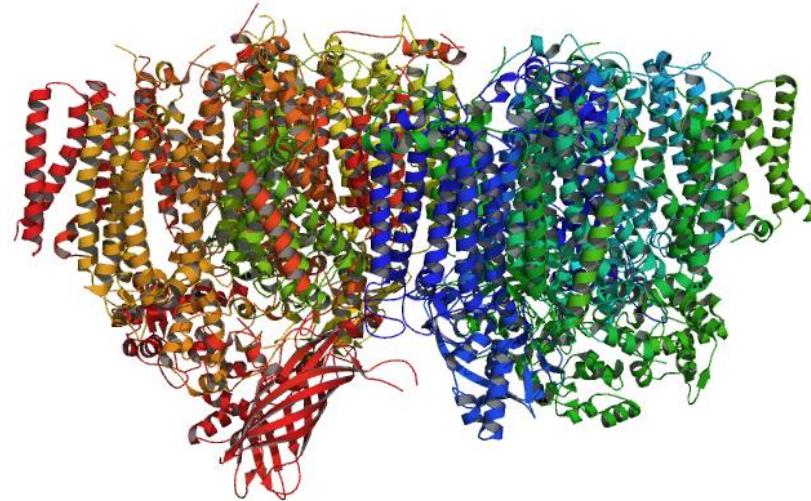
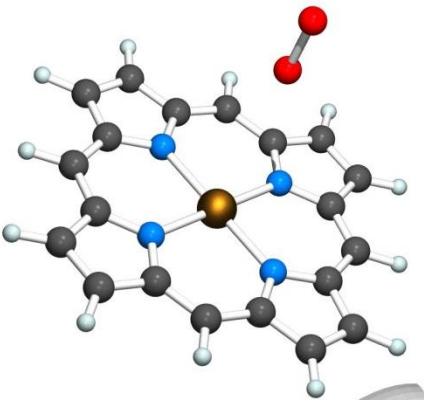
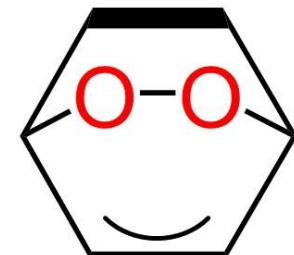


# Bioinorganic Chemistry (BIC)

## IV. Electron Transfer, Respiration, & Photosynthesis



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# Review on Part III

**Hydrolase:** enzymes catalyze **hydrolysis** of a chemical bond.

## General roles of the metal(s):

1. **Structural** role: **bring** the **substrate** into the active site & **orient** the substrate properly for the reactions.
2. **Catalytic** roles: as a **Lewis acid** to **activate** a metal-bound **nucleophile** (forming reactive M-OH), **stabilize** the negative charge in transition states & leaving group.
3. **Non-redox Zn<sup>2+</sup> & Mg<sup>2+</sup>** are commonly used. The **two metal ions** are often required for the reactions.

**Catalytic nucleic acids:** a new class of enzymes.

# Electron Transfer (ET)

The simplest form of redox reactions: **common & important** in *bioinorganic* chemistry (e.g. respiration & photosynthesis).



(D: e-donor & A: e-acceptor)

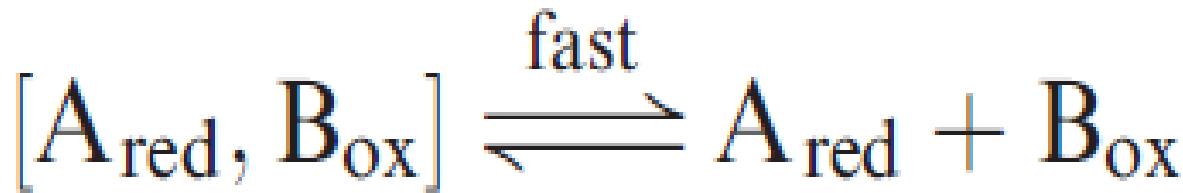
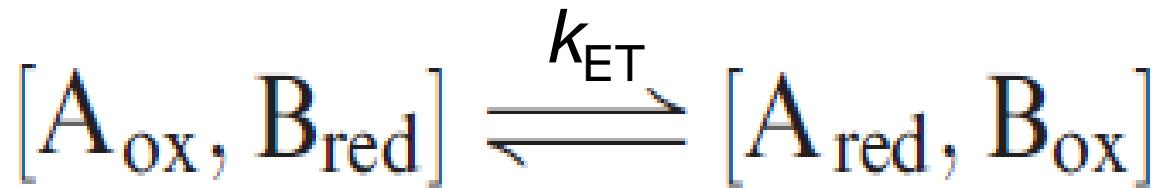
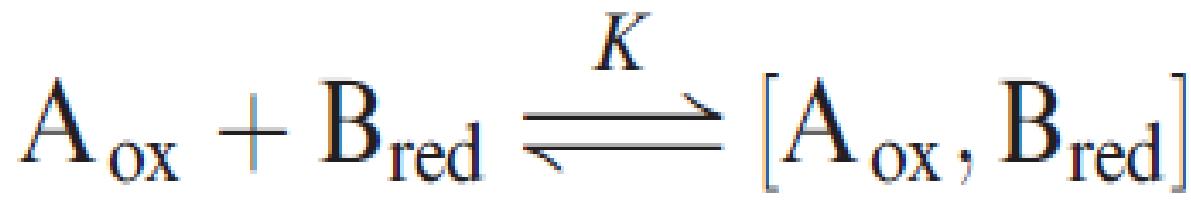
Reductant vs. Oxidant  
(or Lewis Base vs. Lewis Acid)

A bimolecular ET reaction involves:

**(1) Formation** of a **precursor complex**,

**(2) ET** from donor to acceptor, &

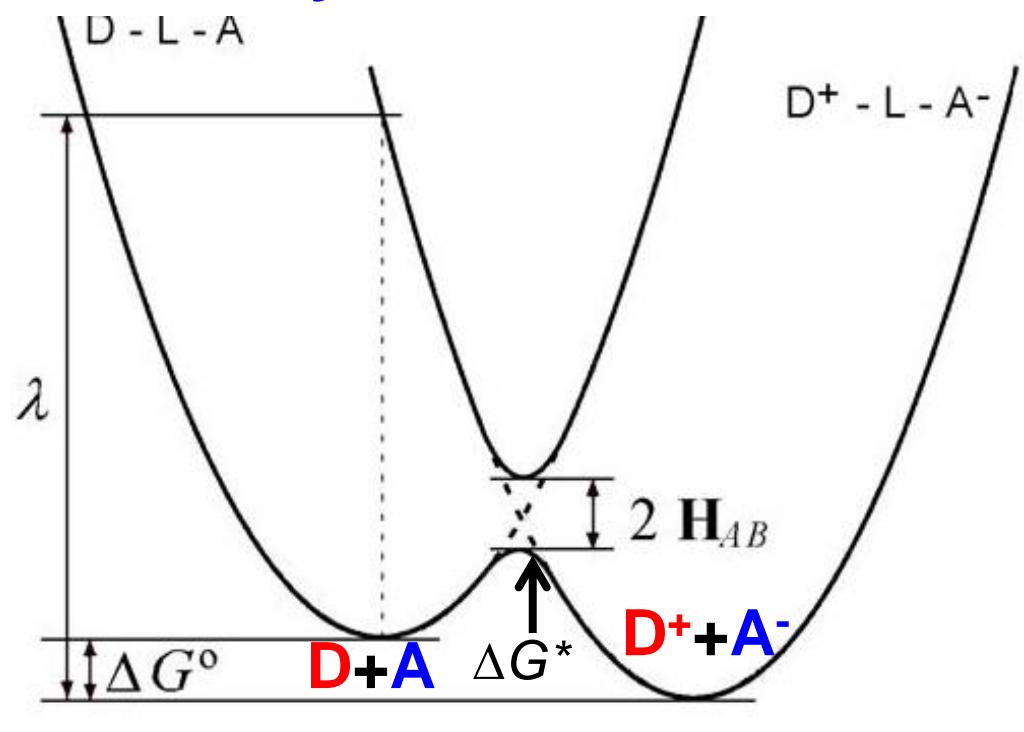
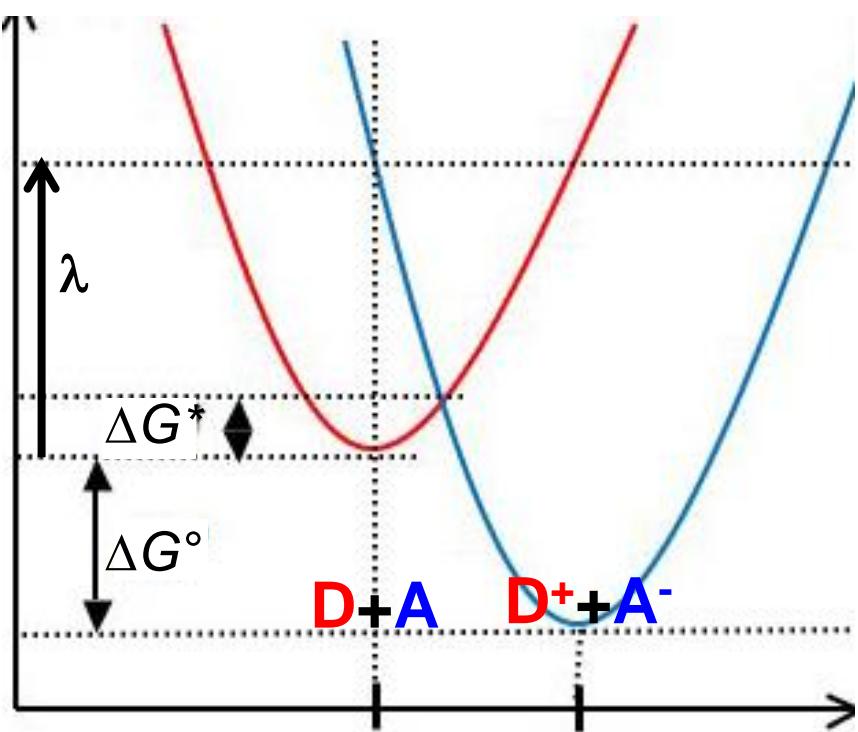
**(3) Dissociation** of the successor complex to products.



$K$ : equilibrium constant

$k_{\text{ET}}$ : ET rate constant

# Marcus Theory

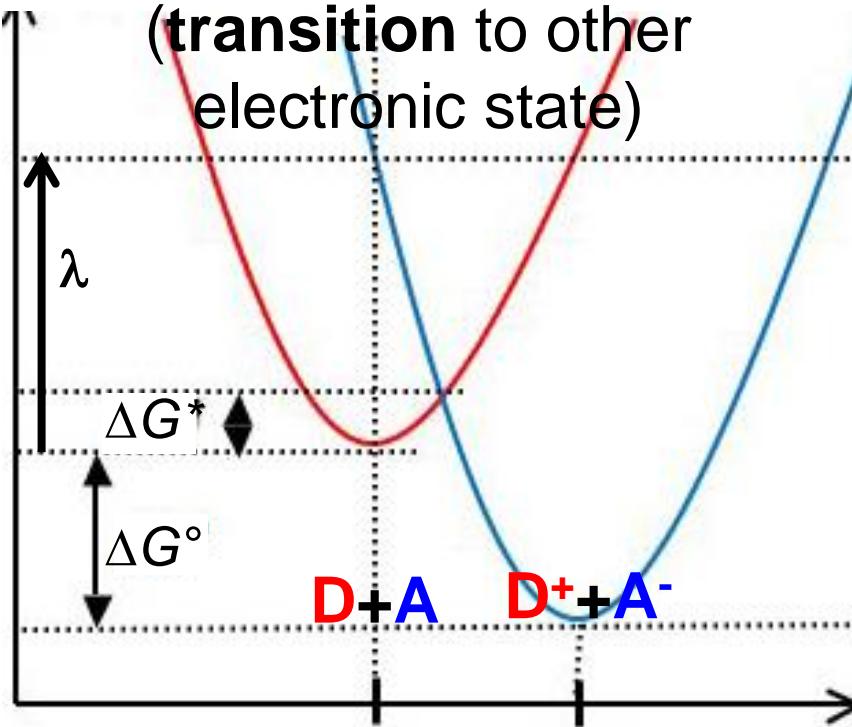


The ET transition state: the intersection of reactant & product surfaces (approximated by parabolas).

The **splitting at the intersection** is equal to  $2H_{AB}$ , ( $H_{AB}$ : *electronic coupling matrix element*).

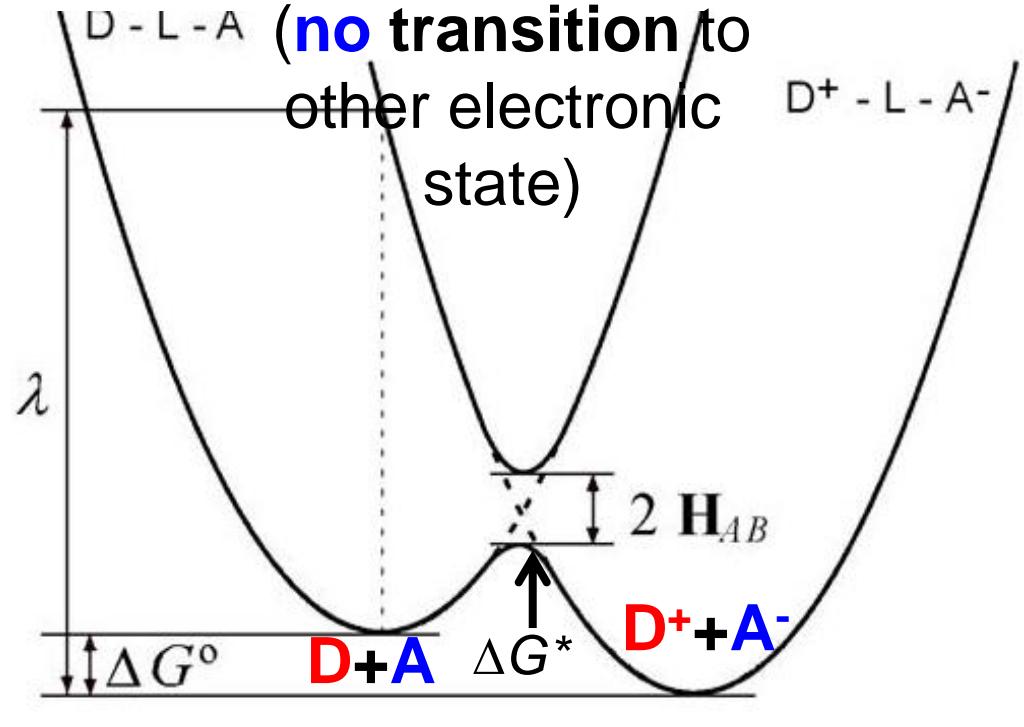
## Non-adiabatic

(transition to other electronic state)



## Adiabatic

(no transition to other electronic state)



- If  $H_{AB}$  is **very small**, the **reactants** ‘jump/hop’ to the **product** potential energy surface with some probability: **non-adiabatic** process.
- If  $H_{AB}$  is **very large**, the **reactants** always cross to the **product** potential energy surface through the transition state region: **adiabatic** process.

On the basis of transition state theory, the rate constant for a bimolecular reaction in solution ( $k$ ):

$$k = \kappa v_N \exp\left(-\frac{\Delta G^*}{RT}\right)$$

- In an adiabatic process, transmission coefficient  $\kappa = \sim 1$ .

$v_N$ : collision frequency, or (if barrierless process) diffusion-limited rate

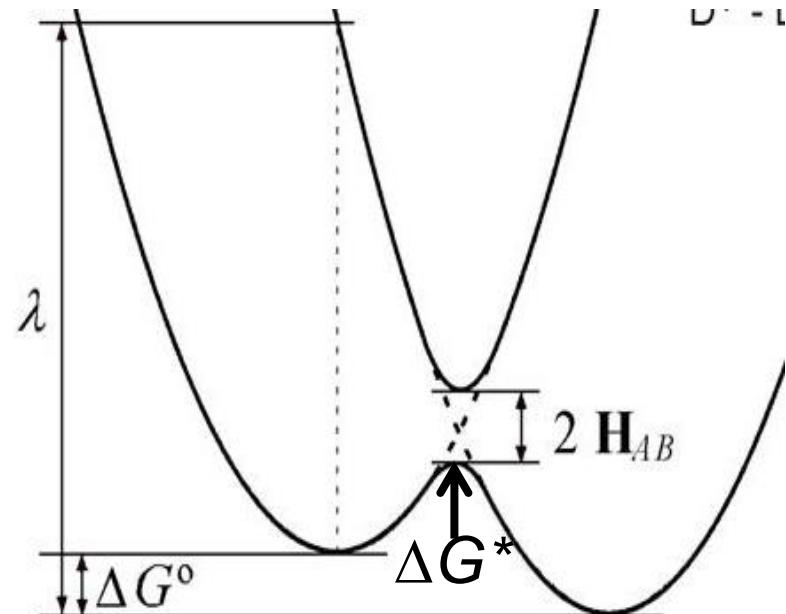
$\Delta G^*$ : Gibbs free energy of the barrier

$\kappa$ : transmission coefficient

- **Marcus** partitioned  $\Delta G^*$ :

$$\Delta G^* = w^r + \frac{(\lambda + \Delta G^{\circ'})^2}{4\lambda}$$

$$\Delta G^{\circ'} = \Delta G^\circ + w^p - w^r$$



**Barrier: a quadratic dependence on  $\Delta G^\circ$  &  $\lambda$**

$\Delta G^\circ$ : Gibbs free energy change of the reaction when the reactants & products are separated by an infinite distance;

$\Delta G^{\circ'}$ : Energy change when they are separated by distance  $r$ ;

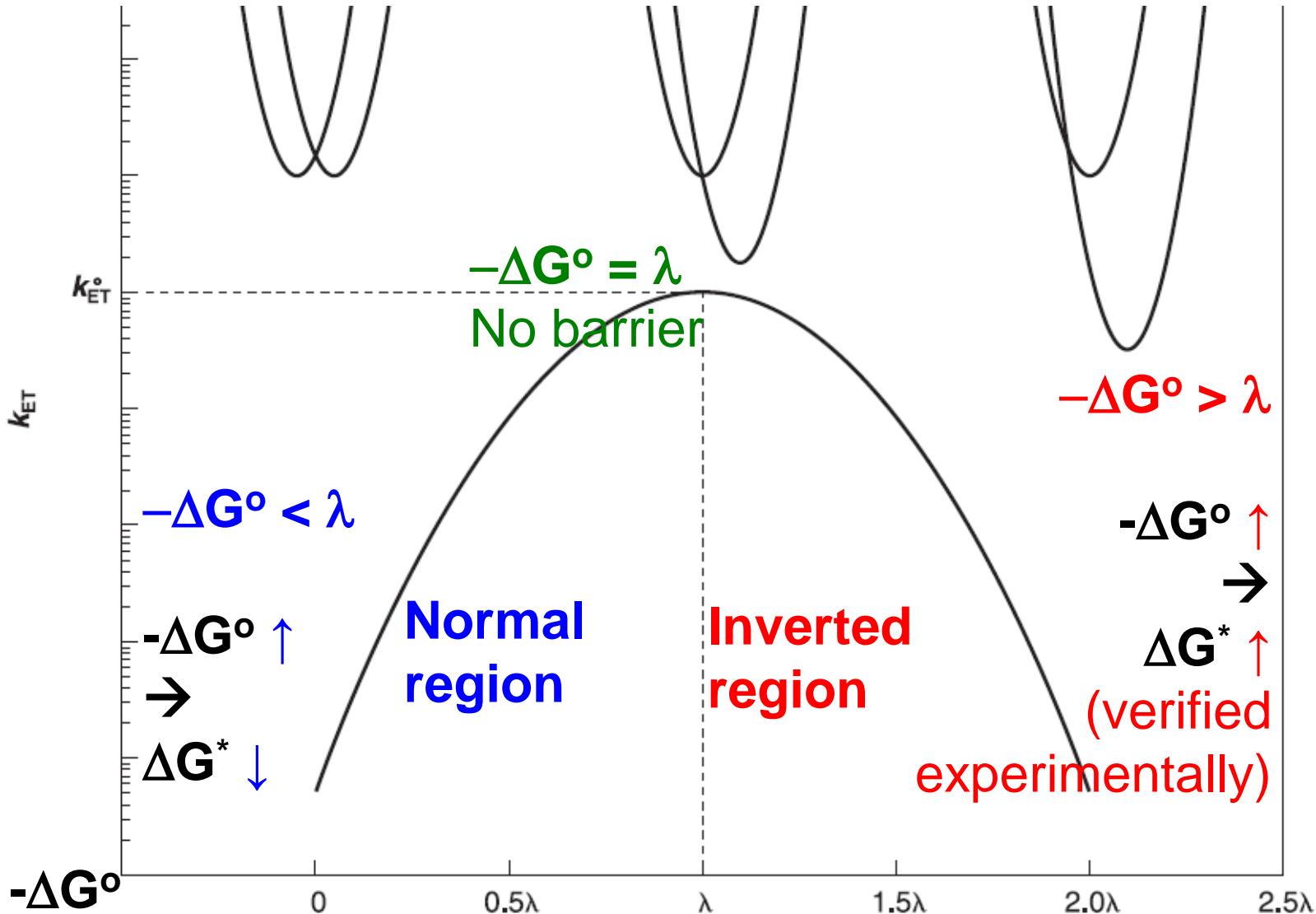
$\lambda$ : Reorganization energy (energy change of geometry & solvation);

$w^r$ : Electrostatic work to bring the reactants together;

$w^p$ : Work for dissociation of the products;

# Marcus theory predicts rate constant for ET:

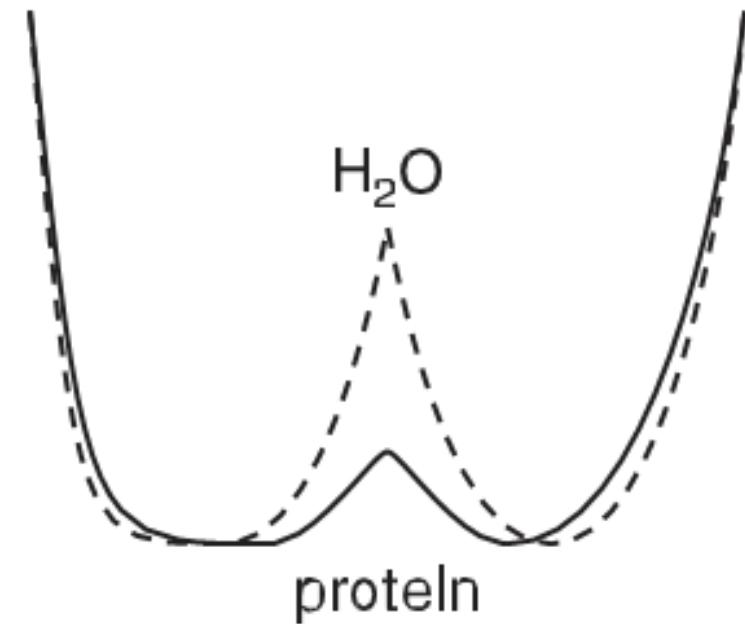
$$k_{\text{ET}} = v_n \kappa \exp \left( -\frac{(\lambda + \Delta G^\circ)^2}{4\lambda R T} \right)$$



- When D & A are separated by a **long distance** (as in proteins), the electronic coupling is very small such that  $k_{\text{ET}}$  can be described by a semi-classical theory:

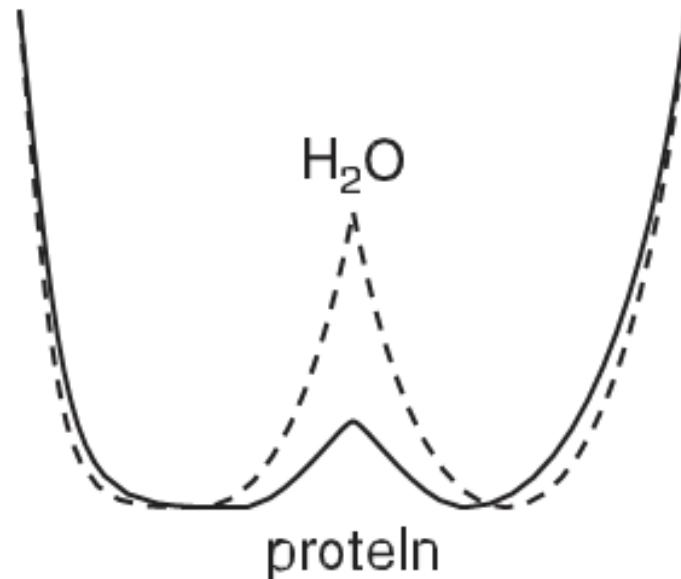
$$k_{\text{ET}} = \sqrt{\frac{4\pi^3}{h^2 \lambda k_B T}} H_{\text{AB}}^2 \exp\left\{-\frac{(\Delta G^\circ + \lambda)^2}{4\lambda k_B T}\right\}$$

$H_{\text{AB}}$ : *electronic coupling matrix element*

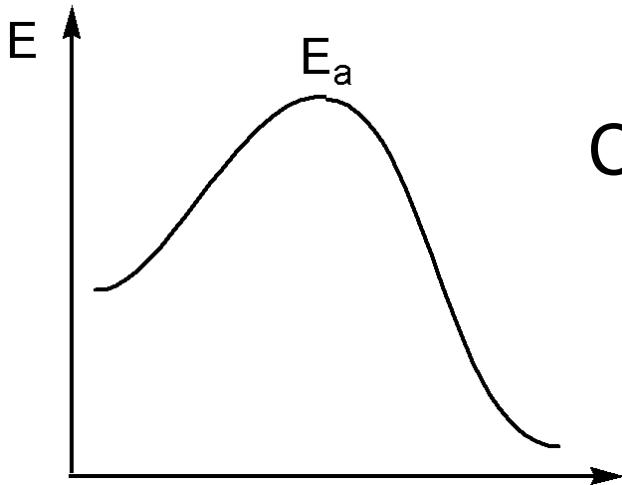


# Medium between redox centers: key for long-range ET

- Time for electron exchange between hydrated Fe(II) & Fe(III) ions is **~ $10^{17}$  years**, if these complexes are separated by 20 Å in a **vacuum**.
- Hydrated Fe(II) & Fe(III) ions **with water**: time for electron exchange decreases **~ $5 \times 10^4$  years**.
- With **electron tunneling** across **hydrocarbon bridges of a polypeptide**, time for electron exchange in the hydrophobic core of a protein could be  **$\mu\text{s-ms}$** . The redox-active metals often in **hydrophobic cavities (medium)**.

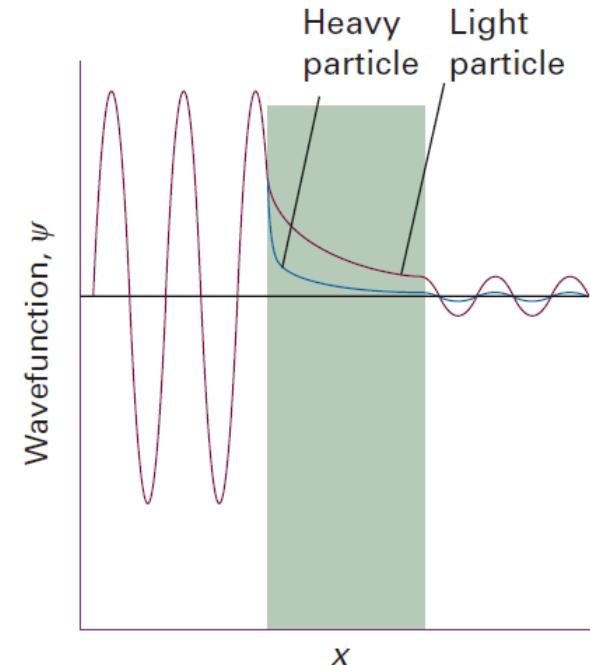


# Quantum-Mechanics Tunneling (QMT)

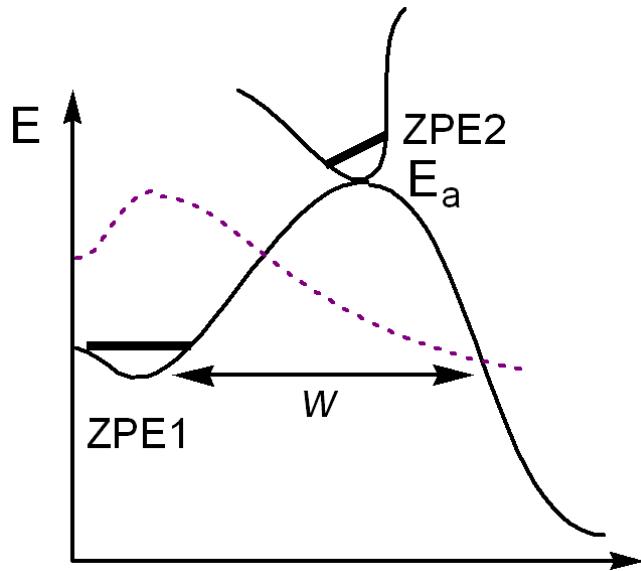


Classic Mechanics

1.  $P = 0$  ( $E < E_a$ )
2.  $P = 1$  ( $E \geq E_a$ )



Quantum Mechanics



Tunneling:

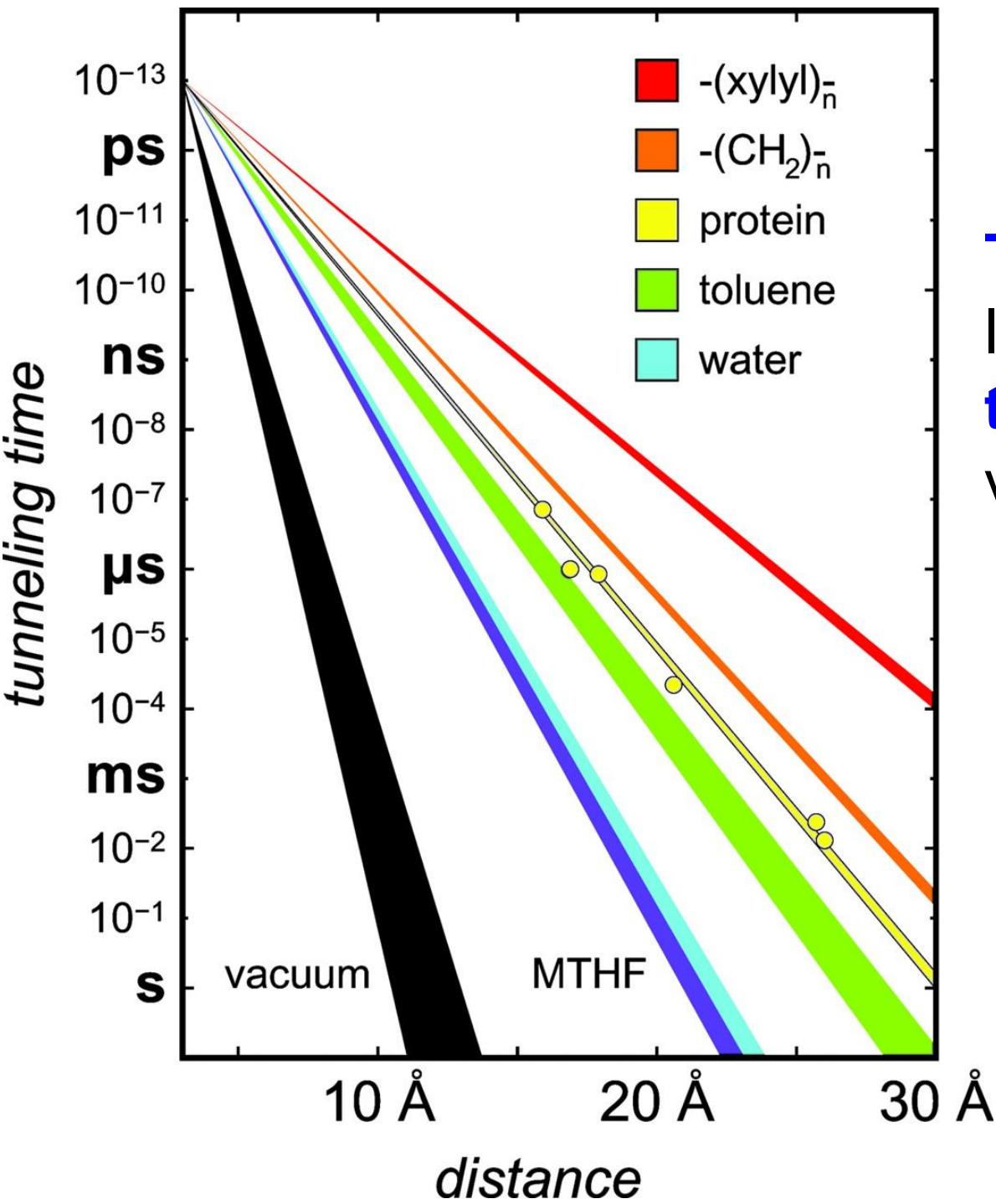
1.  $P \geq 0$  ( $E < (E_a + ZPE_2 - ZPE_1)$ )

Quantum Reflection:

2.  $P \leq 1$  ( $E \geq (E_a + ZPE_2 - ZPE_1)$ )

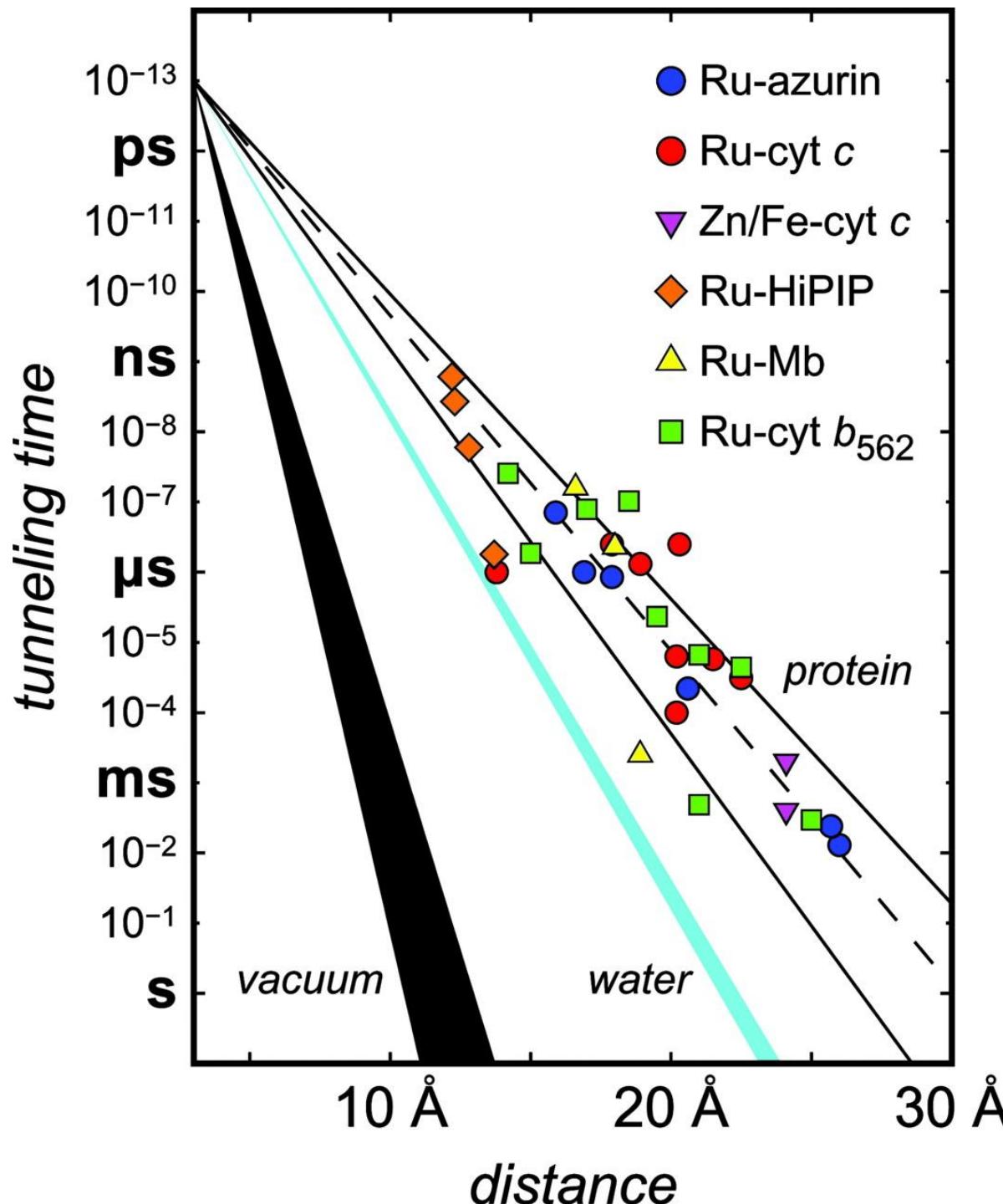
$$P_{QMT} \sim \exp[-w\pi^2(2mE)^{0.5}/h]$$

- $P \uparrow$ : 1.  $\downarrow$  mass ( $m^{1/2}$ ), e.g.  $e^-$ ,  $H$ ;  
2.  $\downarrow$  barrier width ( $x$ )



**Time** for activation-less electron tunneling through various media

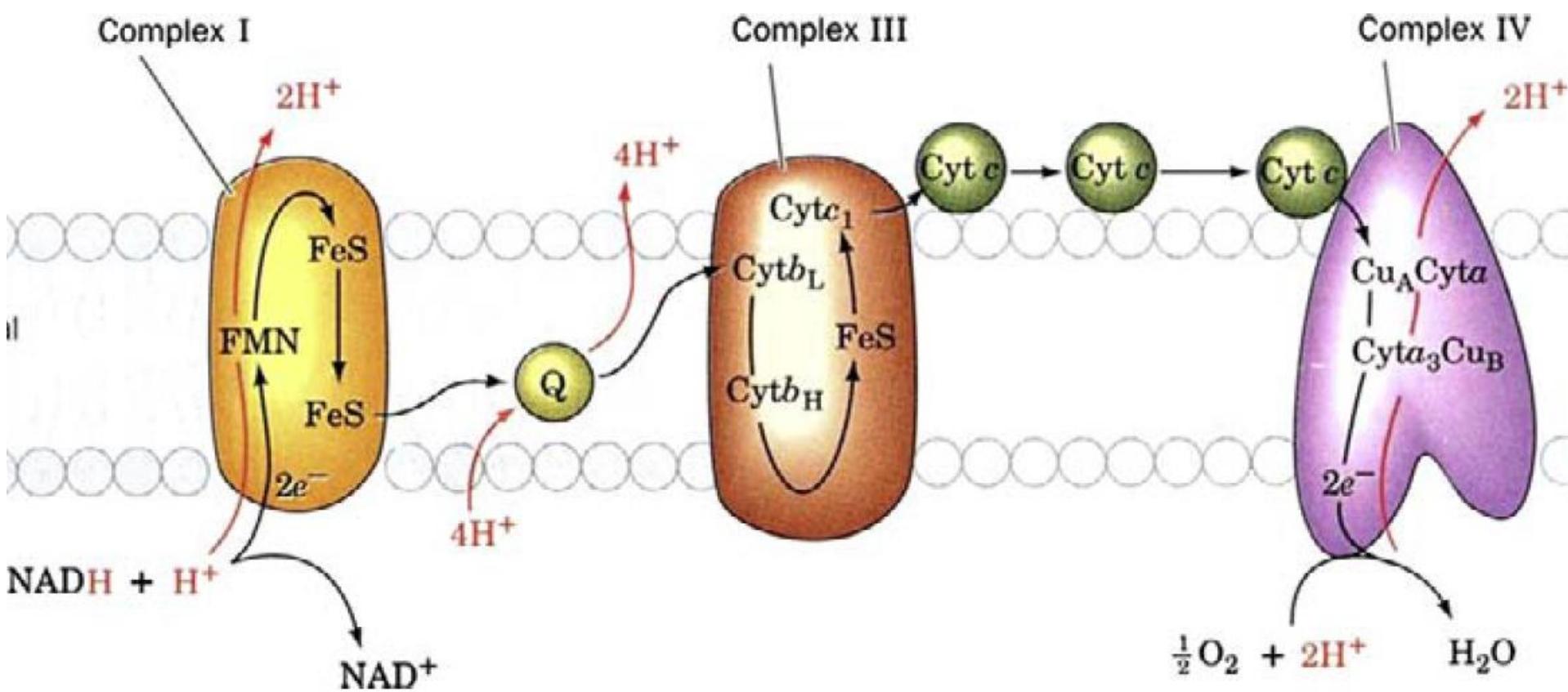
Tunneling time  
for intraprotein  
ET in  
Ru-modified azurin,  
cyt c, myoglobin,  
cyt  $b_{562}$ , HiPIP, &  
for interprotein  
ET Fe:Zn-cyt c  
crystals.



# ET in Biology

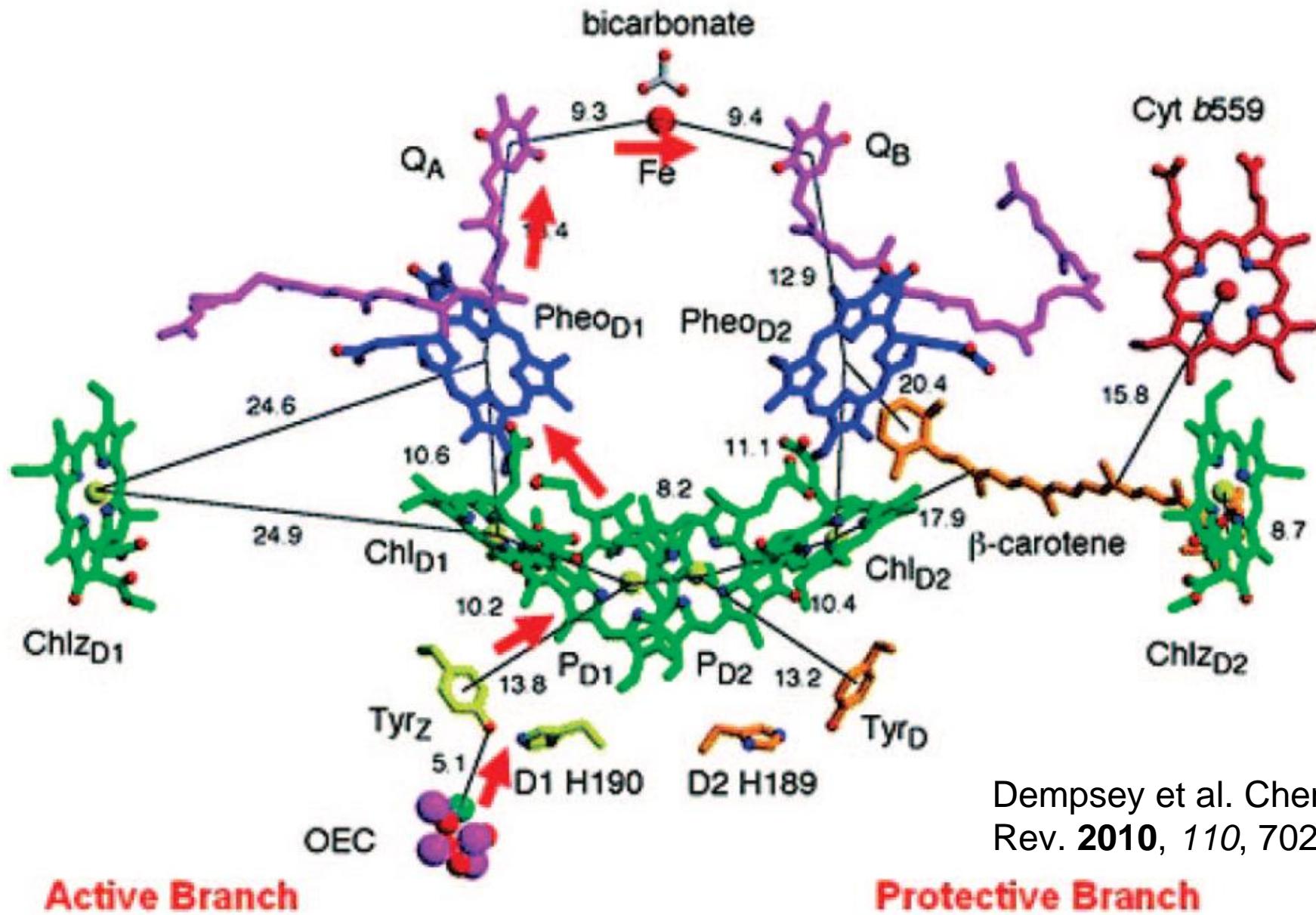
Electron transfer/flow between donors and acceptors in biological systems are usually **separated by large distances**. So, distant ETs are fundamental steps (e.g. in respiration & photosynthesis).

## ET in respiration



# ET in photosynthesis

## Electron transport cofactors



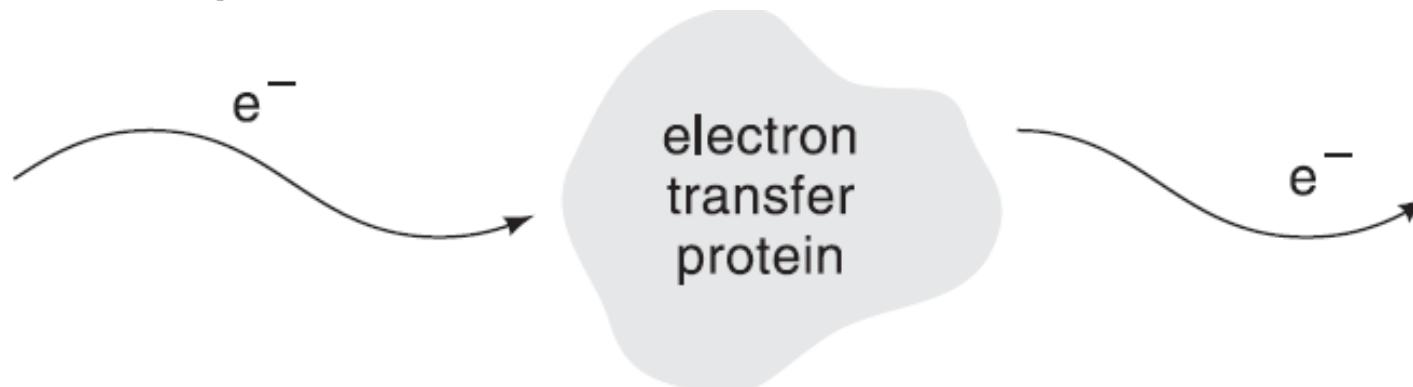
Dempsey et al. Chem.  
Rev. **2010**, *110*, 7024.

Active Branch

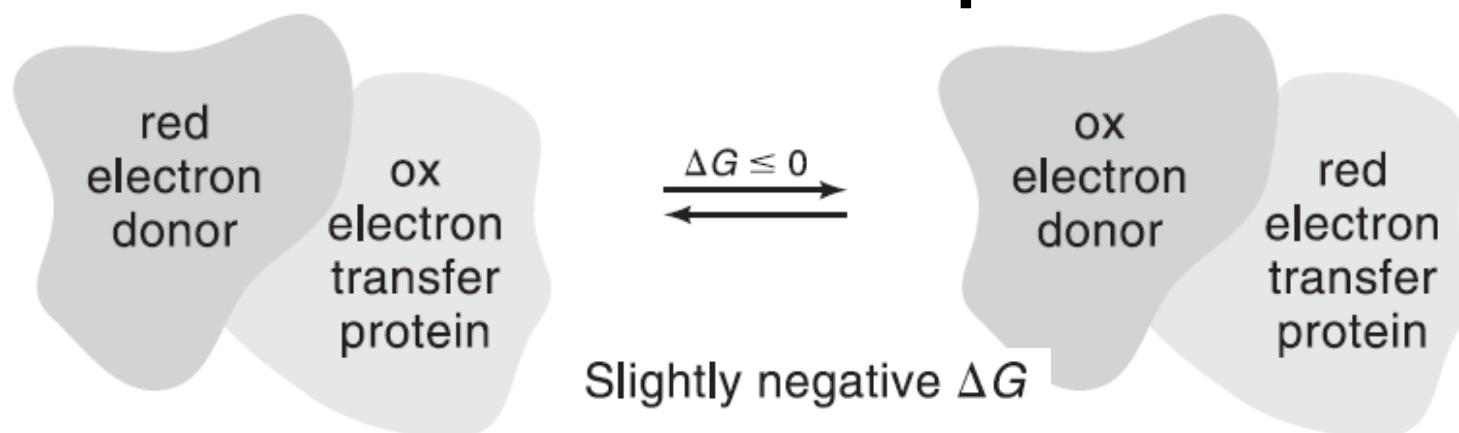
Protective Branch

**Efficient ET in biology** has several requirements:

1. **One electron transfer at a time.** So, the ET protein must be capable of one-electron oxidation-reduction.

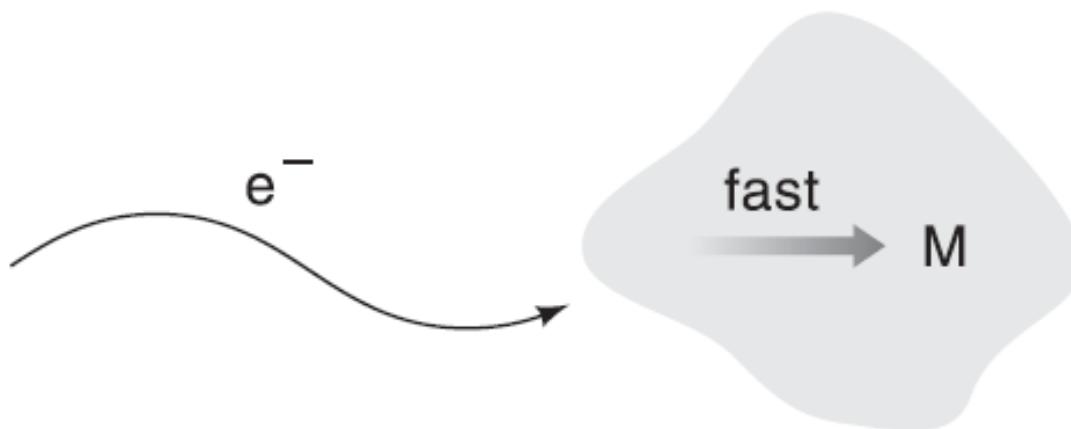


2.  **$\Delta G$  is negative/exergonic** (not too negative). Also, **reduction potential of “electron-relays”** is **fine-tuned** to be in **between the donor & acceptor** in an ET chain.



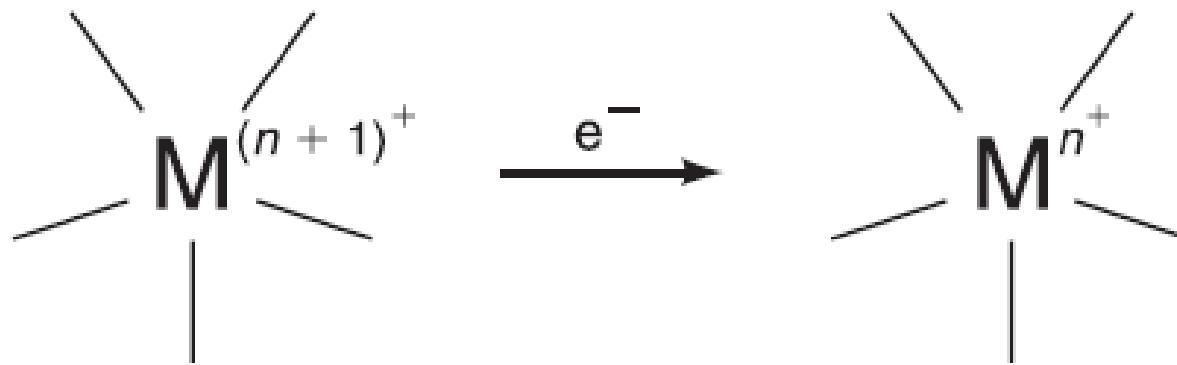
- Reduction potential can be regulated over a wide range by their coordination chemistry and by the electrostatics of environment with the metal ion.

