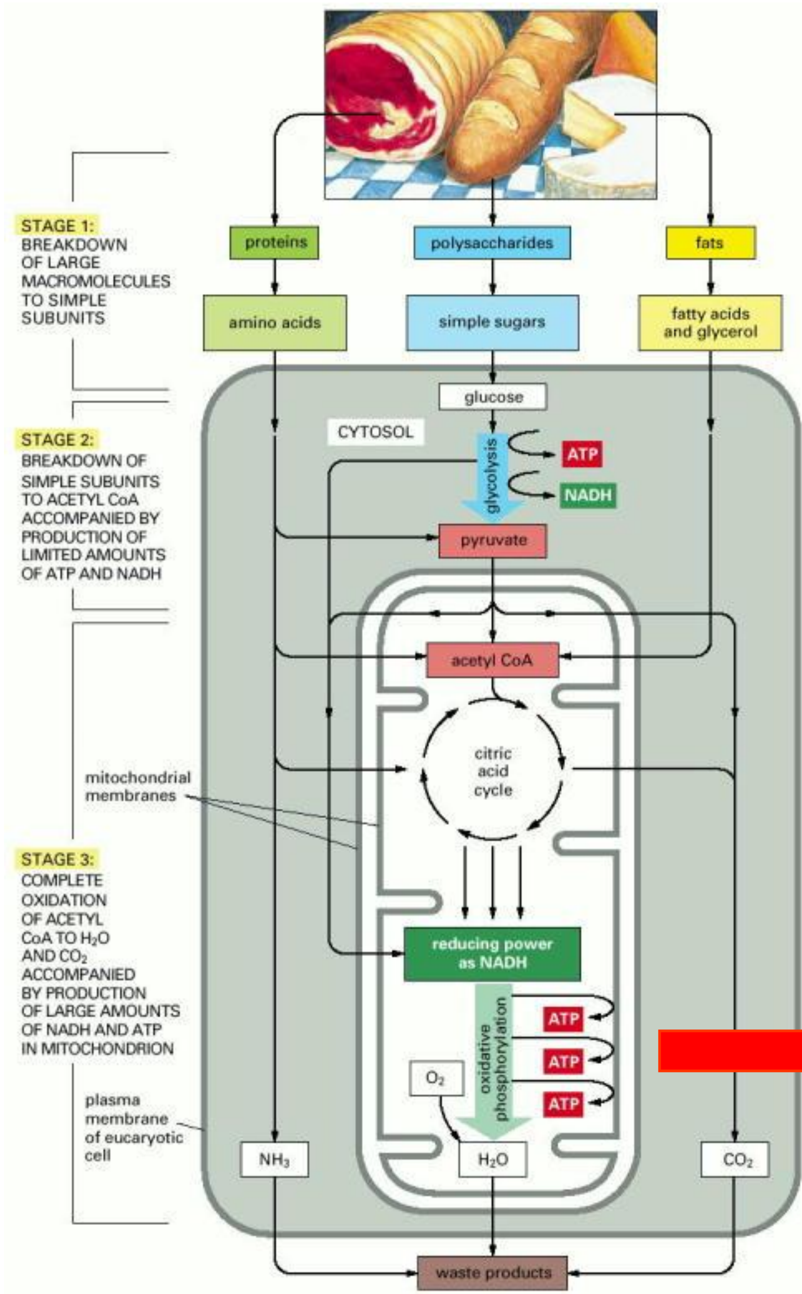
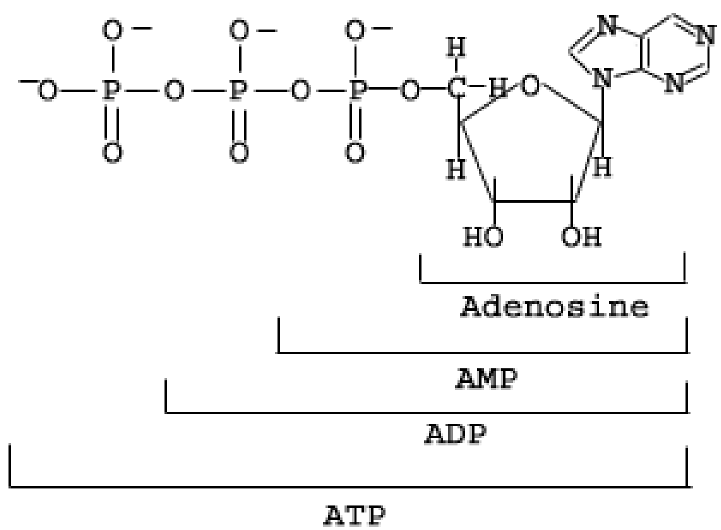
Bioenergetics, catabolism

