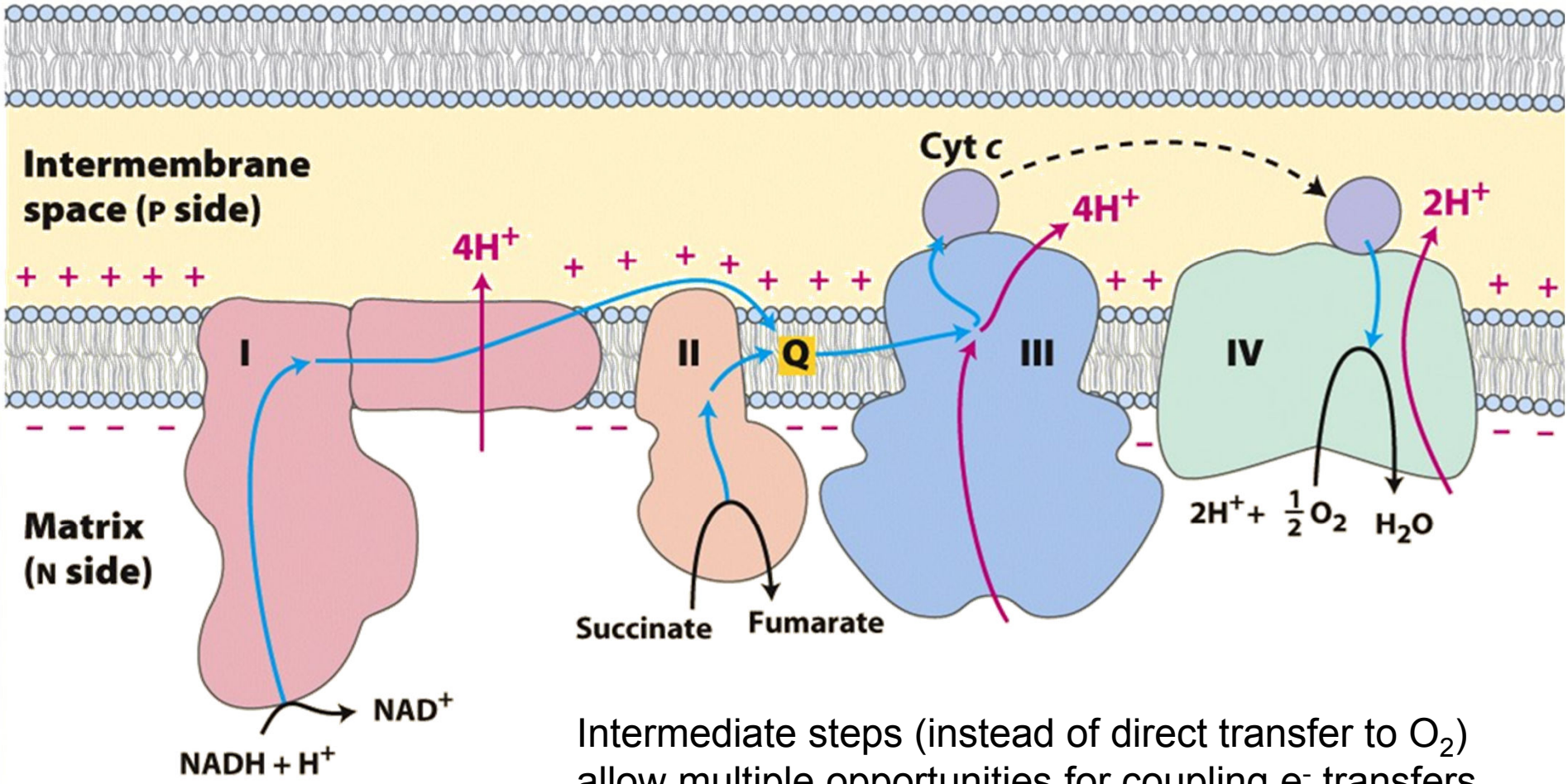
In the ETC, electrons pass through a series of protein complexes and e^- carriers to O_2



Intermediate steps (instead of direct transfer to O_2) allow multiple opportunities for coupling e^- transfers with H^+ translocations

Each protein complex contains multiple redox cofactors used to transfer electrons

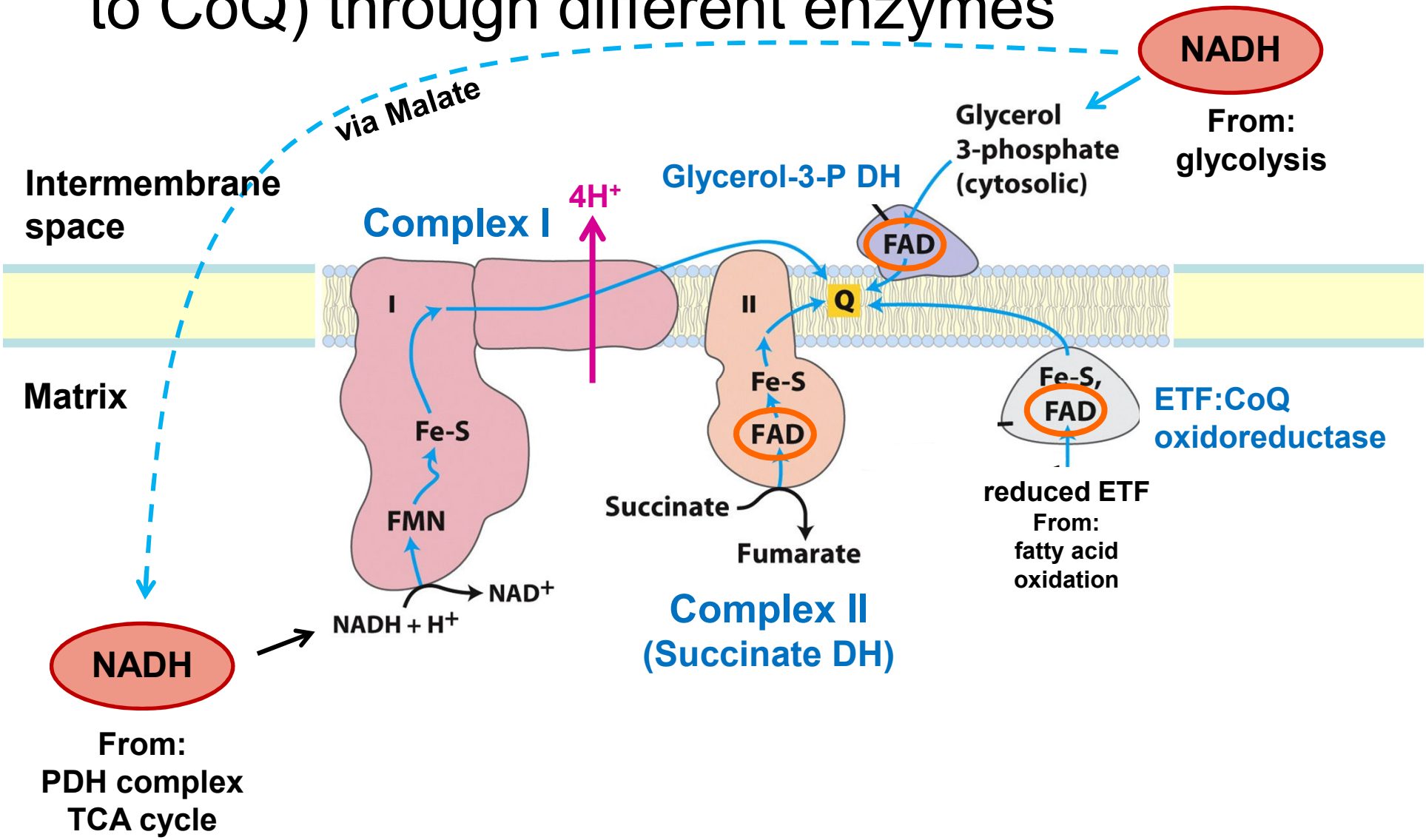
Table 18-1 Reduction Potentials of Electron-Transport Chain Components in Resting Mitochondria

Component	$\mathscr{E}^{\circ\prime}$ (V)
NADH	−0.315
Complex I (NADH–CoQ oxidoreductase; ~900 kD, 46 subunits):	
FMN	−0.340
[2Fe–2S]N1a	−0.380
[2Fe–2S]N1b	−0.250
[4Fe–4S]N3, 4, 5, 6a, 6b, 7	−0.250
[4Fe–4S]N2	−0.100
Succinate	0.031
Complex II (succinate–CoQ oxidoreductase; ~120 kD, 4 subunits):	
FA D	−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

