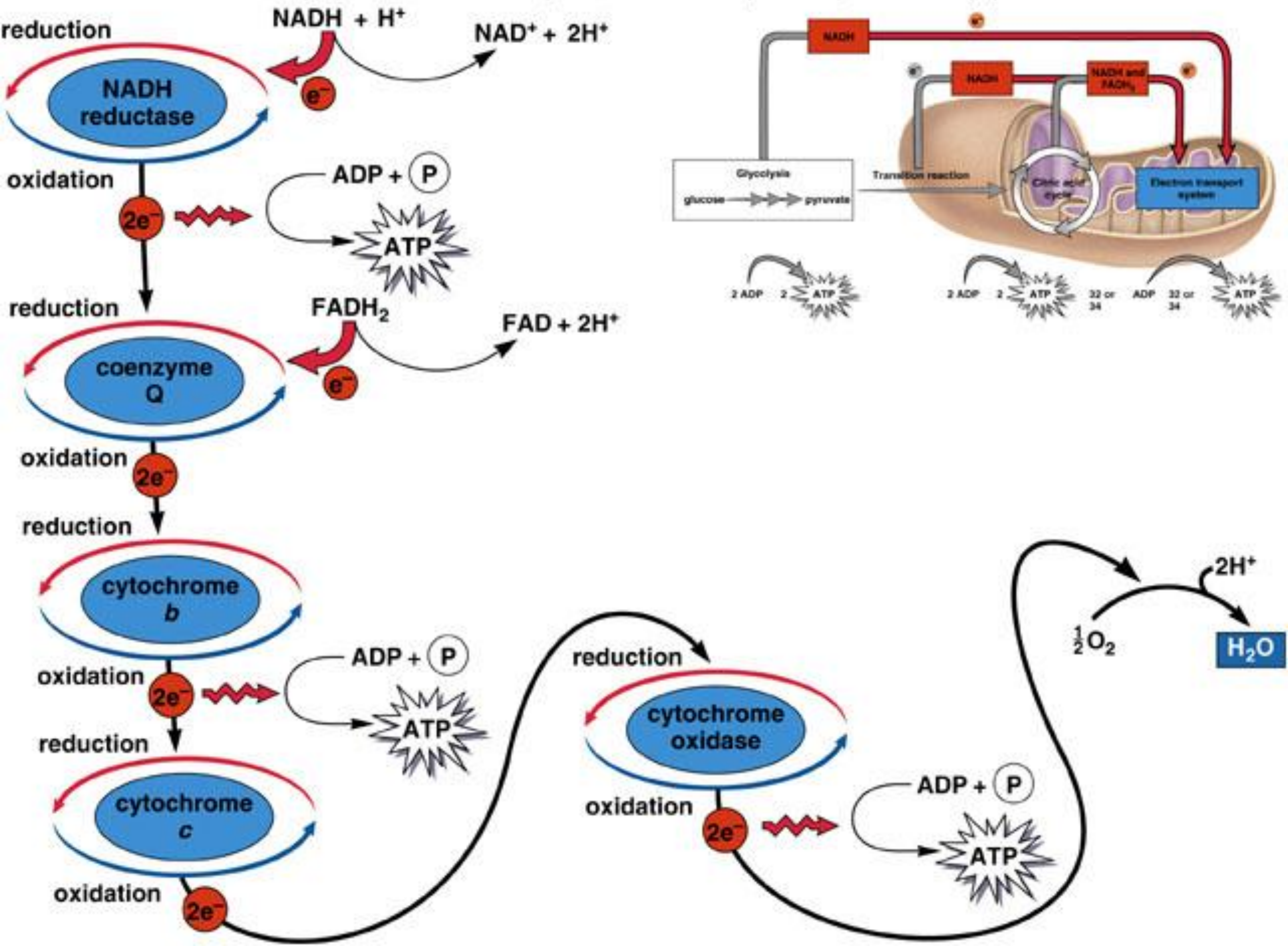
Electron Transport

Dr.Sulieman Al-Khalil



NADH + H^+
NAD^+ + $2H^+$
reduction
NADH reductase
oxidation
e^-
$2e^-$
ADP + P
ATP
reduction
$FADH_2$
FAD + $2H^+$
coenzyme Q
oxidation
$2e^-$
reduction
cytochrome *b*
oxidation
$2e^-$
ADP + P
ATP
reduction
cytochrome *c*
oxidation
$2e^-$
reduction
cytochrome oxidase
oxidation
$2e^-$
ADP + P
ATP
$\frac{1}{2}O_2$
$2H^+$
H_2O
NADH
NADH
NADH and $FADH_2$
Glycolysis
glucose
pyruvate
Transition reaction
Citric acid cycle
Electron transport system
2 ADP
2 ATP
2 ADP
2 ATP
32 or 34 ADP
32 or 34 ATP

1. **Electrons transferred from sugars in glycolysis and the citric acid cycle are further transported between acceptor molecules, ultimately reducing O_2 to H_2O.**

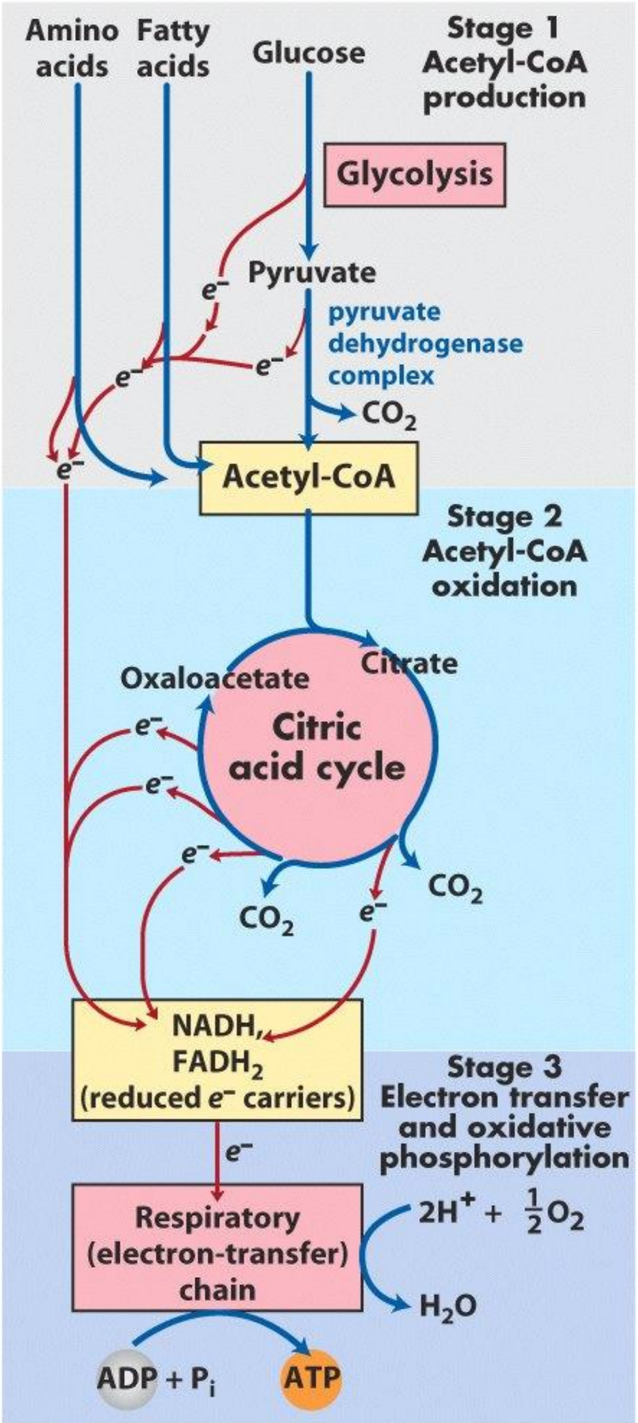
2. **These electron transfers are coupled to the production of a proton gradient across the inner mitochondrial membrane. This proton gradient will be used to generate ATP.**

Important Anaplerotic (Replenishing) Reactions

TABLE 16–2 Anaplerotic Reactions

Reaction	*Tissue(s)/organism(s)*
Pyruvate + HCO_3^- + ATP $\xrightleftharpoons{\text{pyruvate carboxylase}}$ oxaloacetate + ADP + P_i	Liver, kidney
Phosphoenolpyruvate + CO_2 + GDP $\xrightleftharpoons{\text{PEP carboxykinase}}$ oxaloacetate + GTP	Heart, skeletal muscle
Phosphoenolpyruvate + HCO_3^- $\xrightleftharpoons{\text{PEP carboxylase}}$ oxaloacetate + P_i	Higher plants, yeast, bacteria
Pyruvate + HCO_3^- + NAD(P)H $\xrightleftharpoons{\text{malic enzyme}}$ malate + $NAD(P)^+$	Widely distributed in eukaryotes and prokaryotes

