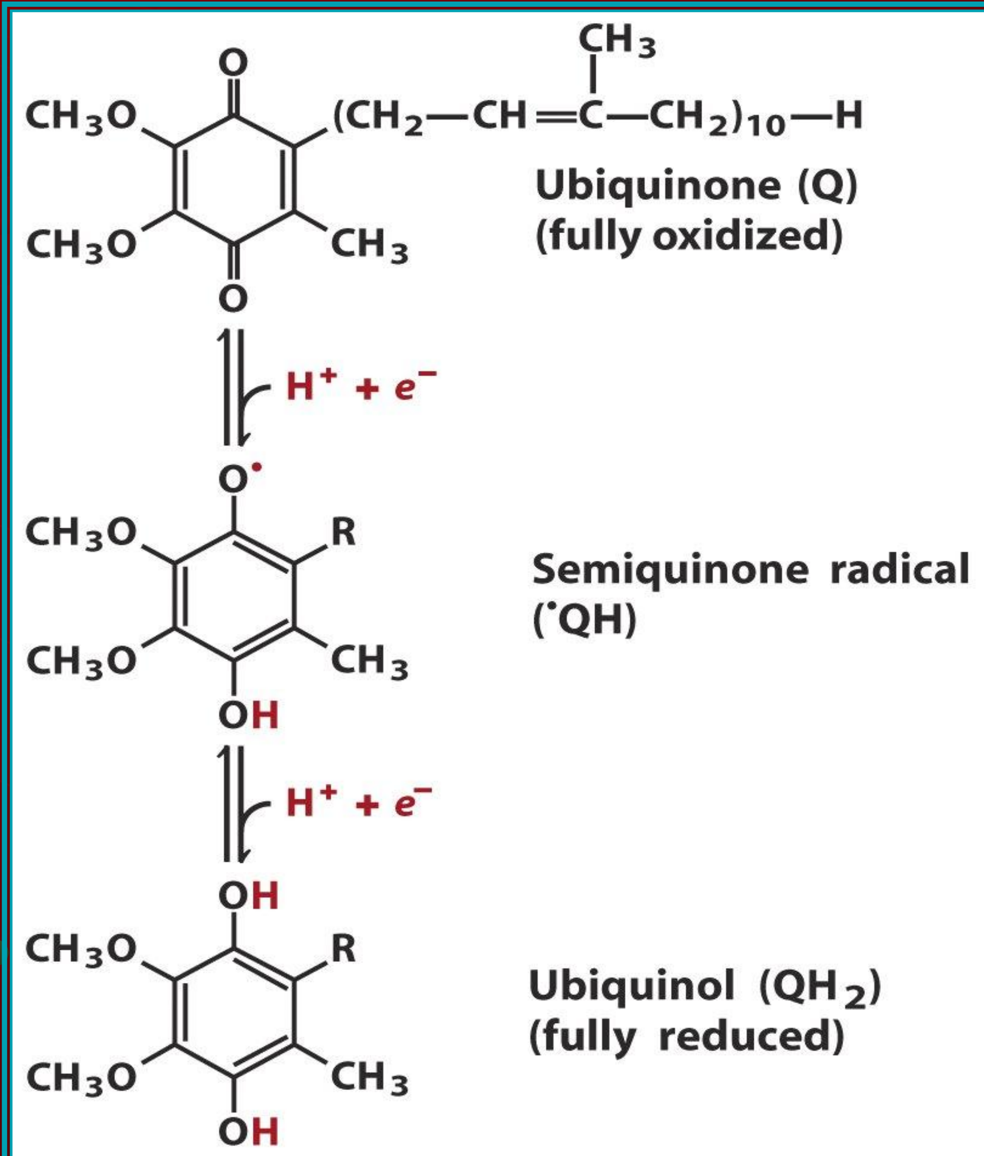
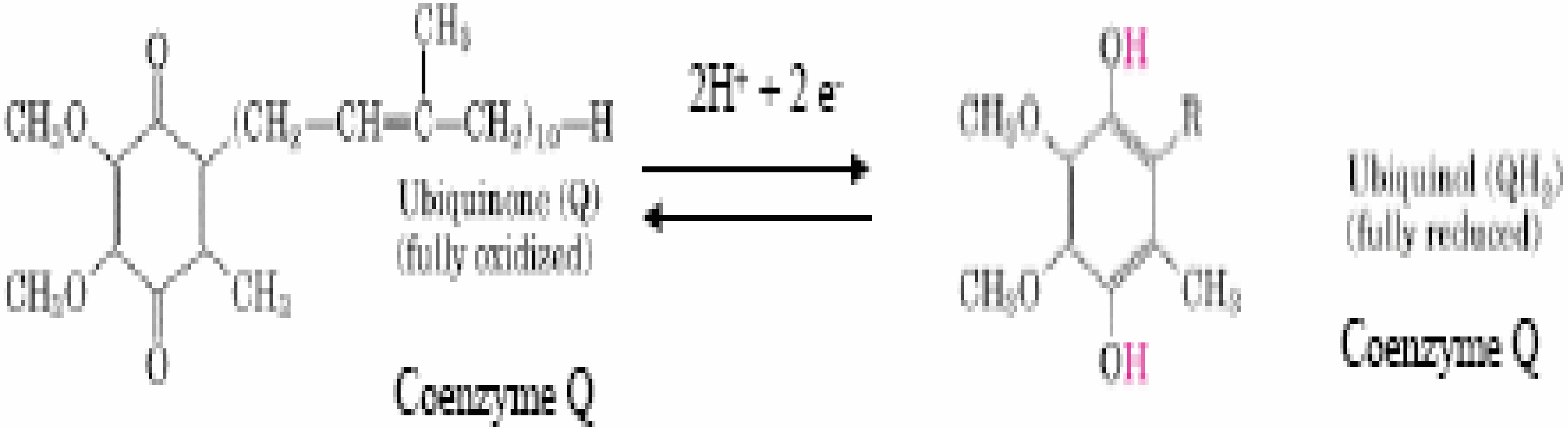
Ubiquinone (Coenzyme Q)



Coenzyme Q is a lipid which undergoes oxidation and reduction with one and two electron transfers.



2. Pathway of electron transport

- The transfer of electrons from reduced coenzymes to molecular oxygen occurs in three successive membrane-bound transfer sequences linked by two mobile electron carriers: coenzyme Q and cytochrome c.
- Electrons flow from NADH or FADH2 to CoQ; from coQ to cyt c; from cyt c to O2.

Electron Transfers in Respiration

TABLE 19–2 Standard Reduction Potentials of Respiratory Chain and Related Electron Carriers

Redox reaction (half-reaction)	E'° (V)
$2H^+ + 2e^- \longrightarrow H_2$	−0.414
$NAD^+ + H^+ + 2e^- \longrightarrow NADH$	−0.320
$NADP^+ + H^+ + 2e^- \longrightarrow NADPH$	−0.324
NADH dehydrogenase (FMN) $+ 2H^+ + 2e^- \longrightarrow$ NADH dehydrogenase ($FMNH_2$)	−0.30
Ubiquinone $+ 2H^+ + 2e^- \longrightarrow$ ubiquinol	0.045
Cytochrome *b* (Fe^{3+}) $+ e^- \longrightarrow$ cytochrome *b* (Fe^{2+})	0.077
Cytochrome c_1 (Fe^{3+}) $+ e^- \longrightarrow$ cytochrome c_1 (Fe^{2+})	0.22
Cytochrome *c* (Fe^{3+}) $+ e^- \longrightarrow$ cytochrome *c* (Fe^{2+})	0.254
Cytochrome *a* (Fe^{3+}) $+ e^- \longrightarrow$ cytochrome *a* (Fe^{2+})	0.29
Cytochrome a_3 (Fe^{3+}) $+ e^- \longrightarrow$ cytochrome a_3 (Fe^{2+})	0.35
$\frac{1}{2}O_2 + 2H^+ + 2e^- \longrightarrow H_2O$	0.8166

- The enzyme complexes responsible for these transport processes are:

A. **Complex I (NADH-ubiquinone oxidoreductase)**

B. **Complex II (Succinate-ubiquinone oxidoreductase)**

C. **Complex III (Ubiquinone-cytochrome c reductase)**

D. **Complex IV (cytochrome reductase)**

- In each of these complexes (except complex II) passage of electrons through the complex is accompanied by pumping of protons across the membrane in which the complex is embedded.
- These processes generate the proton gradient that will be used to drive the synthesis of ATP.

Protein Components of Electron-transfer Chain

TABLE 19–3 The Protein Components of the Mitochondrial Electron-Transfer Chain

Enzyme complex/protein	*Mass (kDa)*	*Number of subunits**	*Prosthetic group(s)*
I NADH dehydrogenase	850	43 (14)	FMN, Fe-S
II Succinate dehydrogenase	140	4	FAD, Fe-S
III Ubiquinone cytochrome *c* oxidoreductase	250	11	Hemes, Fe-S
Cytochrome *c*†	13	1	Heme
IV Cytochrome oxidase	160	13 (3–4)	Hemes; Cu_A, Cu_B

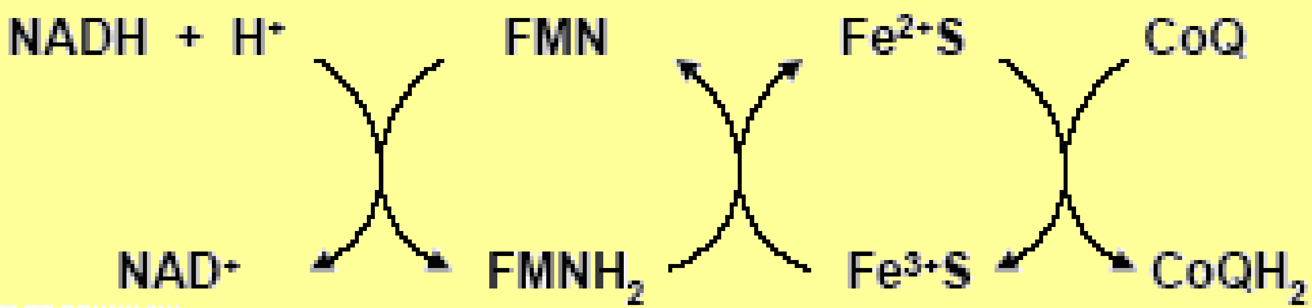
*Numbers of subunits in the bacterial equivalents in parentheses.