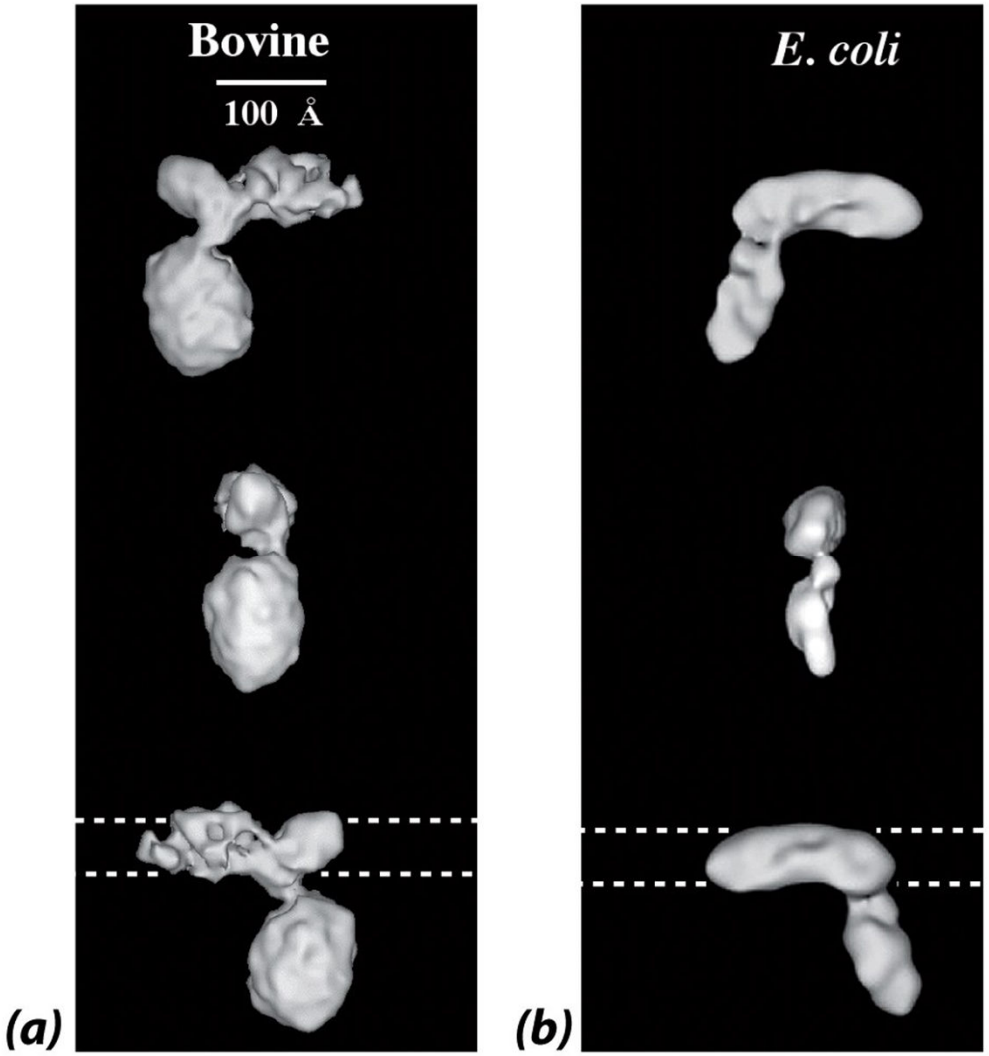
Source: Mainly Wilson, D.F., Erecinska, M., and Dutton, P.L., *Annu. Rev. Biophys. Bioeng.* 3, 205 and 208 (1974); and Wilson, D.F., in Bittar, E.E. (Ed.), *Membrane Structure and Function*, Vol. 1, p. 160,Wiley (1980).

Electrons move from cofactors of lower to higher reduction potential within each complex and from one complex or carrier to the next

Electrons enter the ETC (and are transferred to CoQ) through different enzymes



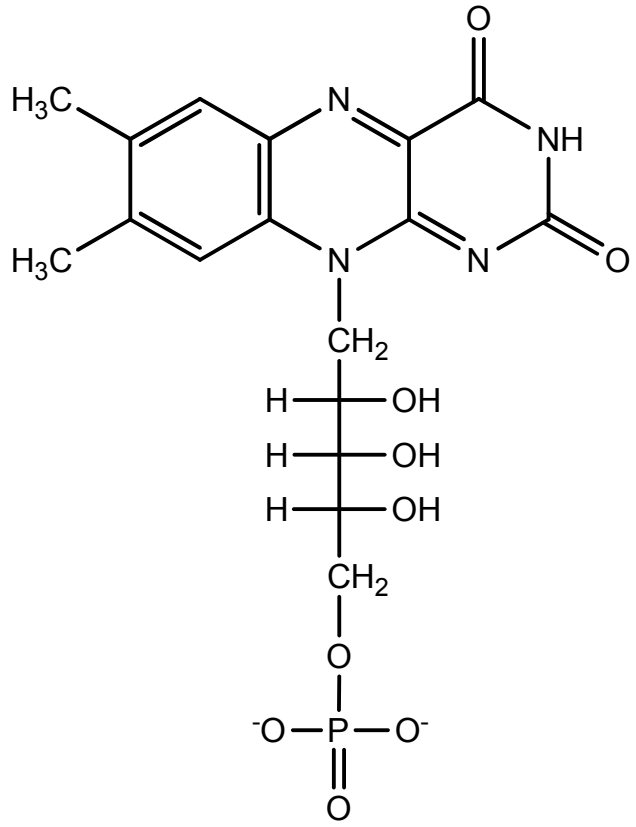
Complex I (NADH-CoQ oxidoreductase) is a large, L-shaped protein complex



Courtesy of Nikolaus Grigorieff, Brandeis University. The *E. coli* structure was determined by Vincent Guénebaut and Kevin Leonard, European Molecular Biology Laboratory, Heidelberg, Germany.

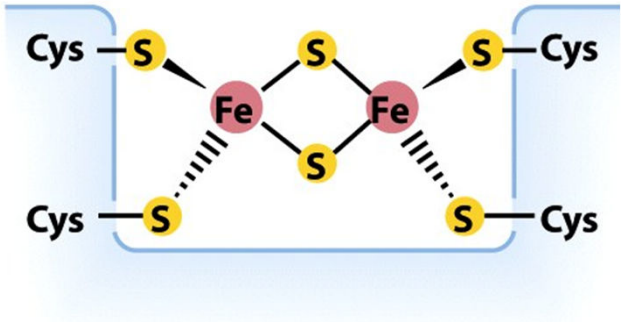
Complex I uses three kinds of redox centers

