

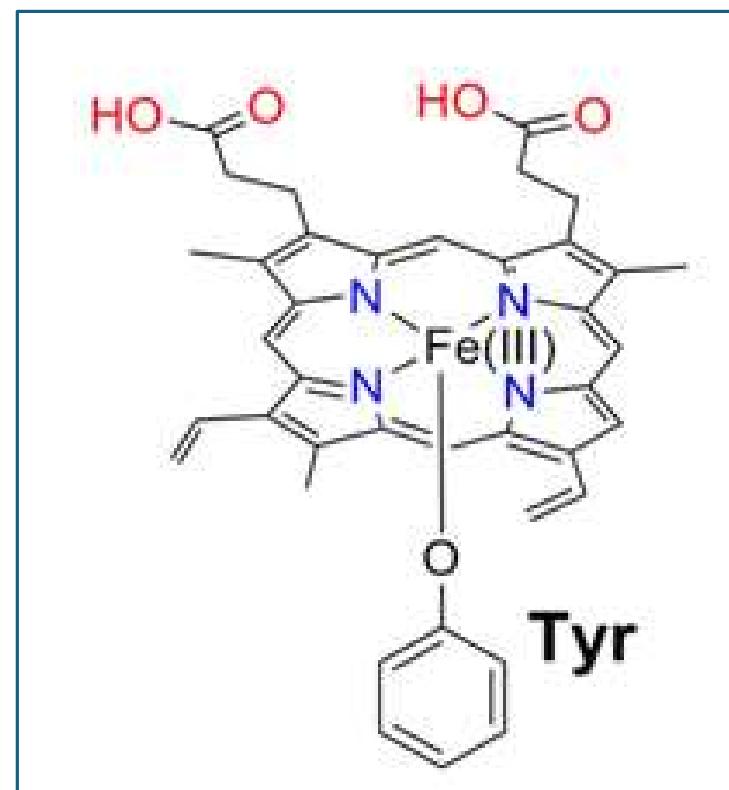
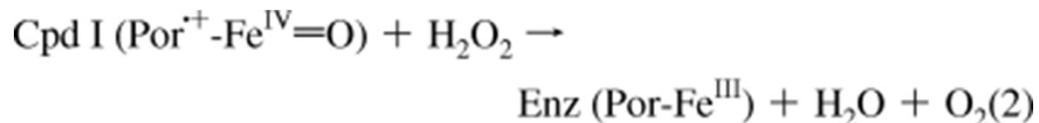
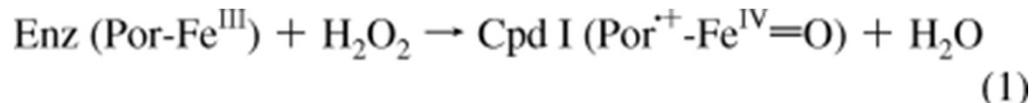
## Catalase

- ✓ Heme catalases, present in almost all aerobically respiring organisms, play an important role in defending cells against oxidative damage by degrading hydrogen peroxide ( $\text{H}_2\text{O}_2$ ) to water and oxygen

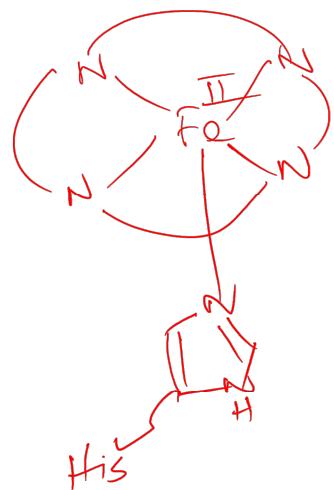


- ✓ Catalases have been implicated as an important factor in inflammation, mutagenesis, prevention of apoptosis, and stimulation of a wide spectrum of tumors.

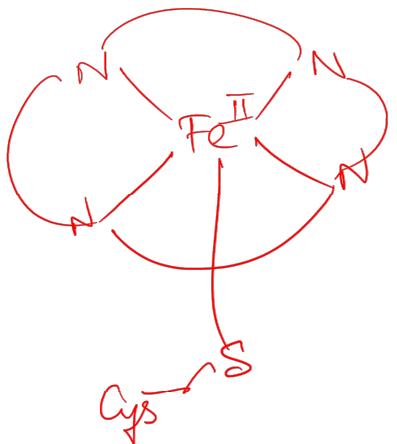
- ✓ Evidence from kinetics studies indicate that once catalase COMPOUND I (cpd I) forms, it rapidly reacts with a second molecule of  $\text{H}_2\text{O}_2$  to generate  $\text{O}_2$  and a water molecule.



