King Saud University
College of Sciences
Biochemistry Department

الأيض (١)

Metabolism (1)

BCH 340

Lecture 4: ETC and oxidative phosphorylation

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Intended learning outcomes (ILOs)

By the end of this lecture, students will be able to:

- Understand the flow of electrons through the electron transport chain.
- Describe the process of oxidative phosphorylation as a final stage of aerobic cellular respiration (where the majority of ATP is generated).
- Identify some inhibitors of the electron transport chain.

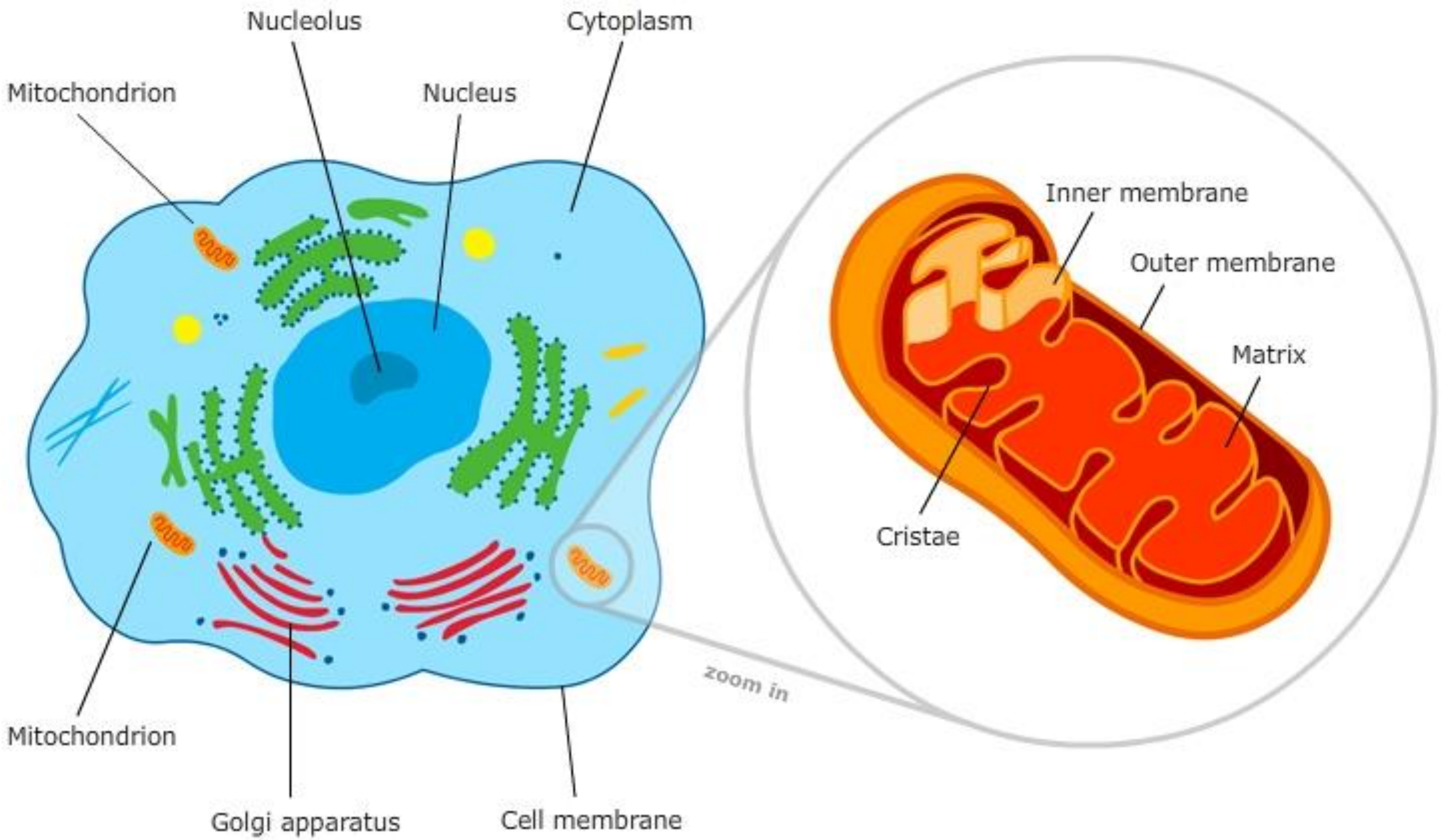
Importance of energy for the cell

- Energy production in cells serves as a fundamental process that sustains life and powers diverse cellular activities, such as:
  - Metabolism
  - Cellular respiration
  - Maintaining cellular homeostasis
  - Cell division and growth
  - Active transport
  - Signal transduction

