Module 11

Oxidative Phosphorylation

Session Slides with Notes

NAD+

nicotinamide

aromatic

hydride

$H:^-$

$2e + 2H^+$

not aromatic

adenosine

NAD+ (oxidized)

NADH (reduced)

standard reduction potential

e^-

e^-

-0.32 V

anode

+0.82 V

cathode

$NAD^+/NADH$

$H^+/\frac{1}{2}H_2$

$H^+/\frac{1}{2}H_2$

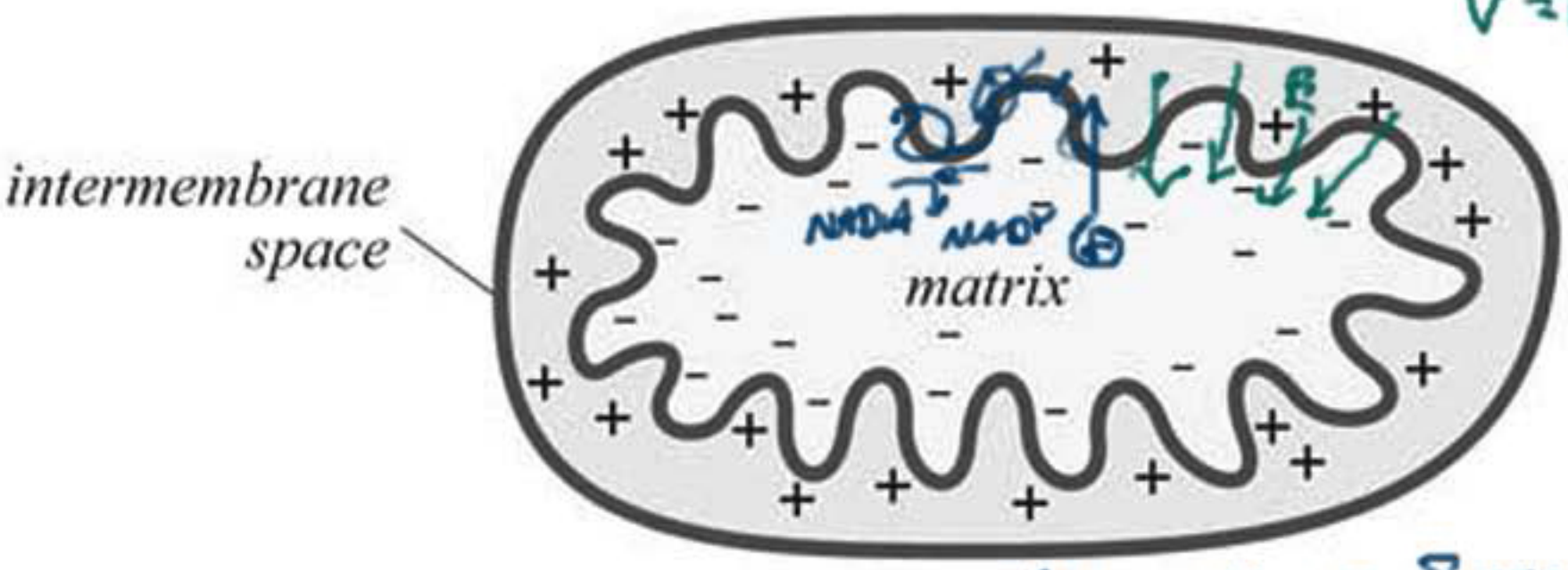
$\frac{1}{2}O_2/H_2O$

standard hydrogen electrode

$$E_{cell} = E^\circ_{cathode} - E^\circ_{anode}$$

$$(0.82) - (-0.32) = 1.14\ V$$

$V = Bl$

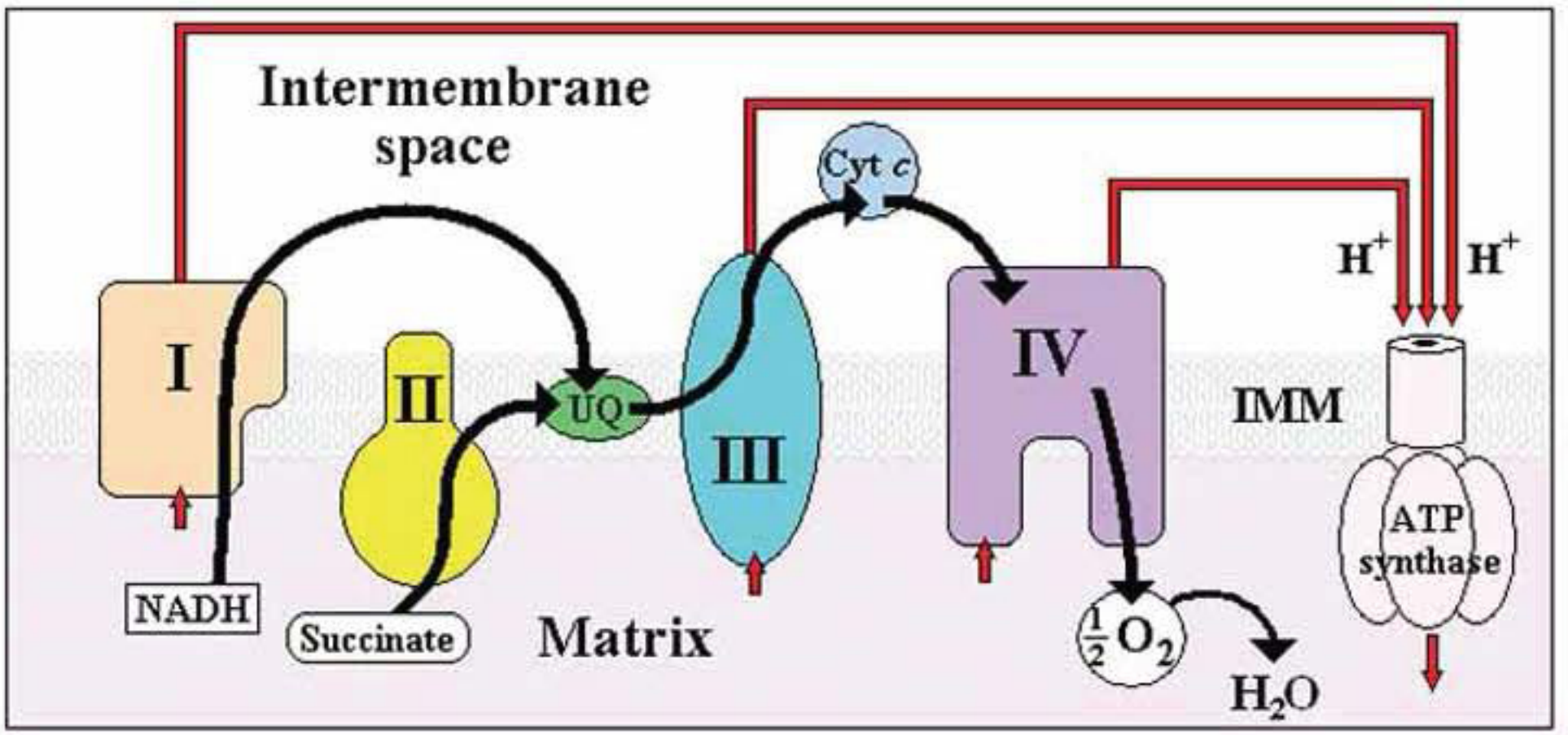


Proton Motive Force

electrostatic potential : 0.16 V

diffusion gradient : 0.05V

210 mV



I - NADH ubiquinone oxido reductase