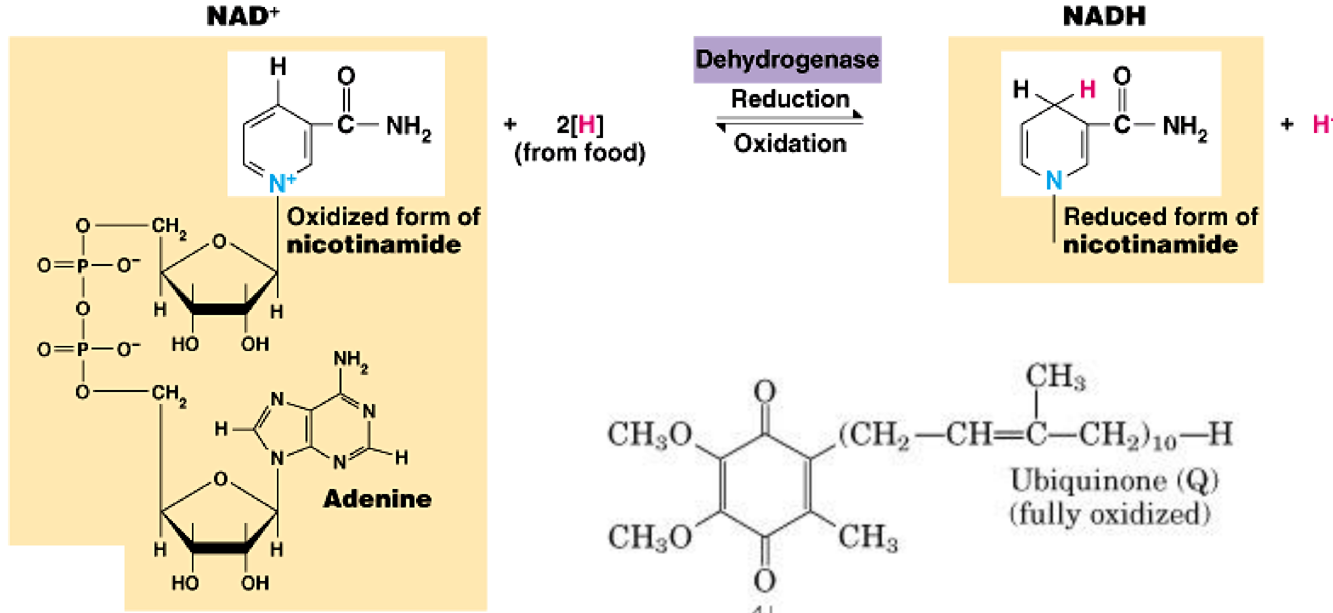


The energy currency:
ATP

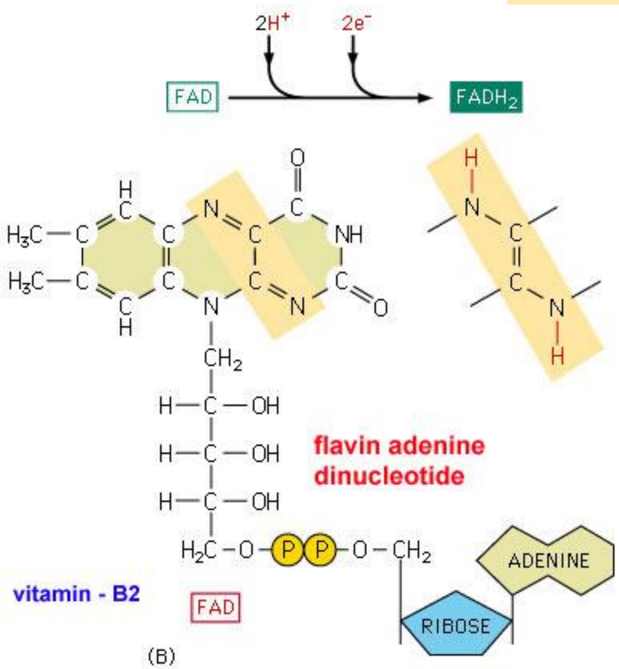


Electrontransfer, the most important electron carriers

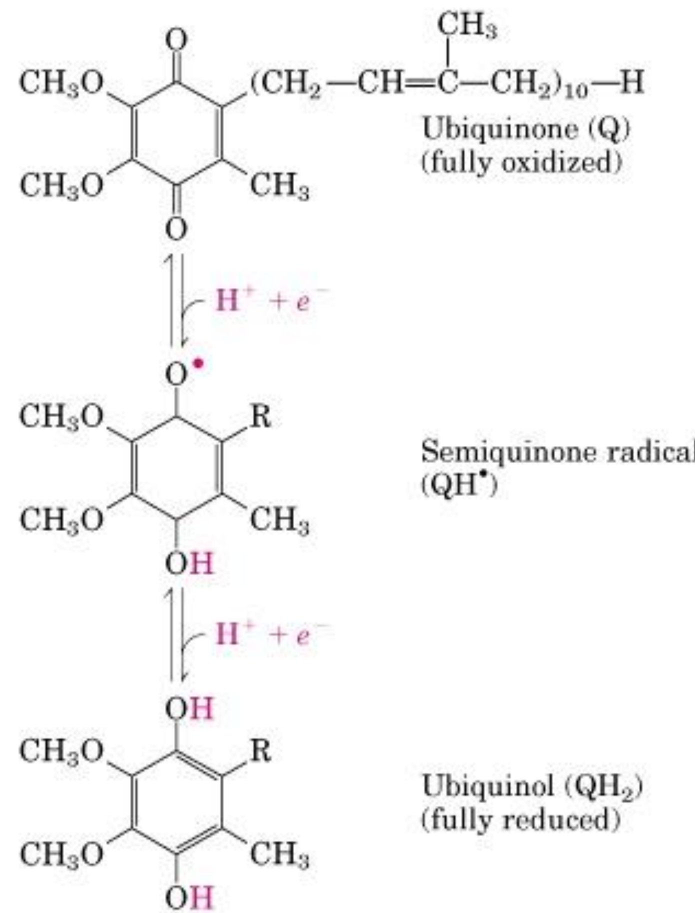
NAD: nicotinamide adenine-dinucleotide

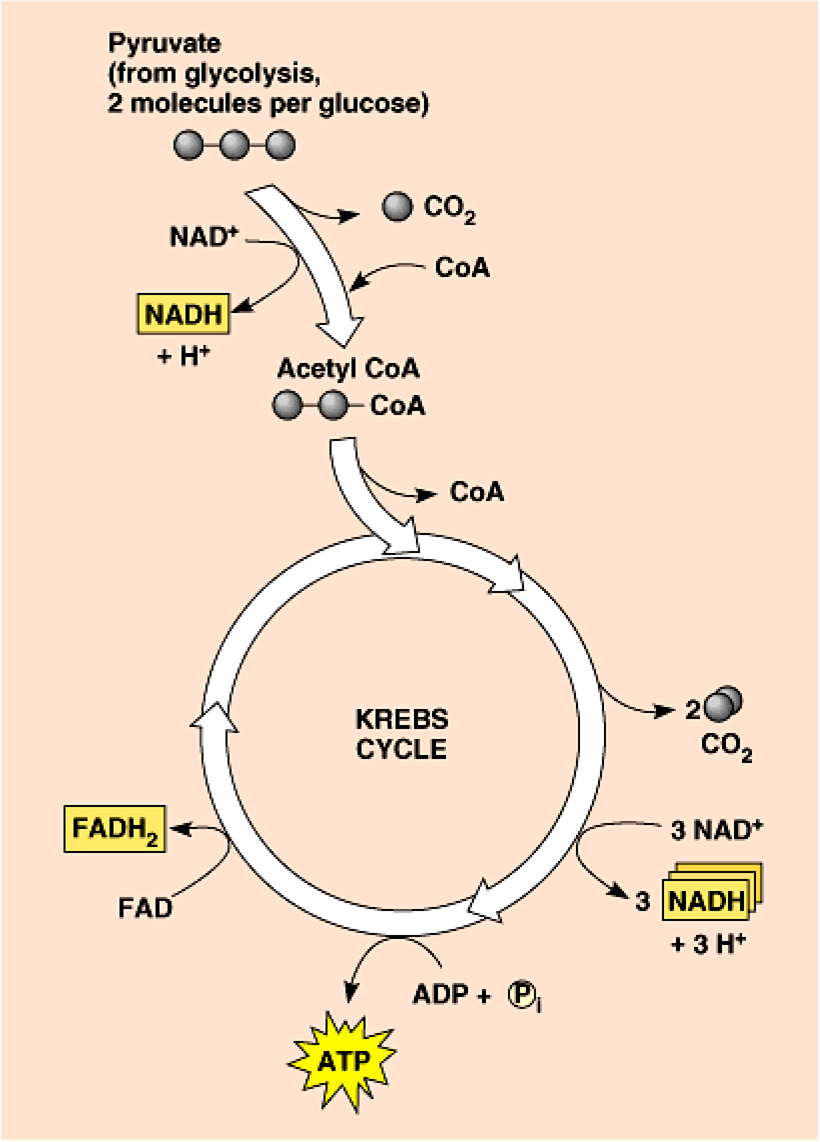


FAD: flavin adenine-dinucleotide



Ubiquinone





Pyruvate
(from glycolysis,
2 molecules per glucose)
CO_2
NAD^+
CoA
NADH
$+ H^+$
Acetyl CoA
CoA
CoA
KREBS
CYCLE
2
CO_2
$3\ NAD^+$
3 NADH
$+ 3\ H^+$
$FADH_2$
FAD
ADP + Ⓟi
ATP

Terminal oxydation, oxidative phosphorylation

Location: inner mitochondrial membrane

Terminal oxidation:

The oxydation of co-factor bonded hydrogen (NADH, $FADH_2$) to water.

$$\frac{1}{2} O_2 + 2H^+ + 2e^- \longrightarrow H_2O$$

$\frac{1}{2} O_2 / H_2O$ $\quad$ $E_0 = +0,82$ V

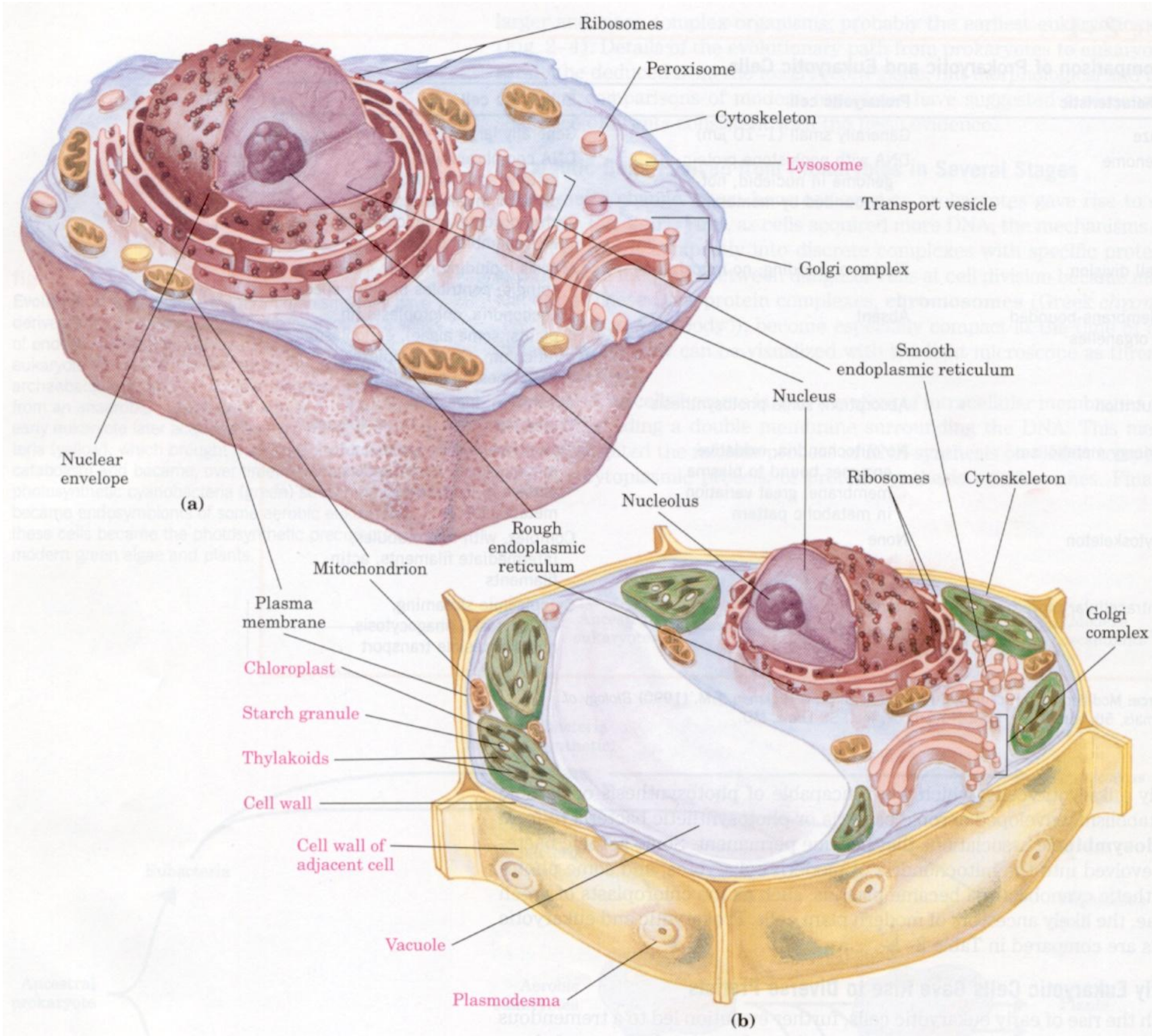
$NADH + H^+ / NAD^+$ $\quad$ $E_0 = -0,32$ V