Cellular respiration

- Cellular respiration is the process through which cells convert biochemical energy from nutrients into ATP (to fuel various cellular activities).
- It's a vital process for all living organisms, as ATP serves as the primary energy source for cells.
- Cellular respiration involves several interconnected metabolic pathways occurring primarily in the cytoplasm and mitochondria of the eukaryotic cells. They include:
  - Glycolysis (in the cytoplasm)
  - Oxidation of pyruvate (in the mitochondrial)
  - Krebs cycle (in the mitochondrial matrix)
  - Electron transport chain (in the inner mitochondrial membrane)
  - Oxidative phosphorylation
  - Anaerobic respiration and fermentation

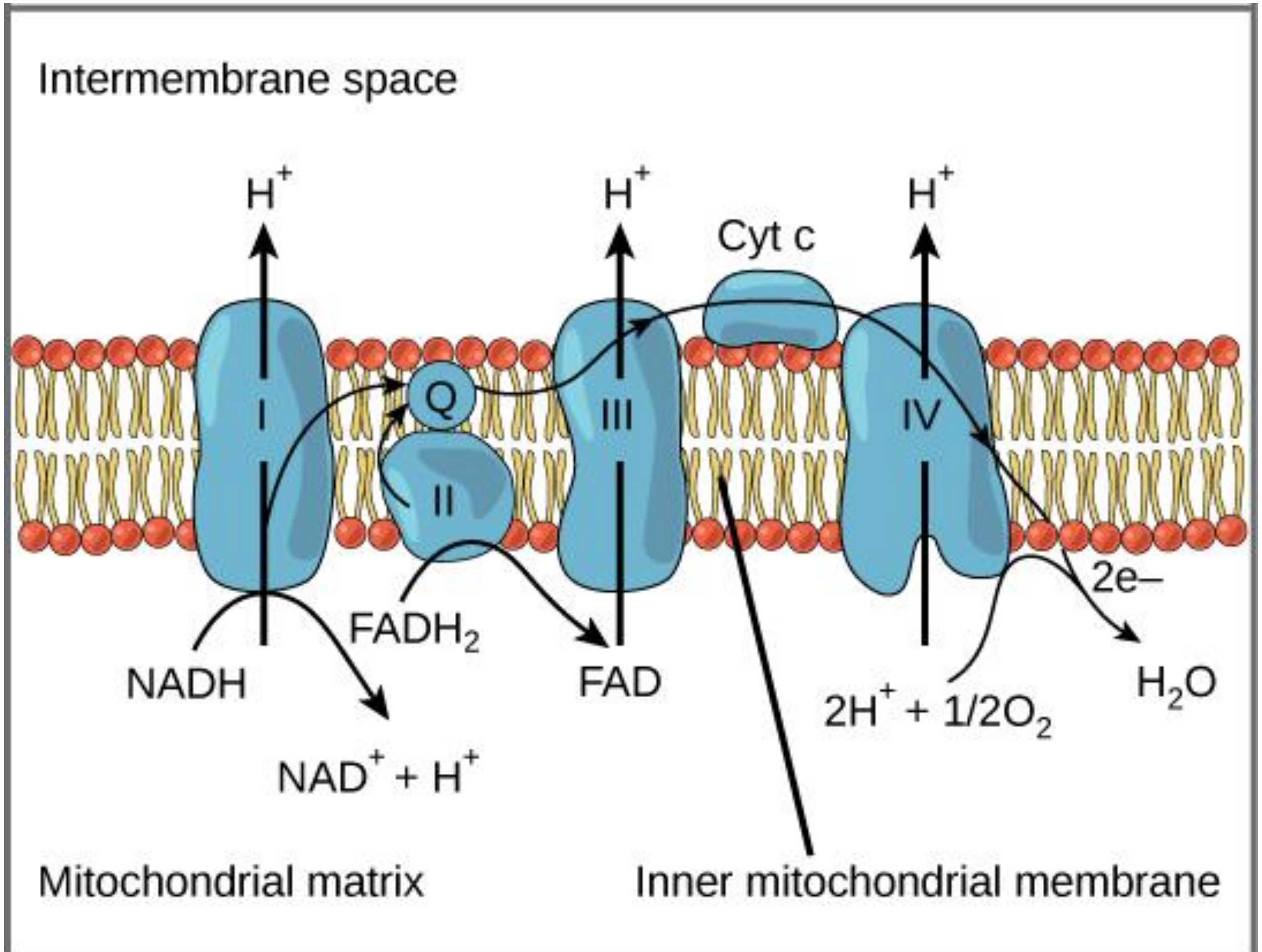
Eukaryotic cell structure



Electron transport chain

- The electron transport chain (ETC) is a critical component of cellular respiration, primarily occurring in the inner mitochondrial membrane of eukaryotic cells.