3. ET pathways connecting the D-A interaction site(s) with the redox site are often shortened by using either a large metal-ligated “conducting” cofactor (e.g. heme) or a “conducting” metal cluster.



Fast intramolecular electron transfer

4. The **reorganization energy  $\lambda$**  (on passing from one redox state to another state) should be **small**: minimizing the geometric changes of the metal in redox step. This may be accomplished by special coordination geometries.



$$k_{\text{ET}} = v_n \kappa \exp\left(-\frac{(\lambda + \Delta G^\circ)^2}{4\lambda R T}\right)$$

# Reduction Potential ( $E$ )



$$E_0(\text{volts}) = -\frac{\Delta G^\ominus}{nF}$$

$E^\circ$ : standard reduction potential (in V or mV)

$\Delta G^\circ$ : standard Gibbs free energy change of the reaction

n: number of the electron(s) transferred

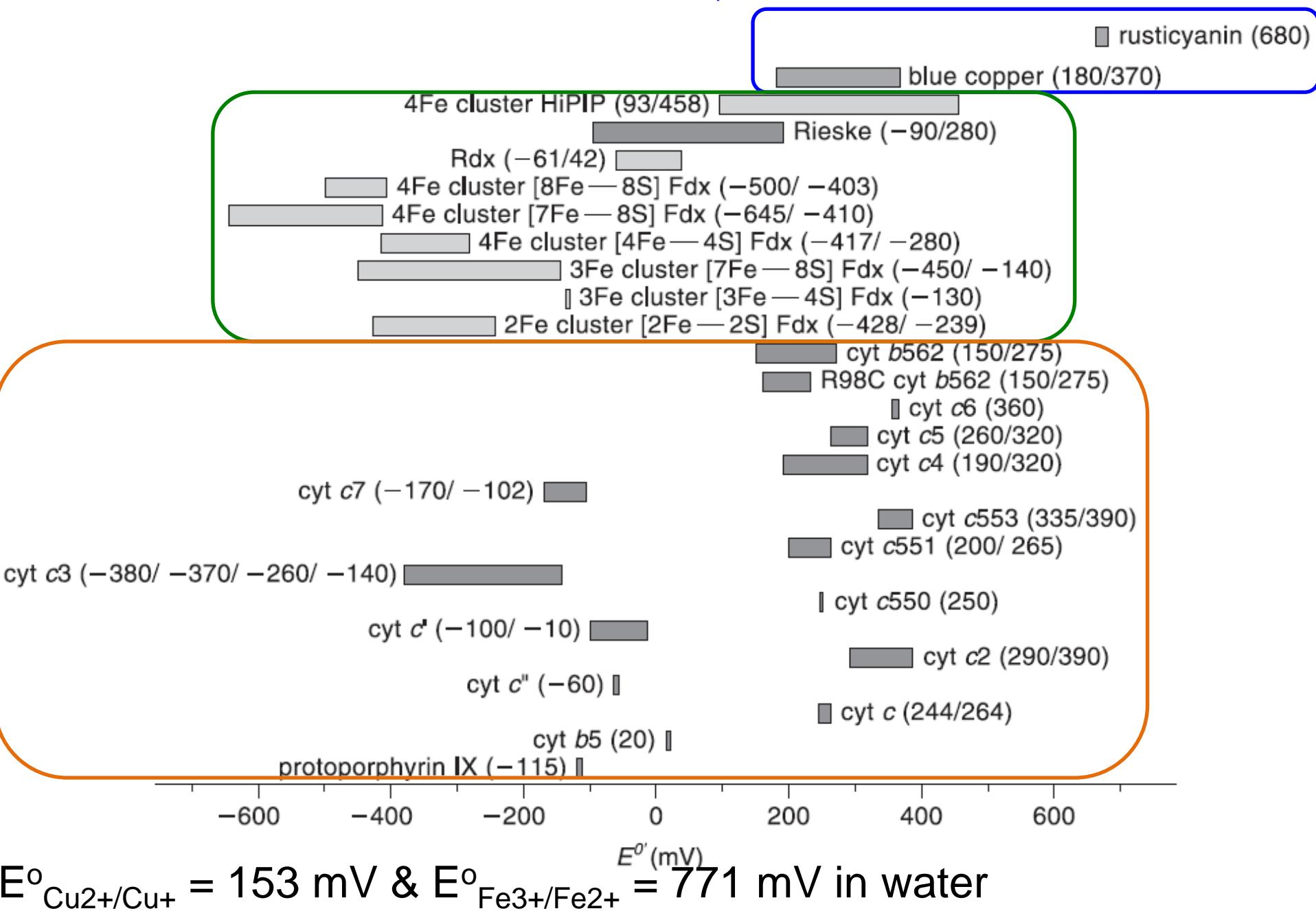
F: the Faraday constant

***What factors can affect the reduction potential??***

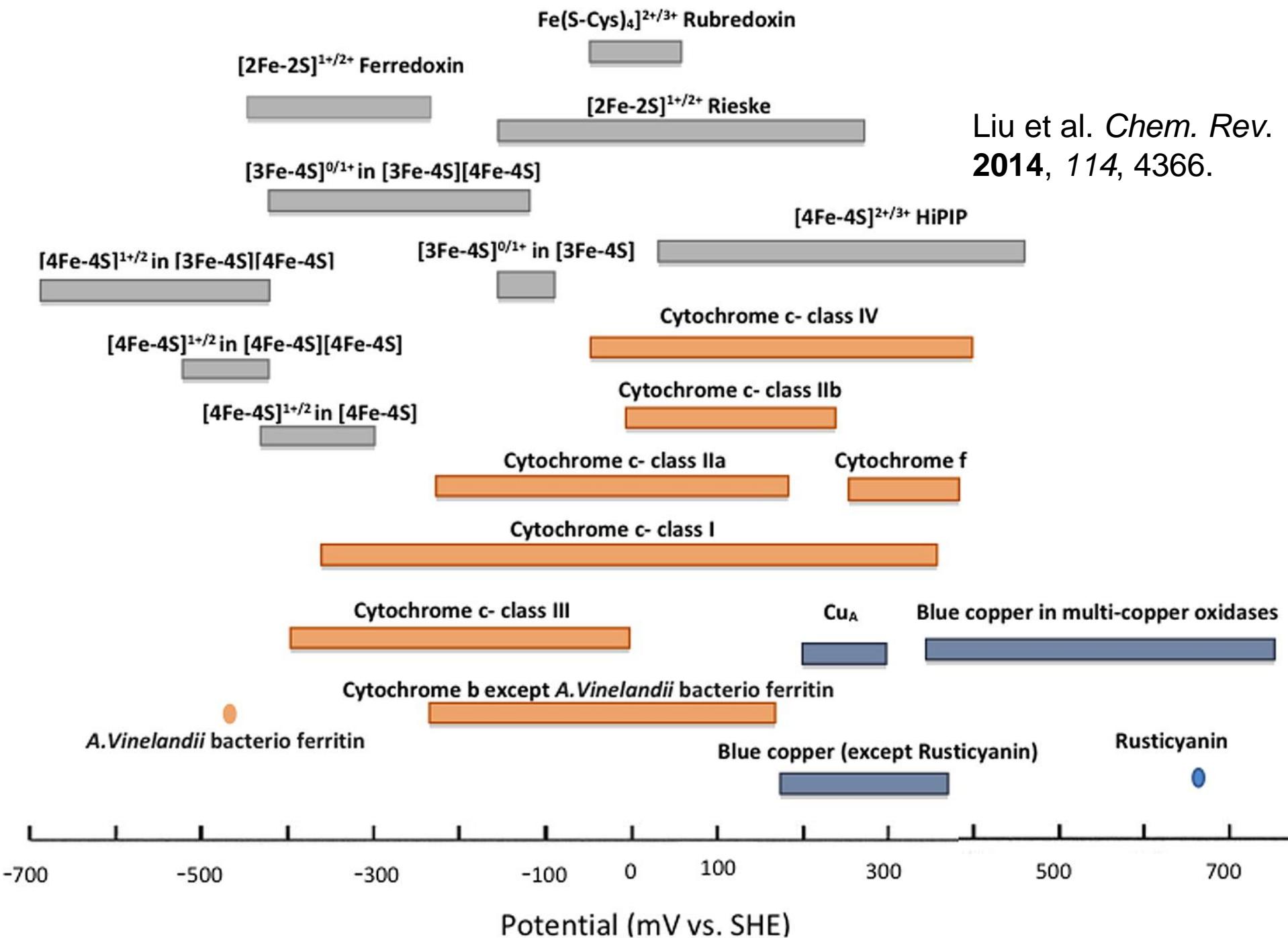
- Nature usually chose **metalloproteins** for ET, as the reduction potentials of metal ions can be more **easily tunable** than organic compounds.
- **Fe & Cu**: the choice of the **metals** for **ET in biology**.
- **Fe-containing ET proteins**: (1) iron-sulfur proteins & (2) heme proteins.
- **Cu-containing ET proteins**: blue copper proteins & its variant, purple copper proteins.
- The **most relevant redox states for ET**:  
**Cu(II)/Cu(I)** & **Fe(III)/Fe(II)** pairs

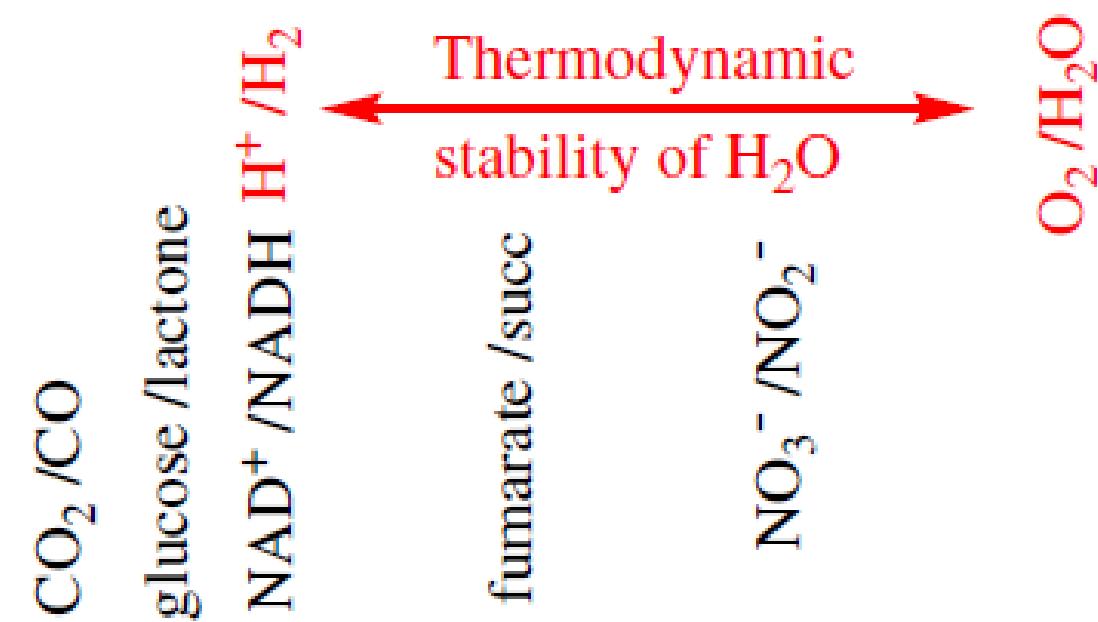
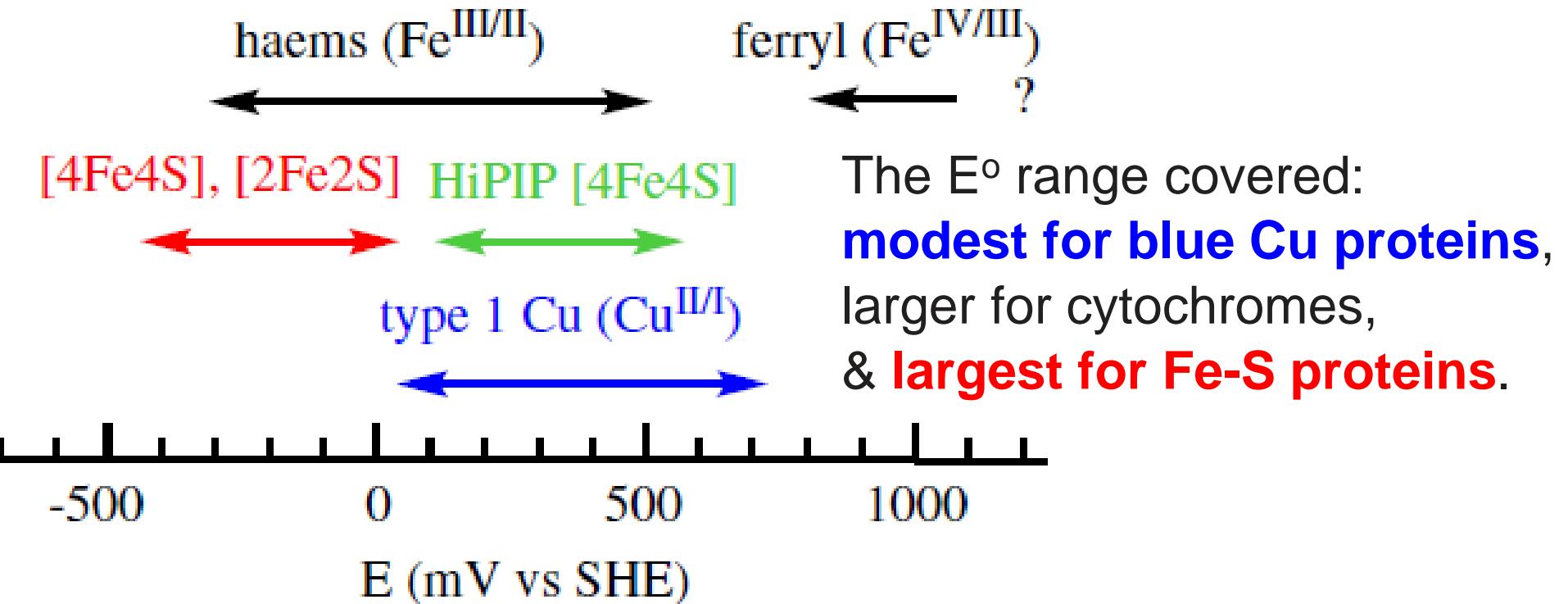
$$E^{\circ}_{\text{Cu}^{2+}/\text{Cu}^{+}} = 153 \text{ mV} \text{ & } E^{\circ}_{\text{Fe}^{3+}/\text{Fe}^{2+}} = 771 \text{ mV} \text{ in water}$$

# Reduction Potentials for Cu, Fe-S & Heme Proteins



Liu et al. *Chem. Rev.*  
2014, 114, 4366.





# **Factors affecting Reduction Potential**

Reduction potential of ET proteins are affected by a combination of the below factors:

- (1) Coordination sphere** (the number and type of ligands).
- (2) Solvent accessibility.**
- (3) More than one metal** clustered together in the same protein.
- (4) (Integer and fractional) Charges of protein residues.**

# 1. Coordination Sphere

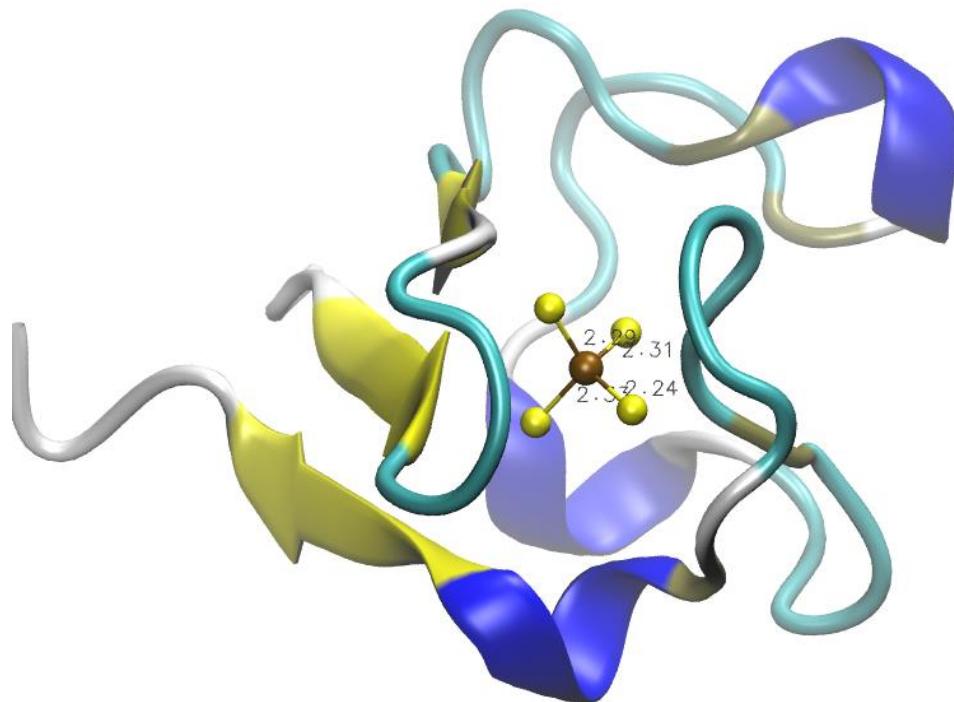
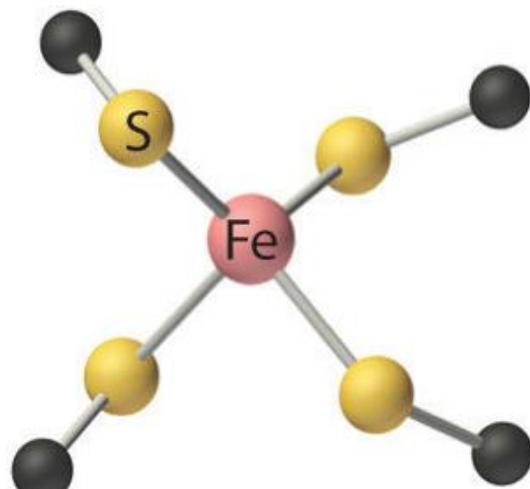
The **most important factor**: **coordination sphere** of the metal:

- **Blue copper proteins**: the **smallest** variability.
- **Cytochromes**: the **nature of the heme (different forms)** can be changed & the ***number and type*** of **axial ligands** are varied.
- **Iron-sulfur proteins** (the **greatest** variability): different **numbers of iron and sulfur ions** & the **various overall charge** of the cluster in different systems.

- The **metal ion**, **ligands** & **geometry** of the coordination polyhedron determine **energy of the d orbitals** that accept/donate an electron (c.f. ligand field theory).

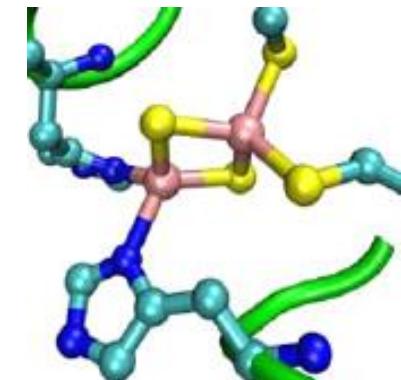
E.g. rubredoxin proteins (Rdx) have the **same overall protein structure** with 1 Fe & 4 Cys, although their sequence similarity may not be high. A narrow reduction potential range of ~100 mV around 0 mV.

Rdx (-61/42)



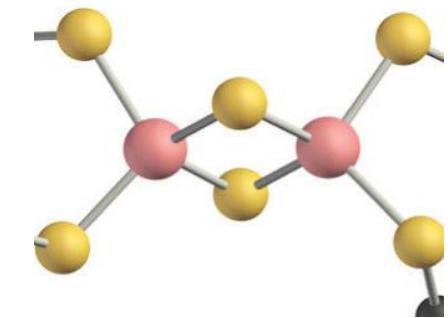
# Effect of Overall Charge of the Metal Center

- **Rieske proteins** (2 Fe with 2 neutral His, with 2 Cys & 2S): a larger reduction potential range & more positive than rubredoxin (Rdx).



diamond structures

- **Ferredoxin** (Fdx, with 2 Fe, 4 Cys & 2 S): a larger reduction potential range, but much more negative potential than Rdx.



Charge (Rieske: 0 → -1; Rdx: -1 → -2;  
Fdx: -2 → -3)



Rdx (-61/42)

2Fe cluster [2Fe—2S] Fdx (-428/-239)

## 2. Solvent Accessibility

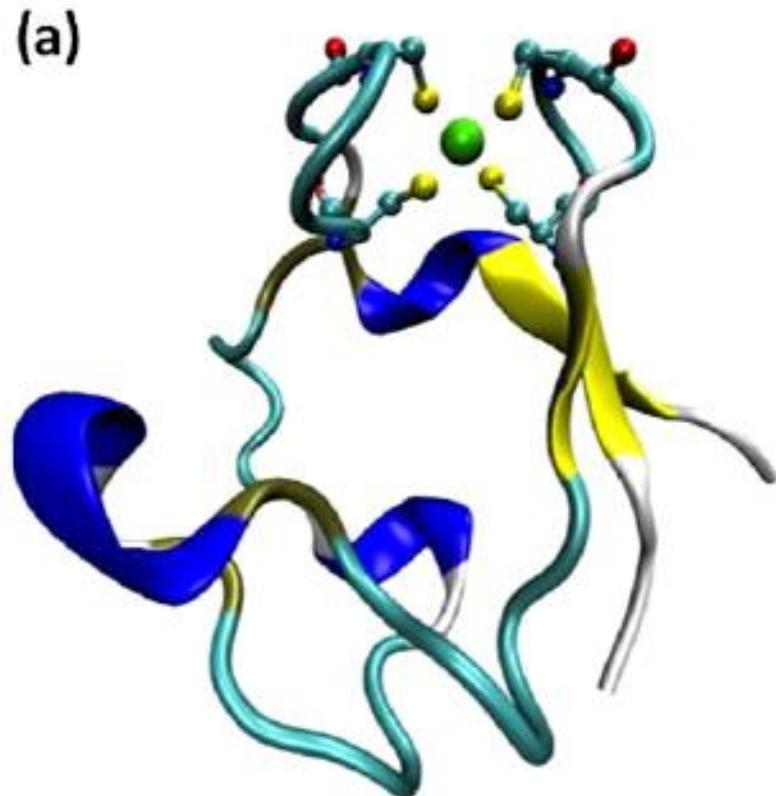
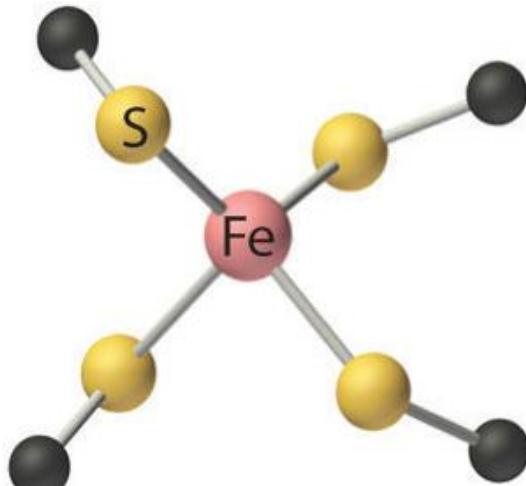
- Reduction is **favored** when addition of the electron reduces or eliminates a positive charge, or **disfavored** when increasing or creating a negative charge.
- An excess of (positive or negative) **charge** can be **stabilized** in a **high dielectric** medium. Dielectric constant of **water**: 80; that of the inner & hydrophobic **protein**: ~2-8.
- An **increase in solvent exposure increases the reduction potential** when the metal center becomes more negatively charged:



E.g. Rdx (with 1 Fe + 4 Cys): the **total charge** of the metal site is **-1** in the **oxidized state**, while it becomes **-2** in the **reduced state**.

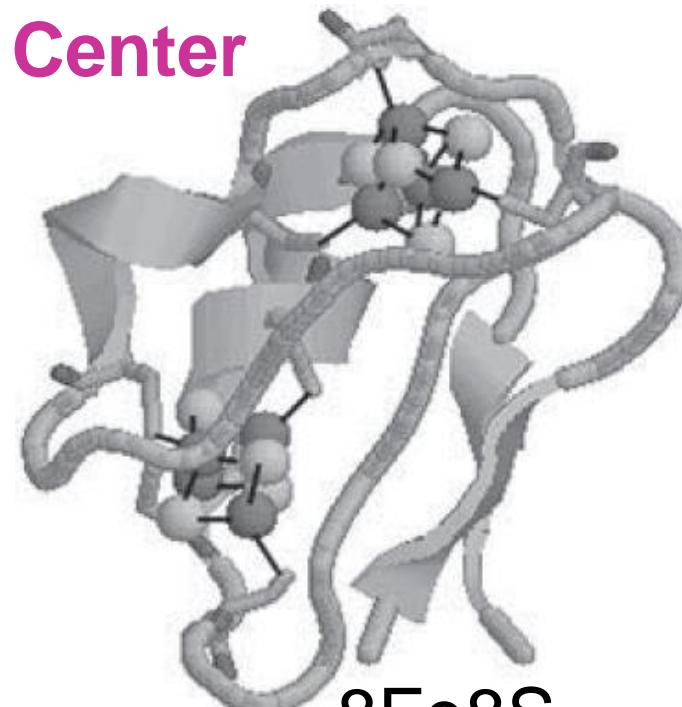
**Reduction is promoted** by a movement of a gate residue which **increases the exposure** of the metal to the **solvent** upon reduction.

Rdx ( $-61/42$ ) 



### 3. Effect of More Than One Redox Center

- Some proteins contain **more than one redox center** which can additionally **modulate** the reduction potential, & allows to **exchange more** than one electron if needed.
- When one of the centers is reduced (with one more negative charge), the reduction **potential of the second center** is **further decreased**. The **electrostatic interaction** in **low-dielectric** proteins is **not negligible**.

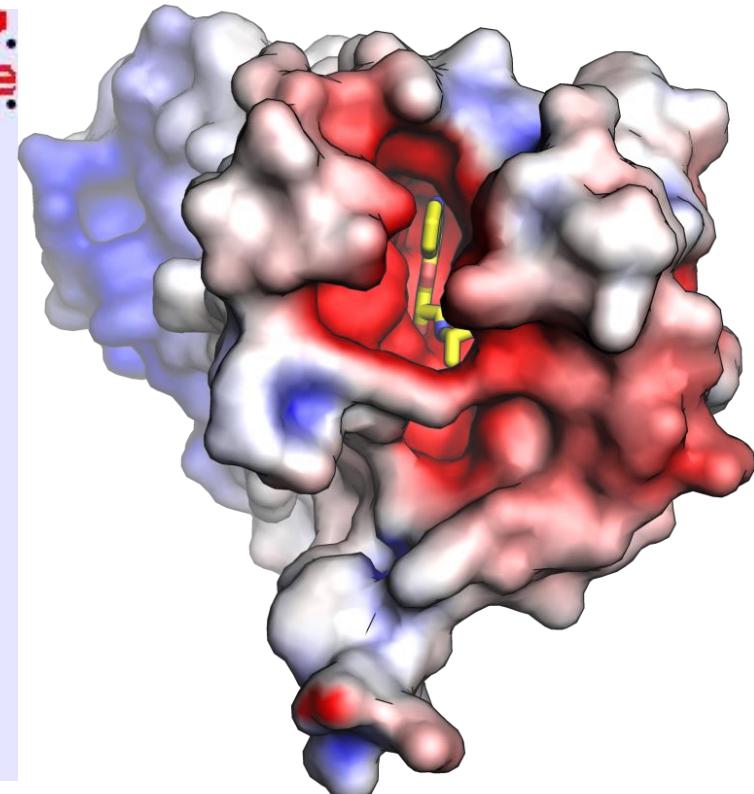
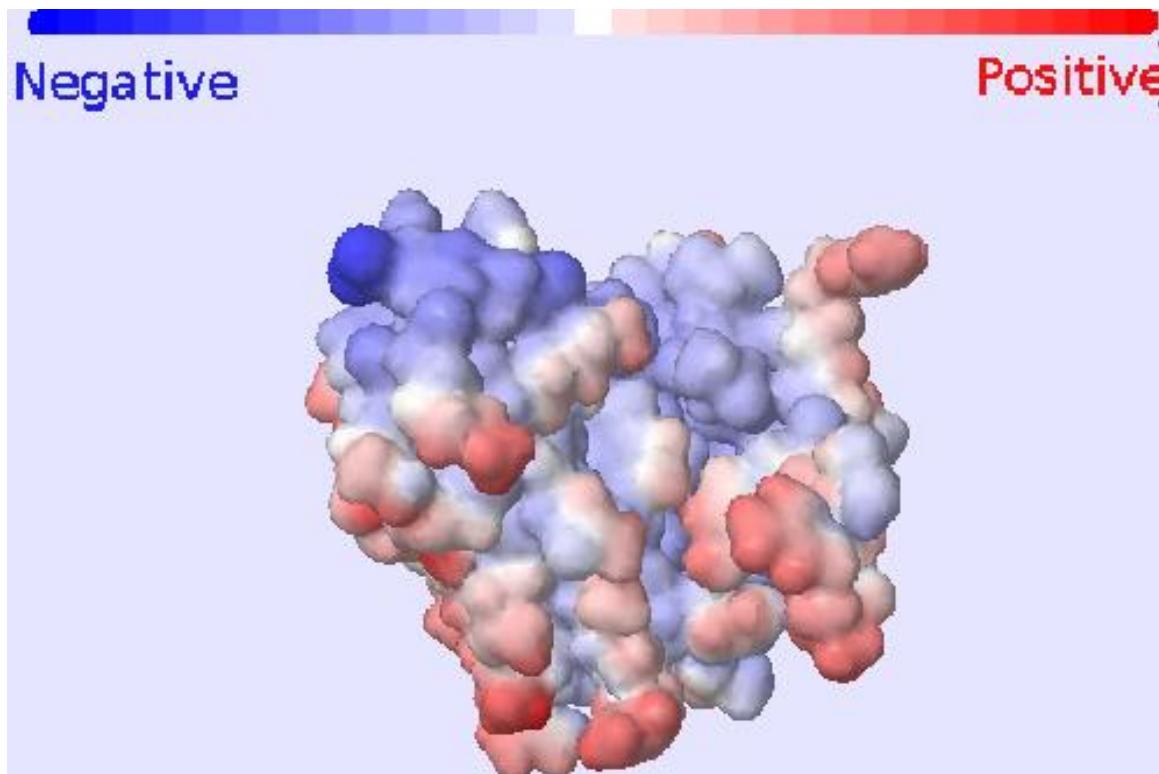


8Fe8S  
ferredoxin

## 4. Effect of Protein Charges

The **protein matrix** can tune the reduction potential:

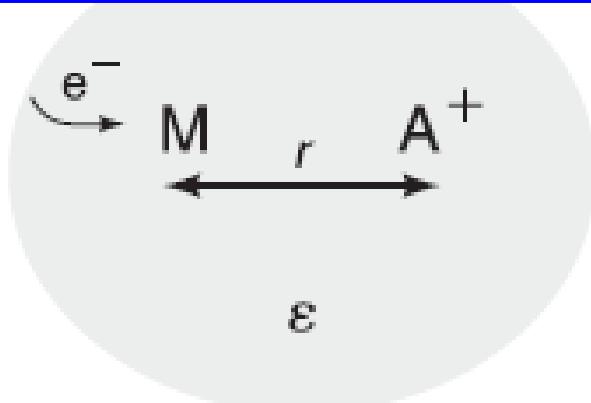
1. Create an **electrostatic field** around the metal center by the combined effect of all (fractional & unit) **charges of the protein atoms**.



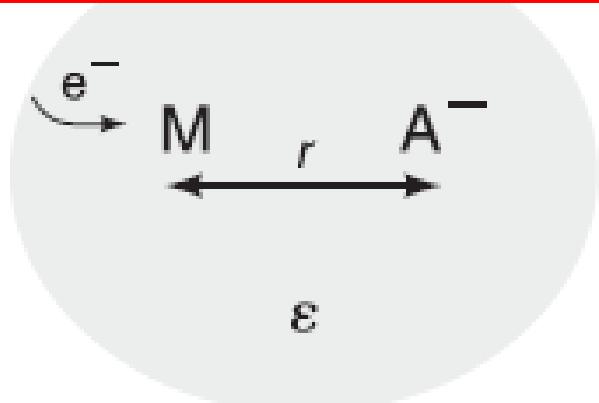
**2. Overall charge** of the metal center (either decrease its positive charge or increase its negative charge) can be **electrostatically favored or disfavored** depending on the **protein electrostatic field**.

**3. Solvent accessibility** can modulate the **dielectric constant ( $\epsilon$ )** of the medium which affects the above-mentioned **electrostatic interactions**.

Reduction favored



Reduction disfavored

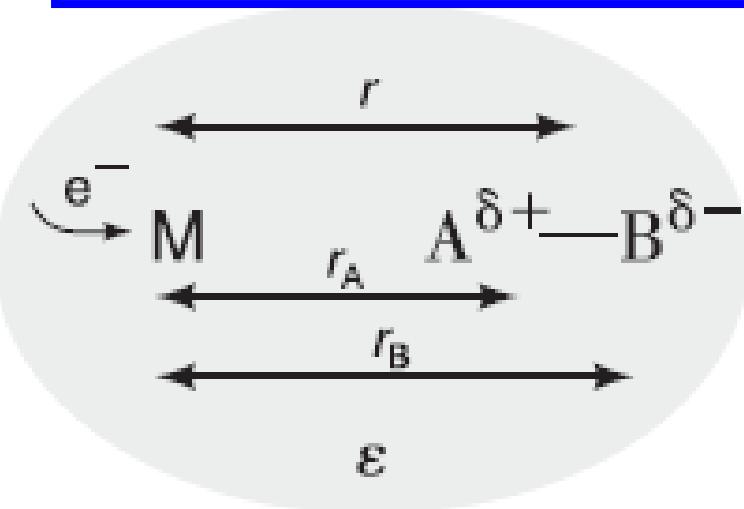


$$E = \frac{k}{\epsilon} \frac{q_e - q_A}{r}$$

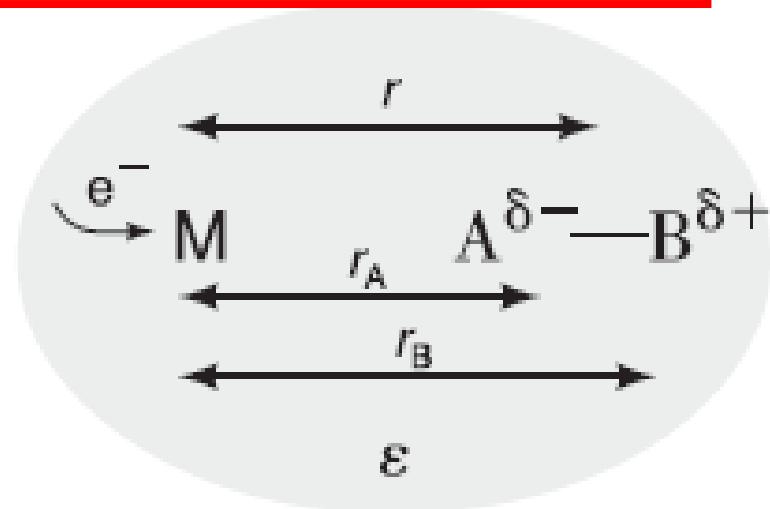
## 4a. Effect of Fractional Protein Charges

- A **positive** fractional charge of a **residue** nearby the metal center **increases** its reduction potential.
- A **negative** fractional charge **decreases** it.

Reduction favored



Reduction disfavored

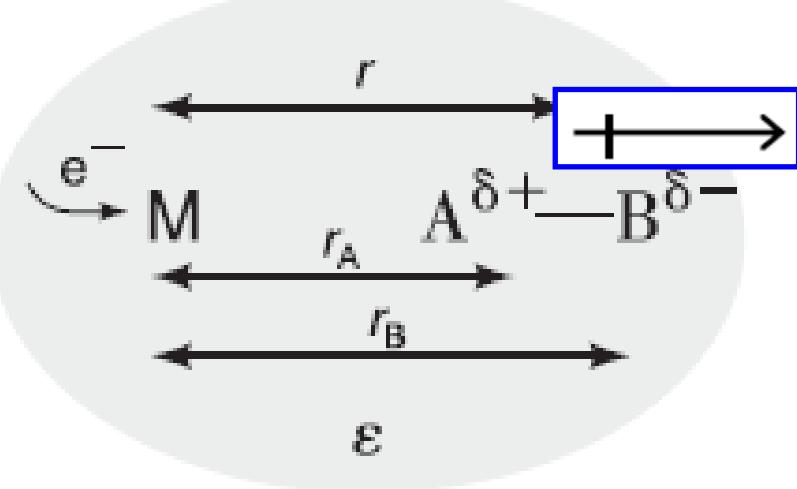


$$E = \frac{K}{\epsilon} \left( \frac{q_{e^-} q_A}{r_A} + \frac{q_{e^-} q_B}{r_B} \right) \approx \frac{K}{\epsilon} \frac{q_{e^-} q_B}{r^2} (r_B - r_A)$$

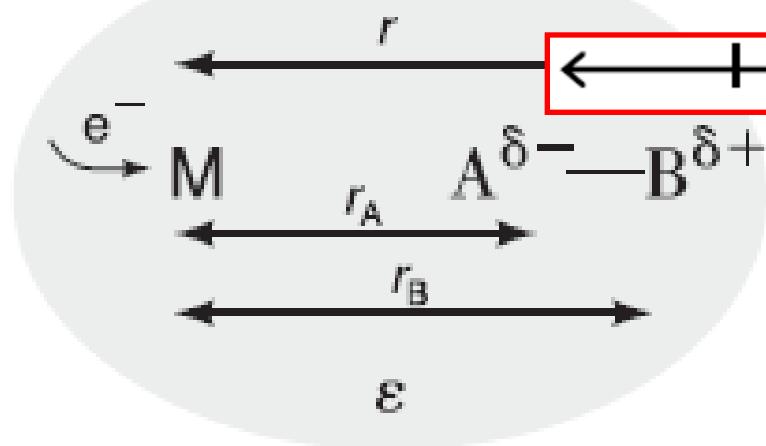
- CONH peptide groups as electric dipoles (with the H (positive end) & O (negative end)): These **dipoles in a low dielectric medium** can affect their nearby metal center.

E.g. the negatively-charged clusters in Fdx ( $-2 \rightarrow -3$ ) is stabilized by some CONH dipoles with their positive end toward the cluster.

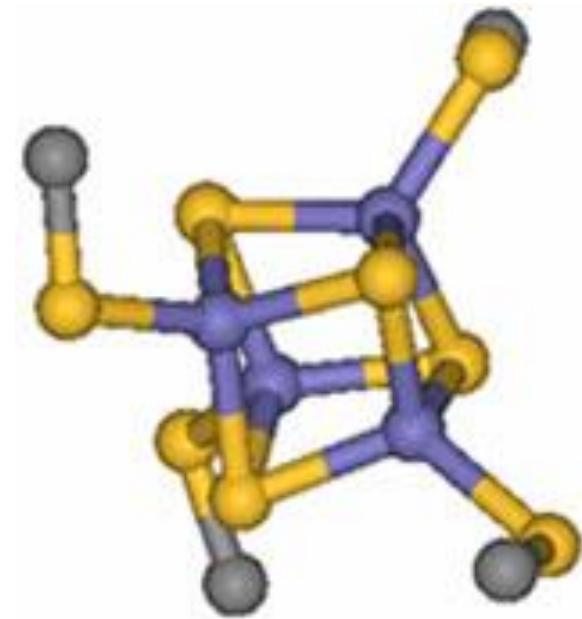
Reduction favored



Reduction disfavored



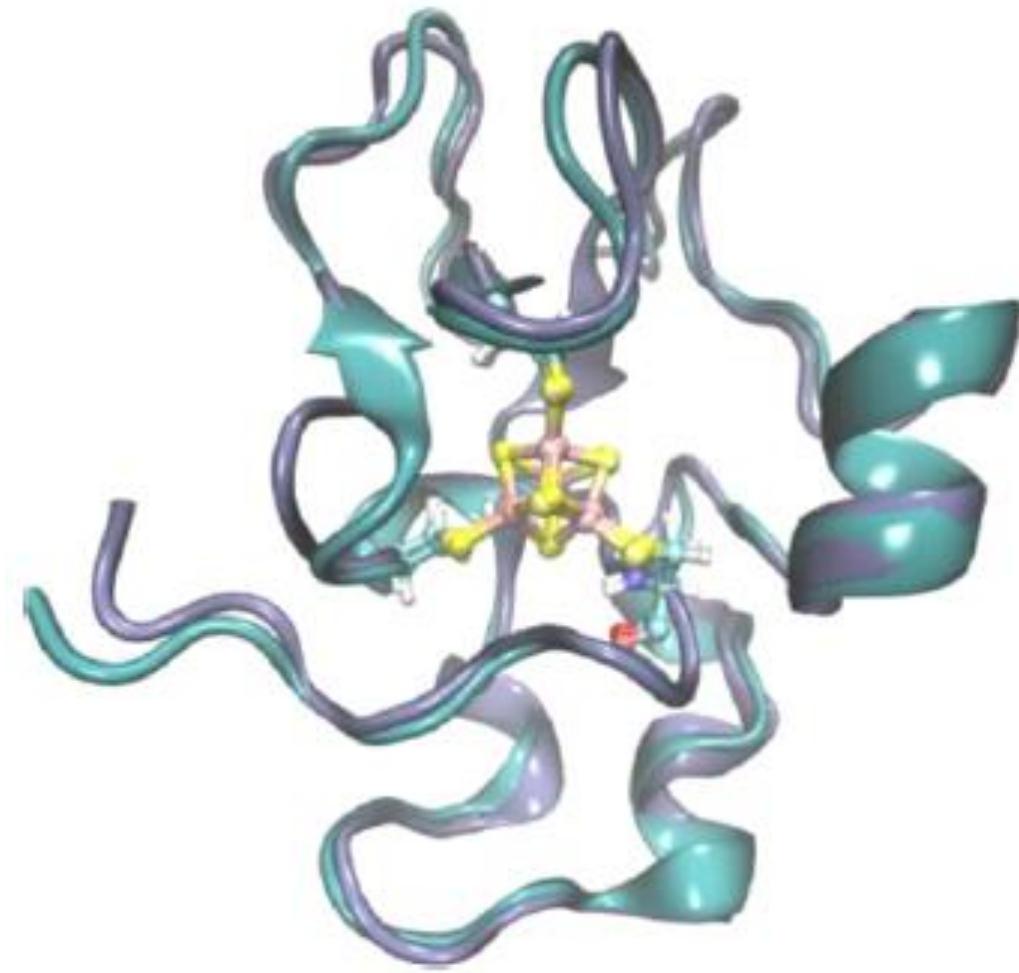
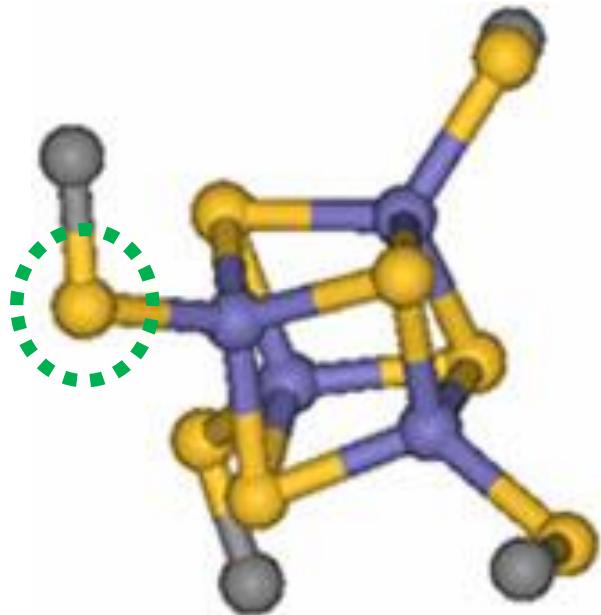
- The combined effect of **solvent exposure** & **protein dipoles**: different redox behavior of 4Fe4S ferredoxin (**Fdx**) & high-potential iron proteins (**HiPIPs**, the highest potential among all iron-sulfur proteins).



4Fe cluster HiPIP (93/458)

4Fe cluster [4Fe—4S] Fdx (-417/-280)

- In **Fdx**, the combined protein-solvent effect stabilizes the  $[\text{Fe}_4\text{S}_4]^{2+/+}$  cluster (overall charges: **-2/-3**). While, it stabilizes the  $[\text{Fe}_4\text{S}_4]^{3+/2+}$  cluster (overall charges: **-1/-2**) in **HiPIPs**.



- **Substitution** of a **Cys (S)** by a (deprotonated) **Ser (O)** in an iron-sulfur cluster **decreases** the reduction potential **modestly** (by a few tens of mV)  
→ **less reducible** (more stabilize the Fe(III) state. Why?)

## 4b. Effect of Unit Charges on the Protein Surface

- **Unit charged** groups (e.g. Lys, Glu) are usually located at the **protein surface**. Their effect on reduction potential should be **less** than inside the protein.
- Charged residues on the surface vary considerably in different proteins (**overall charges** of the proteins: **-14 ~ +3**). A good correlation between total charge & potential. A charged surface residue was estimated to contribute ~15-30 mV to the potential.

# Electrostatic Effects in Electron-Transfer Proteins

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Coordination sphere

The largest determinant is the metal ion. Then the nature and geometry of ligands and the charge of the coordination polyhedron. In polometallic centers, metal–metal interactions.

Solvent accessibility

Affects the dielectric constant, and therefore the energy of electron uptake, up to more than an order of magnitude.

Partial charges and CONH dipoles

Partial charges of atoms affect the overall electrostatic field around the metal center. Sometimes atoms with opposite partial charges are conveniently grouped into clusters of atoms that constitute dipoles (e.g., CONH groups).

Charges inside the protein

Charges inside the proteins have an important role as the dielectric constant inside the protein is small (2–8). Typical examples are given by a negative carboxylate hydrogen-bonded to the proximal His in heme proteins.

Surface charges

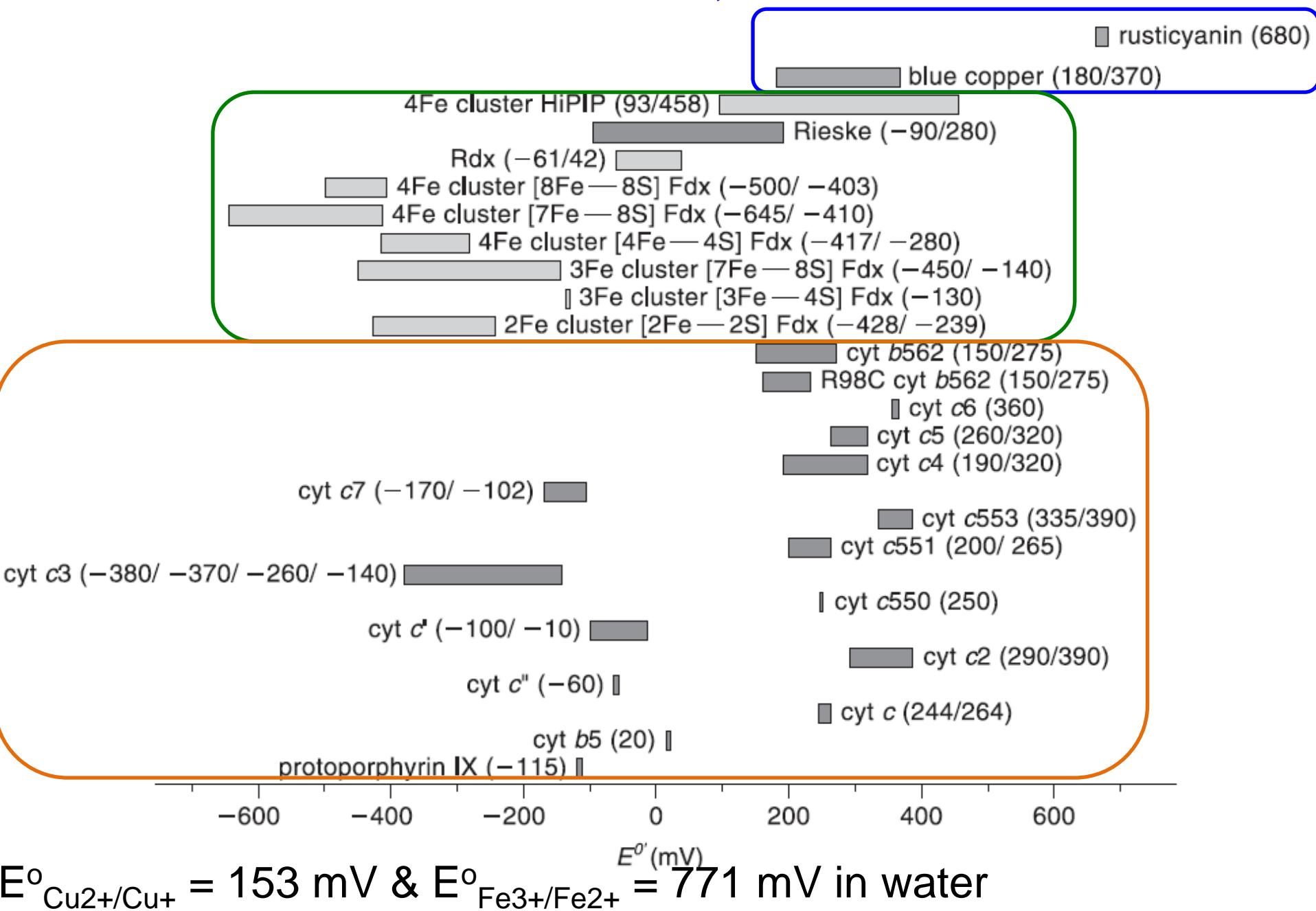
Solvation (in high dielectric media) reduces the effects of these charges and they are meaningful only when all other parameters are essentially constant.