FMN

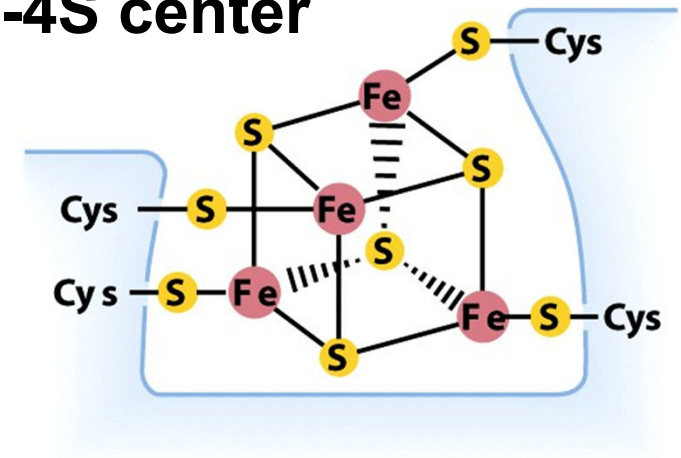


Flavin nucleotides transfer one or two e^- (and H^+) at a time

2Fe-2S center

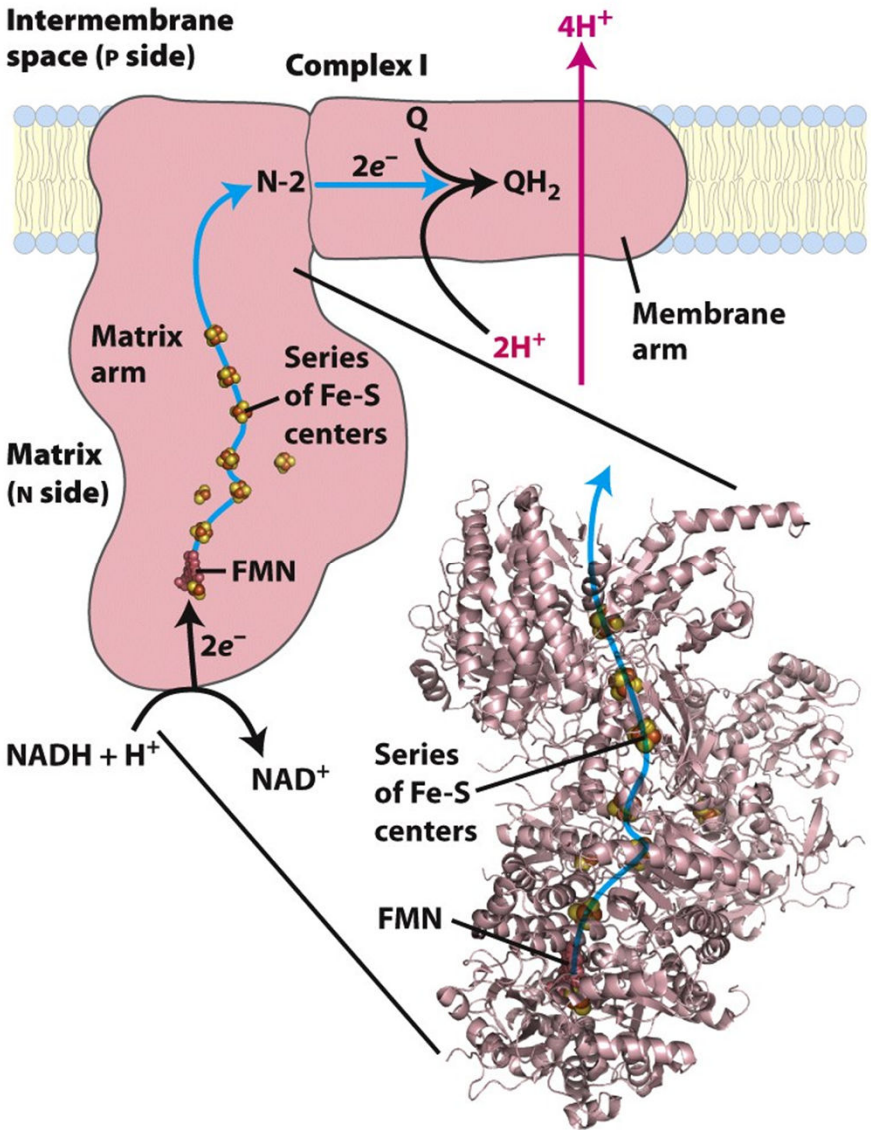


4Fe-4S center

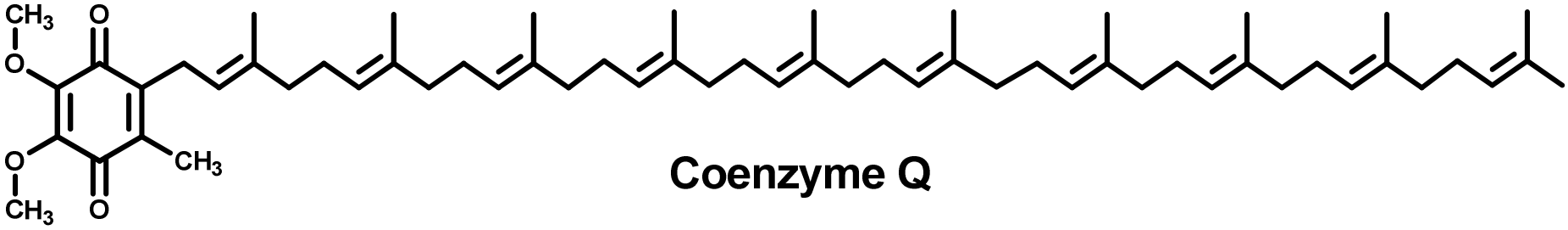


Iron-sulfur clusters transfer only one e^- at a time

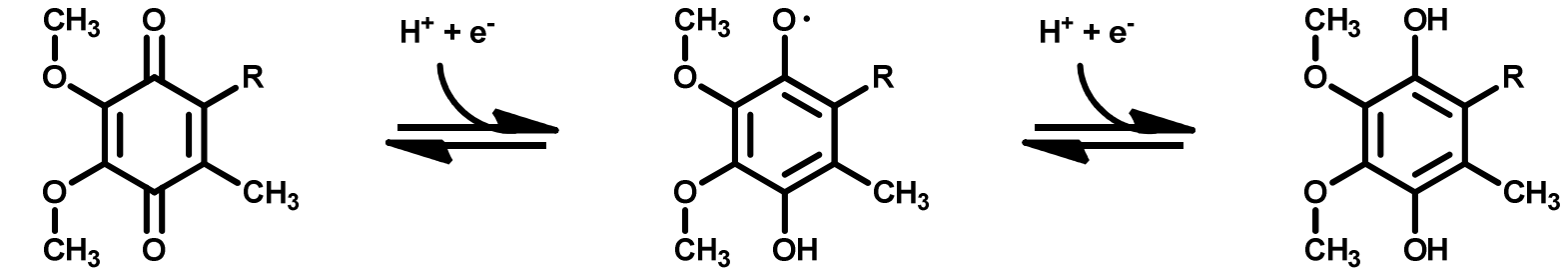
NADH transfers a hydride to FMN, then e^- move one-by-one (via Fe-S centers) to CoQ