  - In prokaryotic cells, it is found in the plasma membrane
- NADH and FADH2 generated from glycolysis, pyruvate oxidation, and the Krebs cycle donate electrons to the ETC.
- Electrons move through a series of protein complexes (Complex I-IV) and coenzymes (Coenzyme Q and Cytochrome c), releasing energy.
- This energy is used to pump protons (H^+) across the inner mitochondrial membrane, establishing an electrochemical gradient.

Electron transport chain (cont.)



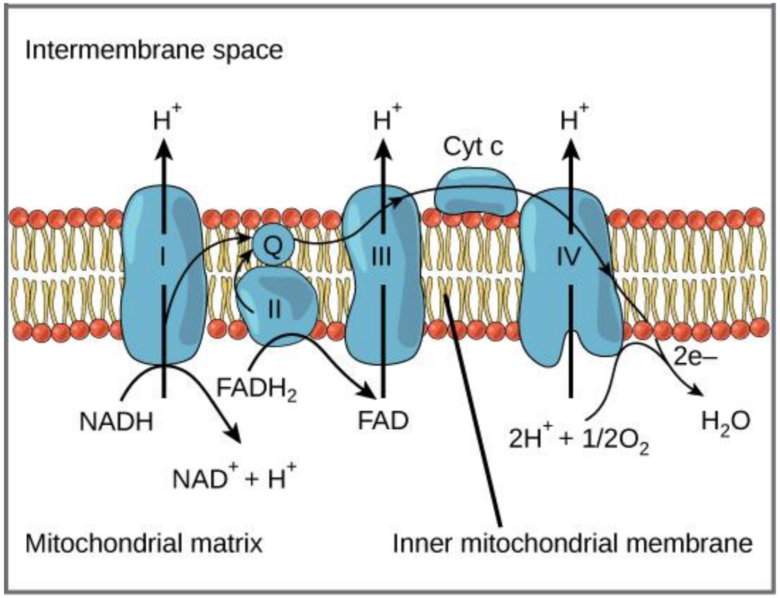
Components of ETC

1. Protein complexes:

The ETC consists of several protein complexes, each containing multiple subunits and cofactors. These complexes facilitate the transfer of electrons along the chain.

Complex I (NADH dehydrogenase):

- Accepts electrons from NADH and passes them to ubiquinone (coenzyme Q).
- It pumps protons (H^+) from the mitochondrial matrix to the intermembrane space.



Components of ETC (cont.)