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## Iron & Blue Copper Proteins

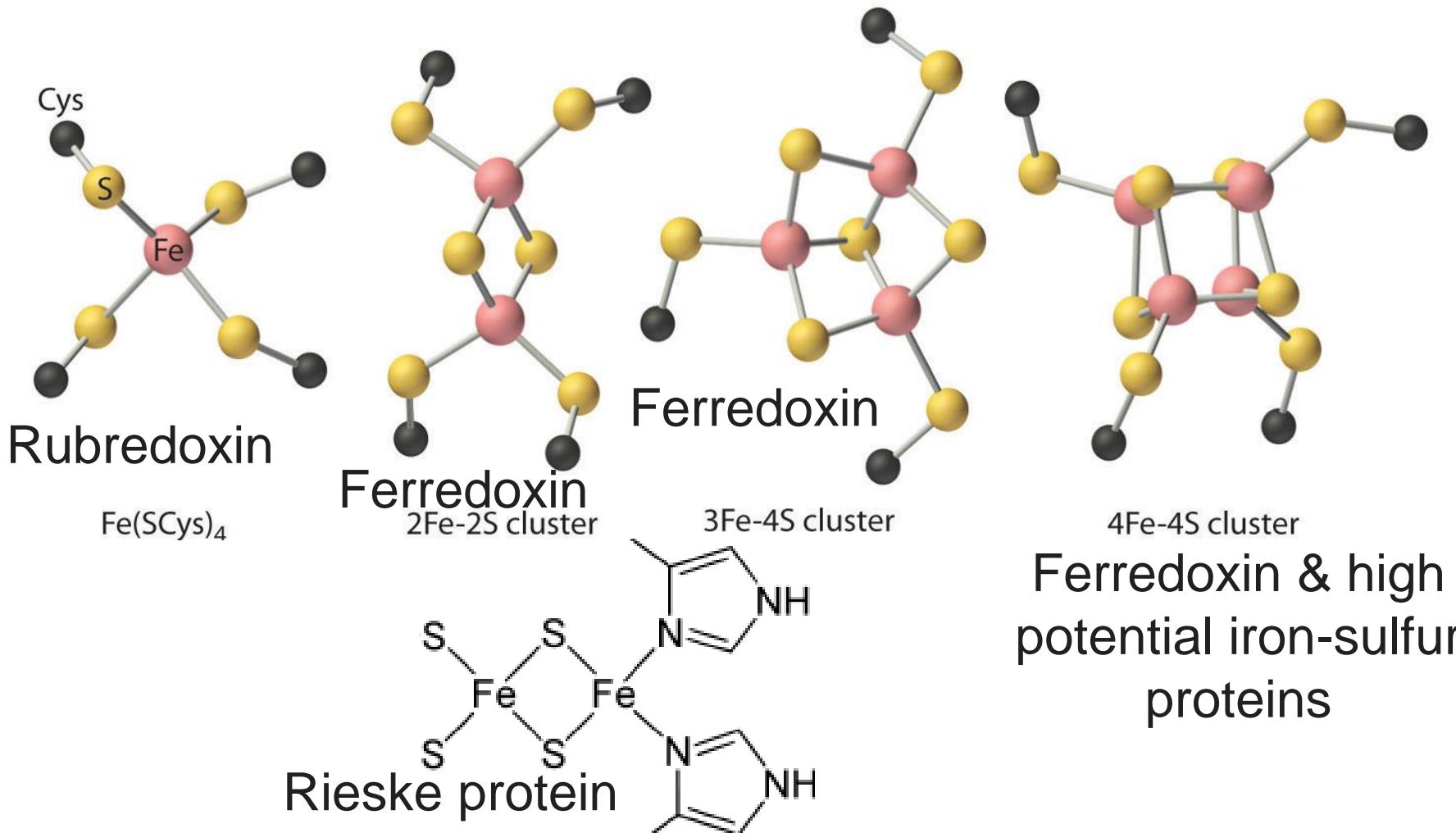
- The average reduction potentials: blue copper proteins  
> iron-hemes > iron-sulfur proteins.
- The **overall charge** of **heme** moiety: **+1/0** (excluding its side chains), ~2 units **more positive than iron-sulfur clusters**. So, potentials for hemes are **more positive** than the negative side.
- The total charge of the metal center in **blue copper proteins**: **+1/0**. They have a **modestly positive potential**, thought Cu(II) intrinsically is harder to be reduced than Fe(III). Nature chose a **less negative environment for Cu**.
- **No special cofactor** for the ET copper proteins (vs. porphyrin for hemes & S<sup>2-</sup> for Fe-S proteins).

# Reduction Potentials for Cu, Fe-S & Heme Proteins



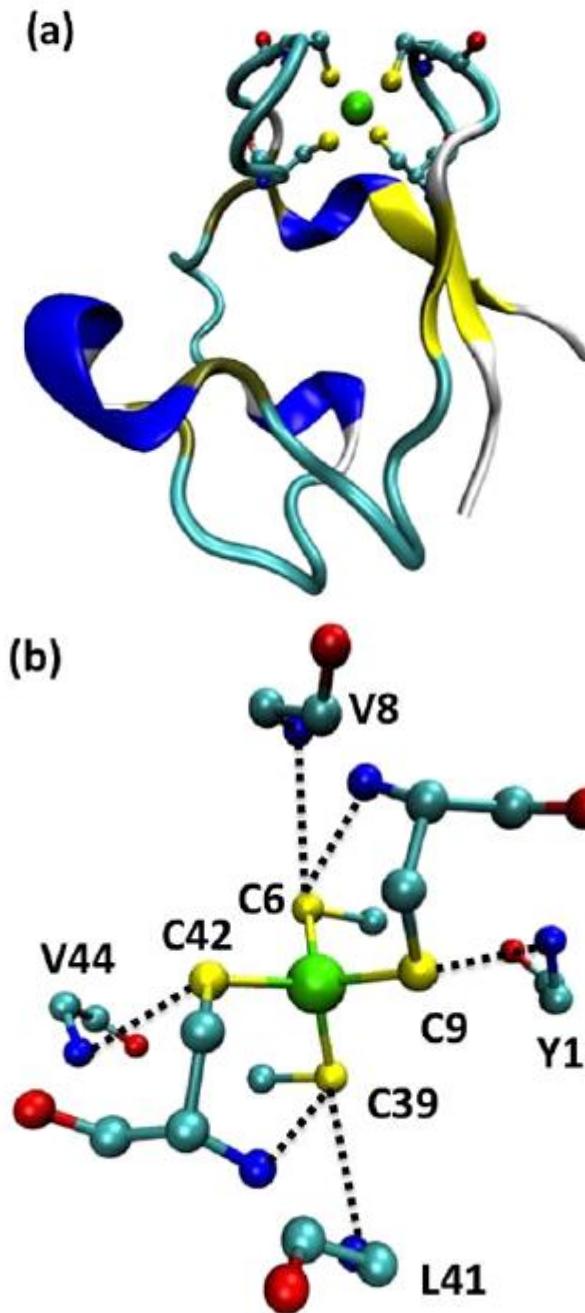
# Iron-Sulfur Proteins

1) **[1Fe-0S]** (Rdx), 2) **[2Fe-2S]** clusters (Fdx & Rieske protein), 3) **[3Fe-4S]** clusters (Fdx) or 4) cubane **[4Fe-4S]** clusters (Fdx & HiPIPs).



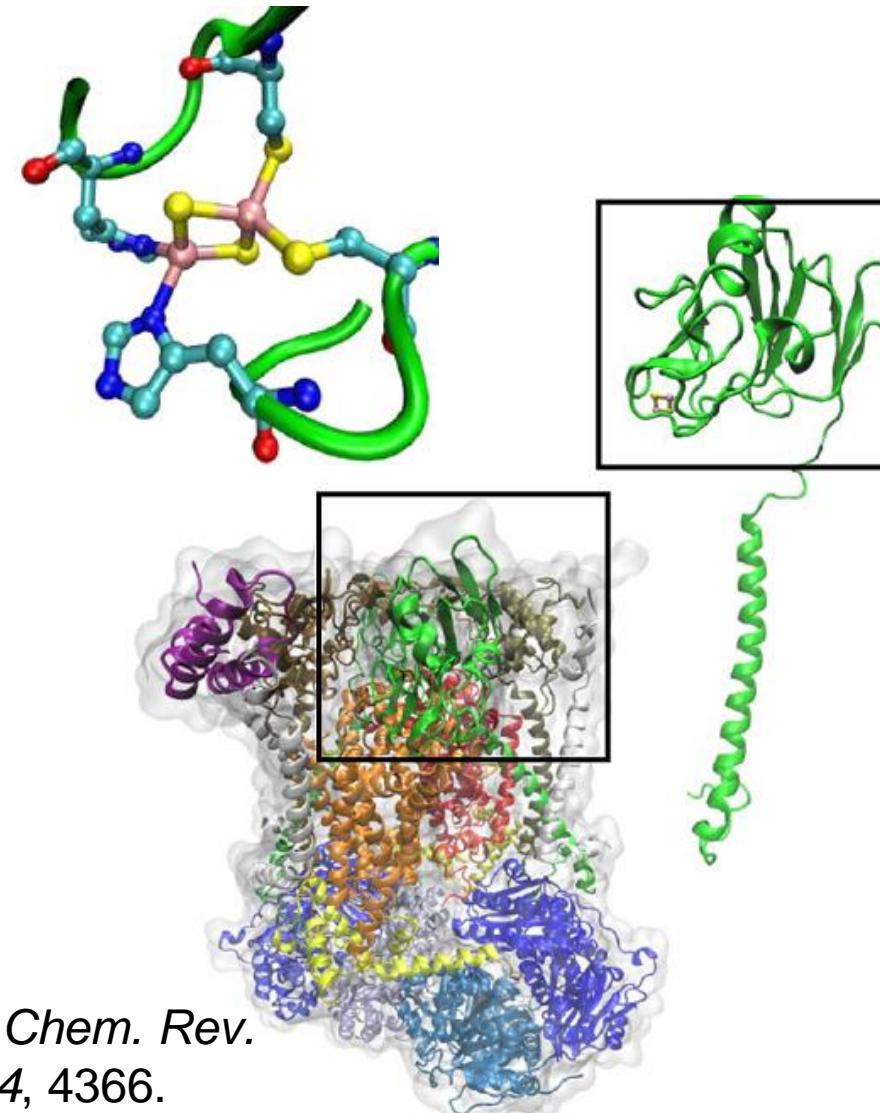
# Rubredoxin (Rdx)

- The **simplest Fe-S** proteins (e.g. bacterial proteins with low molecular weight of ~6-7 K Da).
- **One Fe** ion with **4 Cys** in a distorted tetrahedral redox center.
- The consensus sequence:  
**Cys-Pro-X-Cys-Gly-X<sub>n</sub>-Cys-(X-X)-Cys**
- When one surface Cys is replaced by Ser in CpRdx, the reduction potential can be decreased by 200 mV at most, while such replacement for an internal Cys decreases the potential by 100 mV.



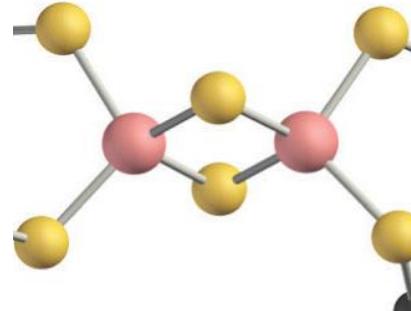
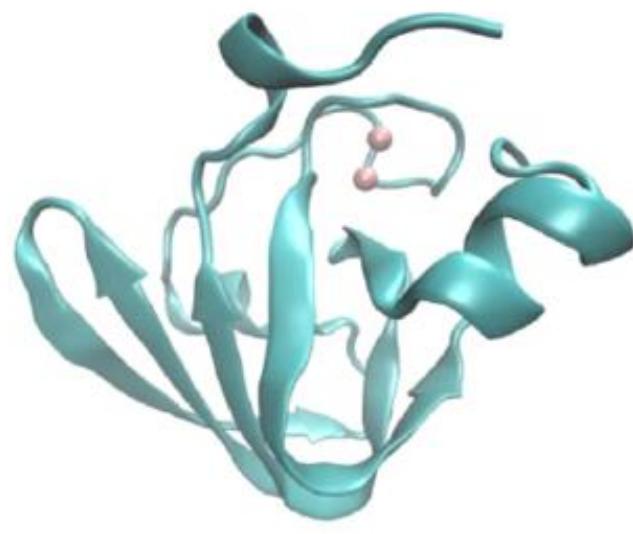
# Rieske Proteins

- They were found in prokaryotes & eukaryotes, & are **ET domains** of more **complex proteins** (e.g. in the bacterial & mitochondrial bc<sub>1</sub> complexes (respiration)) rather than ET proteins.
- **2 Fe ions & 2 Cys, 2S & 2 His** to form a diamond structure with more positive potential (vs. Fdx with 2 Fe & 4 Cys).
- The consensus sequence:  
**Cys-X-His-X<sub>n</sub>-Cys-X-X-His**

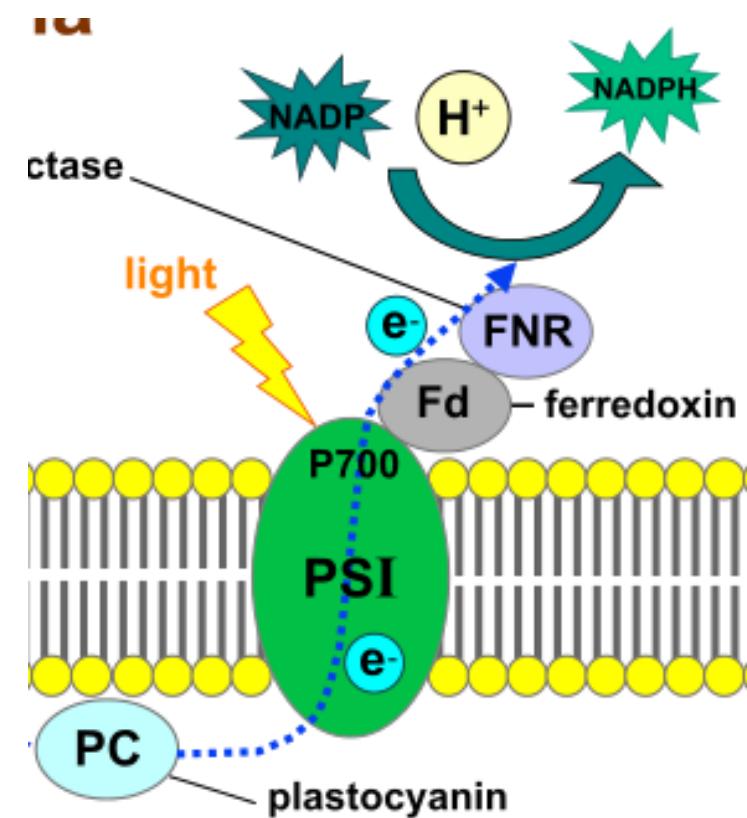


# [2Fe-2S] Ferredoxin

- Contain **2 Fe, 2 S & 4 Cys**. Found in many metabolic reactions from bacteria to humans.
- Can act as terminal electron acceptors of photosystem I in photosynthesis & ET in nitrogen fixation.
- The consensus sequence:  
**Cys-X<sub>4</sub>-Cys-X-X-Cys-X<sub>n</sub>-Cys**



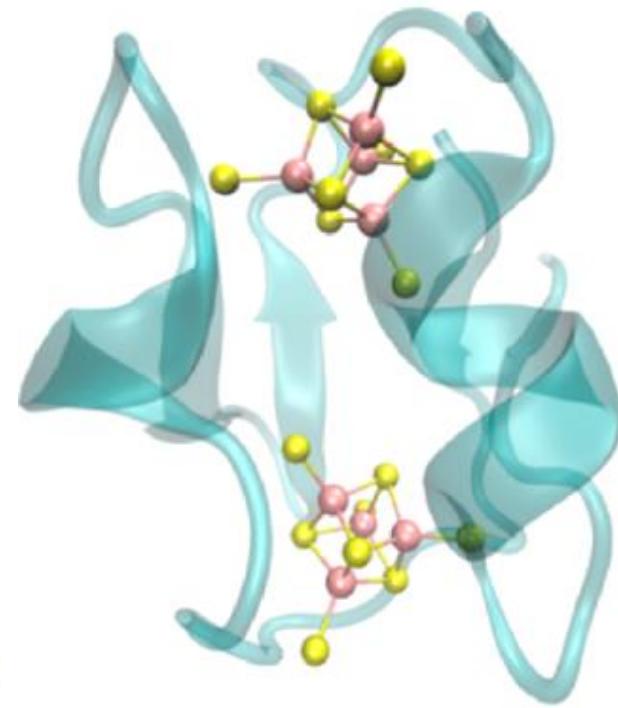
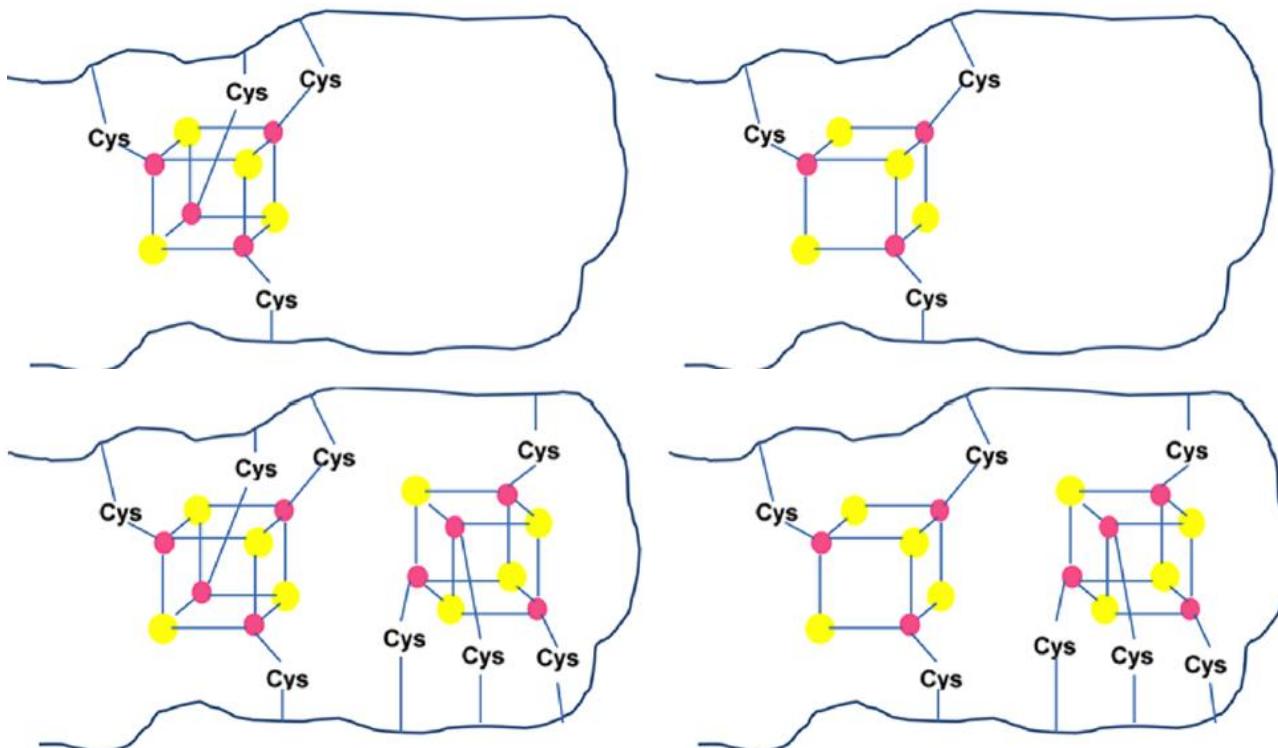
Plant-type ferredoxin

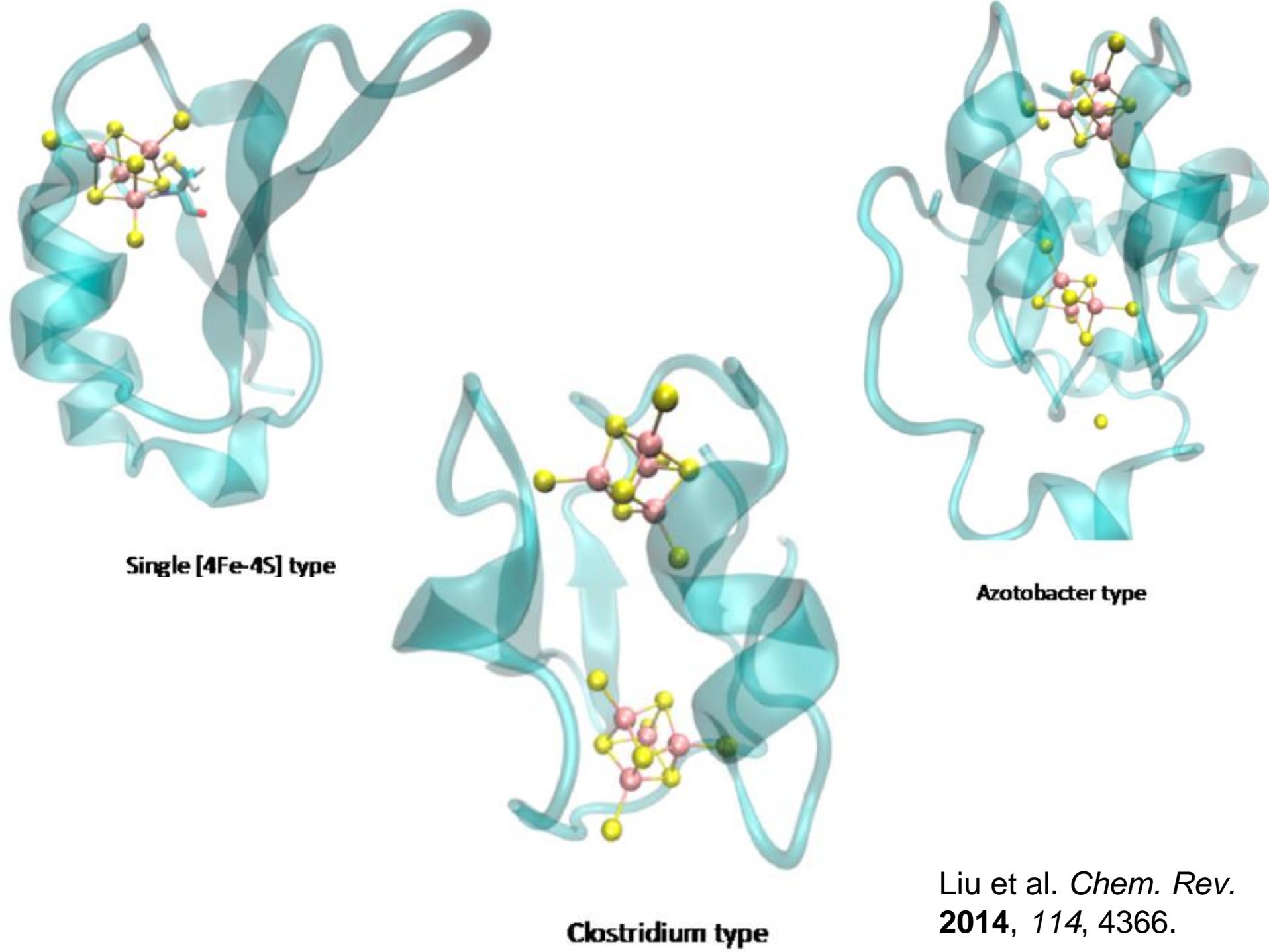


# [4Fe-4S] Ferredoxin

- Contains **4Fe4S cubane (with 4 Fe, 4 S & 4 Cys) clusters.** They can accommodate 3, 4, 7, or 8 Fe ions in 1 or 2 clusters.
- The consensus sequences:

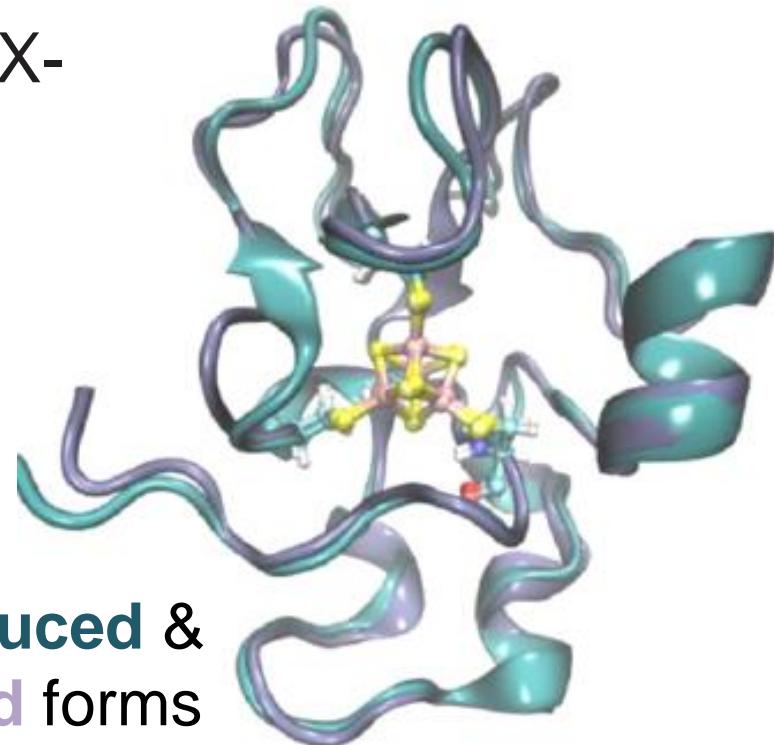
**Cys-X-X-Cys-X-X-Cys-X<sub>n</sub>-Cys A**  
**Cys-X<sub>m</sub>-Cys-X-X-Cys-X-X-Cys B**





# High-Potential Fe-S Proteins (HiPIPs)

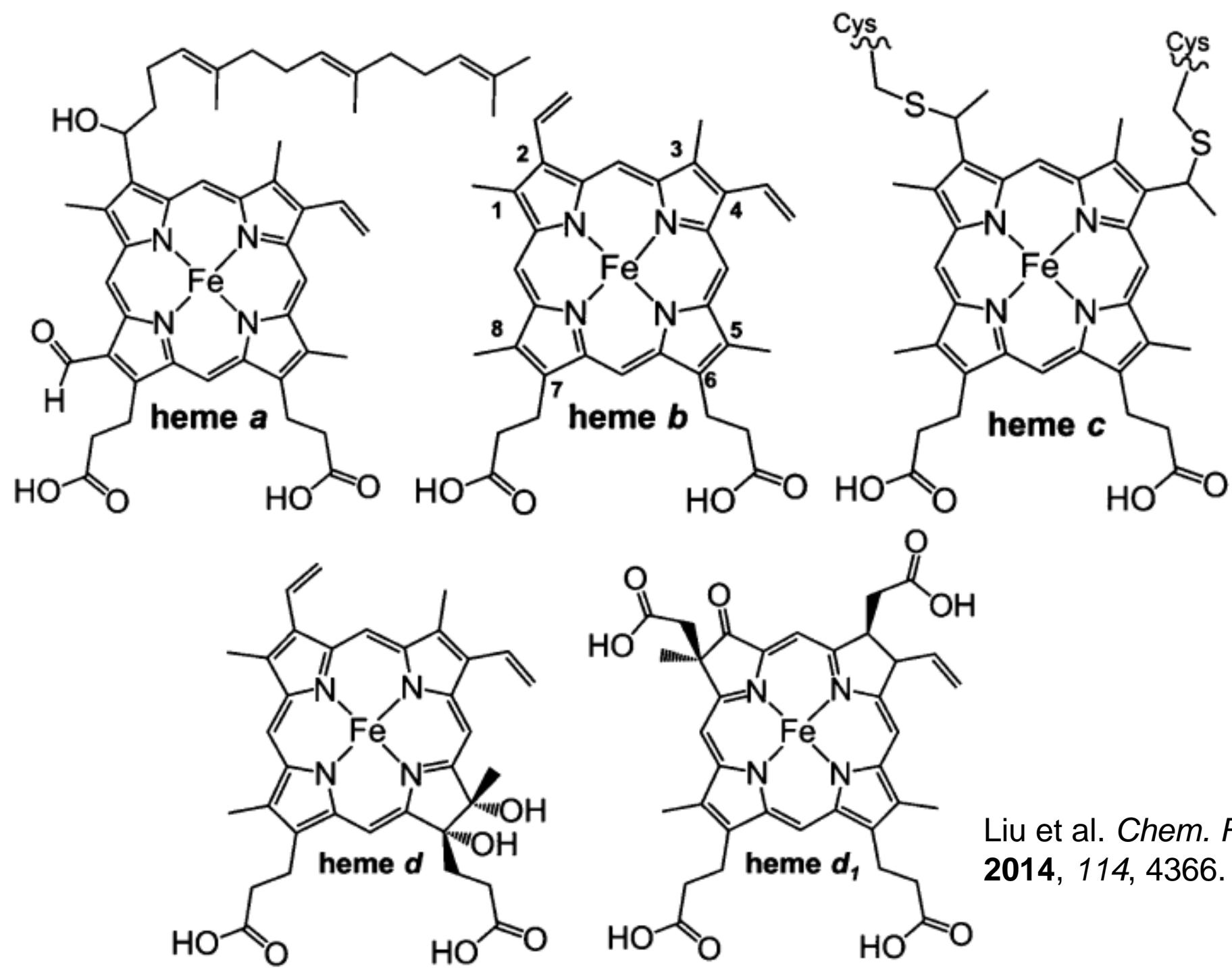
- They have one **4Fe4S cubane** (with 4 Fe, 4 S & 4 Cys) cluster, but have **one less electron** in both the oxidized (with 3 Fe(III) & 1 Fe(II)) & reduced states than Fdx.
- The cluster is almost embedded within the **hydrophobic** environment, stabilizing the **cluster with lower charge**.
- The consensus sequence: **Cys-X-X-Cys-X<sub>8-16</sub>-Cys-X<sub>10-13</sub>-Gly-Z-Cys**  
(Z = Trp or Tyr)
- E.g. acts as electron carriers between the photosynthetic reaction center & the cytochrome *bc<sub>1</sub>* complex.



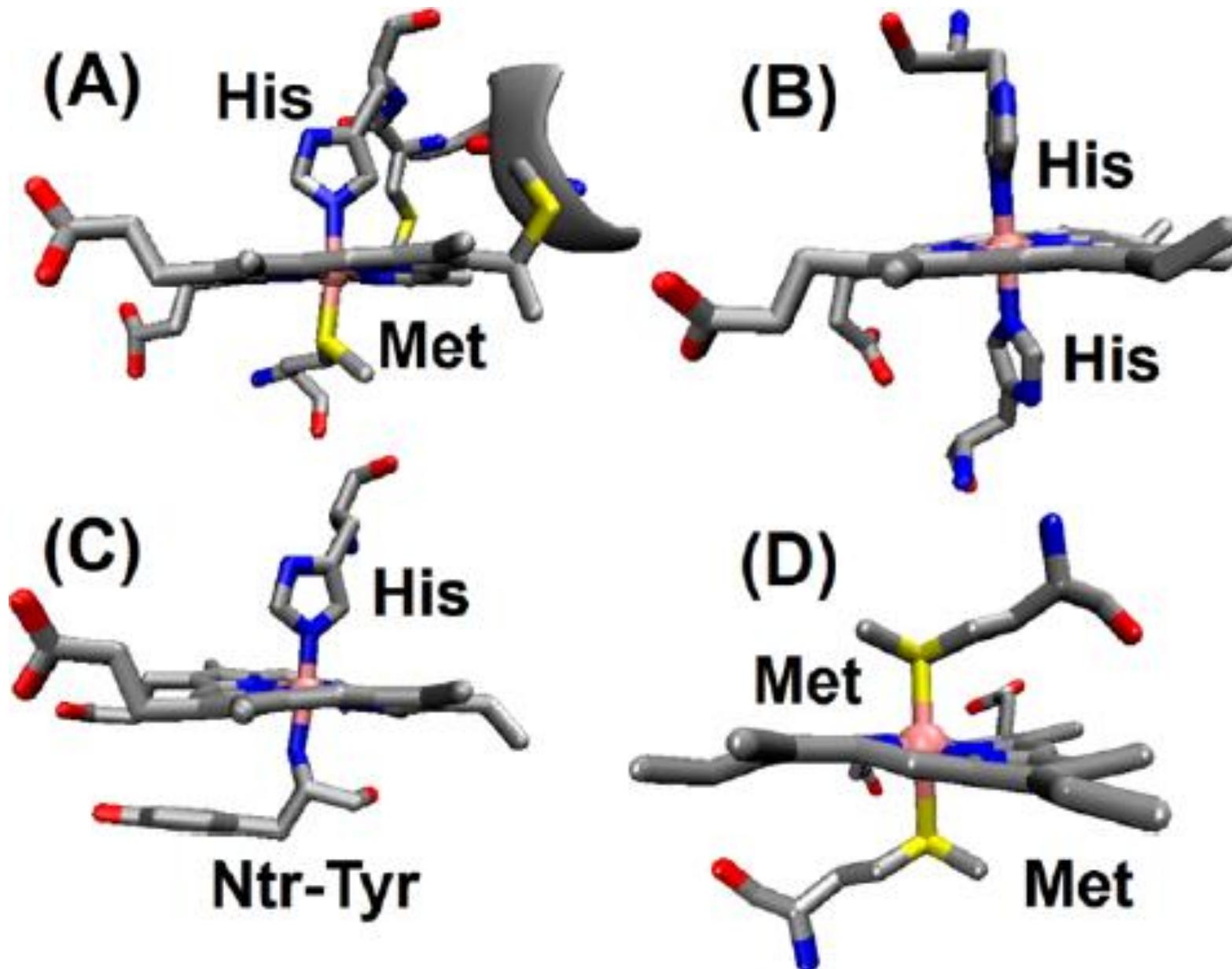
## ET Cytochromes (Cyt, Fe)

- Reduction potentials are tuned mainly by the **number & nature** of the **axial ligands** &, to a minor extent, by the **heme** (*heme a, b, or c* type for ET).
- Have either 2 axial ligands (mainly **2 His or His+Met**), or one axial ligand (**His**).

Donor Atoms	Protein Class
Nε His/Nε His	Cytochrome <i>c</i> oxidase heme <i>a</i> (cyt <i>a</i> ) Cytochrome <i>b/b</i> <sub>6</sub> Cytochrome <i>b</i> <sub>5</sub> Cytochromes <i>c</i> (class III and IV) Cytochrome <i>c</i> <sub>554</sub> (hemes 3 and 4) Cytochrome <i>cd</i> <sub>1</sub> nitrite reductase ( <i>c</i> -domain) Hydroxylamine oxidoreductase (heme <i>c</i> )
Nε His/Nδ His	Cytochrome <i>c</i> <sub>554</sub> (heme 1)
Nε His/Sδ Met	Soluble cytochrome <i>b</i> <sub>562</sub> Cytochromes <i>c</i> (cyt <i>c</i> <sub>1</sub> , class I, class II besides <i>c'</i> , and class IV)
Nε His/Amide N of Tyr1 Sδ Met/Sδ Met	Cytochrome <i>f</i> Bacterioferritin (cyt <i>b</i> <sub>1</sub> ; cyt <i>b</i> <sub>577</sub> )

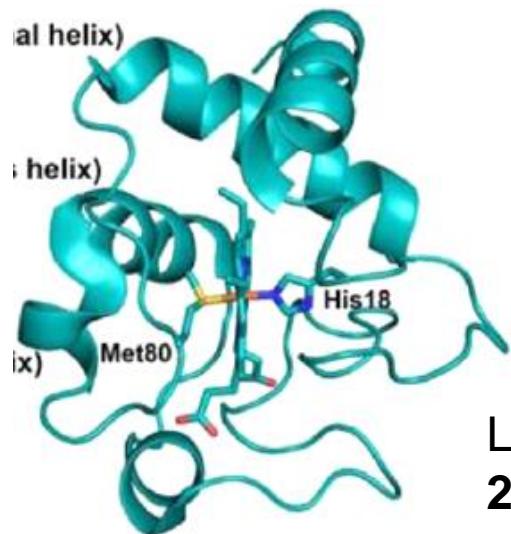


Liu et al. *Chem. Rev.*  
2014, 114, 4366.

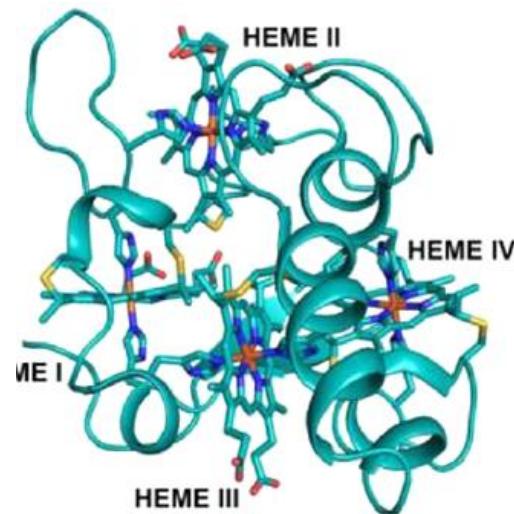


- Cytochromes with **His+Met** as axial ligands are more reducible than those with two **His**. Why?

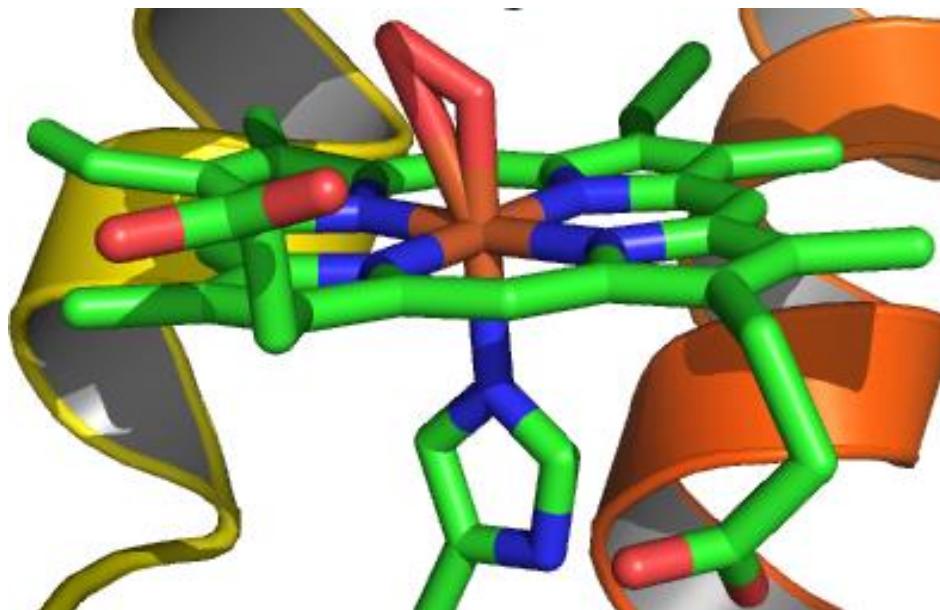
cytochrome	axial ligand	heme type	<i>E</i> (mV) <sup>b</sup>
<i>Nitrosomonas europaea</i> diheme cyt c peroxidase	His/Met	class I	450
<i>Rhodococcus tenuis</i> THRC cyt c		class IV	420
HP1	His/Met		420
HP2	His/Met		110
LP1	bis-His		60
LP2	His/Met		
<i>Rhodopseudomonas viridis</i> THRC cyt c		class IV	380
H1 ( <i>c</i> <sub>559</sub> )	His/Met		330
H3 ( <i>c</i> <sub>556</sub> )	His/Met		20
H2 ( <i>c</i> <sub>552</sub> )	bis-His		-60
H4 ( <i>c</i> <sub>554</sub> )	His/Met		



Liu et al. *Chem. Rev.*  
2014, 114, 4366.

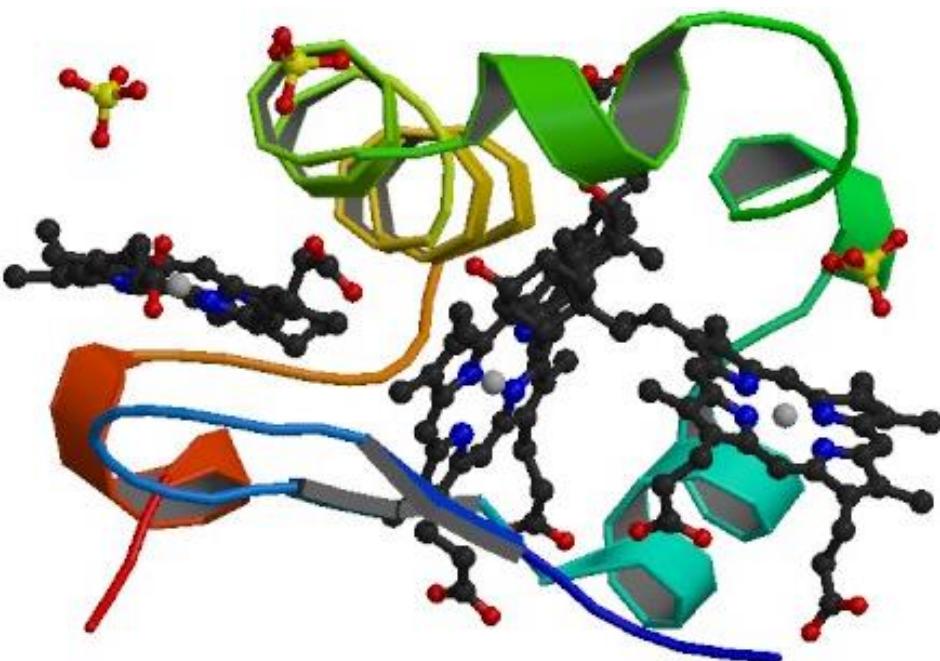


- The **propionate side chains** of the heme can be exposed to solvent → **minor influence** of their two negative charges on the iron center.
- Protonation of these propionate side-chains can increase the reduction potential by ~65 mV for cyt c. When they are substituted with methylesters, the potential can also be increased by ~60 mV. Why?

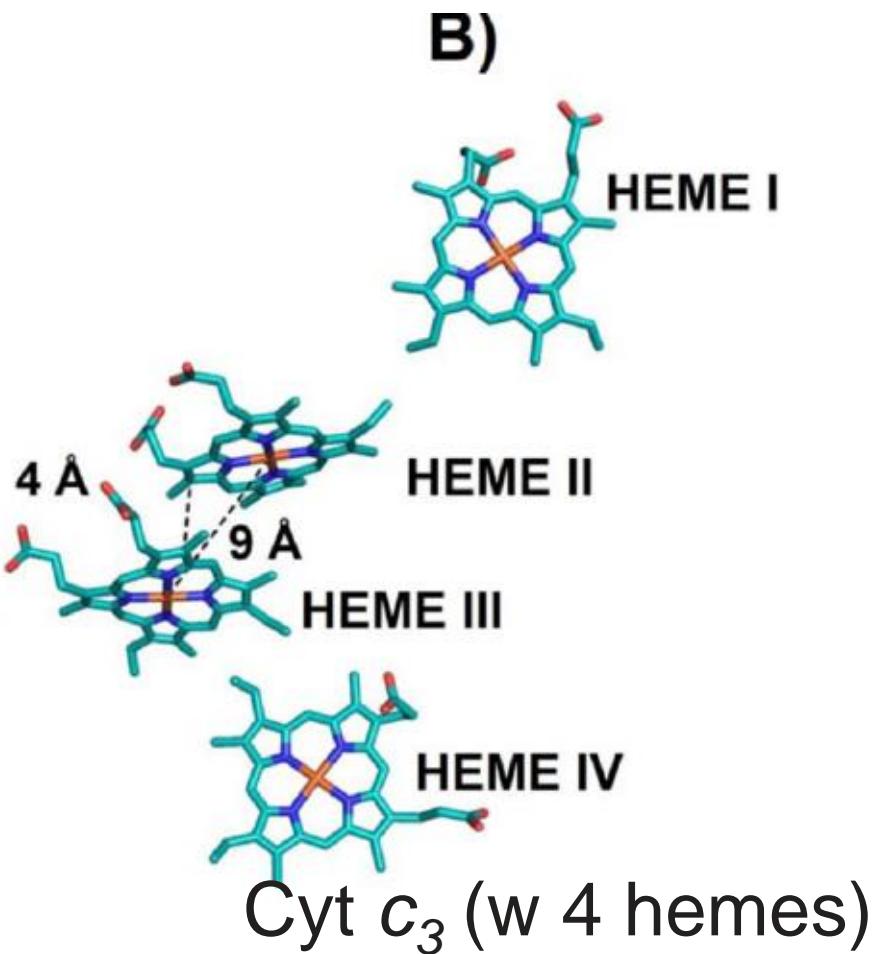


# Multi-Heme Cytochromes

- They are all c-type hemes. Distances between the heme-Fe atoms: ~12-19 Å for Cyt  $c_7$ .
- Solvent exposure is the key factor to low the potentials (-90~400 mV).



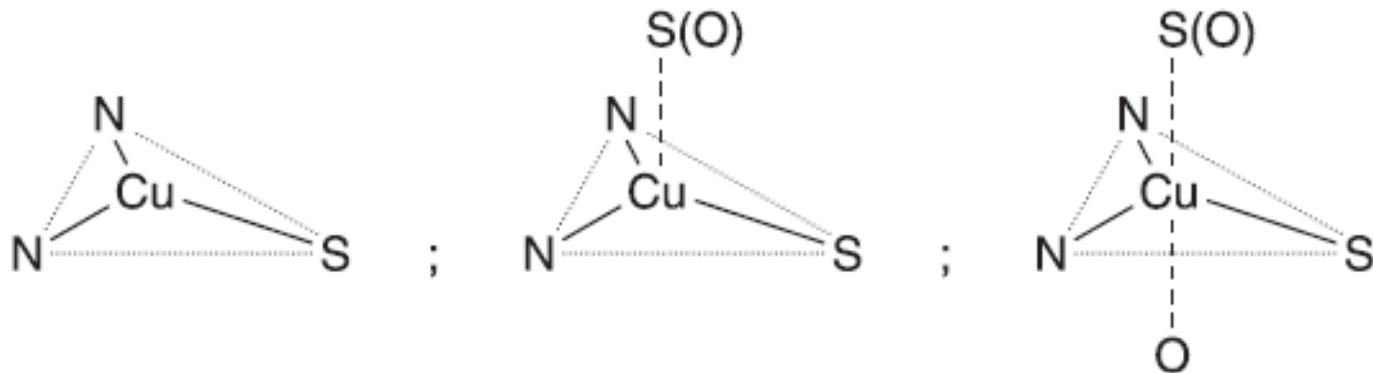
Cyt  $c_7$  (w 3 hemes)



# ET Copper Proteins

- They do **not** need special cofactors in the redox center.
- All Cu proteins can be classified: **(1) type 1 (or blue)**, **(2) type 2 (mononuclear catalytic)**, **(3) type 3 (binuclear Cu(II))** and **(4) Cu<sub>A</sub>** (binuclear Cu(I) or mixed valence).  
The **type 1 & Cu<sub>A</sub>** are used for the Cu **ET** centers.

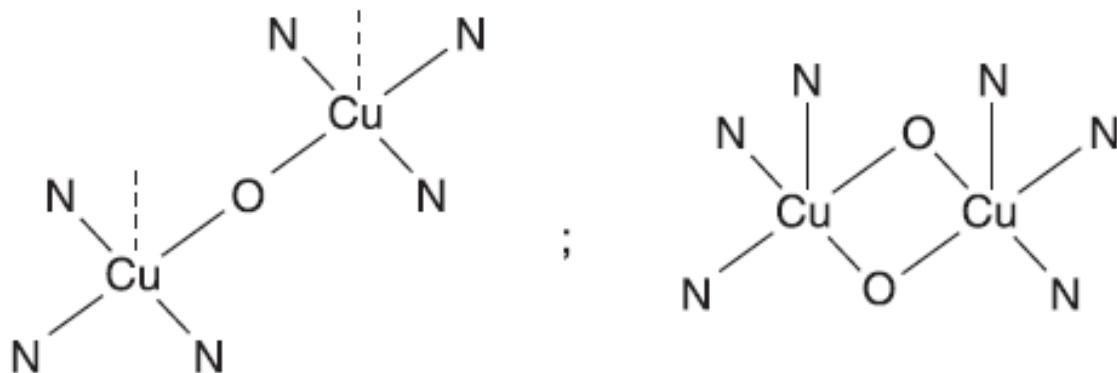
Type 1 copper



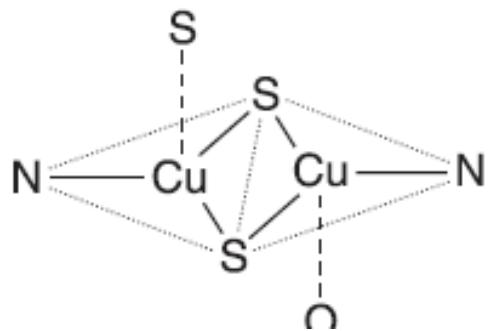
Type 2 copper



### Type 3 copper



**Cu<sub>A</sub>**



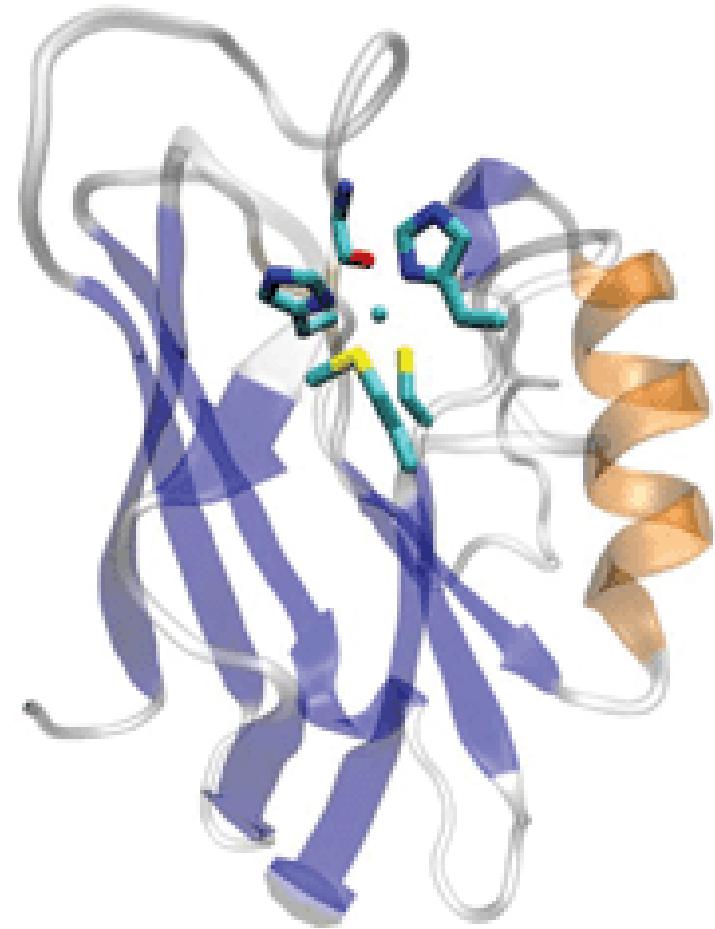
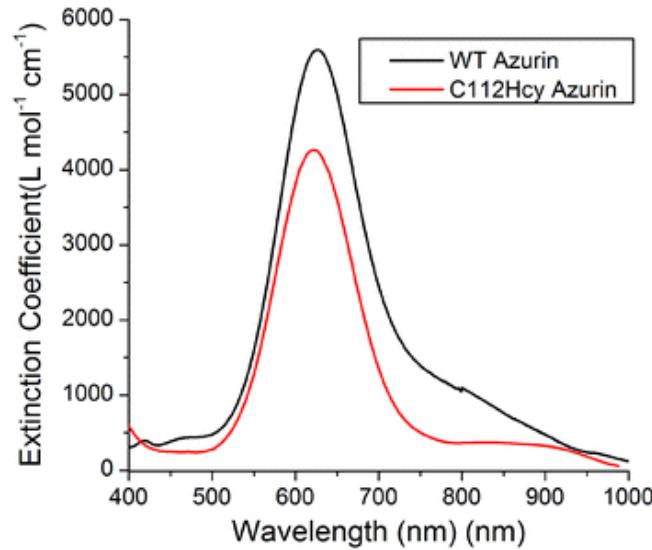
Nuclearity

Donor Atoms

Type 1	1	3 Donors (N, N, S) + 0, 1, or 2 Axial Donors (S, O)
Type 2	1	4 Donors (N <sub>x</sub> , O <sub>4-x</sub> ) + 0 or 1 Axial Donors (N, O)
Type 3	2	3 Donors (N) + 1 or 2 Bridging Donors (O)
Cu <sub>A</sub>	2	3 Donors (N, S, S) + 1 Axial Donor (S, O)

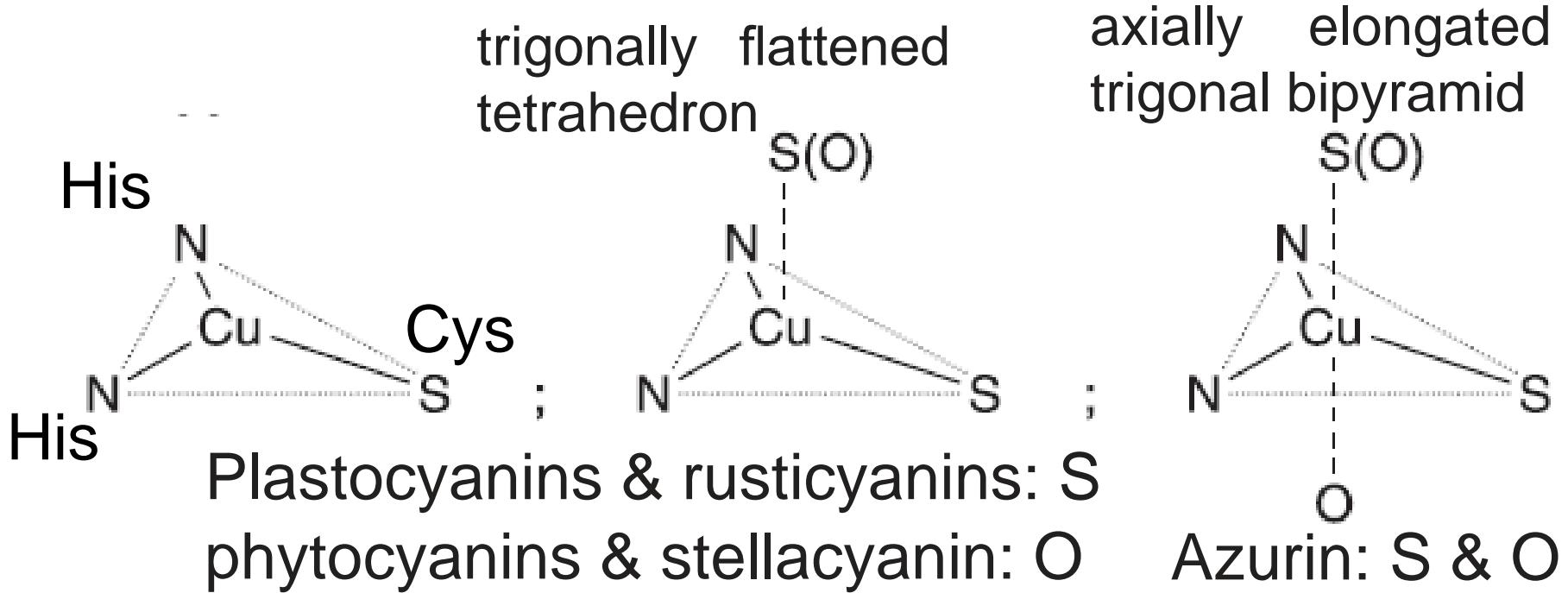
# Blue Copper Proteins

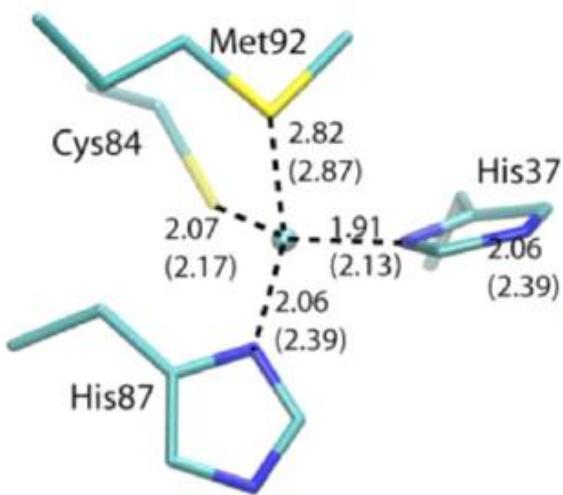
- These soluble type 1 proteins were involved in e.g. photosynthesis & respiration.