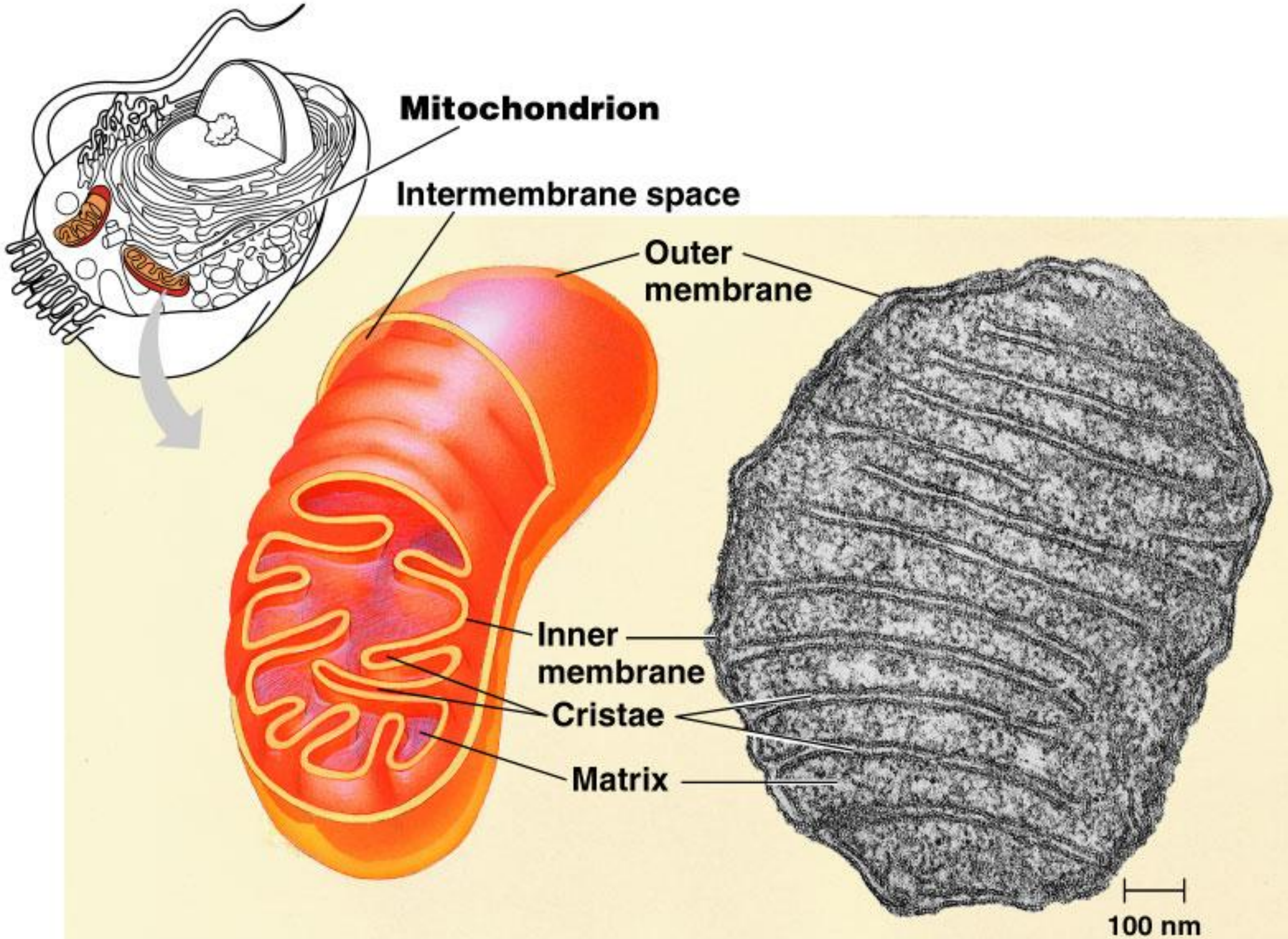
$$\Delta E_o = 1,14 \text{ V} \quad \Delta G^0 = -220 \text{ kJ/mol}$$

Oxydative phosphorylation: The phosphorylation of ADP to ATP

The terminal oxidation and the oxydative phosphorylation are coupled processes.

eukaryotic cells




Mitochondrion
Intermembrane space
Outer membrane
Inner membrane
Cristae
Matrix
100 nm

The structure of mitochondron

Length: 2 μm, diameter: 0,5 μm

Origin: the symbiosys of aerobic bacteria and an ancient eukarytotic cell

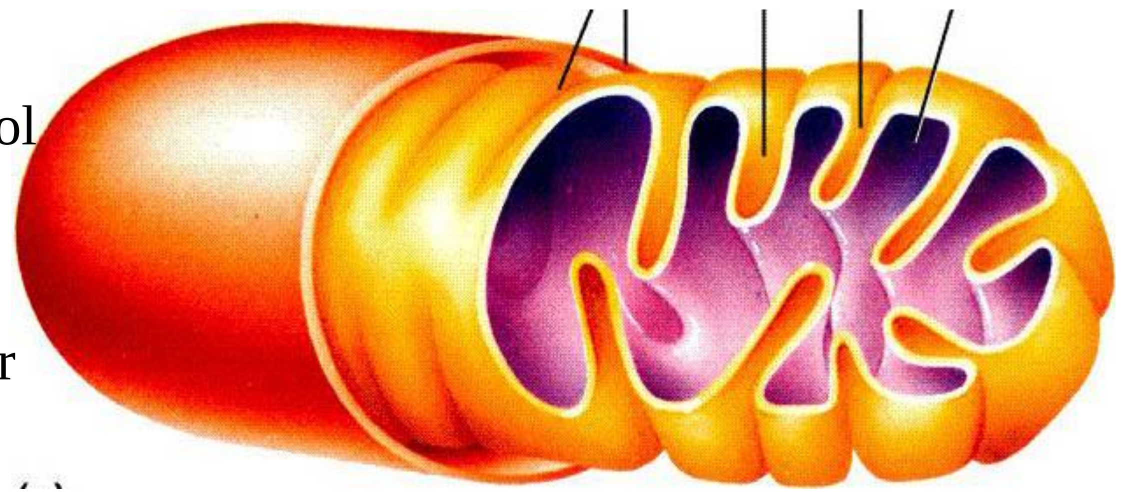
The number of mitochondria differs in different cell types (e.g.: hepatocyte: 800-2500 /cell, red blood cell: 0)