Steps of Aerobic Metabolism



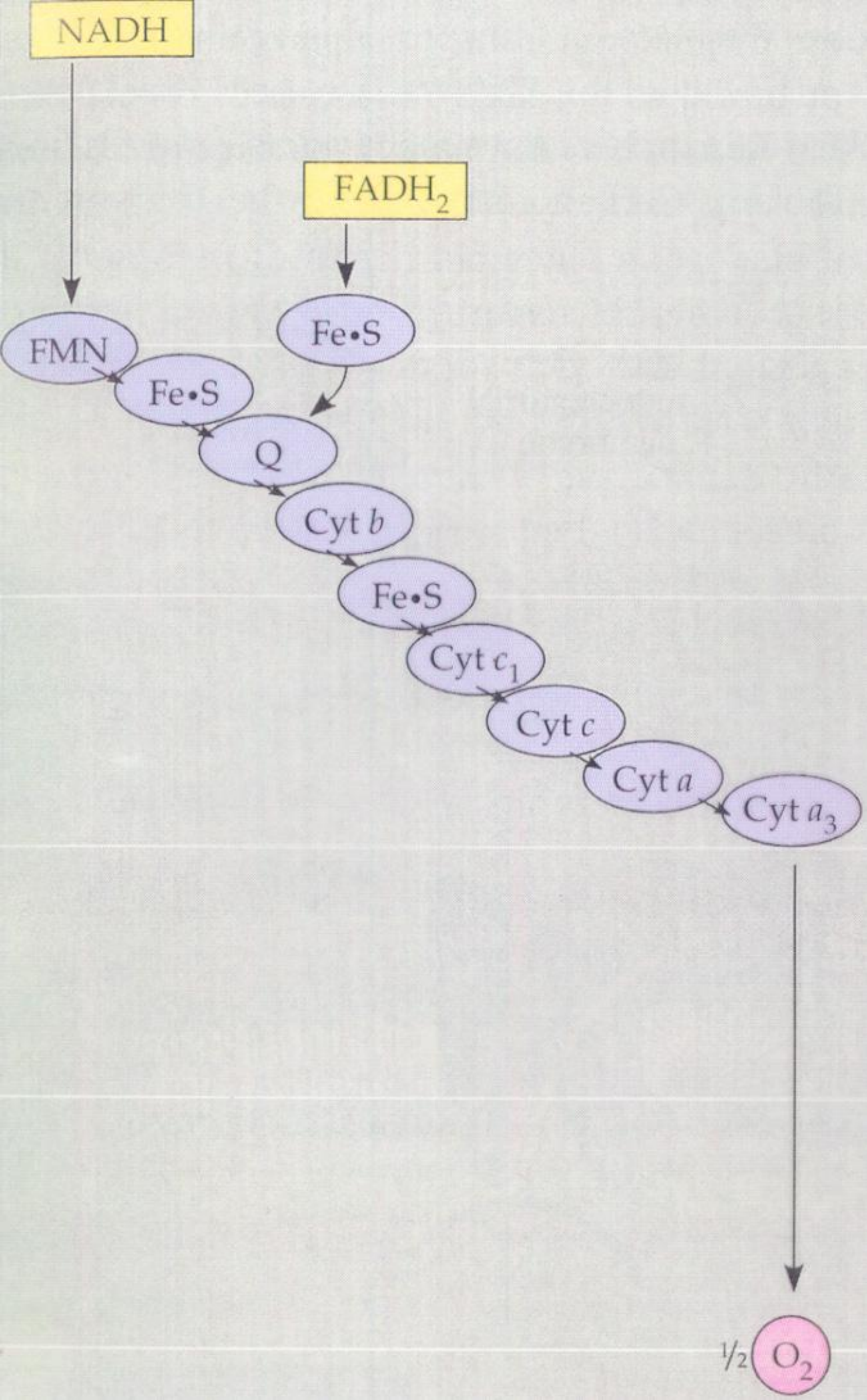
Glycolysis

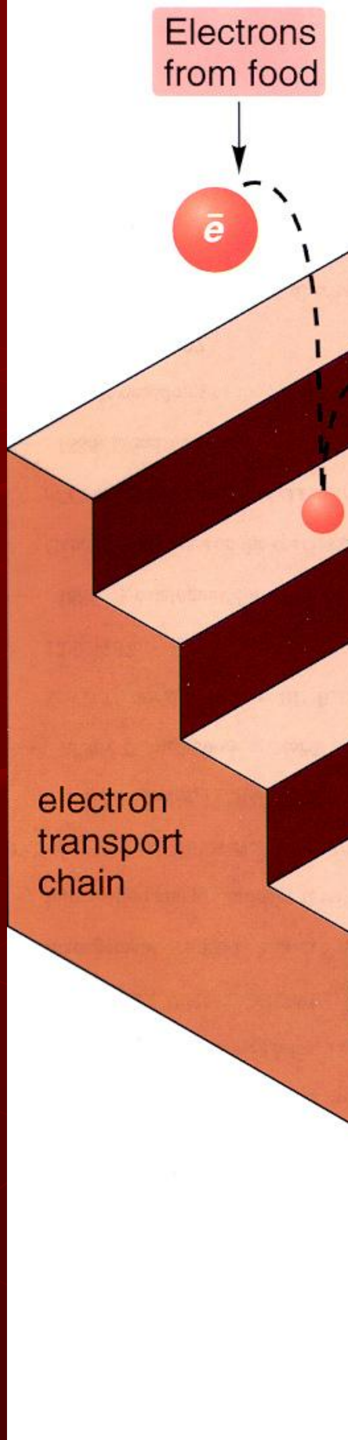
Citric Acid Cycle

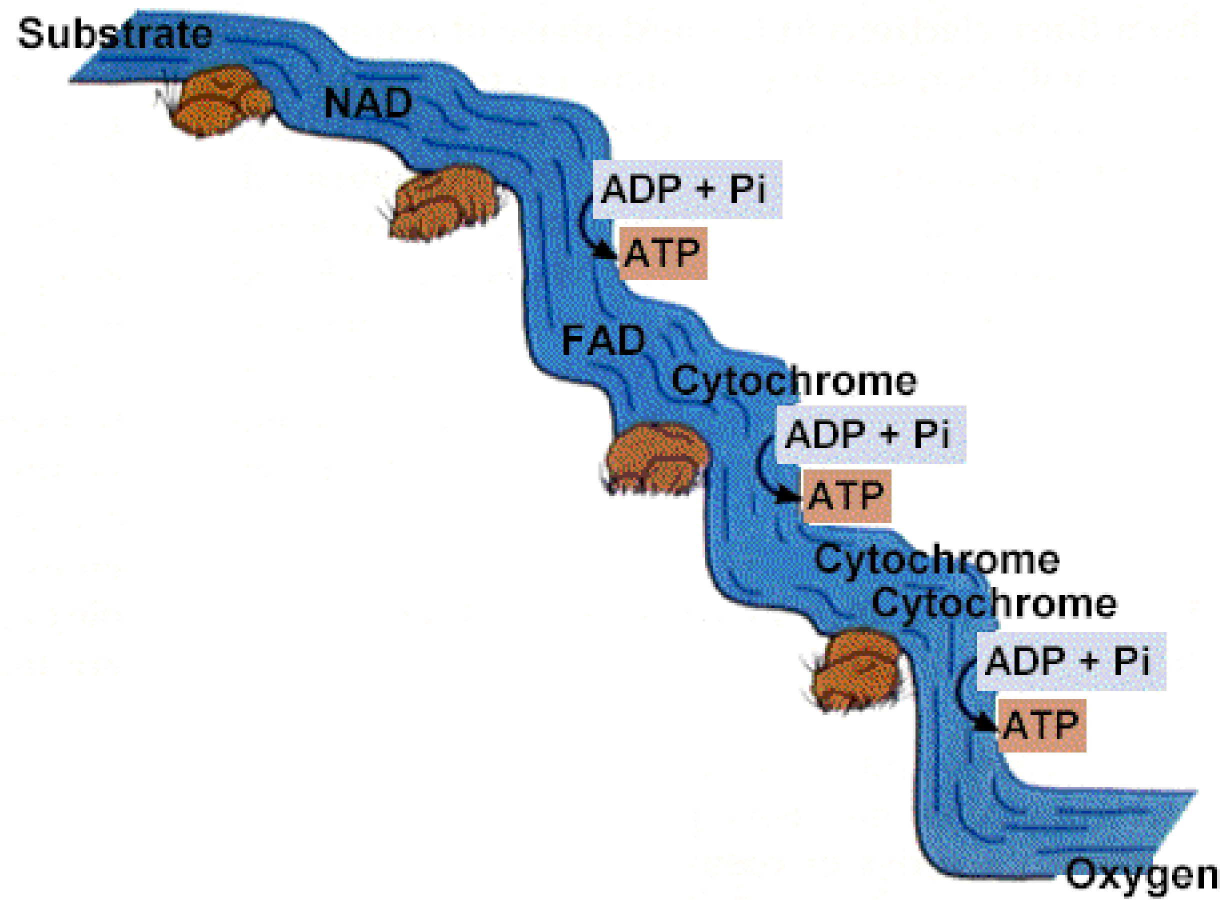
Electron transfer/ Oxidative phosphorylation