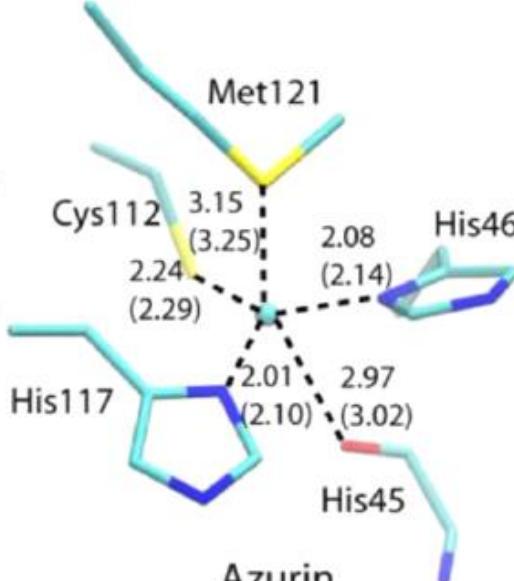
- 5 families of these proteins with different axial ligand:
  - 1) plastocyanin family (plastocyanin, amicyanin, pseudoazurin, & halocyanin); 2) auracyanin; 3) azurin; 4) rusticyanin; & 5) phytocyanin family (plantacyanin, stellacyanin, & uclacyanin).

- Plastocyanins & rusticyanins have 1 Met S ( $2.8\text{-}2.9 \text{ \AA}$ );
- Phytocyanins & stellacyanin have a Gln O ( $\sim 2.2 \text{ \AA}$ );
- Azurin has a Met S & a peptide C=O ( $\sim 3.1 \text{ \AA}$ ).

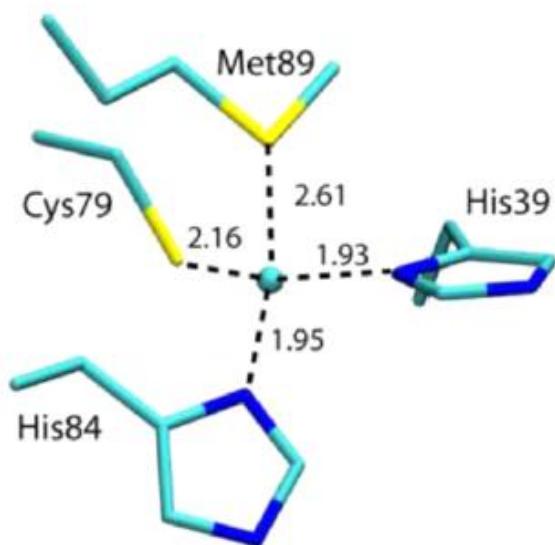




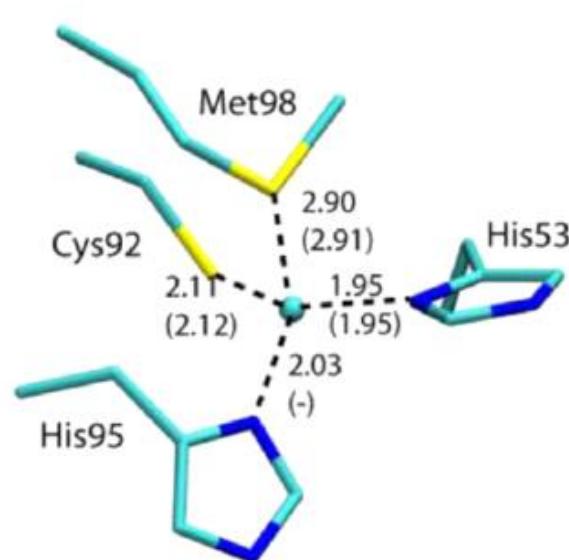
a) Plastocyanin  
1PLC(5PCY)



b) Azurin  
4AZU(1E5Y)



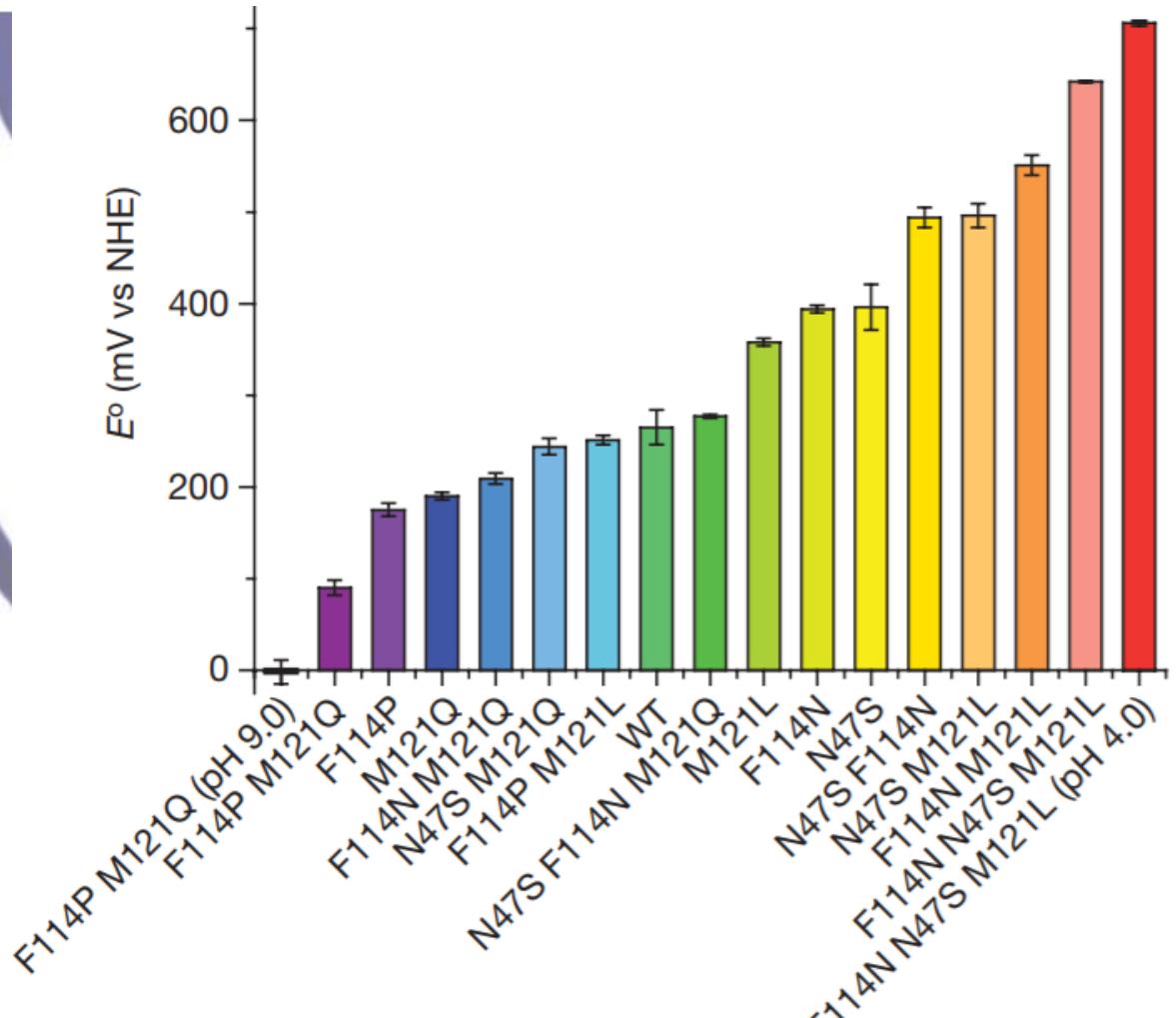
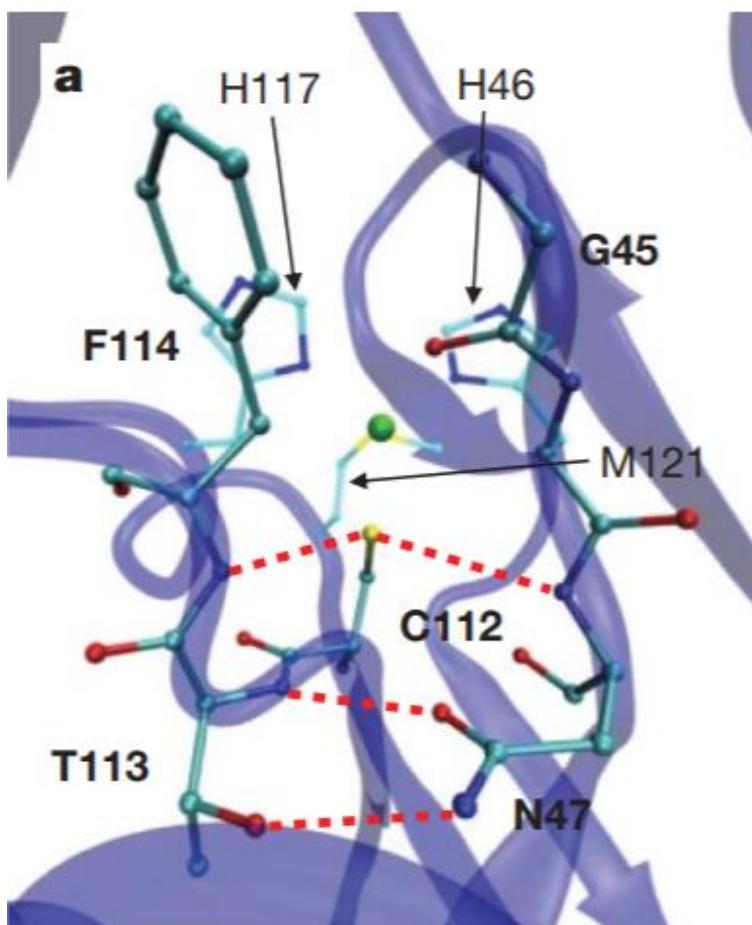
c) Plantacyanin  
(Cucumber basic protein)  
2CBP



d) Amicyanin  
1AAC(2RAC)

name	organism isolated from	PDB code for first structure	ligand set	$E_m$ (mV)
azurin	bacteria		Single Domain	
		1AZU	1Cys, 2His, 1Met, 1 carbonyl oxygen	$310^{1133}$
amicyanin	methylotrophic bacteria	1MDA	1Cys, 2His, 1Met	$260^{1135}$
plastocyanin	plant/algae/cyanobacteria	1PLC	1Cys, 2His, 1Met	$370^{1137}$
pseudoazurin	denitrifying bacteria and methylotrophs	1PAZ	1Cys, 2His, 1Met	$280^{1139}$
rusticyanin	acidophilic bacteria	1RCY	1Cys, 2His, 1Met	$670^{1141}$
auracyanin	photosynthetic bacteria	1QHQ	1Cys, 2His, 1Met	$240^{1142}$
plantacyanin	plants	2CBP	1Cys, 2His, 1Met	$310^{1144}$
halocyanin	haloalkaliphilic archaea <i>Natronobacterium pharaonis</i>		1Cys, 2His, 1Met	$183^{1145}$
sulfocyanin	acidophilic archaea <i>Sulfolobus acidocaldarius</i>		1Cys, 2His, 1Met	$300^{1146}$
nitrosocyanin	autotrophic bacteria	1IBY	1Cys, 2His, 1Glu, 1H <sub>2</sub> O	$85^{1148}$
stellacyanin	plants	1JER	Multidomain Protein with T1 Center	
uclacyanin	plants		1Cys, 2His, 1Gln	$190^{1144}$
			1Cys, 2His, 1Met	$320^{1150}$

# Rationally-Tuning Potential



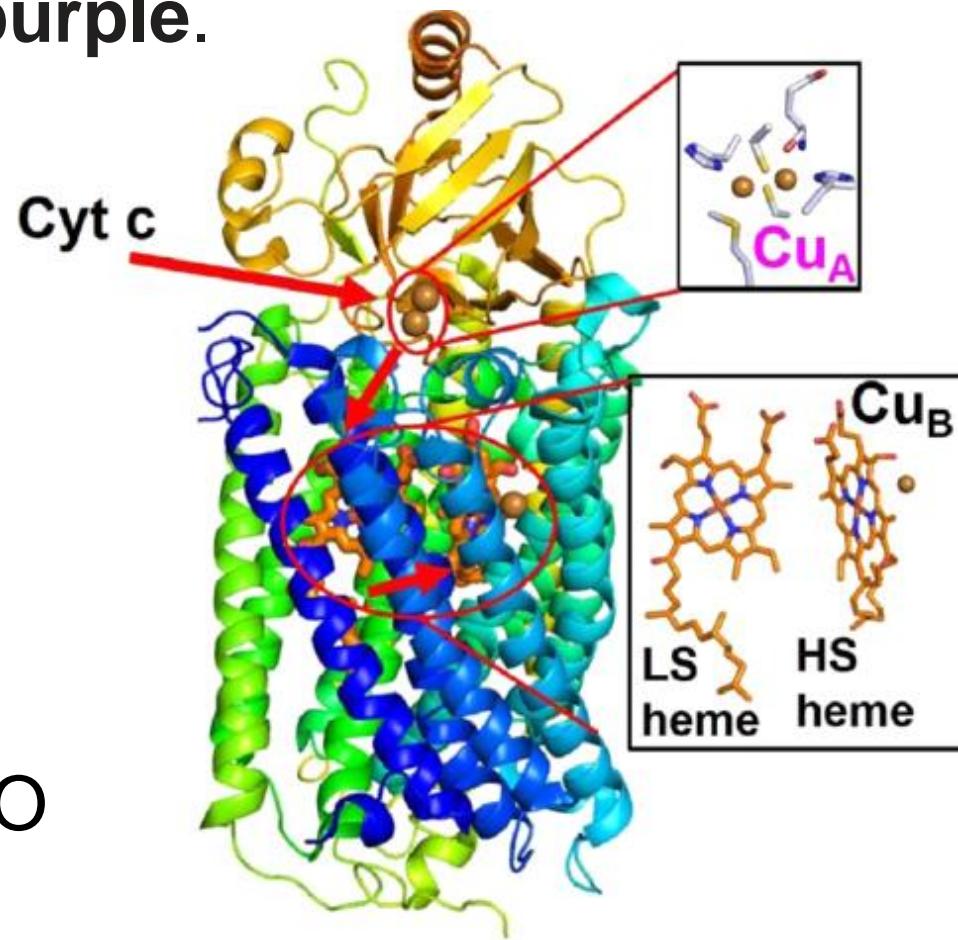
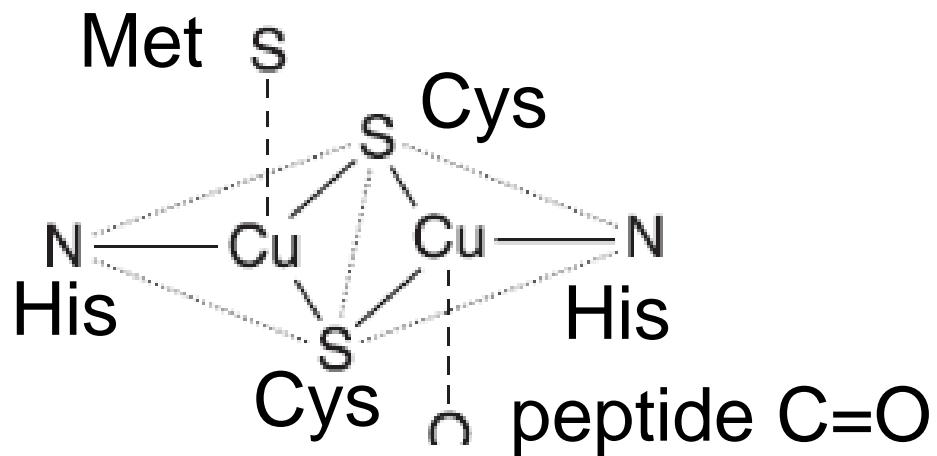
rusticyanin (680)

blue copper (180/370)

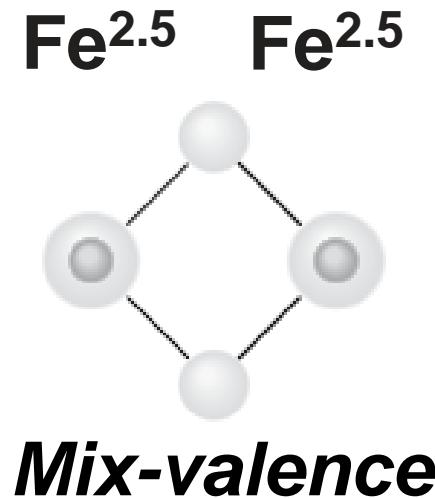
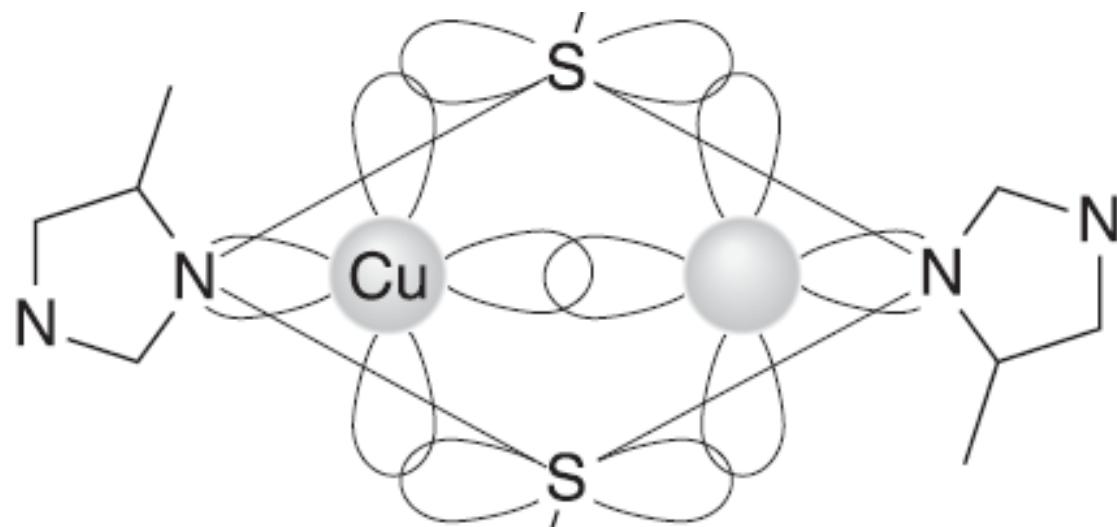
Lu group (UIUC)  
*Nature* 2009, 462, 113.

CuA

- Contains a diamond structure (with **2 Cu ions & 2 Cys**) and was found only as a **domain** in multidomain proteins, e.g. the Cu<sub>A</sub> domain in cytochrome c oxidase.
  - Cu<sub>A</sub> in the oxidized state: **purple**.
  - Consensus sequence:  
**Cys-X-Cys-X<sub>m</sub>-His-X<sub>n</sub>-Met**



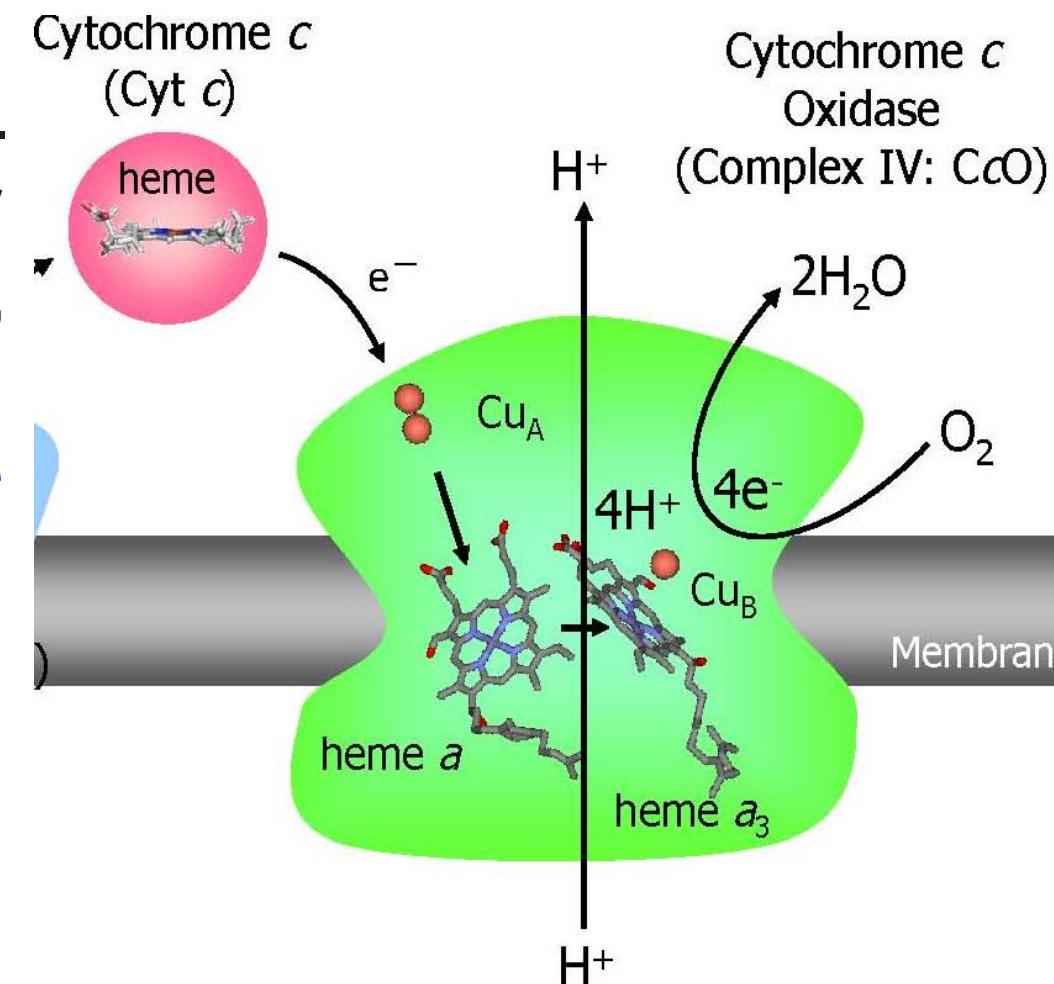
- The unpaired electron in the **oxidized** form is **shared between the 2 Cu centers** due to the orbital overlapping: a **mixed-valence state** of a **Cu(II)** & a **Cu(I)** (*i.e.* **Cu<sup>1.5</sup>**). (Valence delocalization over iron metals was observed in some Fe-S clusters.)
- **2 Cu(I)** in the **reduced** form.
- **Delocalization** over several atoms upon reduction may help **reduce reorganization energy**.



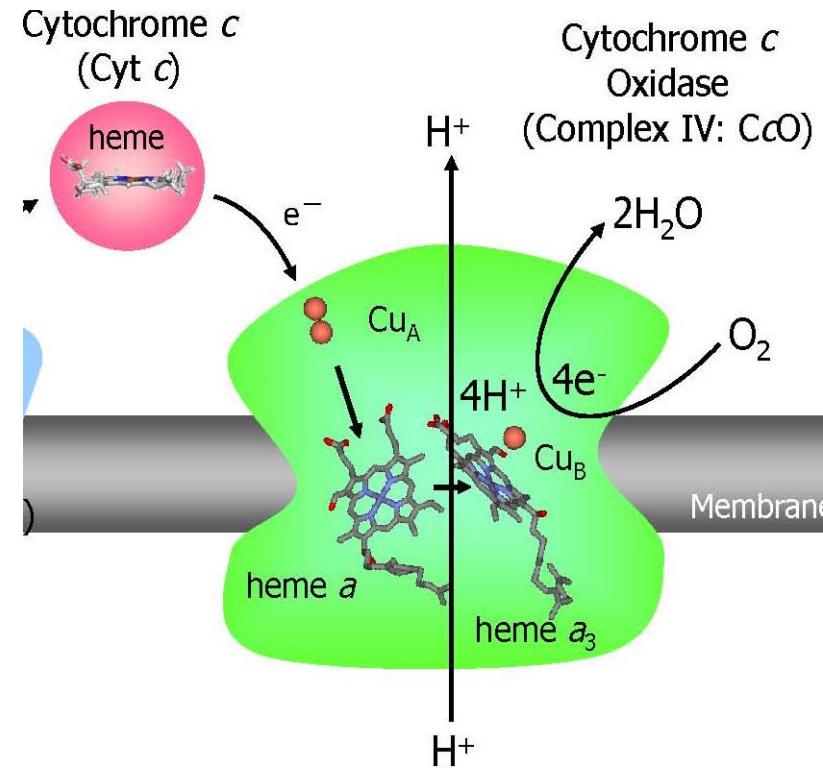
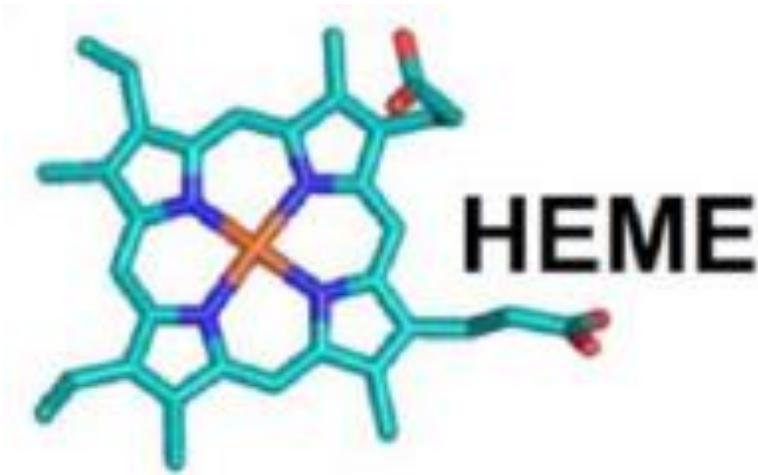
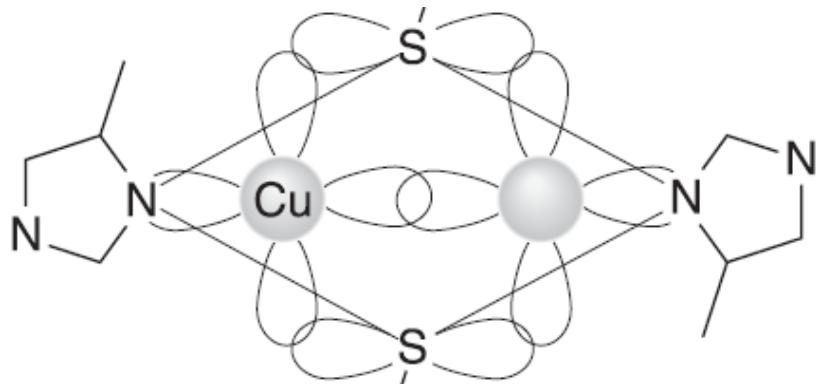
# The Cofactors

- General ET process: **Donor metal center** → donor protein matrix → its surface → acceptor protein surface → acceptor protein matrix → **acceptor metal center**.

- When the **medium** (e.g. cofactors, proteins, water molecules) is **conducting**, an electron can **travel very fast over very large distances**.

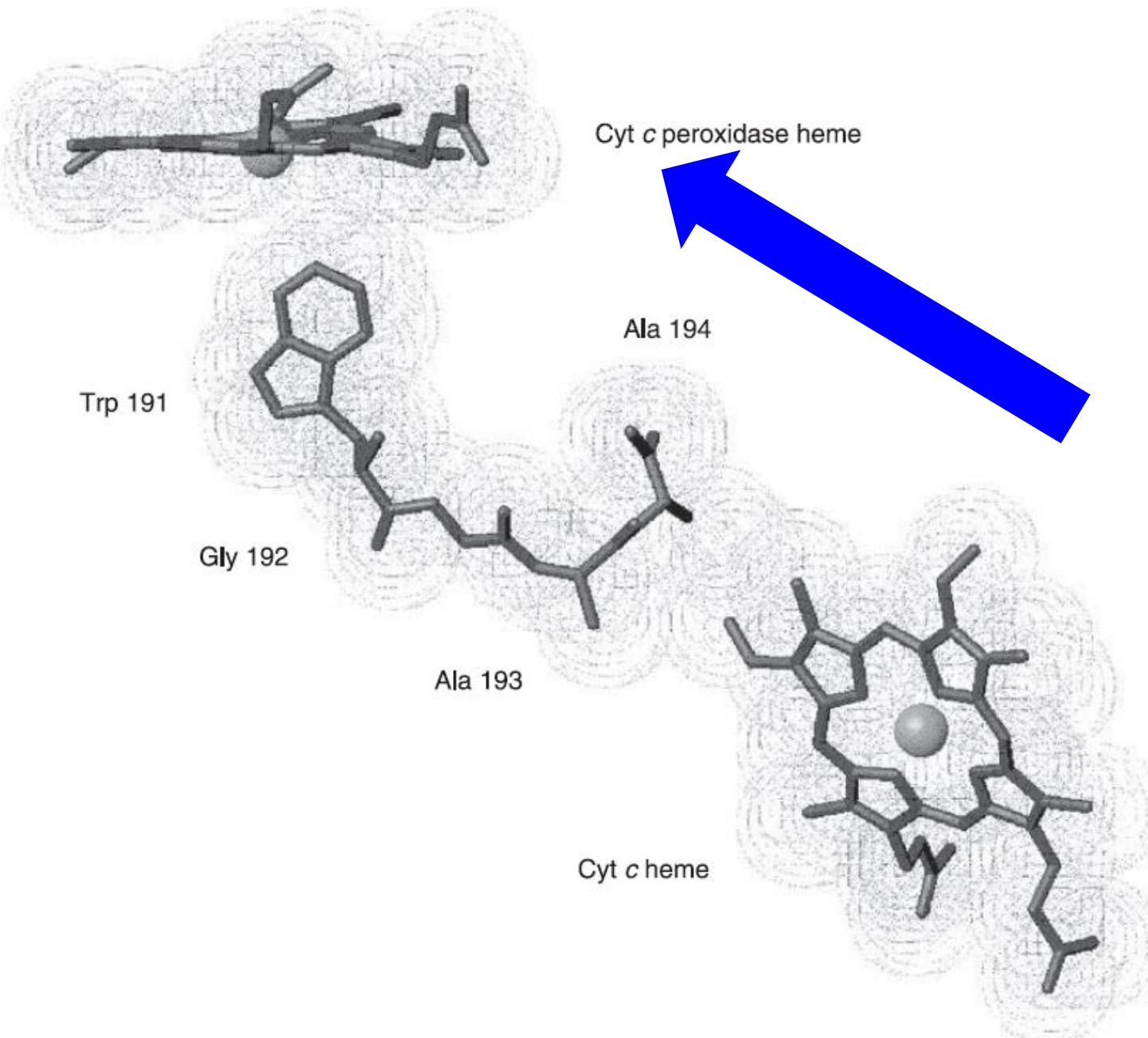


# The Cofactors

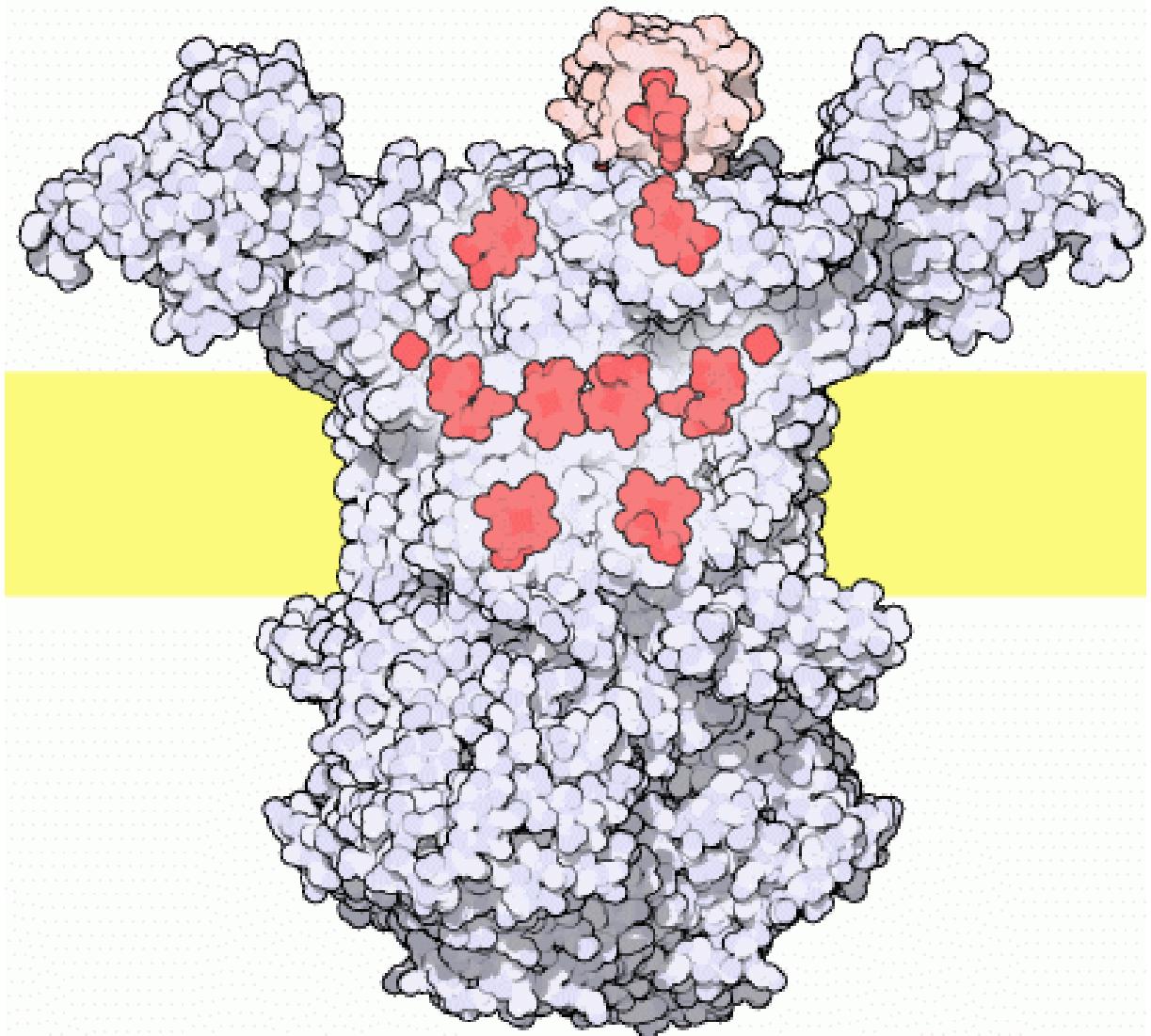


- ET *slows* down for a **long pathway**. So, Nature uses **cofactor(s) or ligands** to **shorten** the pathway. E.g.  $\pi$ -bonds of **His rings** (Cu proteins: ~9-12 Å), **Fe-S** (2Fe-2S: ~6 Å), or a **heme** (~12 Å) as a **ET conductor**.

# Proposed ET Pathway (Cytochromes)

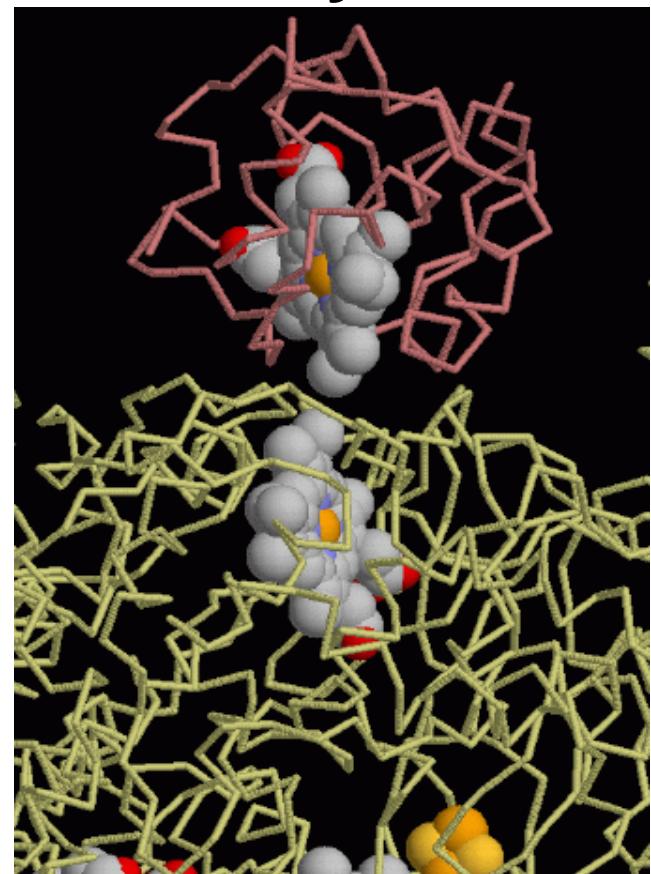


**Cyt c**



**Cyt  $bc_1$**

**Cyt c**



**Cyt  $bc_1$**

Doi:10.2210/rcsb\_pd  
b/mom\_2002\_12

# **ET in Respiration**

# ATP

- The **energy source (“currency”)** in plants, animals, and microorganisms: adenosine triphosphate (**ATP**).



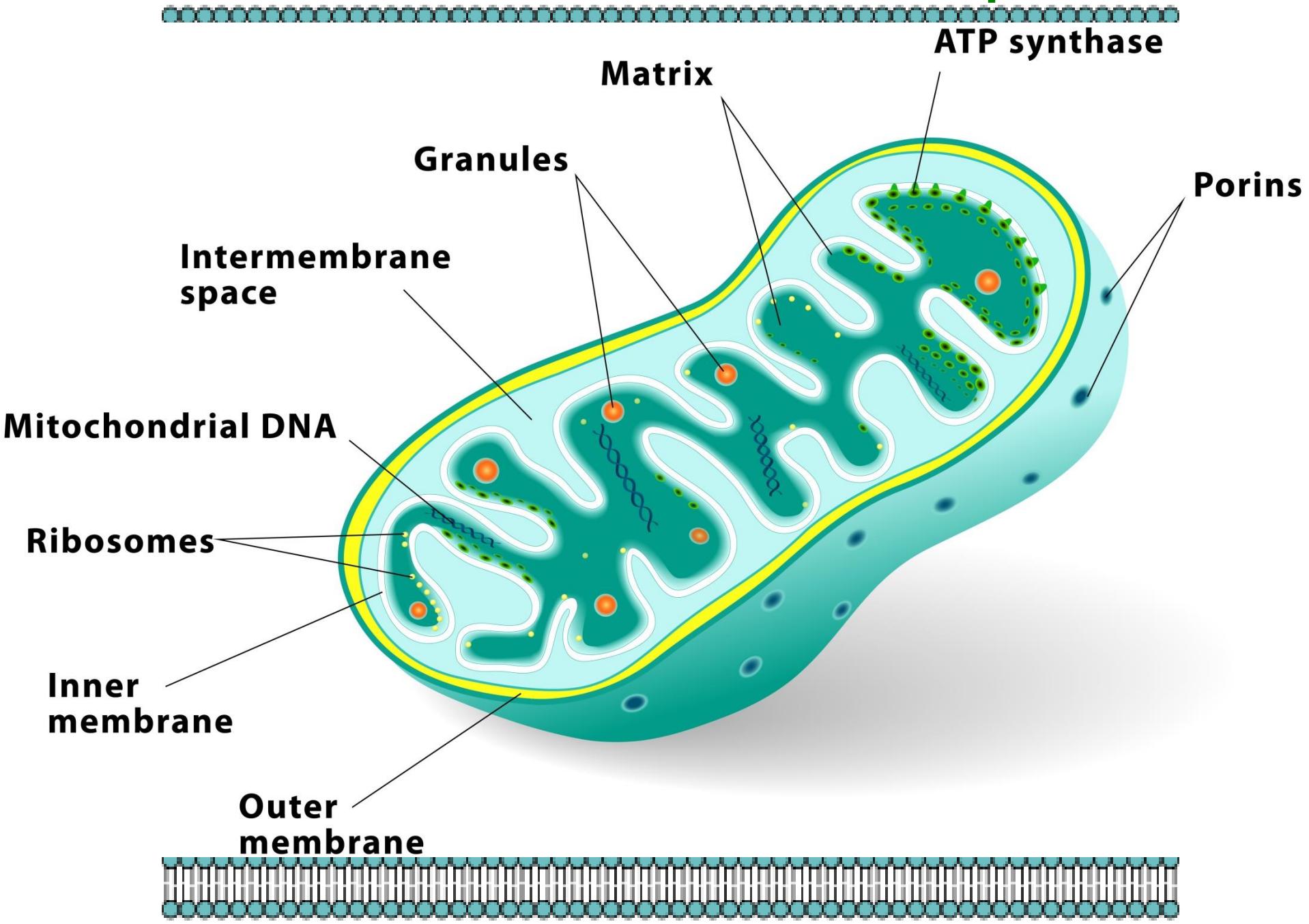
- The above process can release ~8 kcal of energy.

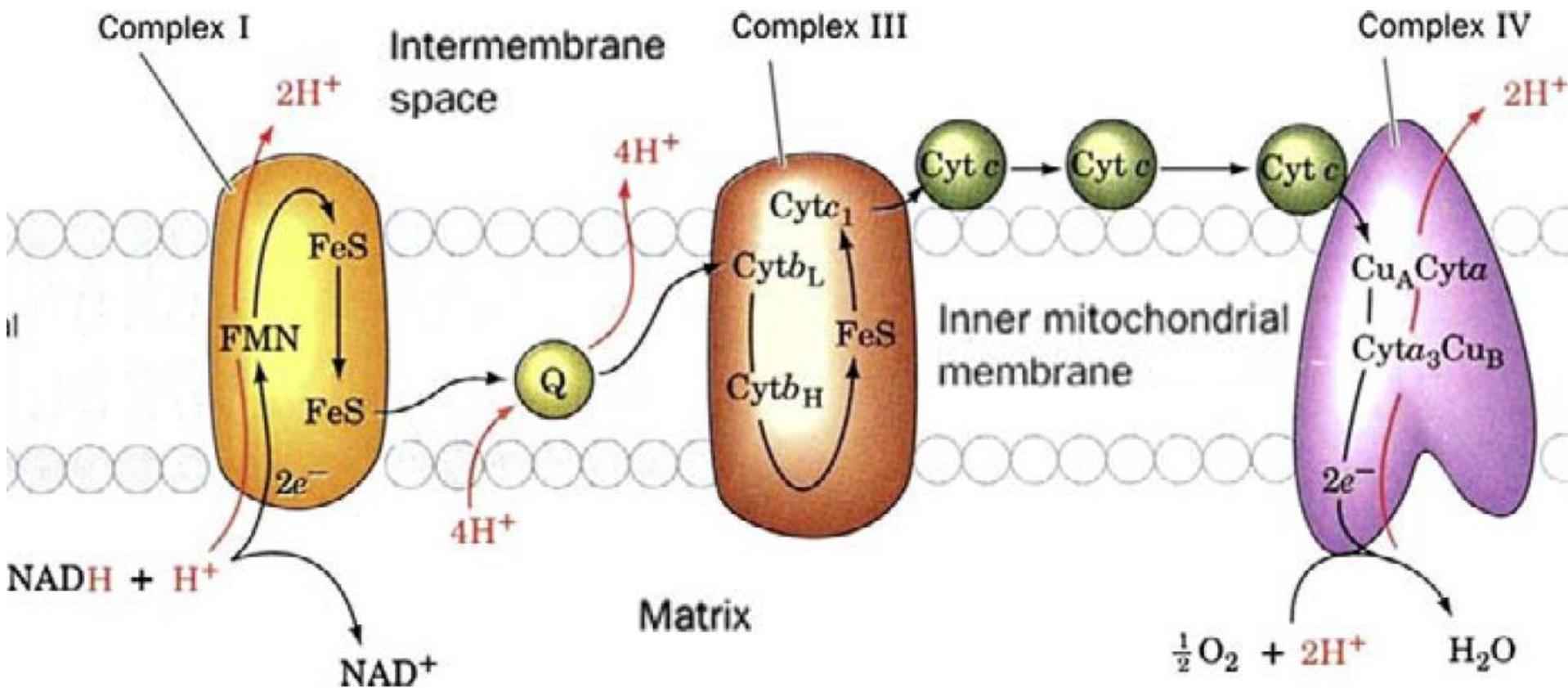
Polypeptide + amino acid → polypeptide elongated by one amino acid  
**endergonic** by ~32 kcal

Polypeptide + amino acid + 4 ATP → new polypeptide + 4 ADP + 4 Pi  
The overall reaction can occur with 4 ATPs

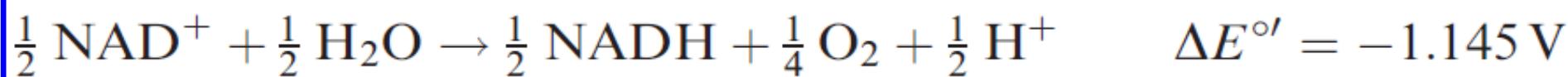
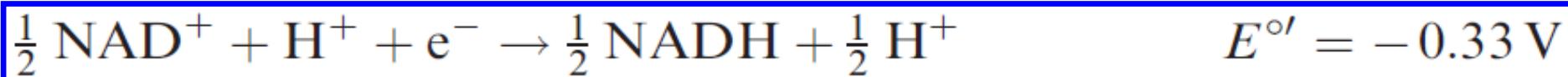
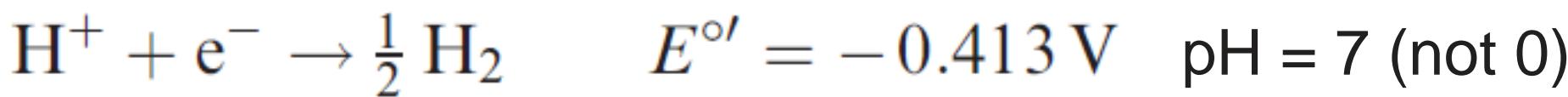
- **Photosynthesis** (in plants, algae, & photosynthetic bacteria) & **respiration** (in these organisms, animals & bacteria) facilitates **ATP formation**.
- Both processes have some common features: **Proton transfer + electron transfer & O<sub>2</sub>** involved for **ATP formation**.

# The Mitochondrial ET Chain in Respiration

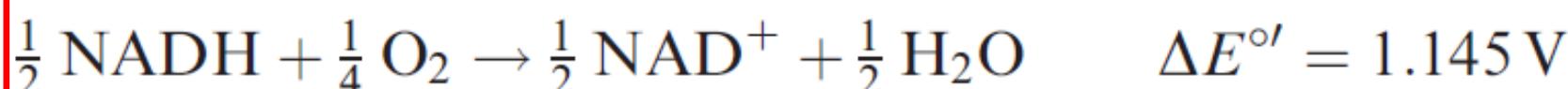
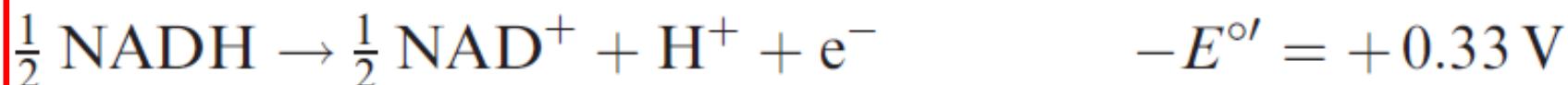




- With **proton & electron transfers**, **O<sub>2</sub>** is **reduced to water** in **respiration**. The soluble cofactor **NADH** (or NADPH) is used as a **carrier (donor)** of electrons & protons.