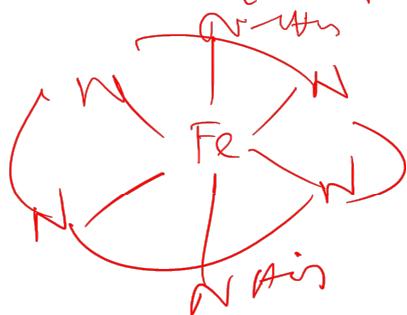
Myoglobin  
oxygen transport



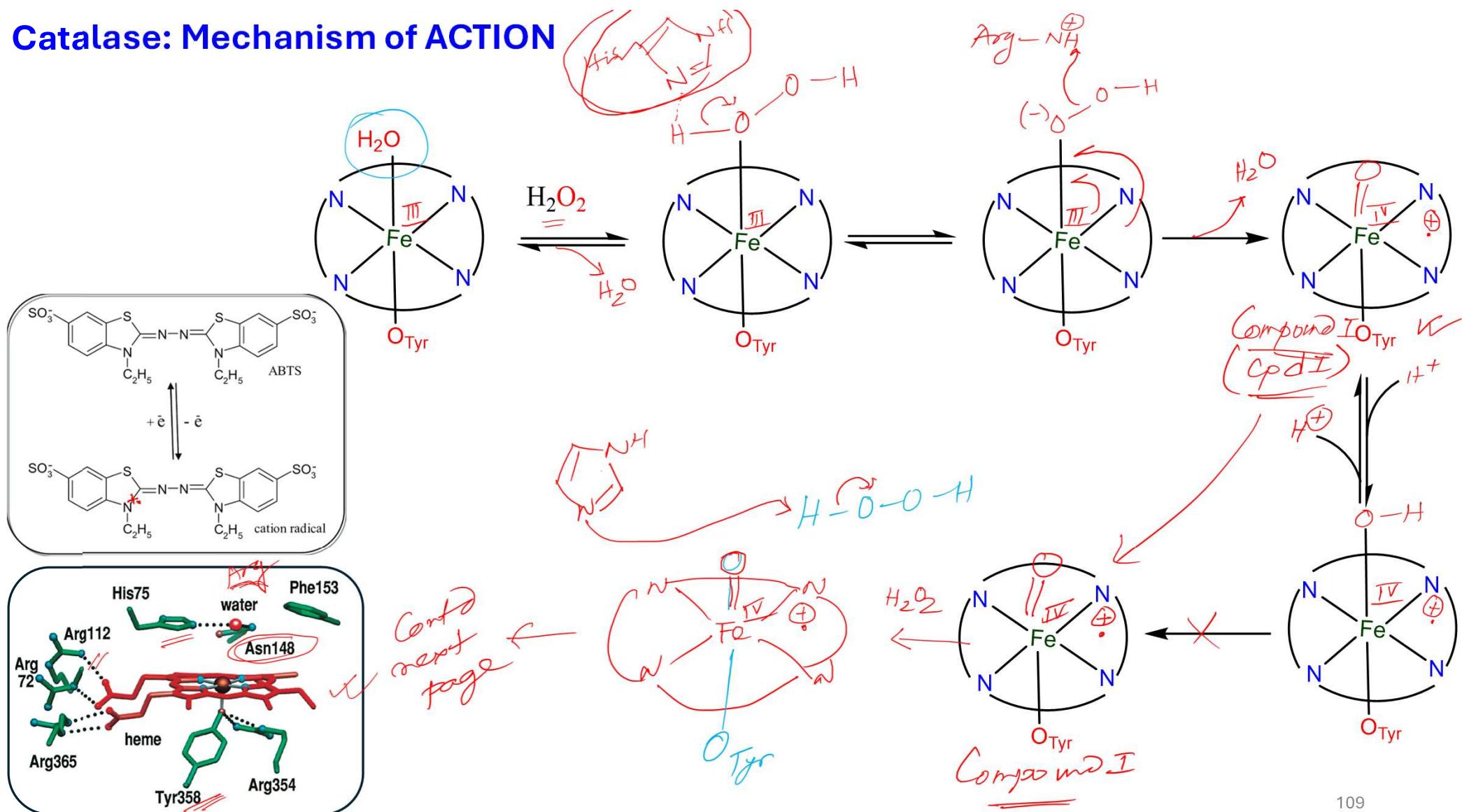
Cytochrome  $\text{c}_{1450}$   
metabolism protein