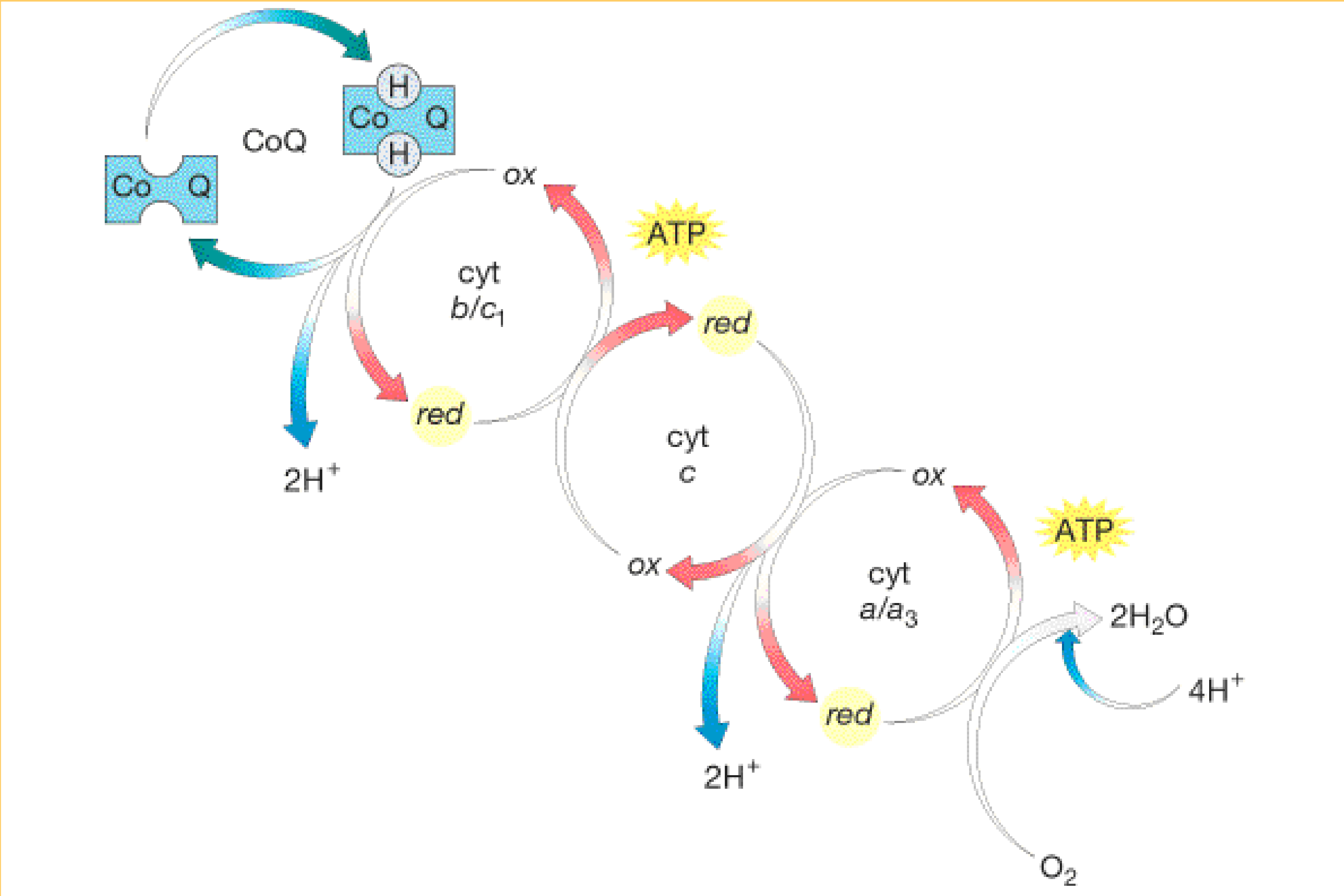
- The oxidation of pyruvate in the citric acid cycle generates five reduced electron carriers per pyruvate: four molecules of NADH and one molecule of $FADH_2$.
- These electrons ultimately are transferred to O_2 in the process of **electron transport**.
- This transport is coupled to the generation of a proton gradient across the mitochondrial membrane, and this gradient is used to synthesize ATP in the process called **oxidative phosphorylation**.

Electron Transport System



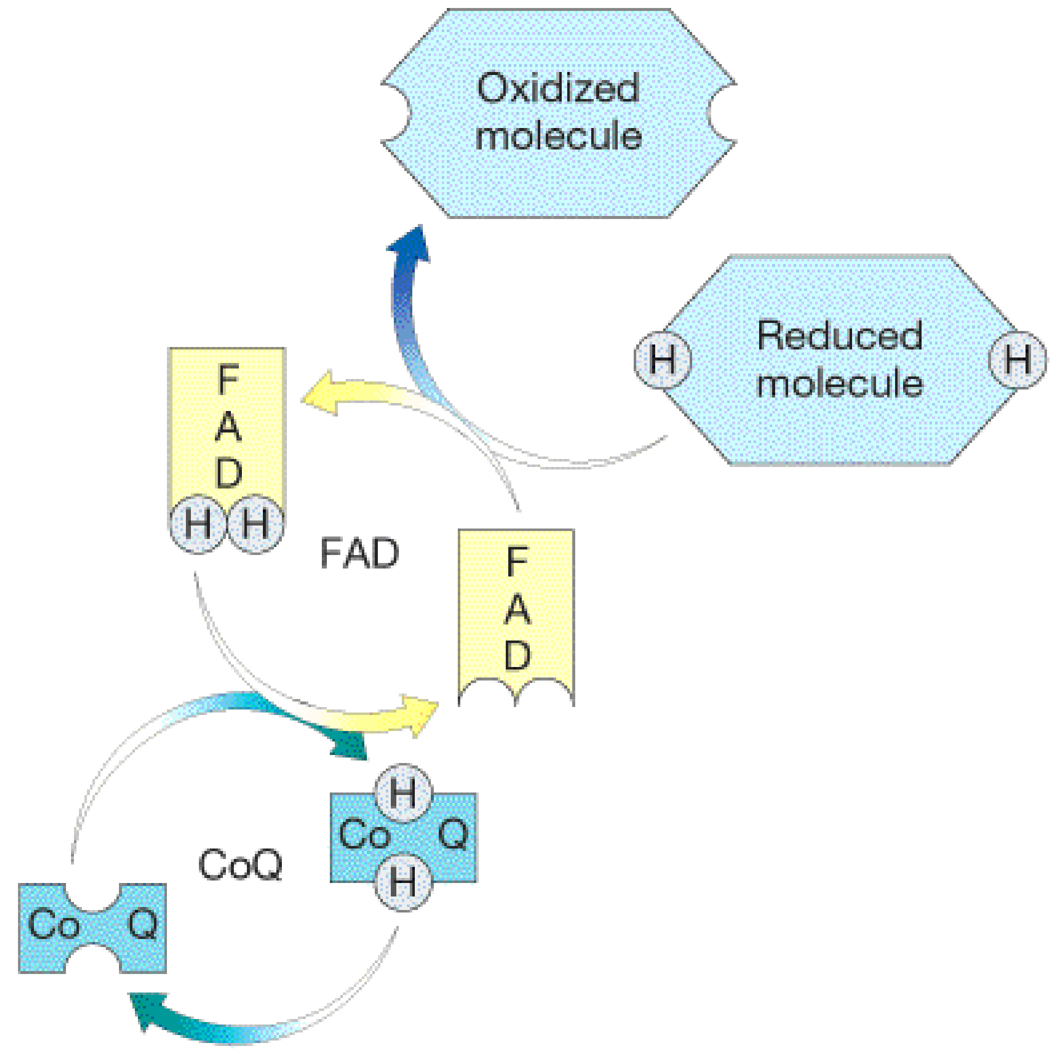


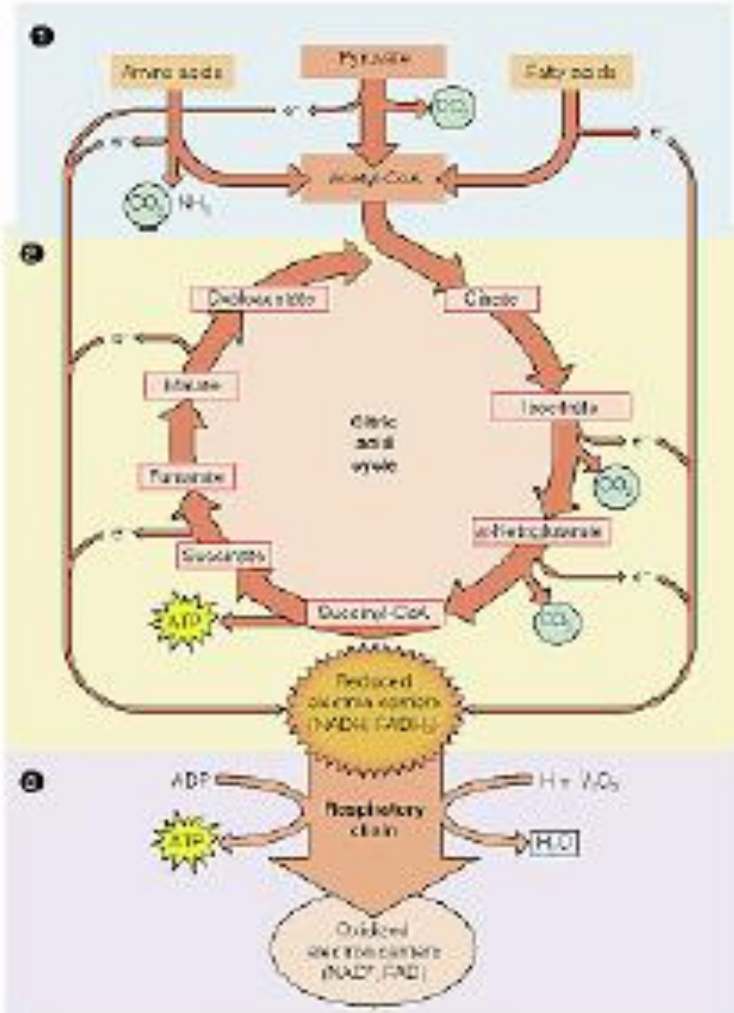

Substrate
NAD
ADP + Pi
ATP
FAD
Cytochrome
ADP + Pi
ATP
Cytochrome
Cytochrome
ADP + Pi
ATP
Oxygen



H
Co
Q
H
CoQ
Co
Q
ox
ATP
cyt
b/c1
red
red
2H+
cyt
c
ox
ox
ATP
cyt
a/a3
2H2O
4H+
red
2H+
O2

- The citric acid cycle enzymes are inside the mitochondrial matrix, so these reduced electron carriers are generated inside the mitochondria.
- In the process of electron transport, the electrons will be transferred to oxygen and protons will be exported out of the mitochondria to generate a gradient.


