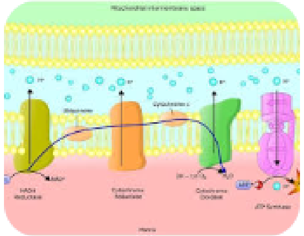
Electron Transport Chain (ETC)



The electron transport chain (ETC) is a series of protein complexes and molecules that transfer electrons from a donor to an acceptor, creating an electrochemical gradient that produces ATP. The ETC occurs in the mitochondria and is involved in both cellular respiration and photosynthesis.

Here are some key points about the ETC:

Components

The ETC consists of four complexes: NADH dehydrogenase (complex I), succinate dehydrogenase (complex II), cytochrome b and c1 (complex III), and cytochrome c oxidase (complex IV).

Electron transfer

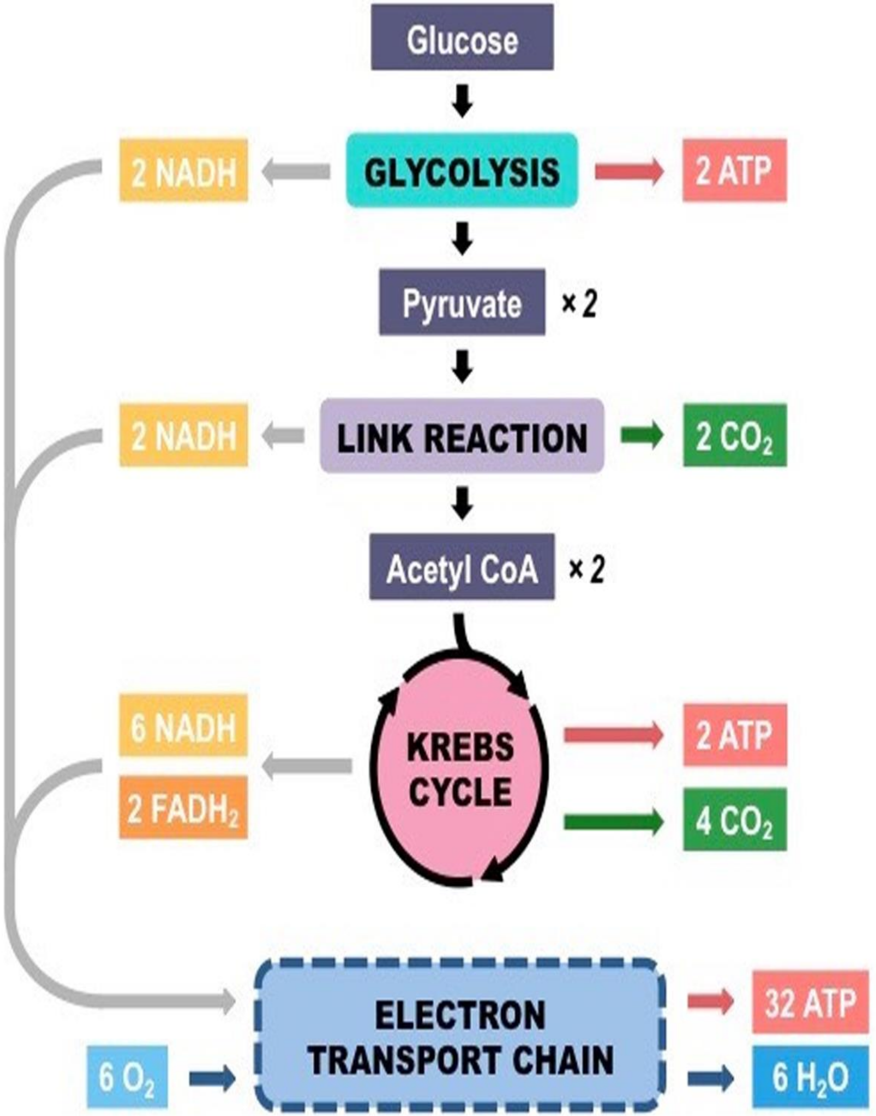
Electrons are transferred from NADH to flavin mononucleotide, then to Fe-S complexes, and finally to Q, which carries them to complex III. In complex IV, electrons are passed from copper to heme a, heme a3, and another copper center. Finally, electrons are received by molecular oxygen to form water.