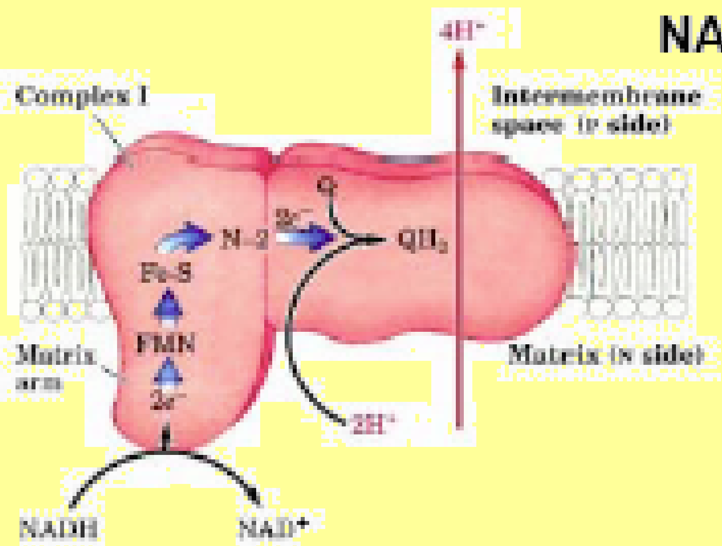
†Cytochrome *c* is not part of an enzyme complex; it moves between Complexes III and IV as a freely soluble protein.

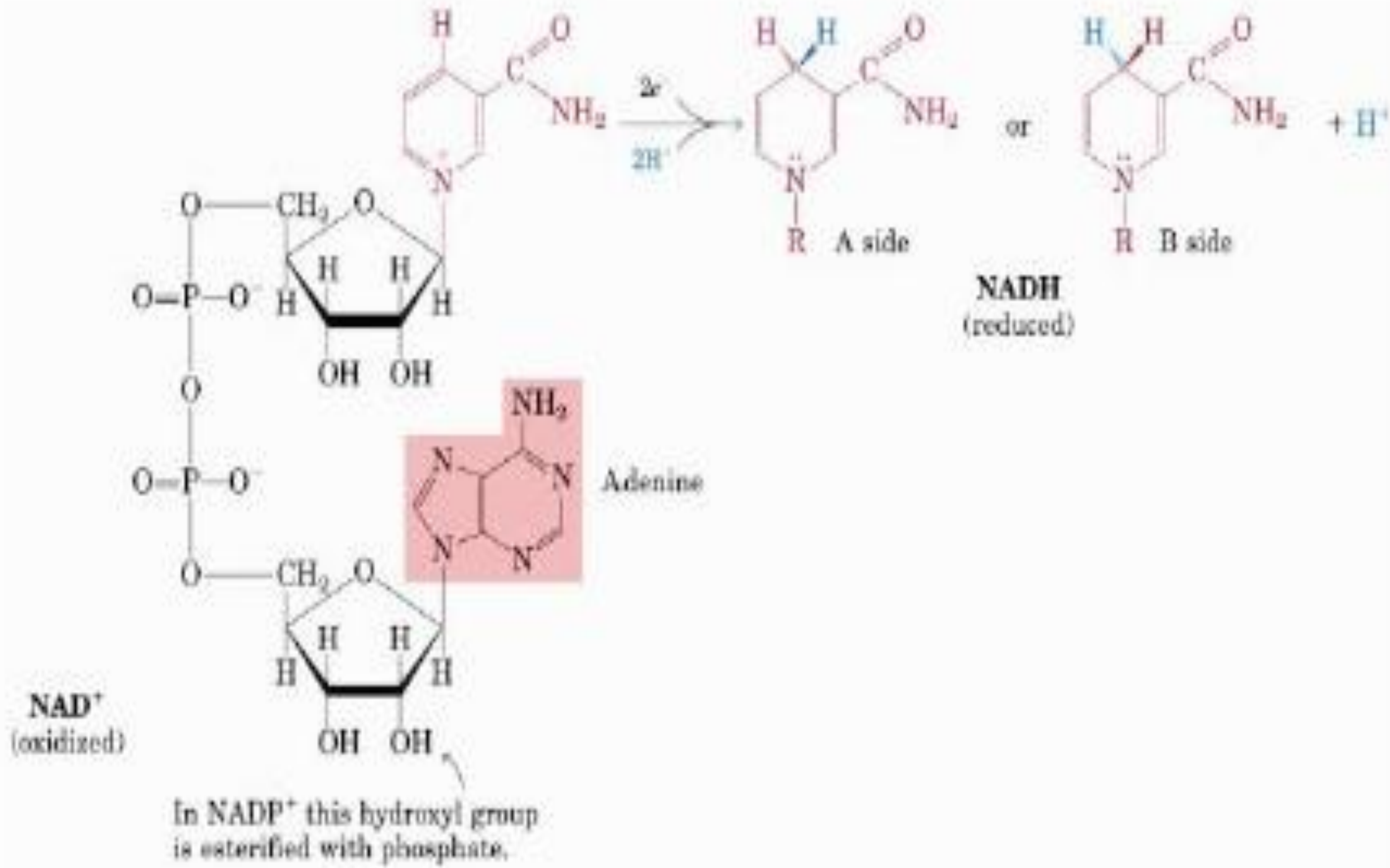
Organization of Electron Carriers

Enzymes associated with these carriers catalyze these electron transfers. These associated proteins are found in the inner membrane of the mitochondrion and can be isolated as complexes which carry out selected portions of the electron transport pathway. For example, NADH dehydrogenase is part of Complex I.

Complex I NADH-Coenzyme Q Reductase

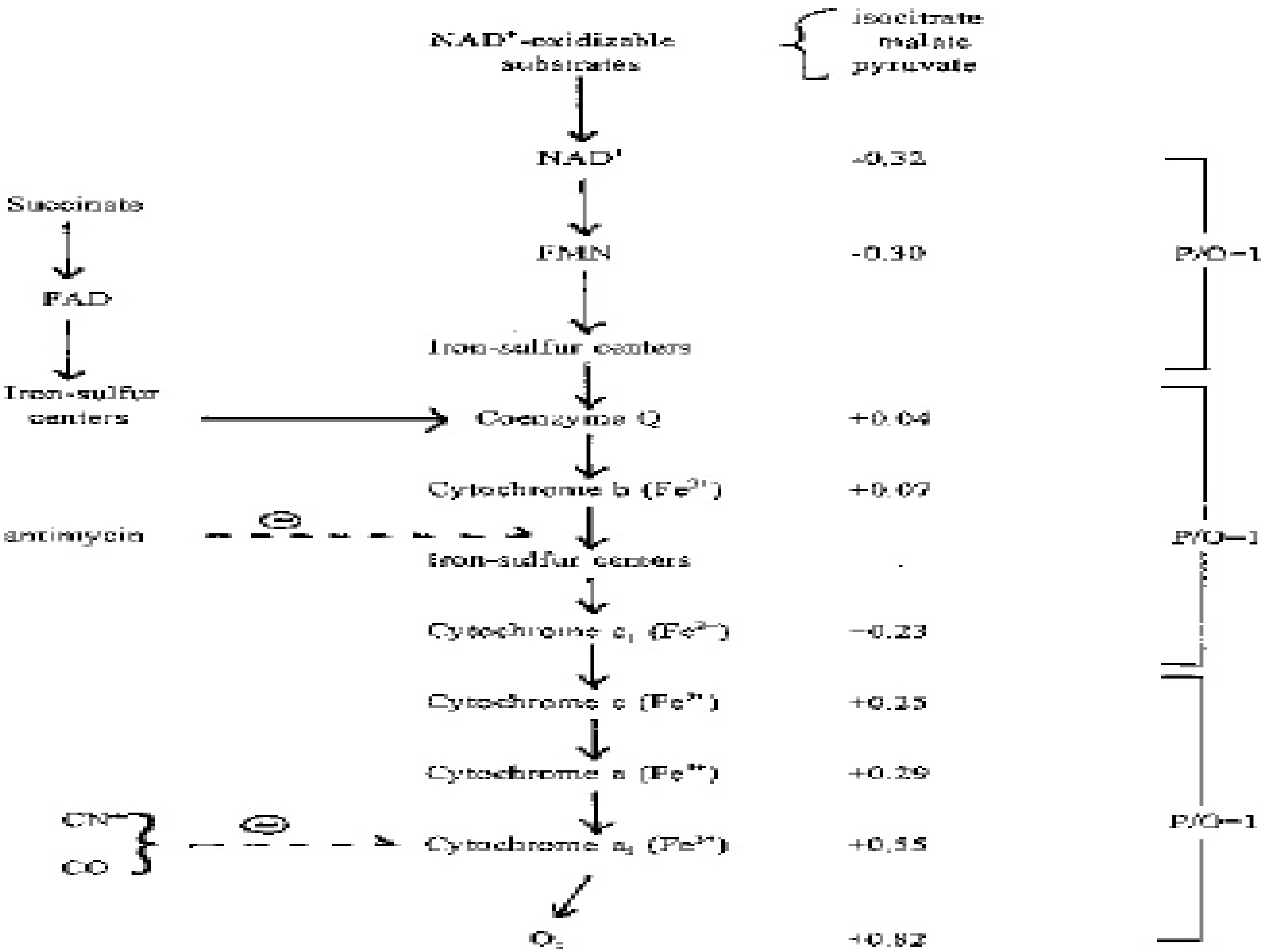





2e⁻
2H⁺
A side
B side
or
+ H⁺
NADH
(reduced)
Adenine
NAD⁺
(oxidized)
In NADP⁺ this hydroxyl group
is esterified with phosphate.