Oxidized molecule
Reduced molecule
H
H
F A D
H H
FAD
F A D
CoQ
Co Q
H
Co Q
H

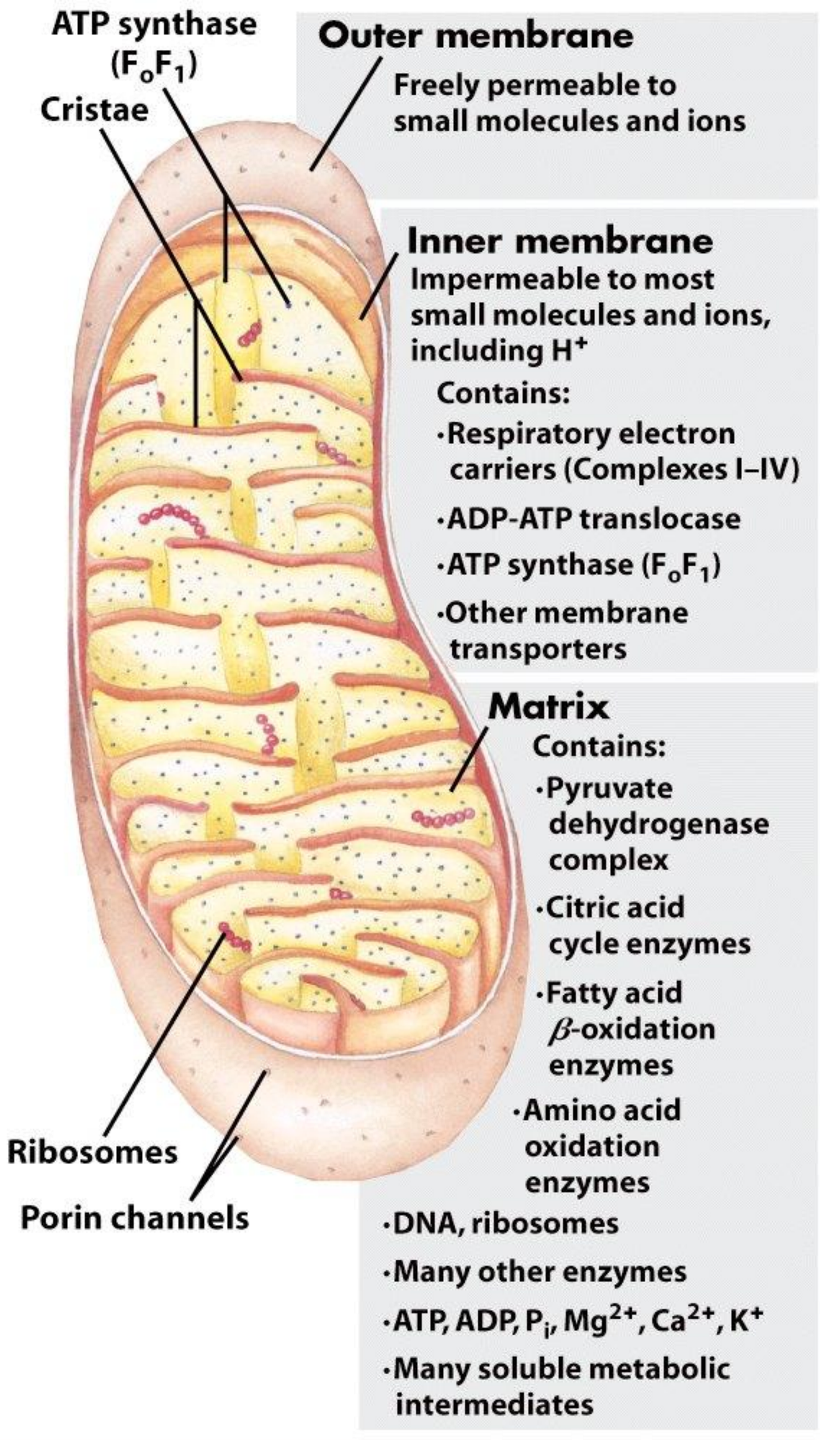


Acetyl CoA Production

Acetyl CoA Oxidation

Electron Transfer

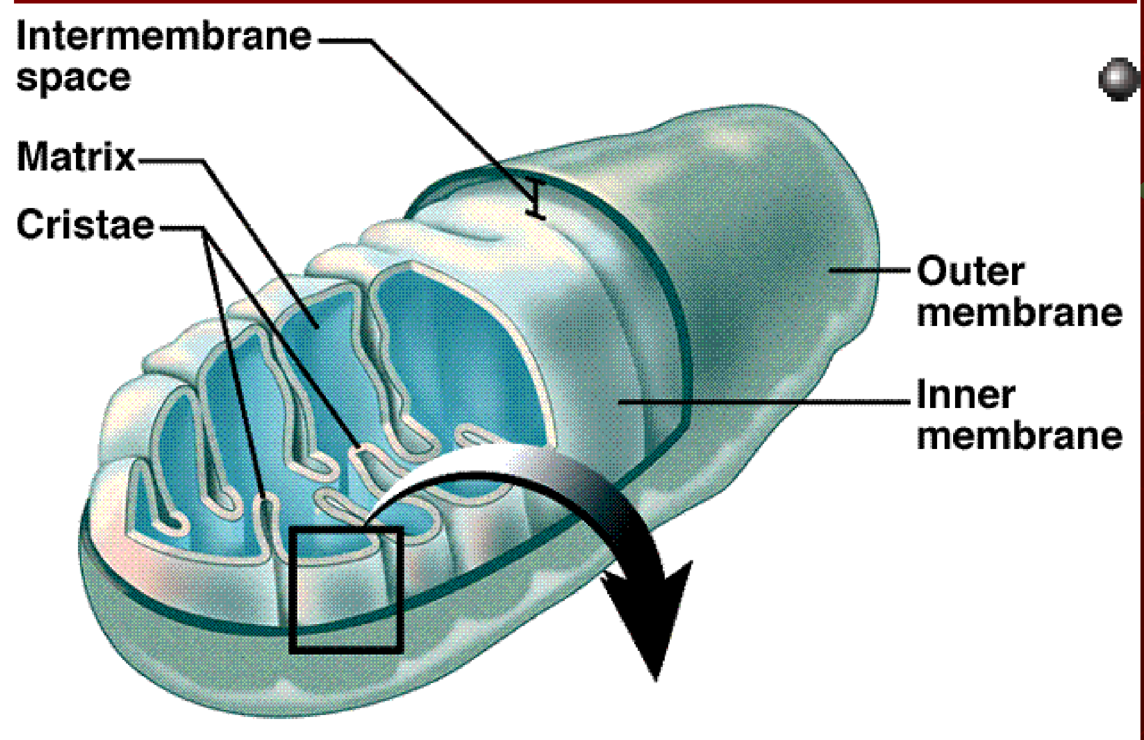
p 485 MVA



Mitochondria: The site of Cellular Respiration

Electron Transport Chain

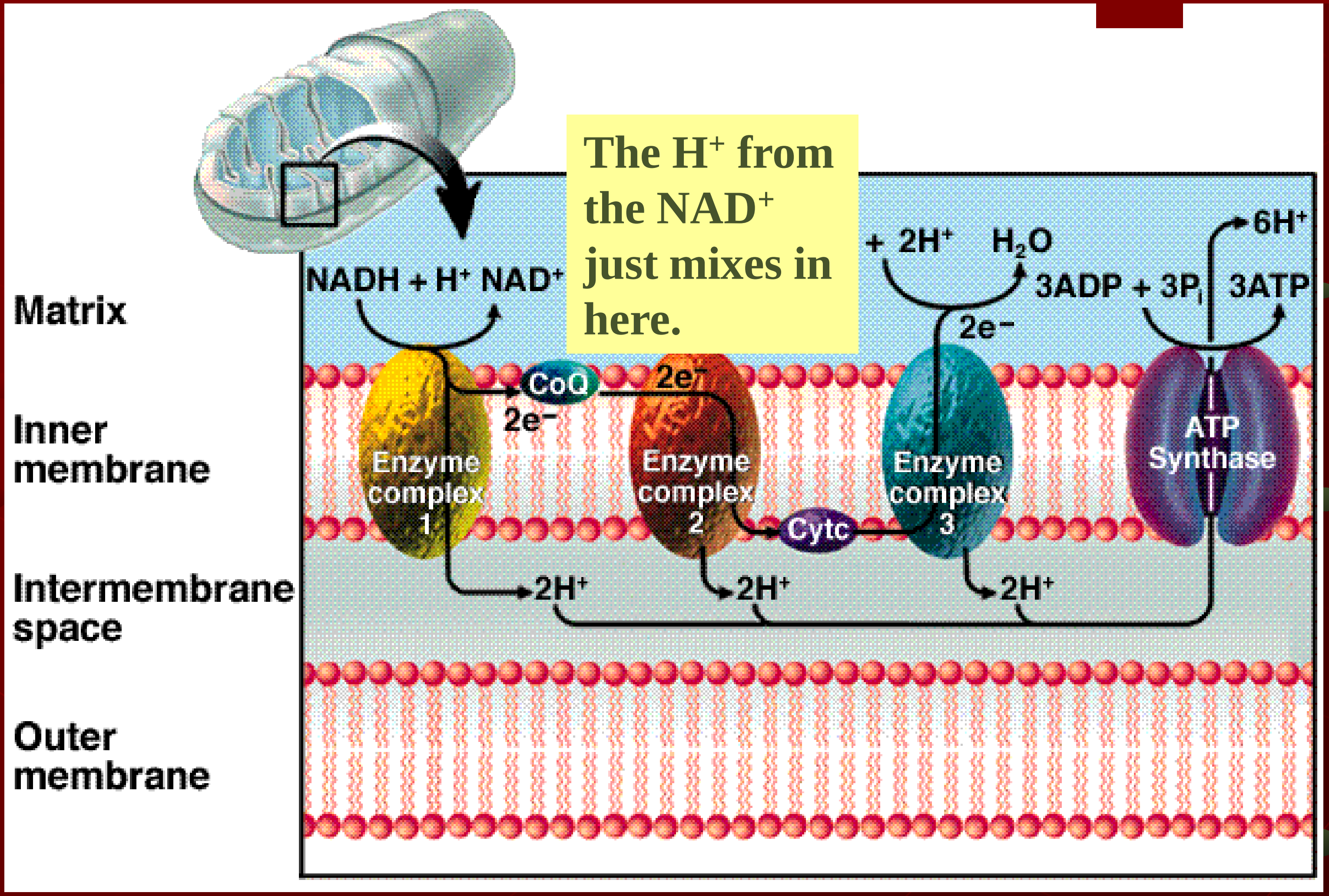
- **10 NADH and 2 $FADH_2$ produced during glycolysis and citric acid cycle**
  - **each one of these contains chemical energy**
  - **need to transfer this energy to ATP**
    - **ATP is used by all parts of the cell**
    - **NAD^+ and FAD need to be recycled**



- chains of enzymes on the ***inner*** mitochondrial membrane are responsible for this.