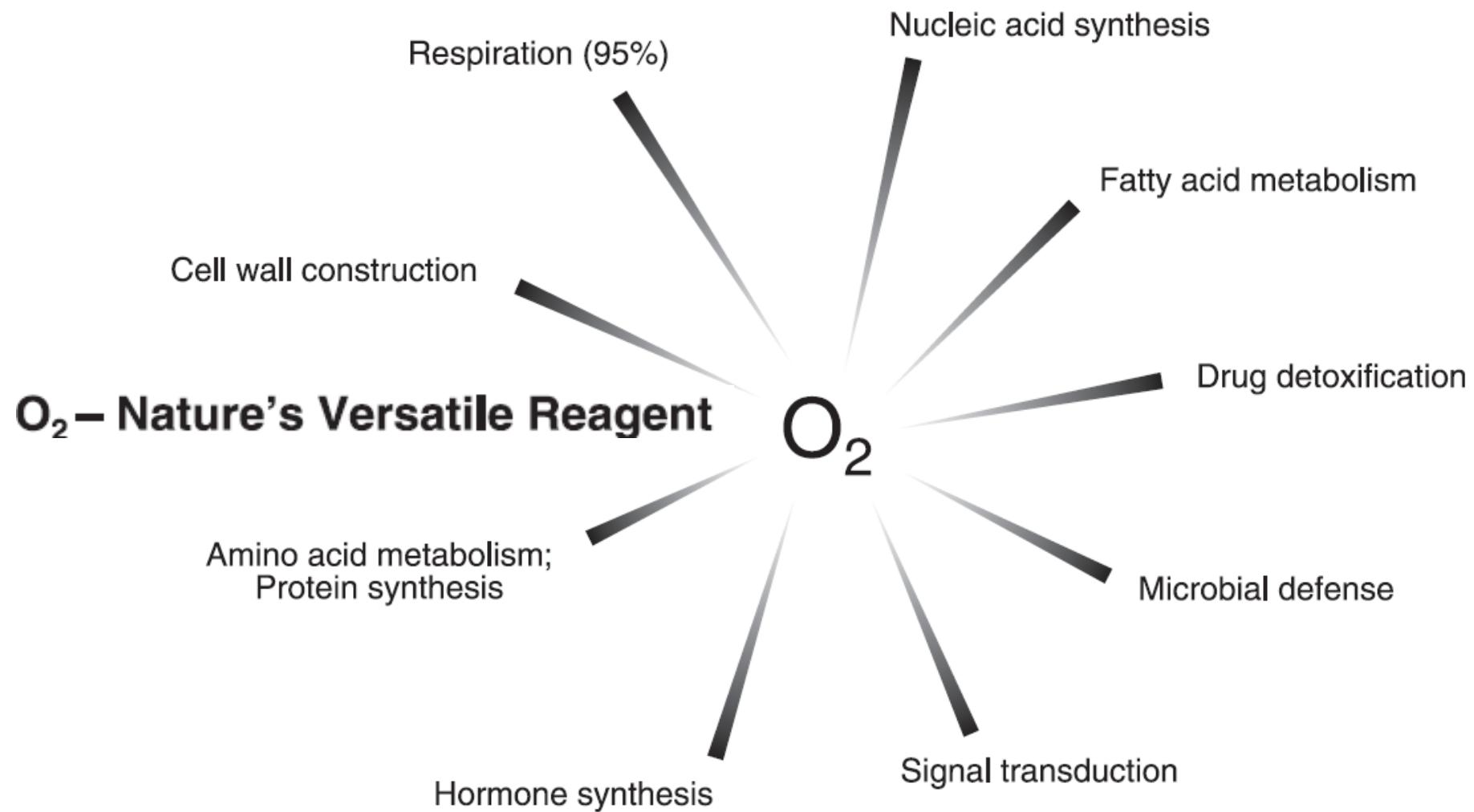


**Unfavorable** by using **H<sub>2</sub>O** as an **electron-donor**



**Favorable** by using **O<sub>2</sub>** as an **electron-acceptor**

- Biochemical oxidation of food stuffs offers a strong reductant NADH for respiration. Extra **energy** (26.3 kcal/mol) is released from the reduction of ~90 %  $O_2$  to promote **ATP formation (H<sup>+</sup> required)** in respiration.



- Both photosynthetic and respiratory systems use a *chain of redox cofactors* that *gradually change their reduction potentials*

from

the **most reducing** compound

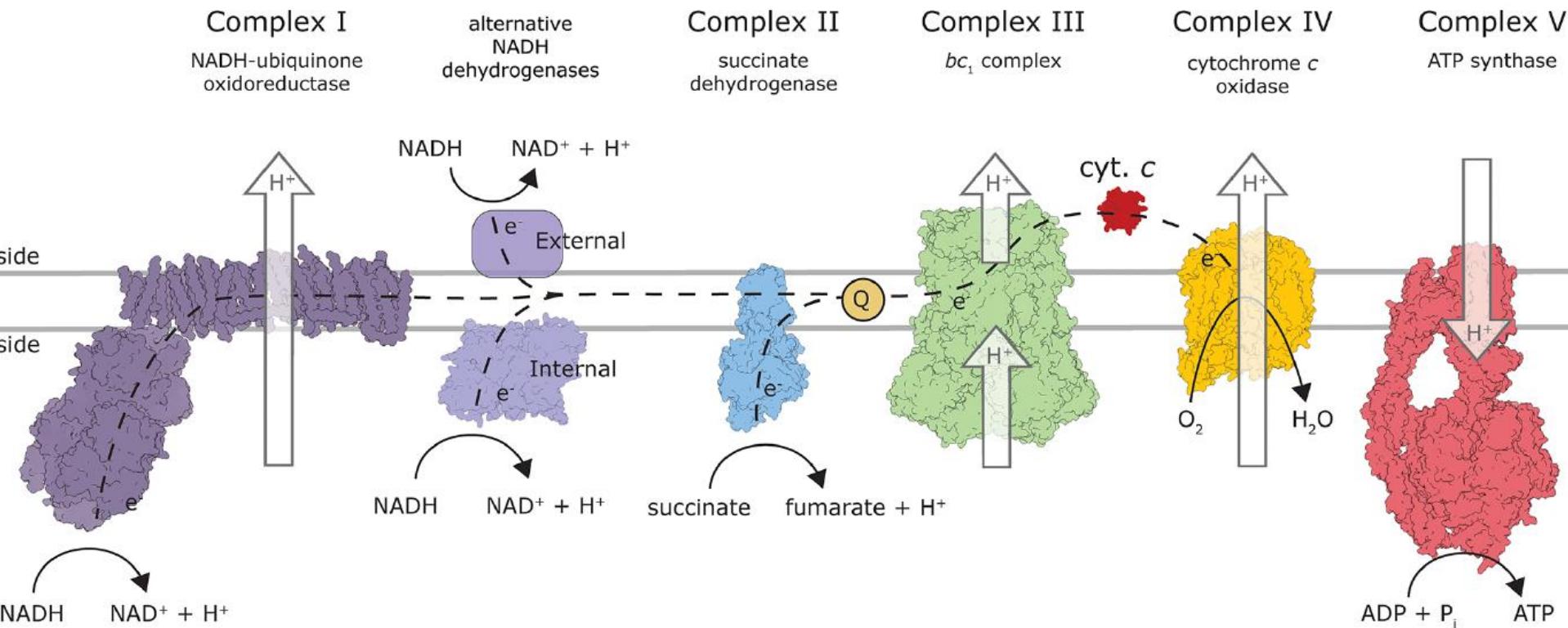
(**NADH** in respiration or **H<sub>2</sub>O** in photosynthesis)

to

the **most oxidizing** terminal component

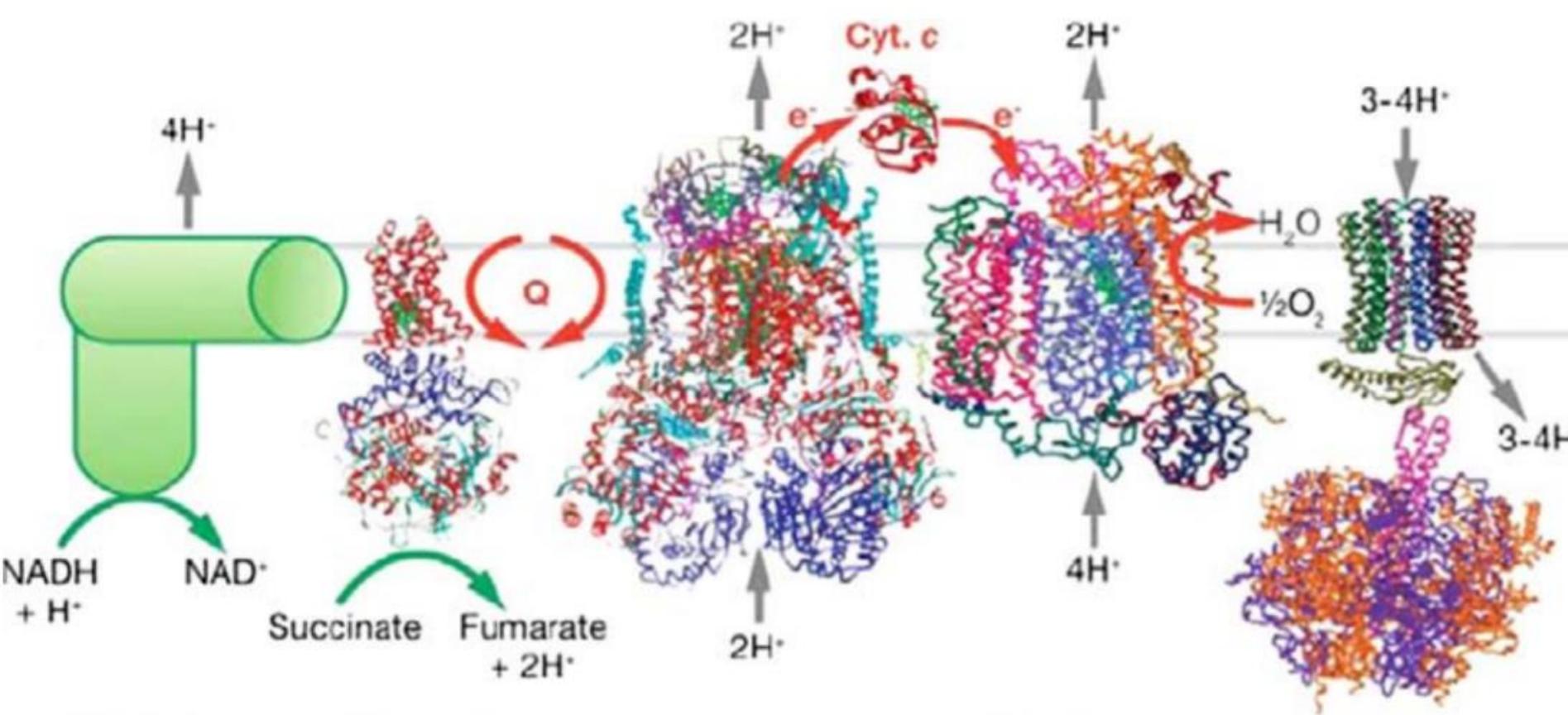
(**O<sub>2</sub>** in respiration & **P700<sup>+</sup>** in oxygenic photosynthesis).

# The Mitochondrial Respiratory Chain



Brzezinski Chem.  
Rev. 2021, 9644.

- 3 metalloproteins **pump  $\text{H}^+$**  across a membrane in series: different redox centers with different potentials → transfer  $e^-$  to the next complex for further using energy.



**Complex I:** NADH-Ubiquinone Oxidoreductase

**Complex II:** Succinate-Ubiquinone Oxidoreductase

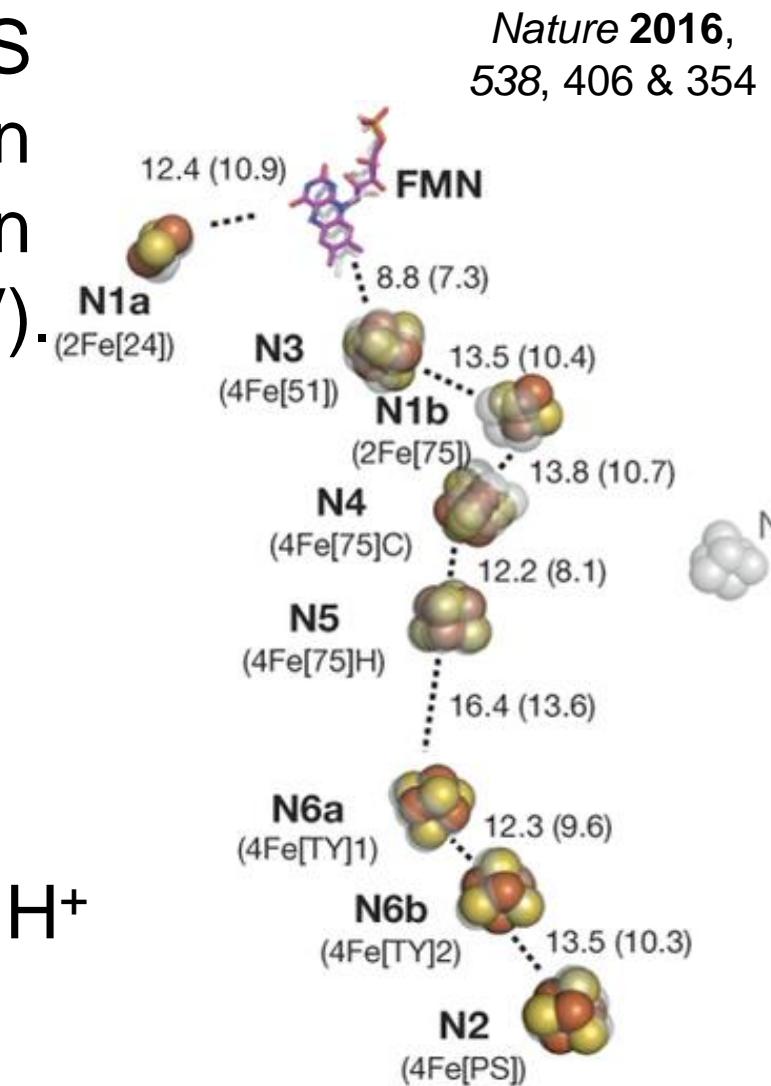
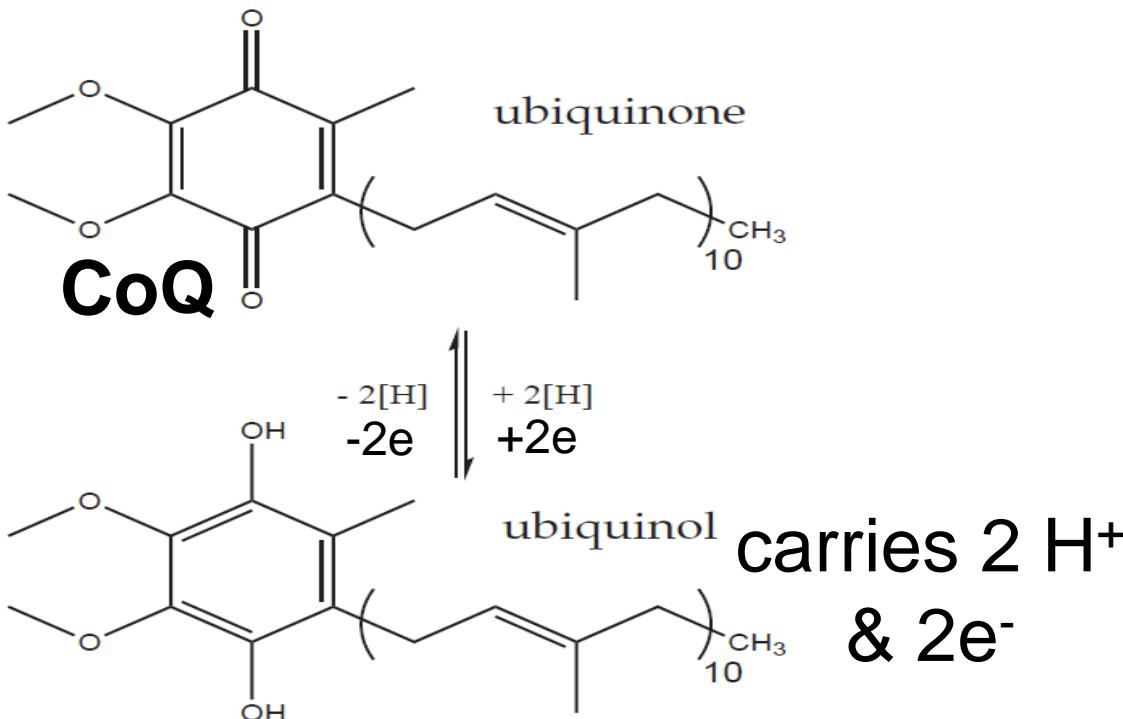
**Complex III:** Ubiquinol-Cytochrome c Oxidoreductase

**Complex IV:** Cytochrome c Oxidase

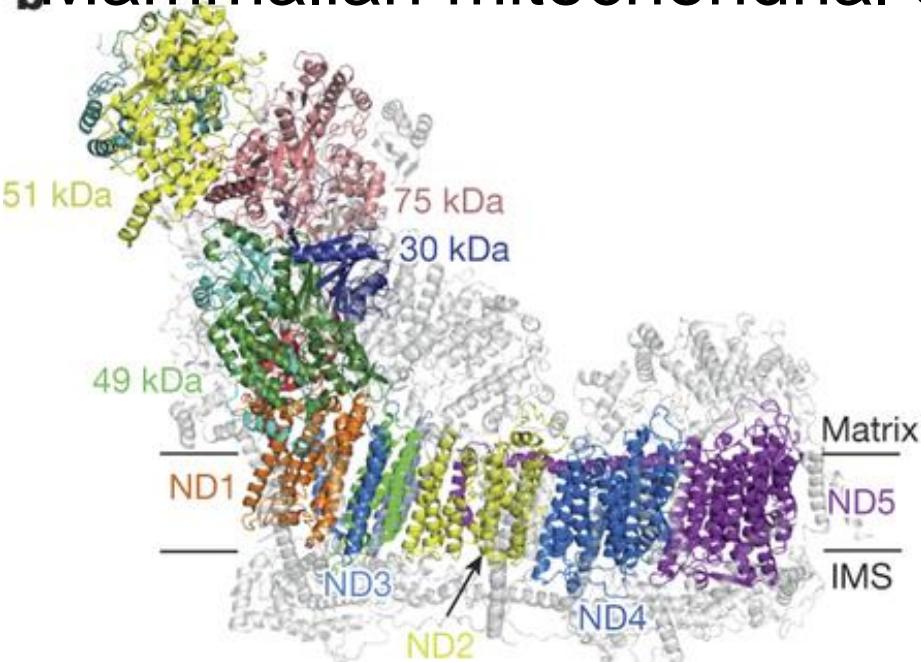
**Complex V:** ATP Synthase

# Complex I: NADH-Ubiquinone Oxidoreductase

- Delivers electrons to a small lipid-soluble acceptor **ubiquinone (CoQ)** to form **ubiquinol**. A flavin mononucleotide (FMN) & 9 Fe-S centers are used for ET between **NADH** (highest-potential electron source, -0.33 V) & CoQ (~0.04 V).

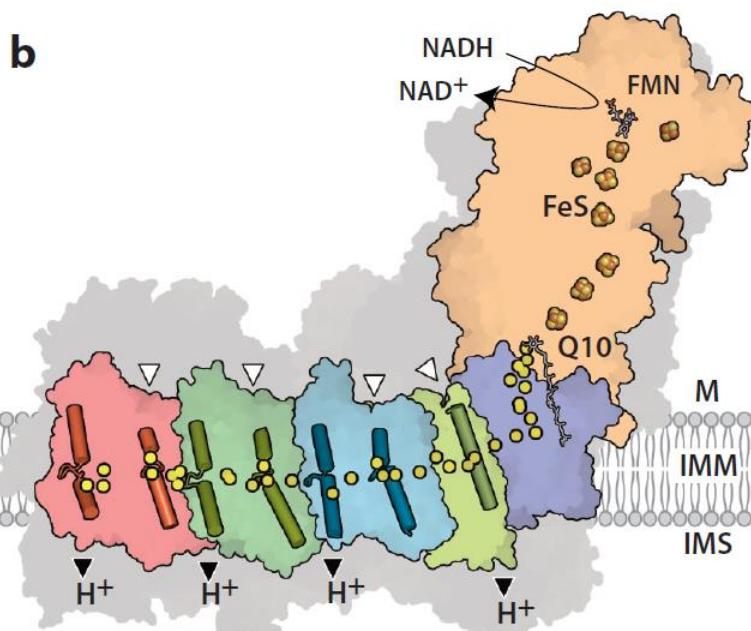
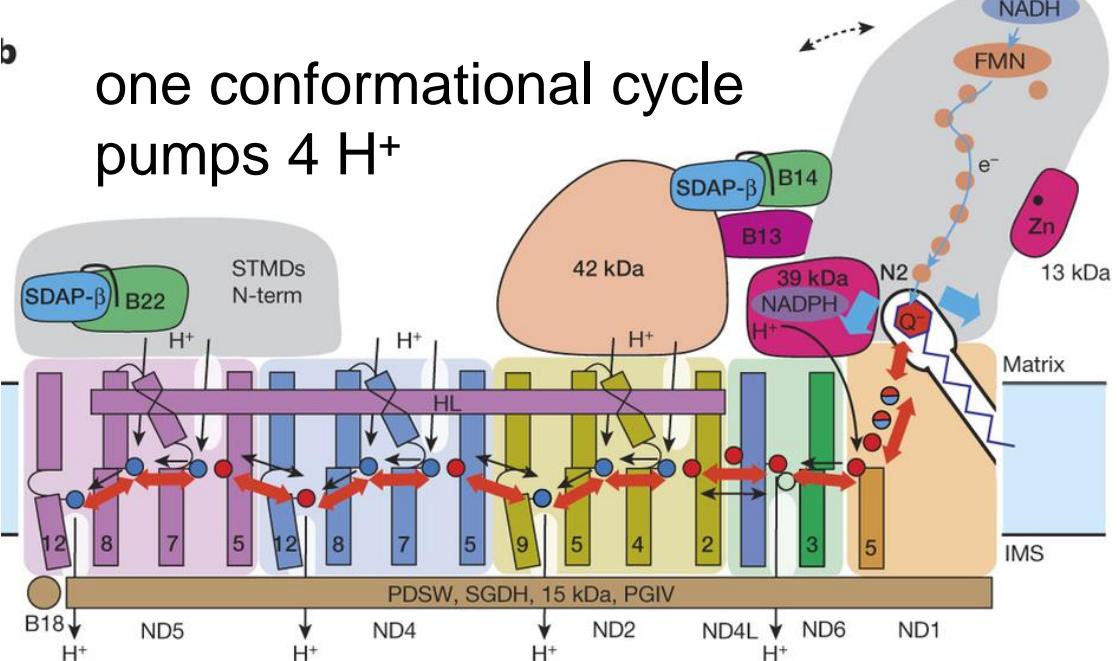


# Mammalian mitochondrial complex I (Cryo-EM, 3.9 Å)

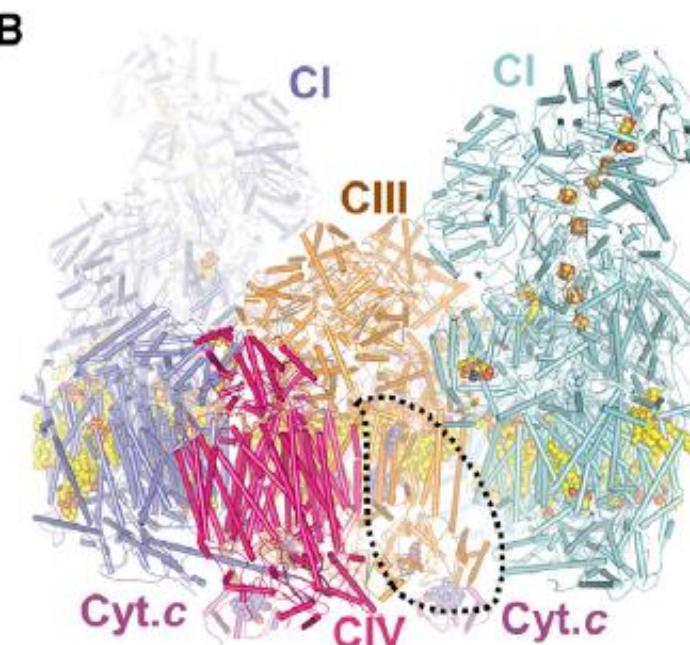
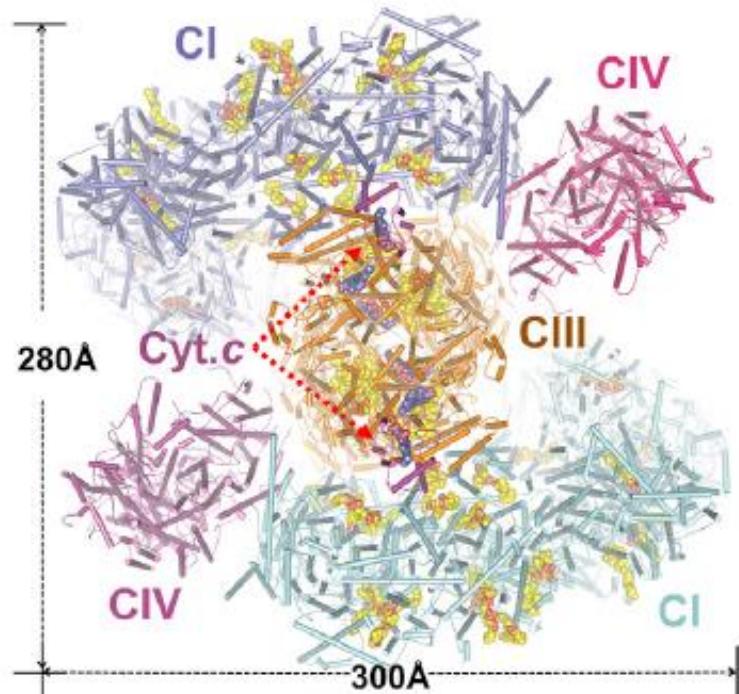
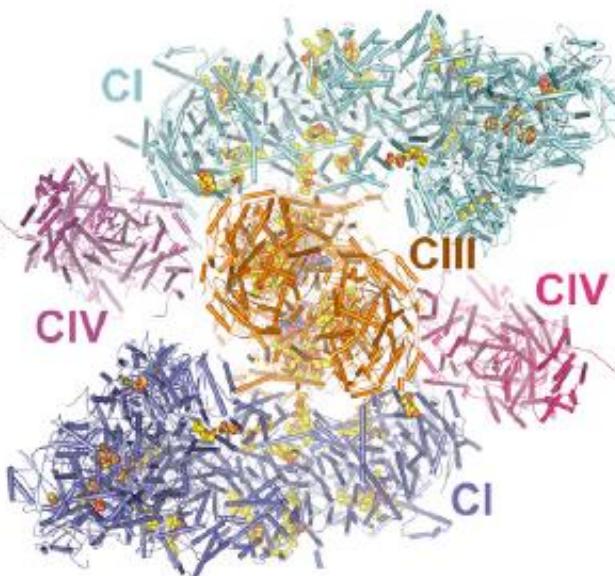
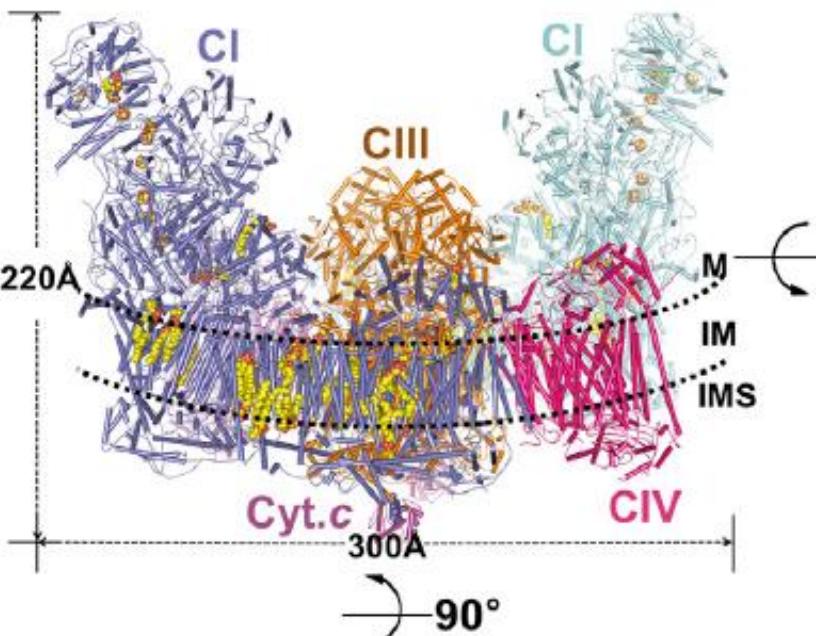


- A redox potential for CoQ: 0.04 V → a loss of potential energy (~0.3 V, 6.9 kcal/mol) → **pump protons** (possibly via conformational change).

one conformational cycle pumps 4 H<sup>+</sup>



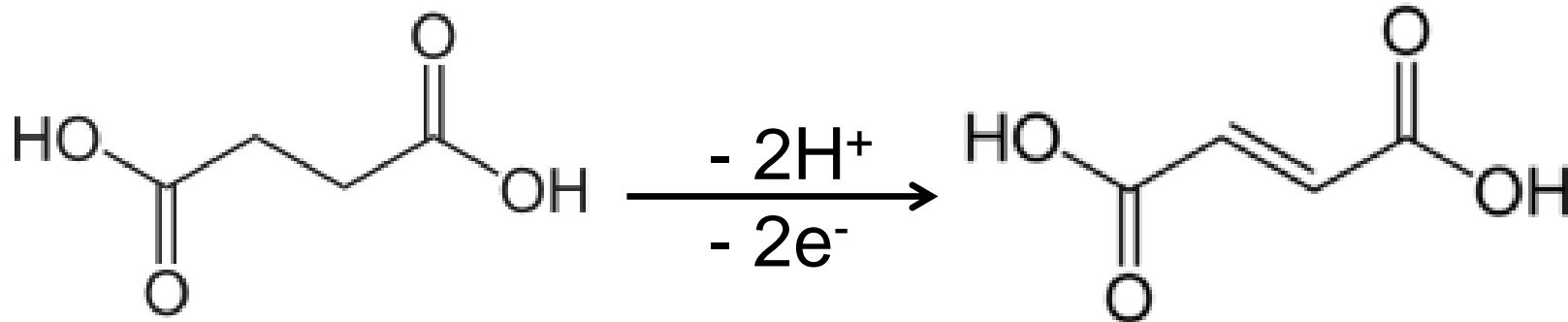
# Human mitochondrial Respiratory Megacomplex $I_2III_2IV_2$ (Cryo-EM)



Maojun Yang  
Cell 2017, 1247,

## Complex II: Succinate-Ubiquinone Oxidoreductase

- This inner-membrane complex is NOT a proton pump, but **another source** of ubiquinol for Complex III, deriving its reducing equivalents from oxidation of succinate to **fumarate** ( $E = 0.1 \text{ V}$ ).

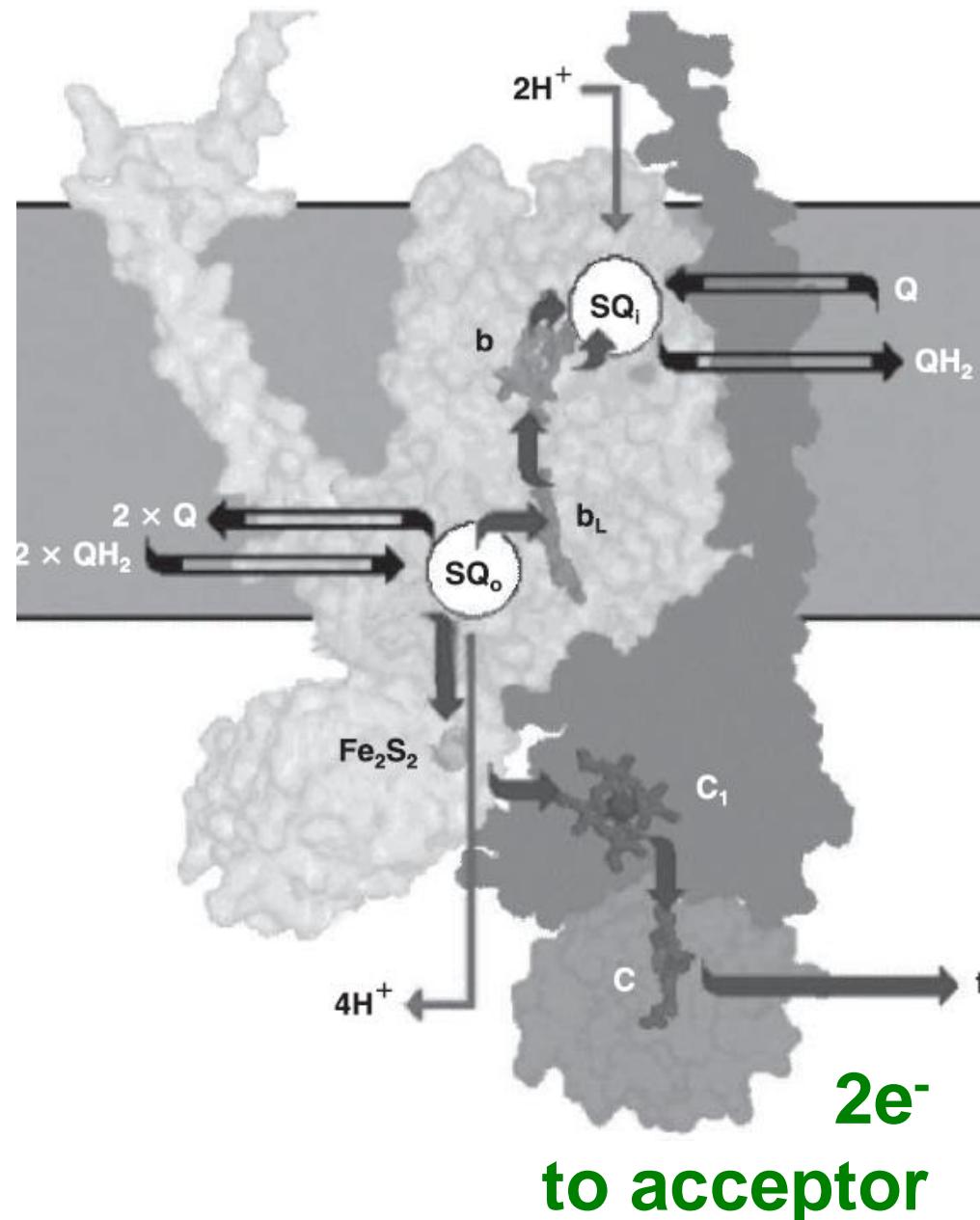


# Complex III: Ubiquinol-Cytochrome c Oxidoreductase

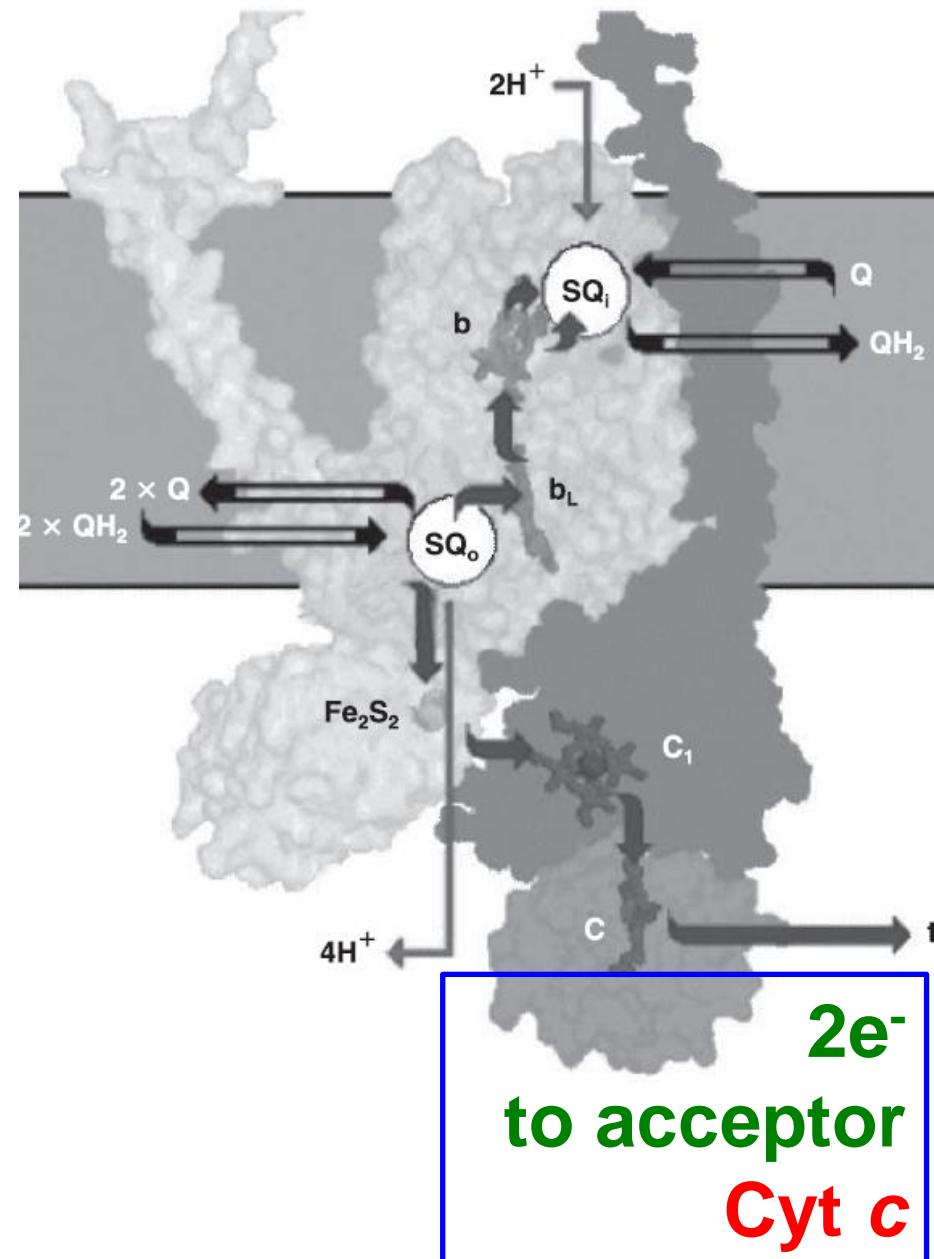
- Electrons from Complex I in an **ubiquinol** form still store potential energy for **proton-pump** in Complex III.

- Contains 2 *b*-type hemes, 1 Rieske (Fe-S) center, & 1 *c*-type heme (Cyt *c*<sub>1</sub>).

- At least 2 binding sites for quinones, (Q<sub>i</sub>) & (Q<sub>o</sub>).

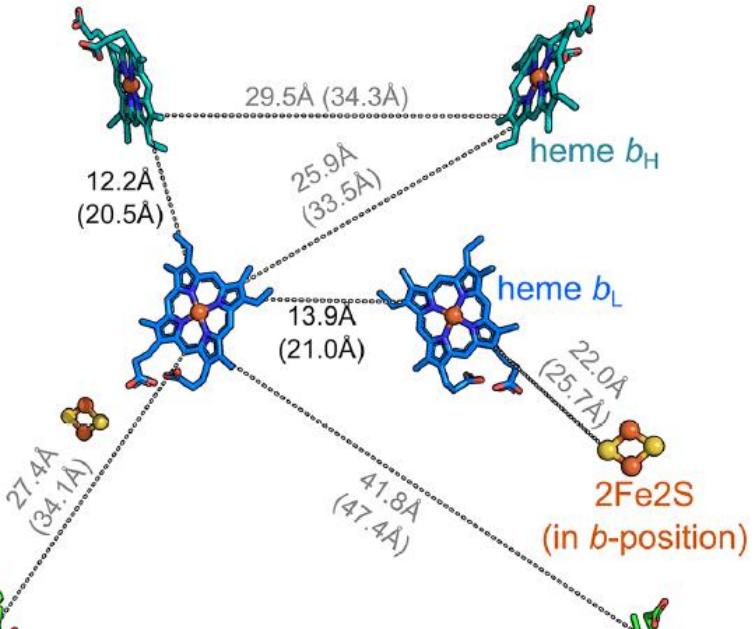
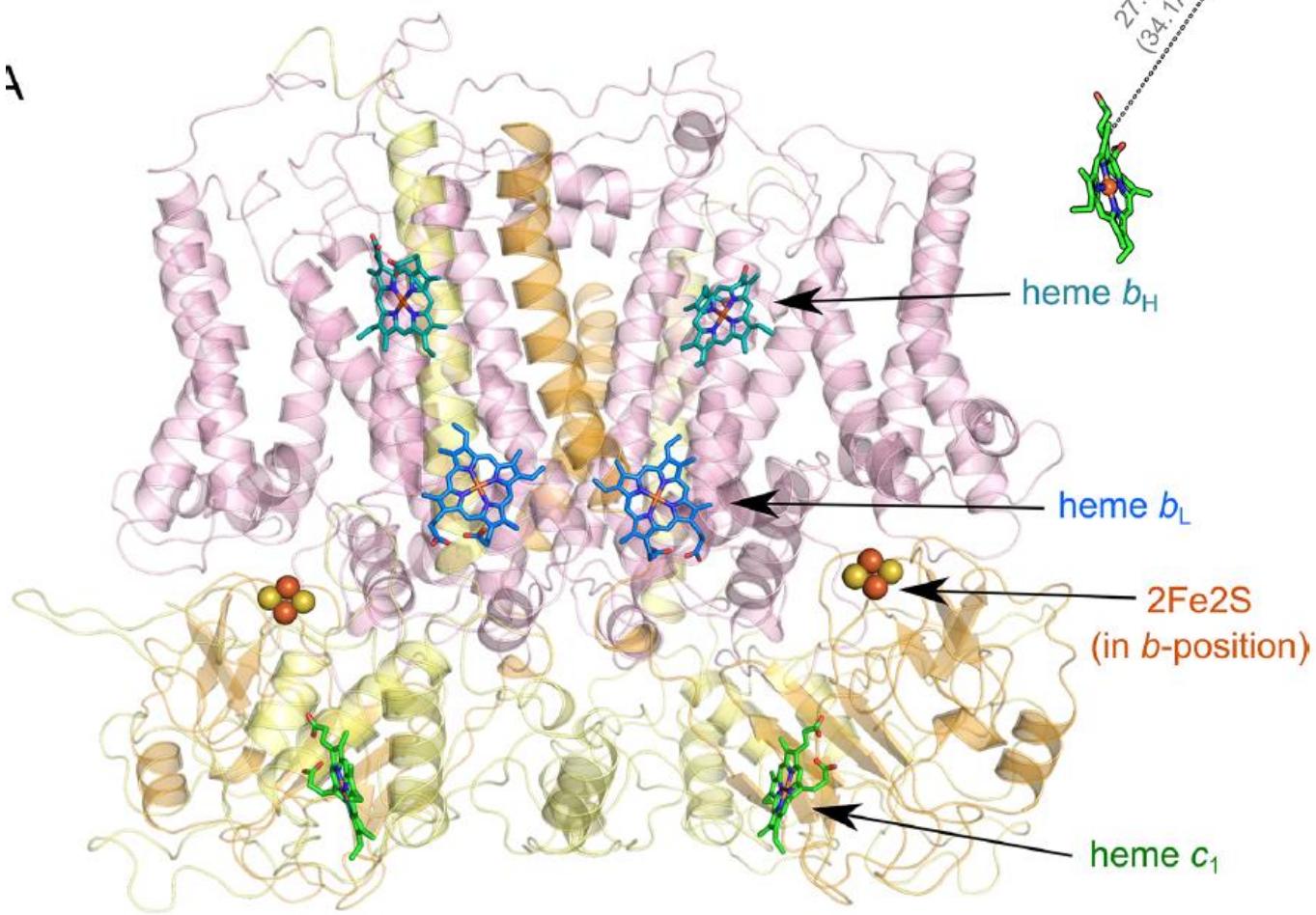


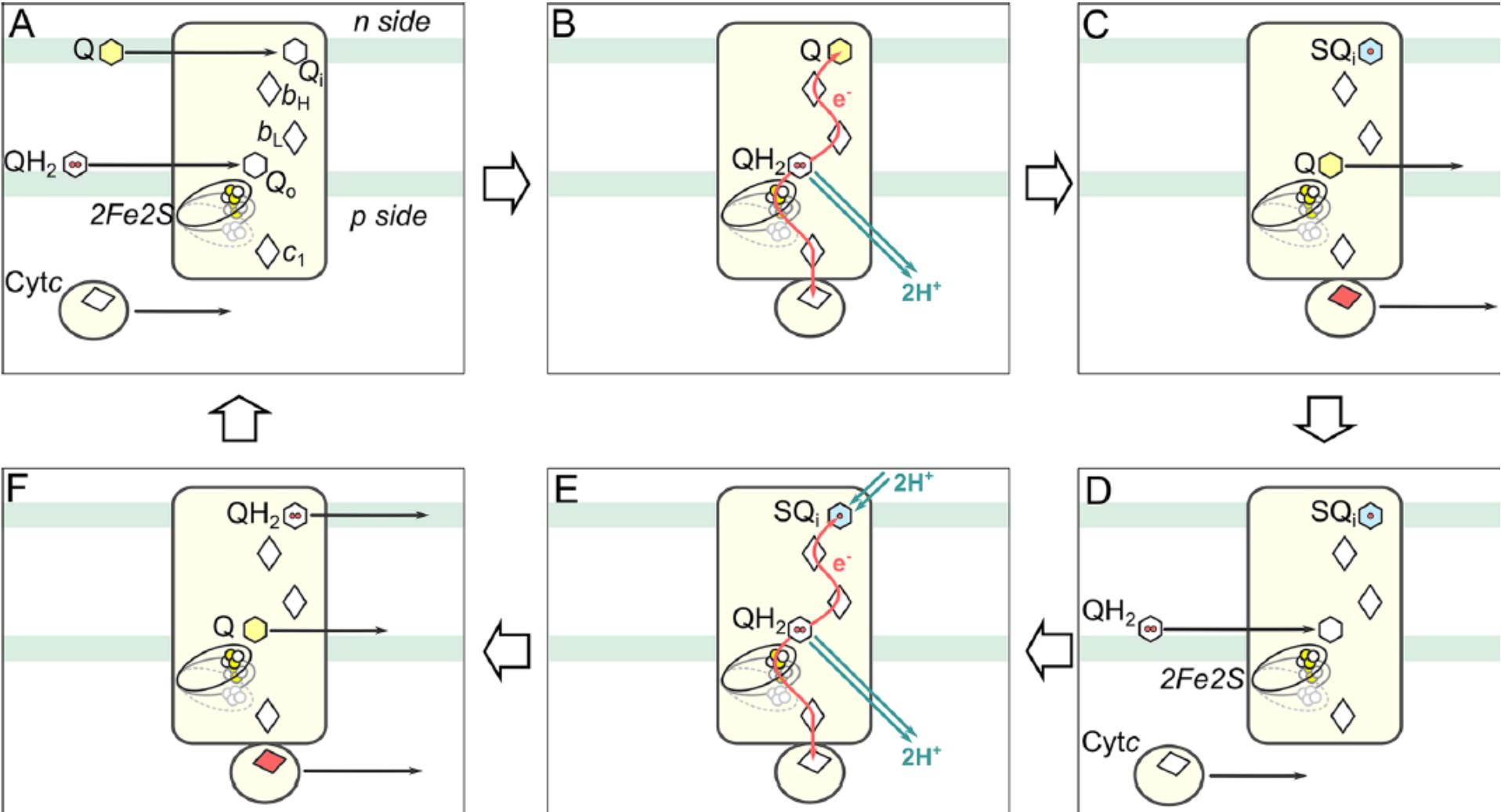
- At least 2 binding sites for quinones, ( $Q_i$ ) & ( $Q_o$ ). .
  - **1<sup>st</sup> ET:**  $QH_2$  ( $Q_o$ )  $\rightarrow$   $Fe_2S_2$  ( $\sim 0.2$  V)  $\rightarrow$  Cyt  $c_1$  ( $\sim 0.23$  V)  $\rightarrow$  **Cyt c** ( $\sim 0.26$  V)
  - **2<sup>nd</sup> ET:** SQ ( $Q_o$ )  $\rightarrow$  Cyt  $b_L$   $\rightarrow$  Cyt  $b$   $\rightarrow$   $Q_i$  site
  - The electrons released to reduce **Cyt c** ( $E = \sim 0.26$  V)  $\rightarrow$  energy change of  $\sim 0.2$  V ( $\sim 5.3$  kcal/mol).