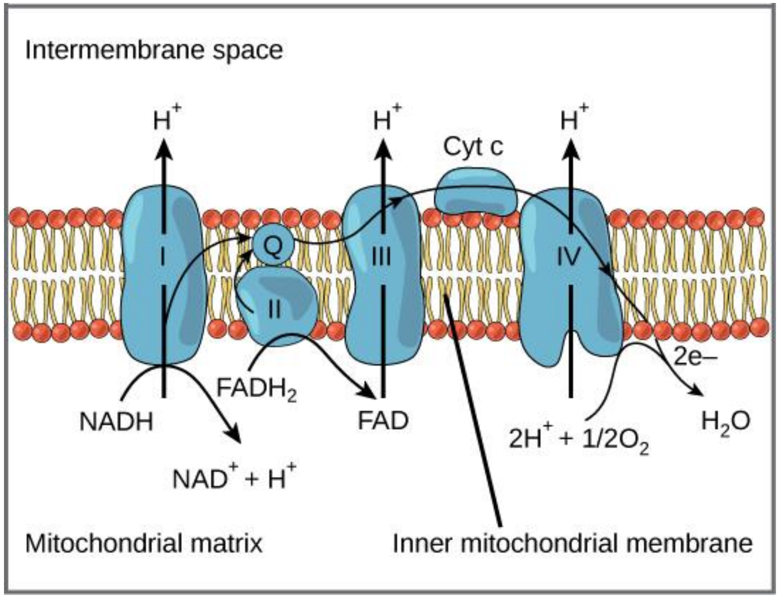
1. **Protein complexes (cont.):**

Complex II (Succinate dehydrogenase):

- Accepts electrons from FADH2 produced in the Krebs cycle and passes them to coenzyme Q.
- It is also involved in the Krebs cycle (Step 6) and does not pump protons.

Complex III (Cytochrome bc1 complex):

- Accepts electrons from coenzyme Q and passes them to cytochrome c.
- It pumps protons from the mitochondrial matrix to the intermembrane space.

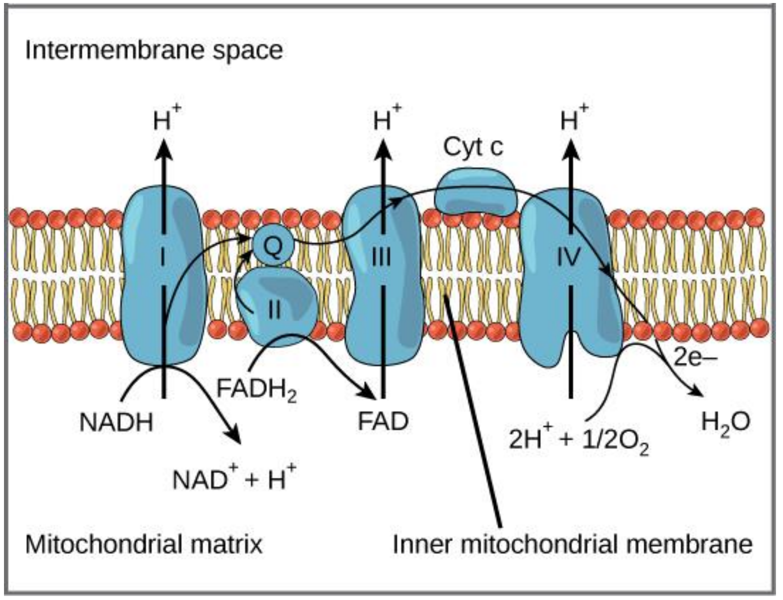


Components of ETC (cont.)

1. **Protein complexes (cont.):**

Complex IV (Cytochrome c oxidase):

- Accepts electrons from cytochrome c and transfers them to molecular oxygen, forming water as a byproduct.
- It pumps protons from the mitochondrial matrix to the intermembrane space.



Components of ETC (cont.)

