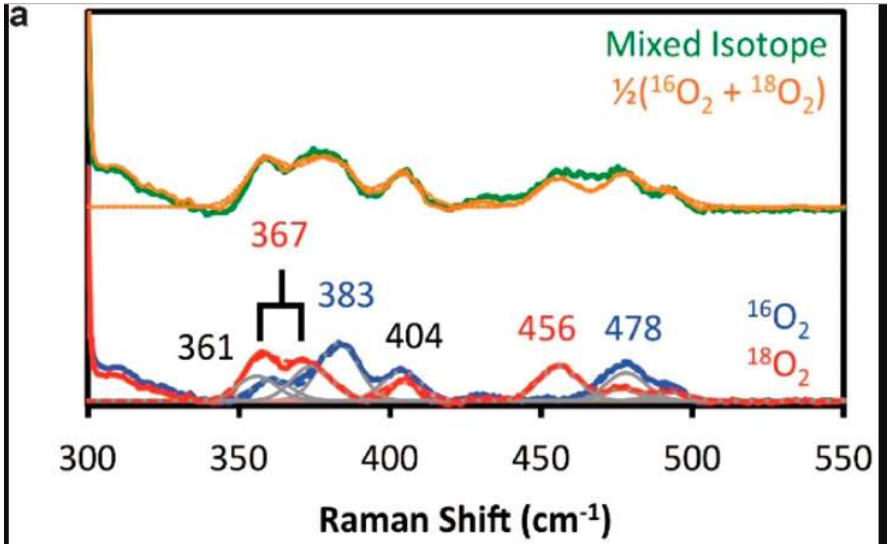
λ_{max} = 360 nm
Cu...Cu = 3.4 Å (EXAFS)
$\nu_{(O-O)}$ = 751 cm^{-1}
$\Delta H_{on}°$ = –81 kJ/mol