Electron Transport Chain

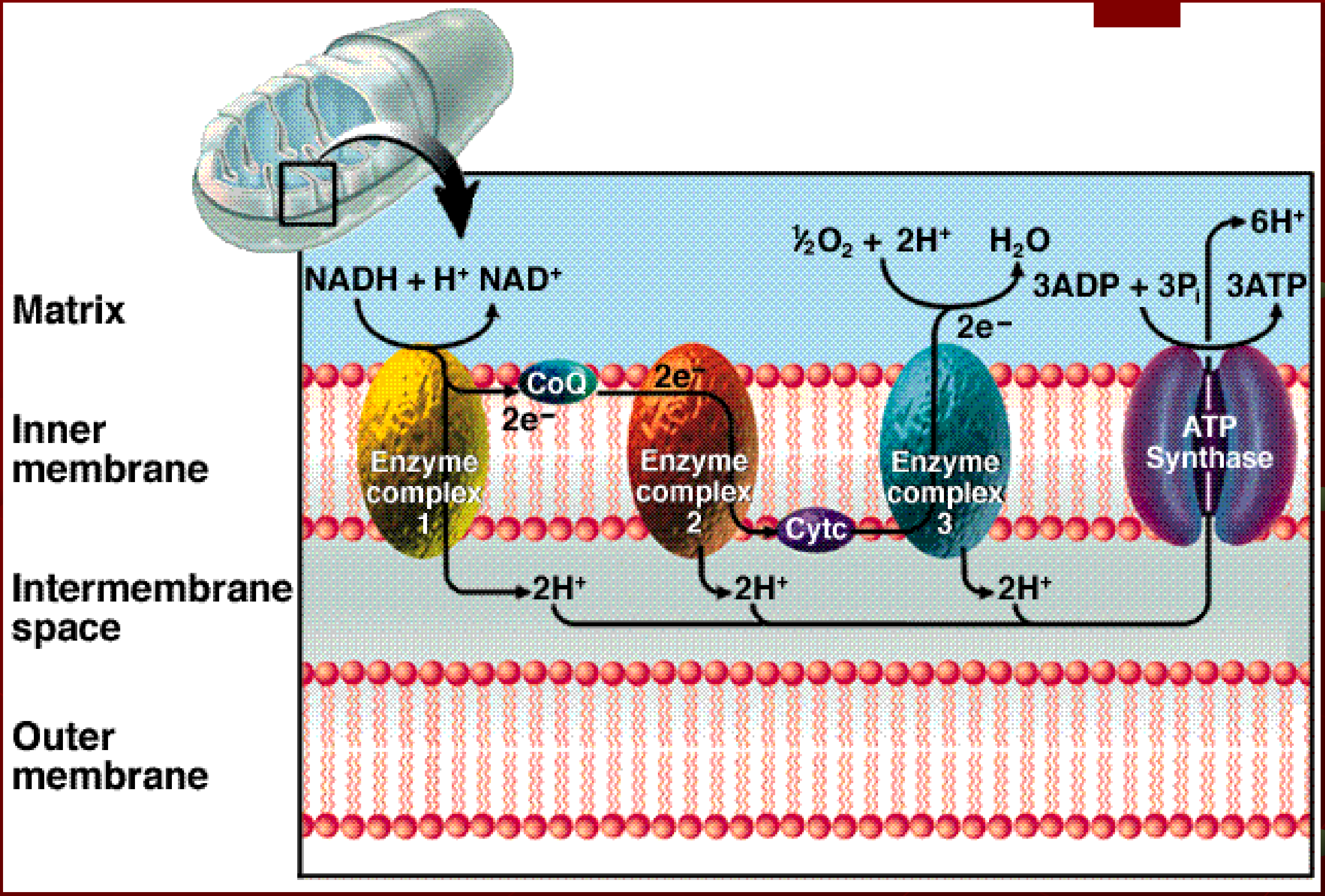
- NADH+H$^+$ hands off high energy e$^-$ to enzyme complex 1
- Energy from the e$^-$ is used to drive the proton pump that moves H+ out of the mito.
- This begins to create a... H$^+$ (proton) gradient



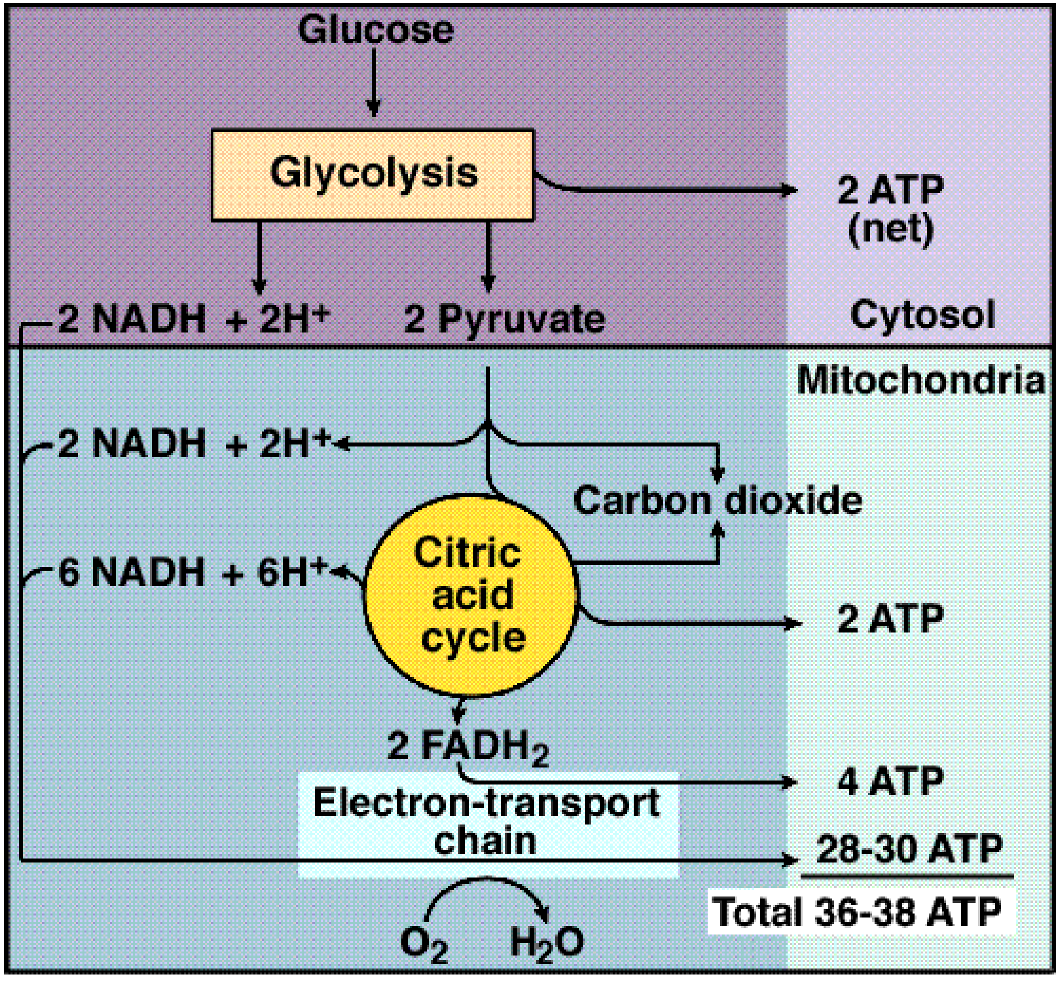
Electron Transport Chain

$$C_6H_{12}O_6 + 6O_2 \longrightarrow 6\ CO_2 + 6H_2O$$

Inhale oxygen, exhale french fries



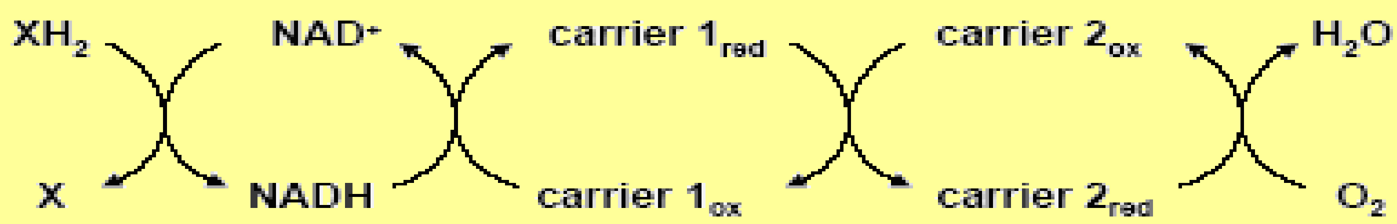
Cellular respiration generates 36-38 ATP molecules for each sugar (glucose) molecule it metabolizes



Electron Transport : In Brief

This process is the mechanism by which cells convert the energy stored in reduced cofactors, NADH and $FADH_2$ into ATP. The electron transport system (ETS) consists of complexes containing about 44 polypeptides and 1 lipid (Coenzyme Q) and involves the transfer of reducing equivalents (hydride ions, hydrogen atoms or electrons) from the reduced cofactors to molecular O_2. Electrons flow uni-directionally along an energy gradient; electrons move from a carrier of high reducing potential (i.e. greater tendency to donate electrons) toward a carrier with greater oxidizing potential (i.e. greater tendency to accept electrons), successively through several carriers to O_2.