Coenzyme Q is a membrane-soluble, diffusible electron (and proton) carrier



Coenzyme Q

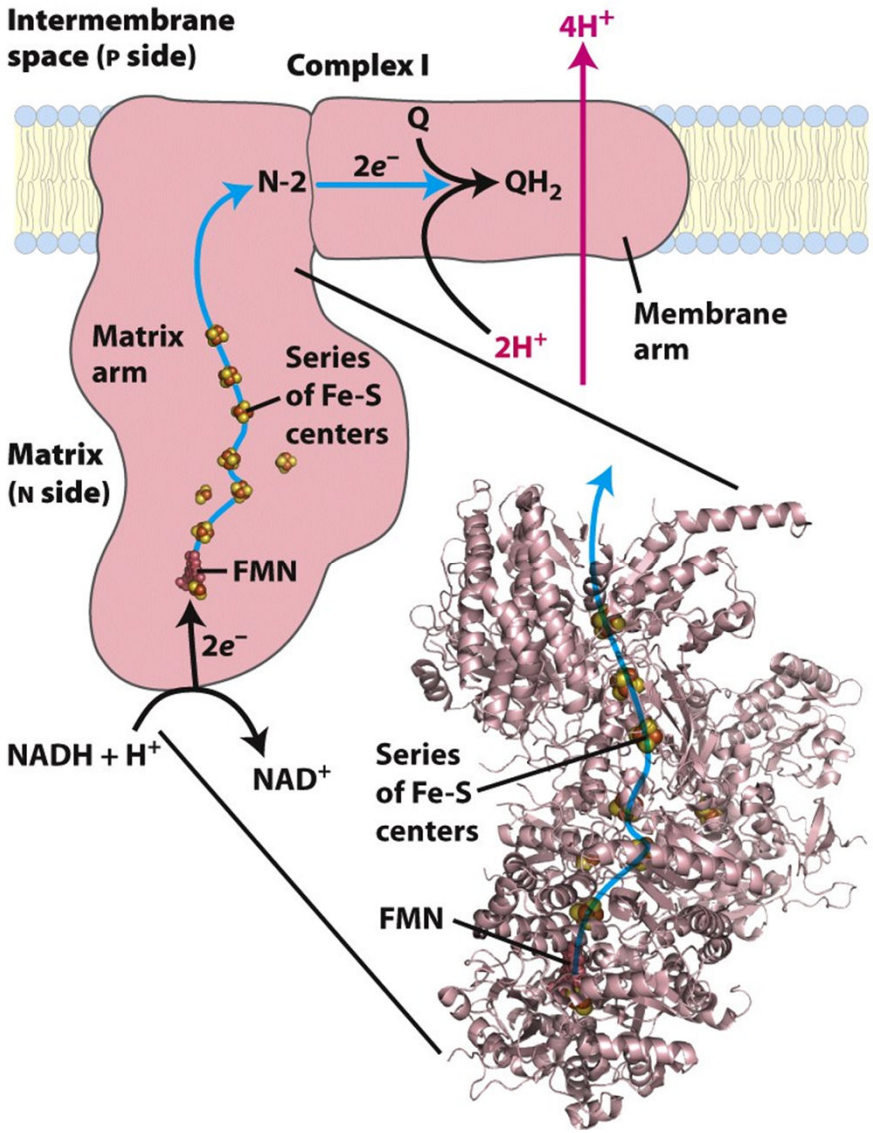


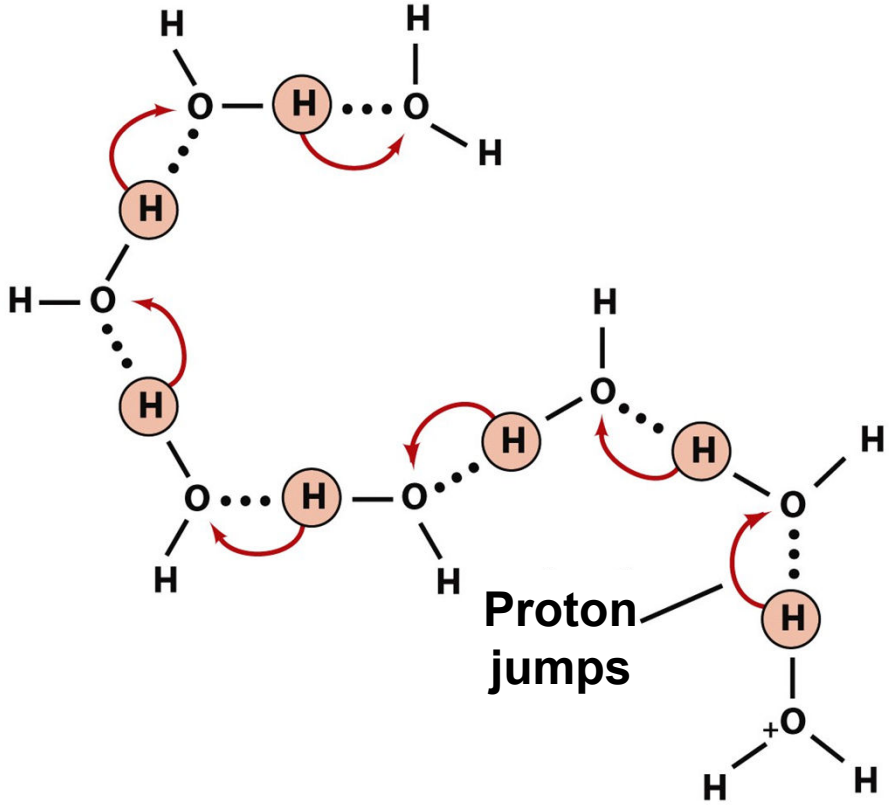
CoQ or Q
(ubiquinone)

$CoQH^{\cdot}$ or $QH^{\cdot}$
(ubisemiquinone)

$CoQH_2$ or QH_2
(ubiquinol)

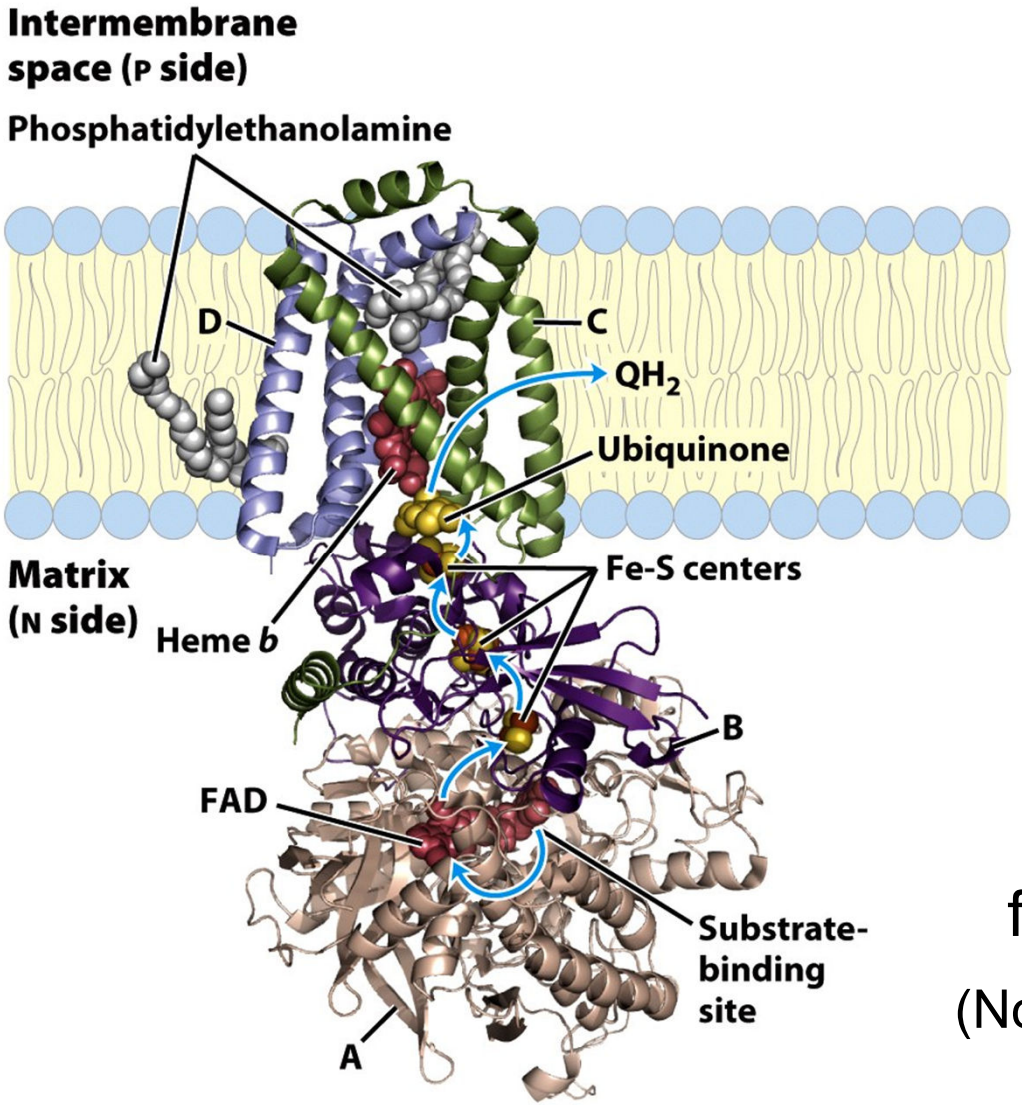
Complex I may translocate protons via proton jumping (involving aa sidechains)





4 protons are translocated for every two electrons transferred

Complex II (succinate-CoQ oxidoreductase) is succinate dehydrogenase from TCA cycle

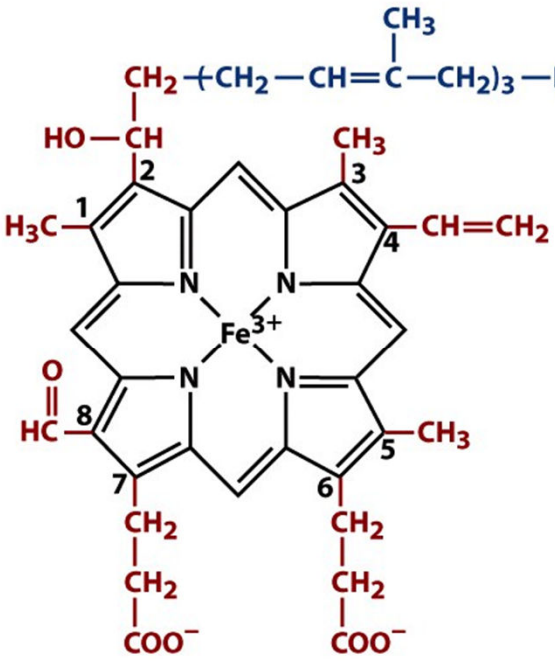


Electrons move one-at-a-time from FAD to CoQ

(No protons are pumped)

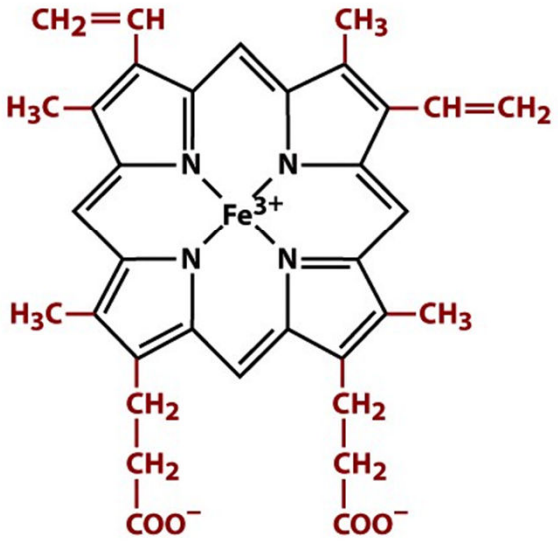
Electron transport involves different kinds of hemes