Structure: double membrane

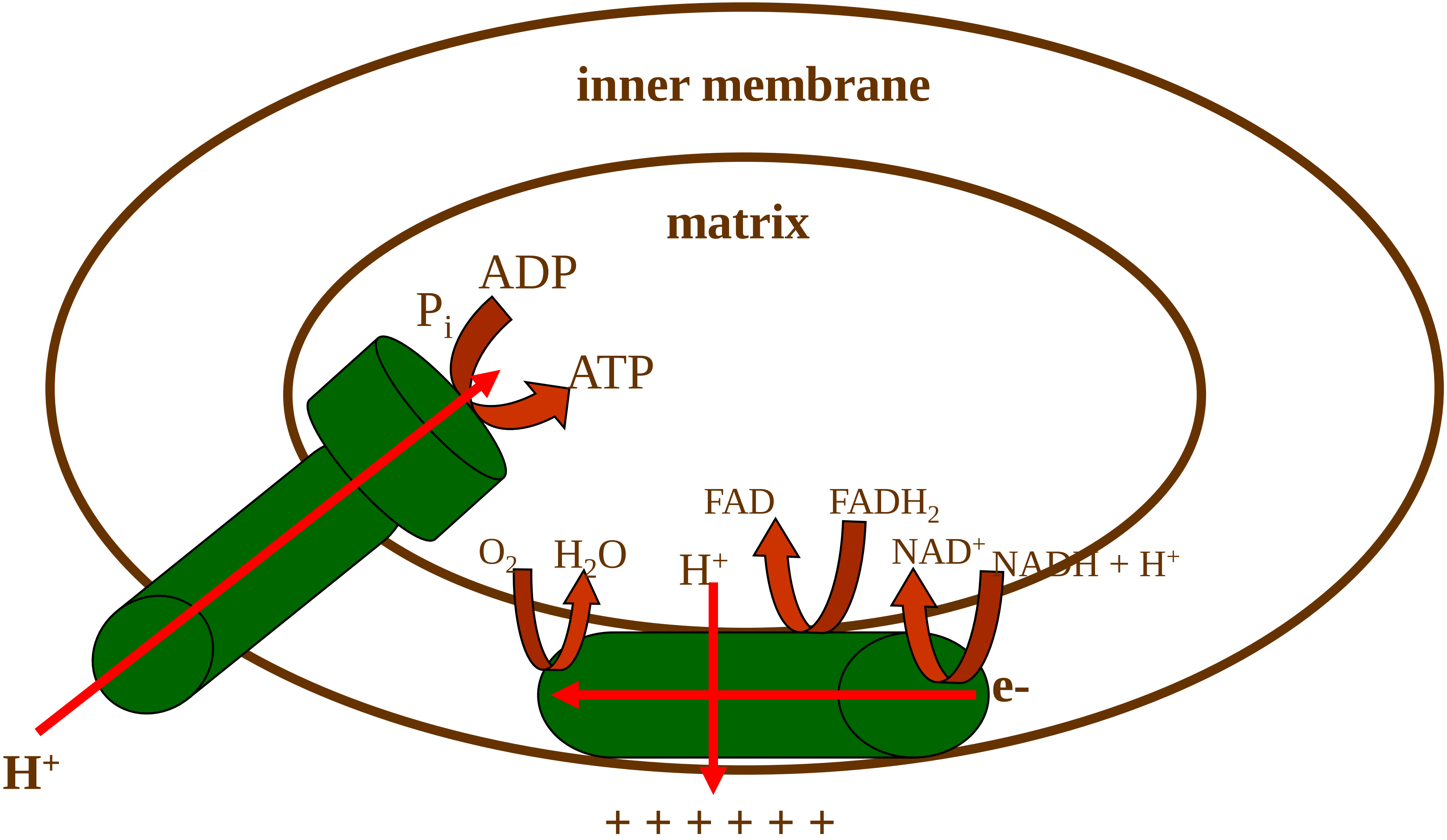
-outer membrane: approx.: 50 % lipid, 50% protein, porin channels: permeable for the intermediers of central metabolism

-inner membrane: 75% protein, non-permeable fol almost all ions

The link between the mitochondrial matrix and cytosol is maintained by the transport systems of inner membrane



The respiratory electron transfer chain and the ATP synthase are loceted here too.



$$O_2 + 4e^- + 4H^+ \longrightarrow H_2O$$

The components of mitochondrial respiratory electron tranfer chain, electron carrier molecules

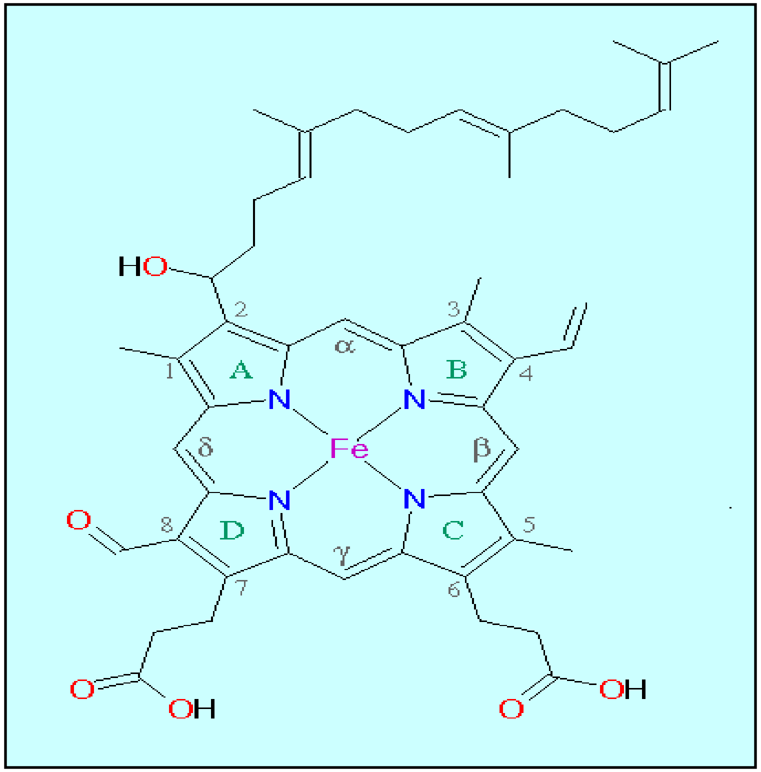
4 complexes: redox proteins with different prosthetic groups

Electron donor: NADH + H^+ , $FADH_2$

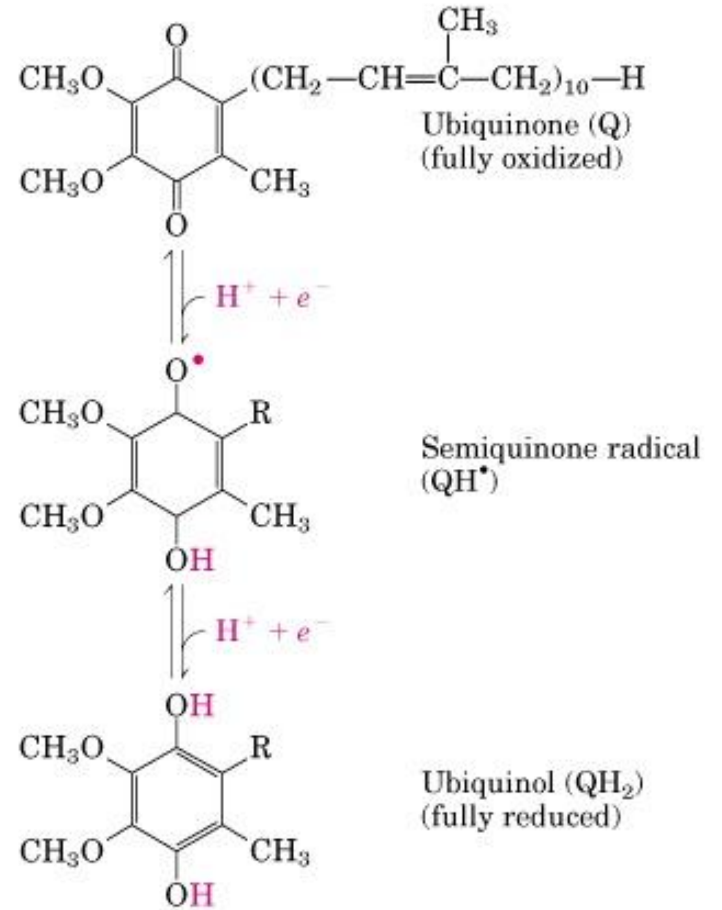
Electron acceptor: O_2

Electron carrier molecules:

1. **Cytochromes**: They contain a hem prosthetic group ($Fe^{2+} \longleftrightarrow Fe^{3+}$) They can be shared on the base of their absorption spectra: a, b, c



2. **Ubiquinone**: benzoquinone derivative, uptake/release of 1 or 2 electrons.