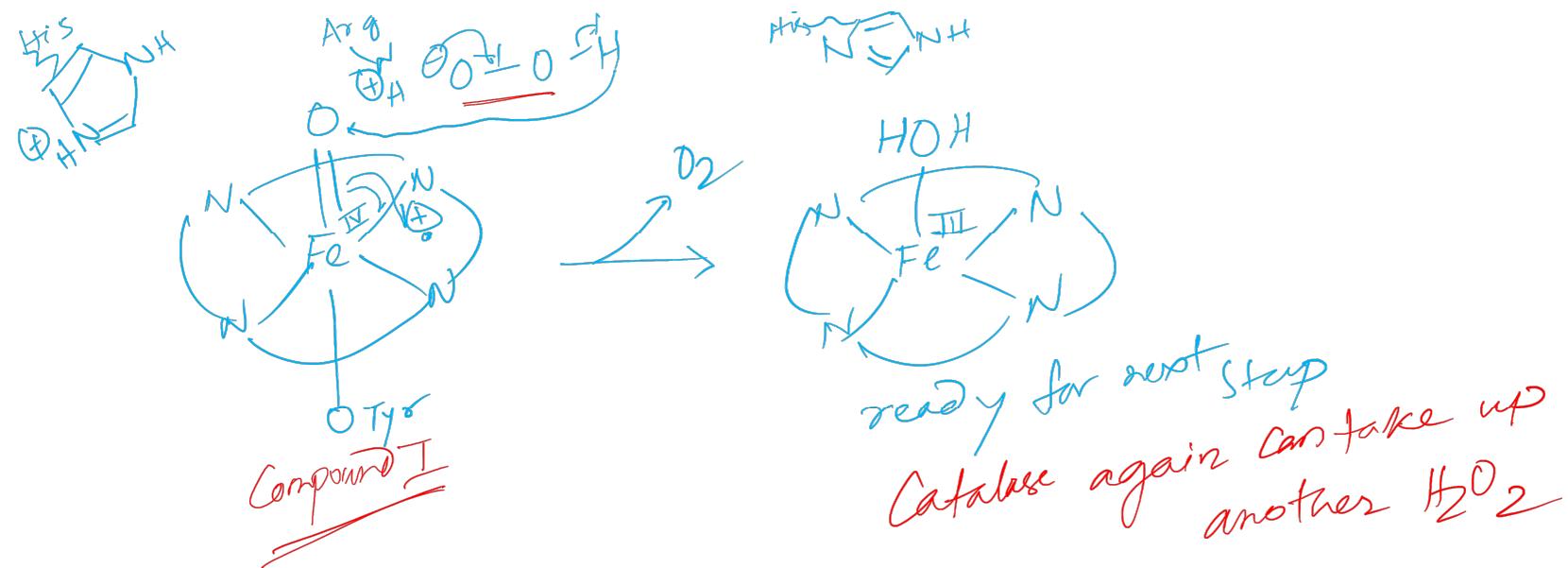


Cytochromes  
 $e^-$  transport



## Catalase: Mechanism of ACTION



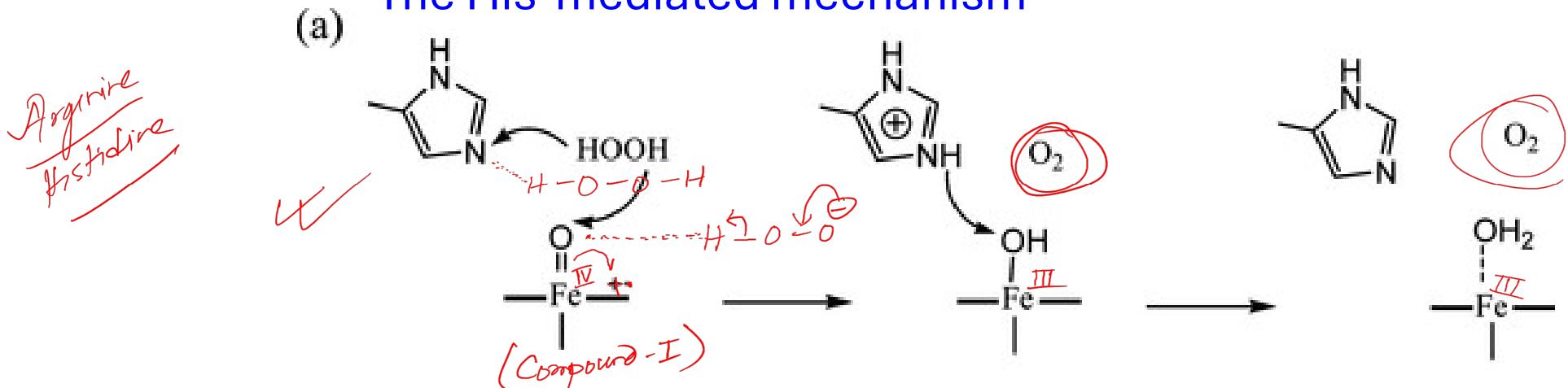


# Proposed mechanisms of Cpd I reduction

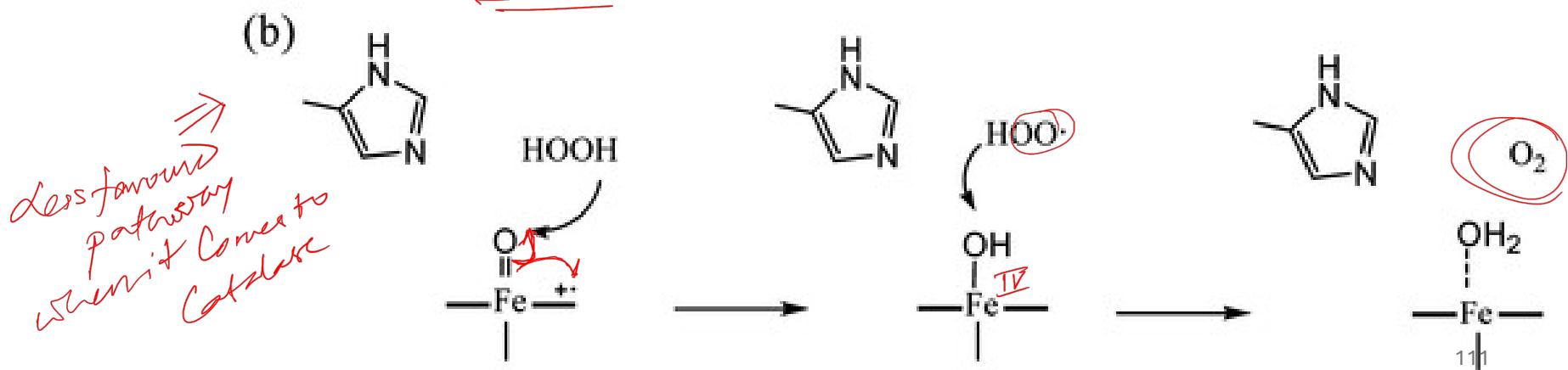
J. Am. Chem. Soc. 2009, 131, 33, 11751–11761