Redox potential

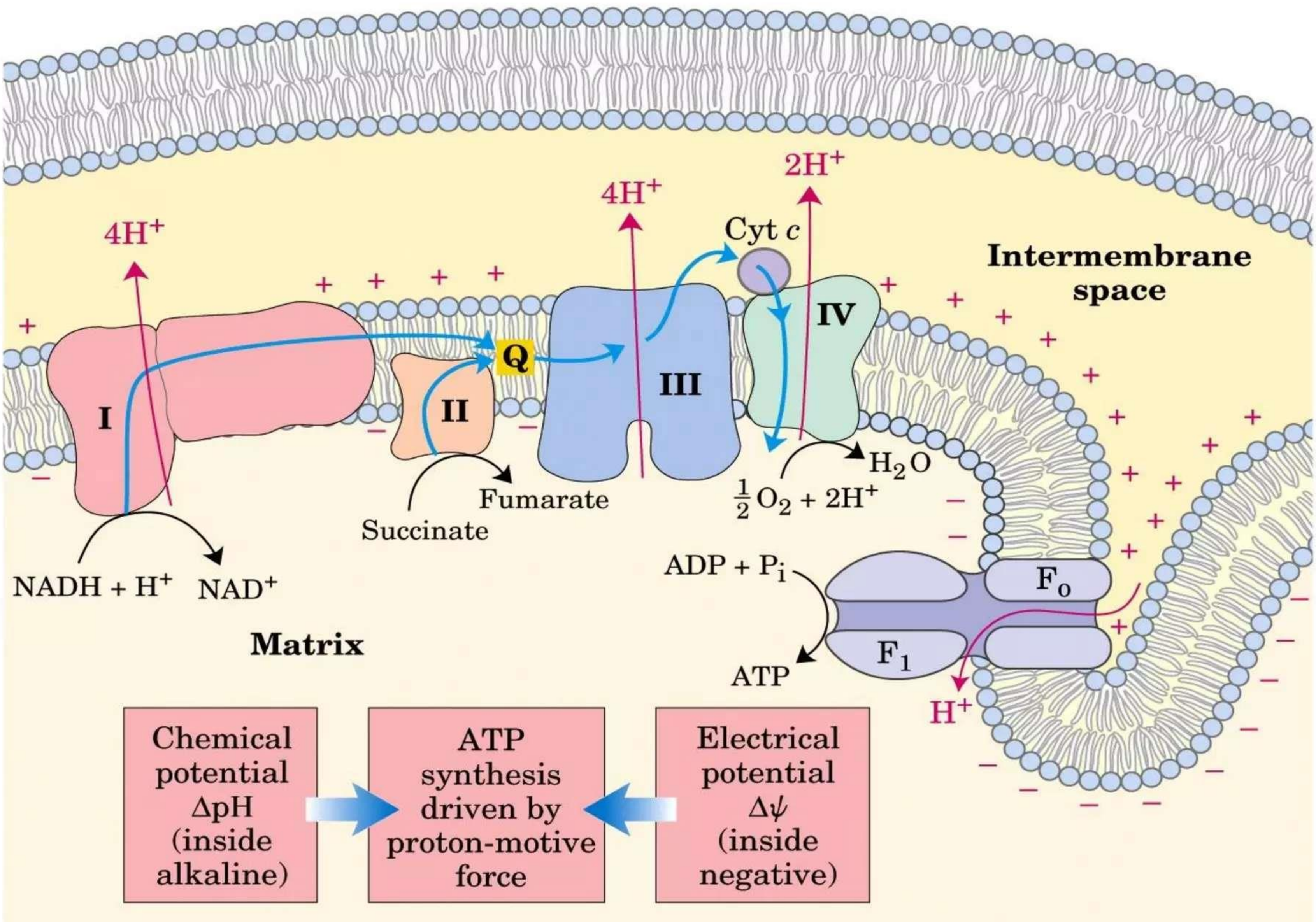
The tendency of a redox pair to transfer electrons can be measured by its redox potential. Electrons move spontaneously from a redox pair with a low redox potential to one with a high redox potential.

Cellular respiration

In cellular respiration, electrons come from breaking down organic molecules and energy is released.


