

The Redox Players I: Fe-S clusters

Table 22-1 Reduction Potentials of Electron-Transport Chain Components in Resting Mitochondria

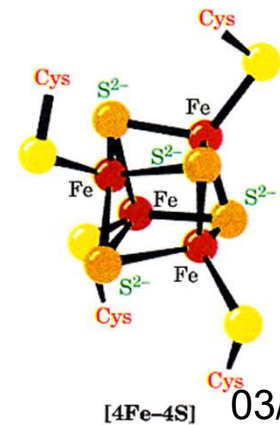
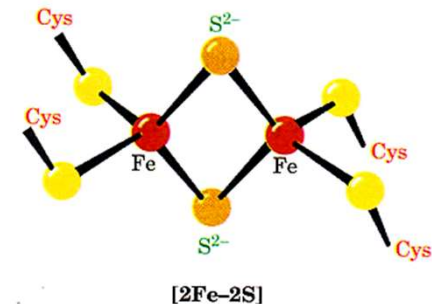
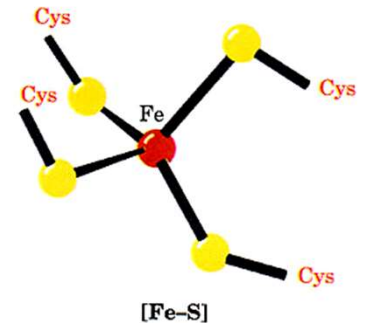
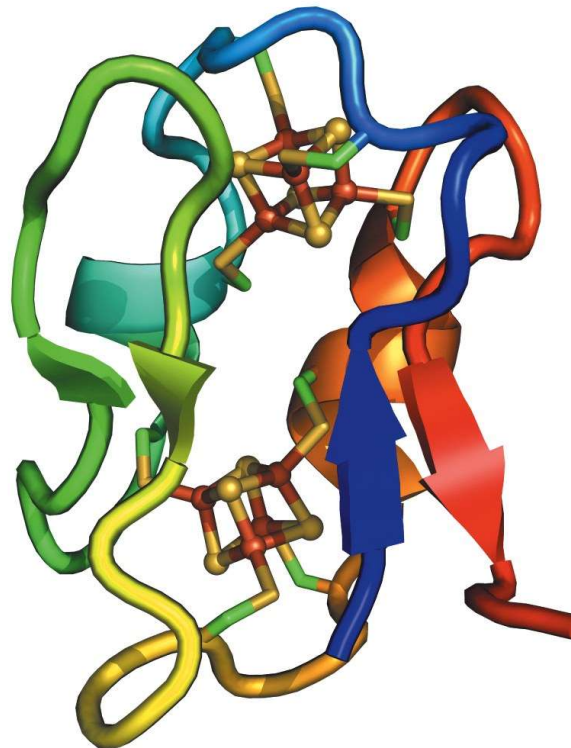
Component	E° (V)
NADH	-0.315
Complex I (NADH:CoQ oxidoreductase; ~900 kD, 45 subunits):	
FMN	-0.380
[2Fe-2S]N1a	-0.370
[2Fe-2S]N1b	-0.250
[4Fe-4S]N3, 4, 5, 6a, 6b, 7	-0.250
[4Fe-4S]N2	-0.150
Succinate	0.031
Complex II (succinate-CoQ oxidoreductase; ~420 kD, 4 subunits):	
FAD	-0.040
[2Fe-2S]	-0.030
[4Fe-4S]	-0.245
[3Fe-4S]	-0.060
Heme b_{560}	-0.080
Coenzyme Q	0.045
Complex III (CoQ-cytochrome c oxidoreductase; ~450 kD, 9-11 subunits):	
Heme b_H (b_{562})	0.030
Heme b_L (b_{566})	-0.030
[2Fe-2S]	0.280
Heme c_1	0.215
Cytochrome c	0.235
Complex IV (cytochrome c oxidase; ~410 kD, 8-13 subunits):	
Heme a	0.210
Cu _A	0.245
Cu _B	0.340
Heme a_3	0.385
O ₂	0.815

Rising reduction potentials = oxidation power

Source: Mainly Wilson, D.F., Erecinska, M., and Dutton, P.L., *Annu. Rev. Biophys. Bioeng.* **3**, 205 and 208 (1974); and Wilson, D.F., In Bittar, E.E. (Ed.), *Membrane Structure and Function*, Vol. 1, p. 160, Wiley (1980).