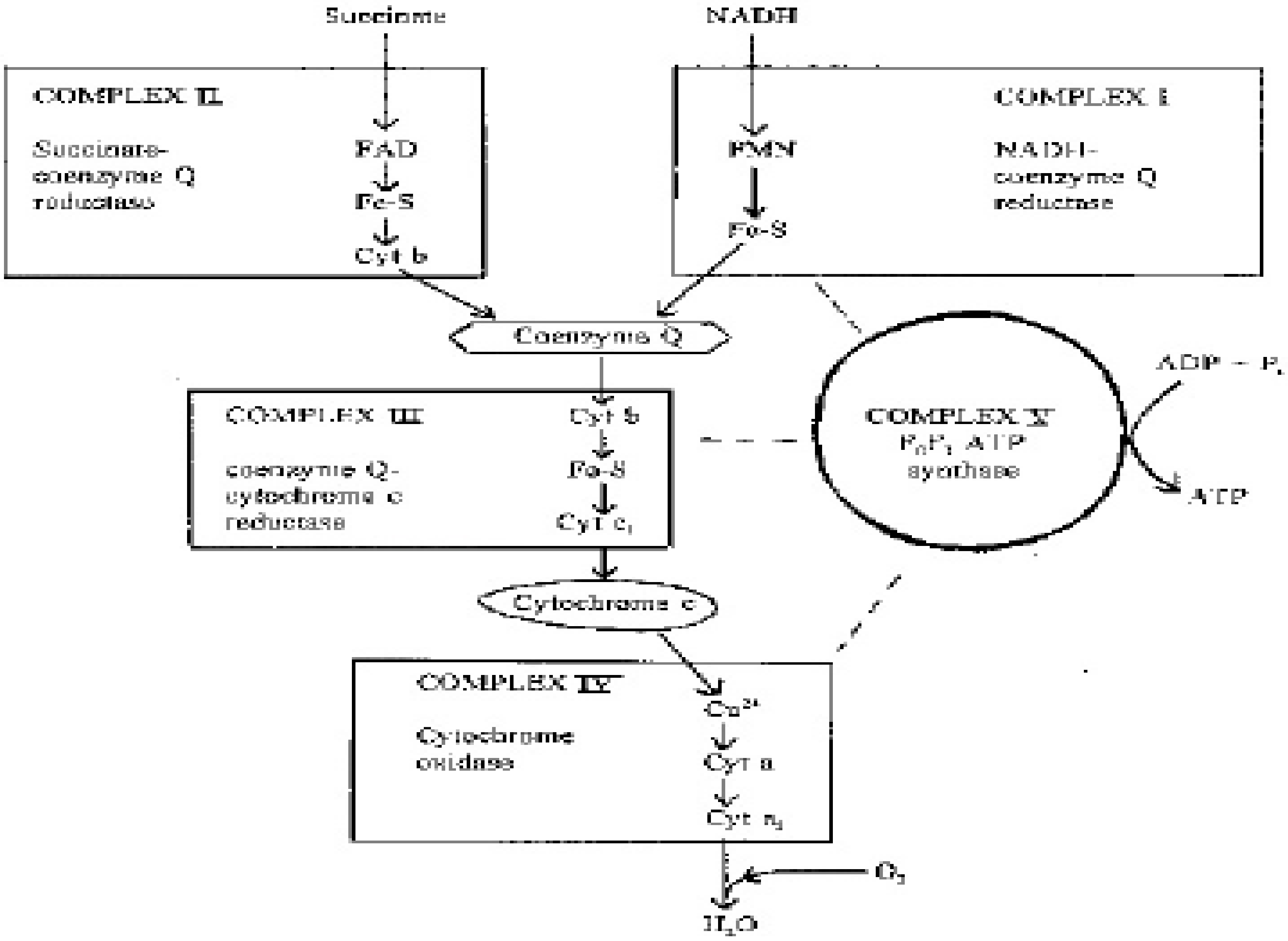
(a)

Sequence of Respiratory Electron Carriers



The arrangement of the other complexes is shown below

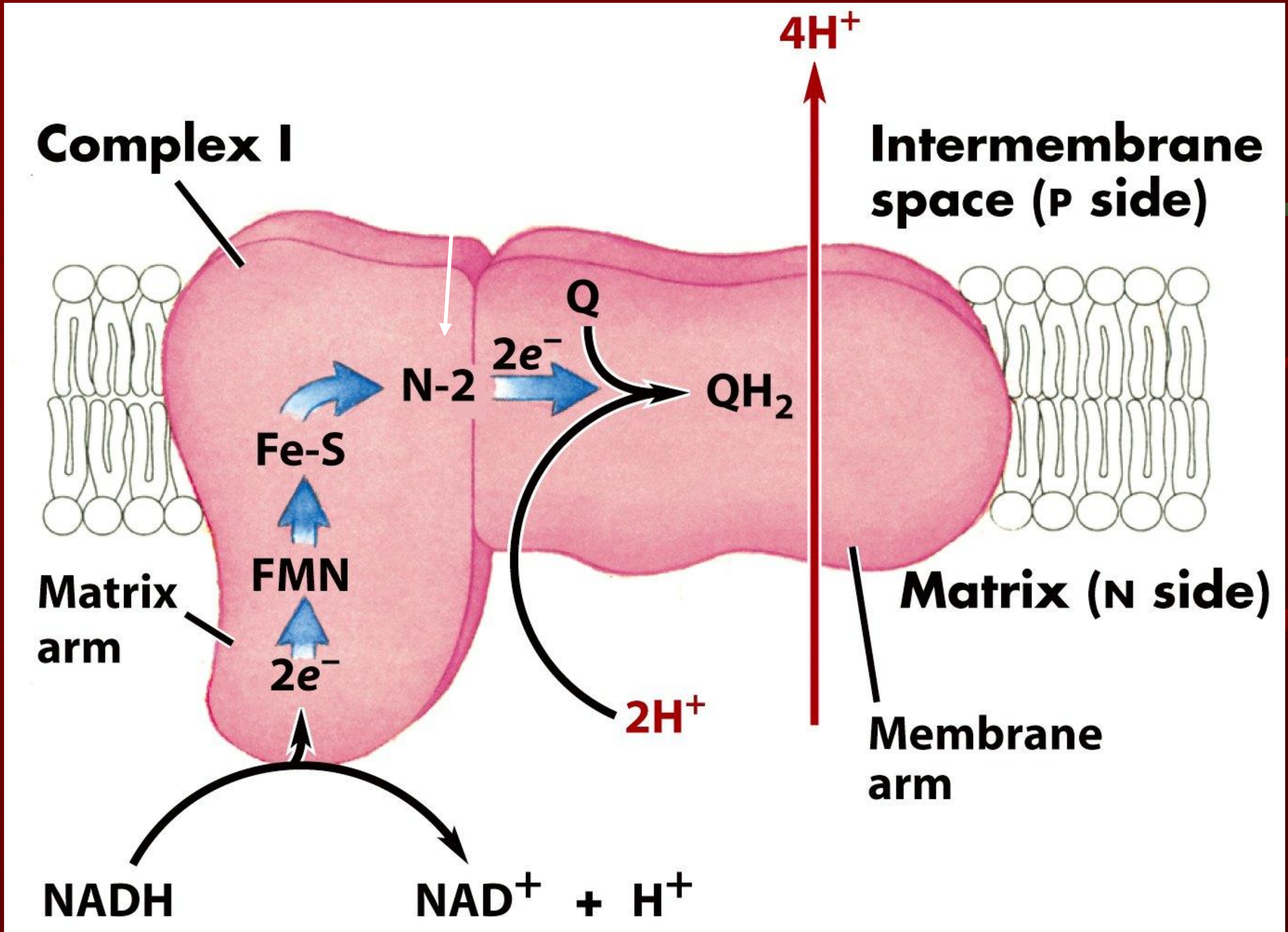
Multiprotein complexes in the Respiratory Assembly



Complex I: NADH-ubiquinone oxidoreductase

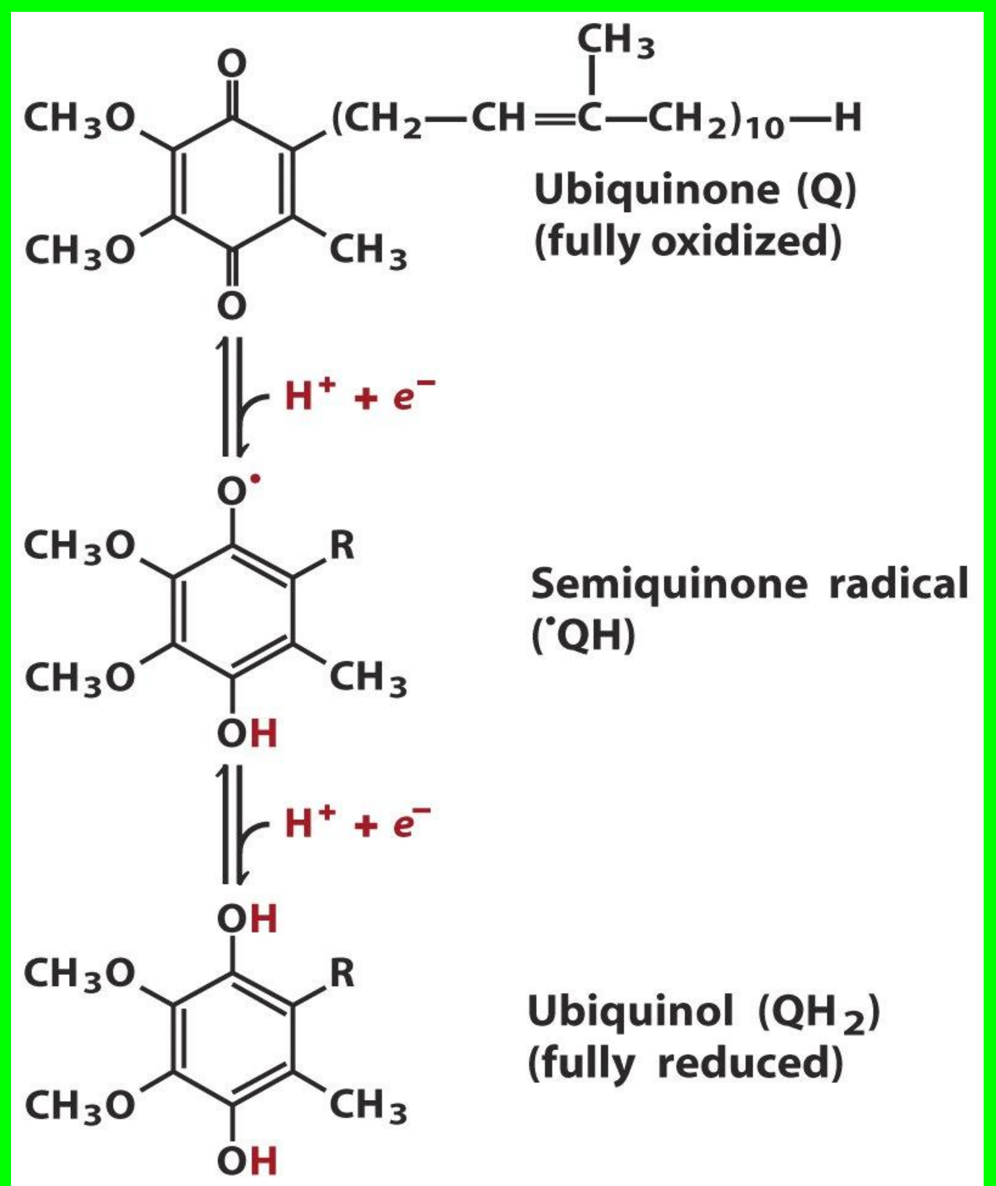
- NADH + H+ + CoQ → NAD+ + CoQH2
- 4 H+ ions are transferred from mitochondrial matrix to intermembrane space
- Large complex composed of 42 polypeptide chains, including an FMN-containing flavoprotein and at least six iron-sulfur centers.