Hemes transfer one electron at a time



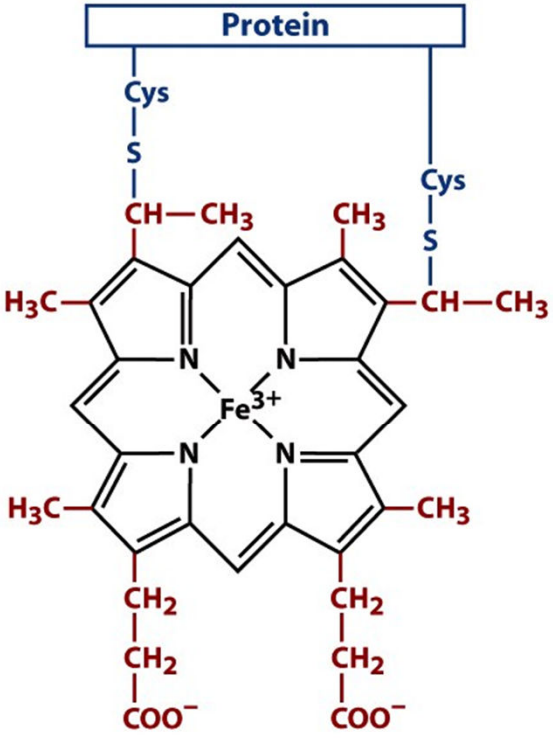
Heme *a*

Complex IV



Heme *b*
(iron–protoporphyrin IX)

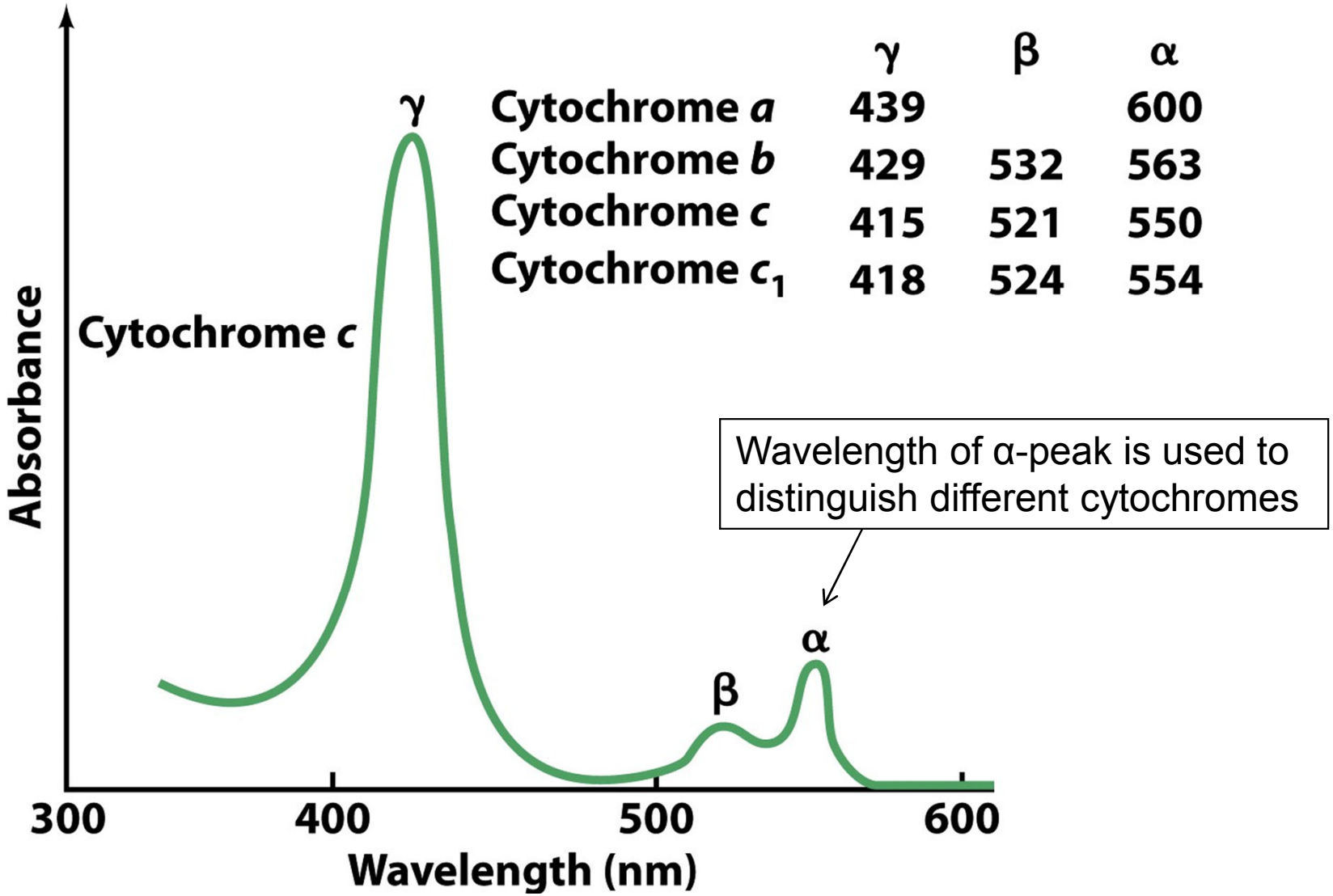
Complexes II and III
(and hemoglobin & myoglobin)