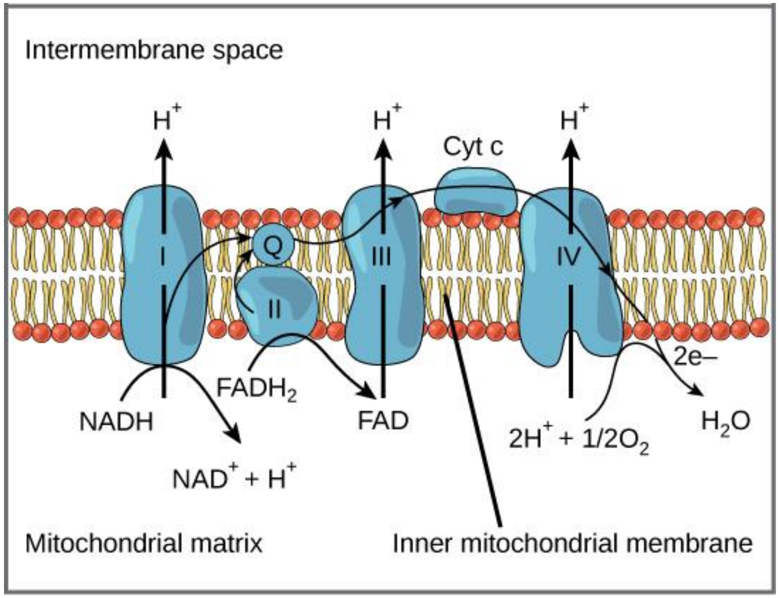
2. Electron carriers

Ubiquinone (Coenzyme Q):

- It acts as a mobile electron carrier between Complexes I/II and III.

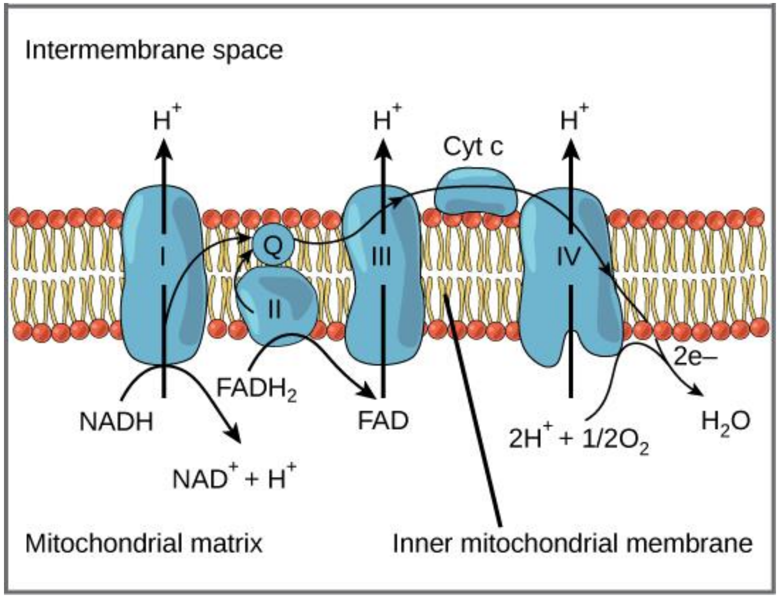
Cytochrome c:

- A small heme protein that shuttles electrons between Complex III and IV.



Formation of proton gradient

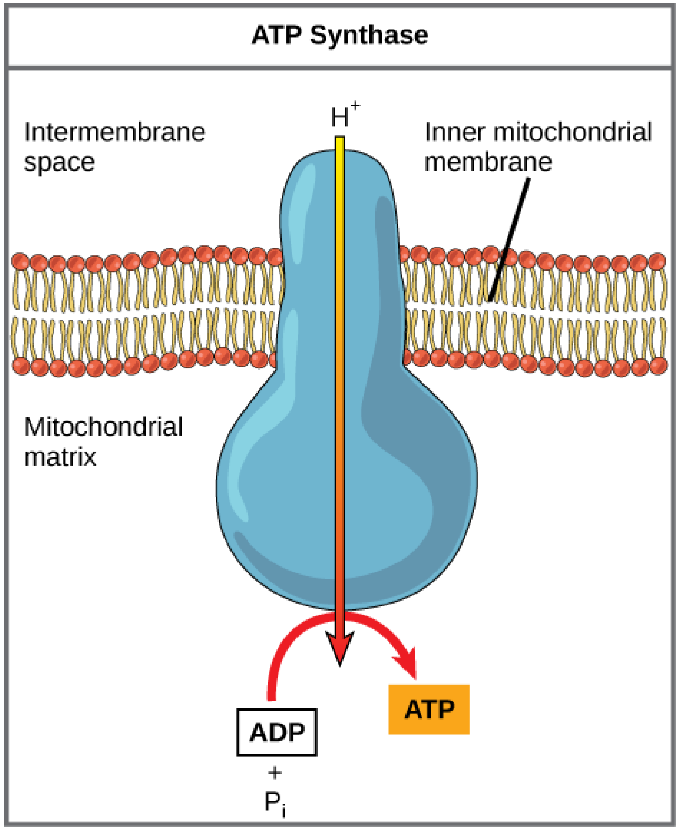
- Electrons from NADH and FADH2 are transferred along the ETC, with each complex successively becoming reduced and oxidized.
- As electrons are transferred, energy is released and used to pump protons from the mitochondrial matrix into the intermembrane space, creating a proton gradient (proton motive force).
- Molecular oxygen serves as the final electron acceptor in the ETC, accepting electrons from Complex IV and forming water along with protons.