For example



The energy drop from NADH $E_o' = -0.32$ V

to O_2 $E_o' = +0.82$ V

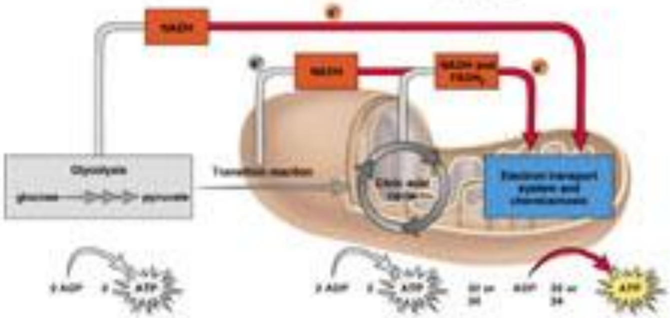
$$\Delta E_o' = +1.14 \text{ V}$$

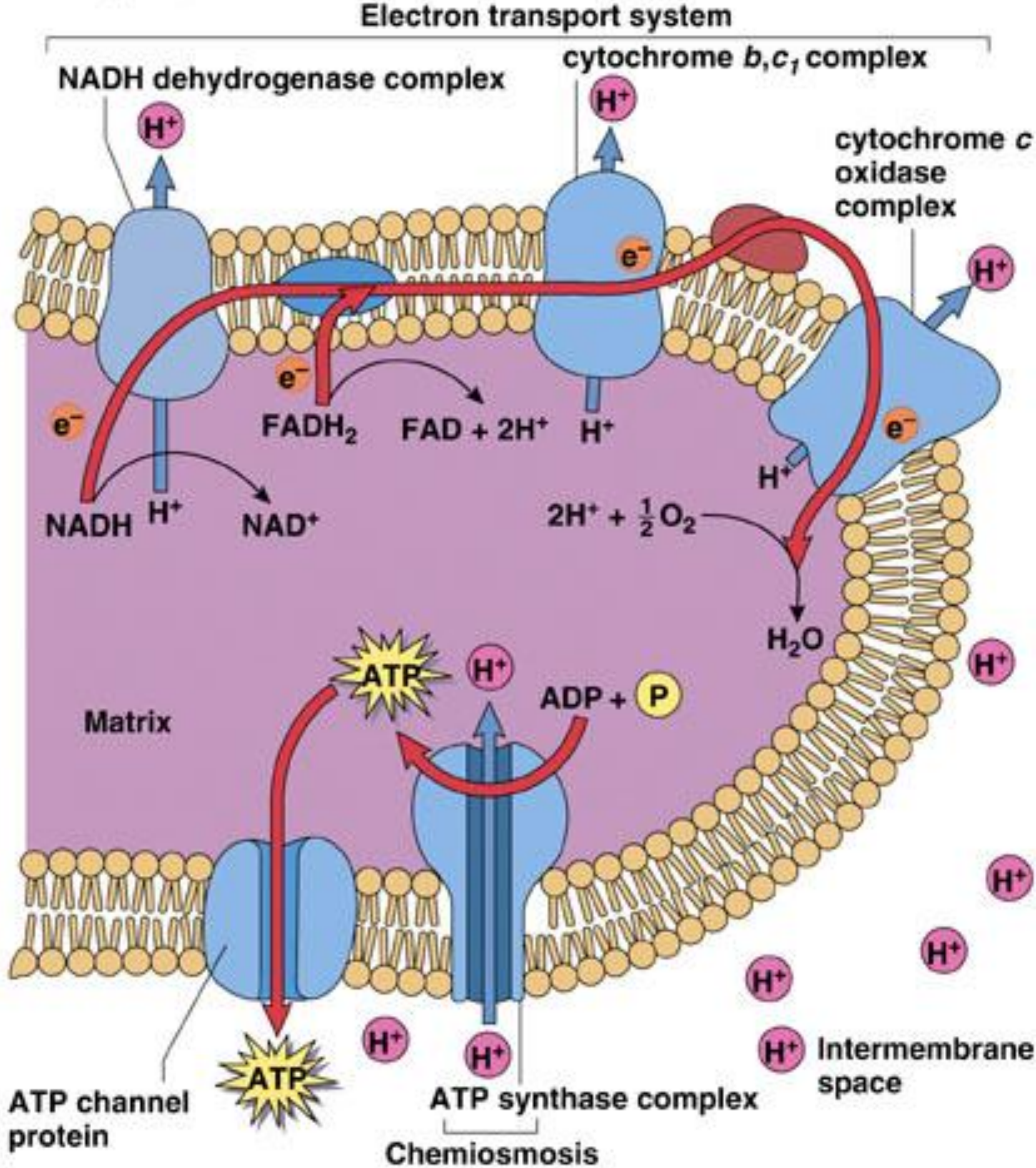
This corresponds to a free energy change of

$$\Delta G^{o\prime} = -nF\Delta E_o' = -220 \text{ kJ/mole}$$

Since the $\Delta G^{o\prime}$ for each ATP is -30.5 kJ/mole, this potential drop is sufficient for the synthesis of several ATPs due to the reduction of O_2 by NADH. Practically it appears that a maximum of 3 ATP can be synthesized for each pair of electrons transported.

Our discussion will center on the character of the ETS and the coupling of electron transport with the synthesis of ATP.




Electron transport system
NADH dehydrogenase complex
cytochrome b,c1 complex
cytochrome c oxidase complex
H+
e−
FADH2
FAD + 2H+
NADH
NAD+
2H+ + 1/2 O2
H2O
Matrix
ATP
ADP + P
ATP channel protein
ATP synthase complex
Chemiosmosis
Intermembrane space

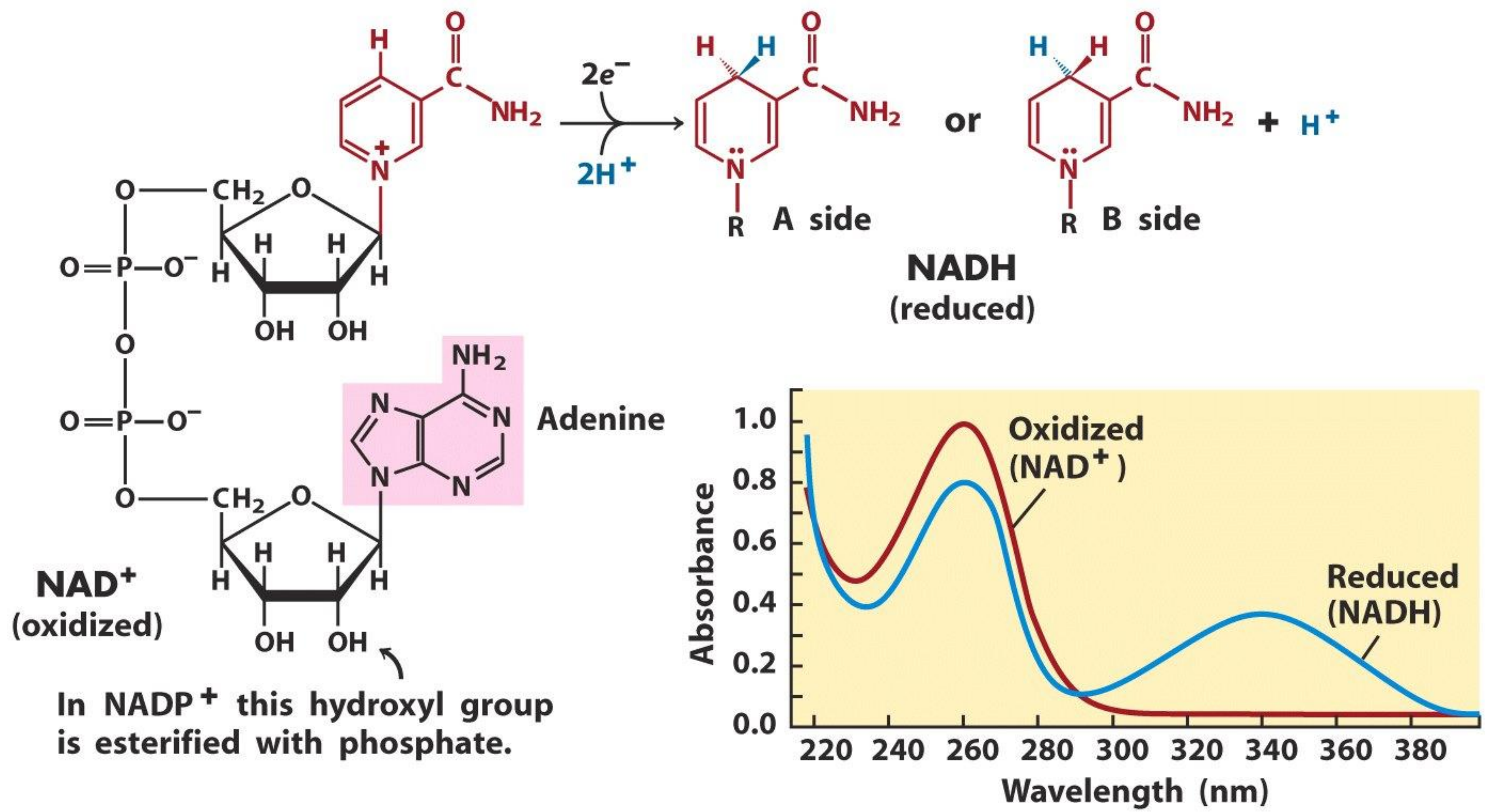
1. Classes of electron-transferring enzymes

- Five types of enzymes are involved in the transport of electrons to O_2.