Prosthetic groups with electron carrier function in the respiratory electron transfer chain:

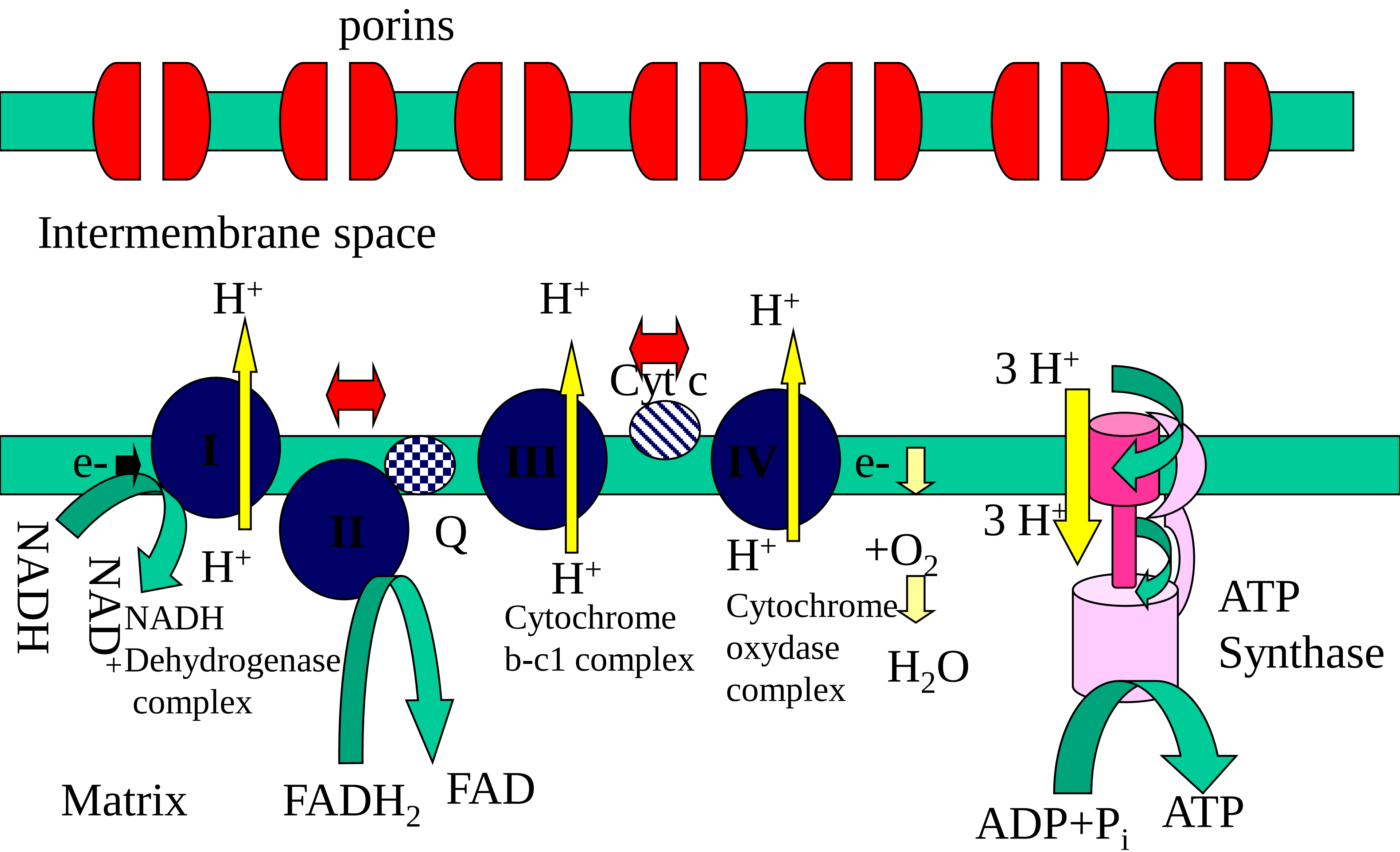
FeS: iron-sulfur complexes. They have non-hem iron: $Fe^{2+} \longleftrightarrow Fe^{3+}$ inorganic S, or Cys S connection.

Copper containing proteins: $Cu^{+} \longleftrightarrow Cu^{2+}$

Redox couple	redox potential (V)
$NAD^+/NADH + H^+$	-0,32
$FAD/FADH_2$	-0,21
Ubiquinone/ubiquinol	+0,045
Cytochrome$_b$ Fe^{3+}/Fe^{2+}	+0,08
Cytochrome $_c$ Fe^{3+}/Fe^{2+}	+0,22
Cytochrome $_a$ Fe^{3+}/Fe^{2+}	+0,29
½ O_2/H_2O	+0,82

direction of electron flow

ATP synthesizing machinery in the mitochondria



Complex I: NADH-UQ-oxidoreductase (NADH-dehydrogenase)

A hugh protein complex with 25 subunits. The NADH binding pocket faces to the matrix. Electrons from complex I flow to ubiquinon It has proton pump activity.

Complex II: succinate-UQ-oxidoreductase

It has a FAD prosthetic group. Succinate dehydrogenase (TCA cycle) is a member of complex II. Electrons from complex II flow to ubiquinon. It has no proton pump activity.

$$\Delta E_{NAD^+/NADH + H^+ : UQ/UQH_2} \quad > \quad \Delta E_{FAD/FADH_2 : UQ/UQH_2}$$

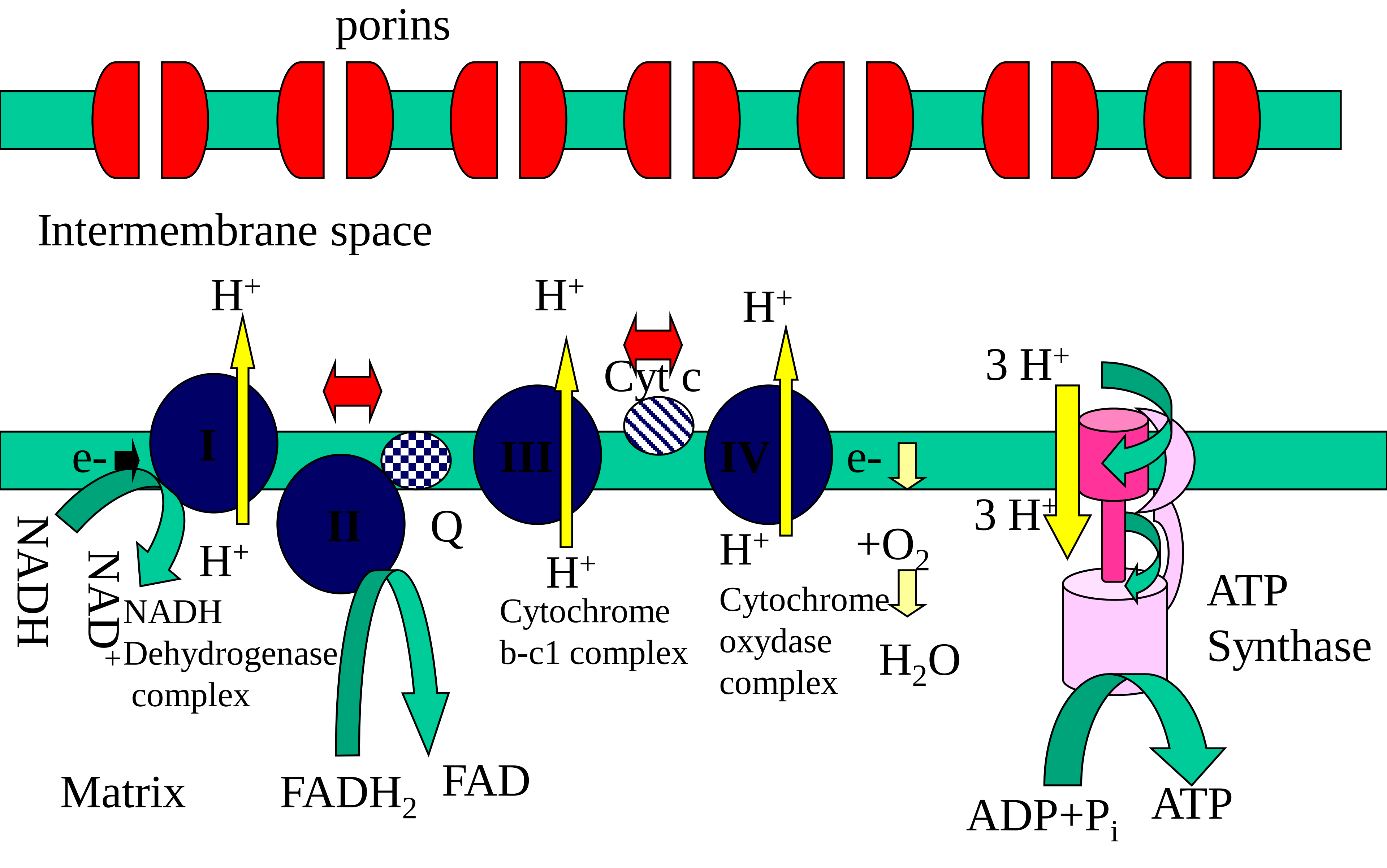
A the difference in redox potential in the FAD/FADH$_2$: UQ/UQH$_2$ redox couples is too low to ride the proton pump.