Complex I: NADH to Q



- The electrons are transferred through these different components, ending in CoQ.
- The mechanism that couples these electron transfers to the proton transfers is not known.
- Ubiquinol (QH2, the fully reduced form) diffuses in the mitochondrial inner membrane to complex III, where it continues the electron transport chain.

Ubiquinone (Coenzyme Q)



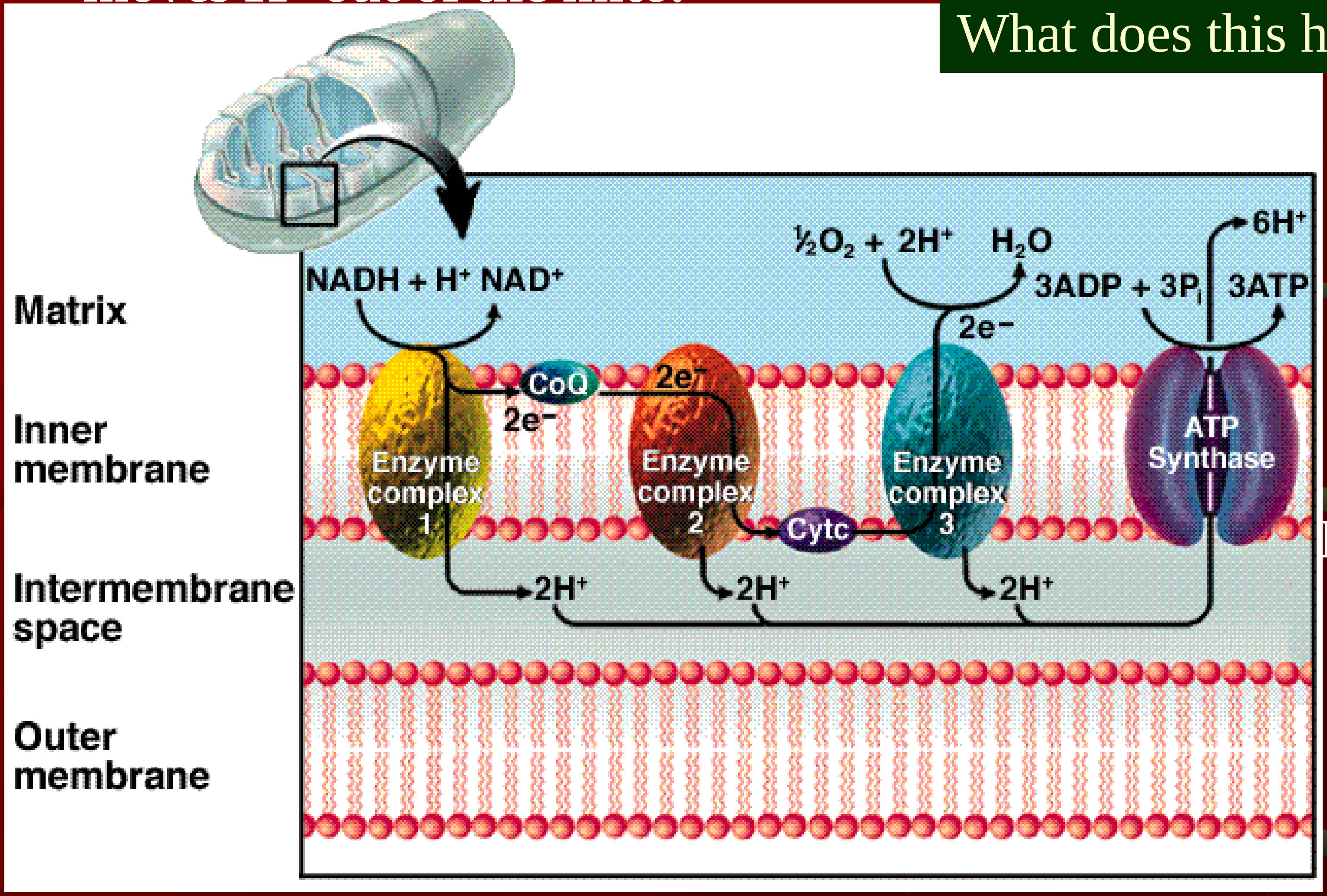
Electron Transport Chain

-enzyme complex 1 passes high energy e^- to coenzyme Q

-coenzyme Q shuttles e^- to enzyme complex 2

- Energy from the e^- is used to drive the proton pump that moves H^+ out of the mito.

What does this help create??