Glucose
2 NADH
GLYCOLYSIS
2 ATP
Pyruvate
× 2
2 NADH
LINK REACTION
2 CO_2
Acetyl CoA
× 2
6 NADH
2 $FADH_2$
KREBS CYCLE
2 ATP
4 CO_2
ELECTRON TRANSPORT CHAIN
6 O_2
32 ATP
6 H_2O

Summary



4H+
4H+
2H+
Cyt c
Intermembrane space
IV
Q
III
I
II
Fumarate
Succinate
H2O
½ O2 + 2H+
NADH + H+
NAD+
ADP + Pi
Fo
F1
ATP
H+
Matrix
Chemical potential ΔpH (inside alkaline)
ATP synthesis driven by proton-motive force
Electrical potential Δψ (inside negative)

Components of ETC

Complex	Name	No. of Proteins	Prosthetic Groups
Complex I	NADH Dehydrogenase	46	FMN, 9 Fe-S cntrs.
Complex II	Succinate-CoQ Reductase	5	FAD, cyt b_{560}, 3 Fe-S cntrs.
Complex III	CoQ-cyt c Reductase	11	cyt b_H, cyt b_L, cyt c_1, $Fe\text{-}S_{Rieske}$
Complex IV	Cytochrome Oxidase	13	cyt a, cyt a_3, Cu_A, Cu_B

CHEMIOSMOTIC HYPOTHESIS

The chemiosmotic hypothesis explains how ATP is produced in the mitochondria of a cell through the process of chemiosmosis:

Proton pumping

Electrons from the electron transfer chain (ETC) pump protons out of the matrix of the inner mitochondrial membrane.

Electrochemical gradient

The energy from the electrons is stored as a transmembrane electrochemical gradient.

ATP synthase

Protons return to the inner membrane through ATP synthase, which uses the energy to convert ADP and inorganic phosphate into ATP.

The chemiosmotic hypothesis was proposed by Peter Mitchell. The ATP synthase enzyme is made up of two parts, F0 and F1. F0 acts as a transmembrane channel to transport protons across the membrane, while F1's configuration changes activate the enzyme.

1 NADH

$$10\ H^+ \times \frac{1\ ATP}{4\ H^+} = 2.5\ ATP$$

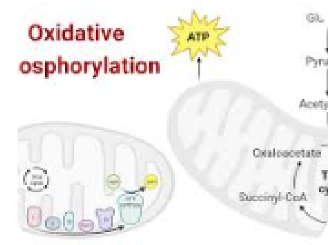
1 $FADH_2$

$$6\ H^+ \times \frac{1\ ATP}{4\ H^+} = 1.5\ ATP$$

ATP Yield from Complete Oxidation of Glucose

Process	Direct Product	Final ATP
Glycolysis	2 NADH (cytosolic)	5*
	2 ATP	2
Pyruvate oxidation (two per glucose)	2 NADH (mitochondrial matrix)	5
Acetyl-CoA oxidation in citric acid cycle (two per glucose)	6 NADH (mitochondrial matrix)	15
	2 $FADH_2$	3
	2 ATP or 2 GTP	2
Total yield per glucose		30 or 32

Oxidative Phosphorylation



Oxidative phosphorylation is a metabolic process that takes place in the mitochondria of cells to produce adenosine triphosphate (ATP), the primary energy molecule for cells. This process is also known as electron transport-linked phosphorylation or terminal oxidation.

Here are some key points about oxidative phosphorylation:

How it works

Oxidative phosphorylation is a series of oxidation-reduction reactions that transfer electrons from NADH and FADH2 to oxygen. These reactions occur in the electron transport chain, which is made up of protein, metal, and lipid complexes in the mitochondria.

Where it happens

Oxidative phosphorylation takes place in the mitochondria, which have a double membrane structure. The inner membrane, called cristae, contains many copies of the respiratory chain components.

Importance

Oxidative phosphorylation is a vital part of cellular respiration and metabolism. It's the reason why many lifeforms require oxygen to survive.

Inhibitors

Certain poisons can inhibit oxidative phosphorylation, including rotenone, carboxin, antimycin A, cyanide, carbon monoxide, sodium azide, and oligomycin.