II - Succinate dehydrogenase

III - Cytochrome c reductase

IV - Cytochrom c Oxidase

Why does NADH in glycolysis yield fewer ATP

Glycolysis

Glyceraldehyde-3-Phosphate Dehydrogenase

1,3-bisphosphoglycerate

Glyceraldehyde-3-phosphate

NADH + H^+

NAD^+

Cytoplasmic Glycerol-3-Phosphate Dehydrogenase

Dihydroxyacetone phosphate

Glycerol-3-Phosphate

Glycerol -3-Phosphate Shuttle

↓ mitochondria

$FADH_2$

FAD

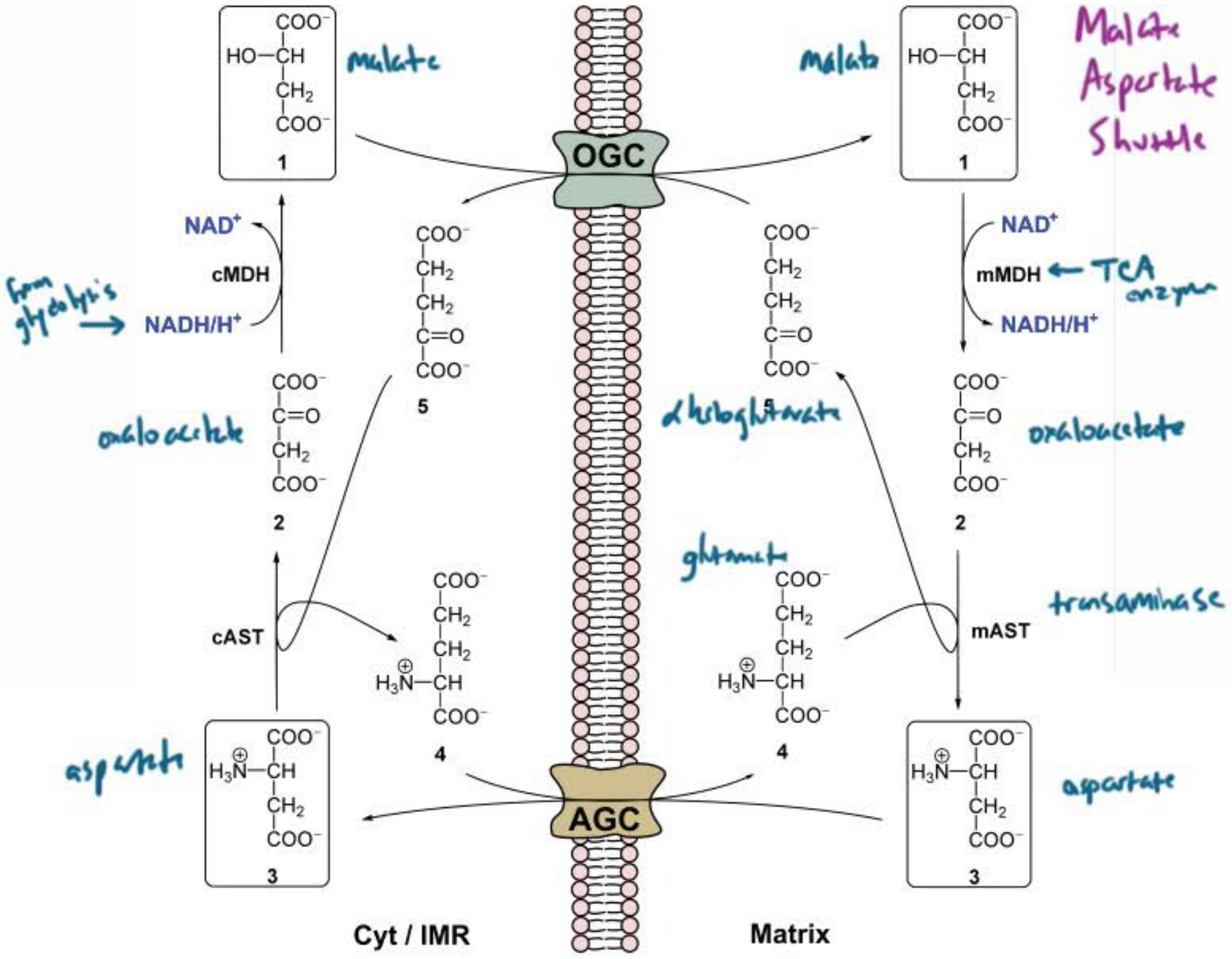
Coenzyme Q

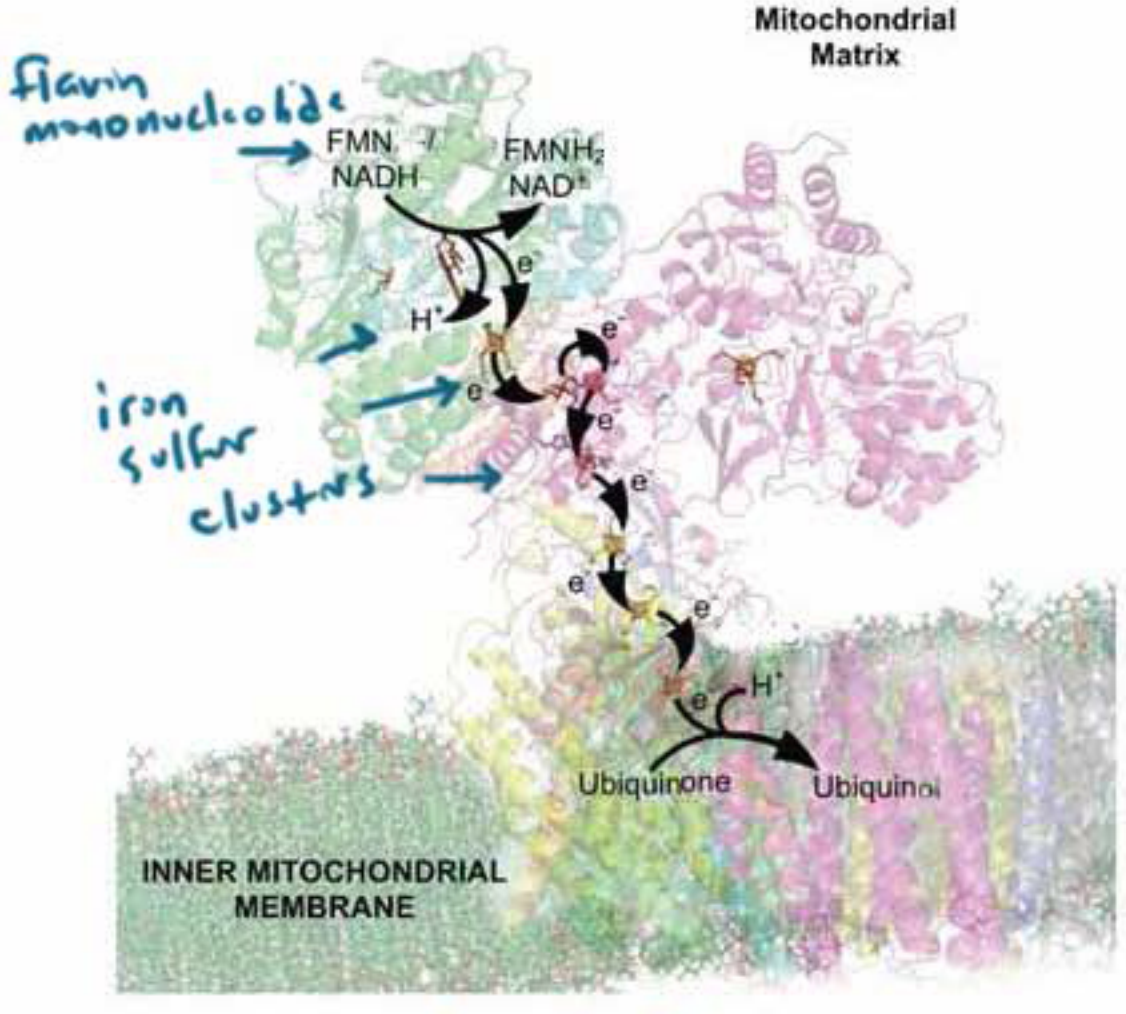
Coenzyme QH_2

Oxidative Phosphorylation

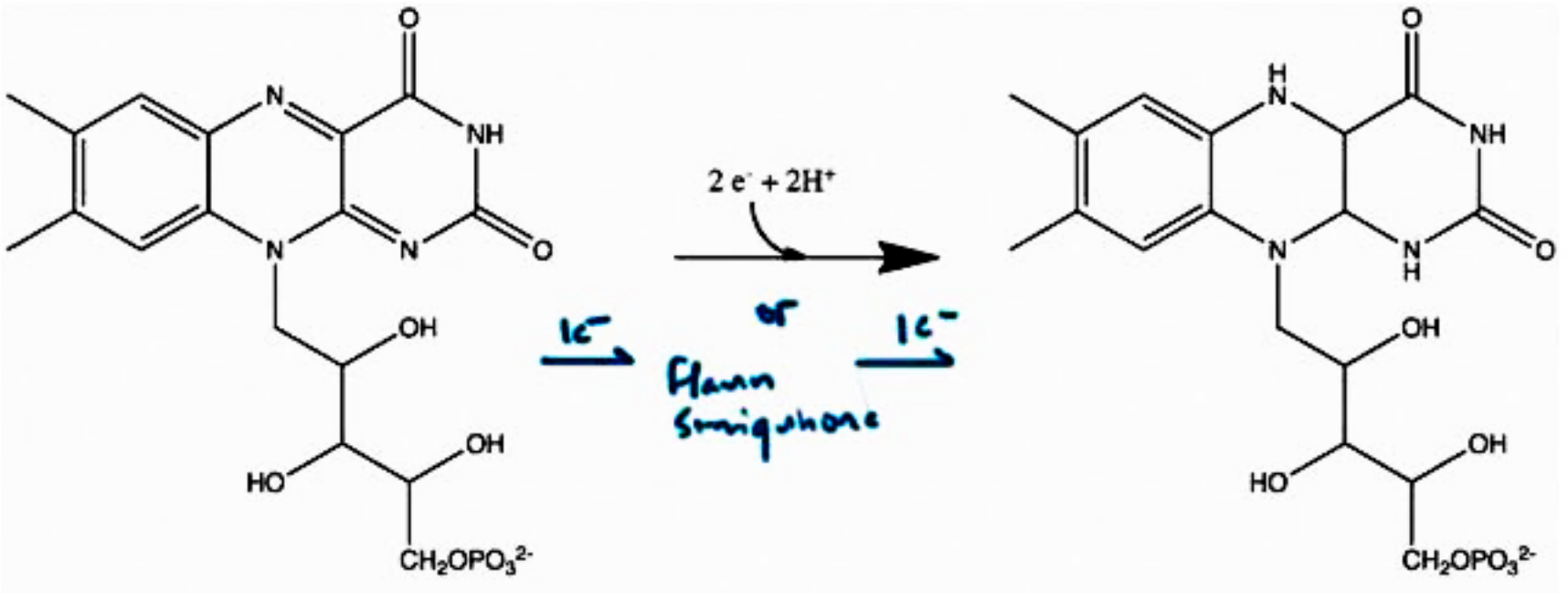
Mitochondrial Glycerol-3-Phosphate Dehydrogenase