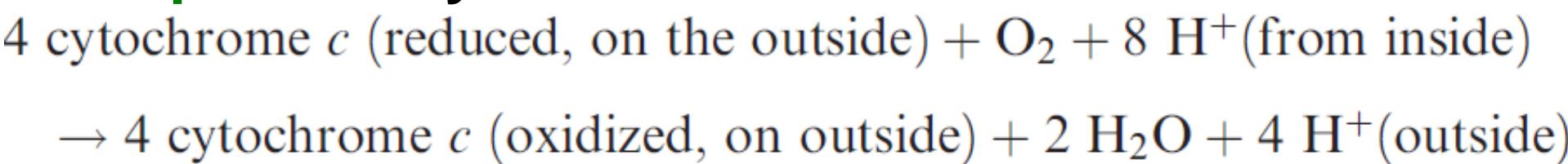
# Cyt<sub>bc1</sub> from *Rhodobacter capsulatus*

A





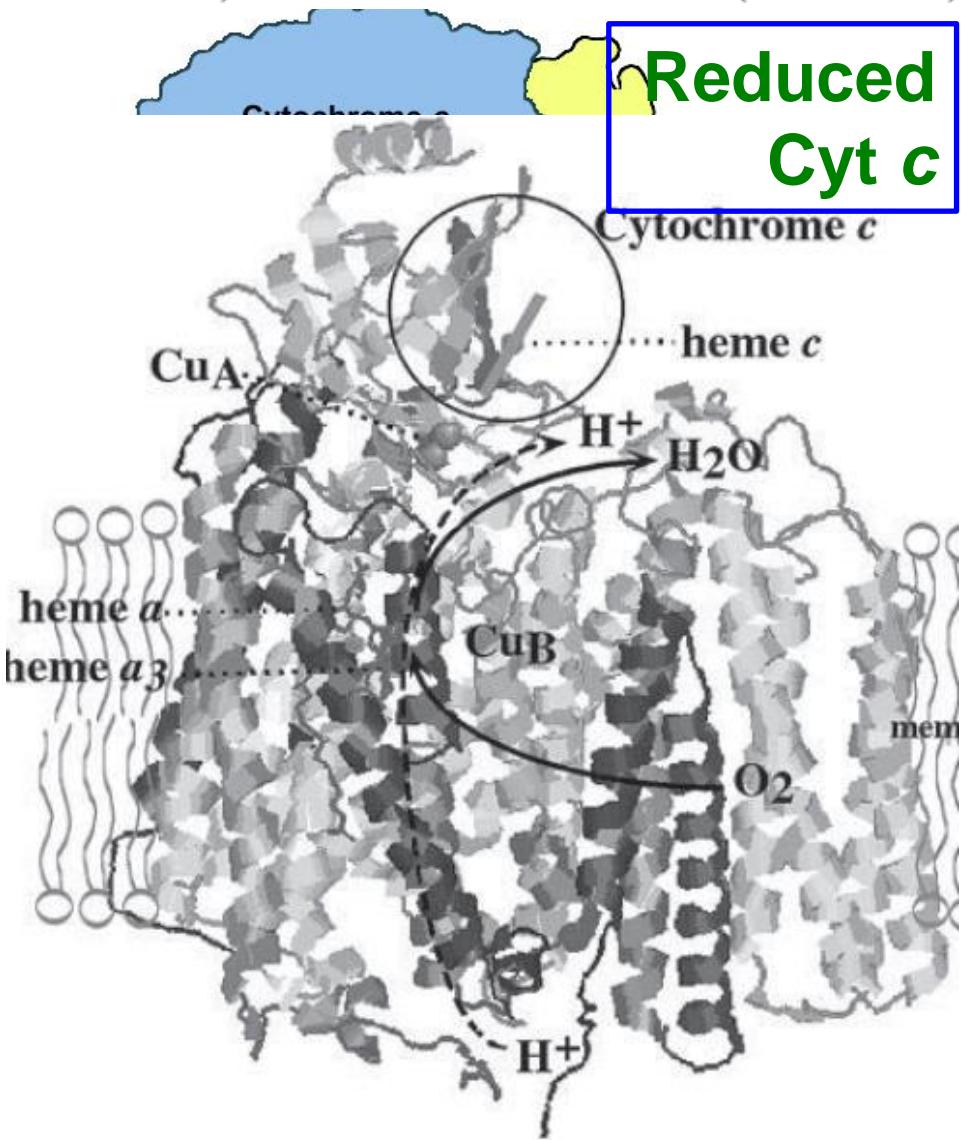
# Complex IV: Cytochrome c Oxidase

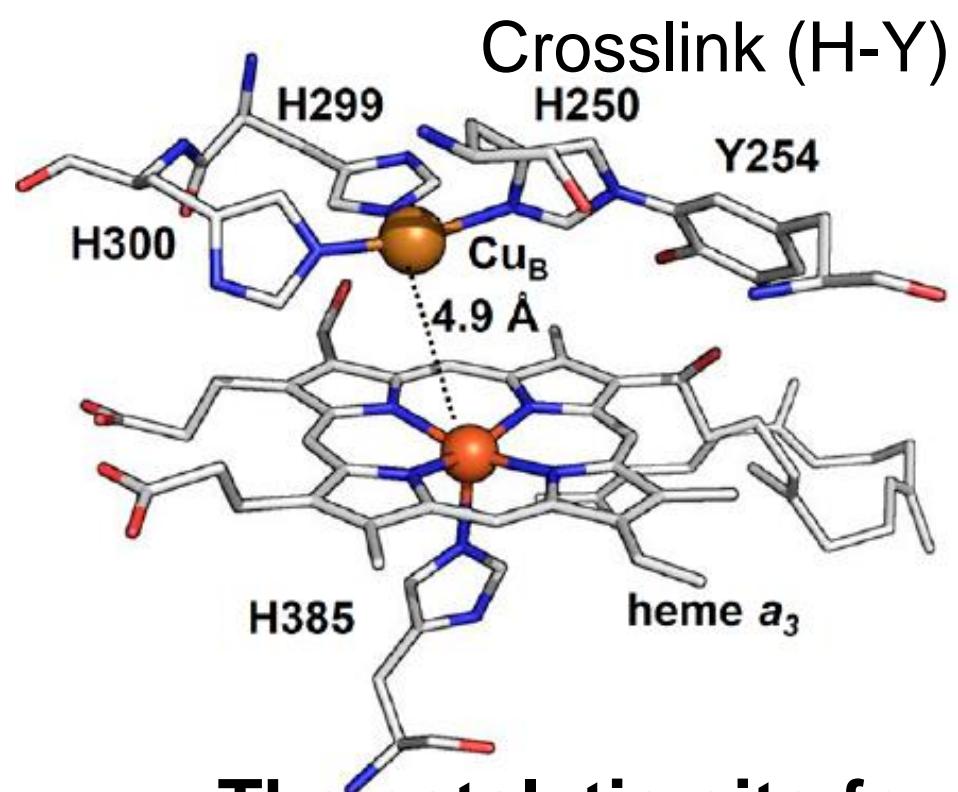
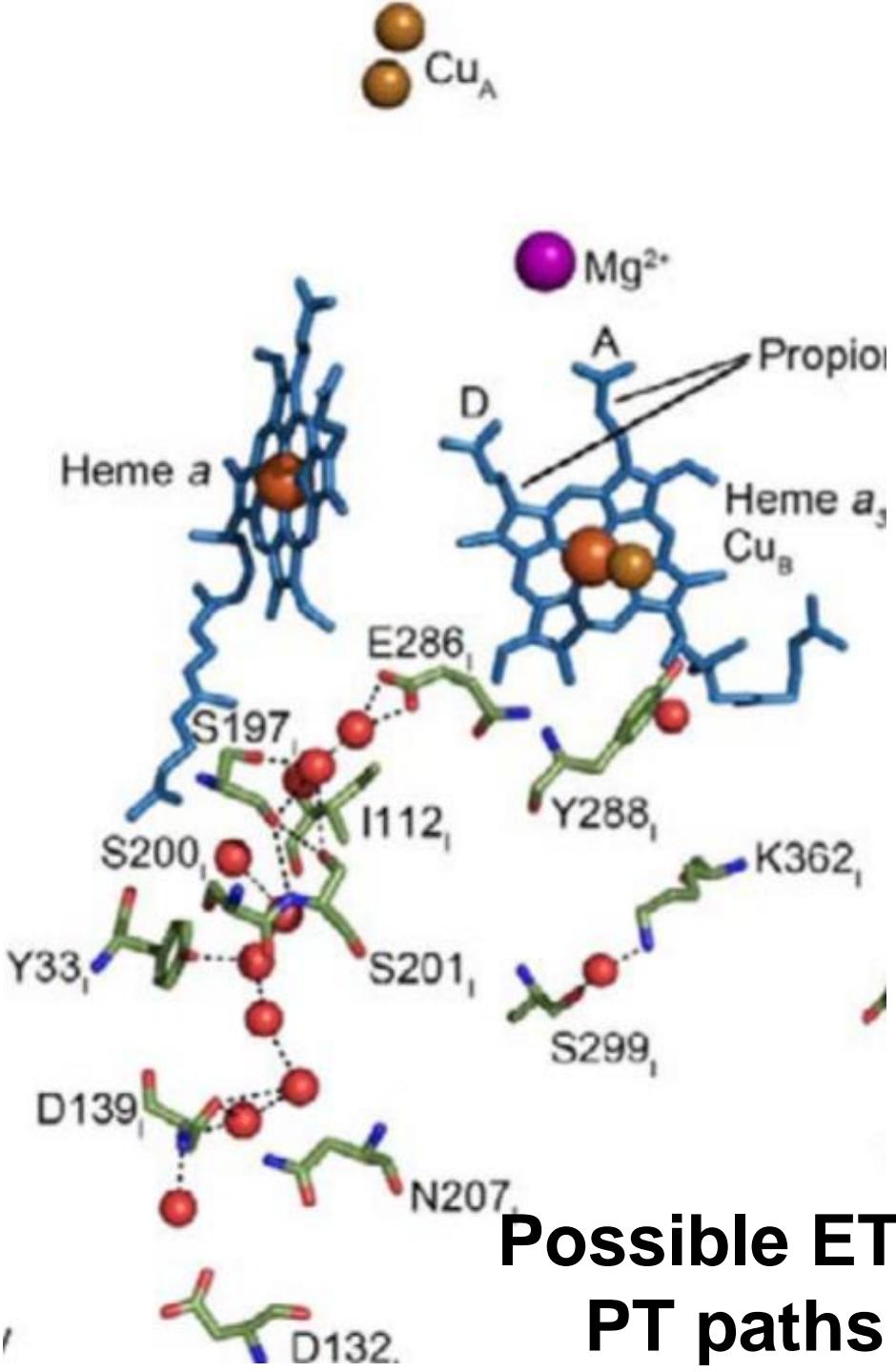


- Contains **Cyt c** (+0.26 V) & its electron acceptor **Cu<sub>A</sub>**, **heme a**, **heme a<sub>3</sub>** & **Cu<sub>B</sub>**.

- With **4e<sup>-</sup>** donated from **Cyt c**, **4 H<sup>+</sup>** are delivered to the heme a<sub>3</sub>-Cu<sub>B</sub> center to reduce **1 O<sub>2</sub>** molecule.

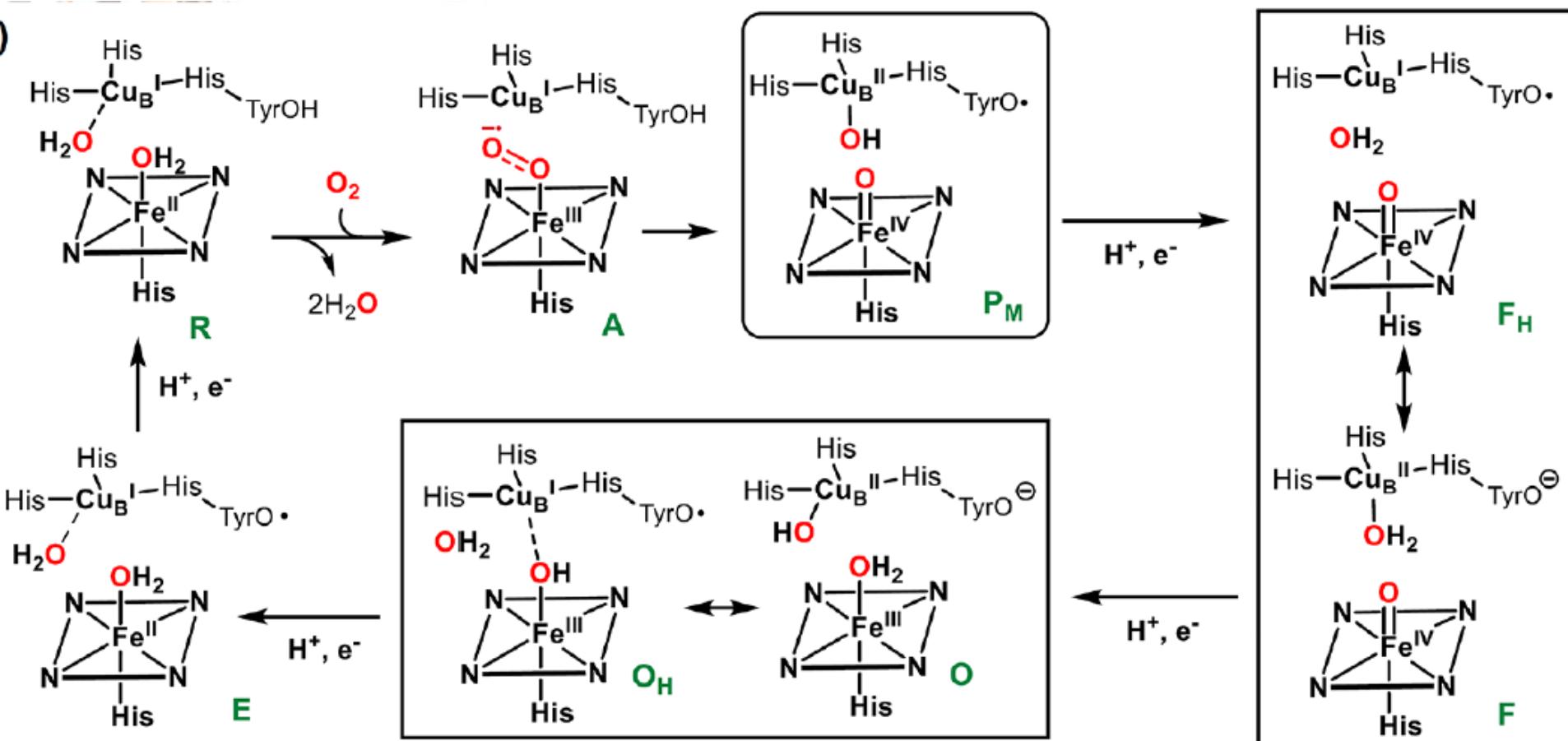
- Another **4 H<sup>+</sup>** are translocated across the membrane.





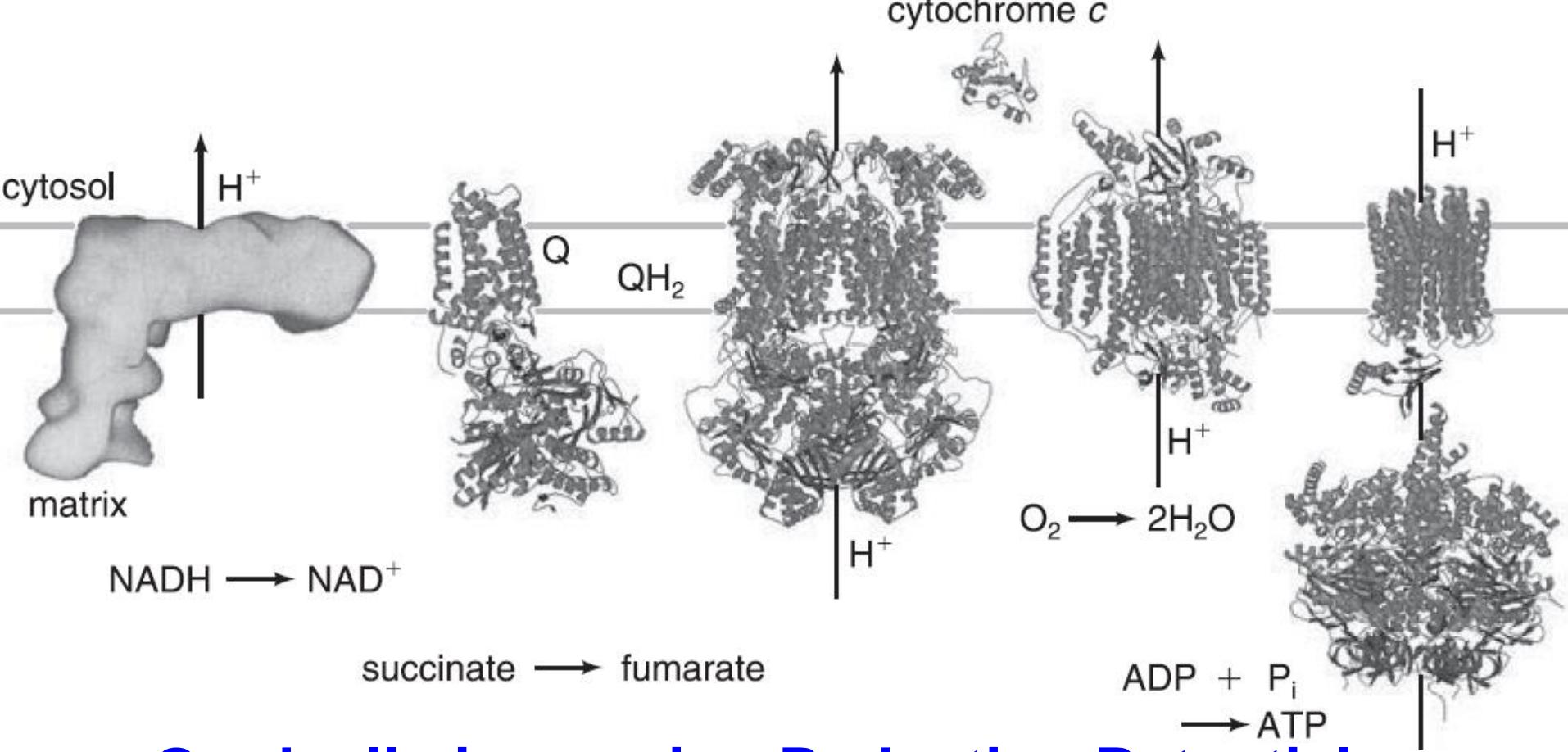
The catalytic site for the  $\text{O}_2$  reduction

- Potential energy change of ~0.59 V  
→ ~54 kcal/mol for reduction of 1  $\text{O}_2$



(Will discuss in detail in part VI)

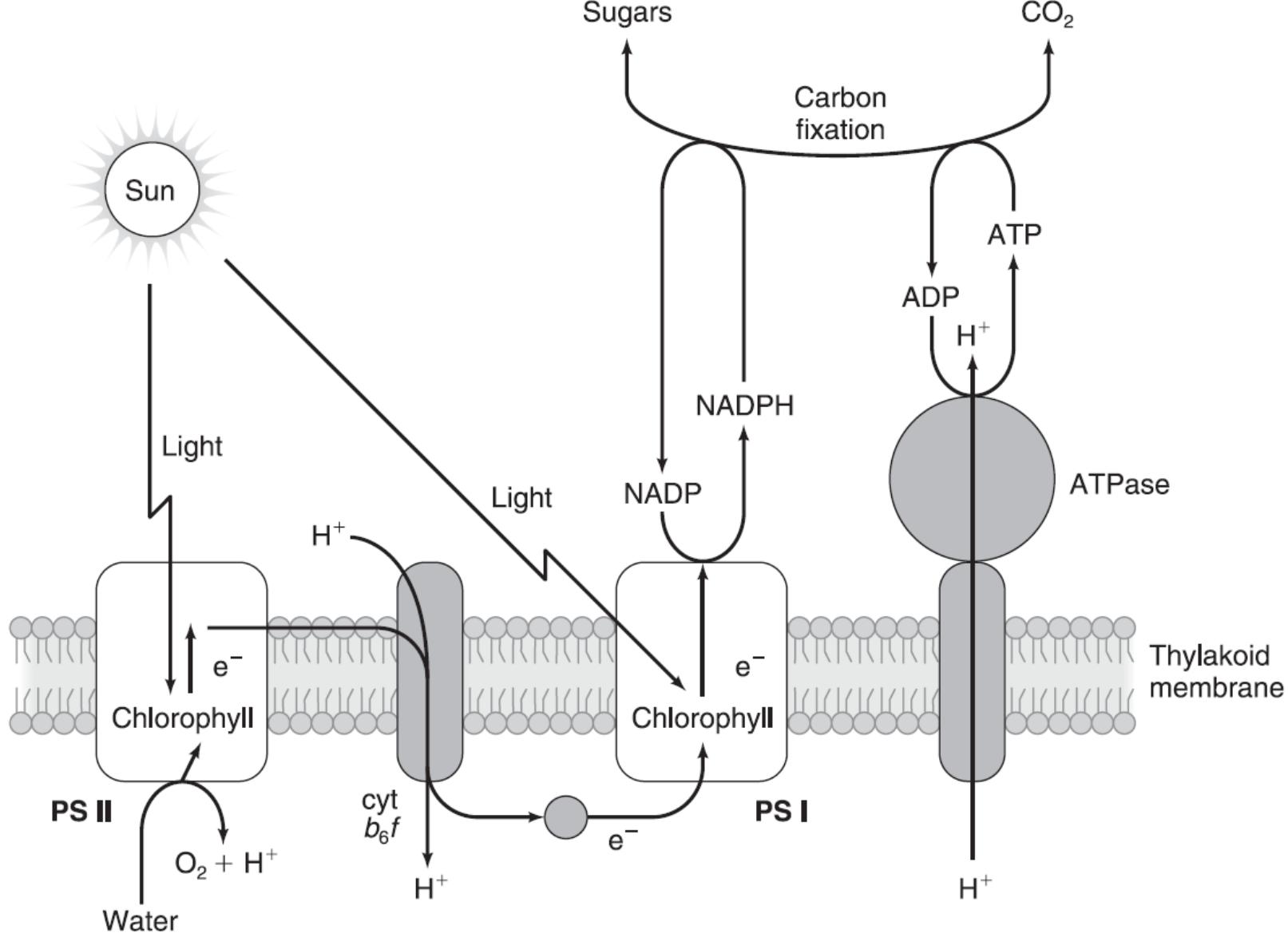
Huang et al. Chem. Rev.  
2018, 118, 2491.



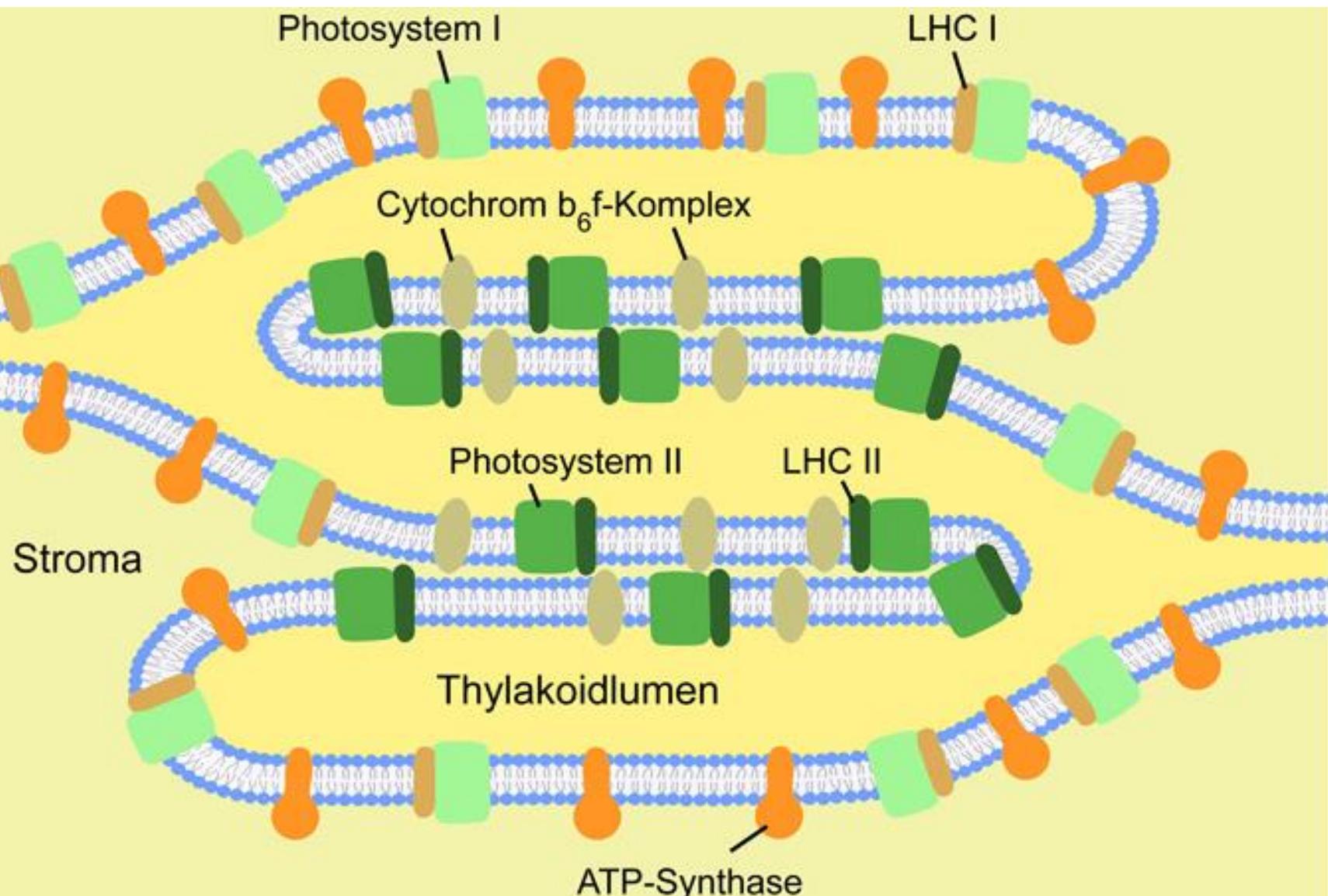
## Gradually-increasing Reduction Potentials:

- **Complex I:** **NADH (-0.33 V)** → CoQ (~0.04 V);
- **Complex II:** Succinate (0.1 V);
- **Complex III:** Rieske center (~0.2 V), Cyt c<sub>1</sub> (~0.23 V), Cyt c (~0.26 V);
- **Complex IV:** **O<sub>2</sub> (0.82 V)**.

# **ET in Photosynthesis**



- Driven by  **$H^+$  &  $e^-$  transfers**, photosynthesis **oxidizes  $H_2O$**  to form  **$O_2$**  & ultimately reduces  **$NADP^+$**  to  **$NADPH$**  by **2 serial light reactions**.

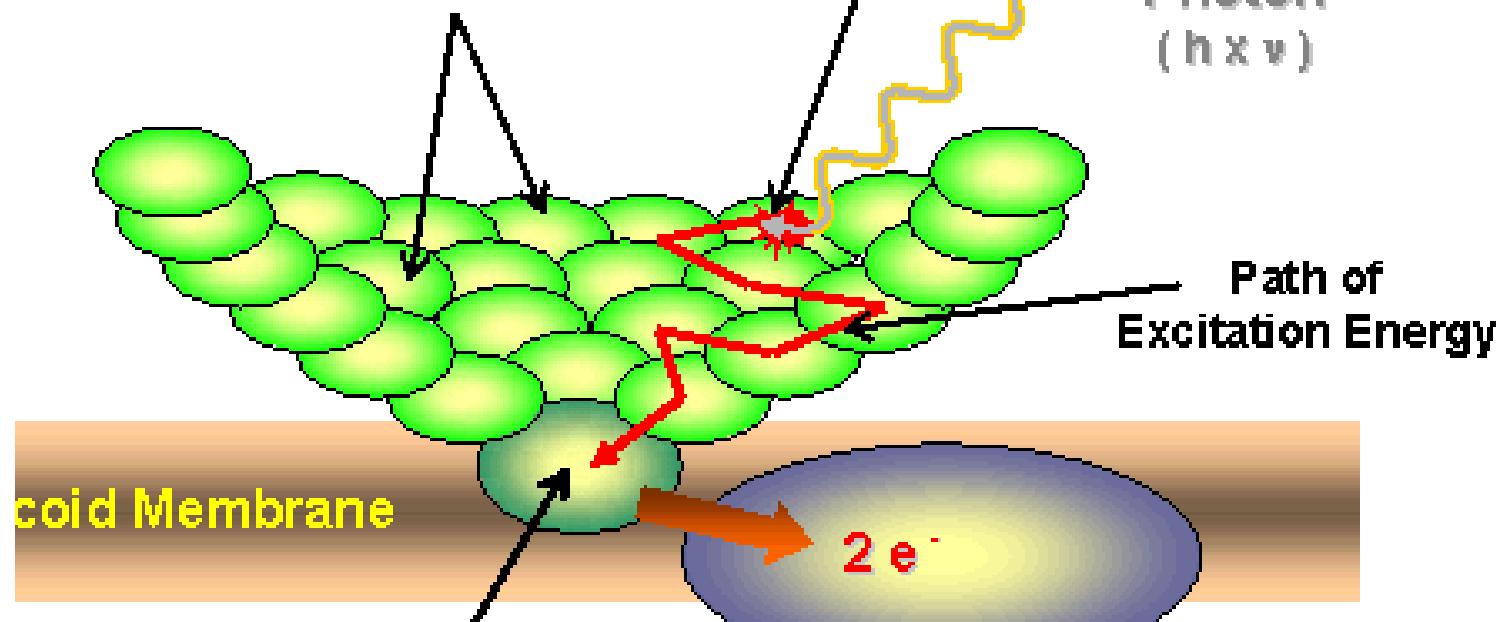


- Photosynthesis occurs in plant, algae, & cyanobacteria. The related redox activity/reactions is localized in chloroplast (叶绿体) in plant & algae.

## Trapping Center or Light Harvesting Complex

### (LHC)

Chlorophyll b &  
Pigment Molecules



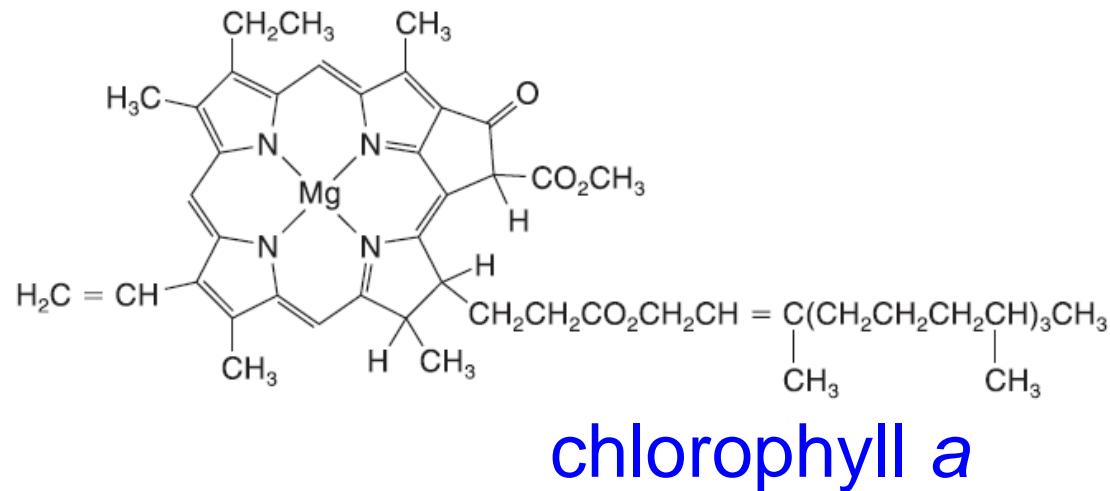
E. Schmid/2003

Reaction Center  
2 Chlorophyll a  
(P-680 or P-700)

Primary Electron-  
Acceptor

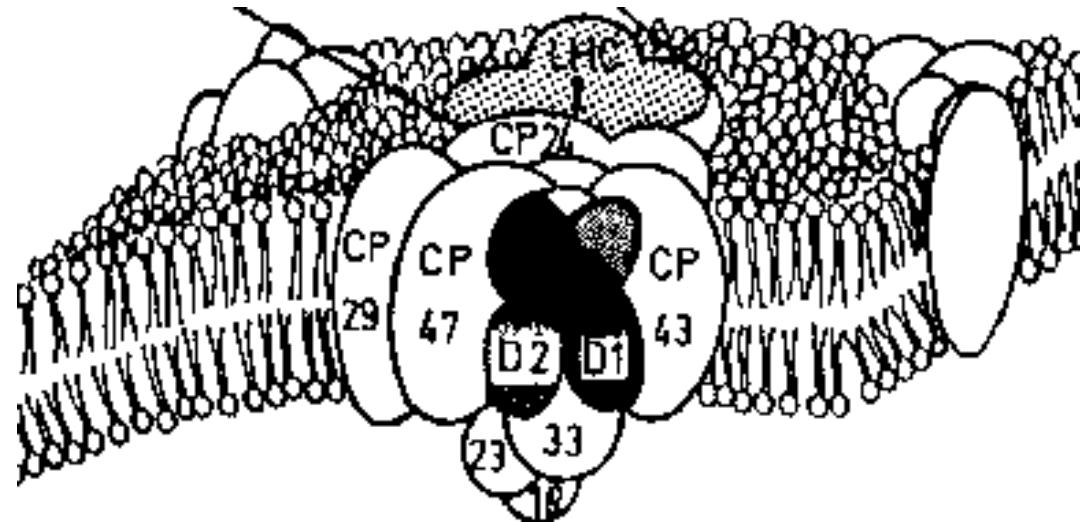
**Photosystem**

- Antenna chlorophylls *a* & *b* were found in **LHC**, e.g. ~13-14 chlorophylls *a* & *b* found in an antenna protein in higher plants.



chlorophyll *a*

- The chlorophylls & other cofactors involved in **light-induced redox activity** were found in two complexes (so-called **reaction centers**), **PSII & PSI**.

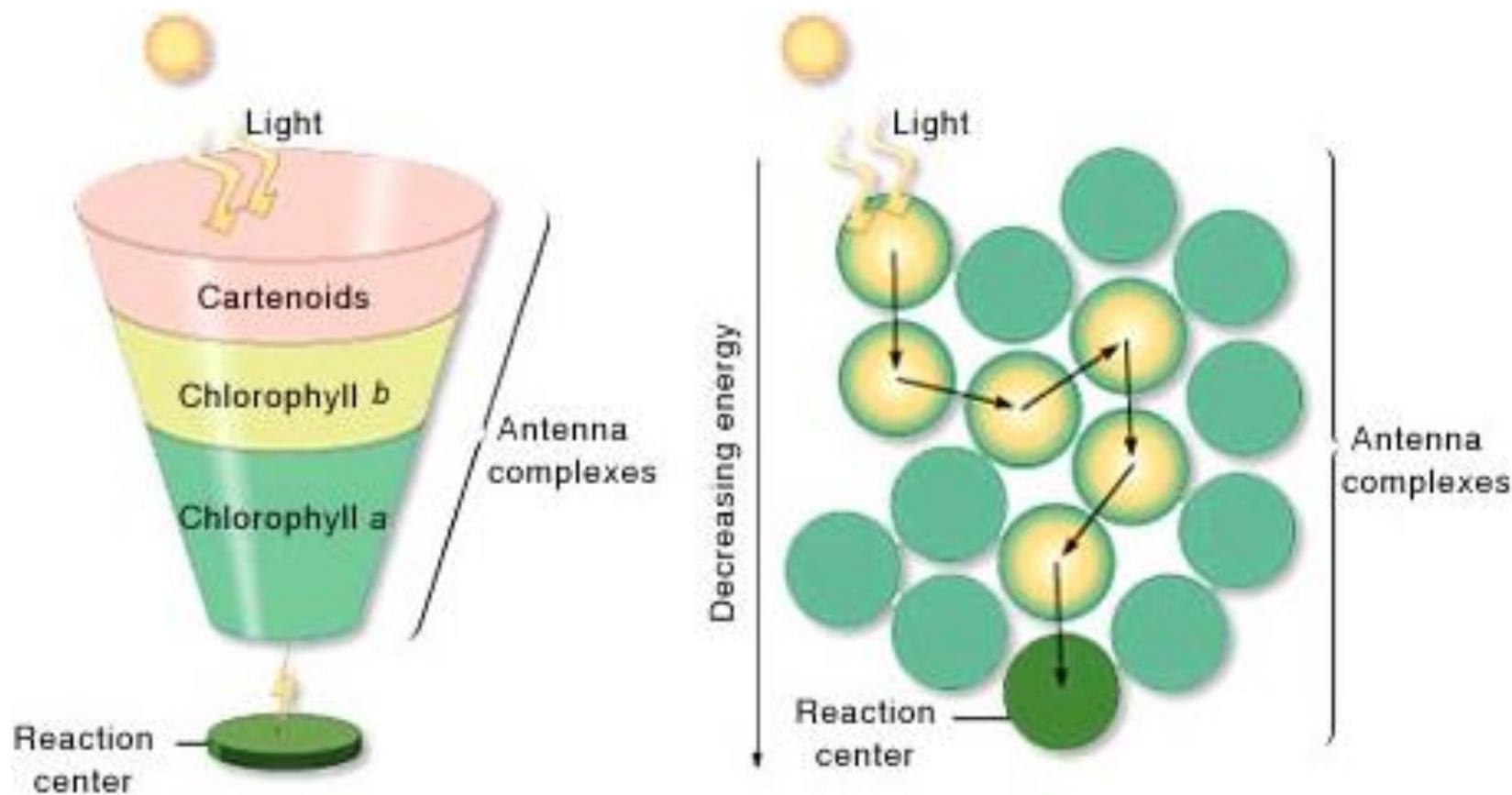


**LHC: Light-Harvesting Complex**

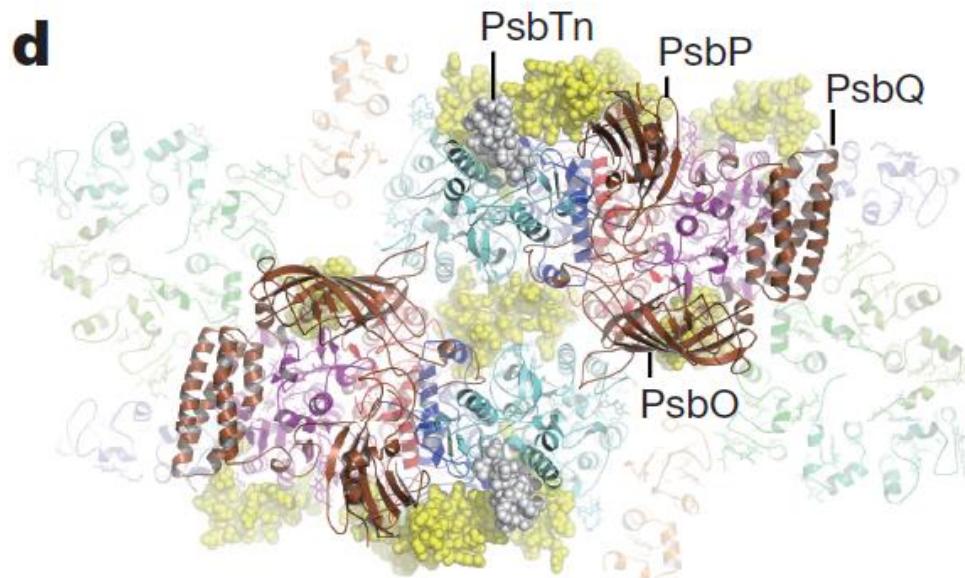
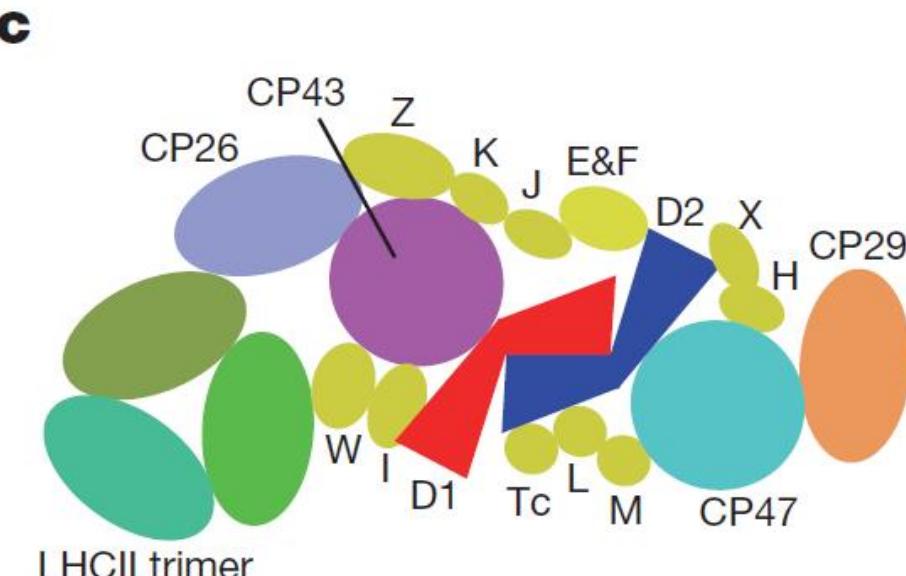
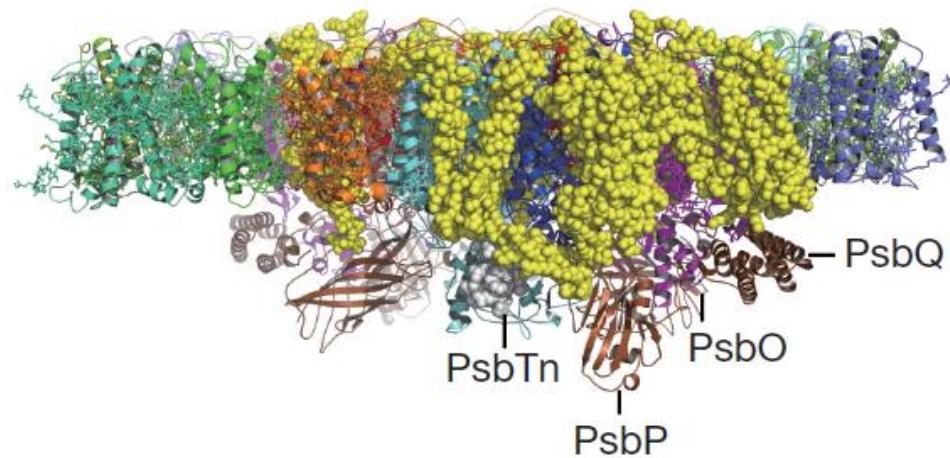
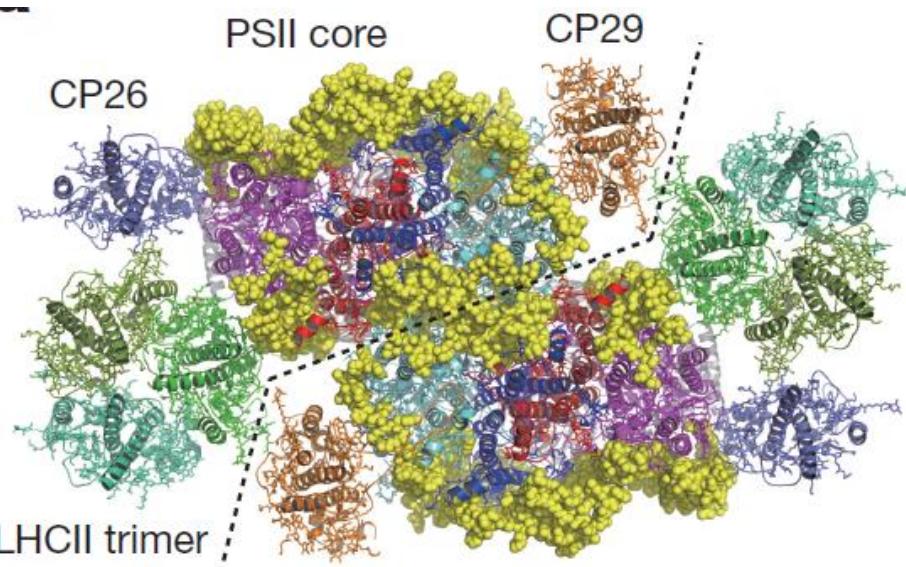
**CP: Core antenna Protein**

**D: Reaction Center**

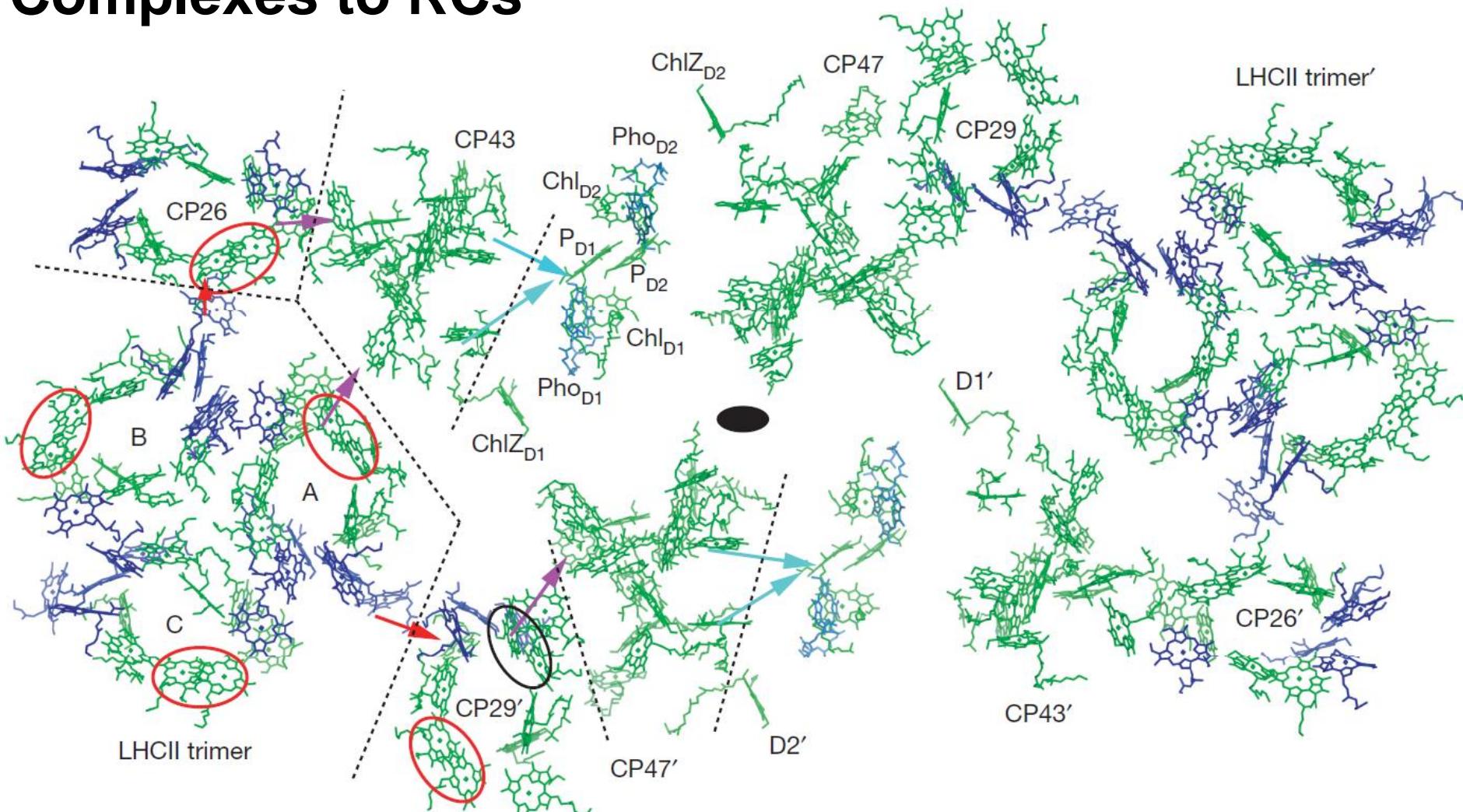
- Almost all the chlorophylls transfer **excitation energy** throughout a bed of pigments.
- Eventually, **energy** arrive at a special chlorophyll a (**P680 or P700**) in a **reaction center** (RC, either **PSII** or **PSI**) that generates oxidized & reduced species.



# Crystal Structure of PS II-LHC II Supercomplex (3.2Å)



# Proposed Energy Transfer Pathways from Antenna Complexes to RCs

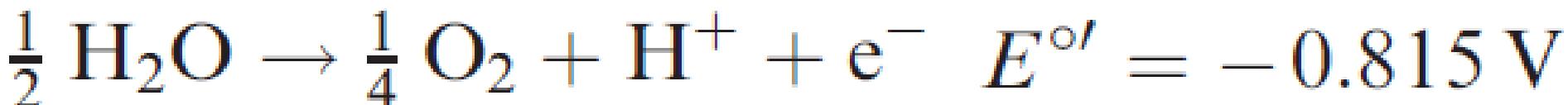


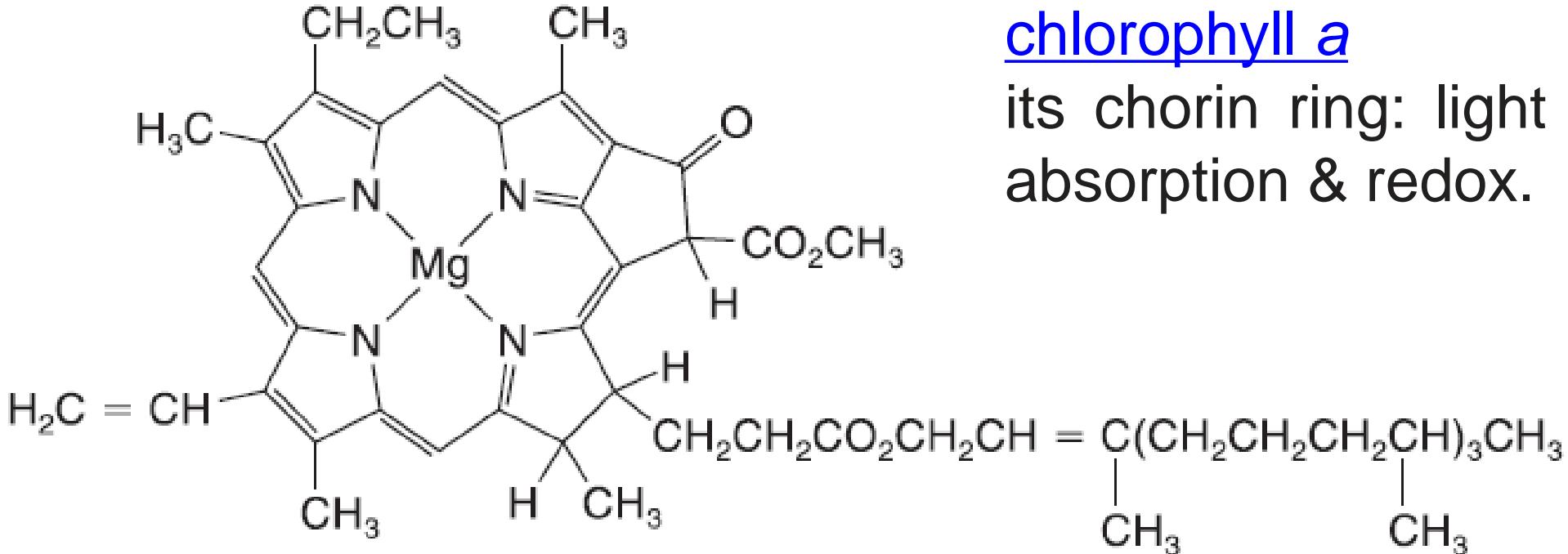
Chl a & Chl b  
Reaction Centers in D1/D2' (cyan)

- The **first** light-induced step: **photosystem II (PSII)** absorbs light to generate **chlorophyll (叶绿素) P680<sup>+</sup>** (absorption: ~680 nm), which **oxidizes H<sub>2</sub>O to give O<sub>2</sub>** & **reduce quinone** (Q) in oxygenic organisms. This lipid-soluble quinone can **transfer electrons to Cyt b<sub>6</sub>f**.



- This water-oxygen cycle in biology stores light energy to energy in O<sub>2</sub>.





## chlorophyll a

its chlorin ring: light absorption & redox.

- The **second** light-induced step: **photosystem I (PSI)** absorbs light to **oxidize** a second & specialized chlorophyll P700 & **reduce NADP<sup>+</sup> to NADPH**.
- **ET** from H<sub>2</sub>O through PSII & Cyt *b*<sub>6</sub>*f* to PSI (P700<sup>+</sup>) is coupled to **H<sup>+</sup> pumping & ATP formation**.