Glycerol-phosphate dehydrogenase

Acyl-CoA dehydrogenase

Other sources of electrons to reduce ubiquinone

ATP synthesizing machinery in the mitochondria



Complex III: UQH_2-cytochrome c-oxidoreductase

Electrons from complex III flow to cytochrome c.

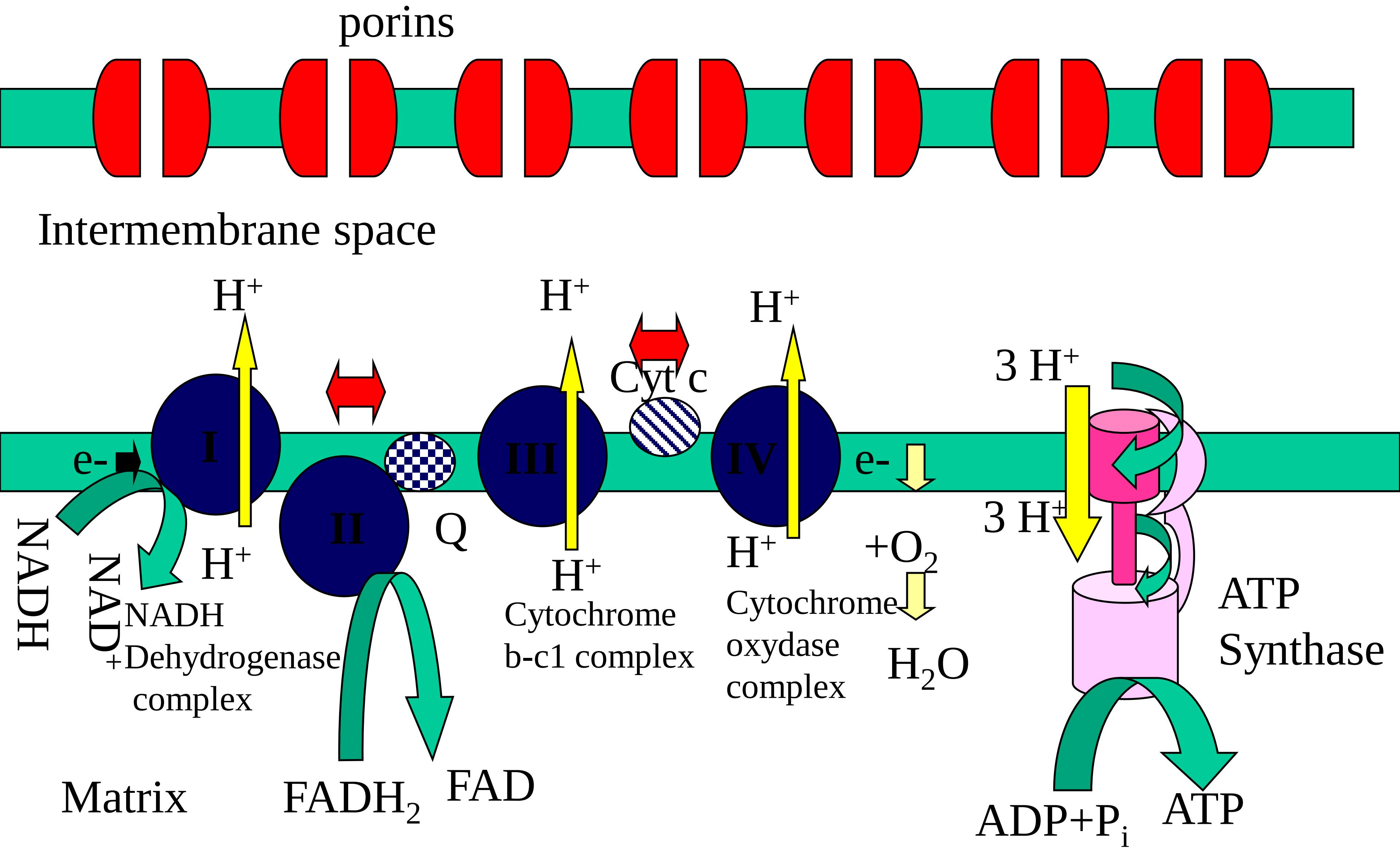
It has proton pump activity.

Complex IV: cytochrome c oxidase

O_2 is reduced to water by this complex.

It has proton pump activity.

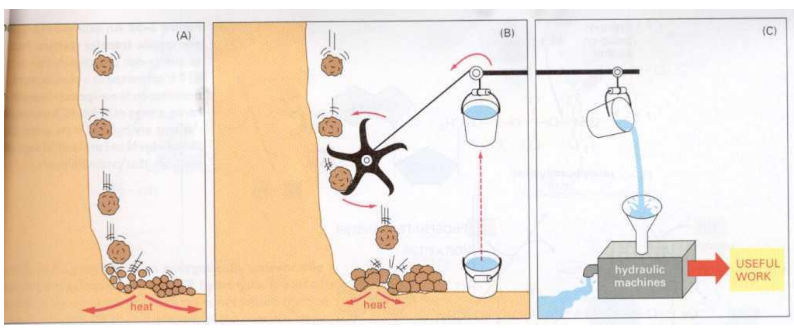
ATP synthesizing machinery in the mitochondria