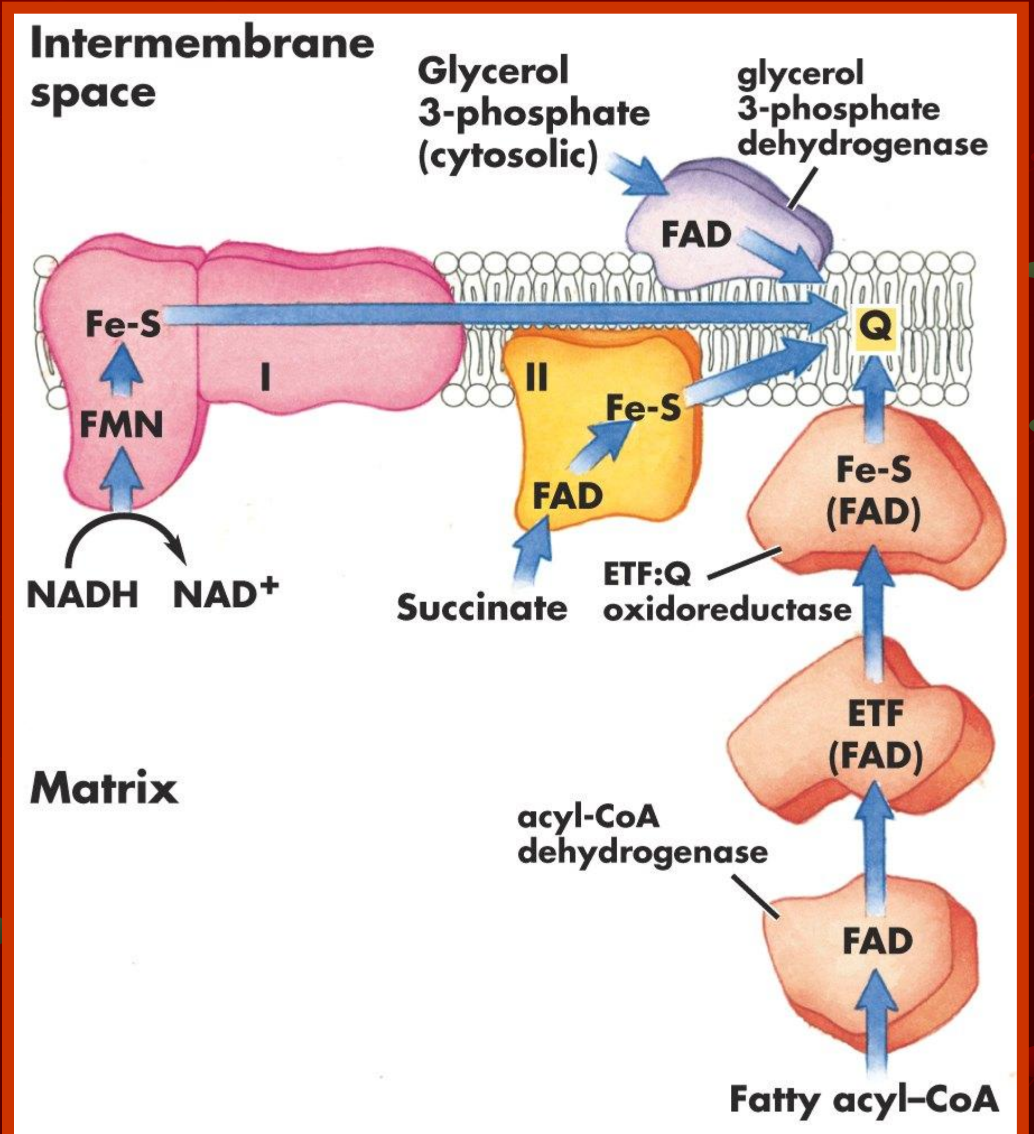


H^+ gradient

Complex II: Succinate – Coenzyme Q reductase

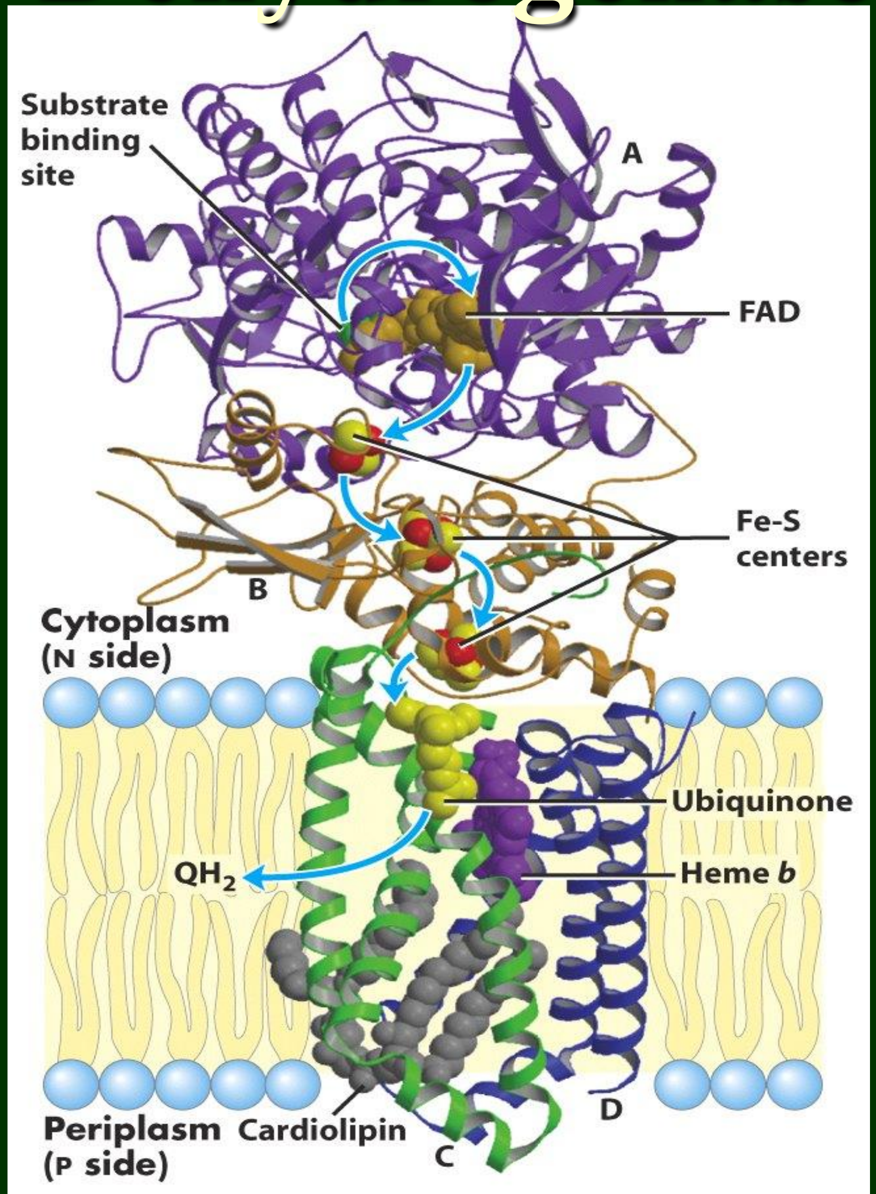
- Complex II is succinate dehydrogenase, which we saw in Chapter 16 as the only membrane-bound enzyme involved in the citric acid cycle.
- Contains one protein with covalently bound FAD and an Fe-S center; also contains a second Fe-S protein.
- Electrons are transferred from succinate to FAD, then through the Fe-S centers to ubiquinone.

Complex II: Succinate Dehydrogenase



- This complex is not involved in proton pumping, only transferring electrons to CoQ (ubiquinone)
- • Other substrates pass electrons into the respiratory chains using other enzymes .
- These different pathways all meet at ubiquinone.

Complex II: Succinate Dehydrogenase

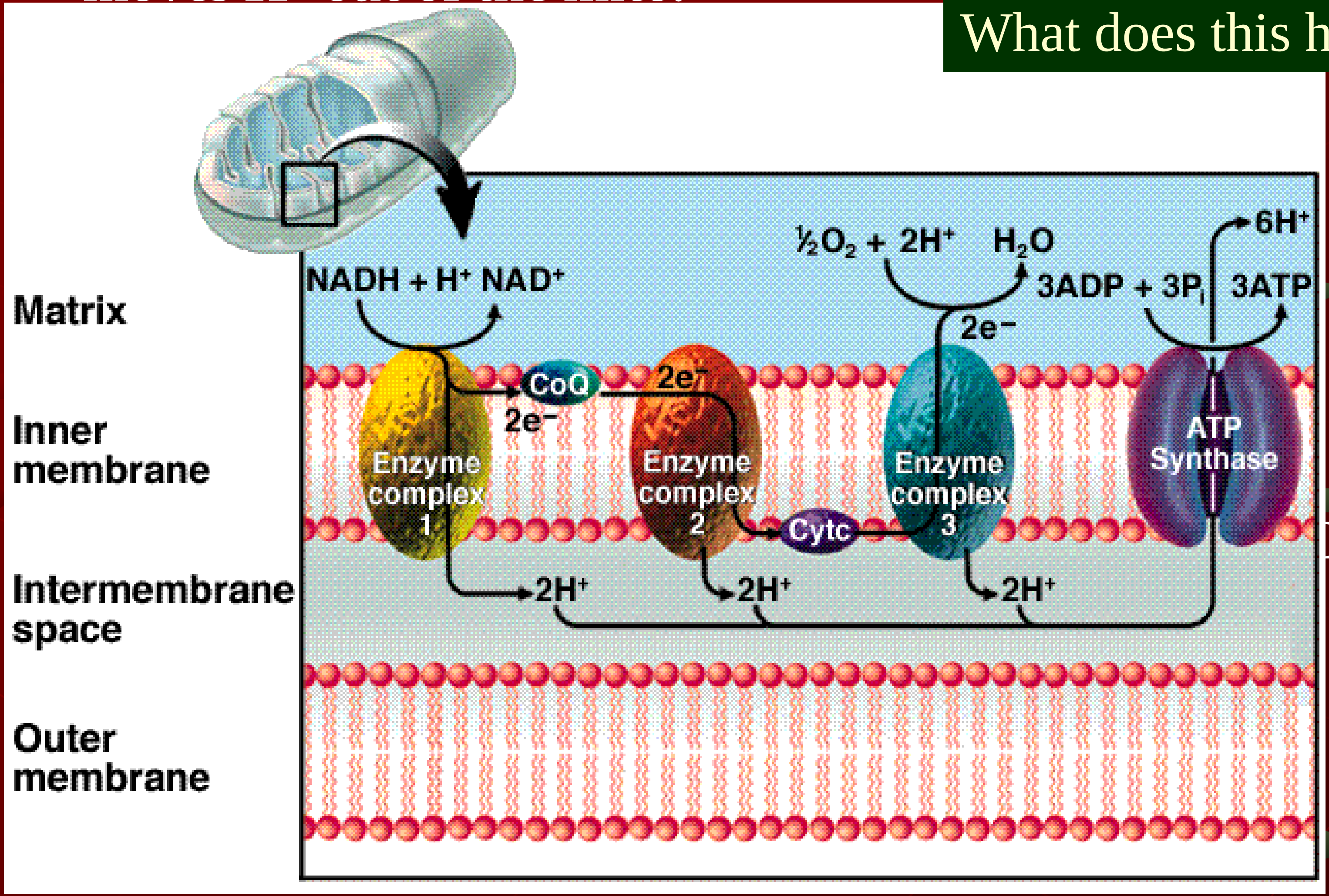


Electron Transport Chain

-enzyme complex 2 passes high energy e^- to cytochrome c

- cytochrome c shuttles e^- to enzyme complex 3
- Energy from the e^- is used to drive the proton pump that moves H^+ out of the mito.

What does this help create??