Heme *c*

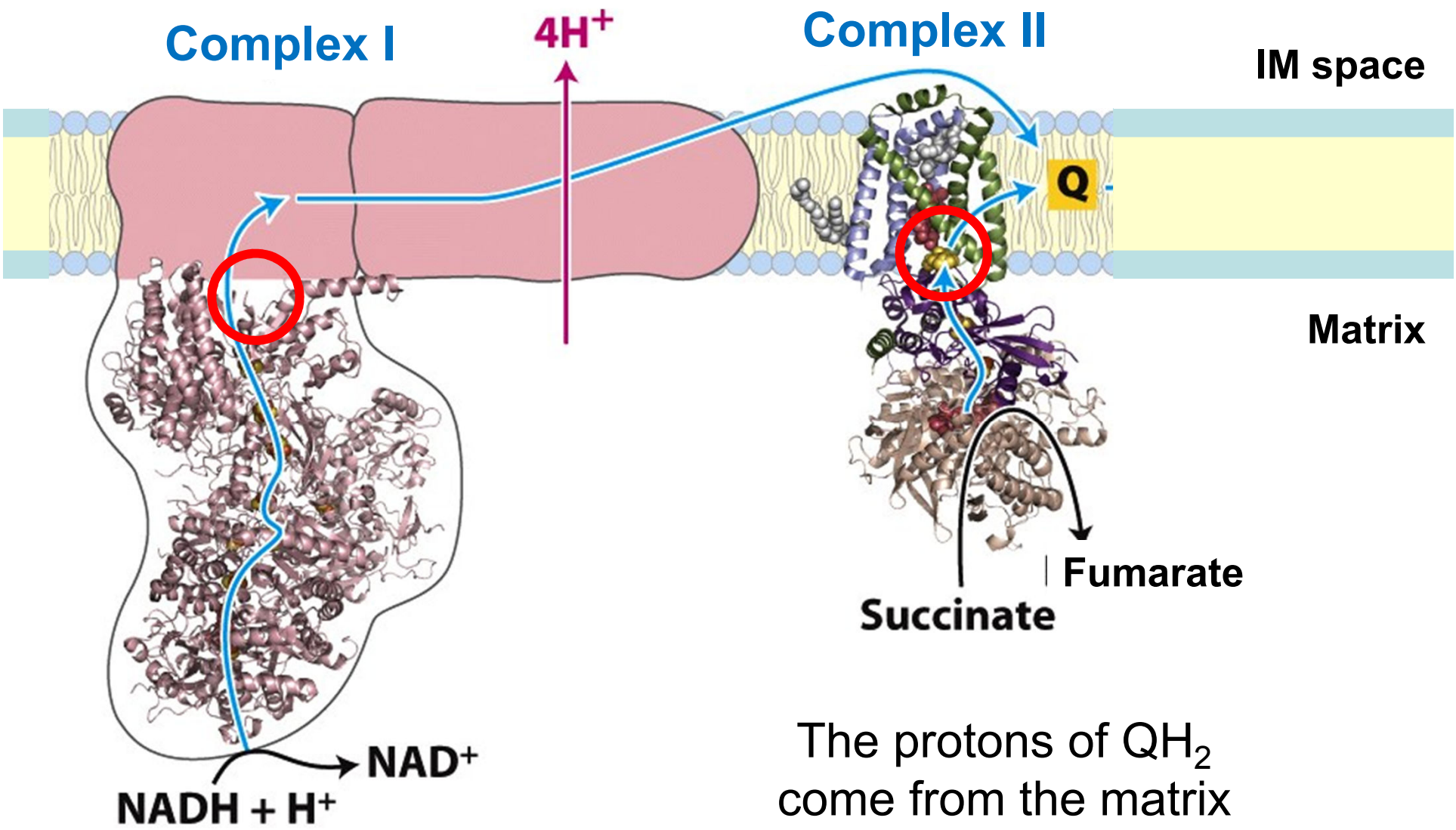
Complex III and
Cytochrome C

Cytochromes (heme-containing redox proteins) are named by heme type



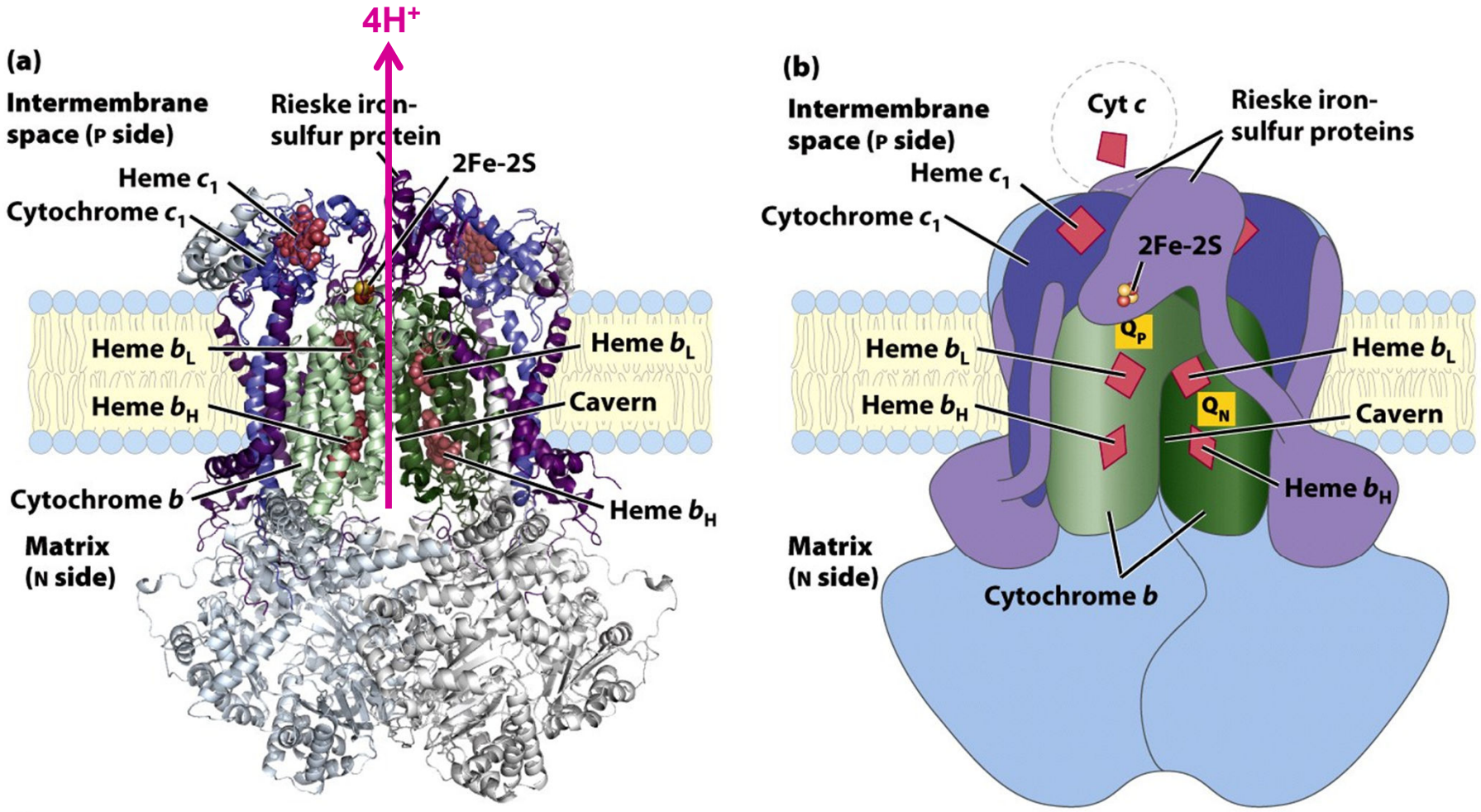
	γ	β	α
Cytochrome *a*	439		600
Cytochrome *b*	429	532	563
Cytochrome *c*	415	521	550
Cytochrome c_1	418	524	554

Q is reduced to QH_2 near the membrane-matrix interface of Complex I or II



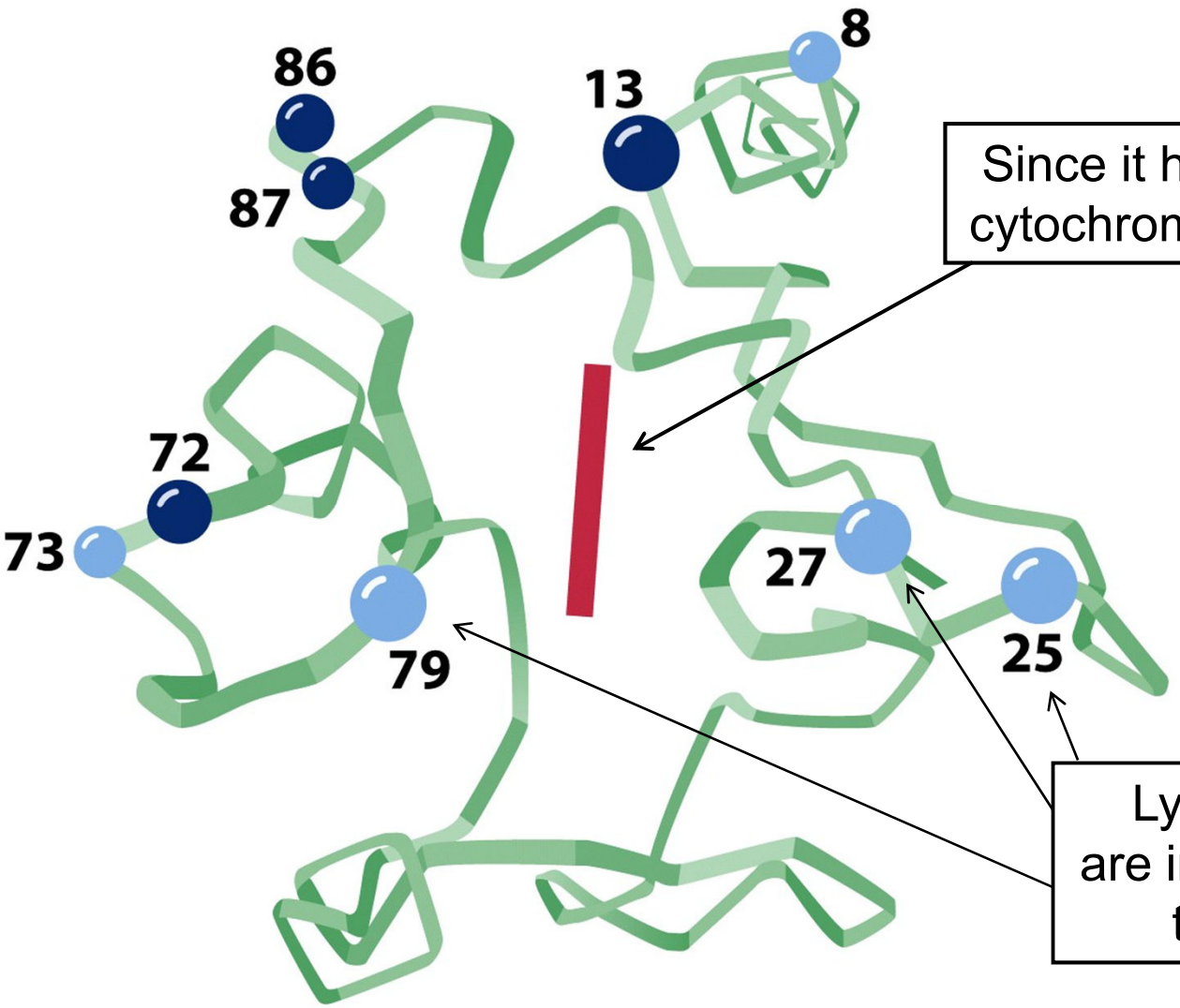
The protons of QH_2 come from the matrix