## The His-mediated mechanism



## The direct mechanism

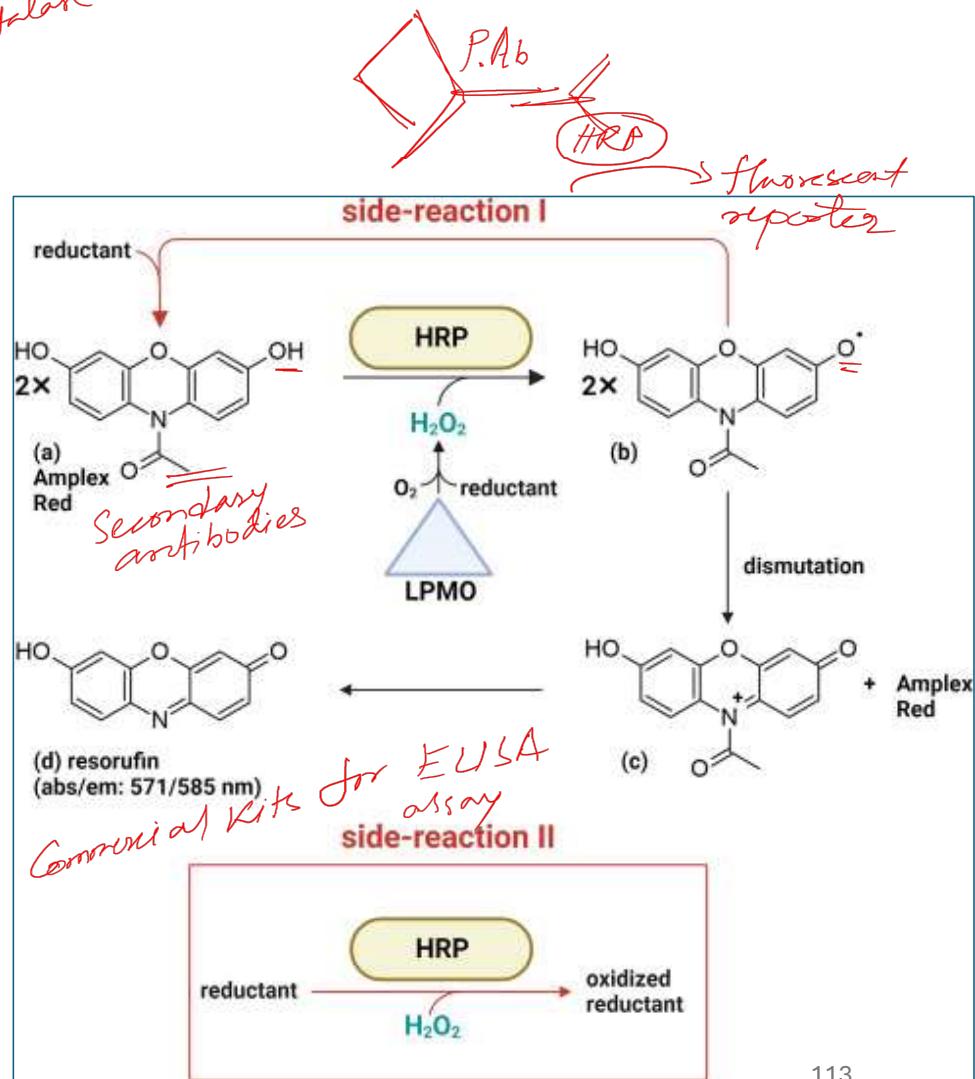
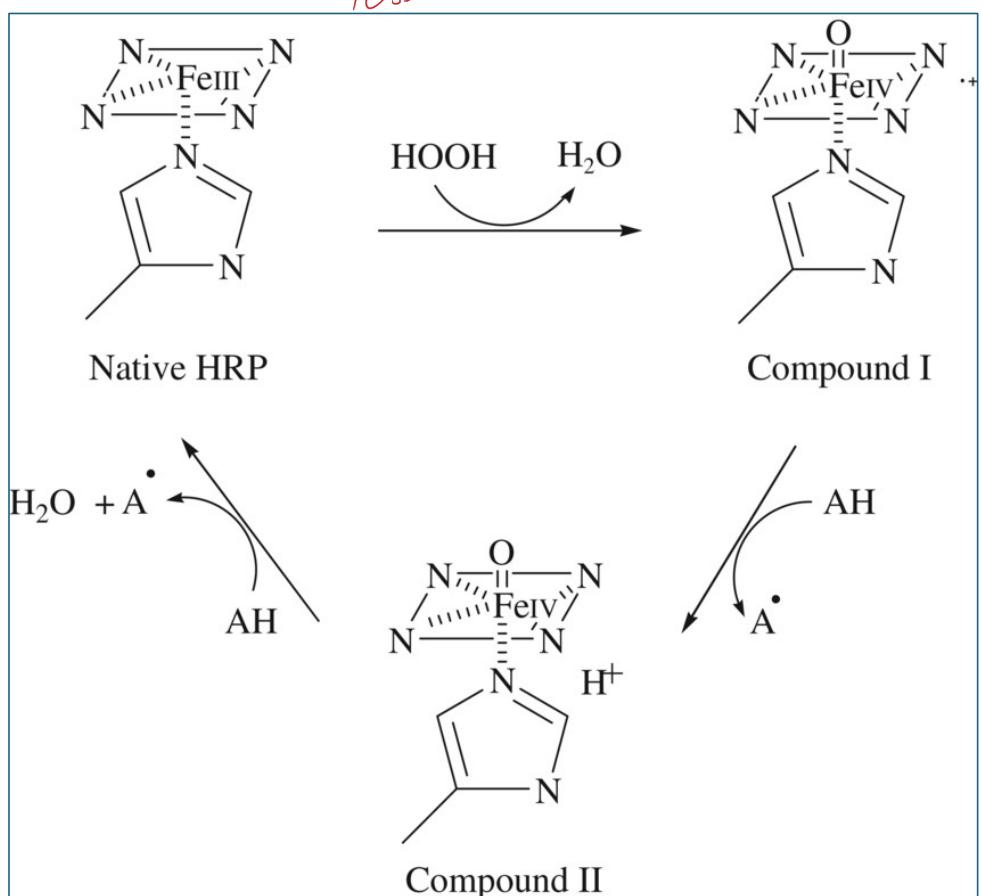