Terminal oxidation (subsequent electron transfers) – exergonic

oxidative phosphorylation
(ADP + P_i $\longrightarrow$ ATP) – endergonic

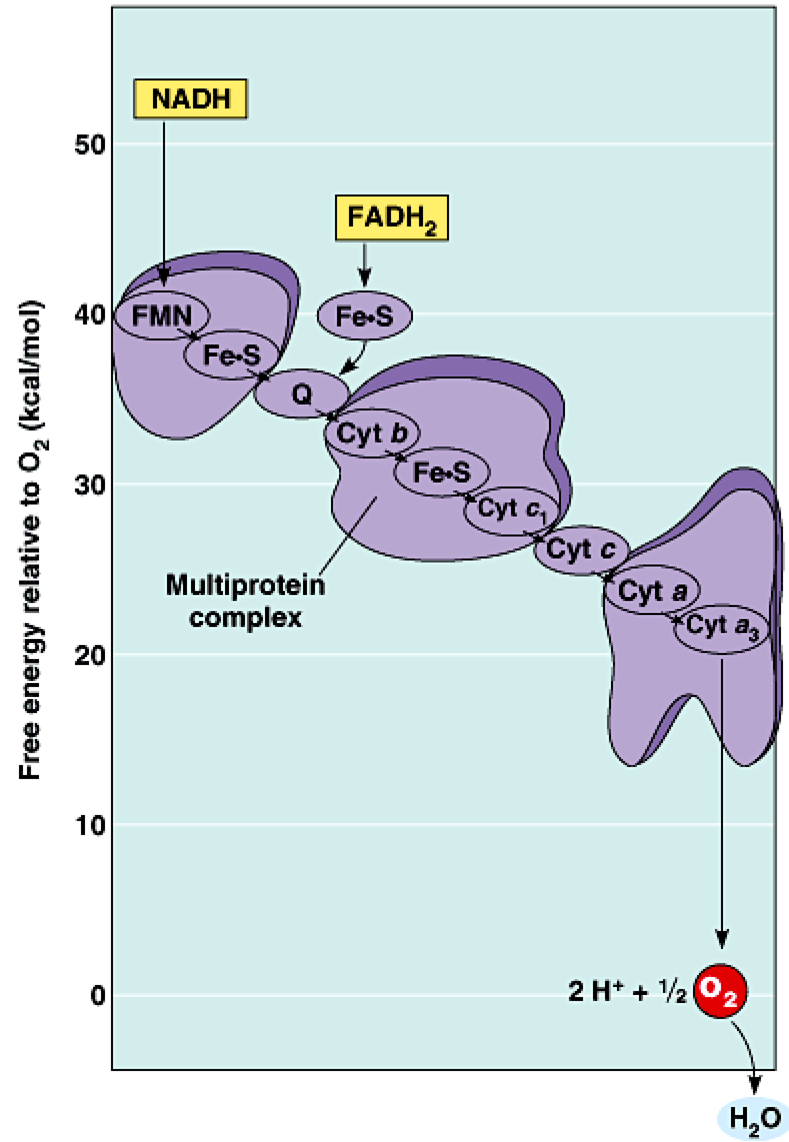
Coupled reactions



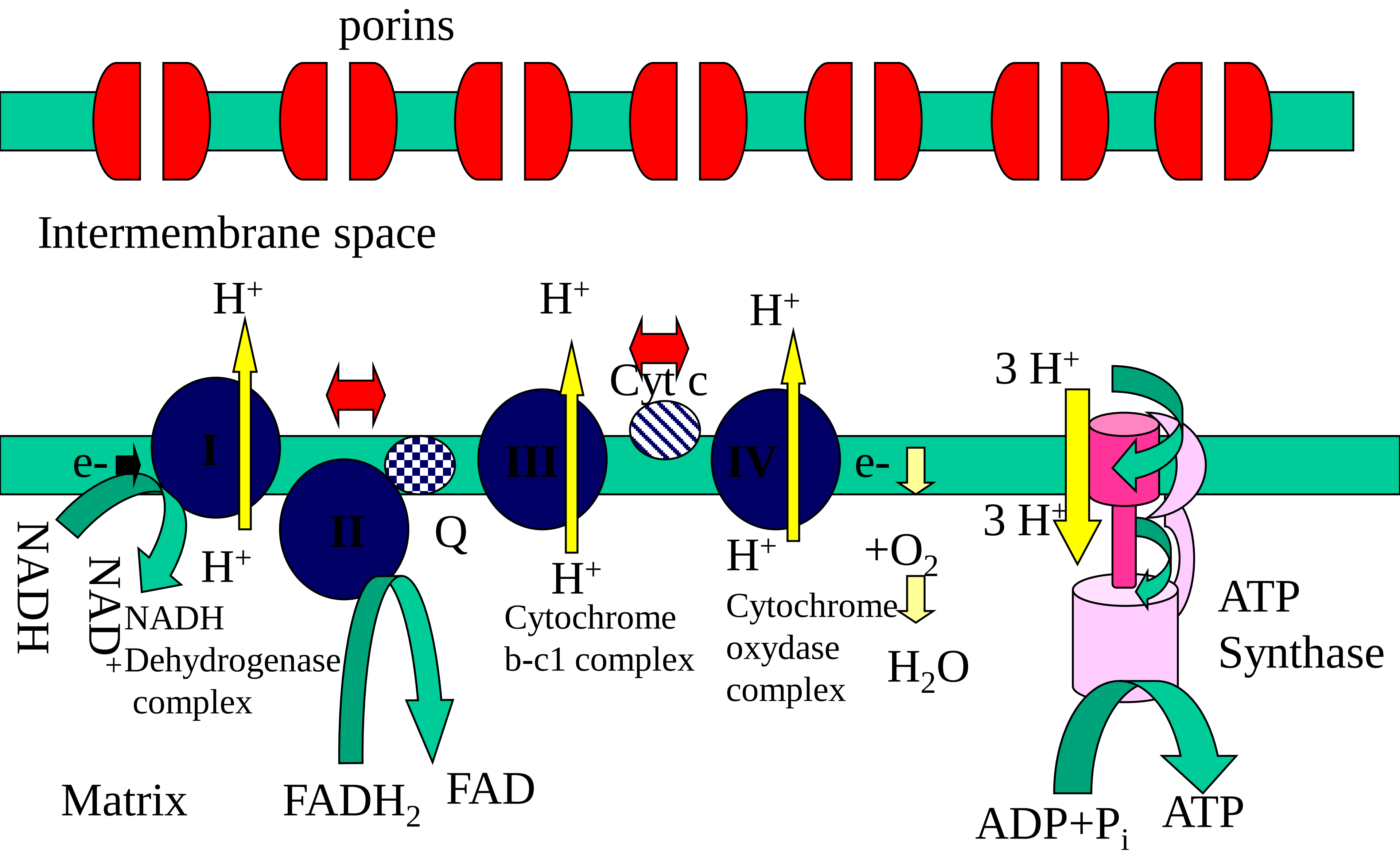
P/O ratio

in case of NADH: 3

in case of $FADH_2$: 2



ATP synthesizing machinery in the mitochondria



ATP syntase

Consist of 2 units: F_1 and F_o

F_1: responsible for the phosphorylation of ADP, F_o: proton channel

Uncoupling agents (e.g.: 2,4-dinitrophenol), uncouple of the terminal oxidation and oxidative phosphorylation

acceptor control

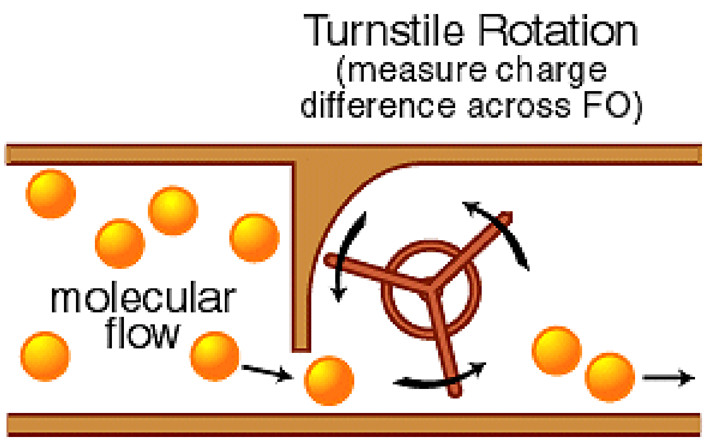
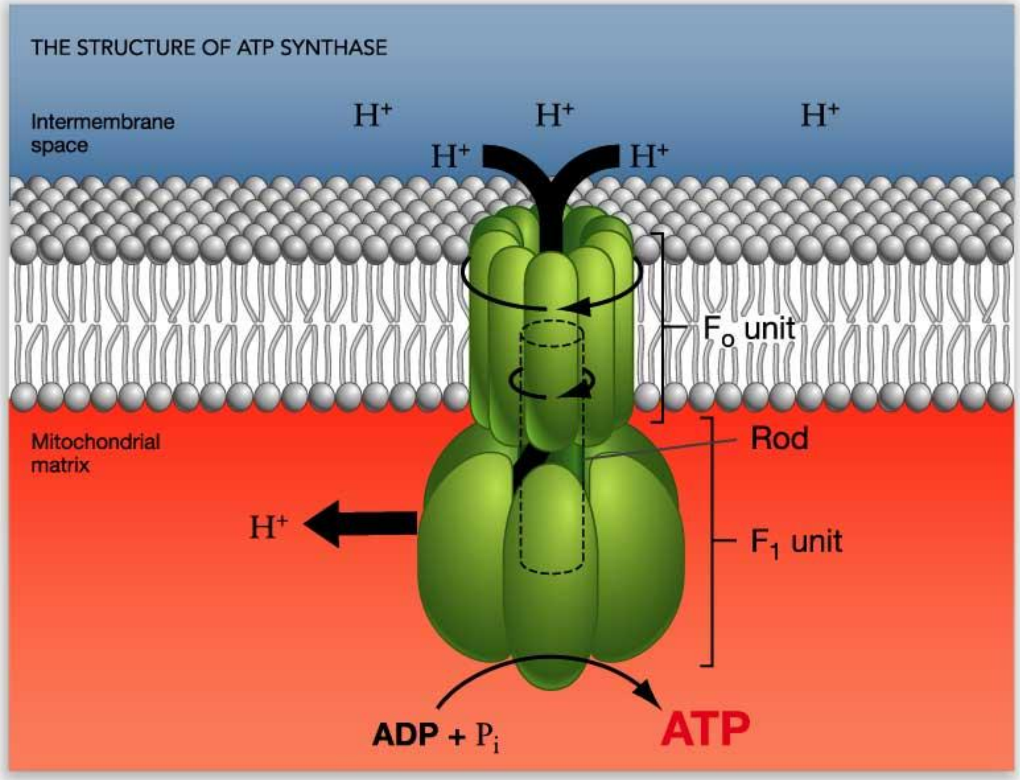


Fig. 4 A nanoscale flow meter based on an ATP synthase enzyme.