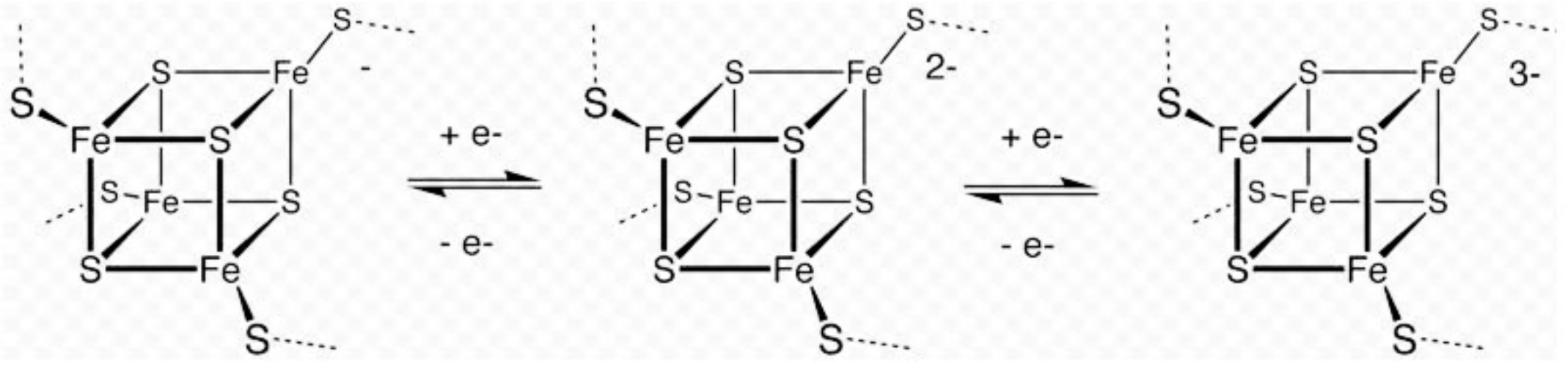
← whoa! another complex? passes to CoQ without pumping protons


malate
OGC
malate
Malate Aspartate Shuttle
NAD+
cMDH
NADH/H+
from glycolysis
NAD+
mMDH
TCA enzyme
NADH/H+
oxaloacetate
α ketoglutarate
oxaloacetate
glutamate
cAST
mAST
transaminase
aspartate
AGC
aspartate
Cyt / IMR
Matrix


Mitochondrial Matrix
flavin mononucleotide
FMN
NADH
FMNH2
NAD+
H+
iron sulfur clusters
e-
Ubiquinone
Ubiquinol
INNER MITOCHONDRIAL MEMBRANE

Complex I


2 e⁻ + 2H⁺
1e⁻
or
Flavin
Semiquinone
1e⁻
FMN (oxidized)
FMNH2 (reduced)

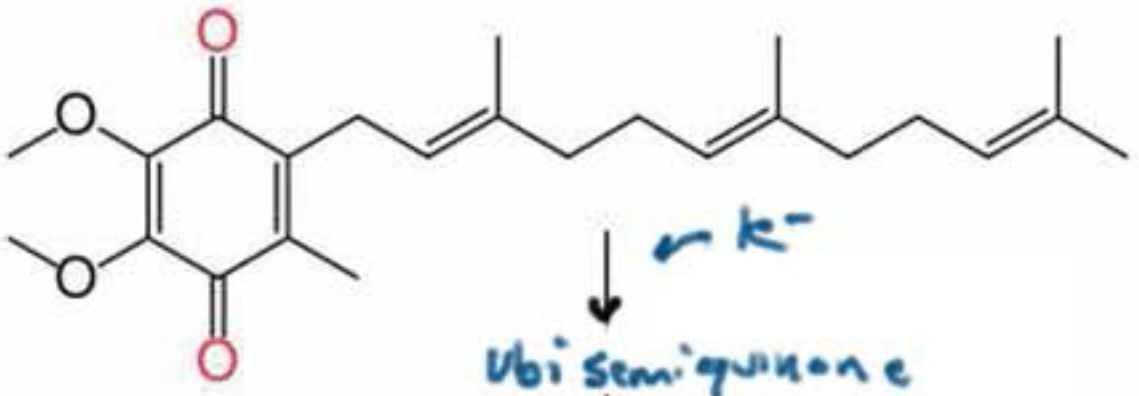


Iron Sulfur Clusters Fe_4S_4

also FeS

Fe_2S_2

Ubiquinone

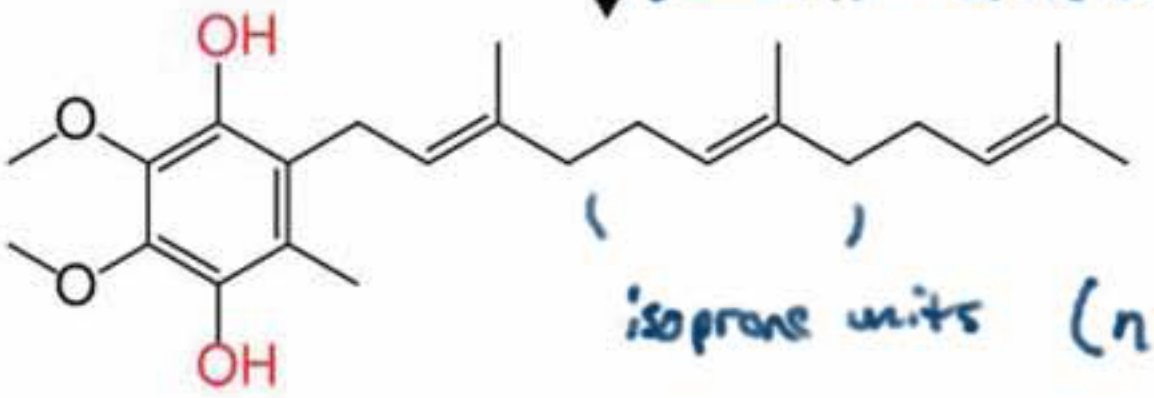


$+ e^-$

Ubisemiquinone

$+ e^-$

$+ 2H^+$ (from the matrix)