## What is probed and known ?

1. Exclusive formation of  $^{18}\text{O}_2$  and  $^{16}\text{O}_2$  from a 50:50 mixture of  $\text{H}_2^{16}\text{O}_2$  and  $\text{H}_2^{18}\text{O}_2$  indicates that  $\text{O}_2$  is formed by two-electron oxidation of  $\text{H}_2\text{O}_2$  without breaking the O-O bond. There are two possible mechanisms on the formation of  $\text{O}_2$  in the reaction of  $\text{H}_2\text{O}_2$  and compound I without showing  $^{18}\text{O}/^{16}\text{O}$  scrambling
2. Mechanism A shows an ionic reaction via initial proton abstraction with the help of the distal histidine acting as a general acid-base catalyst → *I favours this pathway*
3. A similar deprotonation process is involved in the formation of compound I. In mechanism B the reaction starts by a hydrogen atom transfer from  $\text{H}_2\text{O}_2$  to the ferryl species to yield a radical intermediate. The hydrogen abstraction by the ferryl intermediate has been proposed for the alkane hydroxylation by cytochrome P450, its model complexes, and even in non-heme enzymes .

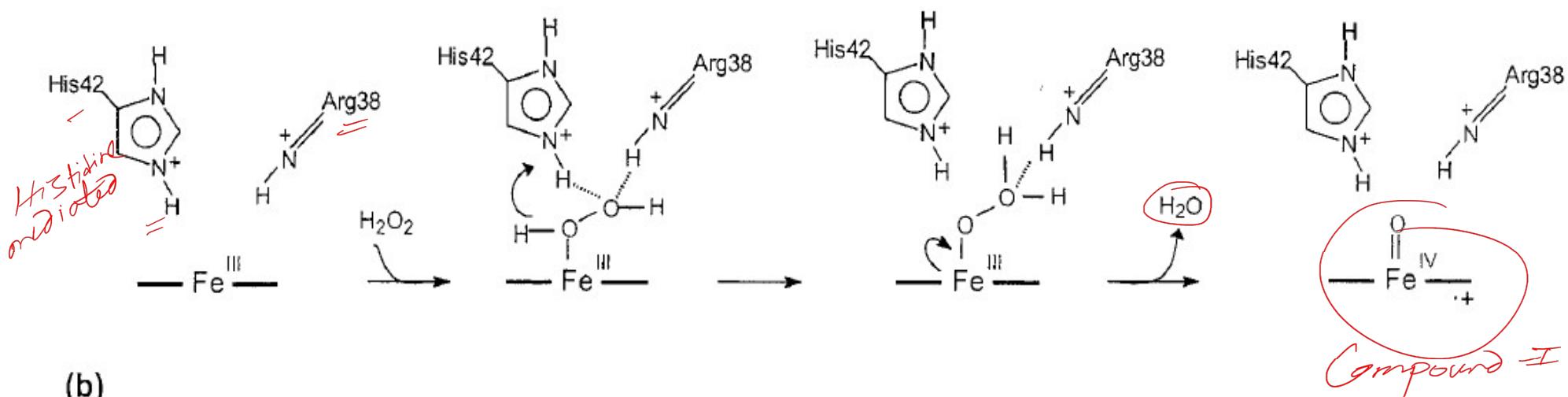
# Horse-Radish peroxidase

*less active than catalyst  
TOF HRP < TOF Catalyst*

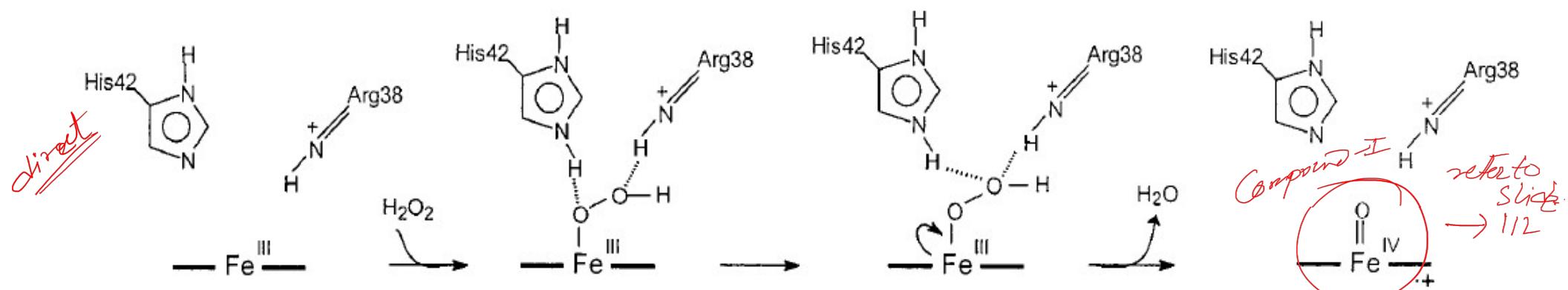


**Scheme 5.** Role of Distal Heme Pocket Residues of HRPC in Compound I Formation<sup>a</sup>

(a)

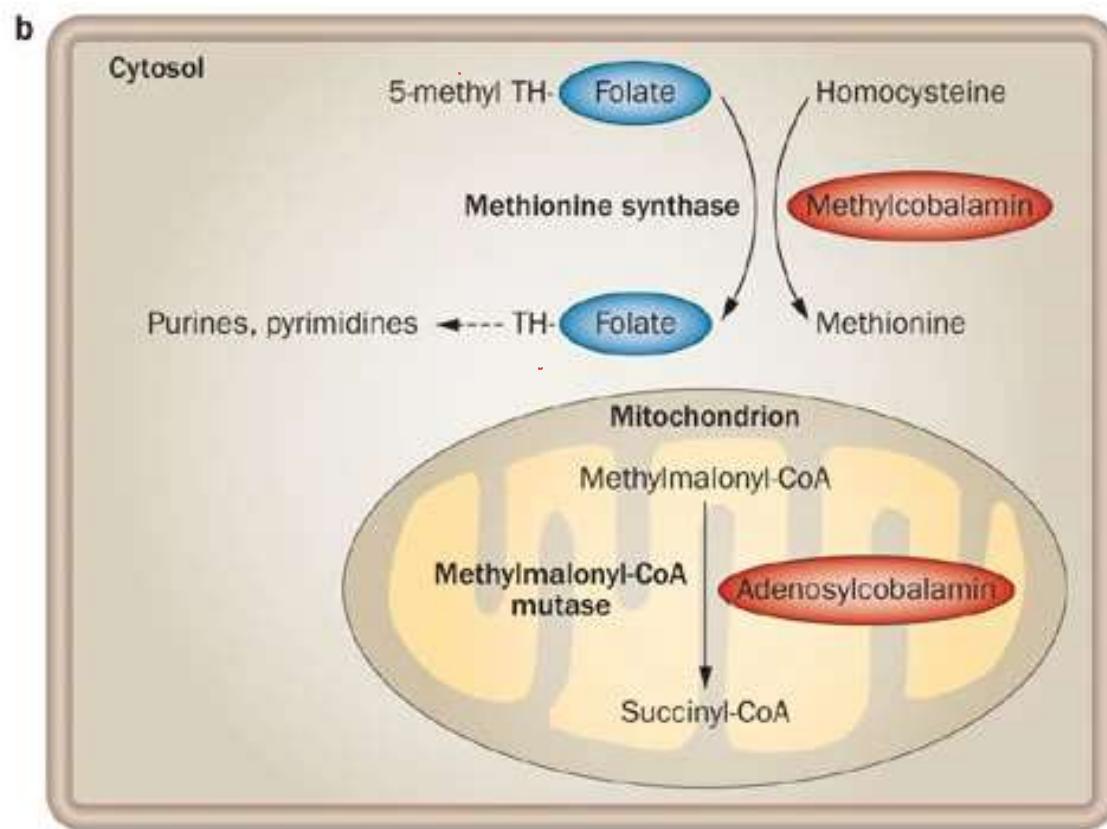
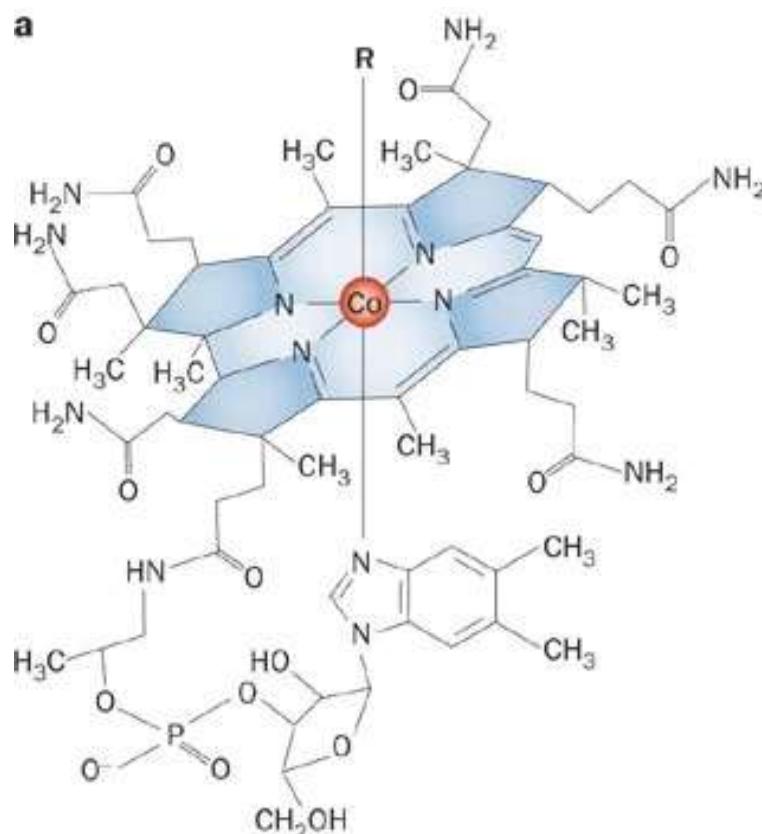