The oxidized and reduced forms of iron-sulfur clusters differ by 1 formal charge in the conjugated system (e.g., $\text{Fe(II)/Fe(III)}_3 \rightarrow \text{Fe(II)}_2/\text{Fe(III)}_2$):

- All irons are tetrahedrally coordinated to Cys or S^{2-}
- Contained in iron-sulfur proteins (= non-heme iron proteins), example ferredoxin:



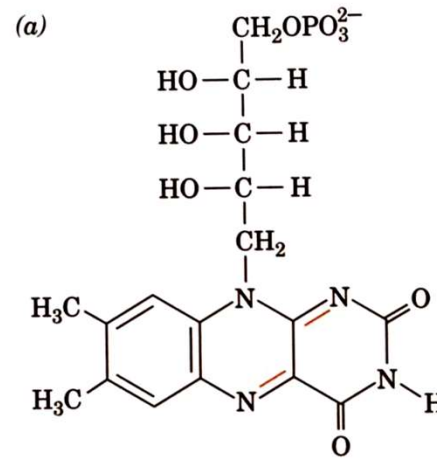
The Redox Players II: Quinones

The coenzymes of Complex I (NADH-Q reductase)

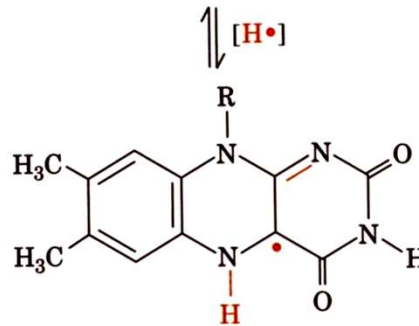
➤ FMN and CoQ are both quinones that are stable as one-electron reduced semiquinones (radicals!) and two-electron reduced hydroquinones

⇒ mediate between 2 e⁻ donor NADH and the 1 e⁻ acceptors (cytochromes) of complexes III and IV

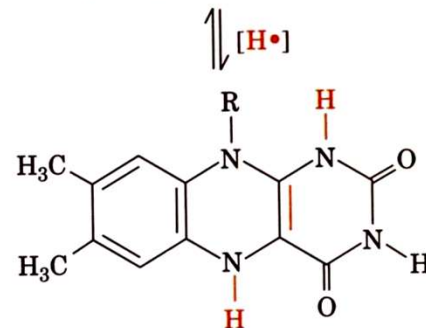
➤ 10 C₅ isoprenoid unit of mammals' CoQ leads to nomenclature "coenzyme Q₁₀" (other organisms Q₆ or Q₈)
⇒ hydrophobic tail that mediates membrane solubility!



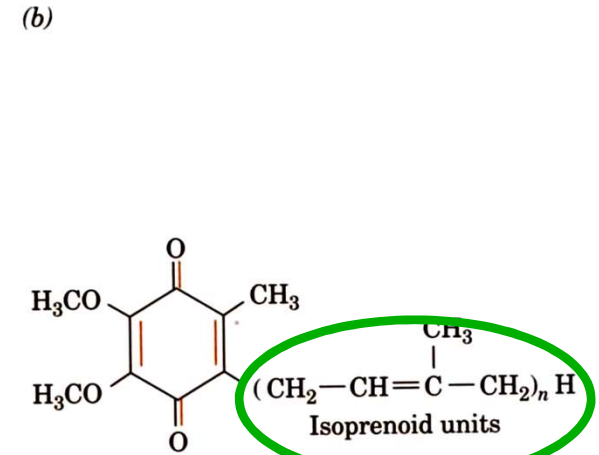
Flavin mononucleotide (FMN)
(oxidized or quinone form)



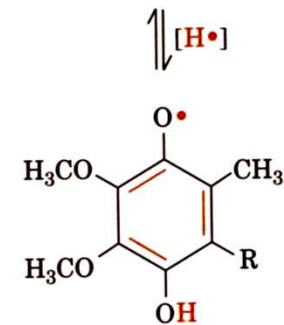
FMN• (radical or semiquinone form)



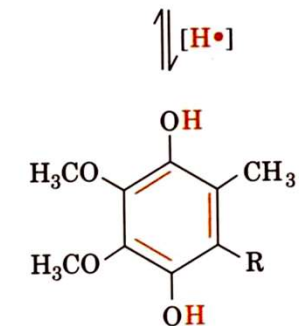
FMNH₂ (reduced or hydroquinone form)



Coenzyme Q (CoQ) or Ubiquinone
(oxidized or quinone form)



Coenzyme QH• or Ubisemiquinone
(radical or semiquinone form)