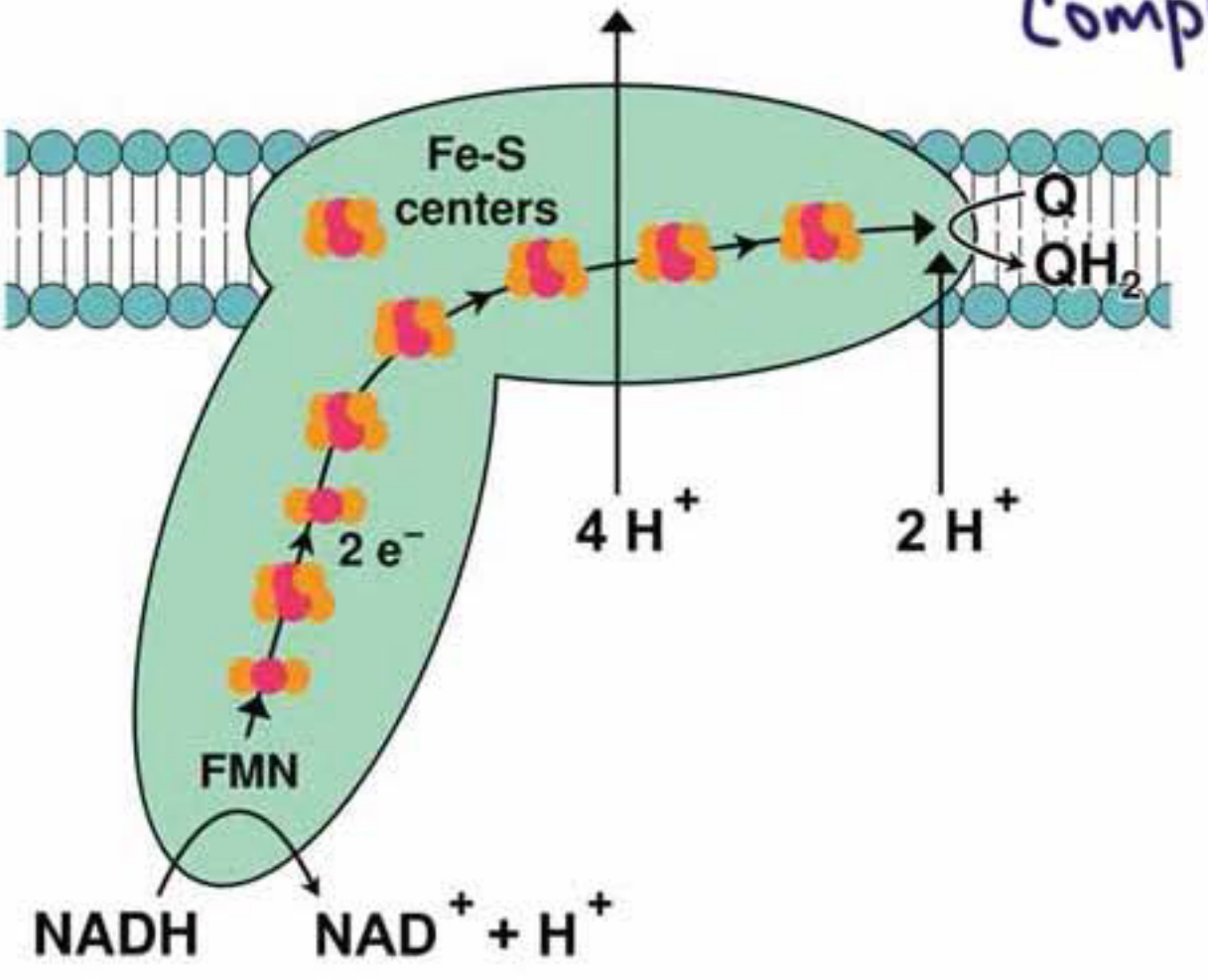


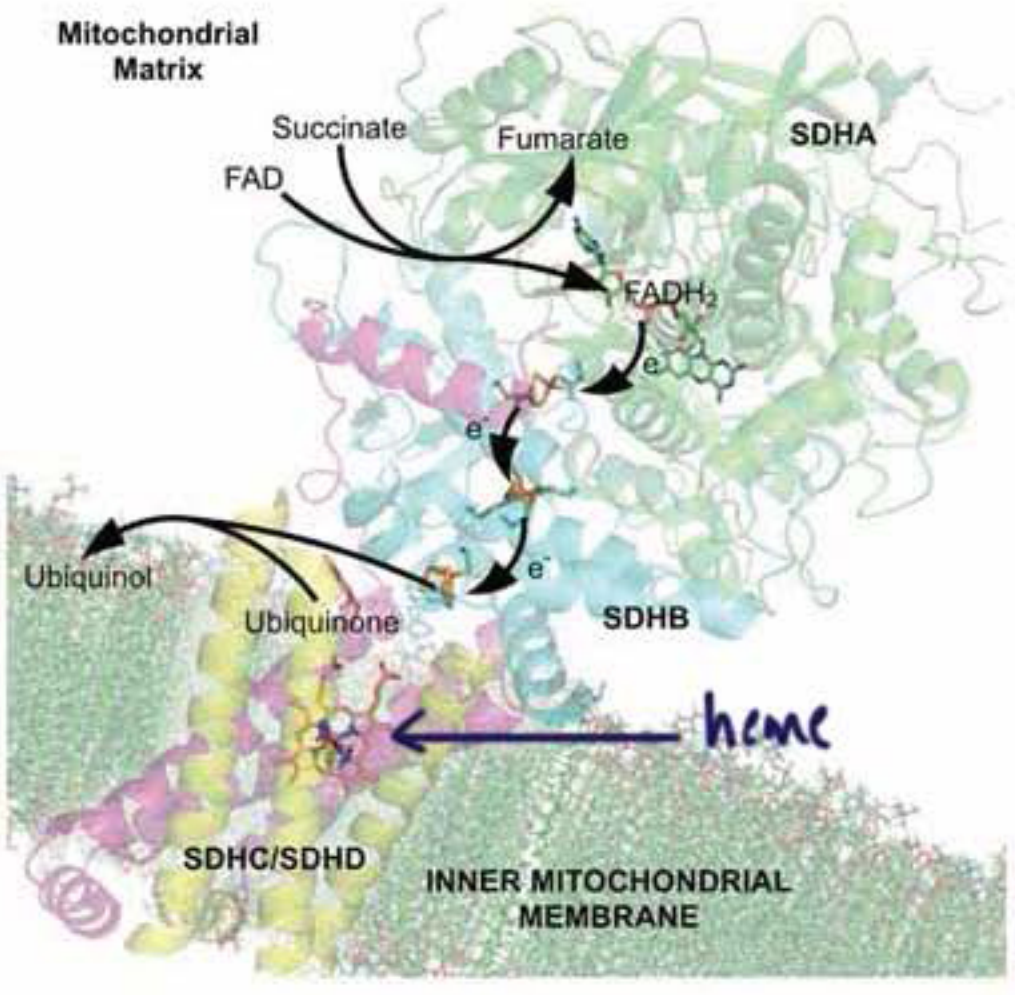
ubiquinol

( )

isoprene units ($n \sim 10$)