Copper-Dioxygen Chemistry

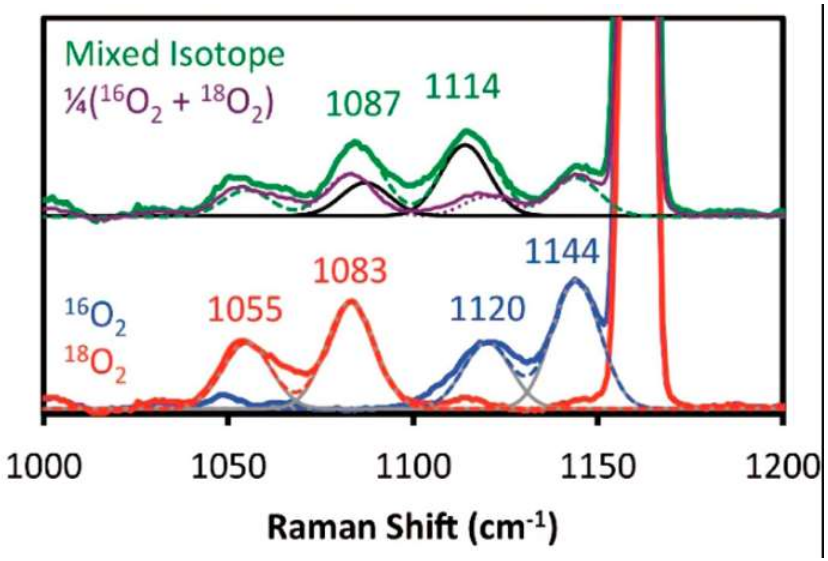


Karlin et al. J. Am. Chem. Soc. 2016, 138, 7055−7066

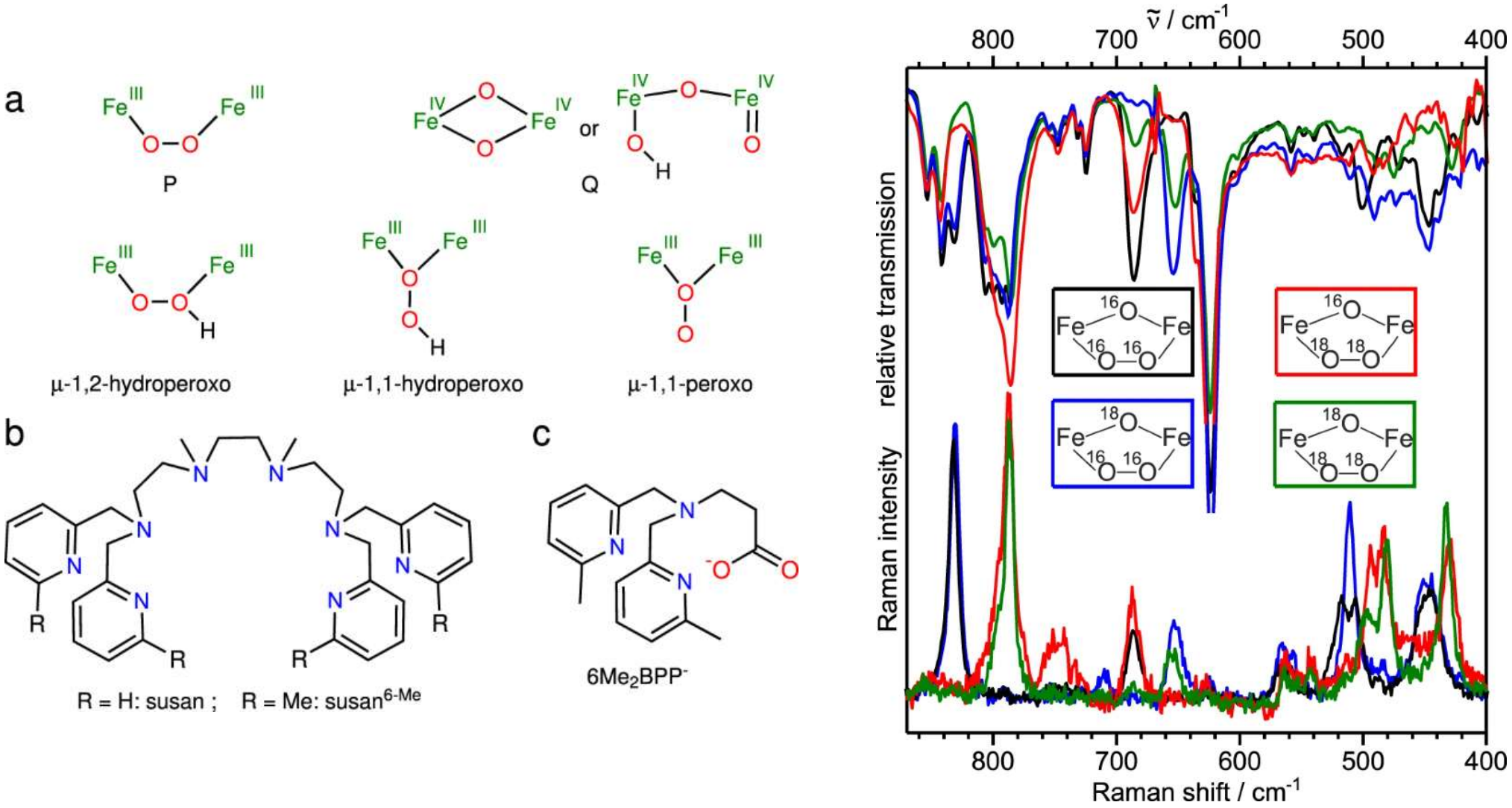
Resonance Raman spectra of **2** with 407 nm excitation; $^{16}O_2$ (blue), $^{18}O_2$ (red), mixed isotope (a 1:2:1 mixture of $^{16}O_2$:$^{16,18}O_2$:$^{18}O_2$ green), 1/4($^{16}O_2$ + $^{18}O_2$) (purple), and 1/2($^{16}O_2$ + $^{18}O_2$) (orange)



Additionally, two oxygen isotope sensitive Cu–O stretches are observed at lower energy (478 cm^{-1} $\Delta^{18}O_2$ and 383 cm^{-1} $\Delta^{18}O_2$



presence of two oxygen isotope sensitive features (1144 cm^{-1} $\Delta^{18}O_2$ and 1120 cm^{-1} $\Delta^{18}O_2$) corresponds to two superoxide O–O stretches indicating the presence of two, distinct superoxide isomers. **The 1144 cm^{-1} feature corresponds to the O–O stretch of the μ-1,2-isomer while the 1120 cm^{-1} stretch results from the μ-1,1-isomer.**



Zimmermann et al Nat. Commun 2022, 10.1038/s41467-022-28894-5