Working of ATP Synthase Complex

The ATP synthase complex in mitochondria works by using the energy of a proton gradient to synthesize adenosine triphosphate (ATP) from adenosine diphosphate (ADP) and inorganic phosphate. The ATP synthase complex is a molecular machine that spans the inner mitochondrial membrane, and its function is as follows:

Proton gradient

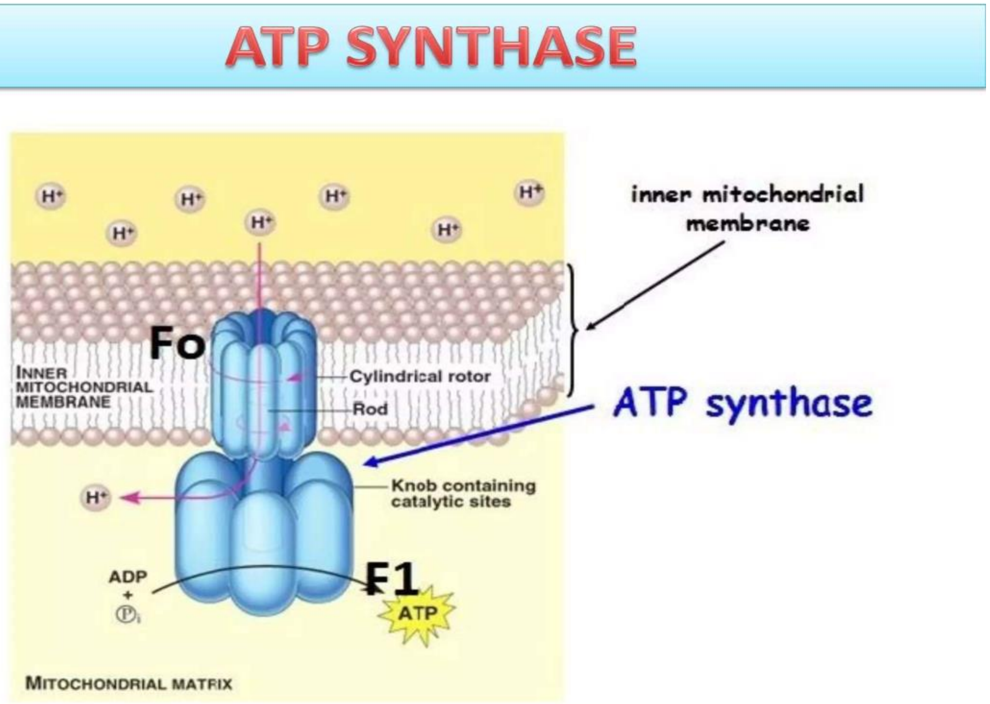
The electron transport chain generates an electrochemical gradient of protons across the inner mitochondrial membrane.

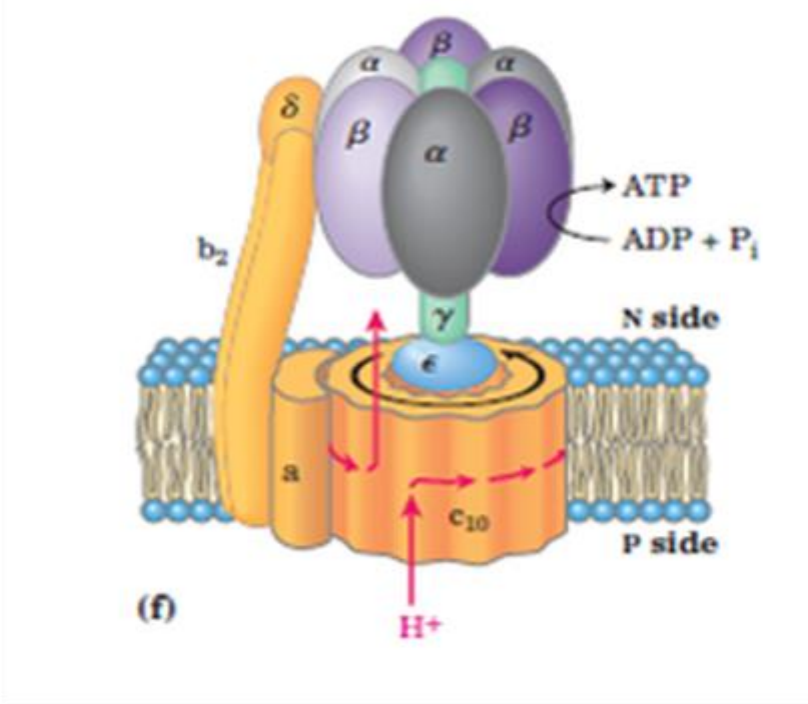
Proton flow

Protons flow through the ATP synthase complex from areas of high concentration to areas of low concentration.