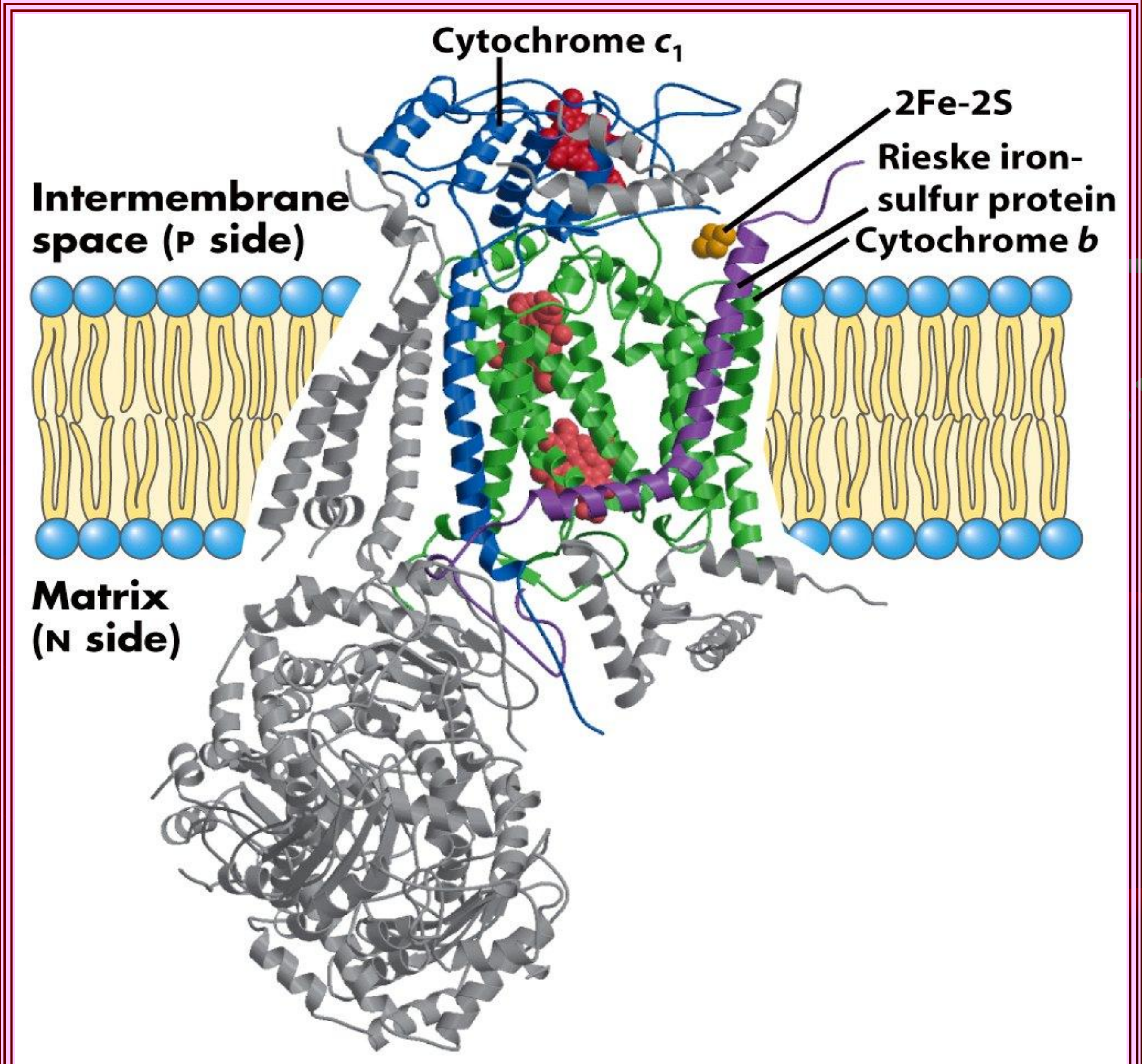


H^+ gradient

<u>Complex III:</u> Ubiquinone-cytochrome *c* oxidoreductase

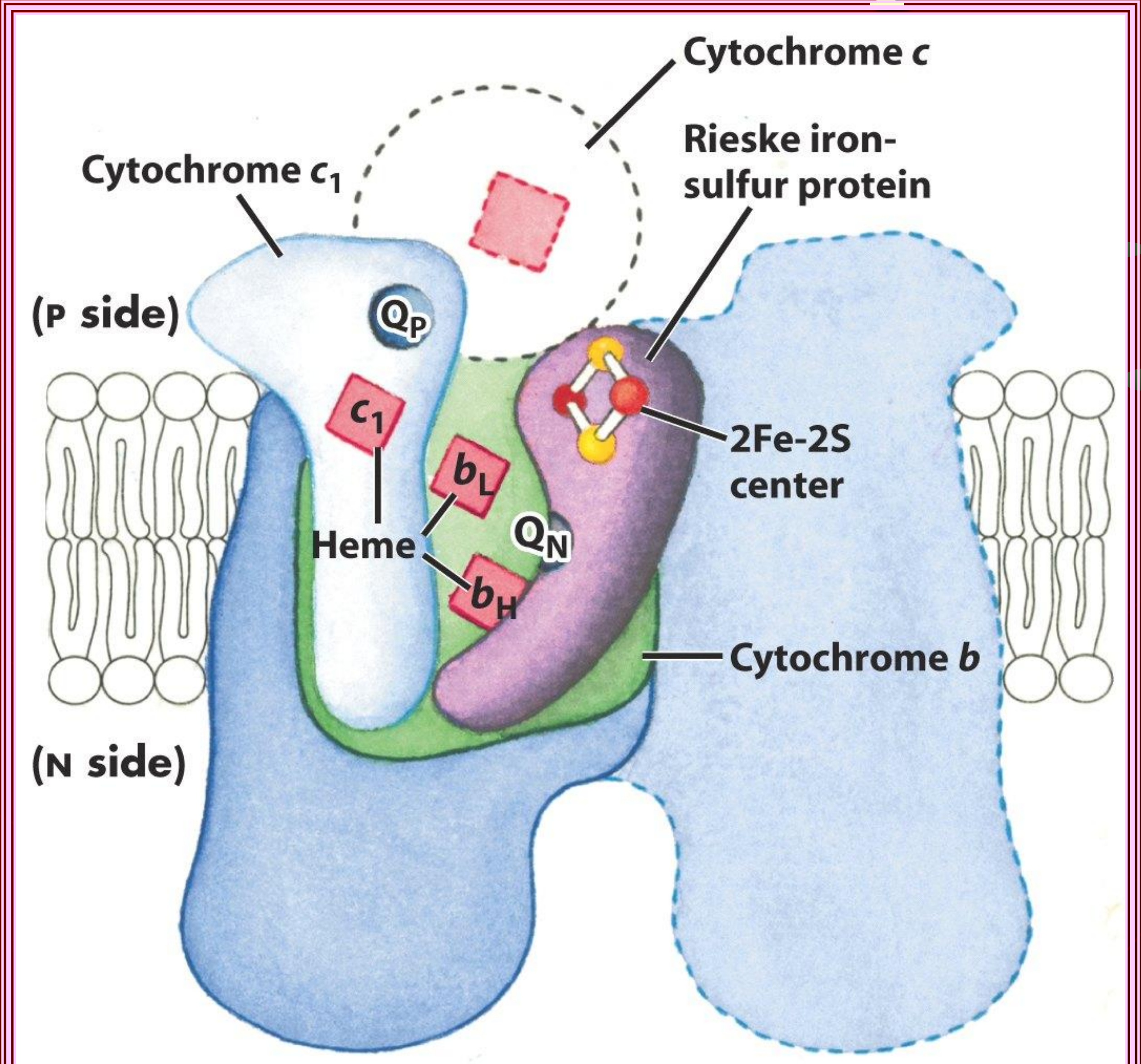
- Transfers electrons from ubiquinone to cytochrome c. Cytochrome c only is reduced by one electron, so two molecules of cytochrome c are reduced for each molecule of CoQ.
- QH2 + 2cyt cox + 2H+in → Q + 2cyt cred + 4H+out
- The net reaction is simple, but within this complex the path of the electron is more complex.

Complex III: Q to cytochrome c

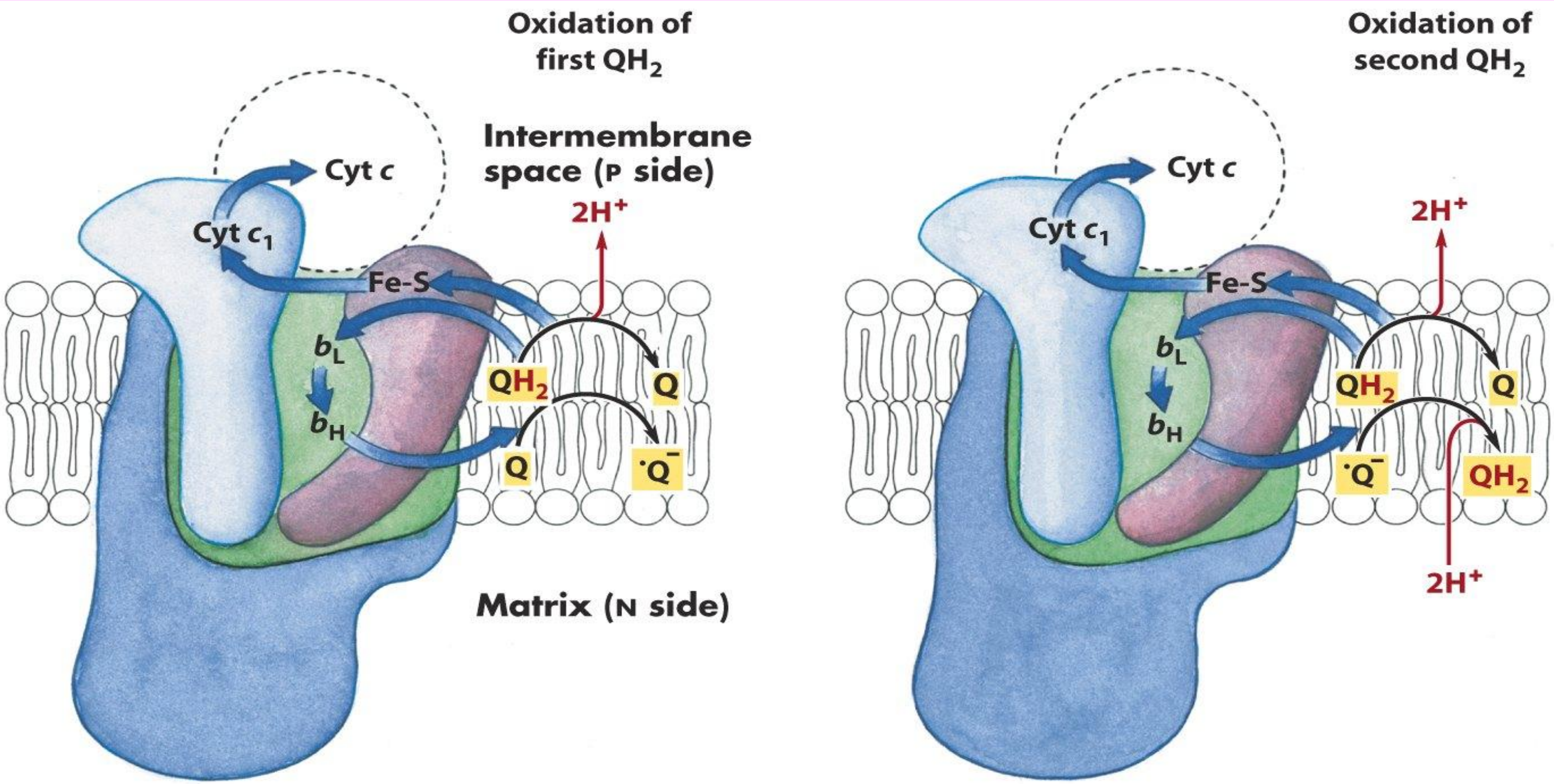


- The complex contains cytochrome *b*, with two hemes, and an iron-sulfur protein.
- Cytochrome c is a soluble protein of the intermembrane space.
- It can freely move through the aqueous solution to Complex IV to continue electron transport.