Complex I

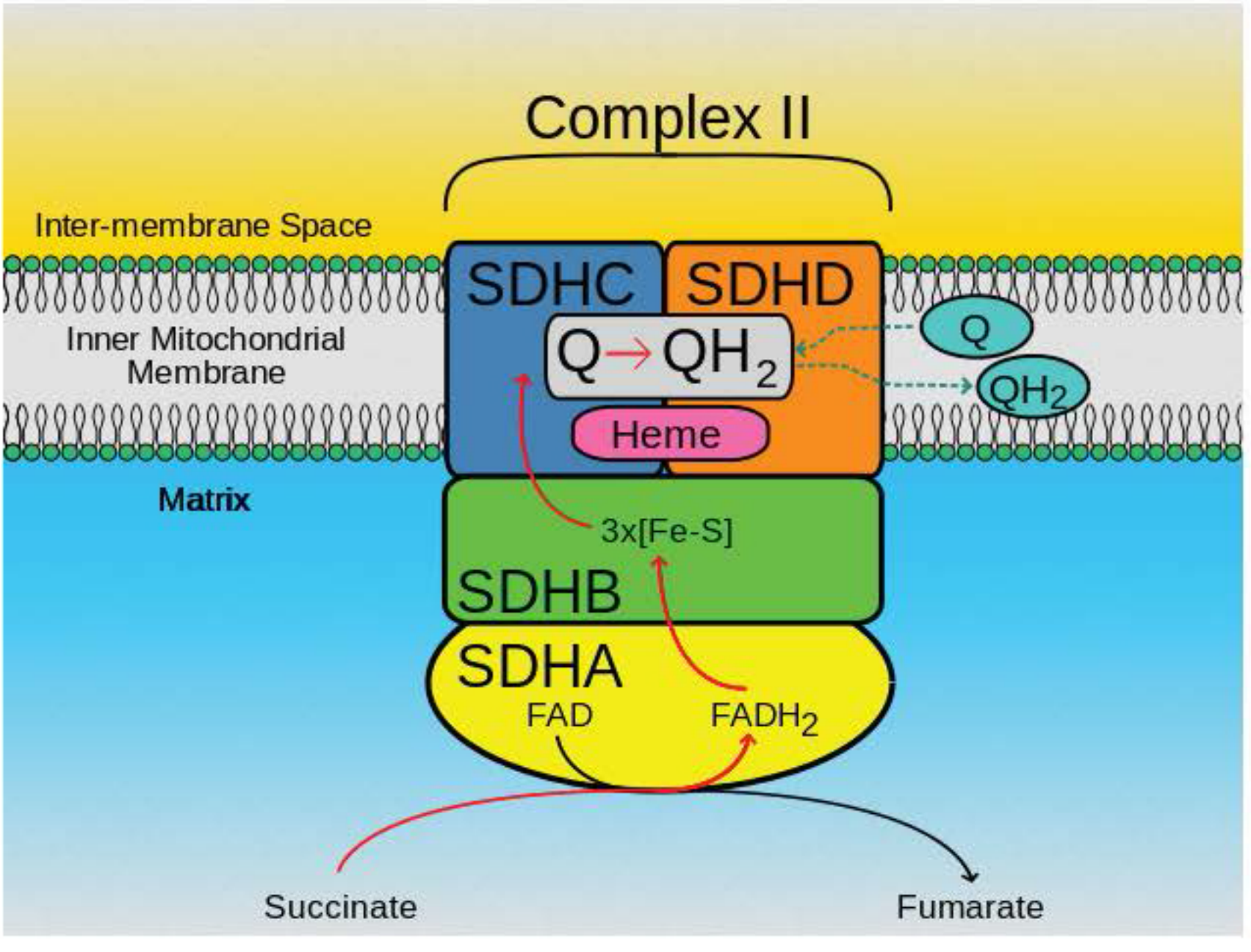


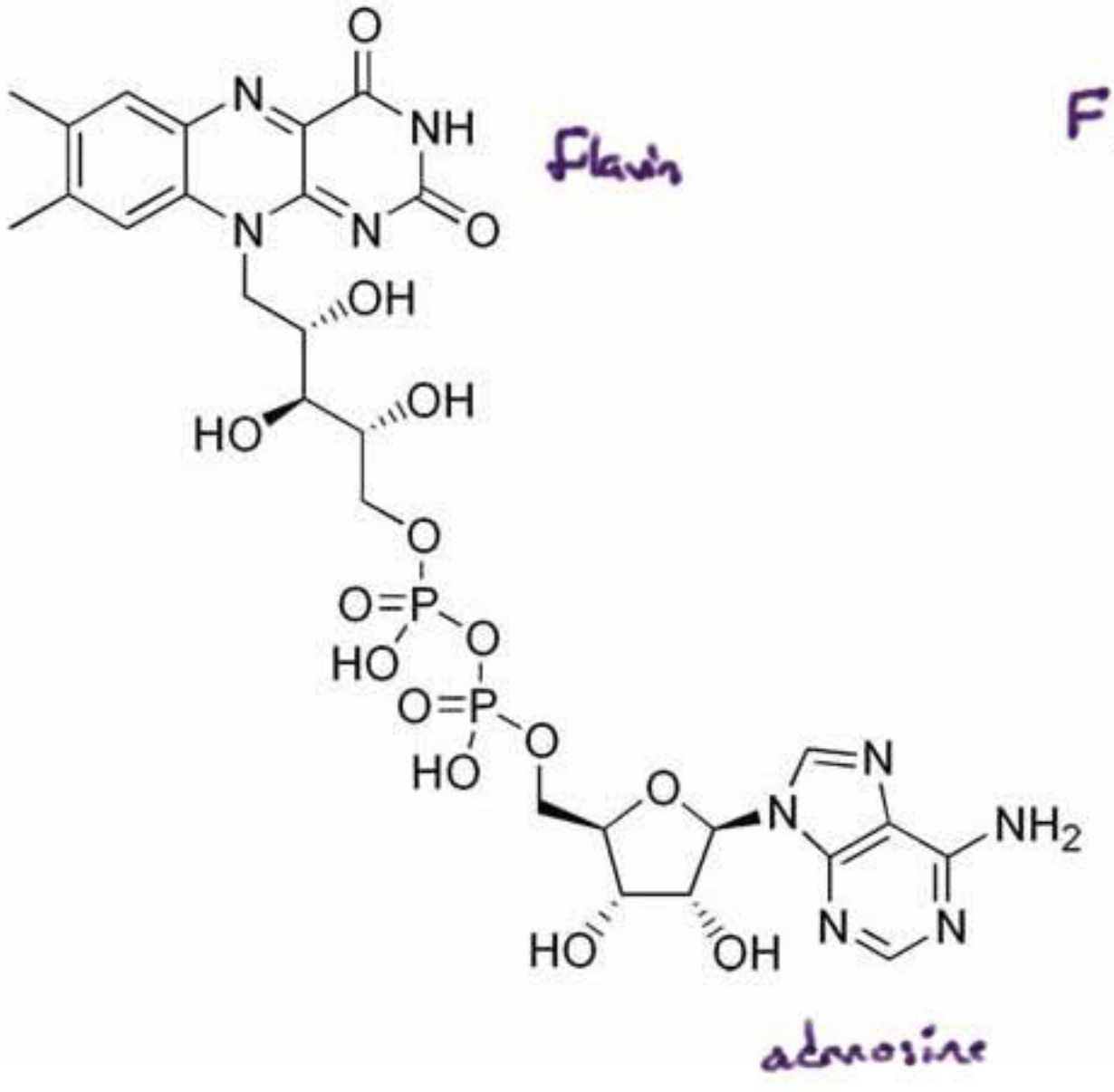


does not pump protons

Complex II

succinate dehydrogenase

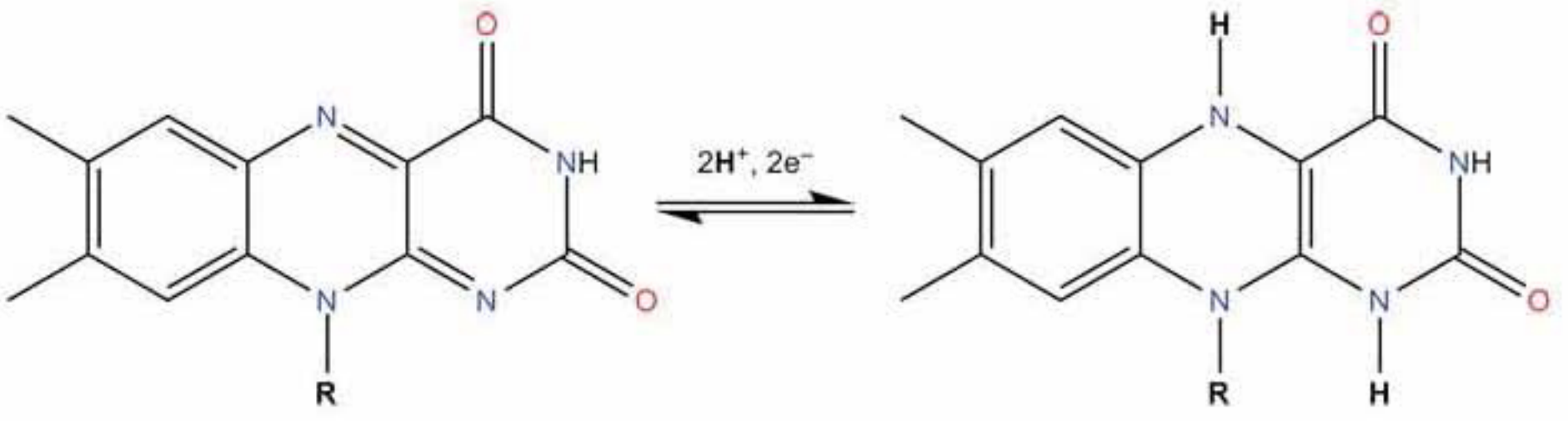

Complex II
Inter-membrane Space
Inner Mitochondrial Membrane
Matrix
SDHC
SDHD
Q → QH2
Heme
Q
QH2
3x[Fe-S]
SDHB
SDHA
FAD
FADH2
Succinate
Fumarate



FAD

Flavin

adenosine

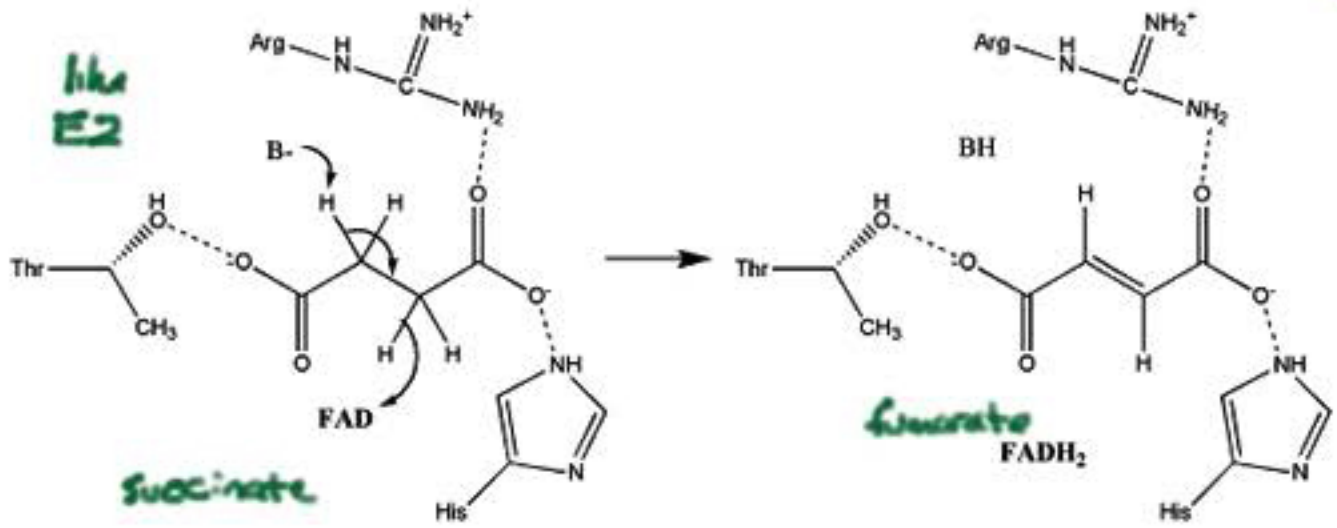


FAD

FADH2

Two alternative proposed mechanisms for succinate dehydrogenase.