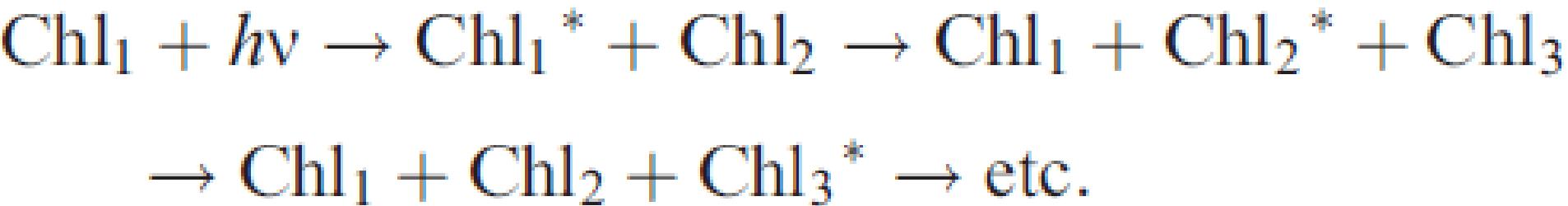
# Photosystem II (PSII)

- A huge membrane-protein complex with ~20 different subunits. Mechanisms of transforming **light energy** into **redox energy** by chlorophyll (Chl):
  - Excited pigment (chlorophyll, Chl\*) has several fates:

1. Decay to the ground state with **fluorescence emission**,

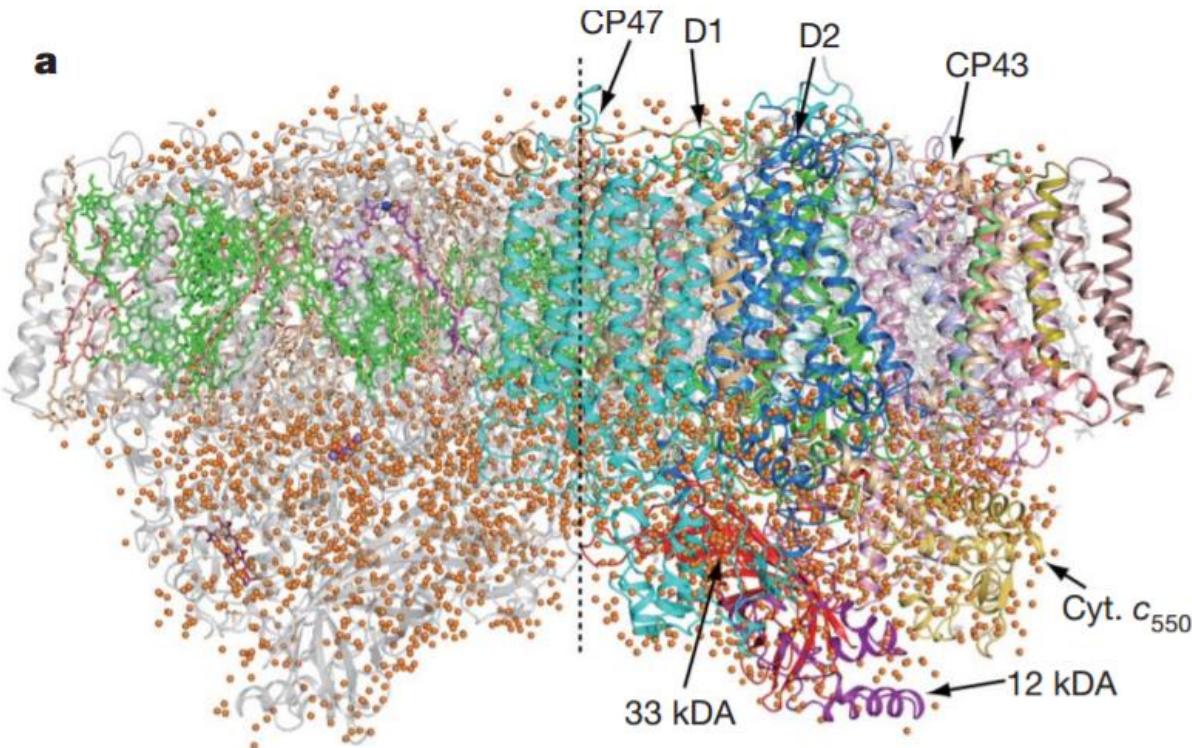
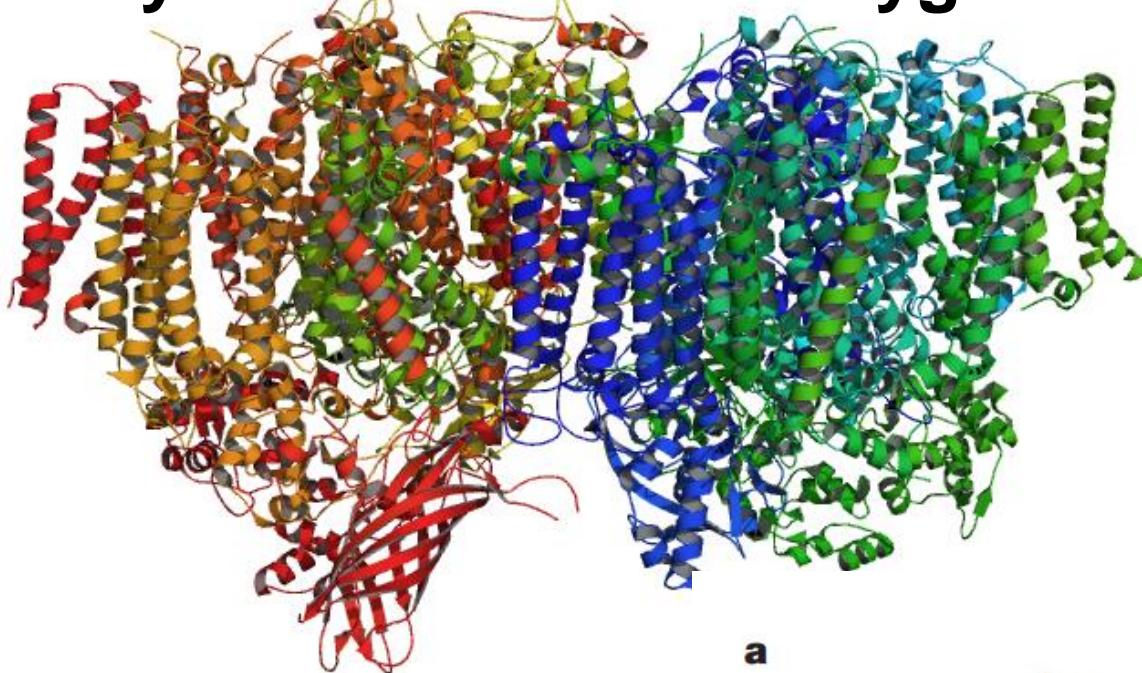


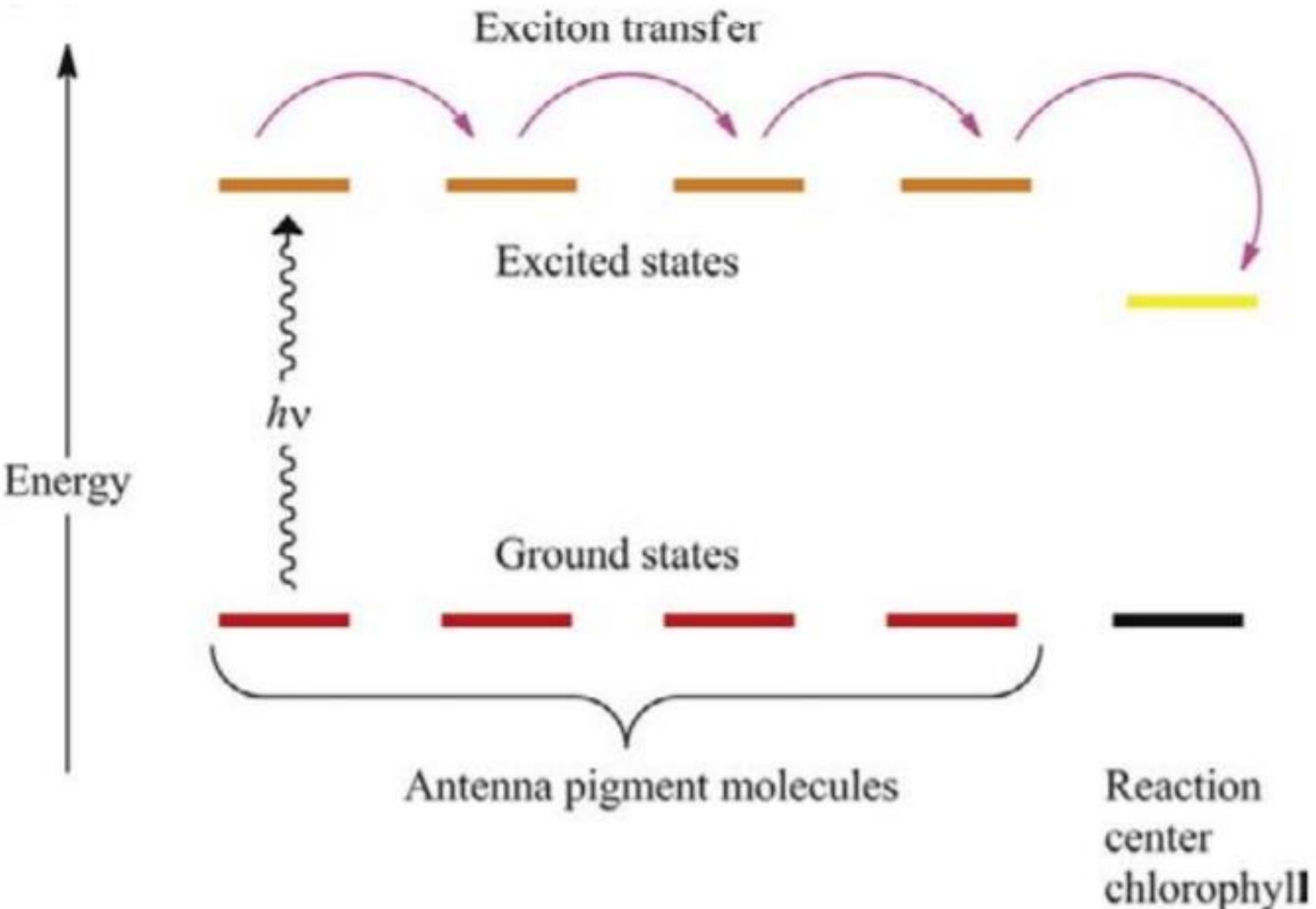
2. **Excitation-energy** (or exciton) **transfers** among Chls,



(Eventually, the exciton either decays to the ground state or is absorbed by a chlorophyll in reaction center)

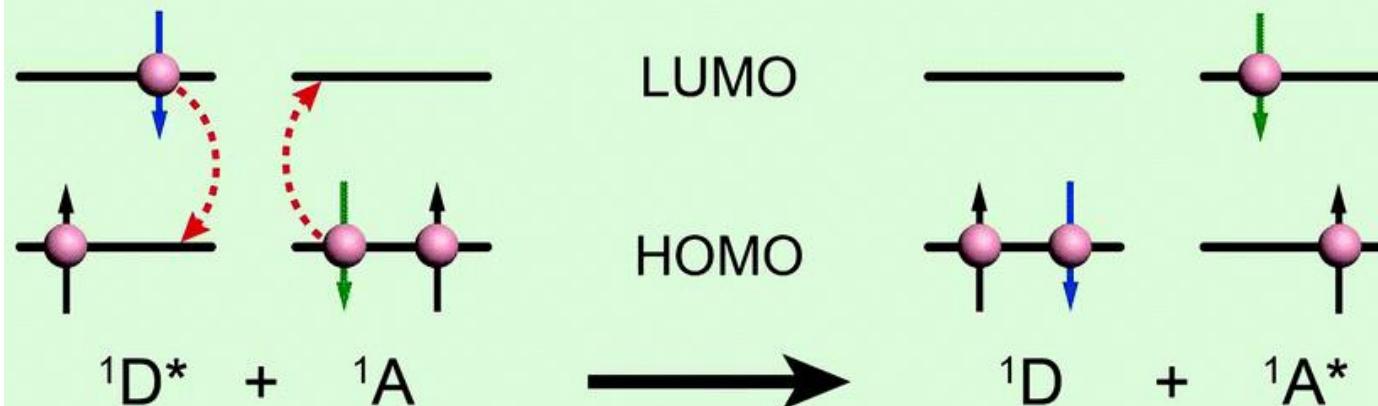
# Crystal Structure of Oxygen-evolving PSII (1.9 Å)



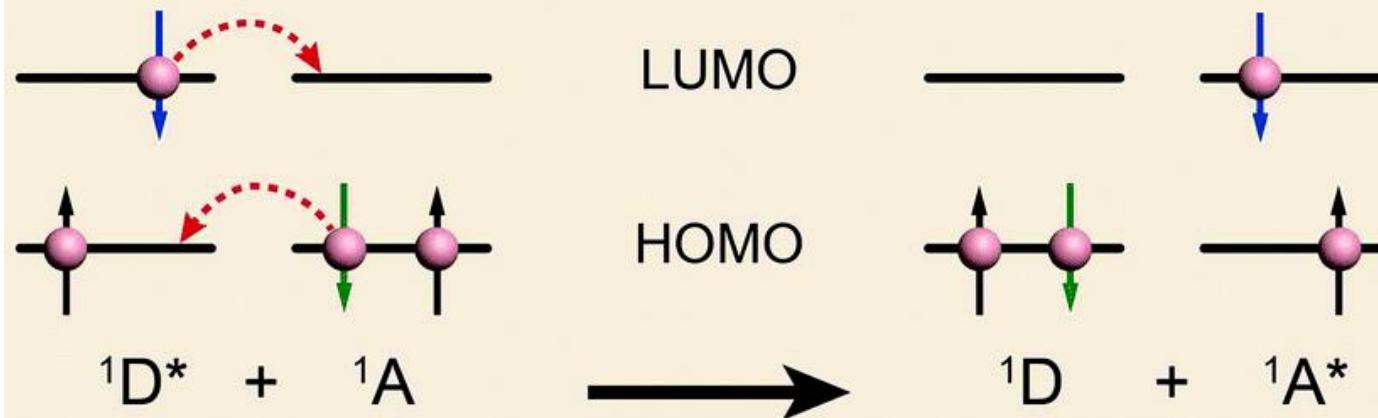


## 2 General Ways for Excitation Energy Transfer

### (a) Singlet-singlet Förster energy transfer



### (b) Singlet-singlet Dexter energy transfer



(a) Förster resonance energy transfer (FRET) through dipole-dipole coupling ( $k_{ET} \sim R^{-6}$ ); (b) Electron exchange.

### 3. Loss of an $e^-$ to form a radical cation & initiate ET.



- The oxidized chlorophyll **radical cation ( $\text{Chl}^+$ )** is highly reactive, & seeks to regain an electron.

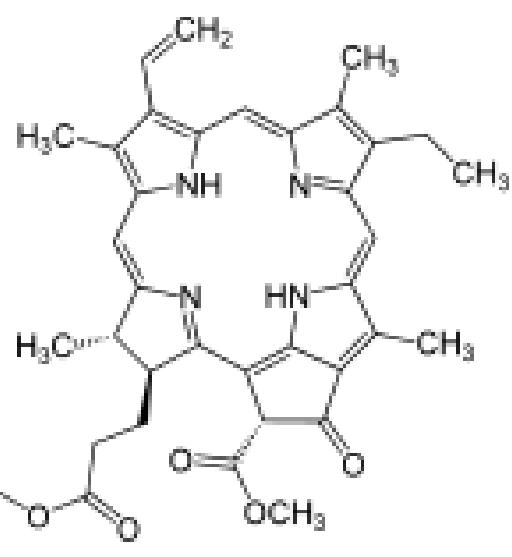
→ Oxidize an  $e$ -donor molecule & regenerate the ground-state pigment ( $\text{Chl}$ ) for another photocycle.



D: electron donor; P: special chlorophyll molecules involving redox reactions; I: Intermediate electron carrier; A: First stable electron acceptor.

# Electron-Transfer Cofactors of PSII and PSI

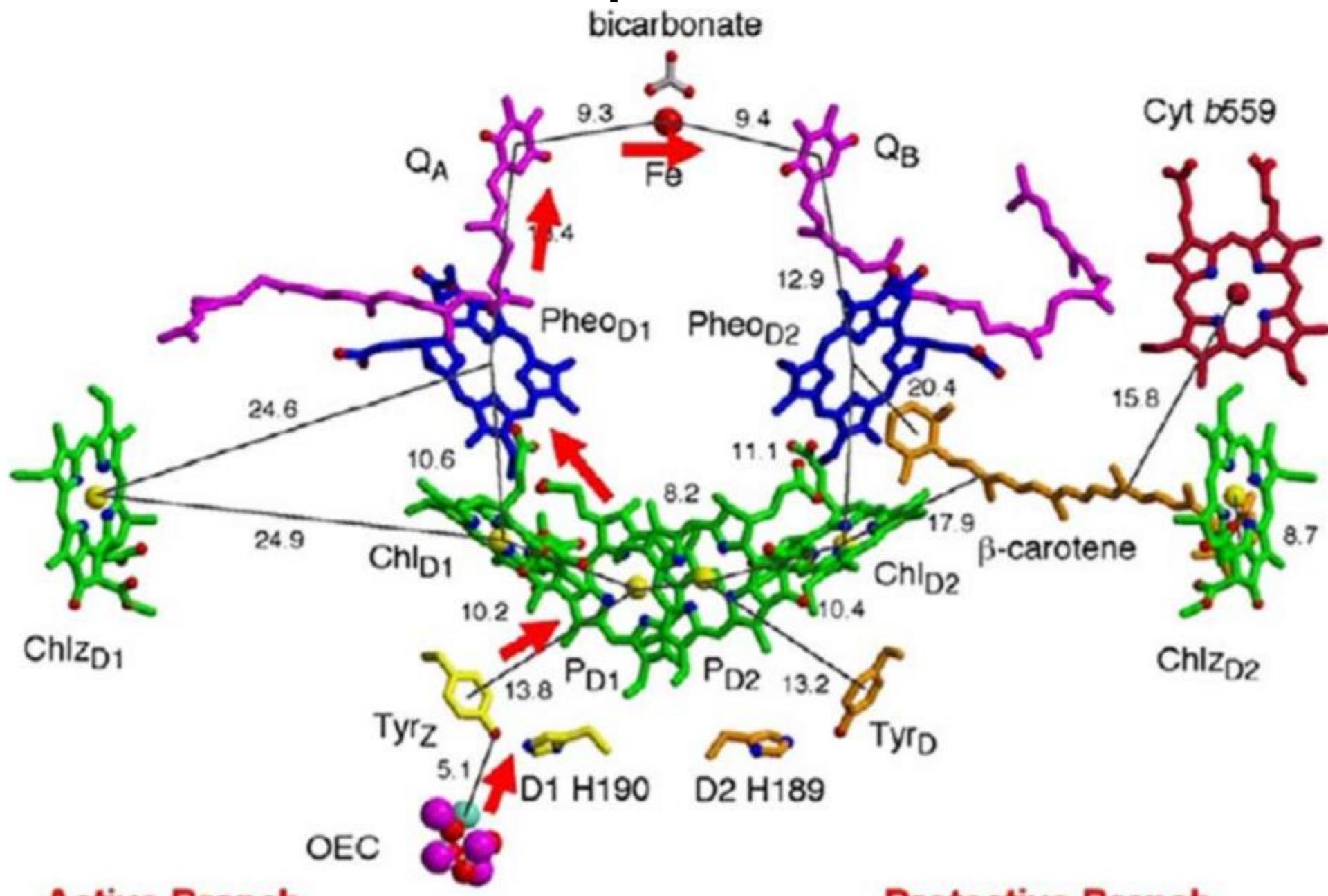
	PSII	PSI
(D) Electron donor $E^{\circ'}$	$[H_2O \rightarrow Mn_4 \text{ cluster} \rightarrow \text{Tyrosine}]$ +0.815 V ca. +0.9 V ca. +1.0 V	Plastocyanin ( $Cu^{+2}$ ) +0.375 V
(P) Reaction center chlorophyll $E^{\circ'}$	P680/P680 <sup>+</sup> ca. +1.2 V	P700/P700 <sup>+</sup> +0.45 V
(I) Intermediate electron carrier $E^{\circ'}$	Pheophytin <i>a</i>  -0.66 V	Chlorophyll <i>a</i> , vitamin K (?) (ca. -1.0 V)
(A) Stable electron acceptor $E^{\circ'}$	Quinone A (Q <sub>A</sub> ) -0.13 V	Fx (4Fe-4S) (-0.7 V)



## Pheophytin

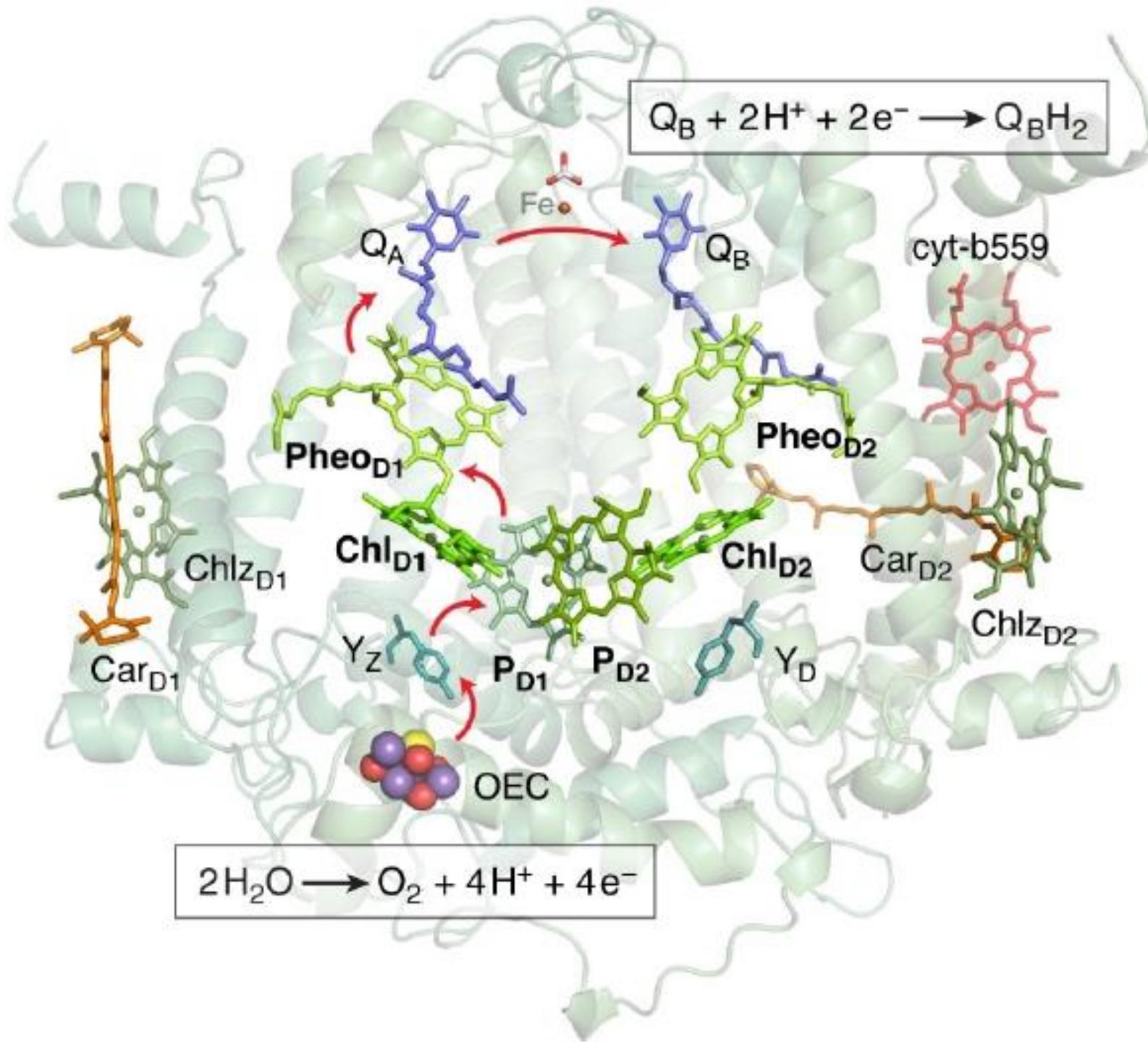
NADPH  
(-0.32 V).

# Electron Transport Cofactors in PSII

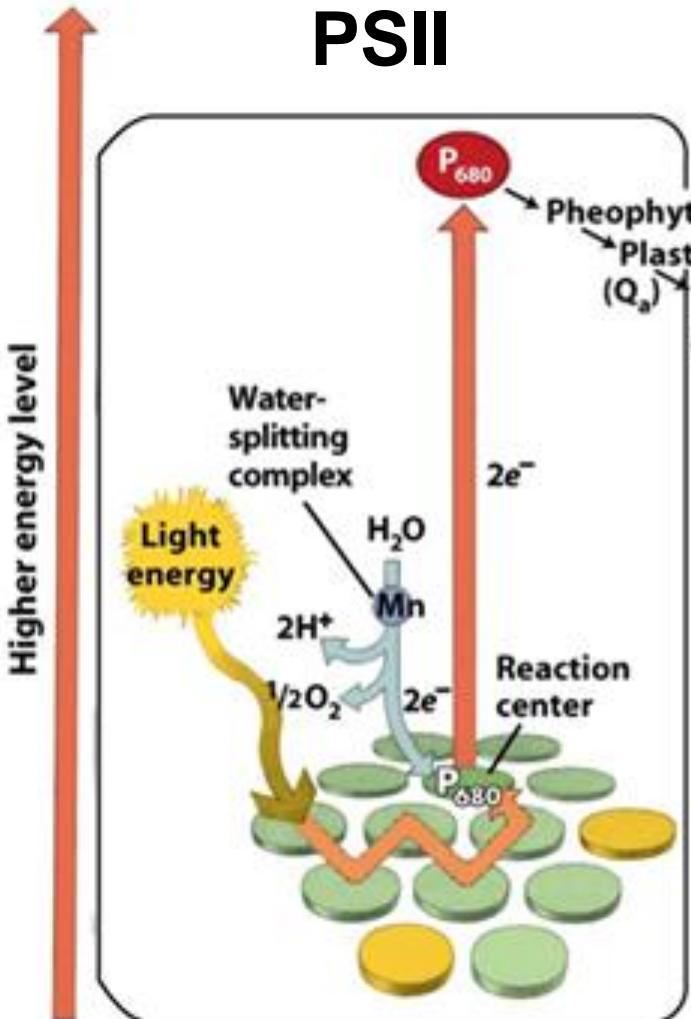


Active Branch

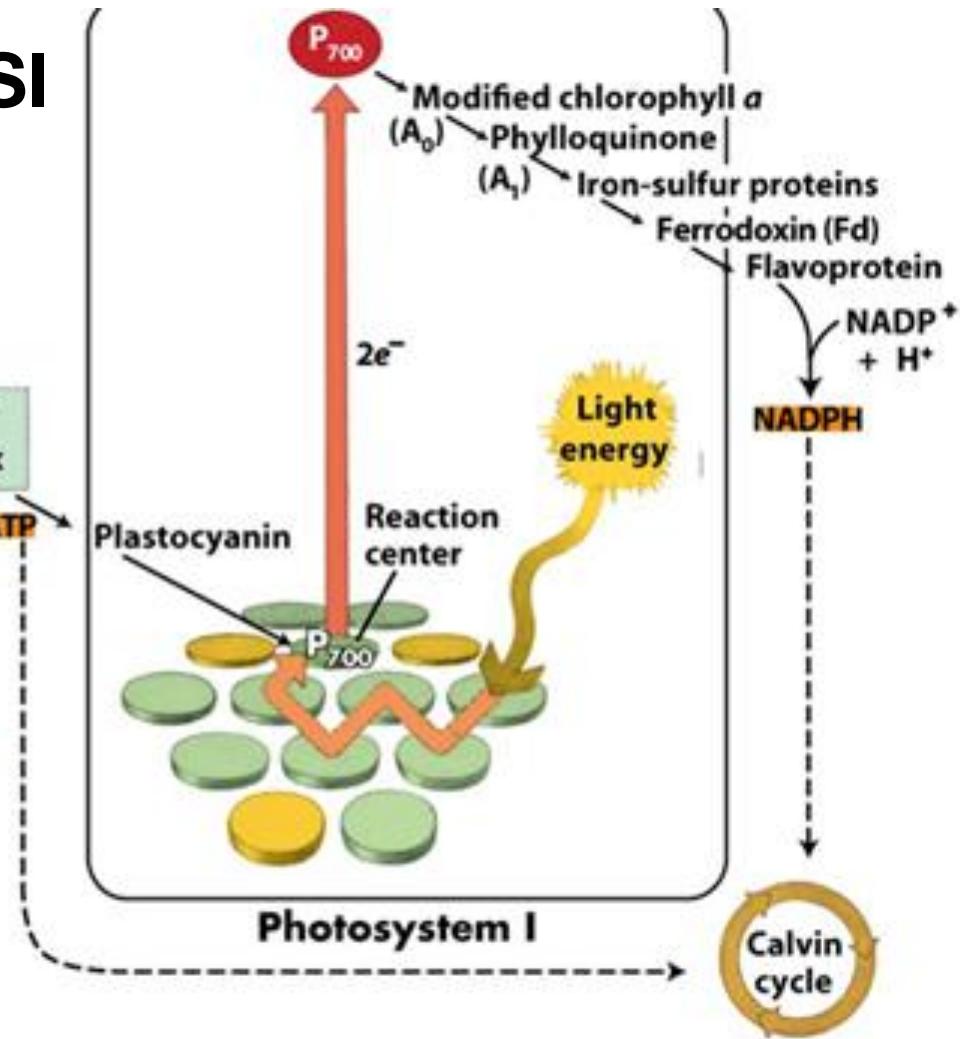
Protective Branch



# PSII



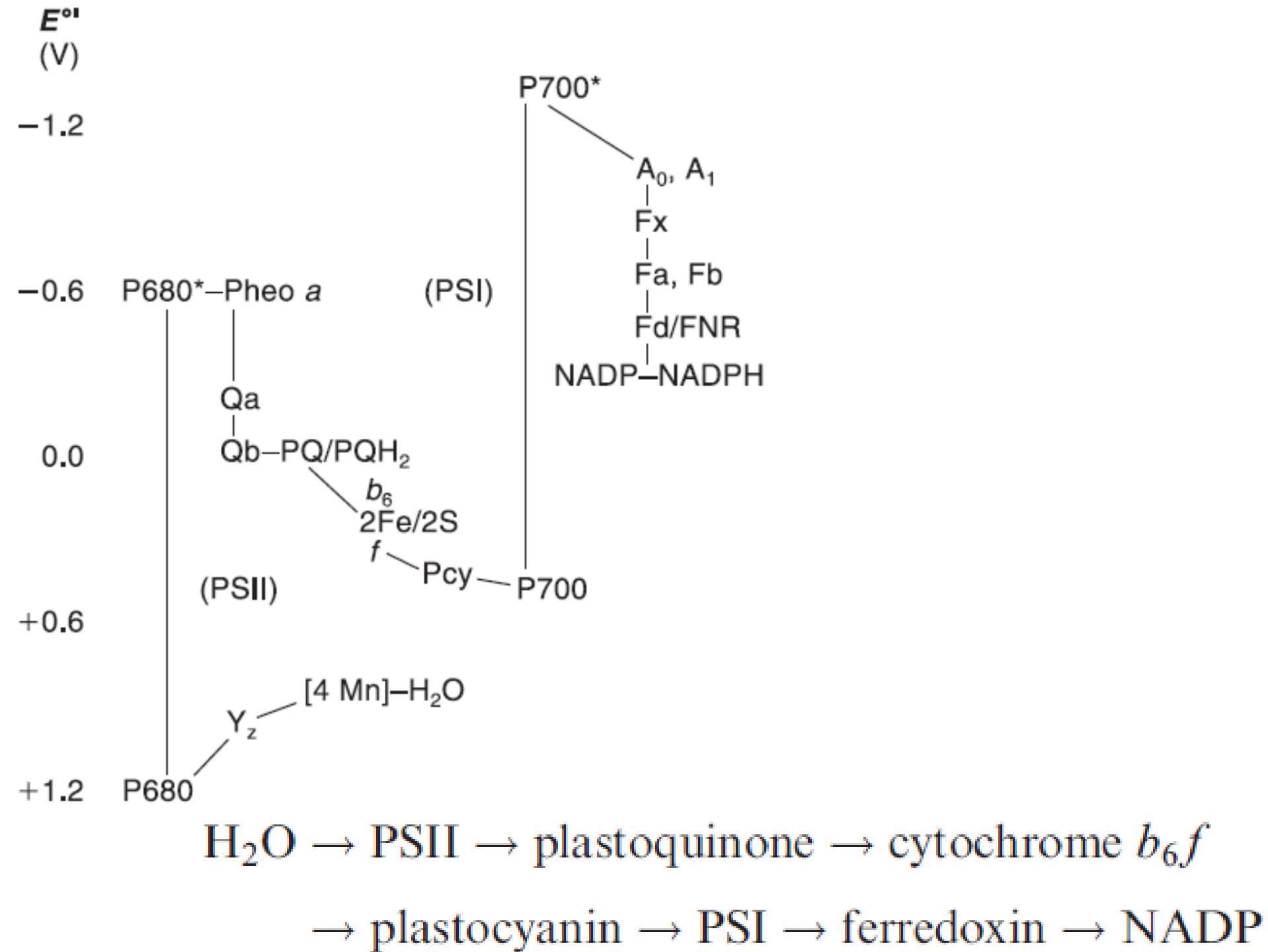
# PSI

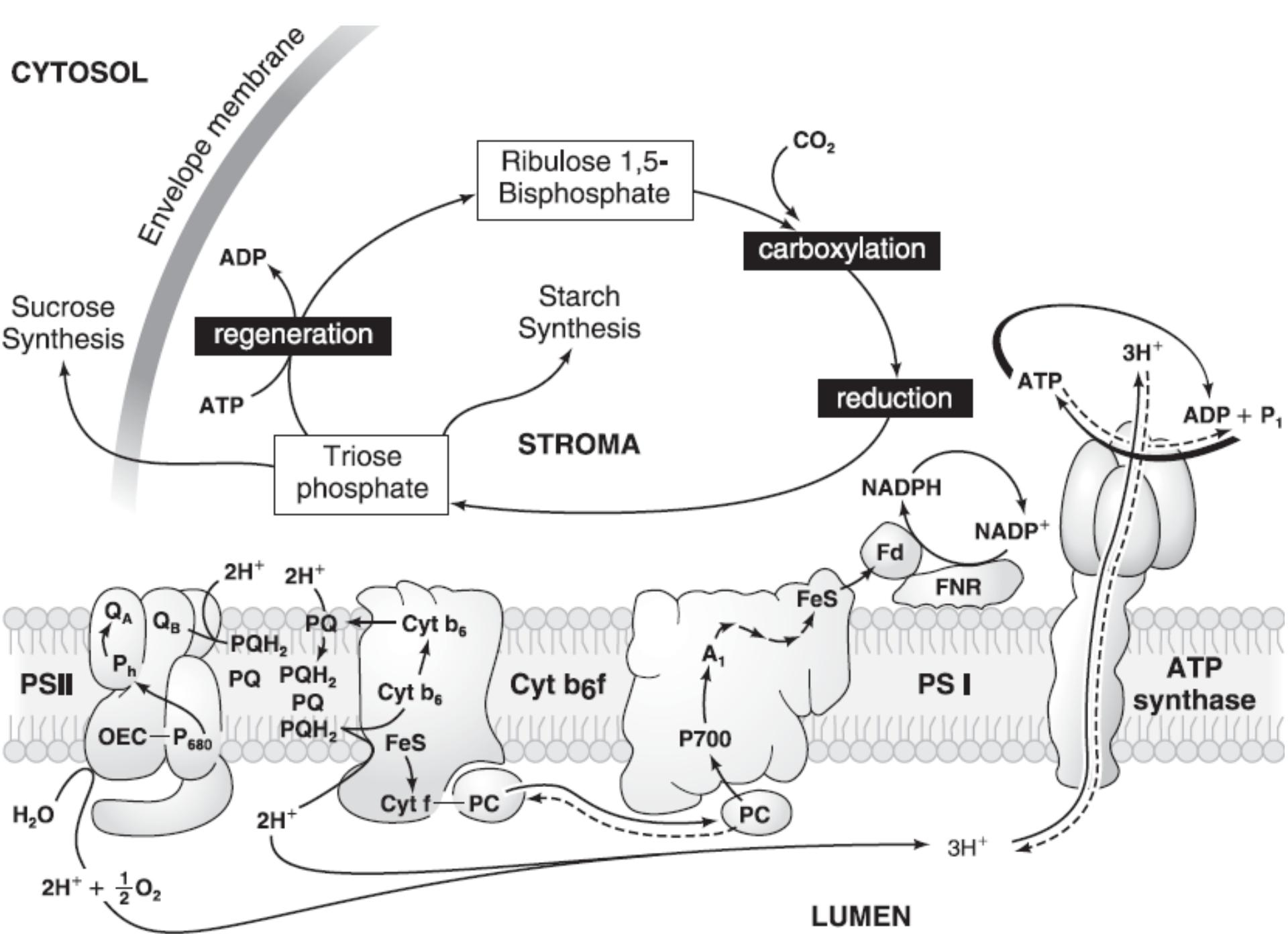


The sequence of  $e^-$  carriers in oxygenic photosynthesis

$H_2O \rightarrow$  PSII  $\rightarrow$  plastoquinone  $\rightarrow$  cytochrome *b*<sub>6</sub>*f*

$\rightarrow$  plastocyanin  $\rightarrow$  PSI  $\rightarrow$  ferredoxin  $\rightarrow$  NADP





- PSII catalyzes the sequential  $2e^-$  reduction of quinone (Q) molecules. One of the quinones, so-called  $Q_A$ , is tightly bound to PSII, while the other plastoquinone (so-called  $Q_B$ ) is less tightly bound & can exchange.



(PQ: the free membrane-soluble form of the quinone)

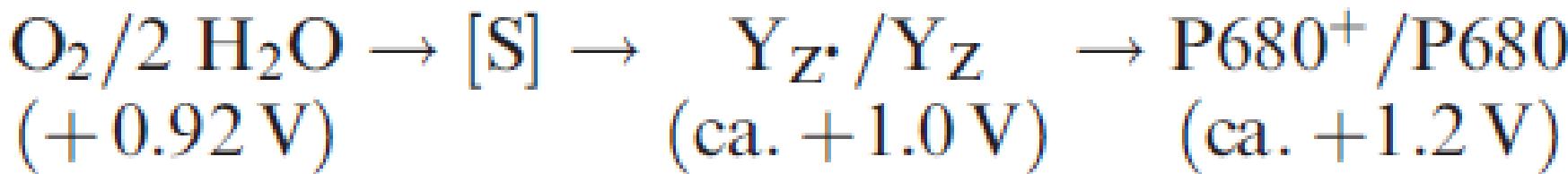
# Electron-Transfer Kinetics in Photosystem II

Forward Electron-Transfer Reaction	$t_{1/2}$	Recombination Reaction	$t_{1/2}$
$P680/\text{Pheo } a \rightarrow P680^+/\text{Pheo } a^-$	<1 ps		
$P680^+/\text{Pheo } a^-/Q_A \rightarrow P680^+/\text{Pheo } a/Q_A^-$	250 ps	$Q_A^-/P680^+ \rightarrow Q_A/P680$	$150\ \mu\text{s}$
$Y_Z/P680^+/Q_A^- \rightarrow Y_Z^\cdot/P680/Q_A^-$	50–250 ns	$Y_Z^\cdot/Q_A^- \rightarrow Y_Z/Q_A$	200 ms
$Y_Z^\cdot/Q_A^-/Q_B \rightarrow Y_Z^\cdot/Q_A/Q_B^-$	100 $\mu\text{s}$	$Y_Z^\cdot/Q_B^- \rightarrow Y_Z/Q_B$	400 ms
$S^N/Y_Z^\cdot/Q_B^- \rightarrow S^{N+1}/Y_Z/Q_B^-$	30 $\mu\text{s}$ –1 ms	$S^{N+1}/Q_B^- \rightarrow S^N/Q_B$	30 s

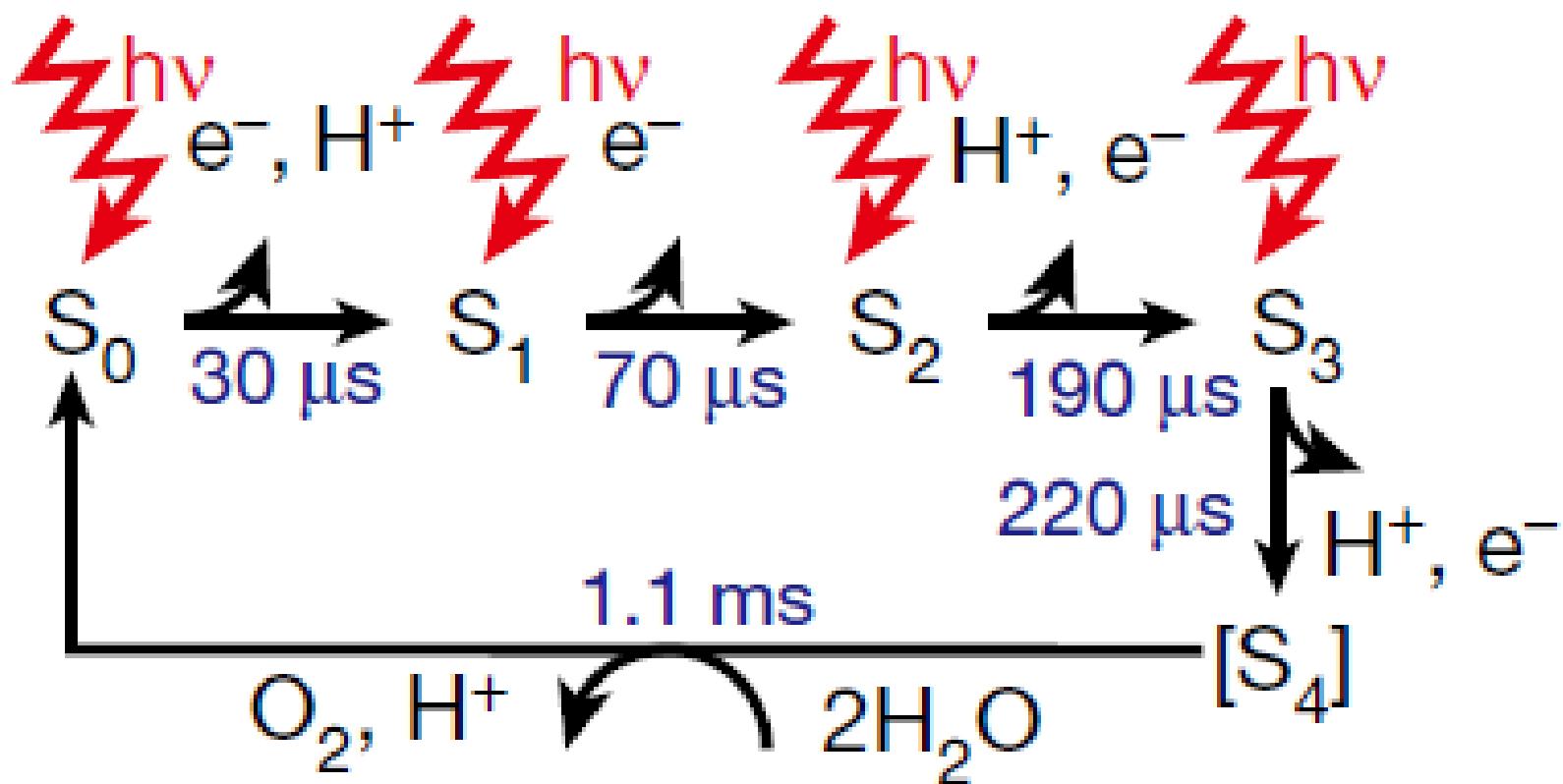
- The **forward ET rates**: **ps-ms**; the forward ET reactions are **much faster than** the **reverse** reactions.
- The overall sequence of the forward ET in PSII



$Y_Z$  : redox-active Tyr161 close to the MnCaO Cluster;  $S_N$  : the nth state of the MnCaO cluster.

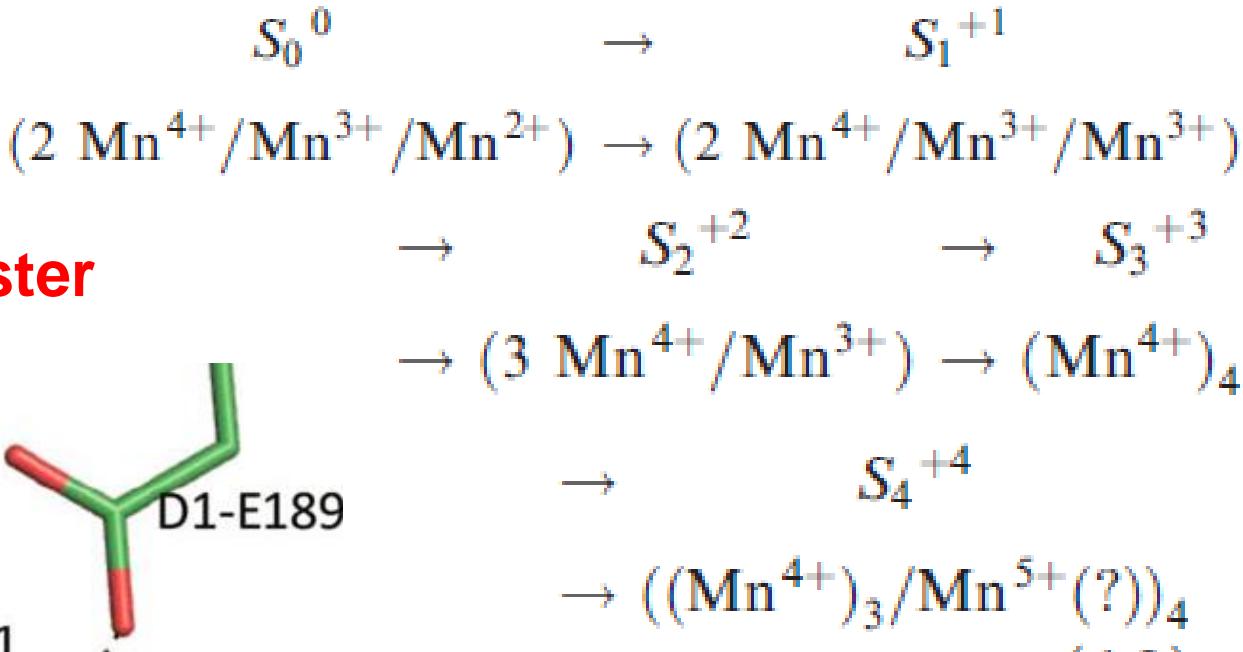
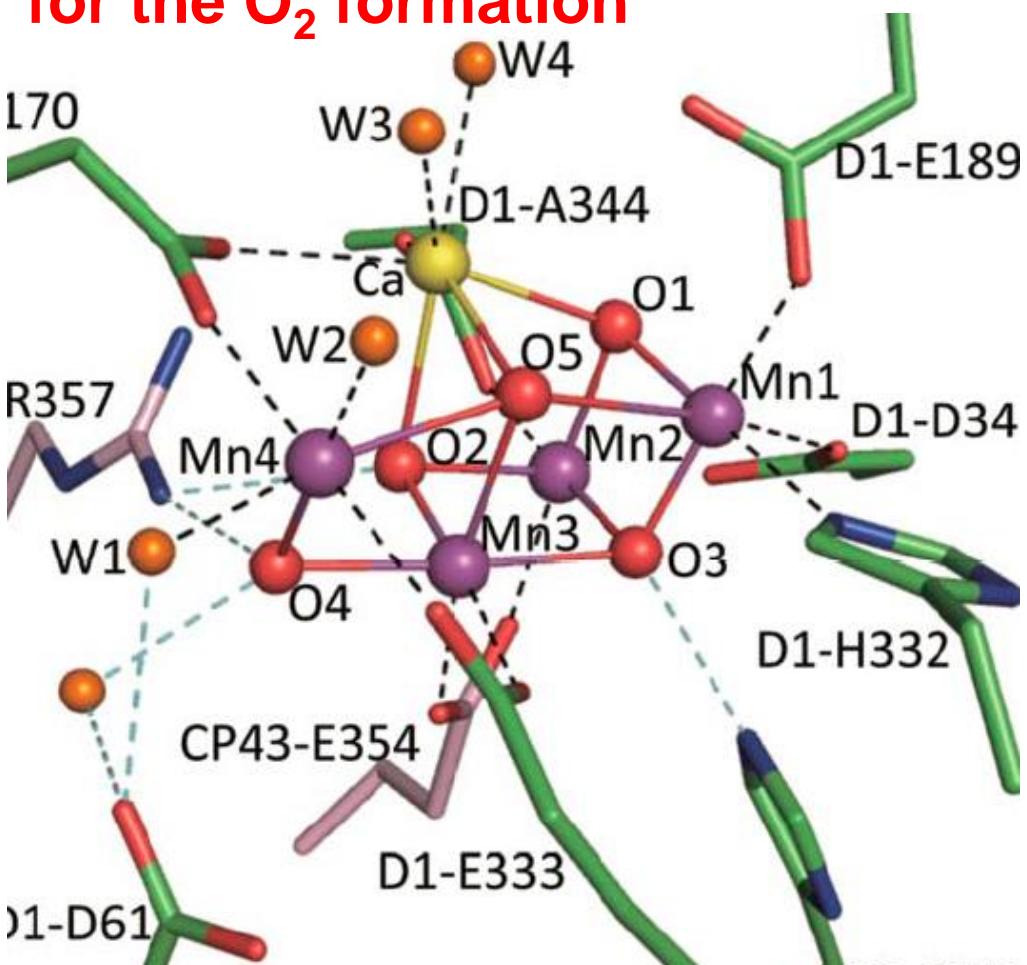


# Redox in Oxygen-evolving Center (OEC)



# Crystal Structure of Oxygen-evolving Center (OEC) in PSII (1.9 Å)

Unique  $Mn_4CaO_5$  cluster  
for the  $O_2$  formation



Proposed  
oxidation states

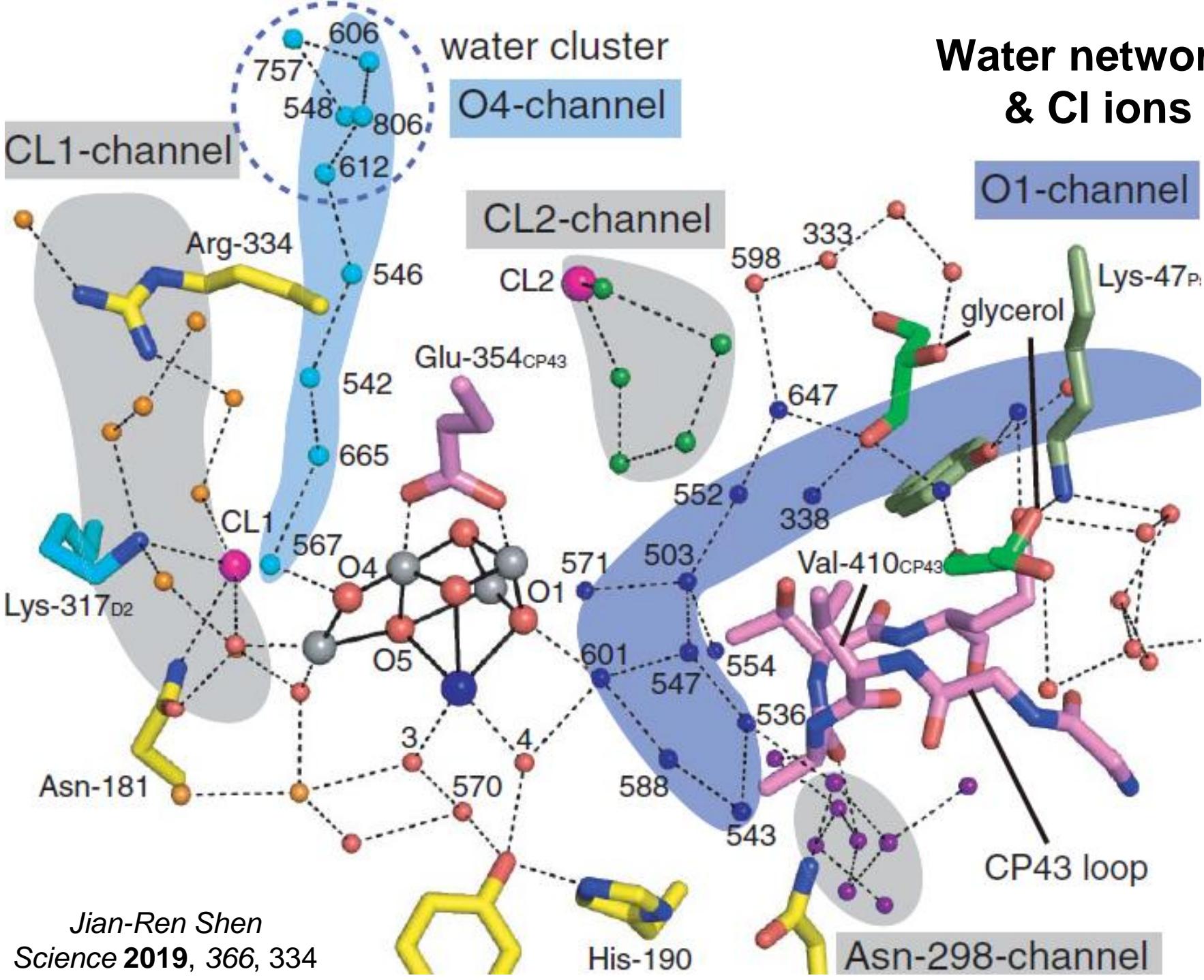
## Inorganic Ion Cofactors of the Dioxygen-Evolving Complex

Cofactor	Substitutes	Inhibitors
4 Mn <sup>n+</sup> ( $n > 2$ )	None	Reducants (Mn <sup>2+</sup> )
1 Ca <sup>2+</sup>	Sr <sup>2+</sup>	Ln <sup>3+</sup> , <sup>a</sup> Cd <sup>2+</sup> , Na <sup>+</sup> /K <sup>+</sup> /Cs <sup>+</sup>
1 Cl <sup>-</sup>	Br <sup>-</sup> > NO <sub>3</sub> <sup>-</sup> > I <sup>-</sup> > NO <sub>2</sub> <sup>-</sup>	Lewis bases (RNH <sub>2</sub> , -OH, F <sup>-</sup> )

<sup>a</sup> Ln<sup>3+</sup> = La<sup>3+</sup>, Pr<sup>3+</sup>, Dy<sup>3+</sup>, Lu<sup>3+</sup>, Yb<sup>3+</sup>.