(b)



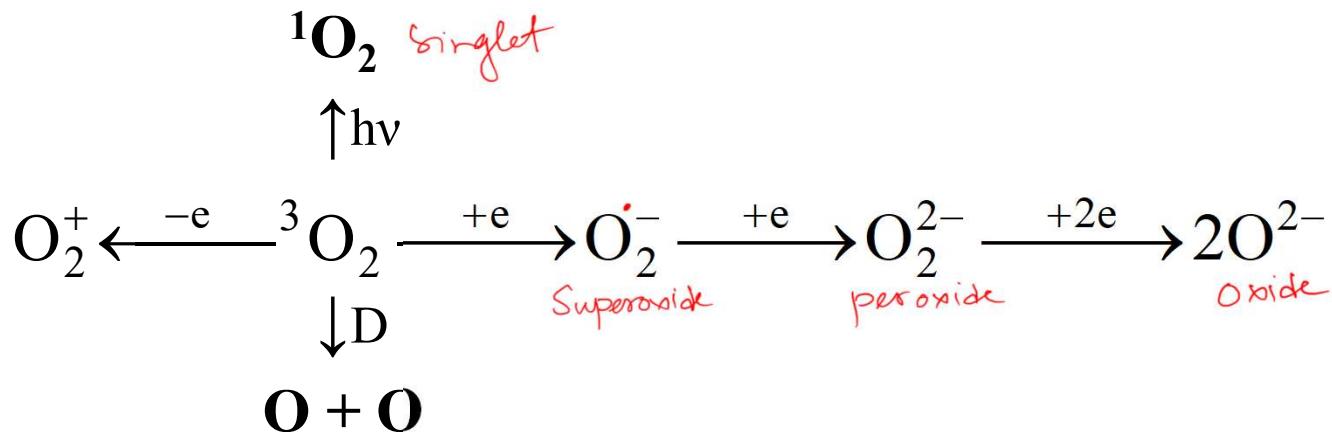
<sup>a</sup> Mechanism of formation of HRPC compound I at (a) acid pH (cationic His42) and (b) neutral or basic pH (neutral His42).

## Vitamin B<sub>12</sub>



**Cyanocobalamin:** This is the most common form of B<sub>12</sub> used in supplements and fortified foods because it is the most stable and cost-effective to produce. The cyanide portion is attached to the central cobalt atom within the molecule. When the body processes cyanocobalamin, it releases the cyanide, which is then detoxified and safely excreted in the urine.

## **Activation and reactions of the oxygen molecule**

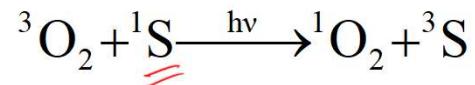


### **1. Generated states:**

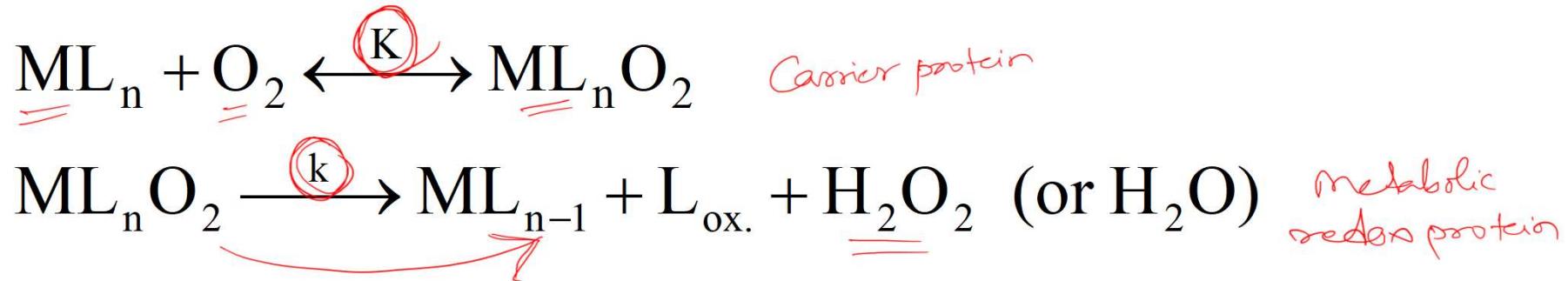
Ground state:  ${}^3\text{O}_2$  (triplet:  $\pi^* \uparrow\uparrow$ )