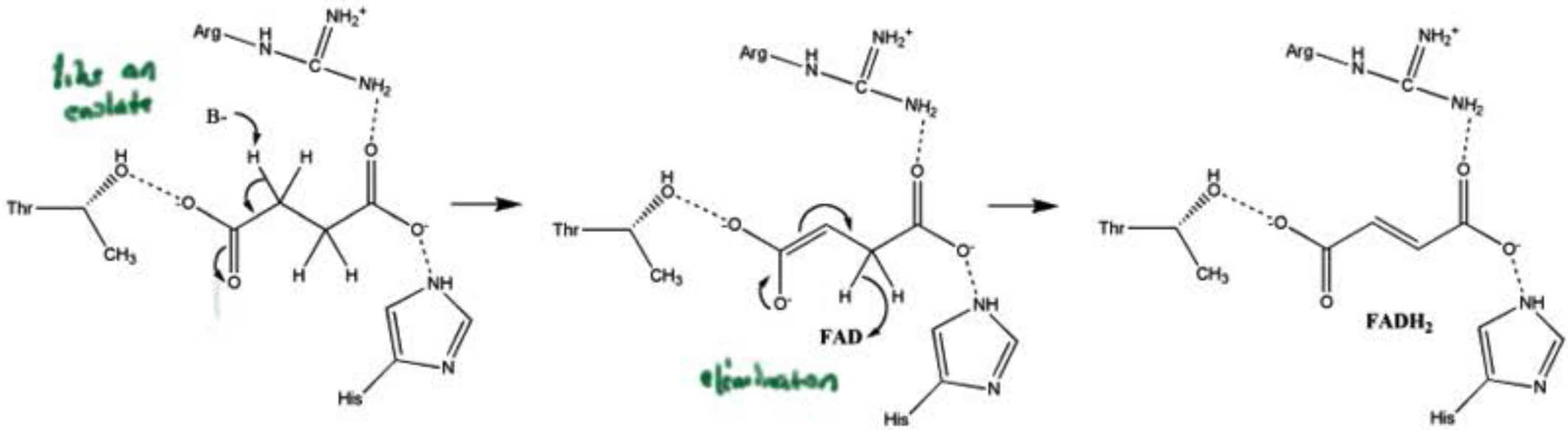
like E2



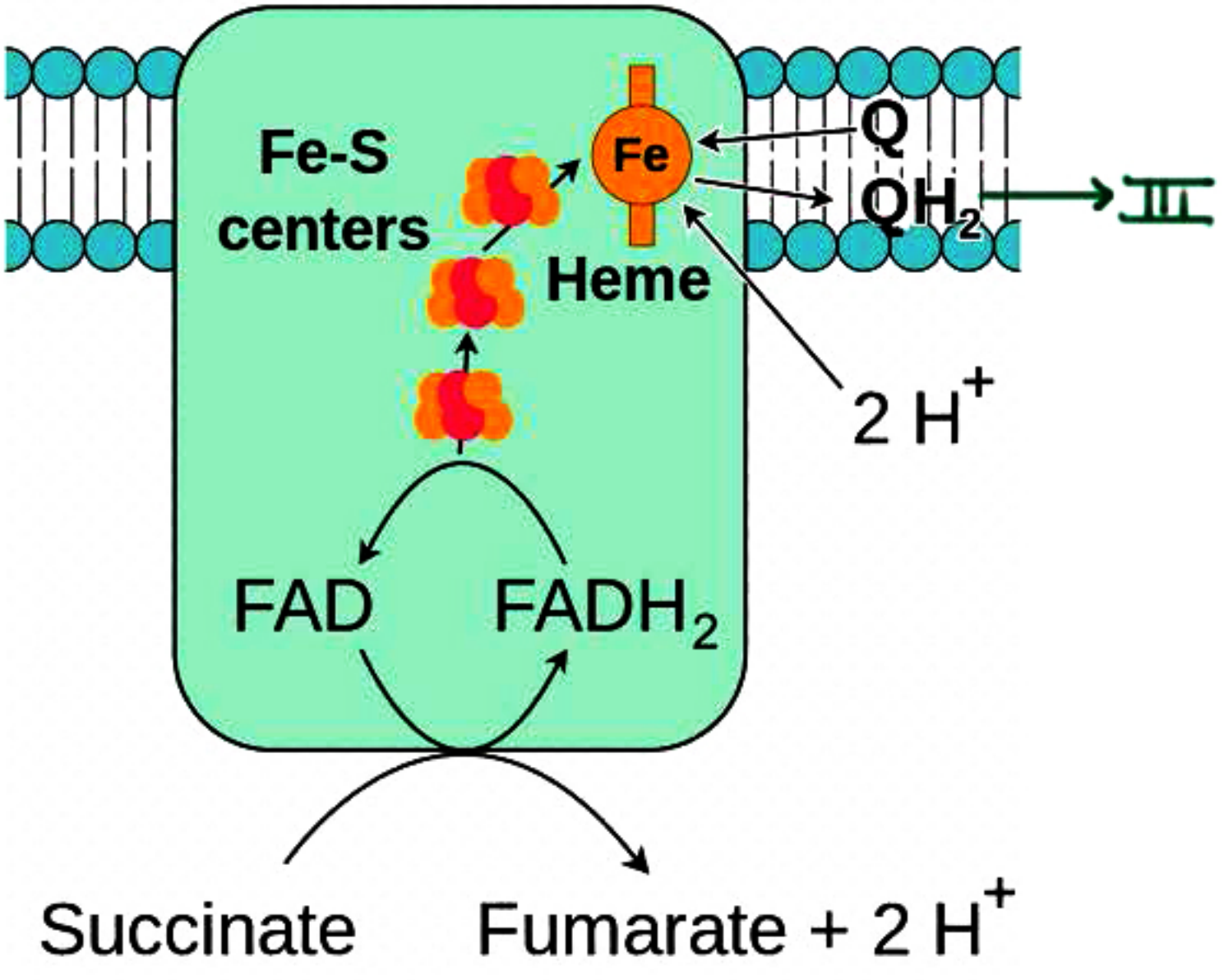
succinate

fumarate

like an enolate

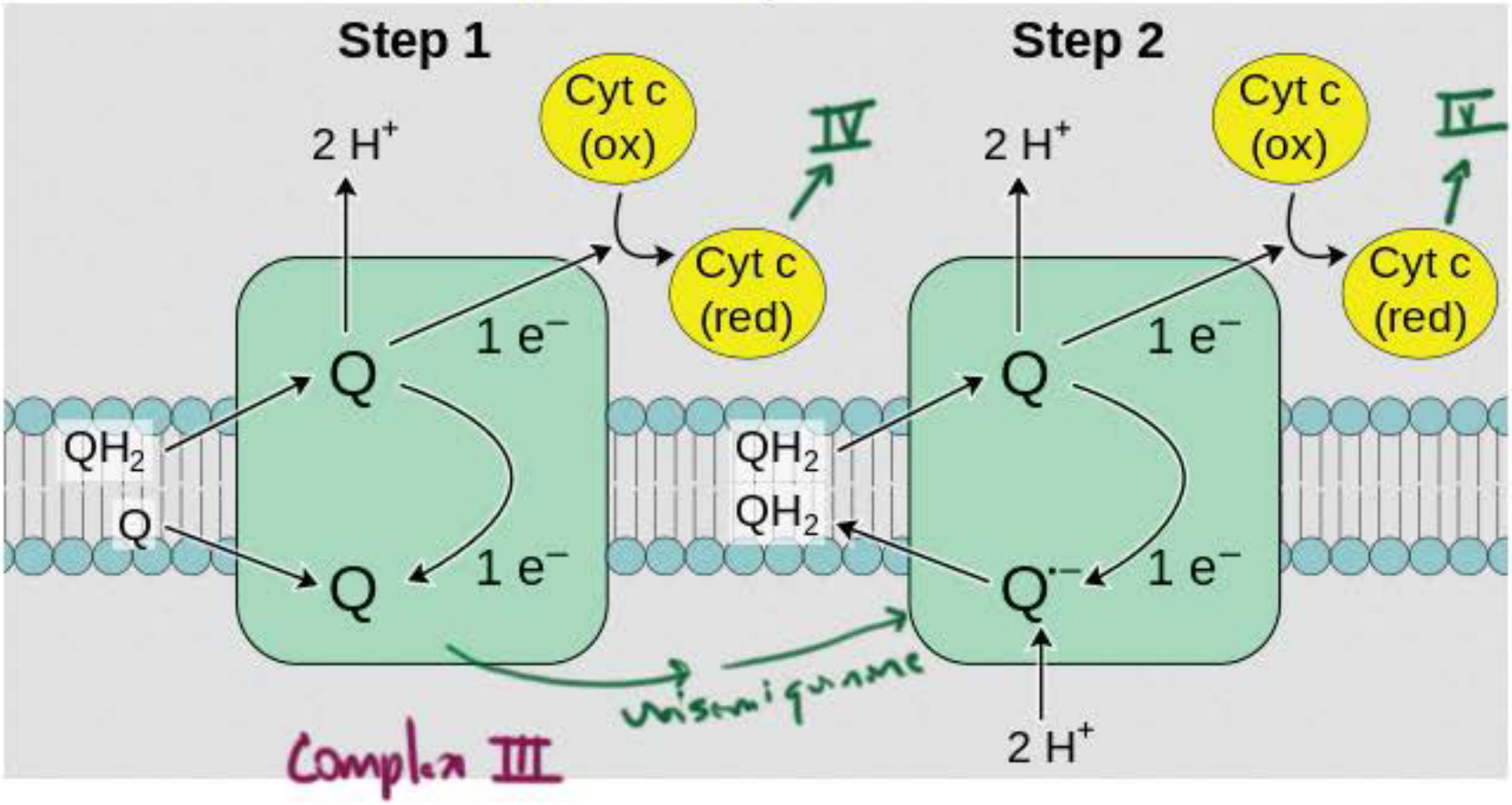


elimination


Fe-S
centers
Fe
Q
QH_2
III
Heme
$2\ H^+$
FAD
$FADH_2$
Succinate
Fumarate + $2\ H^+$

Complex II

Ubiquinone Cycle



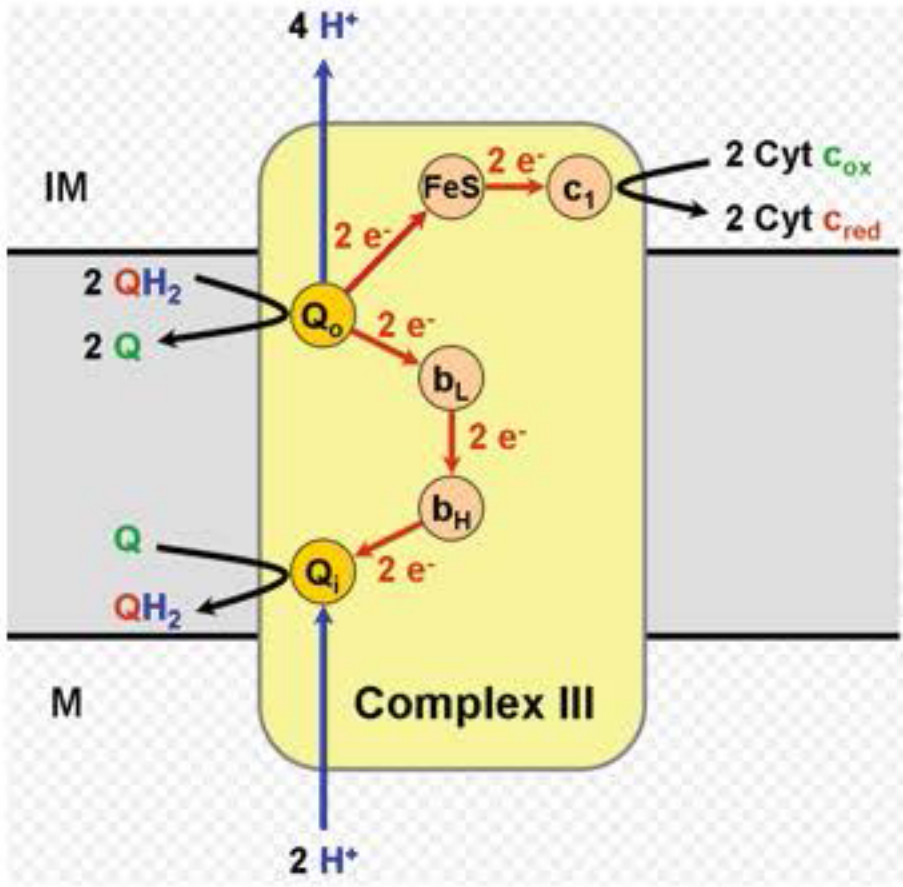
- allows two extra protons to be pumped per ubiquinol

Round 1:

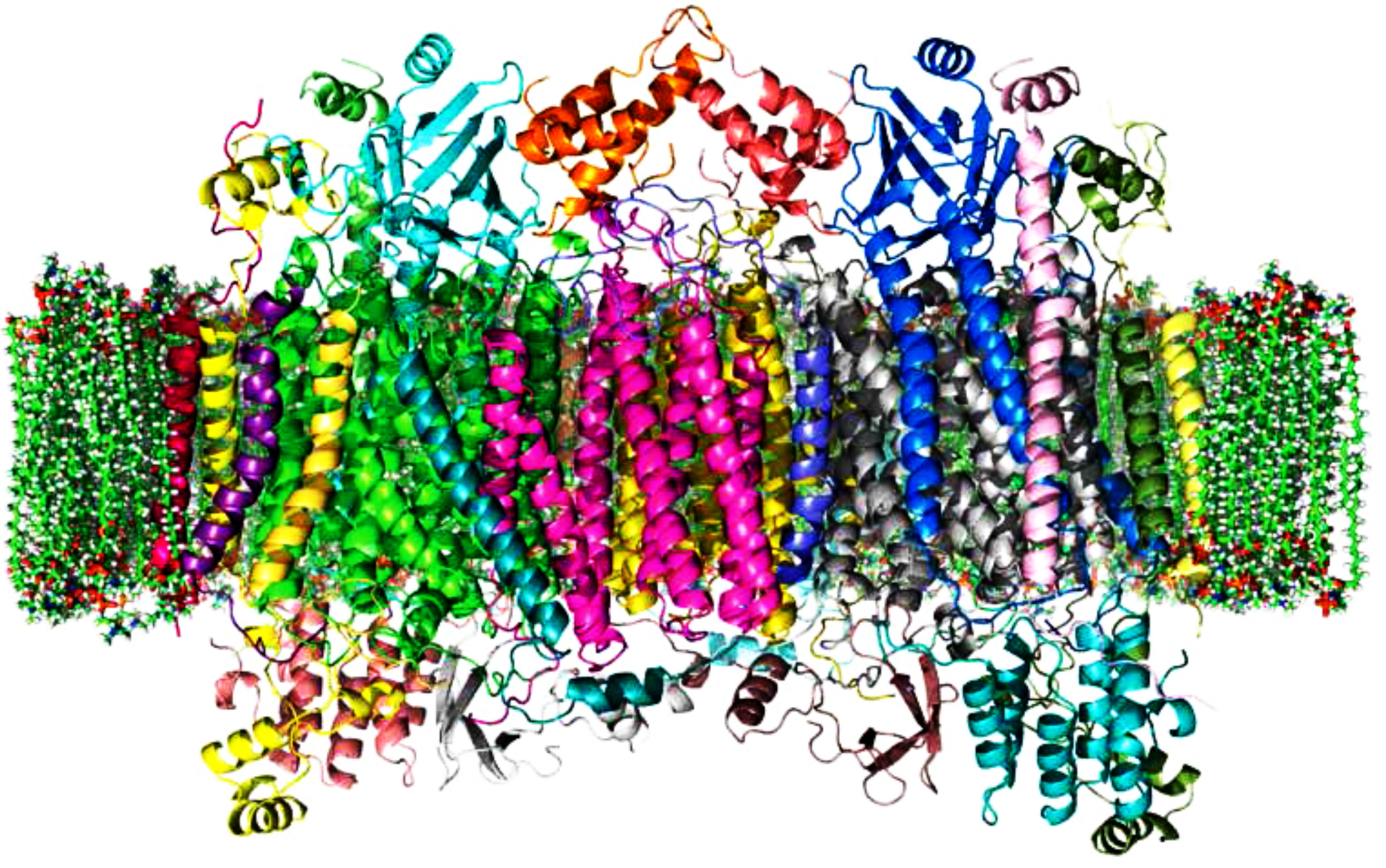
1. Cytochrome b binds a ubiquinol and a ubiquinone.
2. The 2Fe/2S center and B_L heme each pull an electron off the bound ubiquinol, releasing two hydrogens into the intermembrane space.
3. One electron is transferred to cytochrome c_1 from the 2Fe/2S centre, while another is transferred from the B_L heme to the B_H Heme.
4. Cytochrome c_1 transfers its electron to cytochrome c (not to be confused with cytochrome c_1), and the B_H Heme transfers its electron to a nearby ubiquinone, resulting in the formation of a ubisemiquinone.
5. Cytochrome c diffuses. The first ubiquinol (now oxidized to ubiquinone) is released, whilst the semiquinone remains bound.

Round 2:

1. A second ubiquinol is bound by cytochrome b.
2. The 2Fe/2S center and B_L heme each pull an electron off the bound ubiquinol, releasing two hydrogens into the intermembrane space.
3. One electron is transferred to cytochrome c_1 from the 2Fe/2S centre, whilst another is transferred from the B_L heme to the B_H Heme.
4. Cytocrome c_1 then transfers its electron to cytochrome c, while the nearby semiquinone picks up a second electron from the B_H heme, along with two protons from the matrix.
5. The second ubiquinol (now oxidised to ubiquinone), along with the newly formed ubiquinol are released.

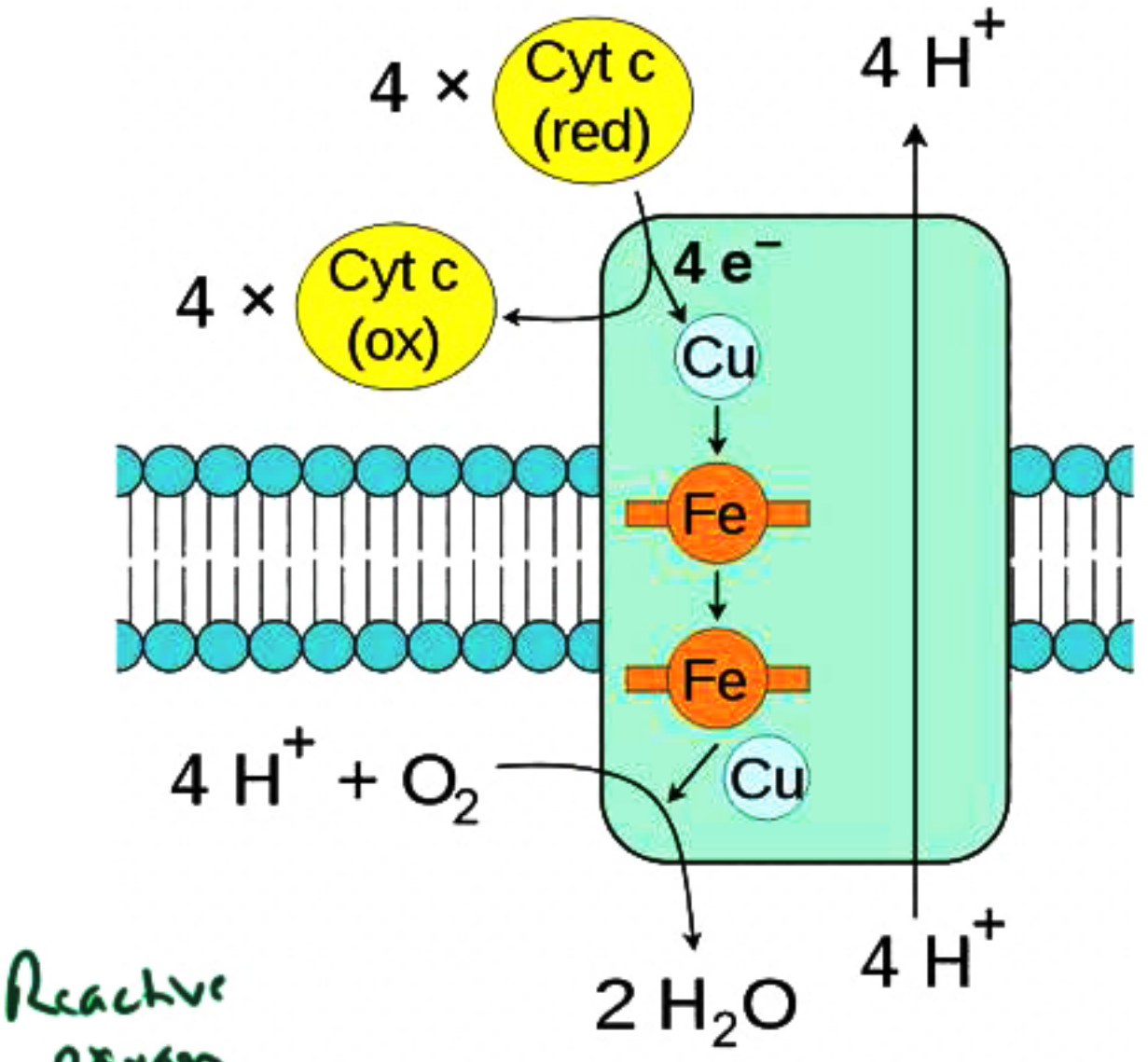


Supplemental reading



$$4\ Fe^{2+}\text{-cytochrome } c + 8\ H^{+}_{in} + O_2 \rightarrow 4\ Fe^{3+}\text{-cytochrome } c + 2\ H_2O + 4\ H^{+}_{out}$$