Formation of proton gradient (cont.)

- The proton gradient generated across the inner mitochondrial membrane drives protons back into the mitochondrial matrix through ATP synthase (a protein complex embedded in the membrane).

- ATP synthase harnesses the energy of proton flow to catalyze the phosphorylation of ADP to ATP (a process known as oxidative phosphorylation).



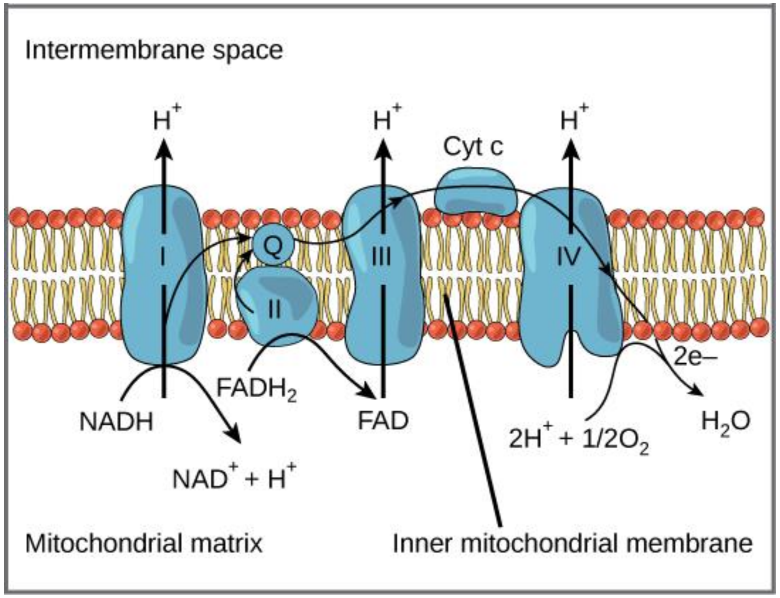
Role of oxygen in ETC

End of metabolic pathway of ETC:

- Oxygen serves as. the final electron acceptor in the ETC (accepting electrons from Complex IV) and combining with protons to form water

- The presence of oxygen ensures the continued flow of electrons through the ETC and the maintenance of the proton gradient necessary for ATP synthesis.

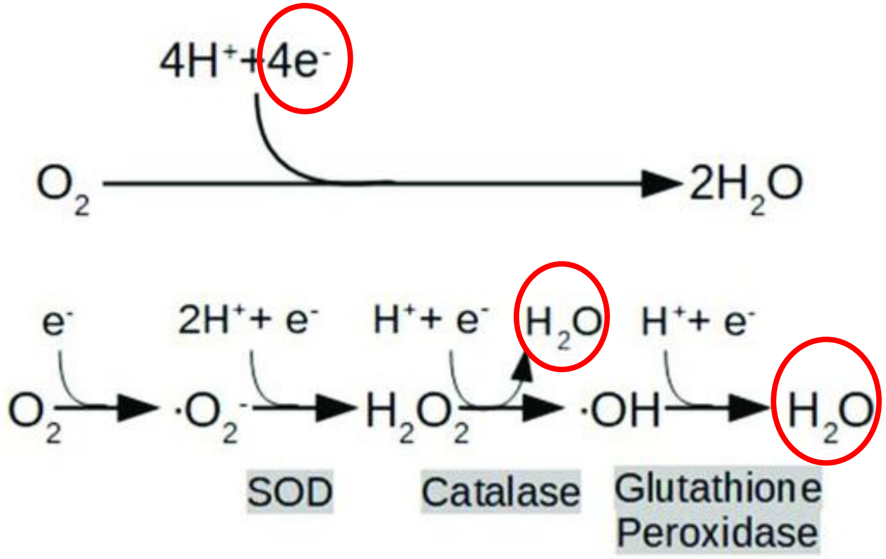
- In the absence of oxygen, electron transport ceases, and ATP synthesis cannot occur efficiently, leading to a decrease in cellular energy production.