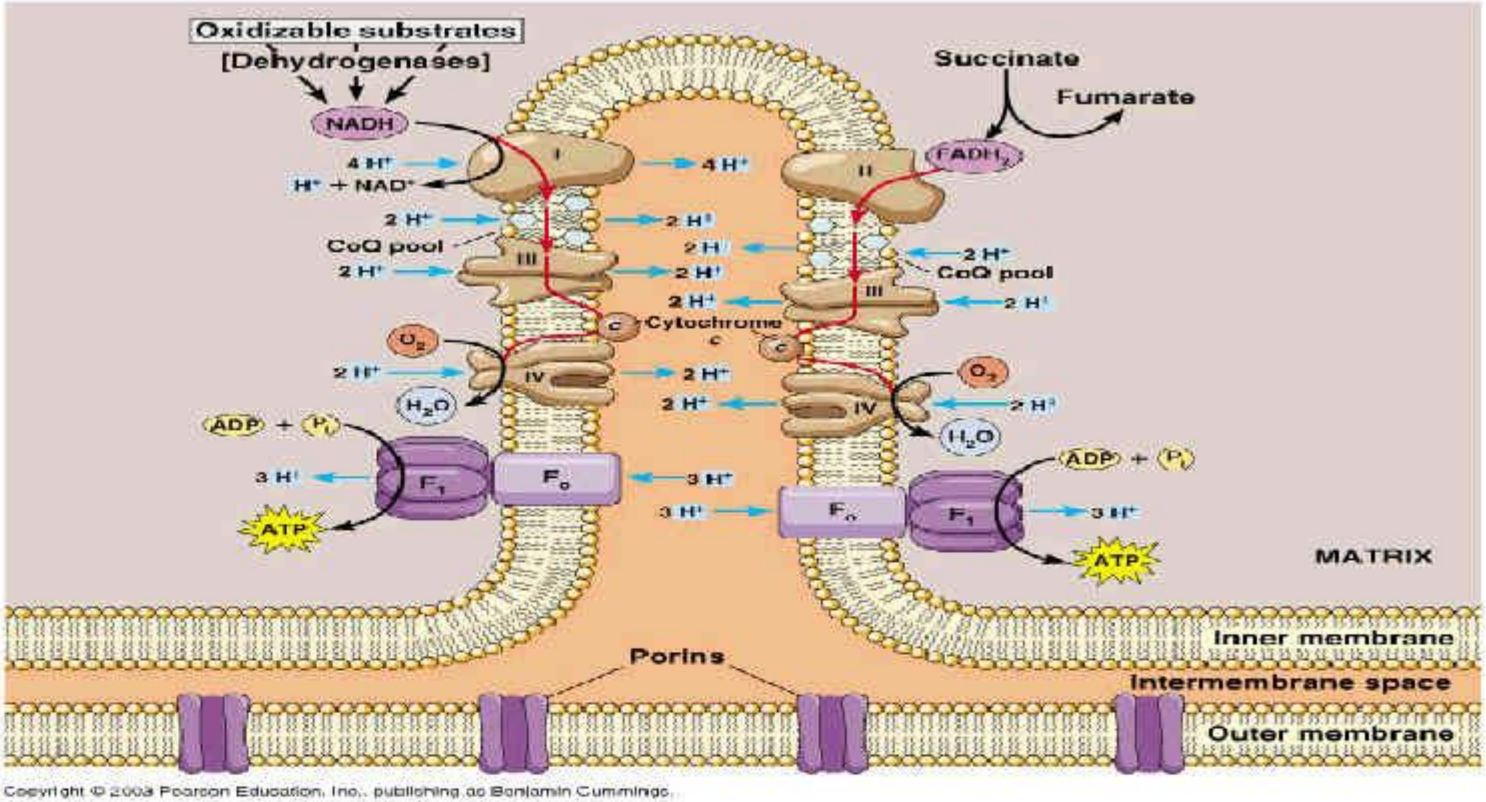


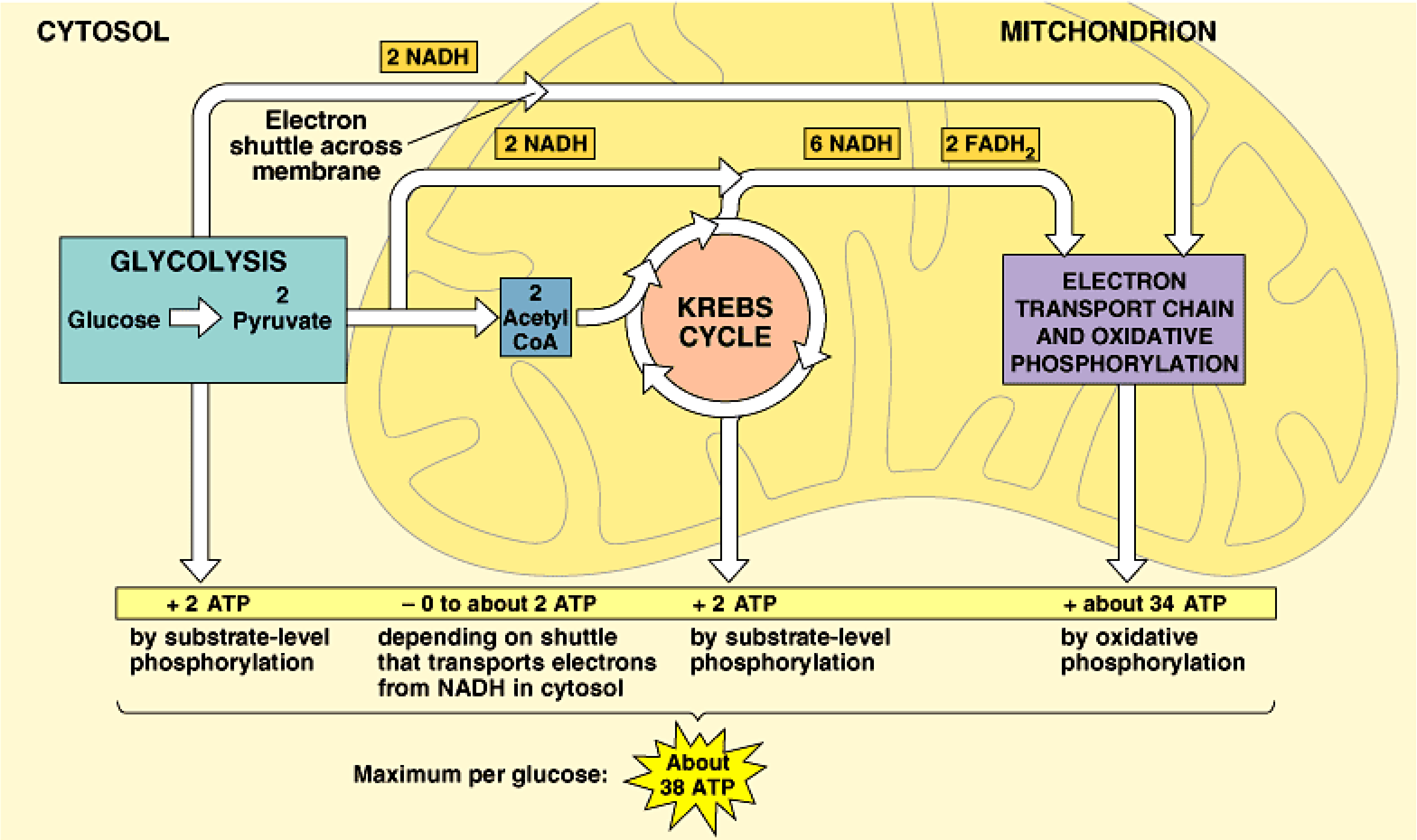
Mitchell's chemiosmotic theory

Membrane potential

proton motor force:

Delta in H^+ ion concentration




CYTOSOL
MITCHONDRION
2 NADH
Electron shuttle across membrane
2 NADH
6 NADH
2 $FADH_2$
GLYCOLYSIS
Glucose
2 Pyruvate
2 Acetyl CoA
KREBS CYCLE
ELECTRON TRANSPORT CHAIN AND OXIDATIVE PHOSPHORYLATION
+ 2 ATP
by substrate-level phosphorylation
– 0 to about 2 ATP
depending on shuttle that transports electrons from NADH in cytosol
+ 2 ATP
by substrate-level phosphorylation
+ about 34 ATP
by oxidative phosphorylation
Maximum per glucose:
About 38 ATP