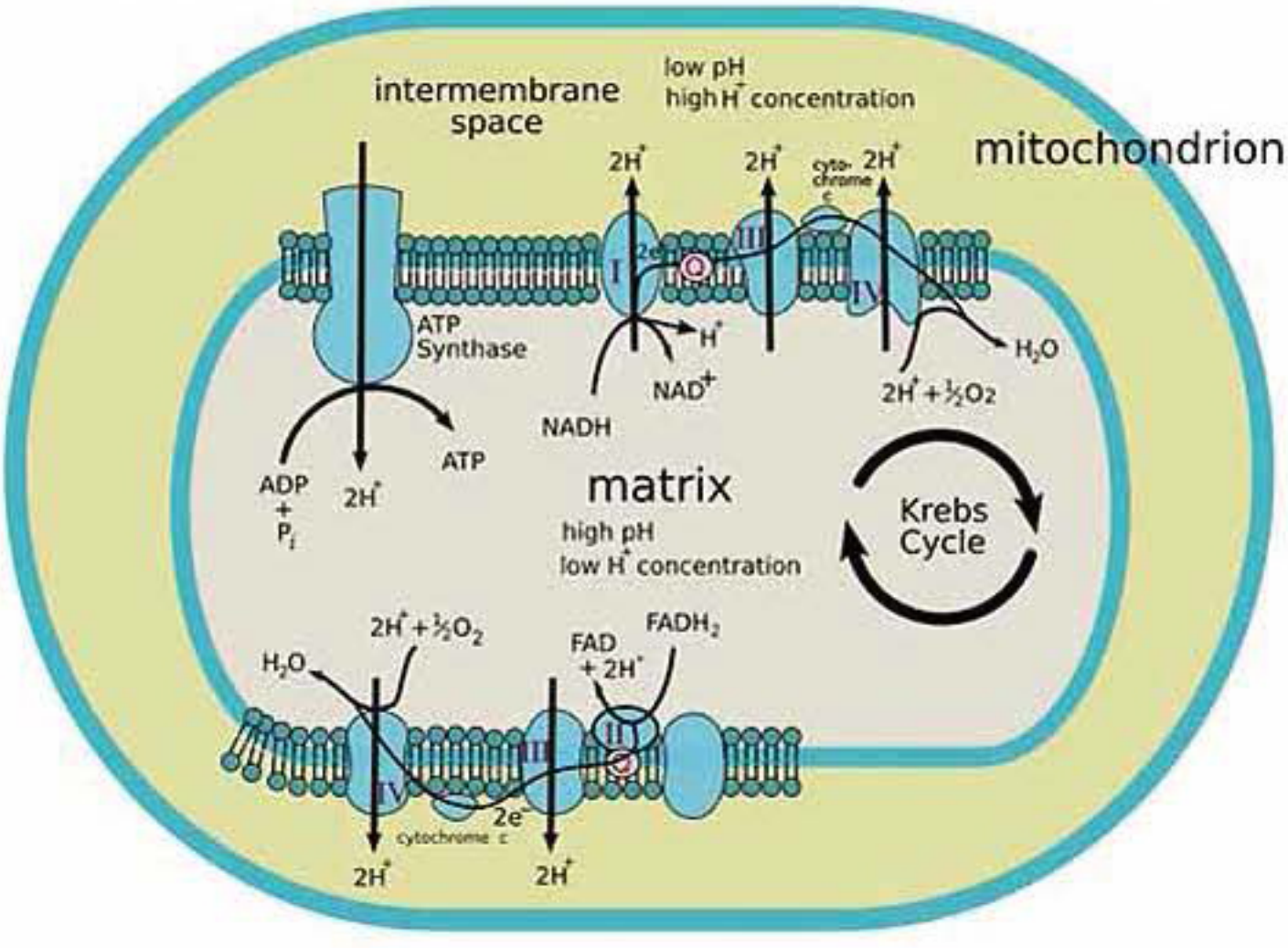
Complex IV



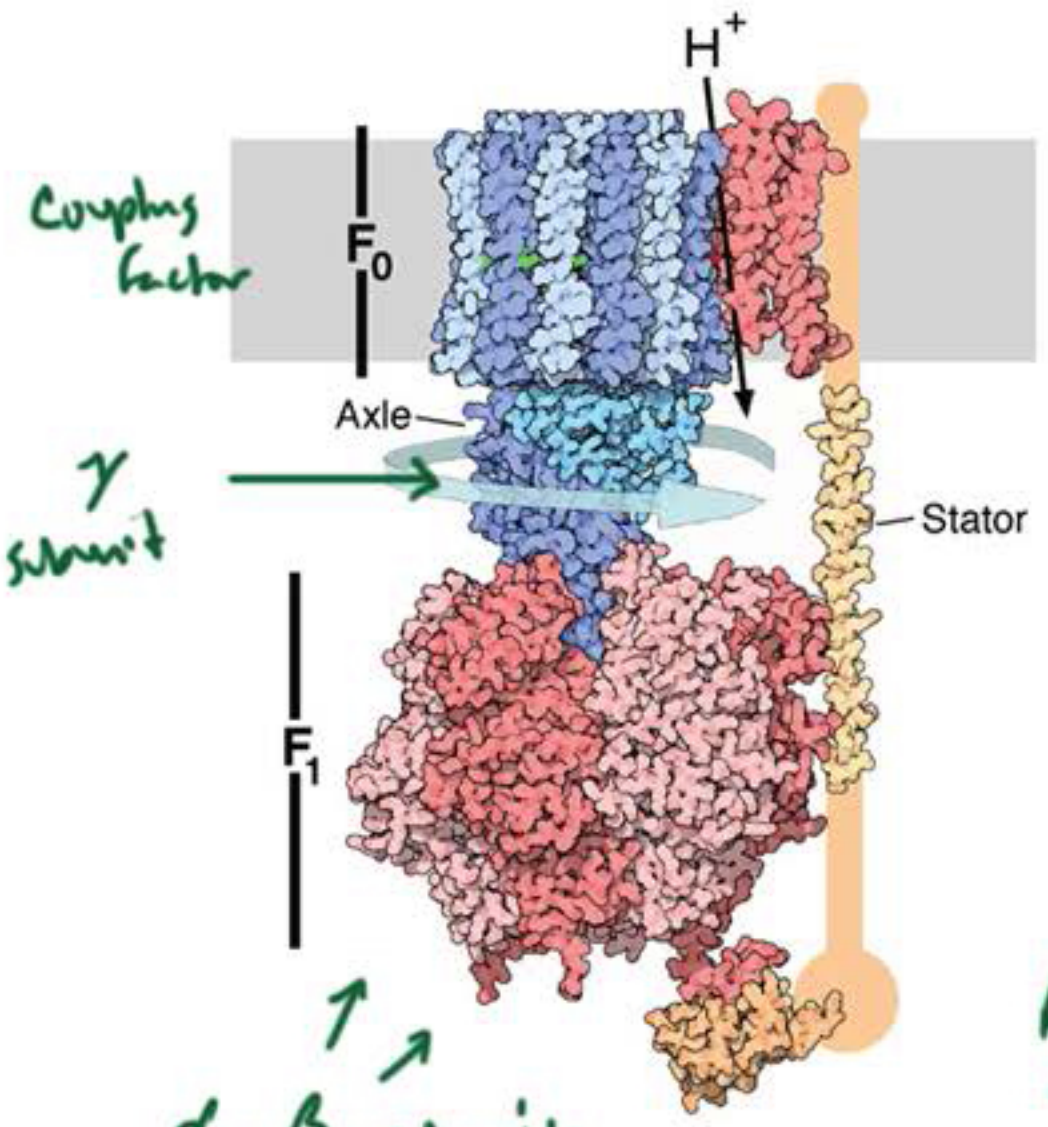
Reactive oxygen species may form here

R.O.S.

Mitochondrial Electron Transport Chain

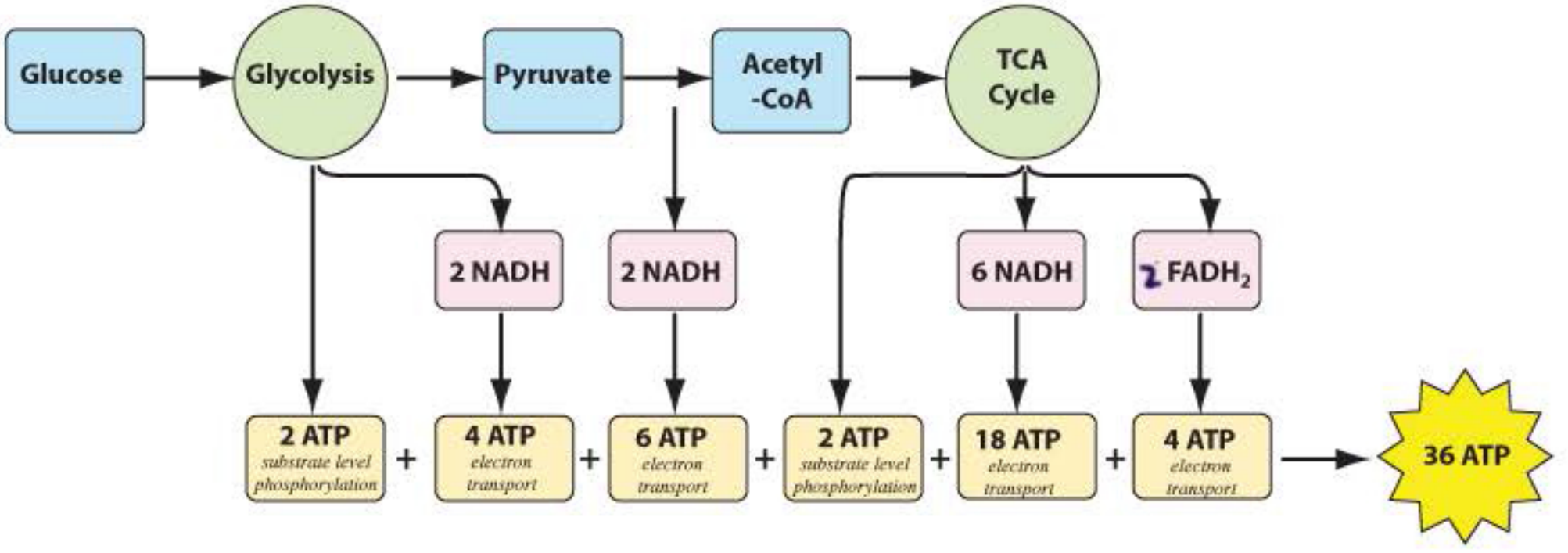


ATP Synthase



β subunits undergo conformational change

1) open - ADP & Pi to enter
2) loose - binds loosely
3) tight - forms ATP


Glucose
Glycolysis
Pyruvate
Acetyl -CoA
TCA Cycle
2 NADH
2 NADH
6 NADH
2 FADH2
2 ATP substrate level phosphorylation
+
4 ATP electron transport
+
6 ATP electron transport
+
2 ATP substrate level phosphorylation
+
18 ATP electron transport
+
4 ATP electron transport
36 ATP