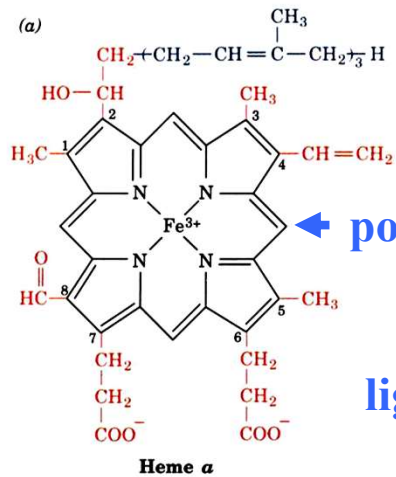
Coenzyme QH₂ or Ubiquinol
(reduced or hydroquinone form)

The Redox Players III: Cytochromes

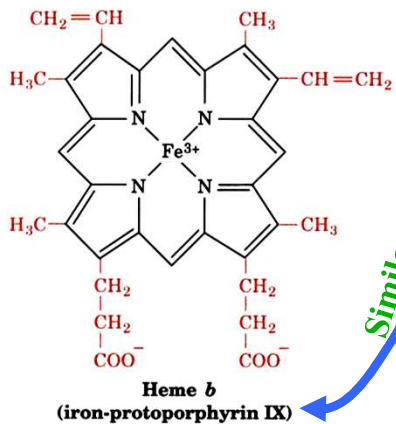
Cytochromes = Redox-active proteins with heme groups:
 $\text{Fe(II)} \rightleftharpoons \text{Fe(III)}$

Cytochromes transfer electrons through sigma bonds over distances of 10-20 Å at physiologically significant rates!

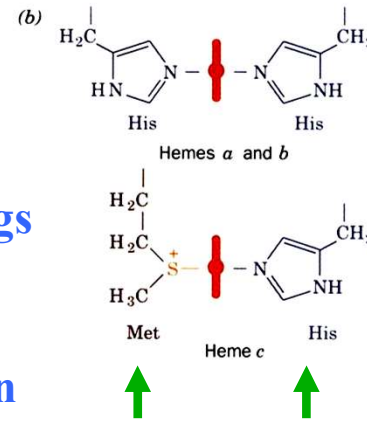
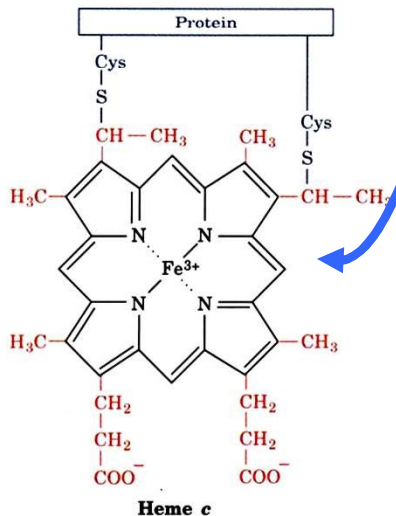
➤ have visible absorption spectra with α , β , and γ (Soret) bands
⇒ can easily and specifically be detected:



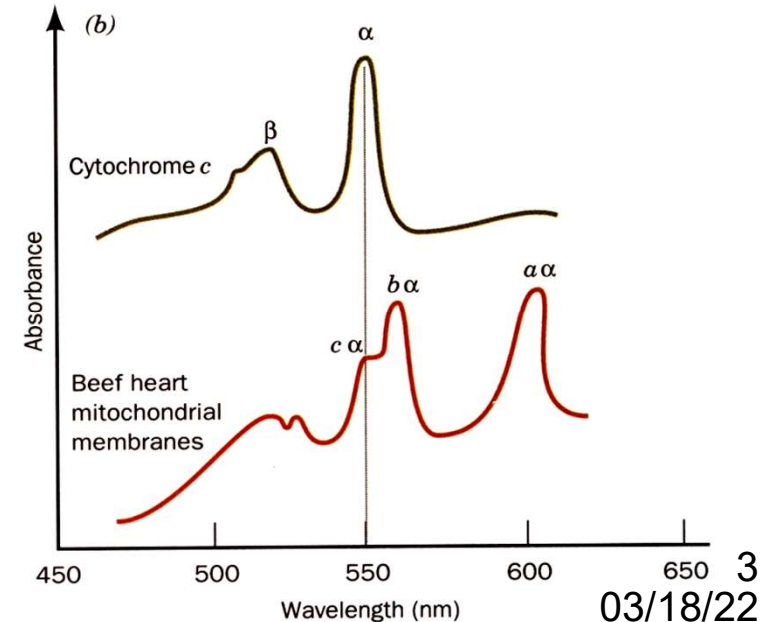
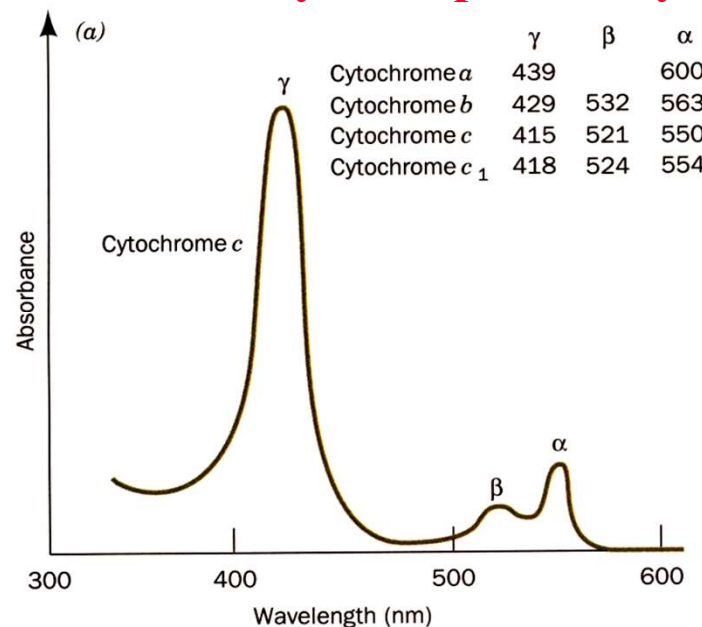
porphyrin rings
are the
equatorial
ligands to iron