Role of oxygen in ETC (cont.)

End of metabolic pathway of ETC (cont.):

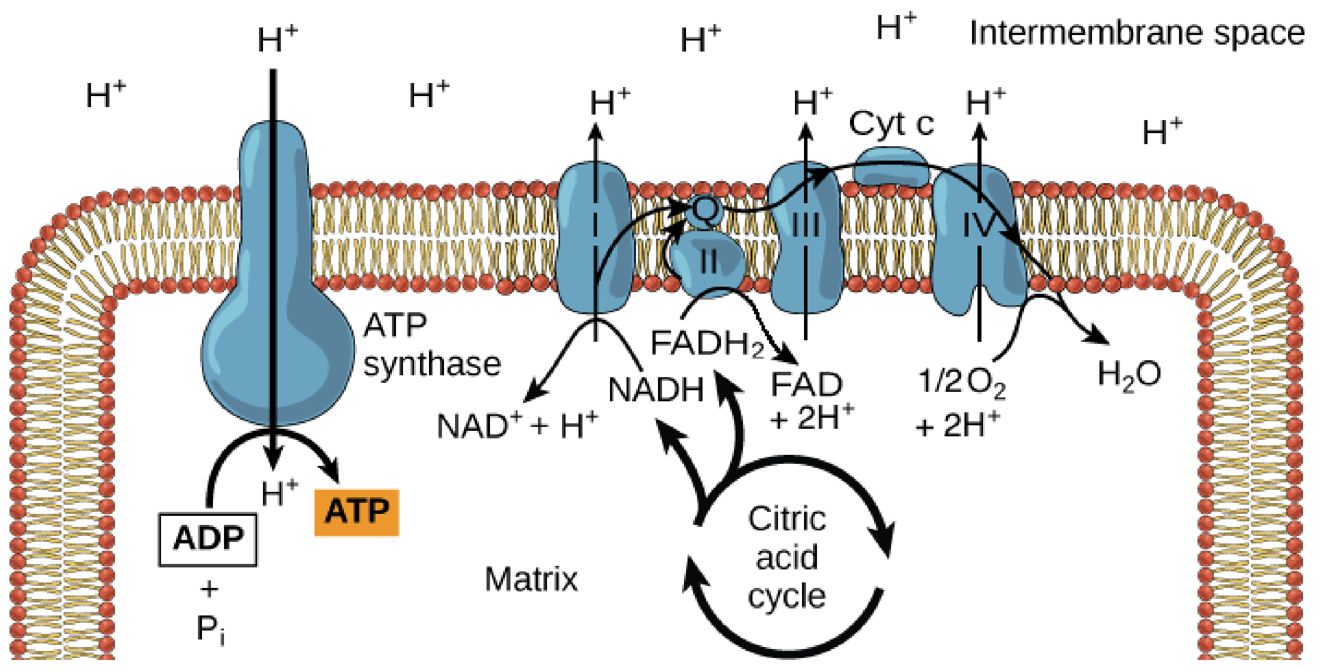
- The reduction of molecular oxygen to water and the formation of reactive oxygen spices.



SOD = Superoxide dimutase.

Oxidative phosphorylation

- Oxidative phosphorylation is the final stage of cellular respiration (occurring in the mitochondria of eukaryotic cells) where the majority of ATP is generated.
- It involves the coupling of electron transport through the ETC with the phosphorylation of ADP to form ATP.



Oxidative phosphorylation (cont.)

- During the ETC, electrons from NADH and FADH2 are transferred through a series of protein complexes, leading to the pumping of protons (H^+) from the mitochondrial matrix to the intermembrane space.
- This creates a proton gradient across the inner mitochondrial membrane, with a higher concentration of protons in the intermembrane space compared to the mitochondrial matrix.
- The proton gradient established drives protons back into the mitochondrial matrix through a protein complex called ATP synthase (Complex V).

Note:

The flow of protons across the membrane (proton motive force), coupled with the synthesis of ATP (by ATP synthase) is called chemiosmosis.