- No Ca<sup>2+</sup> or Cl<sup>-</sup>, S<sub>1</sub> → S<sub>2</sub> was observed, but no further oxidation.
- When Ca<sup>2+</sup> is replaced by Sr<sup>2+</sup>, the ET activity is reduced by 50 %.

# Water networks & Cl<sup>-</sup> ions

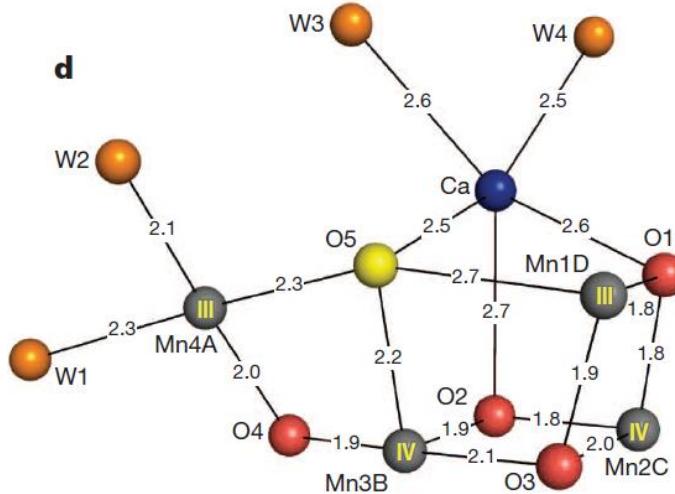


Jian-Ren Shen

Science 2019, 366, 334

# Native Structure by fs X-ray Pulses

6

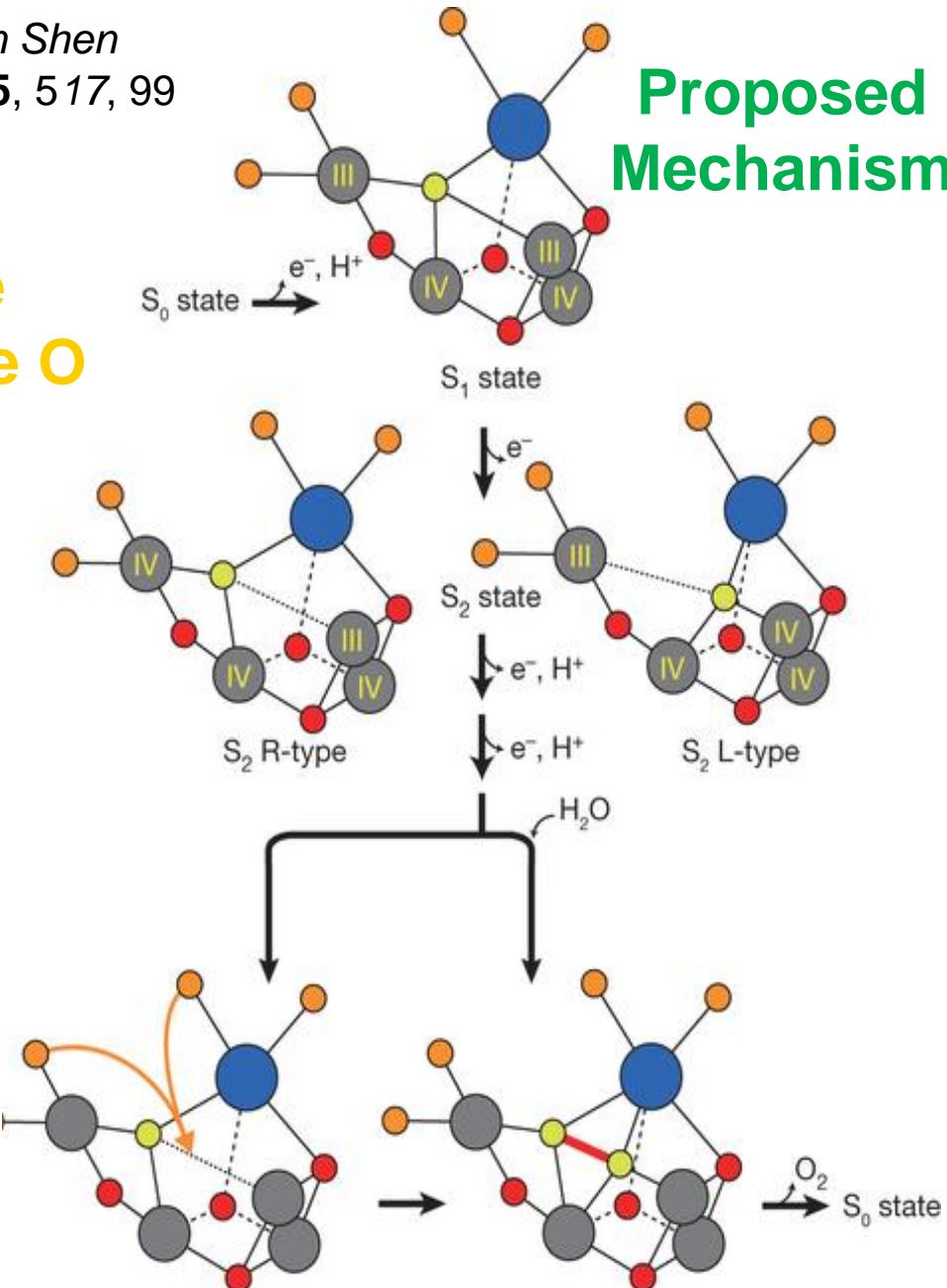


Jian-Ren Shen  
Nature 2015, 517, 99

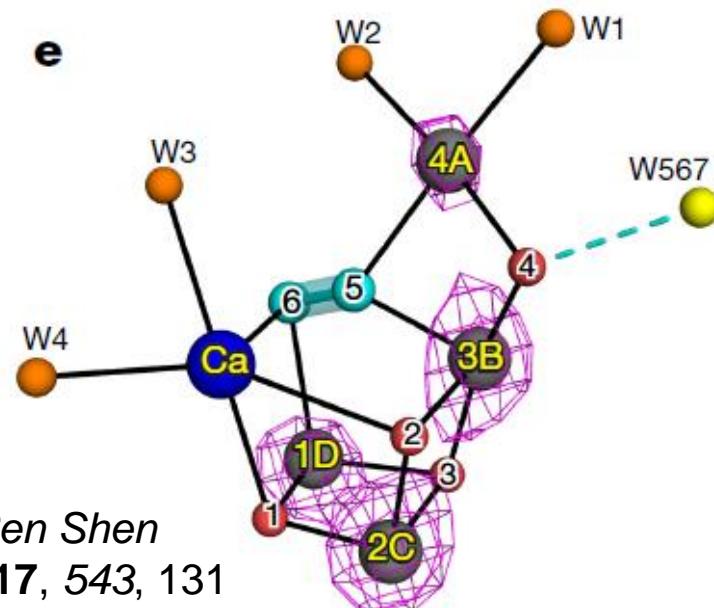
# O5: OH & the substrate O

# Time-resolved serial fs crystallography with X-ray free e- laser upon 2-flash illumination

# Proposed Mechanism



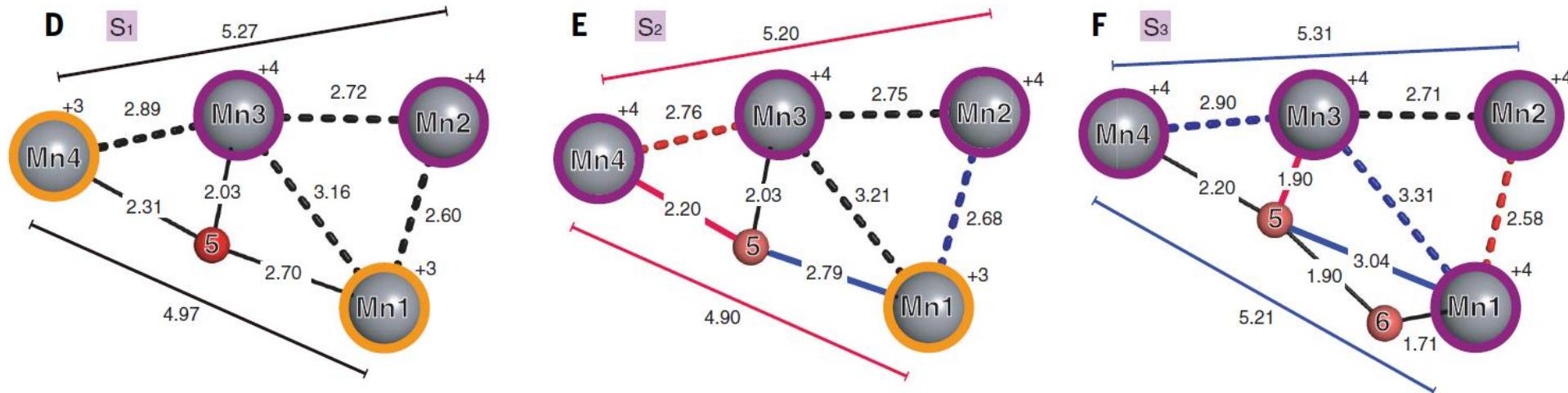
e



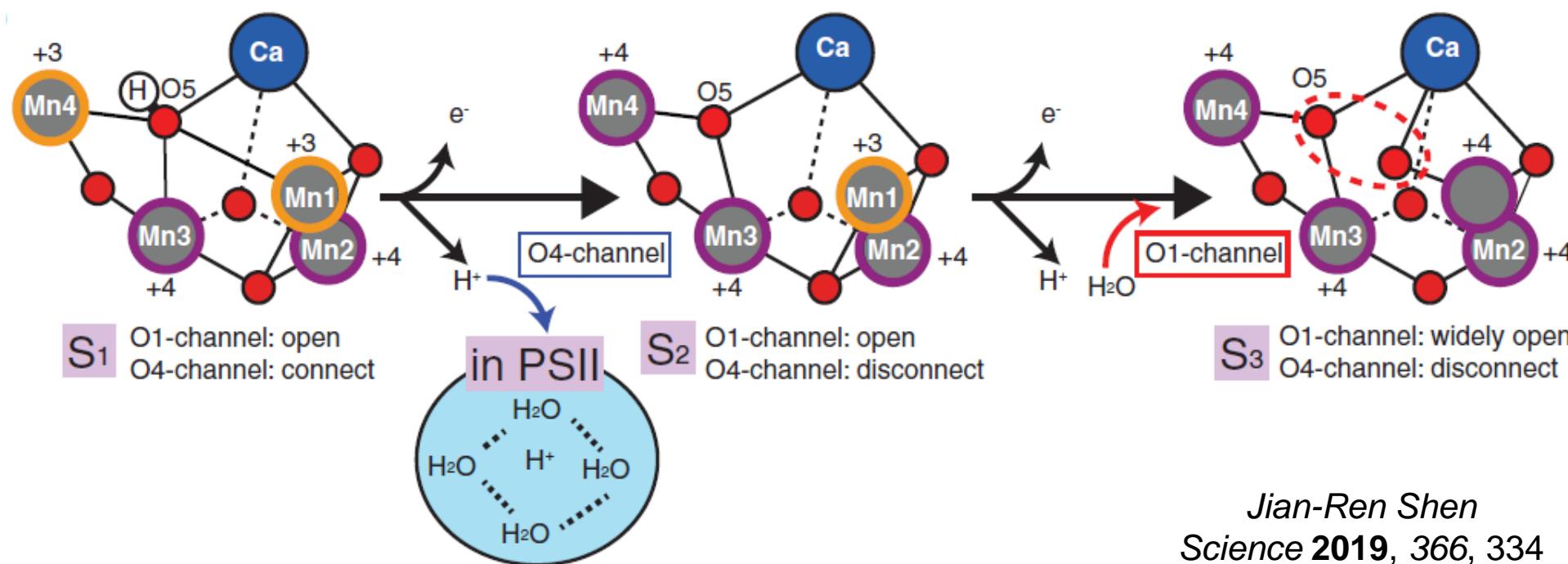
Jian-Ren Shen

*Nature* 2017, 543, 131

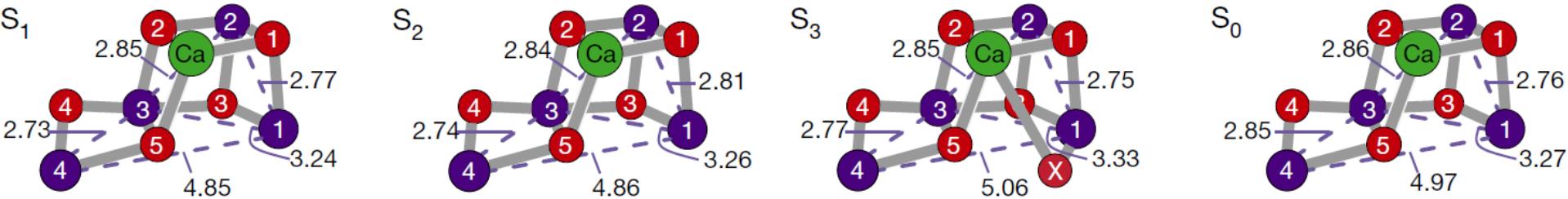
# S1-S3 States observed by serial X-ray free-e laser



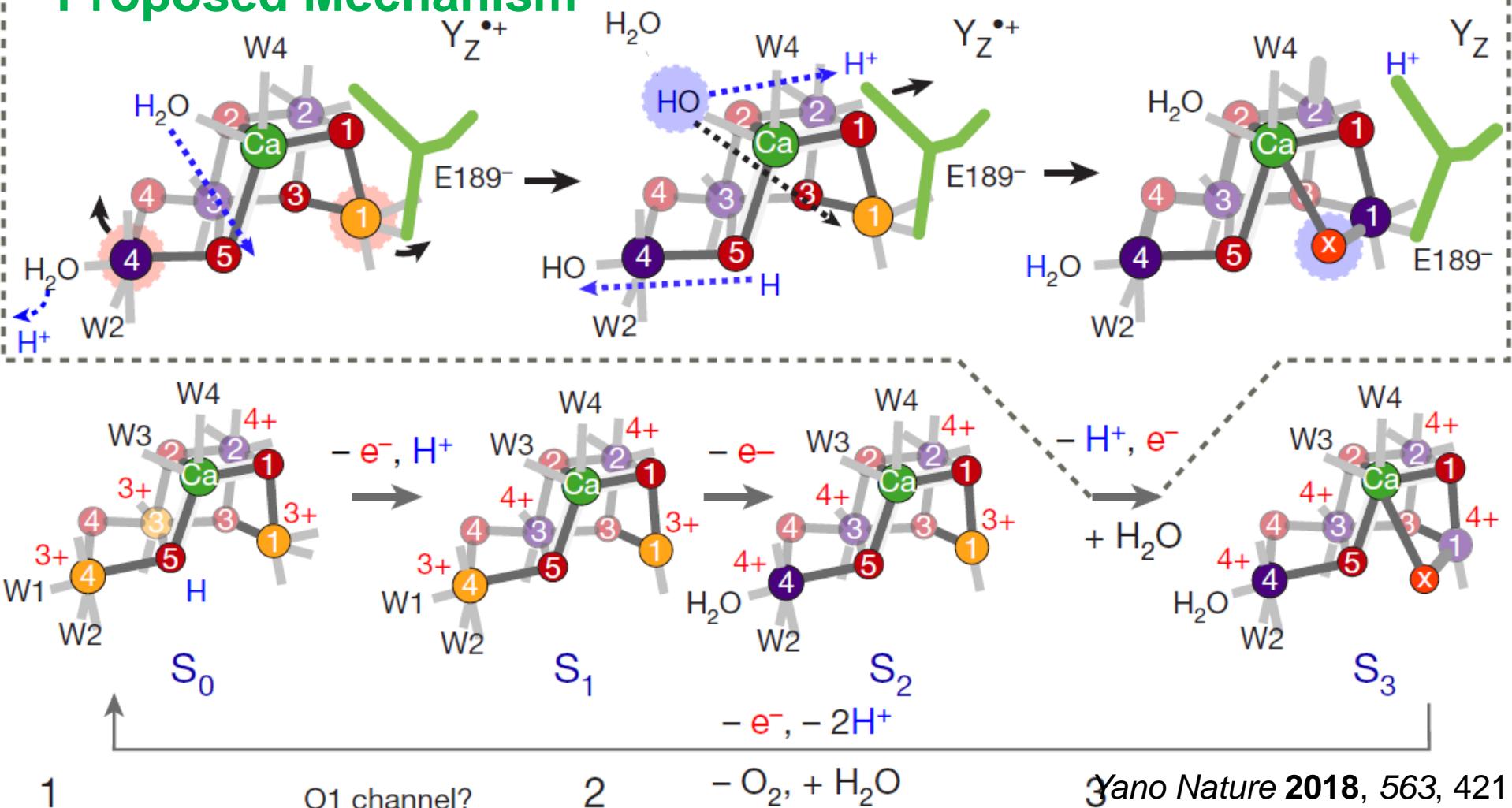
## Proposed Mechanism



# S1-S3 States observed by serial fs X-ray ( $\sim$ 2.0-2.1 Å)

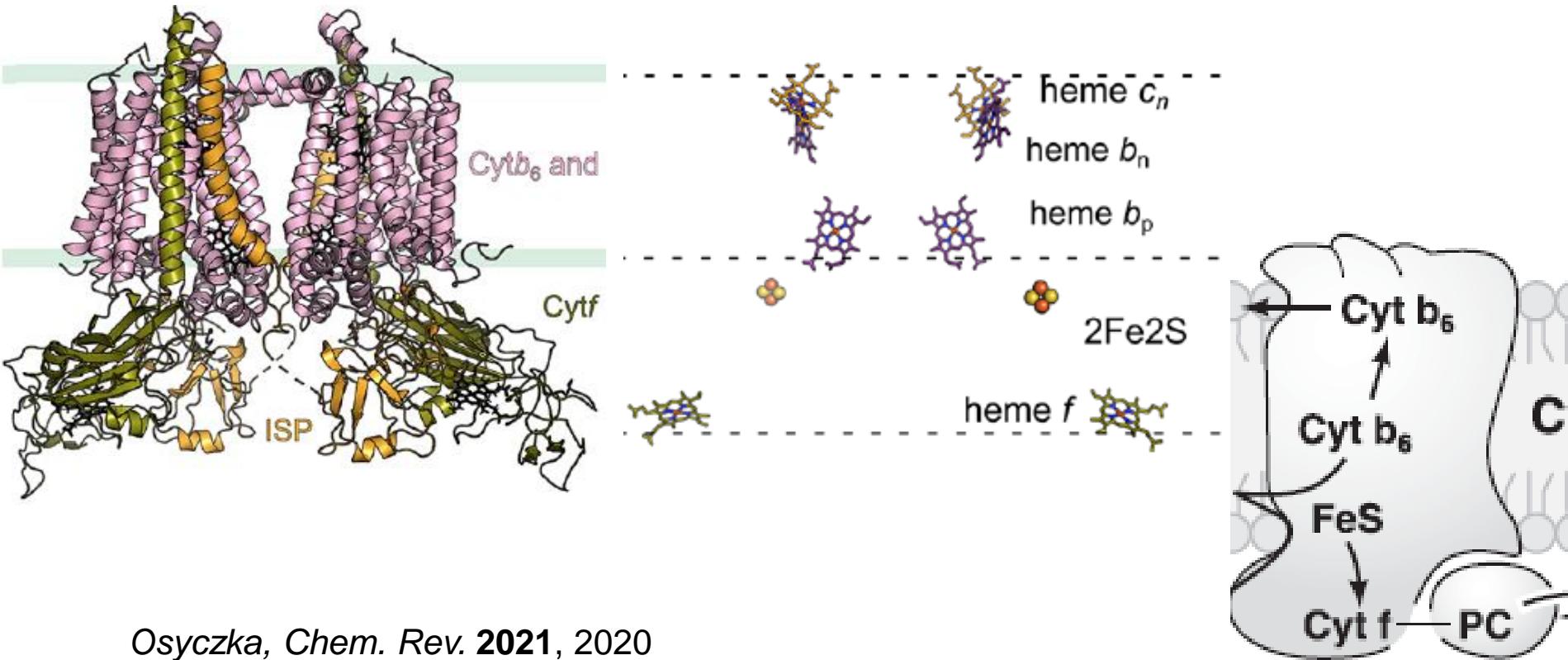


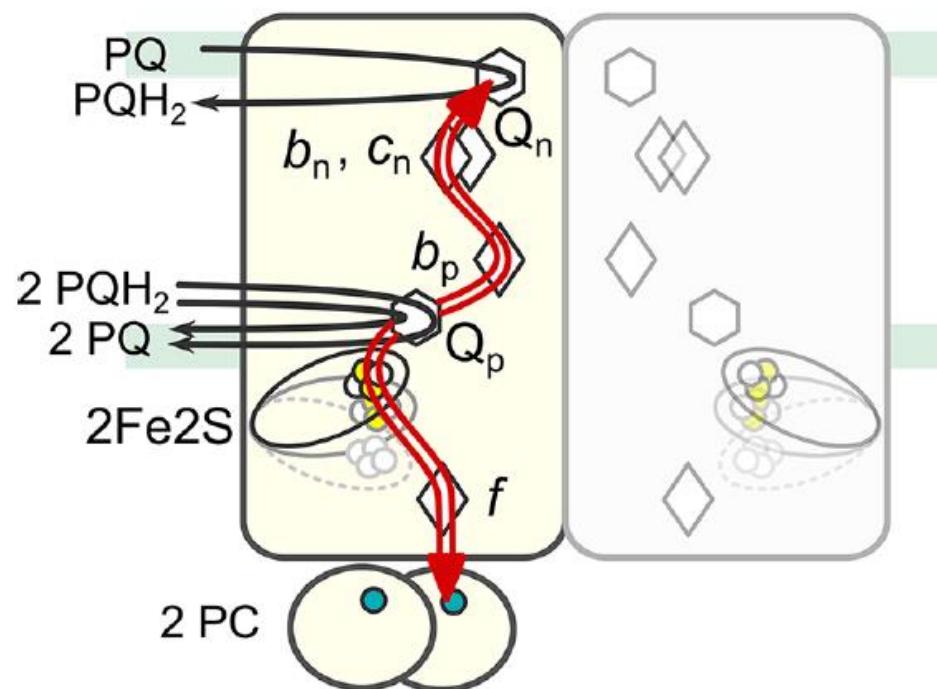
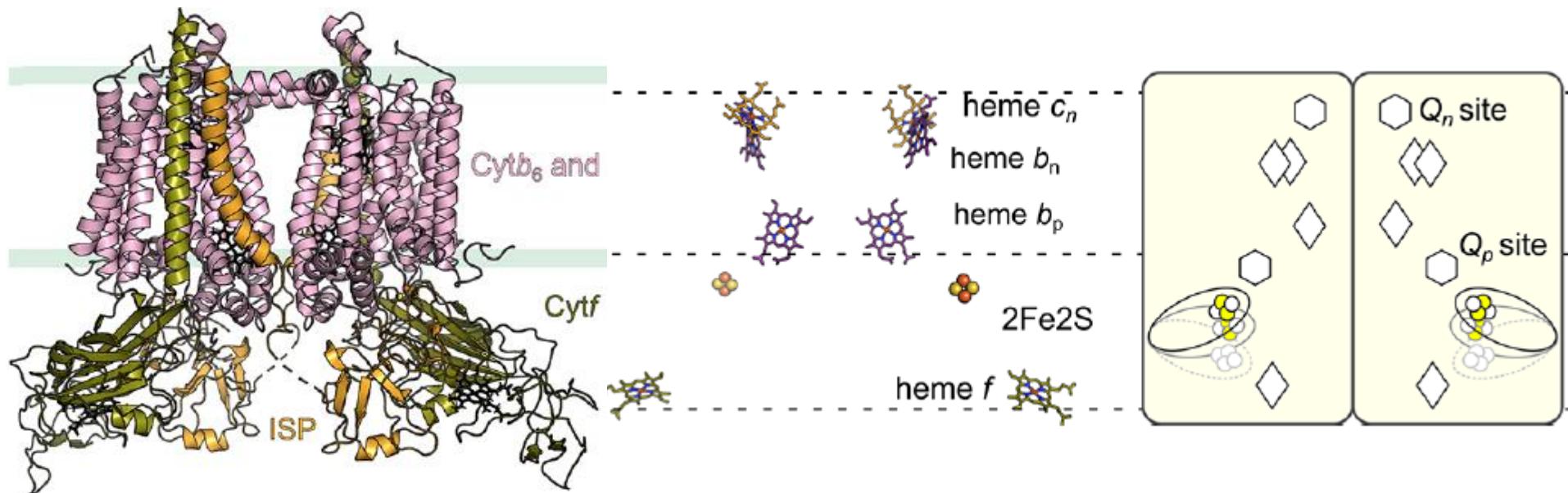
## Proposed Mechanism



# Cyt *b*<sub>6</sub>*f* Complex

- Contains 2 *b*-type hemes (*b*<sub>6</sub>, E = -150 (b<sub>L</sub>) & -50 mV (b<sub>H</sub>)), a c<sub>1</sub>-type heme Cyt *f* (E = 340 mV), & a Rieske 2Fe2S cluster (E ~300 mV).
- **Oxidize PQH<sub>2</sub>** to release 2e<sup>-</sup> + 2H<sup>+</sup> and **reduce** the water-soluble **blue copper protein** plastocyanin (**PC**, E = 0.375 V, a Cu ion with 2 His & 1 Cys & 1 Met).

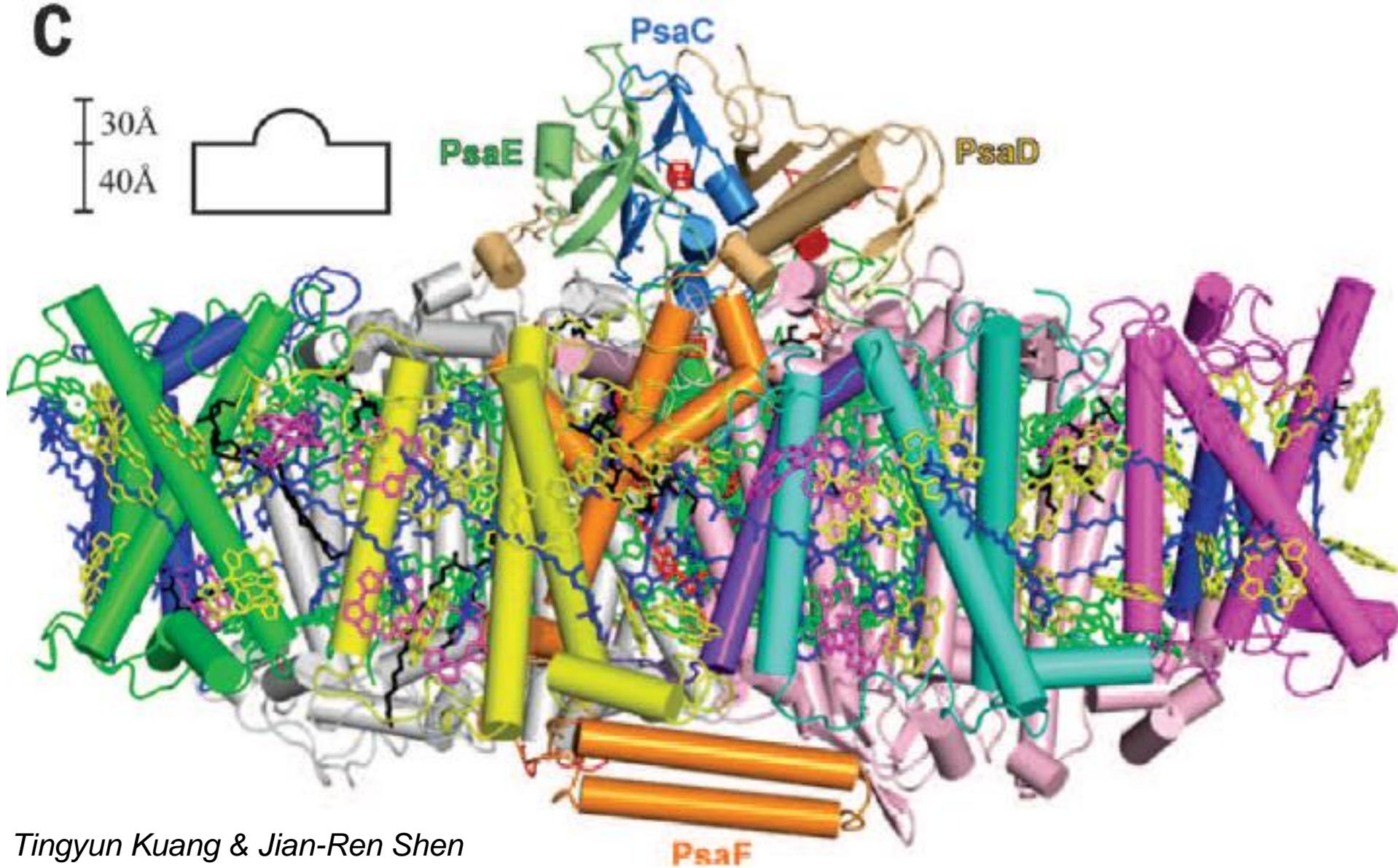


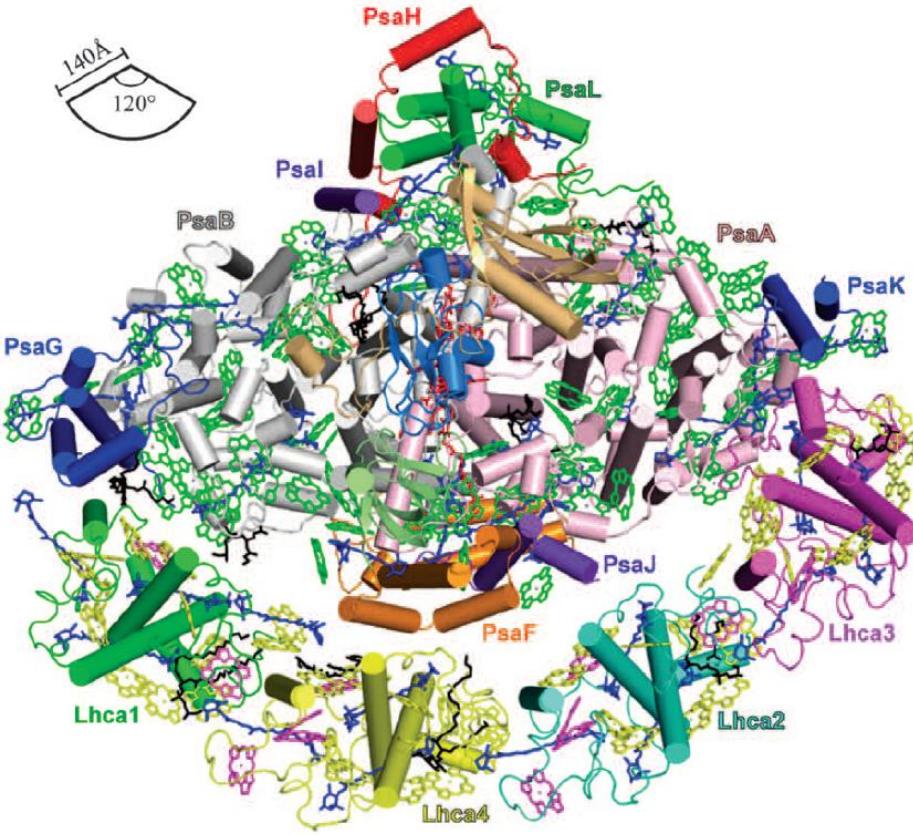


# Crystal Structure of PS I-LHC I Supercomplex (2.8Å)

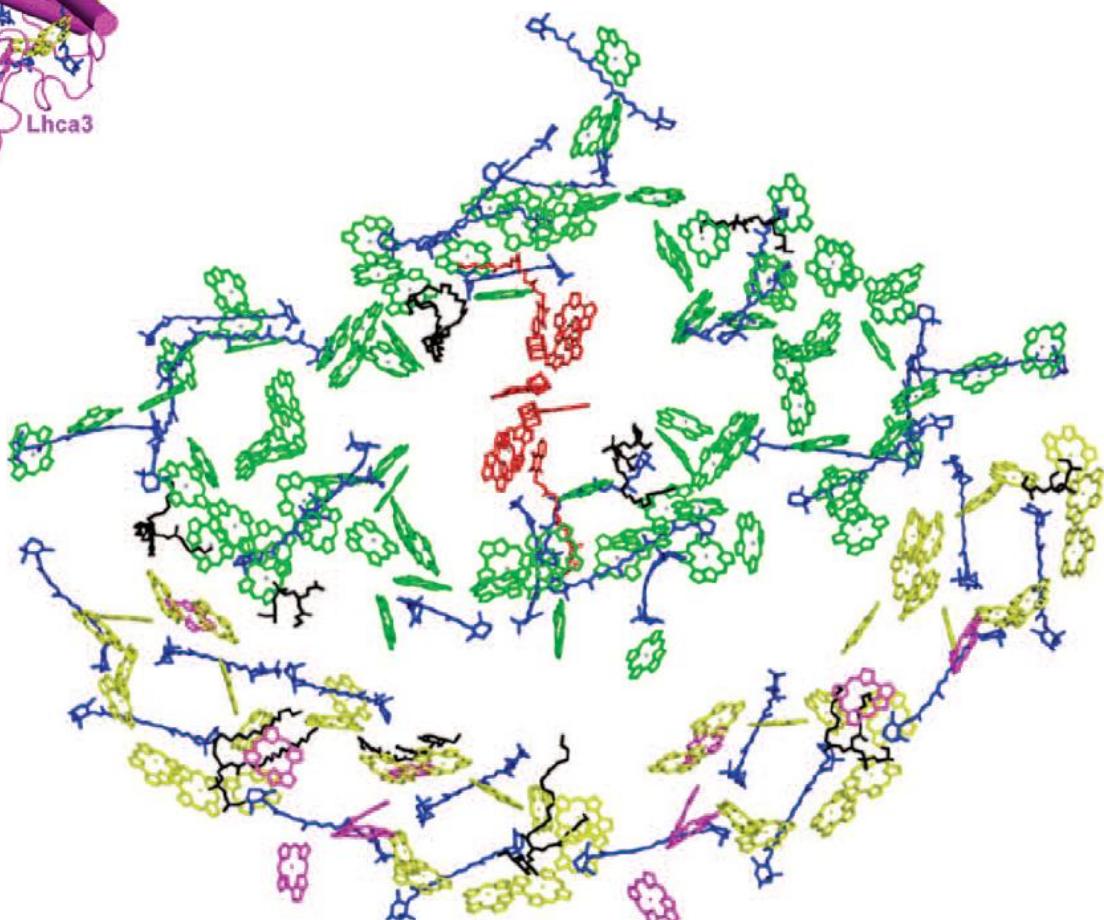
C

30Å  
40Å



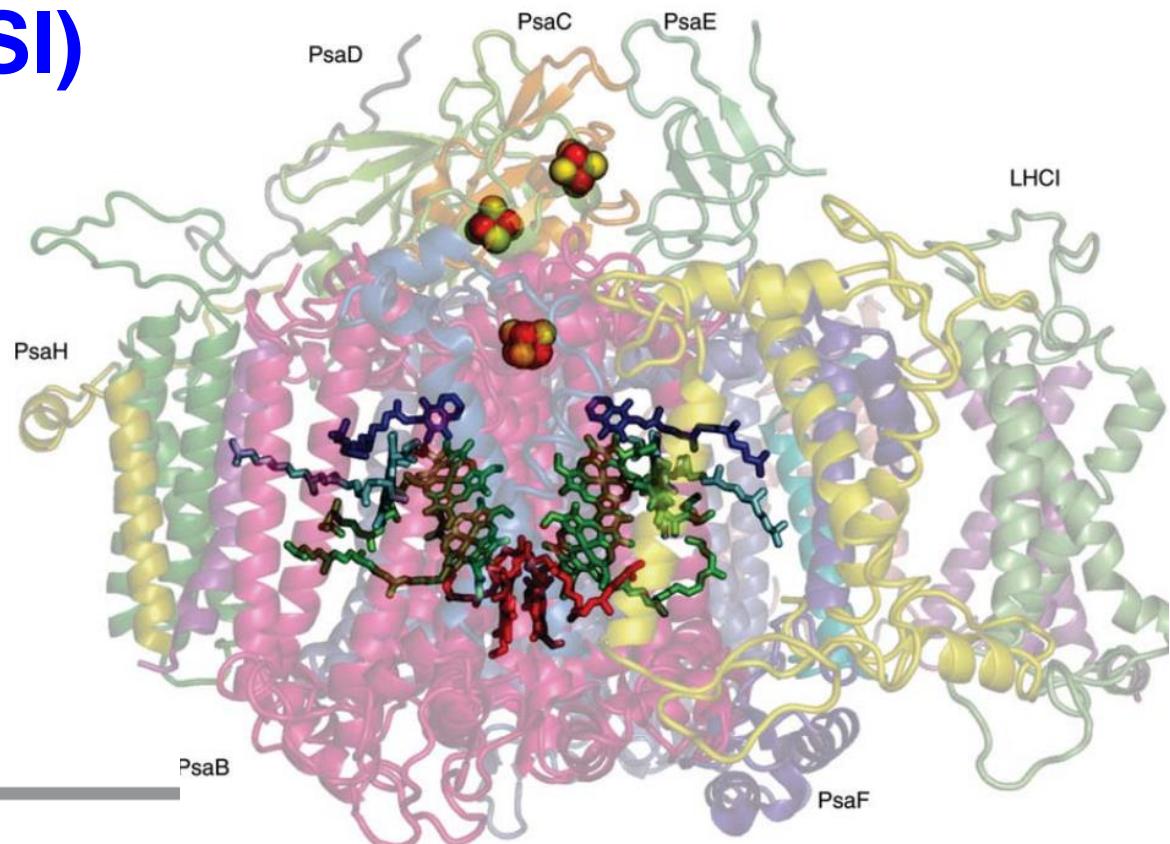


## Arrangement of pigments & other cofactors



# Photosystem I (PSI)

- The electron donor to the photooxidized PSI, P<sub>700</sub><sup>+</sup> (a dimer of chl a molecules): Plastocyanin (Cu(I))

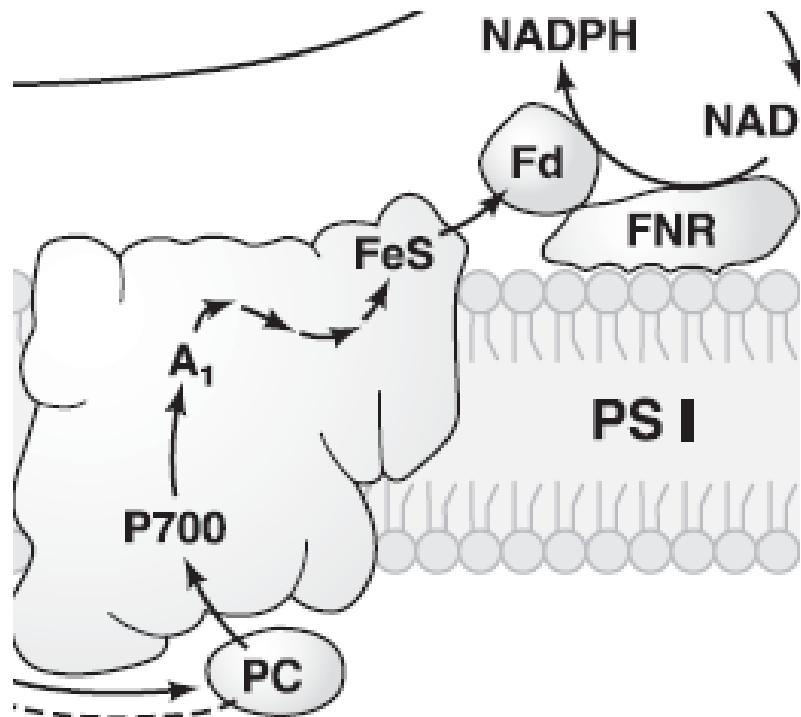
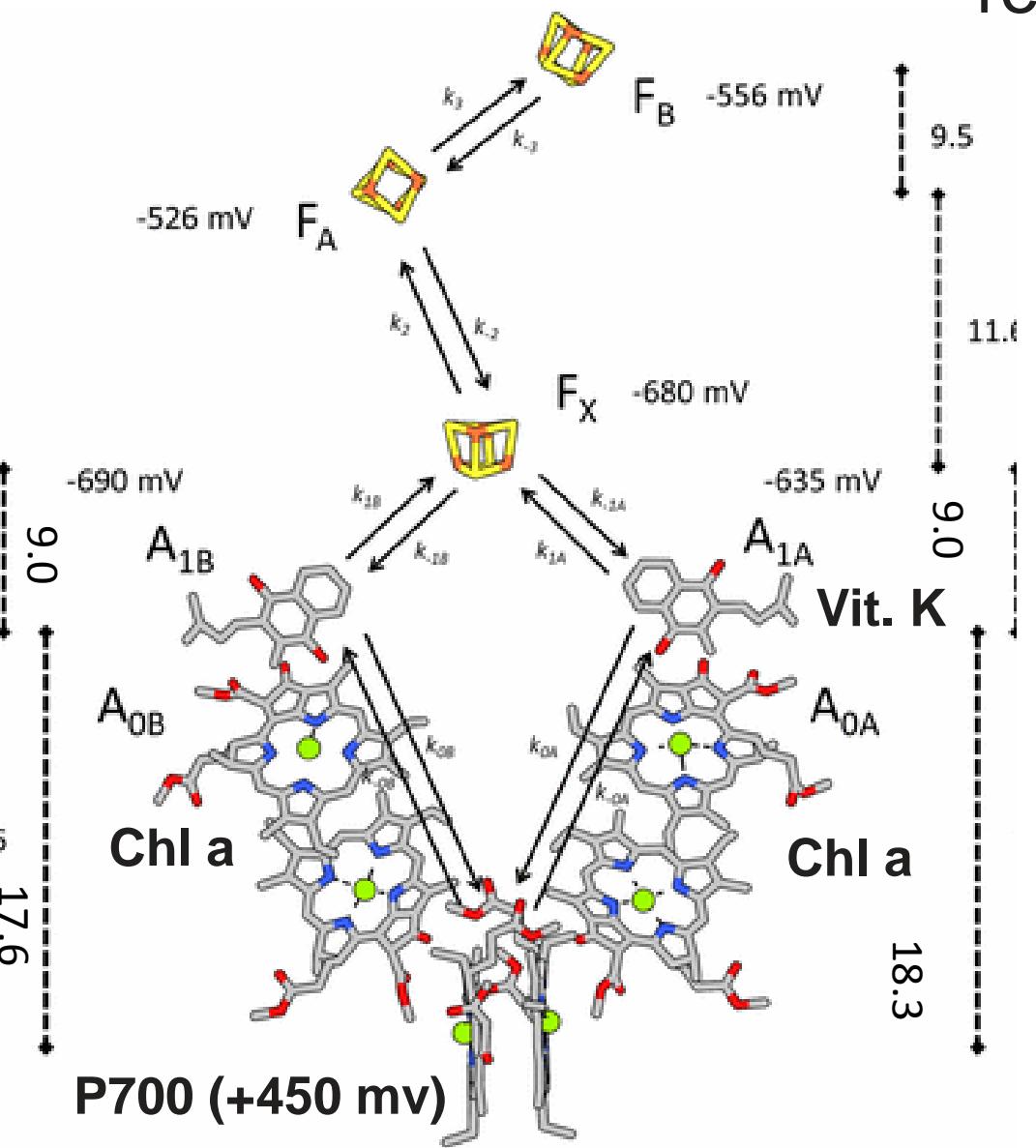


## Electron-Transfer Cofactors

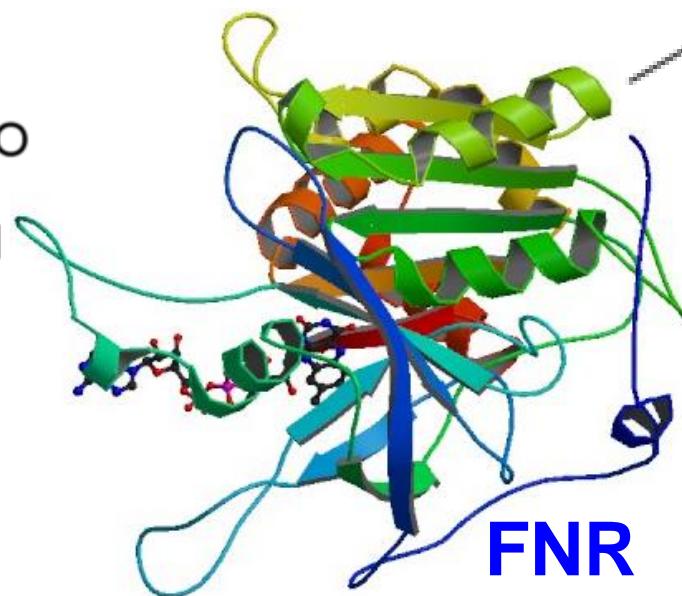
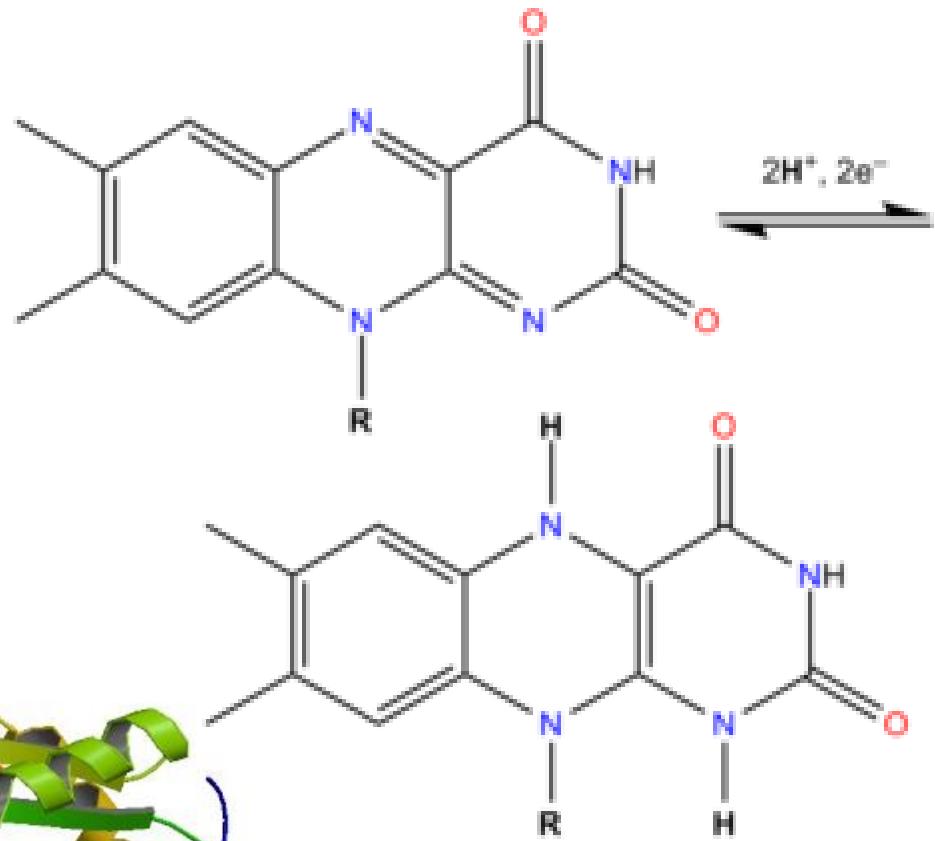
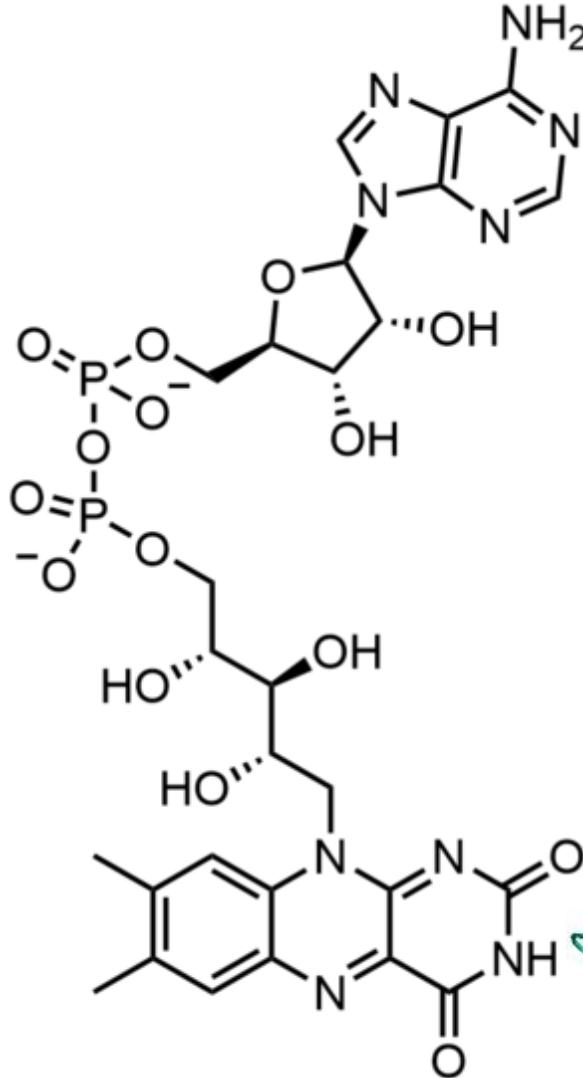
### PSI

(D) Electron donor $E^{\circ'}$	Plastocyanin (Cu <sup>+</sup> ) + 0.375 V
(P) Reaction center chlorophyll $E^{\circ'}$	P <sub>700</sub> /P <sub>700</sub> <sup>+</sup> + 0.45 V
(I) Intermediate electron carrier $E^{\circ'}$	Chlorophyll <i>a</i> , vitamin K (?) (ca. -1.0 V)
(A) Stable electron acceptor $E^{\circ'}$	F <sub>d</sub> (4Fe-4S) (-0.7 V)

- ET pathway:  $P700 \rightarrow \text{Chl } a \rightarrow \text{Vit. K} \rightarrow 4\text{Fe4S}$  clusters  $\rightarrow$  ferredoxin (Fd); Fd reduces ferredoxin-NADP reductase (FNR, with FAD) & finally reduces  $\text{NADP}^+$ .



# FNR & Flavin adenine dinucleotide (FAD)



**Reduction of  
FAD to FADH<sub>2</sub>**

**FNR**

# Key Summary

- **ET**: the simplest redox rxn; common & key in biology.
- **Efficient & distant ET** in biology: **slightly negative  $\Delta G$ , shorter ET pathways** (via “conducting” cofactors) & **small reorganization energy, medium & tunneling**.
- Usually **Fe- or Cu-containing metalloproteins (Fe-S, Cytochromes (types a-c hemes), blue copper & Cu<sub>A</sub> proteins)** **for ET** with wide range of reduction potentials.  
Their **redox states: Cu(II)/Cu(I) & Fe(III)/Fe(II)**.
- **Reduction potential** can be tuned by combined effects of **coordination sphere** (e.g. ligand field, HASB & charge), **solvent accessibility**, **electrostatic interactions** with the others (proteins and cofactor).

- Proton + electron transfers via a chain of redox cofactors with gradually increasing their reduction potentials &  $O_2$  is also involved to facilitate ATP formation in photosynthesis & respiration.
- In respiration, a reductant NADH is used as energy/e<sup>-</sup> source to reduce  $O_2$  to form  $H_2O$ .
- Whereas, in photosynthesis, solar energy & reductant  $H_2O$  as the e<sup>-</sup> source are used to form  $O_2$  & reduce NADP<sup>+</sup> to form NADPH.
- A heme & Cu<sub>B</sub> center involves in the  $O_2$  reduction in respiration. While, Mn<sub>4</sub>CaO<sub>5</sub> cluster involves in the  $O_2$  formation in photosynthesis.

**Thank You for Your  
Attention!  
Any Questions?**