Generated state:  ${}^1\text{O}_2$  (singlet:  $\pi^* \uparrow\downarrow$ )

*The generated state is usually formed through a „mediator molecule” (photosensibilisator, S):*



## ***Interactions of the Oxygen molecule with metal complexes***



### Two extreme possibilities:

1. “K” is high and “k” is low: oxygen carrier complexes

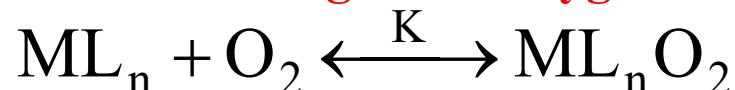
(e.g. hemoglobin, myoglobin, hemocyanin, etc.)

2. “K” is low, but “k” is high: redox catalysis

(e.g. oxygenases, oxidases, etc.)

## **Reactions of the oxygen molecule in biology I.**

### **1. Reversible binding of the oxygen molecule:**

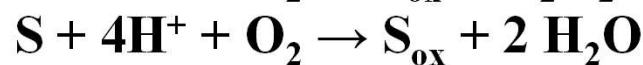
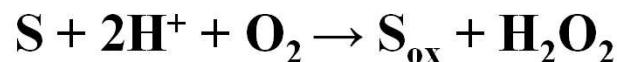


#### **Binding of oxygen in different forms:**

- ✓ -  $M^{n+} + O_2 \leftrightarrow M^{n+}O_2$  → (molecular form)
- ✓ -  $M^{n+} + O_2 \leftrightarrow M^{n+1}(O_2^-)$  → (superoxide radical)
- ✓ -  $M^{n+} + O_2 \leftrightarrow M^{n+2}(O_2^{2-})$  → (peroxide, monomer)
- ✓ -  $M^{n+} + O_2 \leftrightarrow (M^{n+1})_2(O_2^{2-})$  (peroxide, dimer)

### **2. Oxidases (dehydrogenases)**

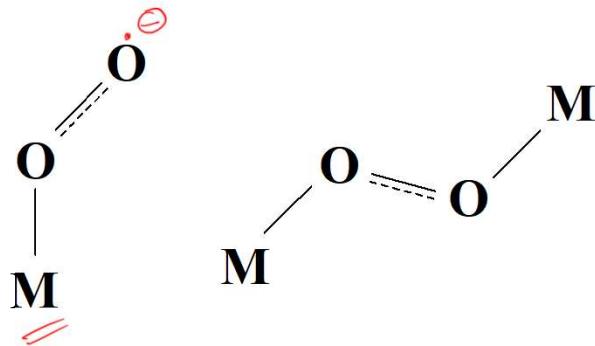
*(Oxygen is reduced to peroxide or to water, it does not built in the substrate)*



*(e.g. cytochrome c oxidase, blue copper oxidases, etc.)*

## The possible binding modes of $O_2$

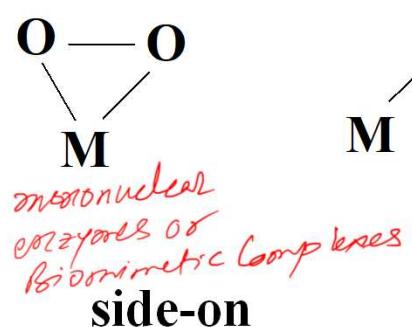
as superoxo ligand



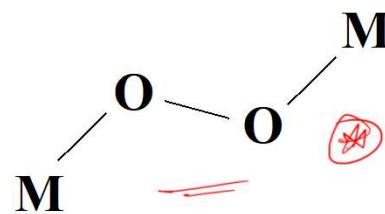
Bended (end-on)

*(class test on 11 Nov 25  
5-6pm during class time  
6-7pm (ideal answers discussion))*

as peroxy ligand

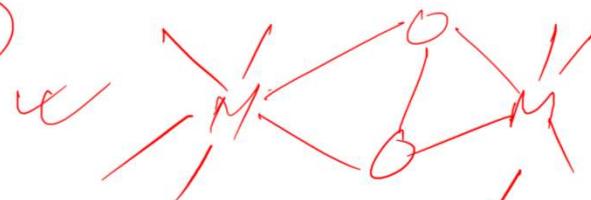


side-on



bridging

*(\*) Two mononuclear complexes come together  
(\*) or a dinuclear complex favoring such oxygen bonding*



*upto this slide in class test-II  
no questions from class test-I syllabus*