  1) - Pyridine-linked dehydrogenases (NAD, NADP).

- We have already seen these dehydrogenases, which transfer a hydride ion to NAD.

NAD and NADP

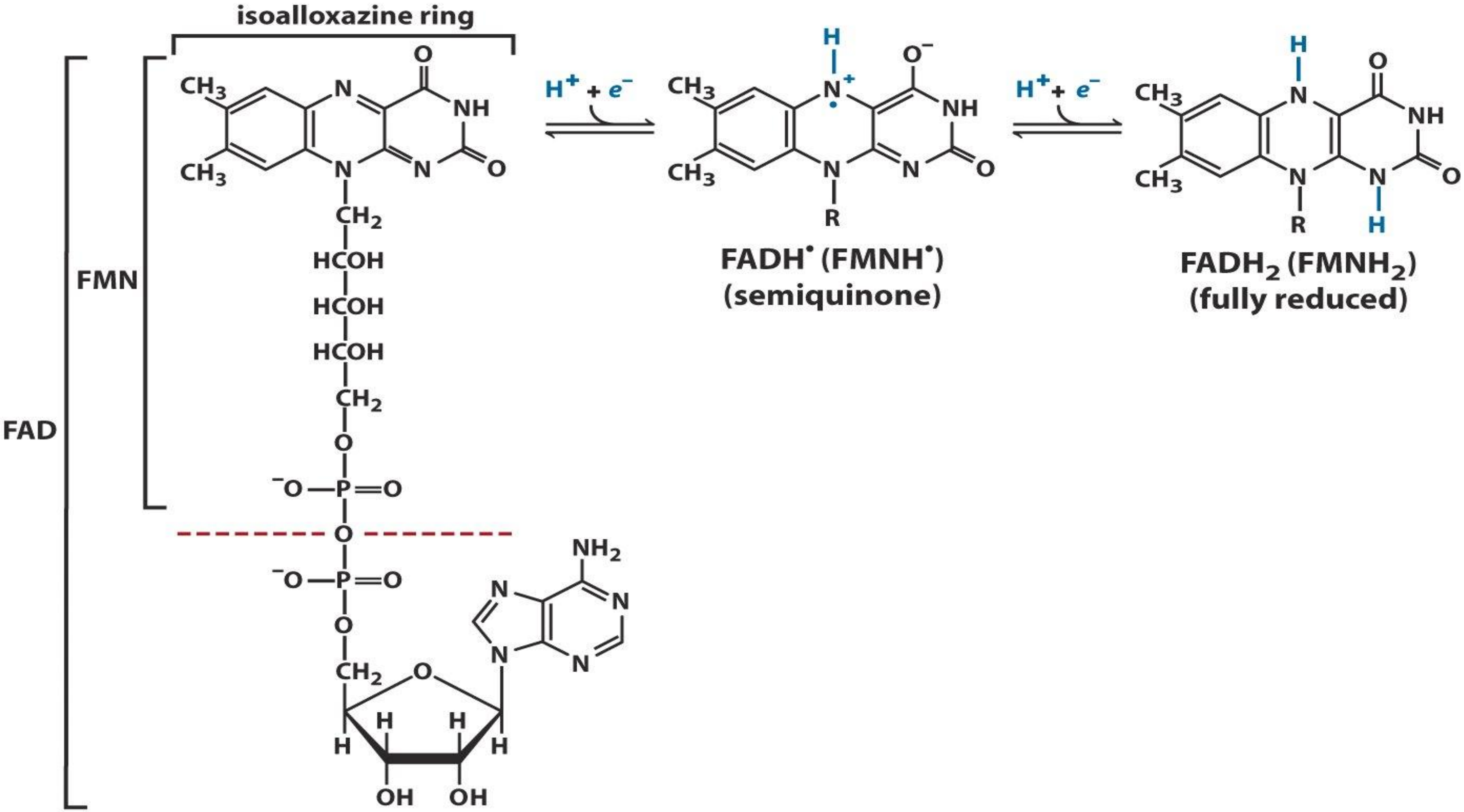


H
O
C
NH2
N
2e−
2H+
H H
A side
R
or
B side
+ H+
NADH
(reduced)
O
CH2
O=P—O−
H
OH OH
NH2
N
Adenine
NAD+
(oxidized)
In NADP+ this hydroxyl group
is esterified with phosphate.
1.0
0.8
0.6
0.4
0.2
0.0
Absorbance
Oxidized
(NAD+)
Reduced
(NADH)
220 240 260 280 300 320 340 360 380
Wavelength (nm)

2) - Flavoproteins.

- These contain a tightly bound, sometimes covalently bound, flavin nucleotide, either FMN or FAD.
- We have also seen these before (*i.e.* succinate dehydrogenase).

Reduced and Oxidized FAD and FMN

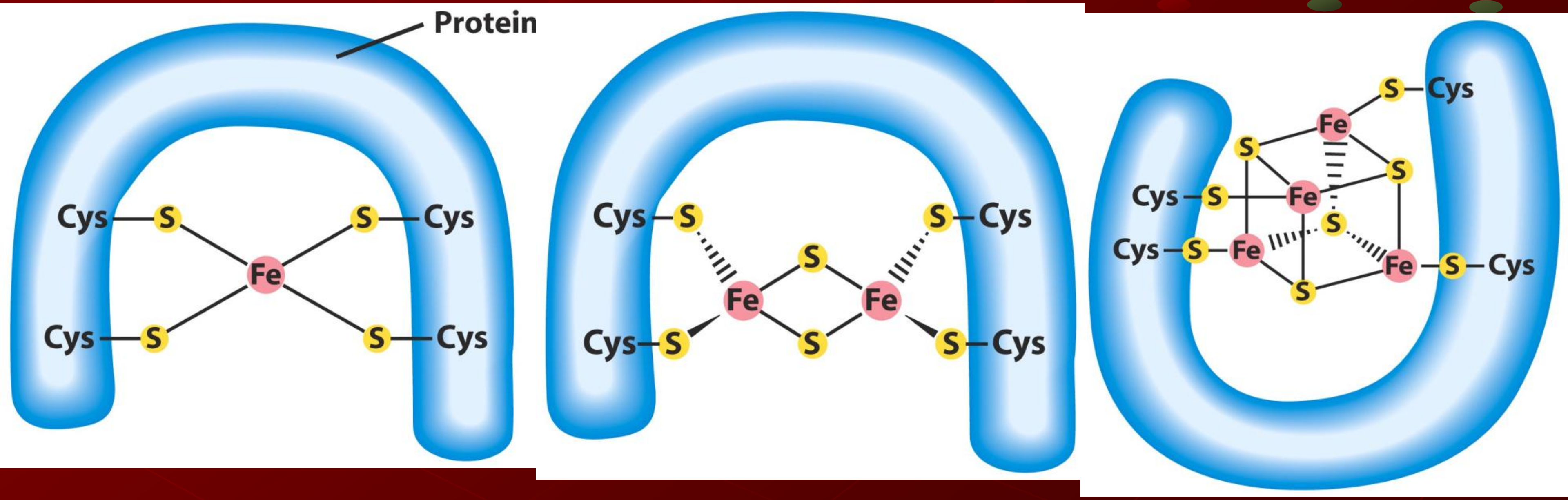


Flavin adenine dinucleotide (FAD) and
flavin mononucleotide (FMN)

3) - Iron-sulfur proteins :

- These contain Fe and acid-labile sulfur in equimolar amounts.
- 2Fe-2S and 2Fe-4S are the most common.
- They undergo reversible Fe(II)-Fe(III) transitions.
- These are single electron transfers only.
- (Fe(III) results from the loss of one electron from Fe(II)).

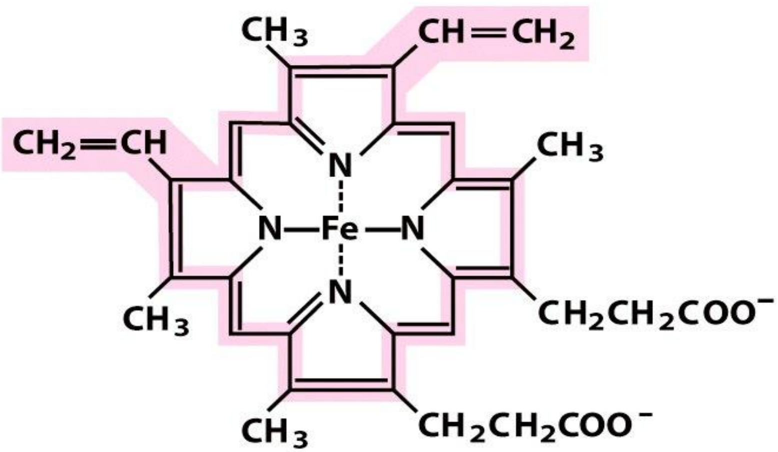
Iron-sulfur proteins are electron carriers



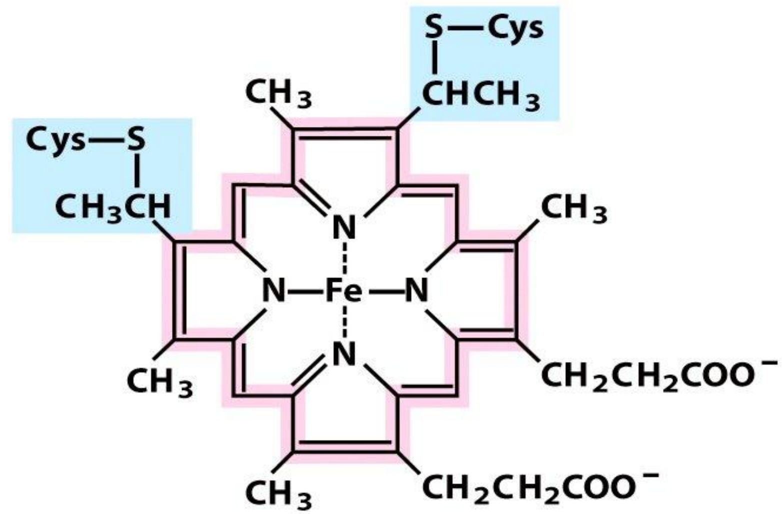
4) - Cytochromes :

- These proteins contain heme groups.
- The Fe, coordinated between four pyrrole groups, can alternate between Fe(II) and Fe(III) states.
- These proteins also undergo single electron transfers.
- There are three types of cytochromes in mitochondria, *a*, *b*, and *c*.
- The iron in cytochromes absorbs light in the visible range and the absorbance is sensitive to the redox state, allowing experimental observation of electron transfers of these proteins .