Schematic of Complex III



The Q cycle



QH_2 + cyt c_1 (oxidized) $\longrightarrow$ $\cdot Q^-$ + $2H_P^+$ + cyt c_1 (reduced)

QH_2 + $\cdot Q^-$ + $2H_N^+$ + cyt c_1 (oxidized) $\longrightarrow$ QH_2 + $2H_P^+$ + Q + cyt c_1 (reduced)

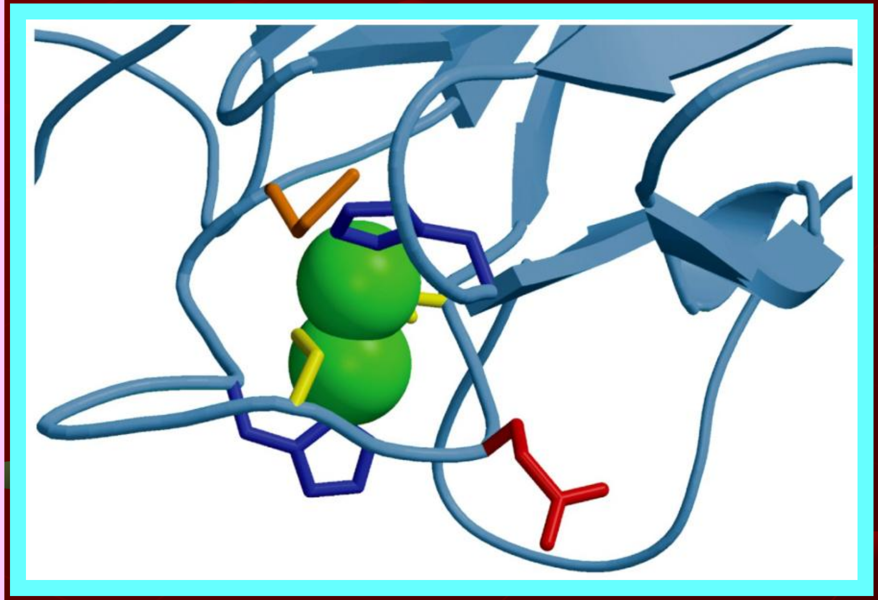
Net equation:

$$QH_2 + 2\,\text{cyt}\ c_1\ (\text{oxidized}) + 2H_N^+ \longrightarrow Q + 2\,\text{cyt}\ c_1\ (\text{reduced}) + 4H_P^+$$

<u>Complex IV</u>: Cytochrome *c* oxidase complex

- This is the last segment of the electron transfer chain: electrons are transferred from cytochrome *c* to O2, reducing it to H2O.
- 4 cyt cred + 8 H+in + O2 → 4 cyt cox + 4 H+out + 2 H2O
- The reduction of O2 requires that 4 electrons be transferred from cytochrome *c*, one at a time, without release of oxygen intermediates (*e.g*. hydrogen peroxide, hydroxyl radicals), which would be highly reactive .

Critical Subunits of Complex IV



- Large enzyme complex, 13 subunits, Mr 200,000. The crystal structure was determined in 1999.
- Comparison of mitochondrial and bacterial enzyme complexes suggests that three subunits are critical.
- Subunit II contains two Cu ions complexed with the –SH groups of two Cys residues in a binuclear center that resembles 2Fe-2S clusters.
- Subunit I contains two heme groups and another Cu ion.
- Subunit III is apparently essential but poorly understood.