Complex III (CoQ-cytochrome c oxidoreductase) pumps protons with the help of CoQ



"Q-cycling" allows for the release of 4 protons to the IM space (from QH_2) for every $2e^-$ transferred to Cytochrome c

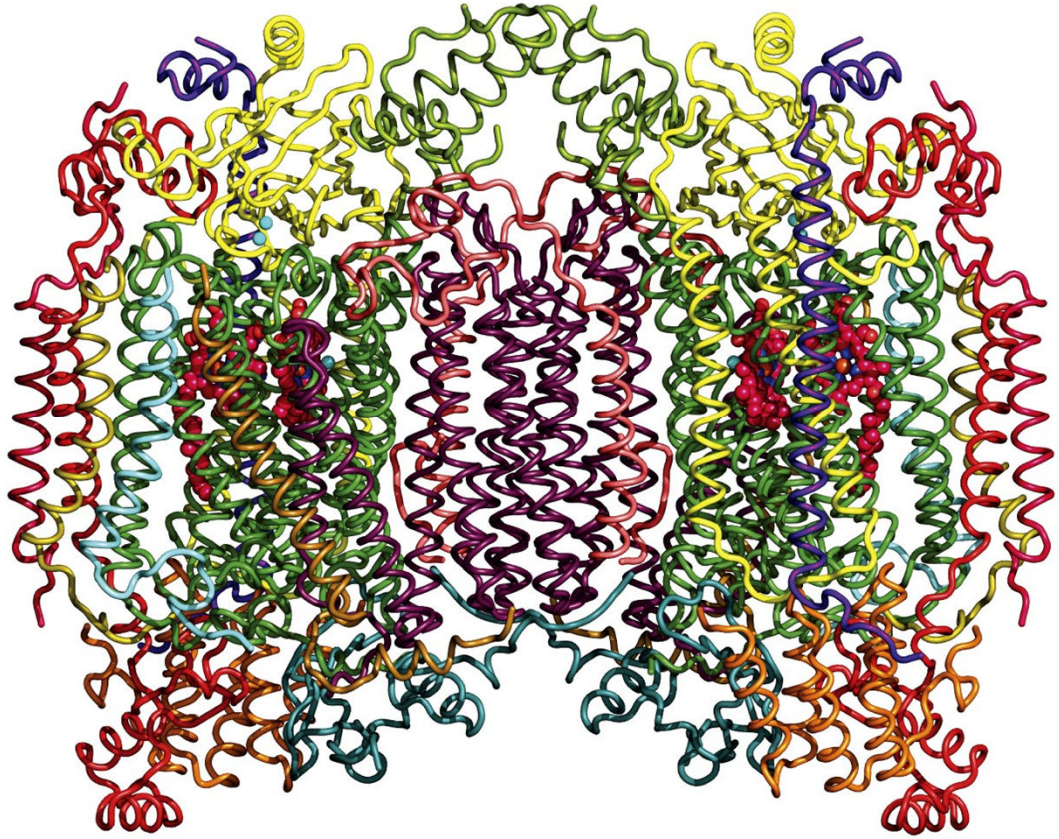
Cytochrome c is a small peripheral mb protein that diffuses in the IM space

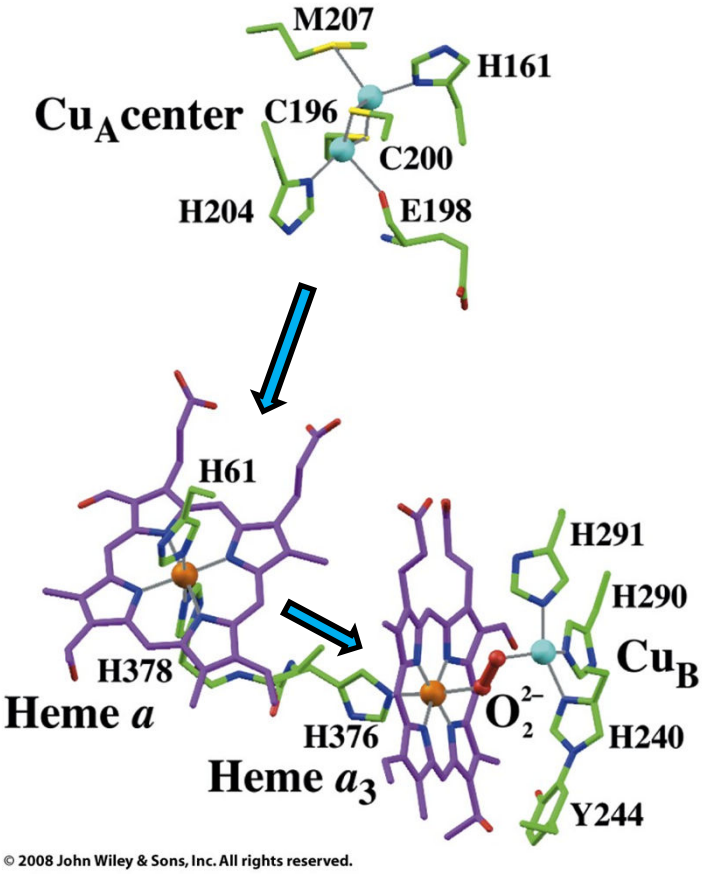


Since it has just one heme, cytochrome c is a $1e^-$ carrier

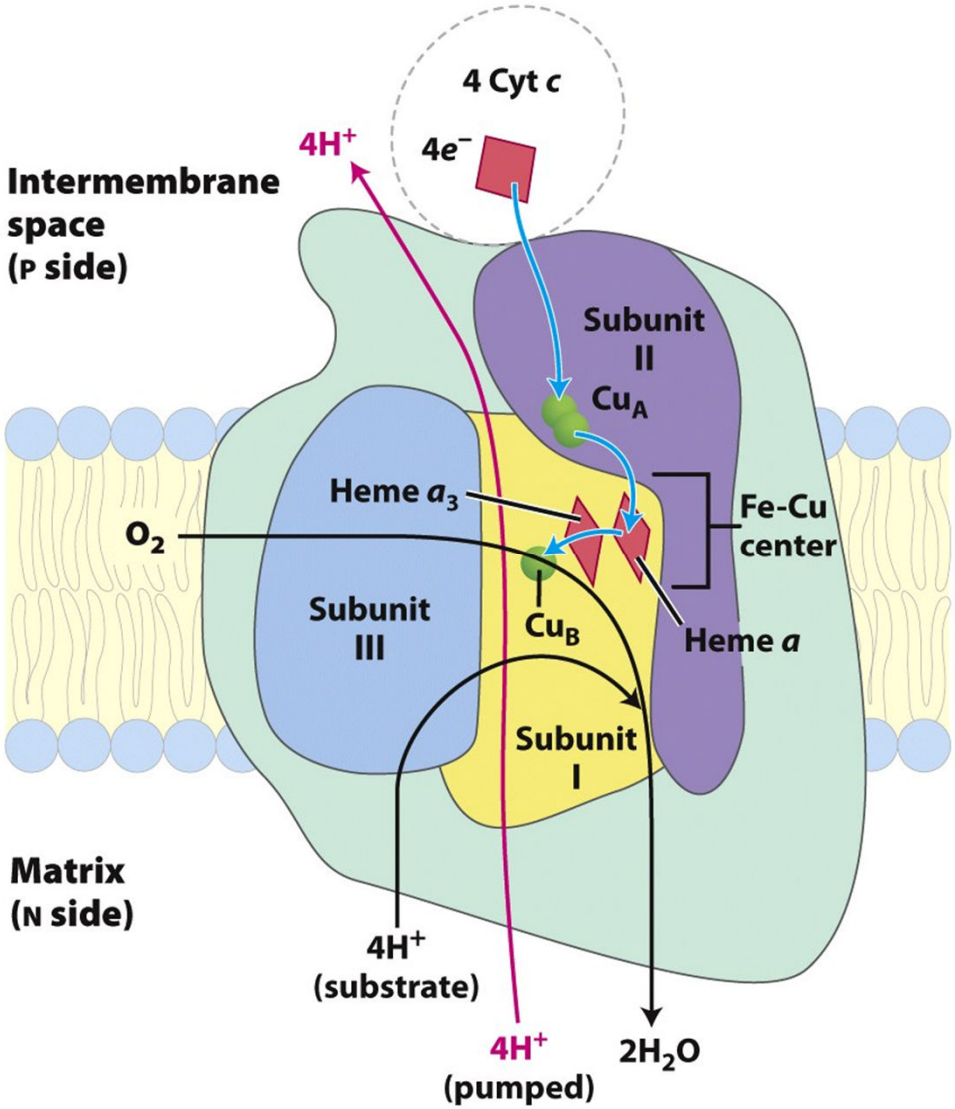
Lysine sidechains are involved in binding to Complex IV