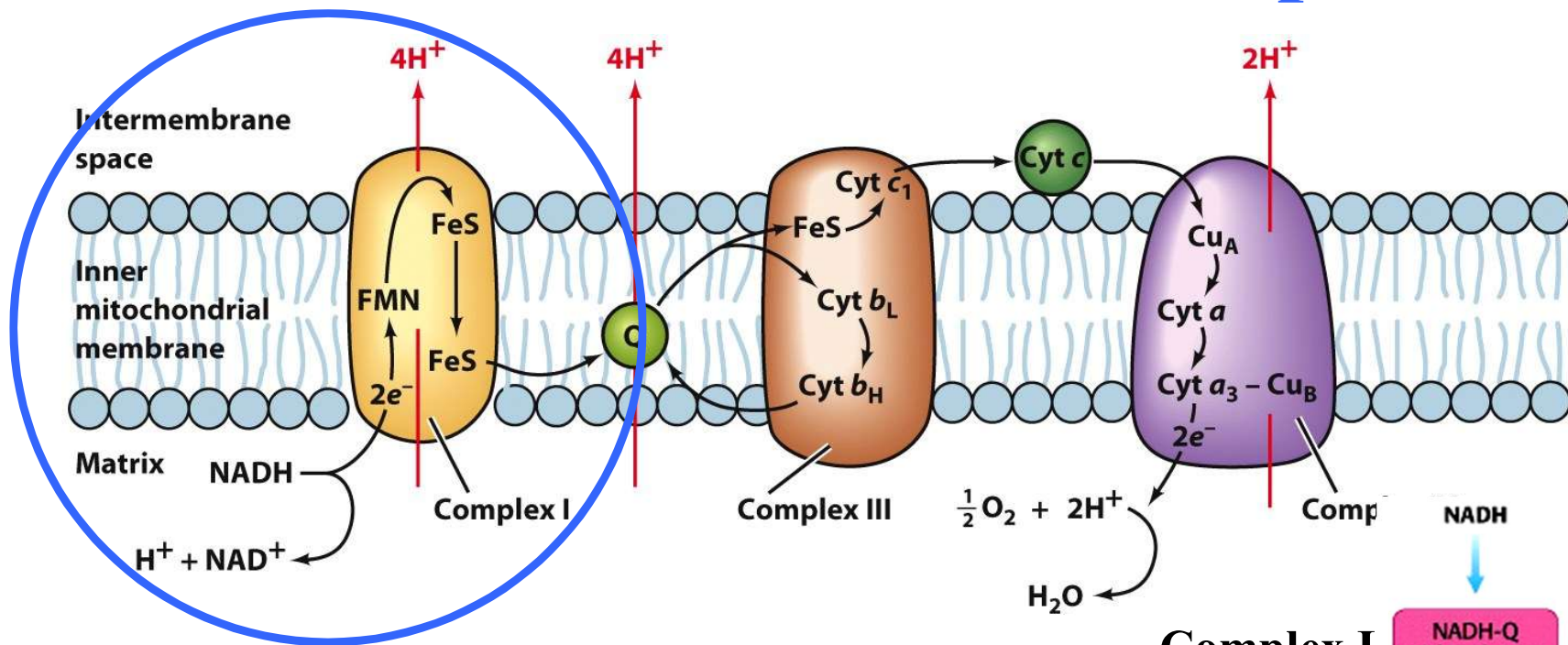
Similar to hemoglobin



Met and His are
the axial ligands to
iron (and shield it
from O_2 !)