Path of Electrons Through Complex IV

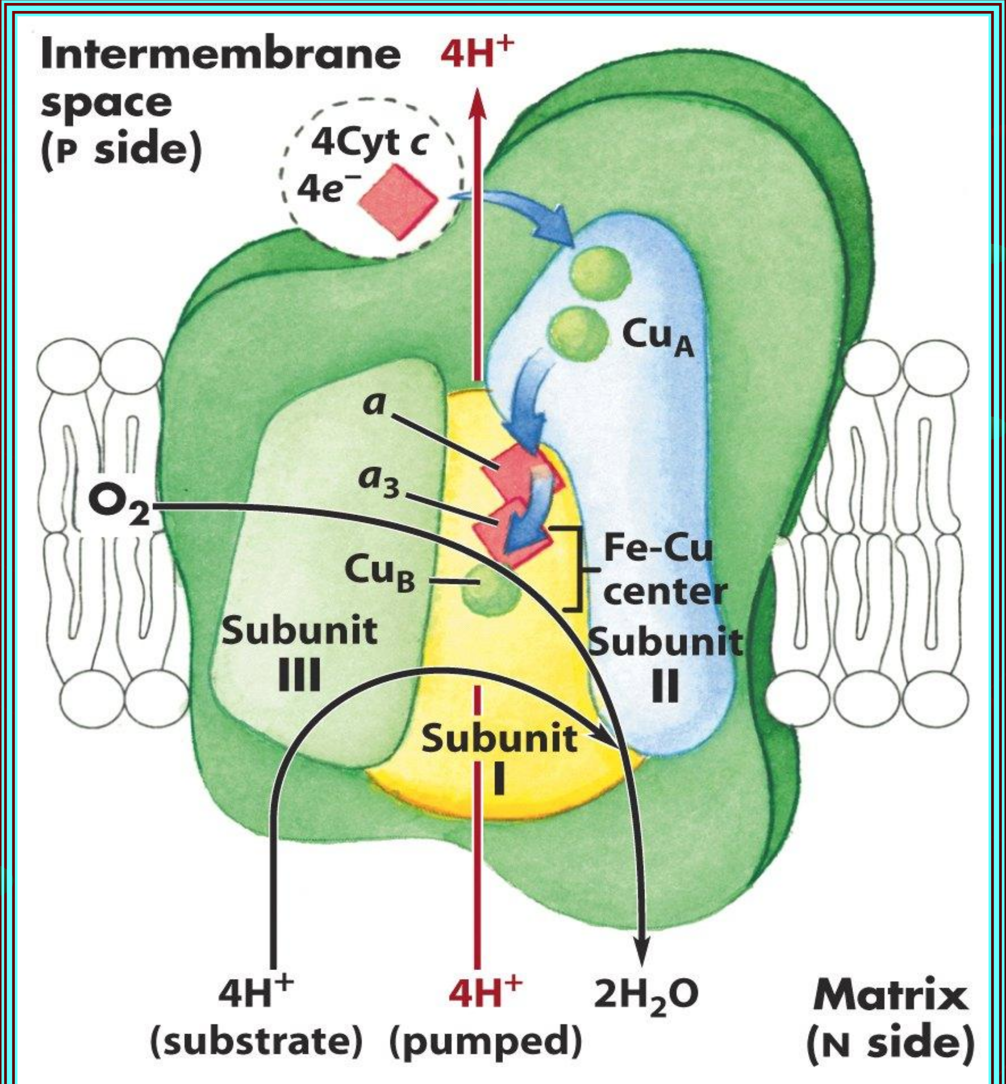
O_2

↓

O_2^{2-}

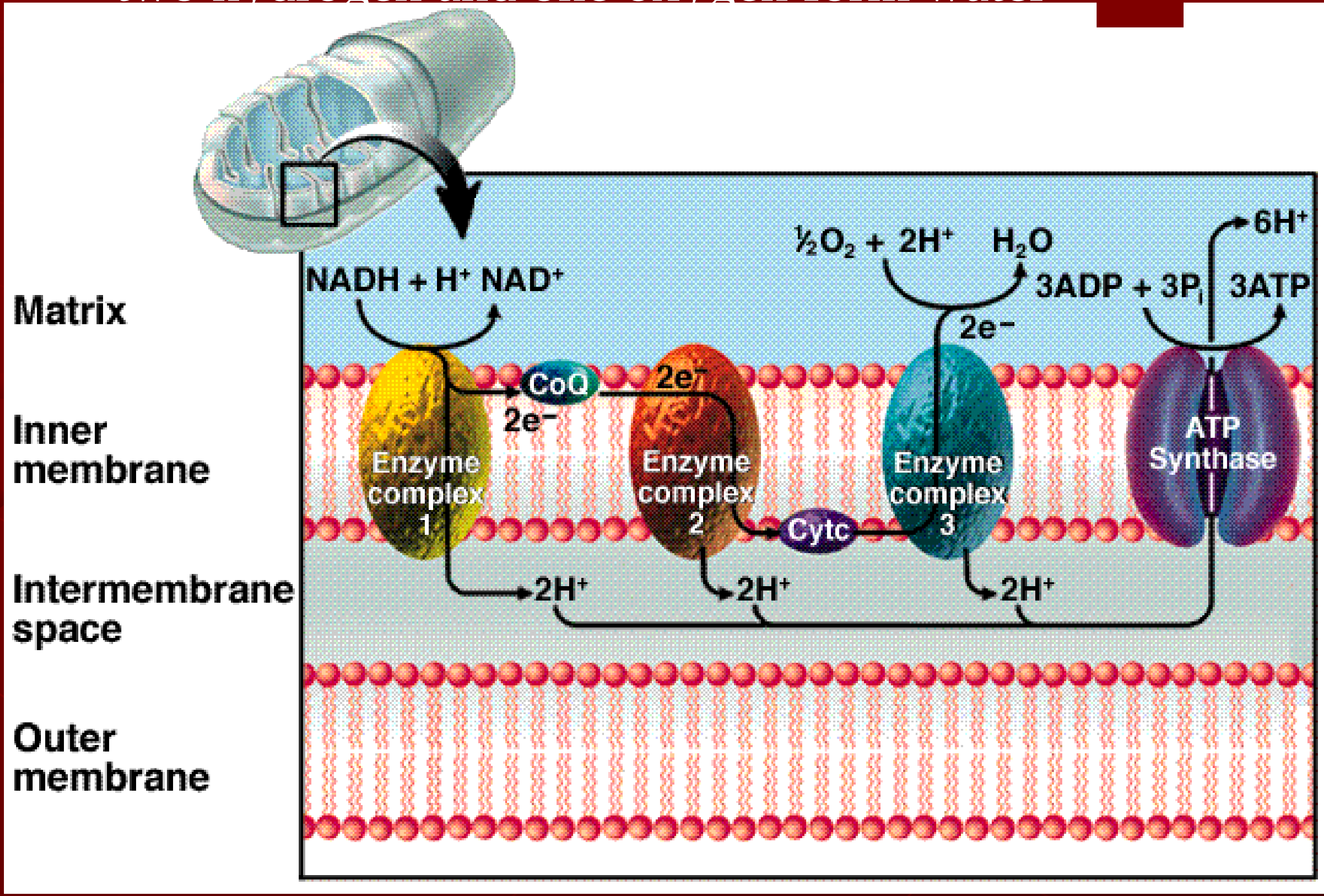
↓

$2H_2O$



Electron Transport Chain

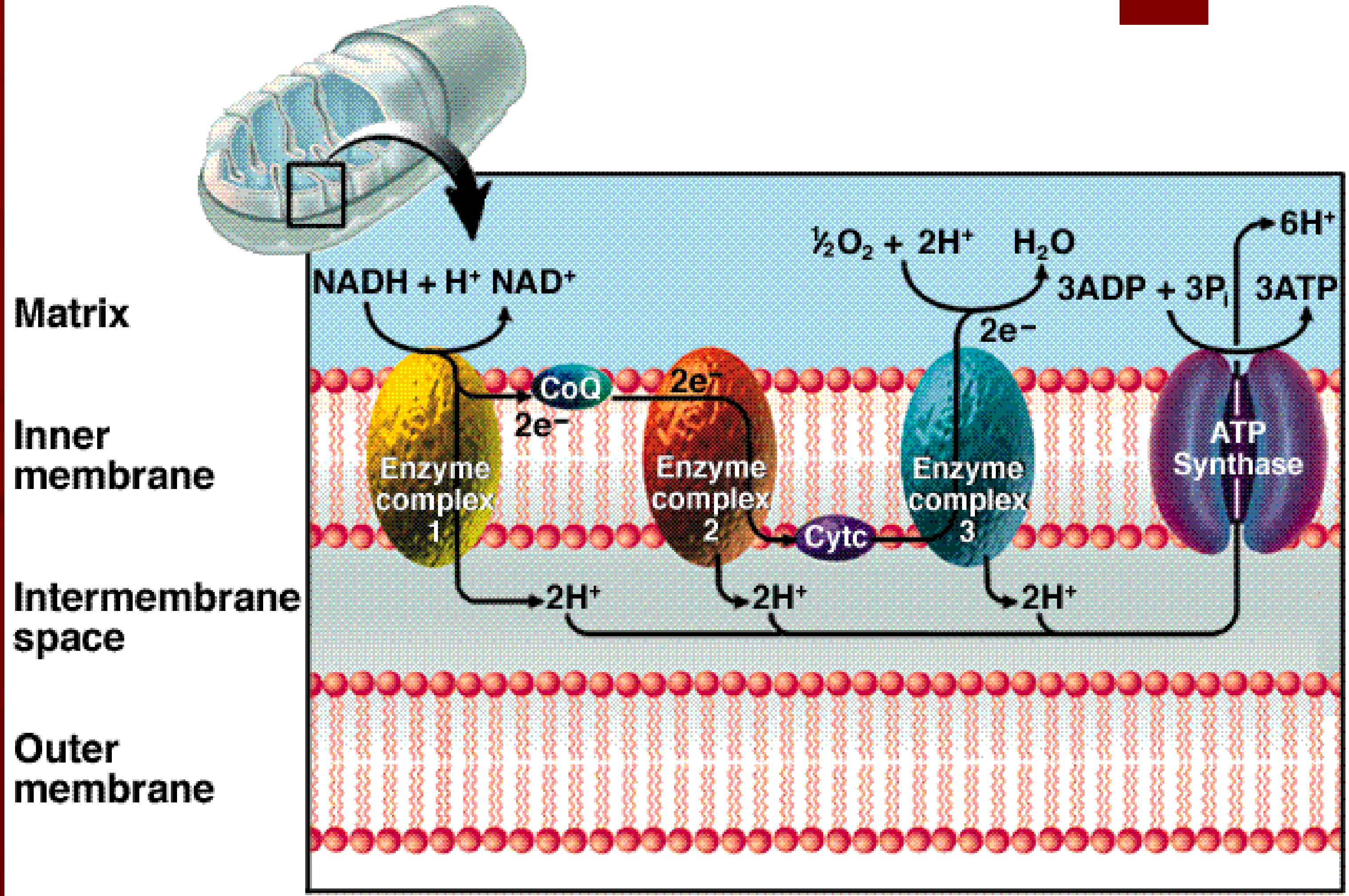
-by now, those electrons are not so high energy anymore...
- the low energy electrons combine back with hydrogen and are finally added to an oxygen atom
- two hydrogen and one oxygen form water



Electron Transport Chain

We still have not done anything with the H^+ gradient we created:

- H^+ runs down it's concentration gradient to provide energy for the enzyme ATP synthase
- ATP synthase uses the energy from the H^+ gradient to...



Convert ADP + P into **ATP**

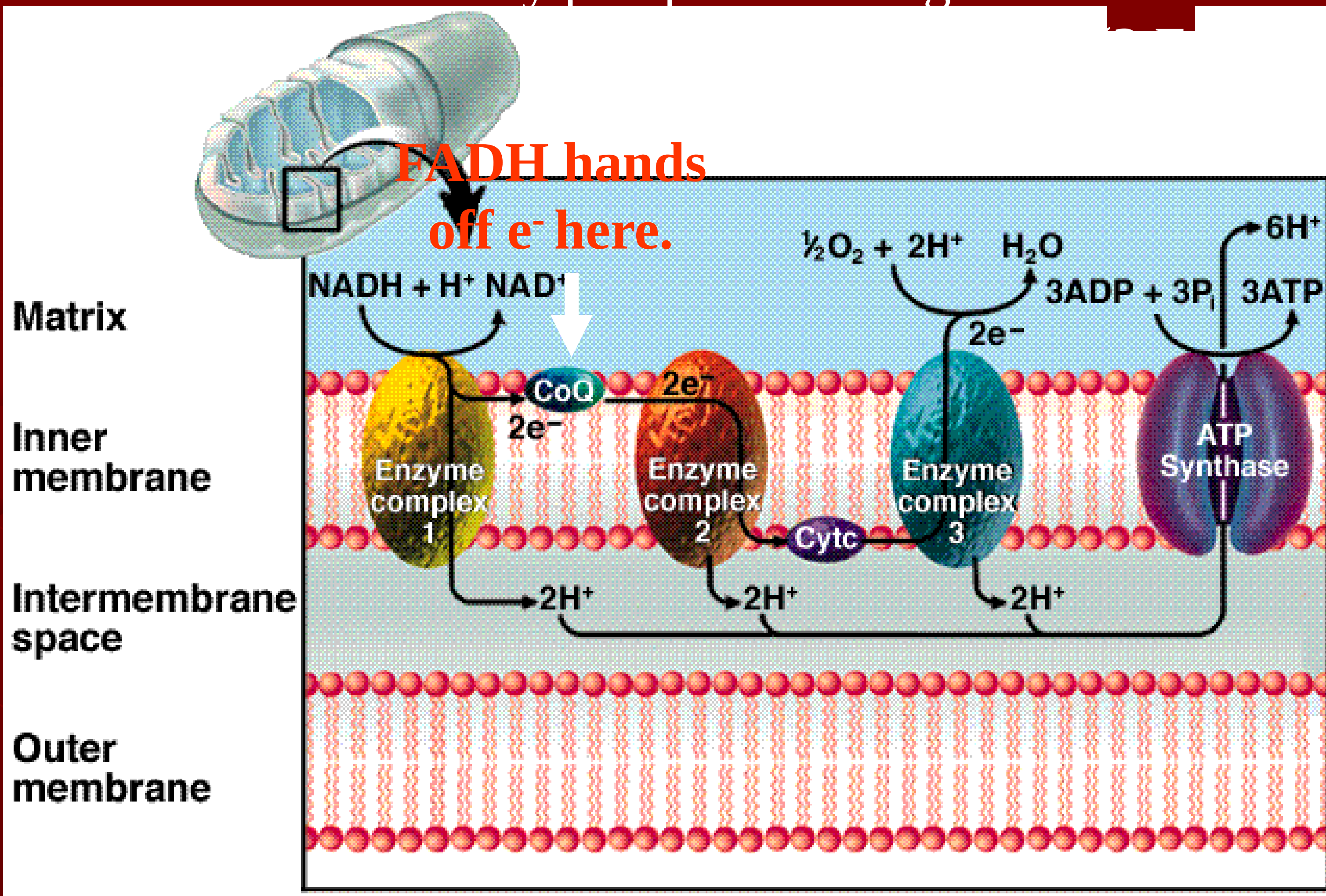
Electron Transport Chain

-Each NADH carries two electrons which pump out enough H^+ to make **3 ATP molecules** (10 NADH yield 30 ATP).

- Each FADH carries two electrons but…

-So each FADH only pumps out enough H^+ to make

[redacted] yield 4 ATP).



Respiratory chain - sequence of electron transfers from substrate fuels to O_2

Goal Achieved -- transfer electrons in a series of small steps, some of which are sufficiently exergonic to drive the synthesis of ATP

Where do electrons come from?

Two classes of electron funneling - they are quite different.

-- ①from NADH and
-- ②from flavins in flavoprotein enzymes

1. ***NADH funnel*** - several metabolites reduces NAD via specific enzymes. NADH diffuses and is re-oxidized by NADH dehydrogenase.

Isocitrate → α-KG
lactate → pyruvate
NAD → **malate → oxaloacetate** → NADH
other oxidations

↙

NADH Dehydrogenase

↘CoQ