Complex IV (Cytochrome c oxidase) transfers electrons to O_2 (reducing it to H_2O)



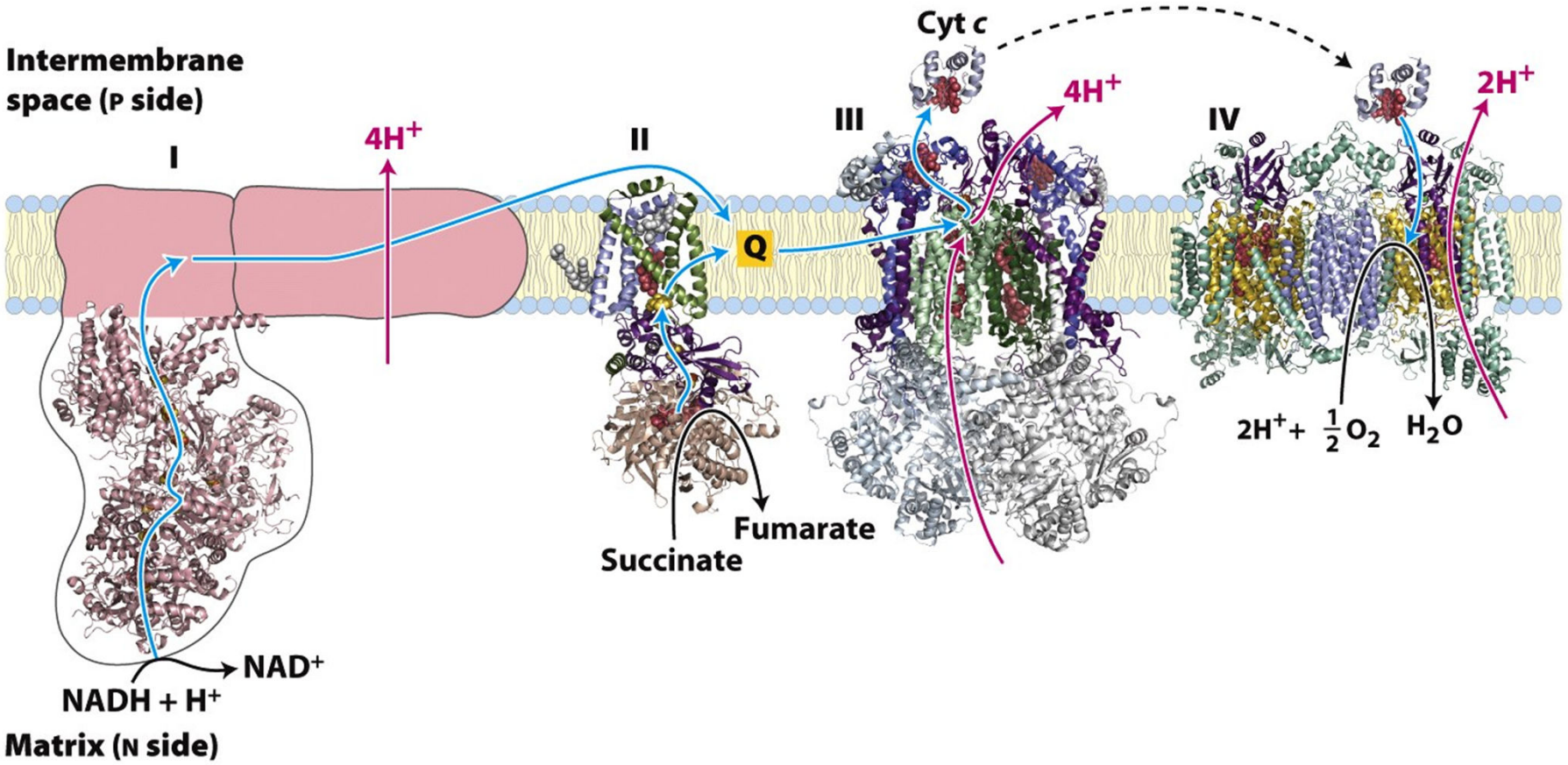


4 electrons (and 4 matrix protons) are used to reduce one molecule of O_2 to 2 H_2O



2 protons are translocated for every two electrons transferred

2-electron transfers from NADH→O_2 result in 10H^+ translocated; from $FADH_2$→O_2, 6H^+



The electrochemical potential of the proton gradient is used to drive ATP synthesis

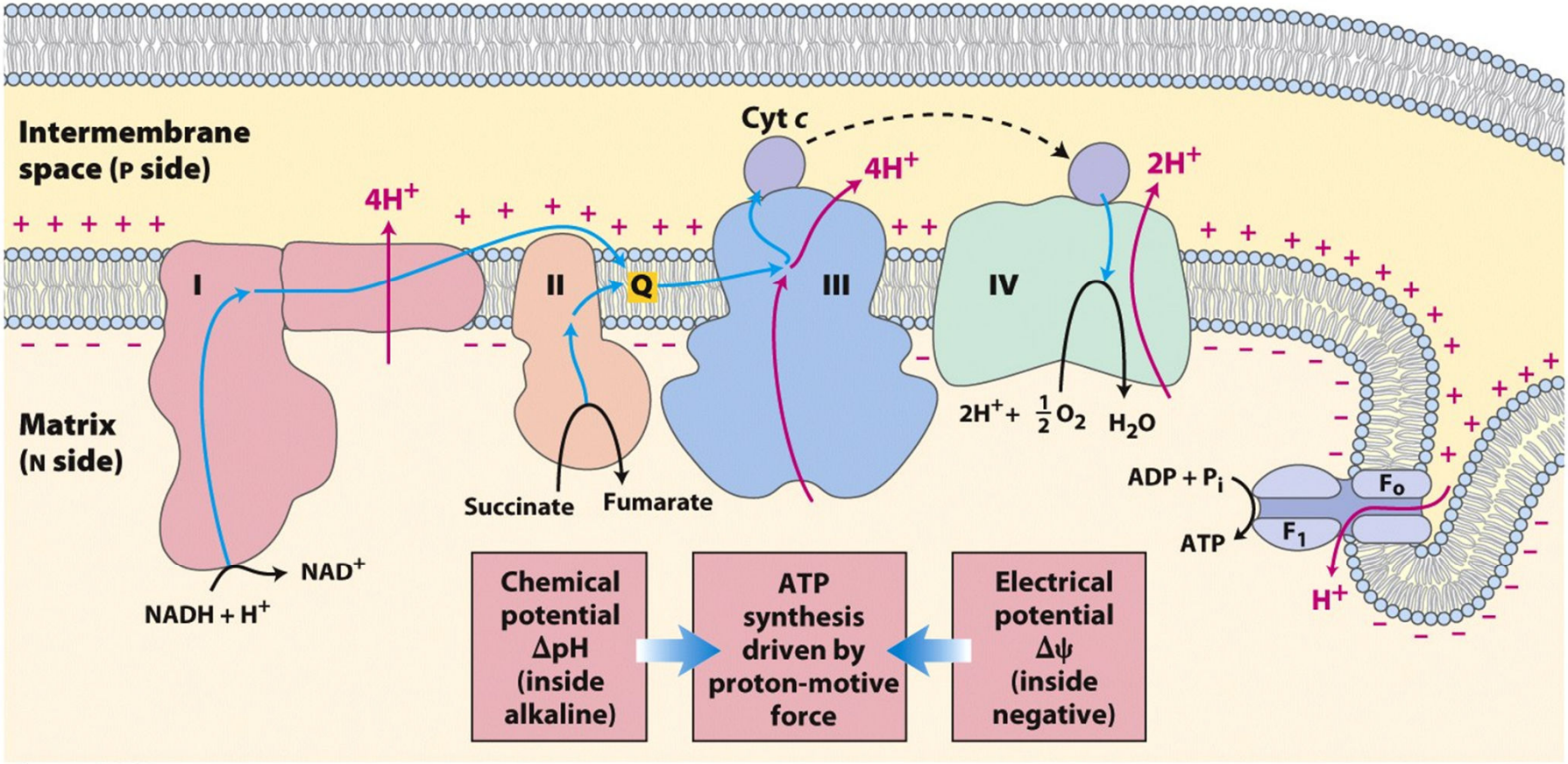


Figure 19-19
Lehninger Principles of Biochemistry, Fifth Edition

To make ATP, $4H^+$ move back into the matrix;
∴ 10/4 = 2.5 ATP per $2e^-$ from NADH;
6/4 = 1.5 ATP per $2e^-$ from $FADH_2$