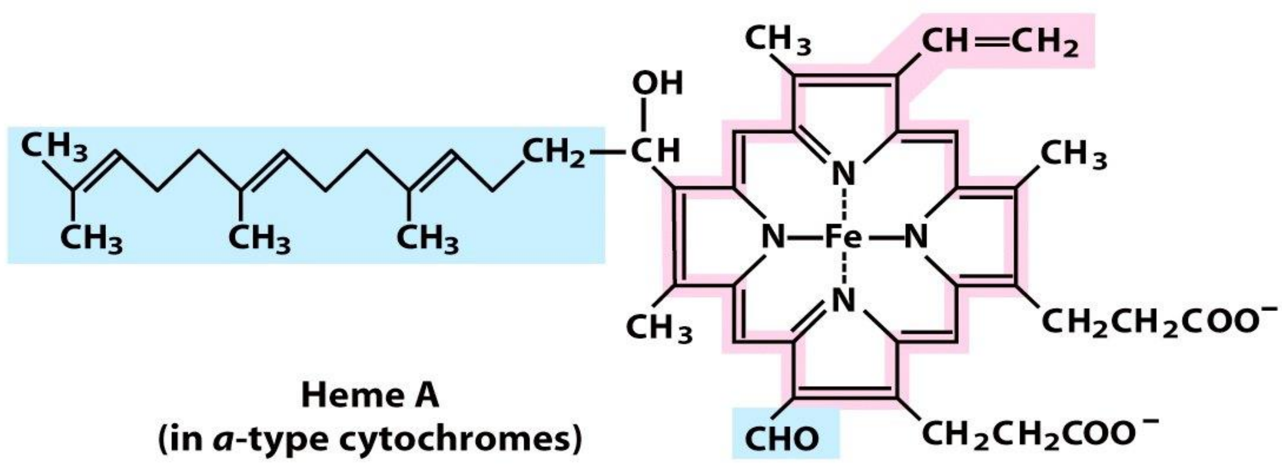
Cytochromes: one-electron carriers



Iron protoporphyrin IX
(in *b*-type cytochromes)



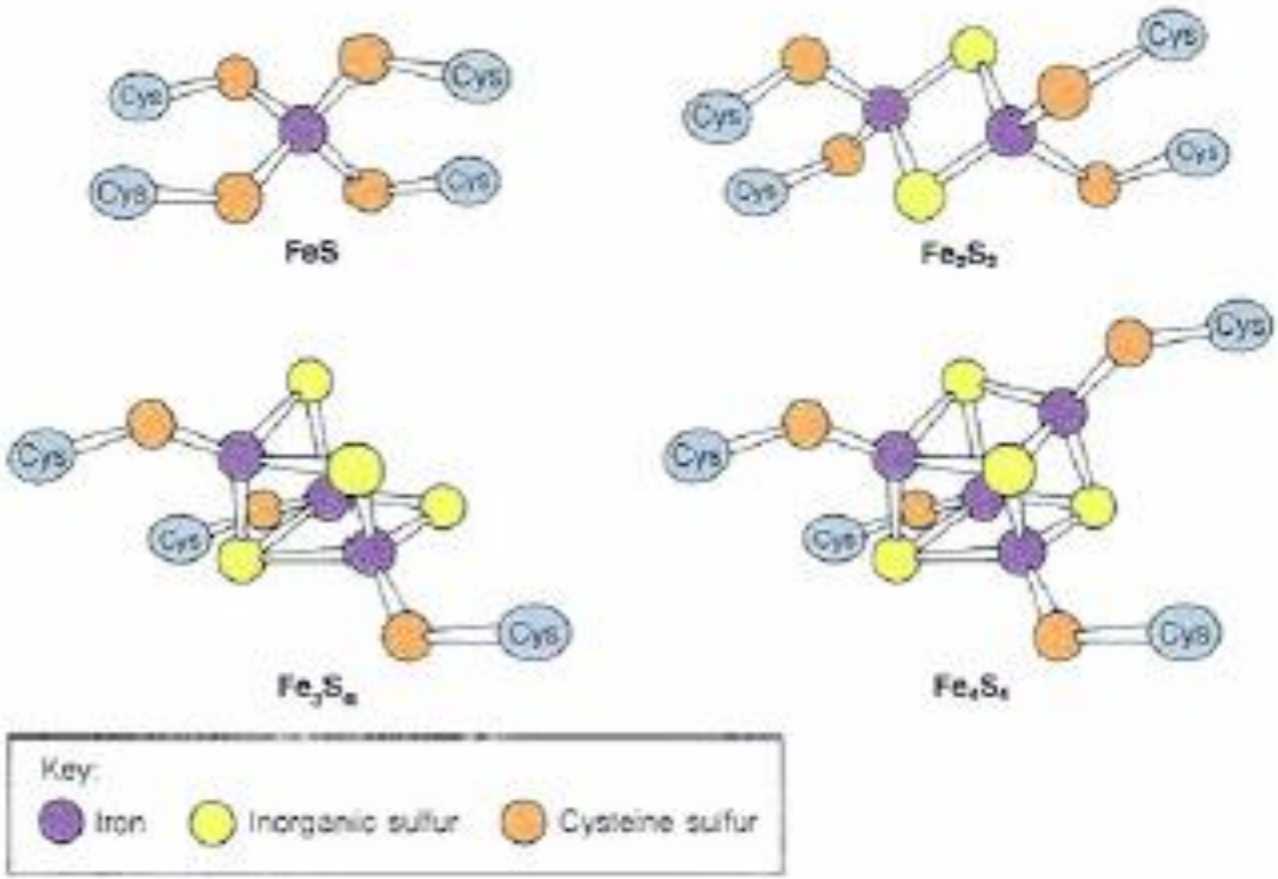
Heme C
(in *c*-type cytochromes)



Heme A
(in *a*-type cytochromes)

Fe sulfur proteins (contain no heme) but undergo similar oxidation/ reduction reactions exhibited by the cytochromes to enable the transfer of electrons along the transport pathways.

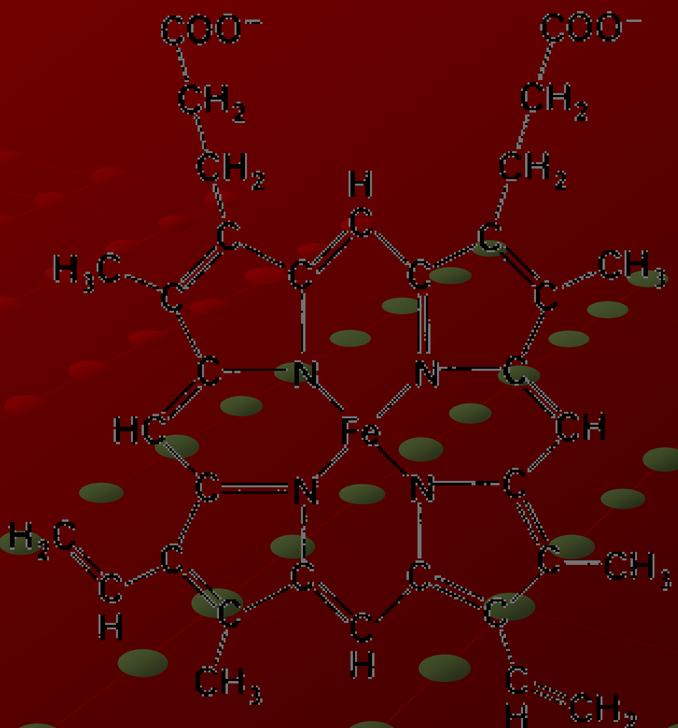
$e^- + Fe^{3+} \rightleftharpoons Fe^{2+}$



p 530 MVA

Cytochromes - proteins in ETS

- Carries electrons
- Contain heme or heme-like group
- Heme based on porphyrins with iron in center, usually as Fe(II), and is tightly bound at sides, sometimes covalently
- Contrast heme in cytochromes & hemoglobin


Heme
(Fe-protoporphyrin IX)

Hemoglobin vs Cytochromes

-- **For the hemoglobin heme group:**

a) Fe has *his* bound from above and O_2, comes in below to bind.
b) Fe remains as Fe(II) & no electrons are transferred.

☛ **Just carries O_2**

--For ***cytochrome heme***,

a) all 6 sites of Fe are filled (4 from porphyrin, 2 above and below from protein) = no *molecule* can approach

b) carries electrons only:

$Fe(III) + e^- \leftrightarrows Fe(II)$

Note: Only *one* electron is transferred at a time.

-- Cytochromes in respiration are on ***inner mitochondrial membrane***

☛ ***cytochromes b, c_1, c, a, a_3 ,*** relay electrons (one at a time, in this order) ☚

5)- Ubiquinone, or coenzyme Q :

- This is a lipid-soluble benzoquinone with a long non-polar (isoprenoid) tail.
- It can accept one or two electrons.
- It carries both electrons and protons, allowing it to play a critical role in coupling electron flow to proton movement.