How It All Works: Electron Transport Chain



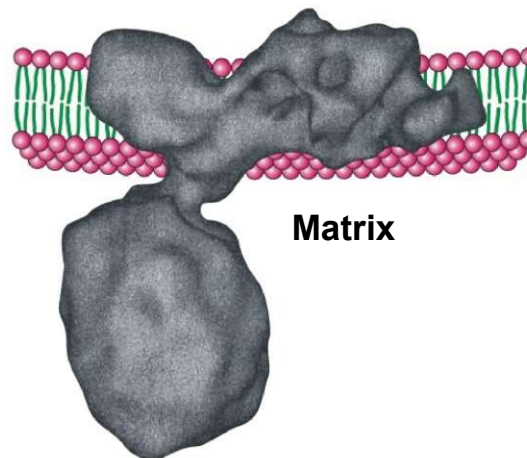
➤ Complex I:

- ♣ electrons are transferred from the 2 e⁻ carrier NADH to the 1 or 2 e⁻ carrier FMN and the Fe-S clusters;
- ♣ they are then passed on to Coenzyme Q that is lipid soluble and takes them to Complex III;
- ♣ 4 H⁺ are concomitantly pumped out of the matrix

♣ 880kD in 34

polypeptide chains;

♣ large, NADH binding matrix arm:

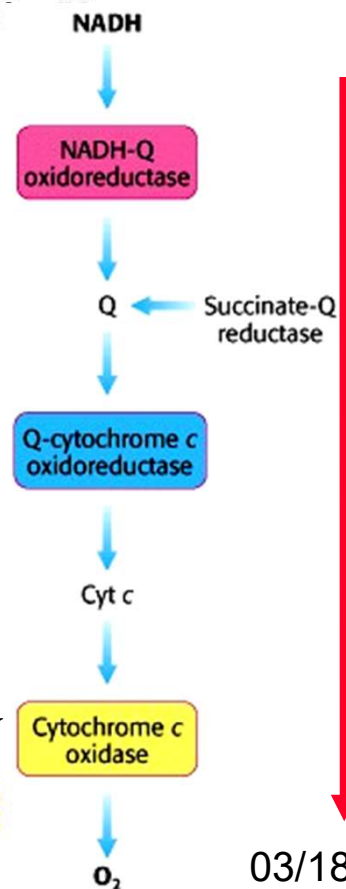


Complex I

Complex III

Complex IV

Nils Walter: Che

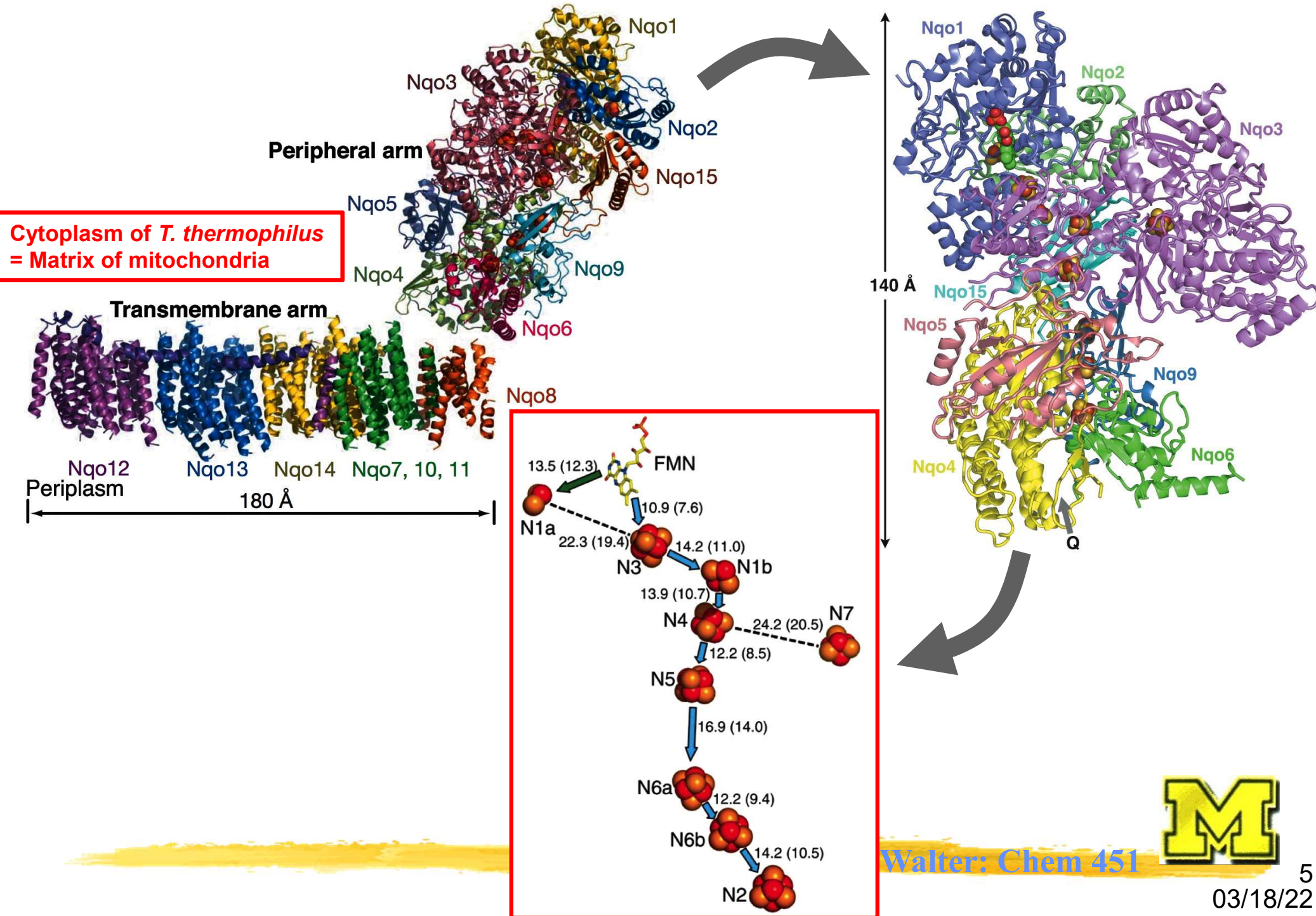


Rising reduction potentials = oxidation power

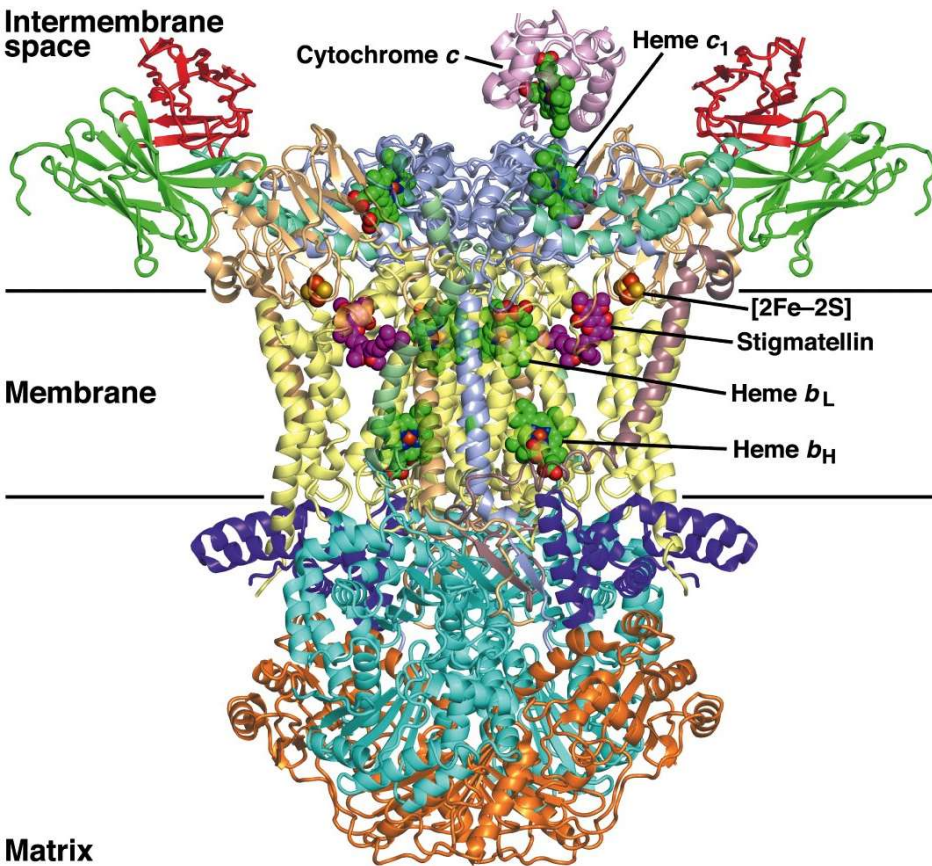
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Details of Complex I from *T. thermophilus*