Rotary catalysis

The energy from the proton flow rotates two rotary motors in the ATP synthase complex, which provides the energy for ATP synthesis.





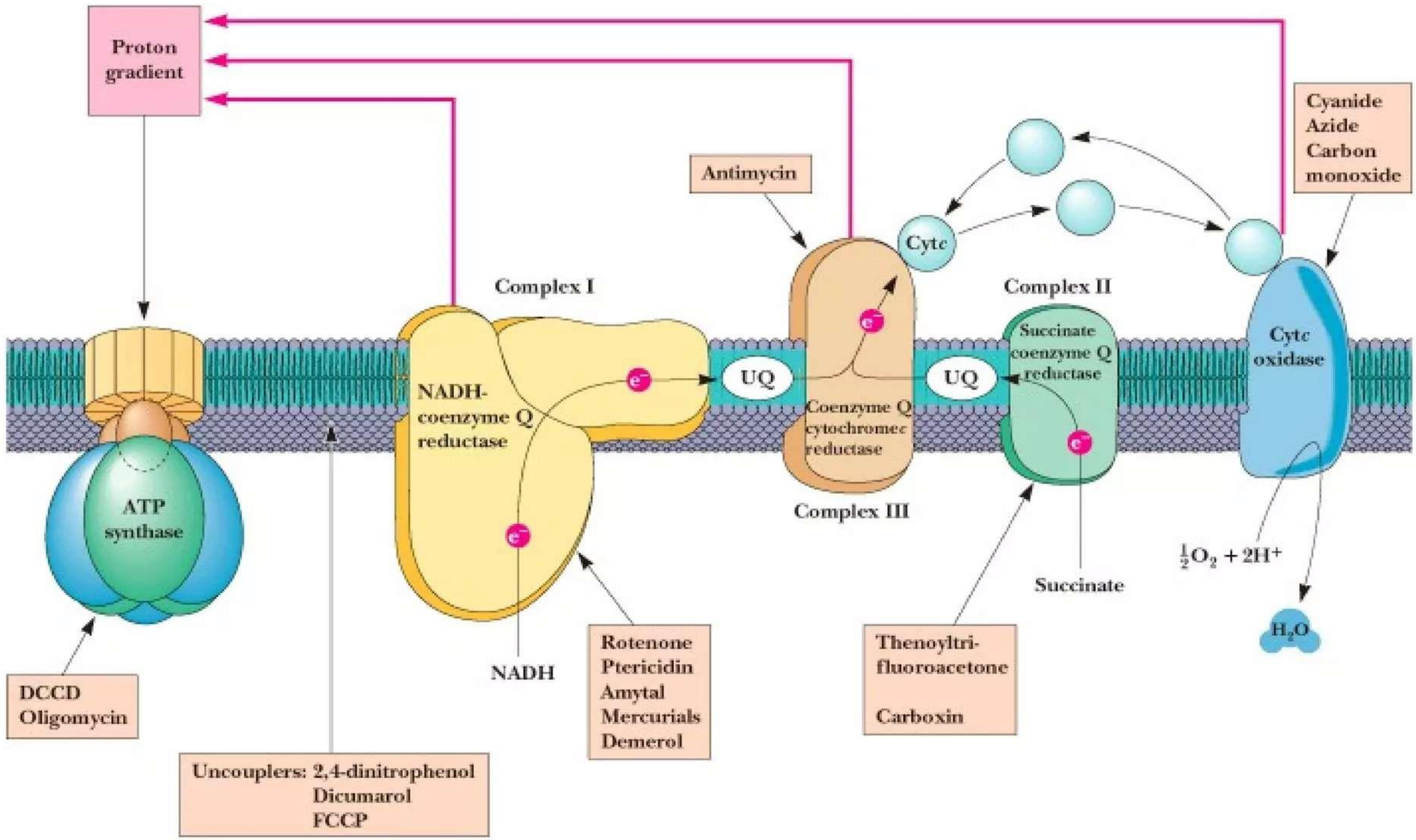
Inhibitors of the ETC

Some inhibitors of the electron transport chain (ETC) include:

- Carbon monoxide: Binds to Complex IV and prevents electrons from passing through.
- Cyanide: Inhibits Complex IV.
- Rotenone: Inhibits Complex I.
- Antimycin C: Inhibits Complex III.
- Oligomycin: Inhibits Complex V.
- Amytal: Blocks the ETC between NADH dehydrogenase (Complex I) and CoQ.
- Metal chelating agents: Such as o-phenanthroline, sali- cylaldoxim, 8-hydroxyquinoline, and EDTA.
- Hg-compounds: Can act on the NADH-flavoprotein segment.

Inhibitors block oxidation and reduce oxygen consumption and ATP generation.

Garrett & Grisham: Biochemistry, 2/e
Figure 21.30



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Uncouplers of ETC

Uncouplers, also known as uncoupling agents, are molecules that disrupt the electron transport chain (ETC) by preventing the formation of ATP. They do this by:

Disrupting the membrane

Uncouplers disrupt the phospholipid bilayer of membranes, making them more fluid and disorganized. This allows protons to flow more freely, weakening the electrochemical gradient.

Short-circuiting the proton-motive force

Uncouplers act as H+ carriers, providing a pathway for protons to flow across the inner mitochondrial membrane. This bypasses the ATP synthase, preventing the cell from using the proton-motive force to make ATP.

Releasing heat

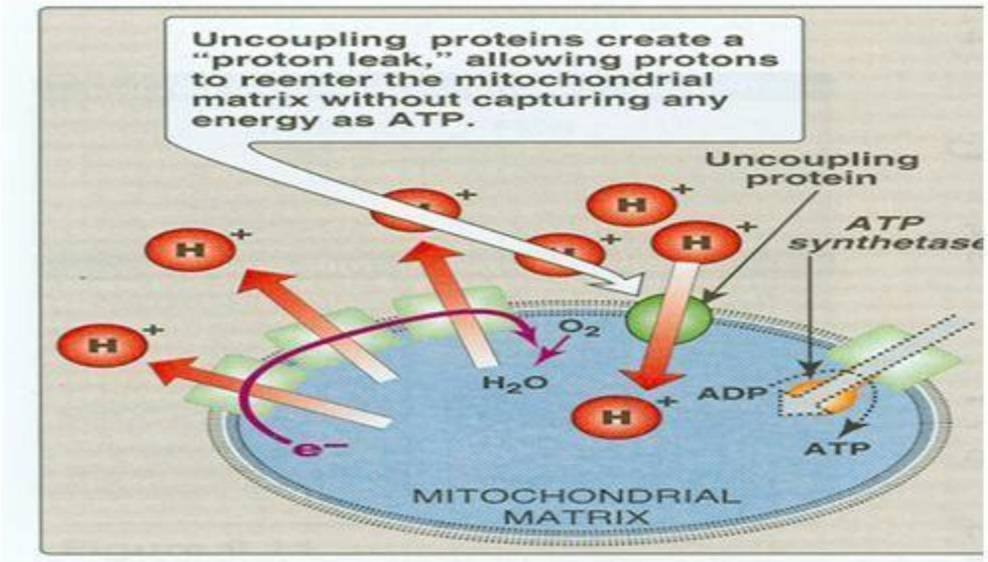
When protons are released across the membrane, the energy is released as heat instead of being used to create a phosphate bond.

Some examples of uncouplers include:

- 2,4-dinitrophenol: A low-molecular-weight organic compound that can be used as a diet aid. Poisoning from dinitrophenol can lead to hyperthermia, tachycardia, and tachypnea.
- Salicylic acid: An uncoupler and inhibitor of the mitochondrial electron transport. Salicylate poisoning can cause tinnitus, tachypnea, respiratory alkalosis, and metabolic acidosis.
- Valinomycin: A common uncoupler.

Uncouplers

- Compounds that can uncouple or delink the electron transport chain from oxidative phosphorylation, such compounds are known as Uncouplers.
- These increase the permeability of IMM to protons (H+).
- Thus an Uncoupler allows ETC but blocks the establishment of proton gradient across the IMM.



- The result is that ATP synthesis does not occur.
- The energy linked with the transport of electrons is dissipated as heat.