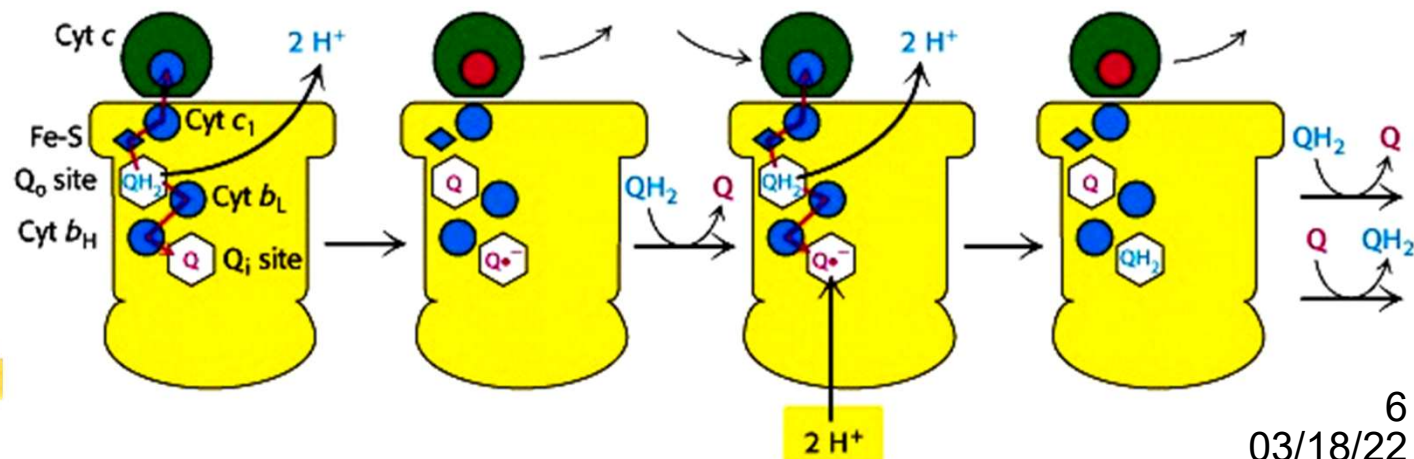
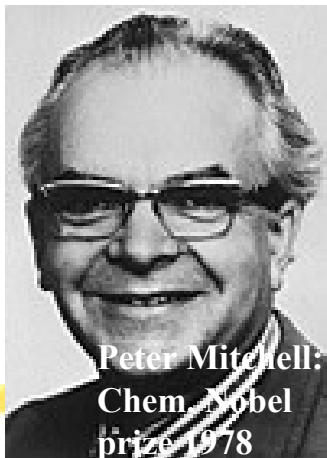


Complex III: Q-Cytochrome c Reductase

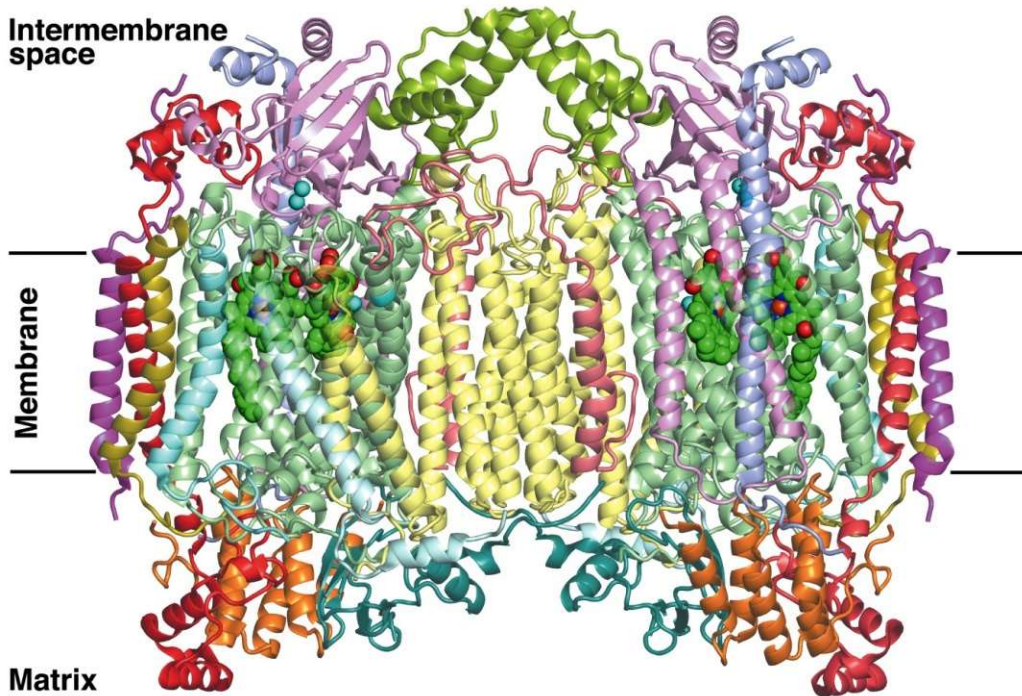


➤ Complex III:

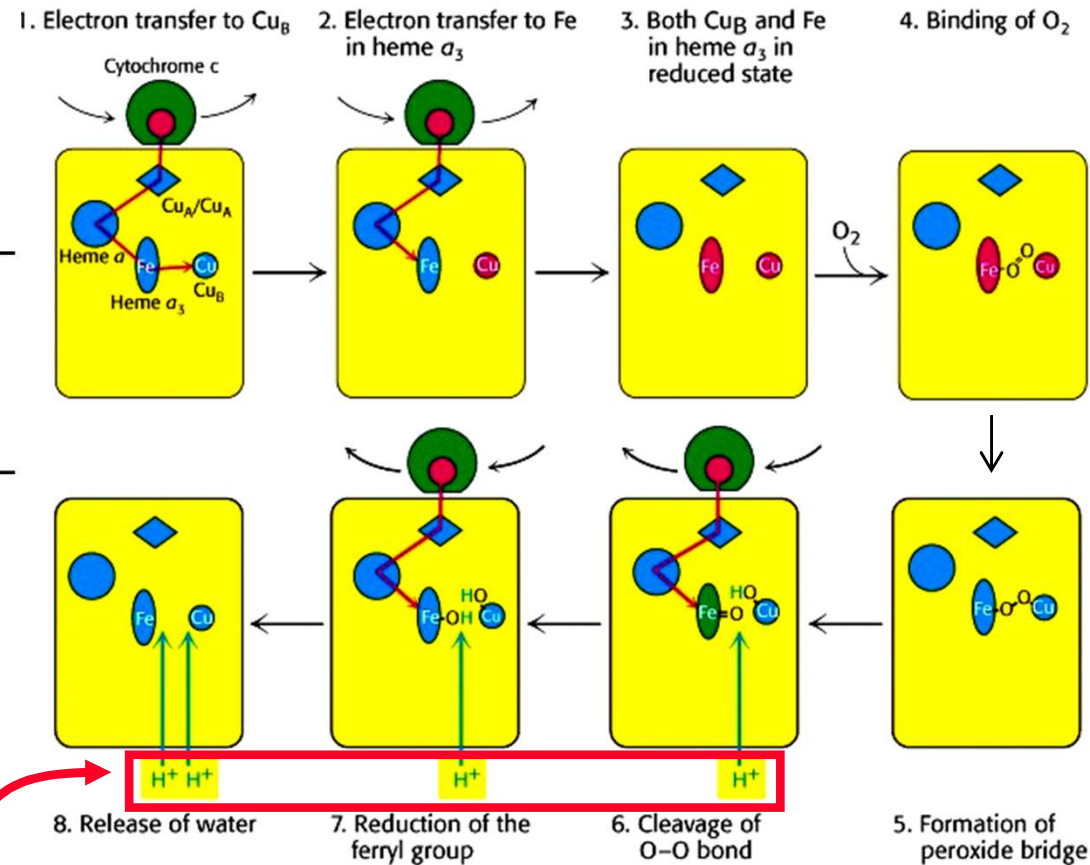
- ♣ dimer with 11 polypeptide chains/monomer;
- ♣ hemes b_L (for Low affinity) and b_H (for High affinity) within cytochrome b, one c-type heme in cytochrome c_1 ;
- ♣ contains one 2Fe-2S cluster (Rieske center) with one Fe coordinated by two His (instead of Cys)
⇒ stabilizes reduced form = raises reduction potential!
- ♣ oxidizes CoQ, reduces cytochrome c
- ♣ 4 H^+ are pumped out of the matrix during the “Q cycle”:



Complex IV: Cytochrome c Oxidase



Mechanism:



➤ Complex IV:

- ♣ ~200kD; 13 polypeptide chains, 3 encoded in mitochondrial genome;
- ♣ contains 2 hemes a and 3 copper ions (shuttle between Cu(II) and Cu(I));
- ♣ catalyzes:



⇒ removes 4 H^+ from matrix!

➤ in addition: pumps 4 more H^+ for a total of 8 H^+ removed from matrix;

how may such pumping occur?

- ♣ charge neutralization of e^- in protein core by H^+
- ♣ conformational changes that guide H^+ from matrix to cytosolic side (as in bacteriorhodopsin!)