Oxidative phosphorylation (cont.)

ATP synthase:

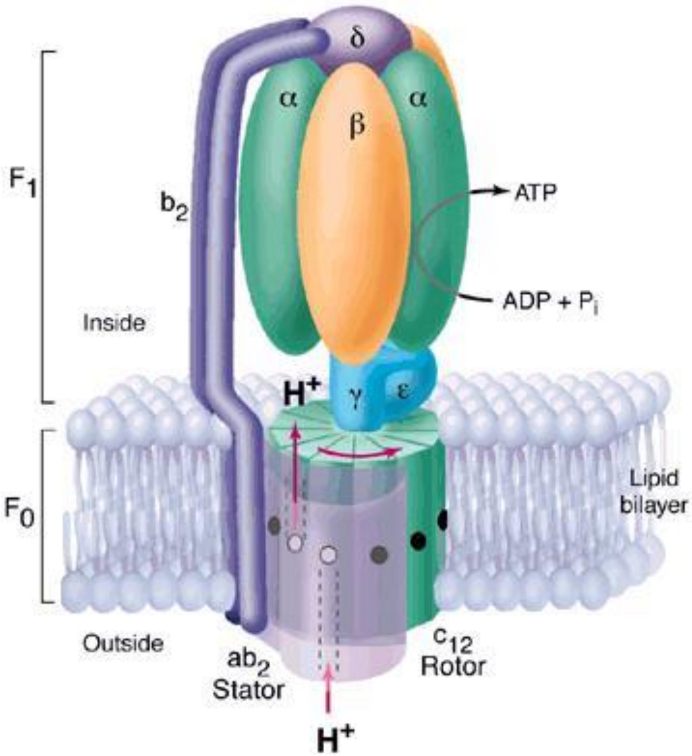
- ATP synthase acts as a molecular engine, harnessing the flow of protons to catalyze the phosphorylation of ADP to ATP.

- ATP synthase consists of two main components, F_o and F_1.

F_o (water-insoluble integral transmembrane protein):

- It spans the inner mitochondrial membrane and forms a proton channel through which protons flow.

- It consists of multiple subunits vary depending on the organism.



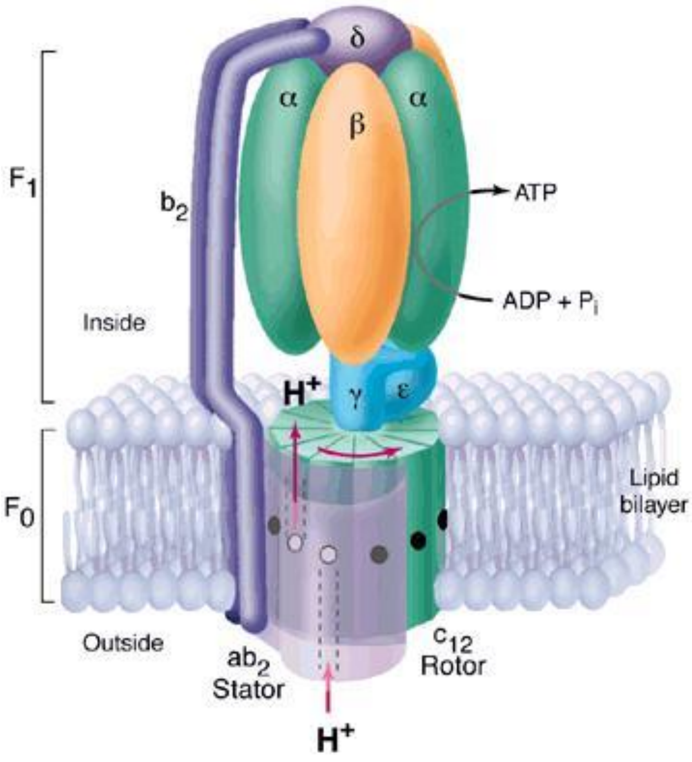
Oxidative phosphorylation (cont.)

ATP synthase (cont.):

F_1 (water-soluble peripheral membrane protein):

- It is located in the mitochondrial matrix and contains the catalytic sites responsible for ATP synthesis.

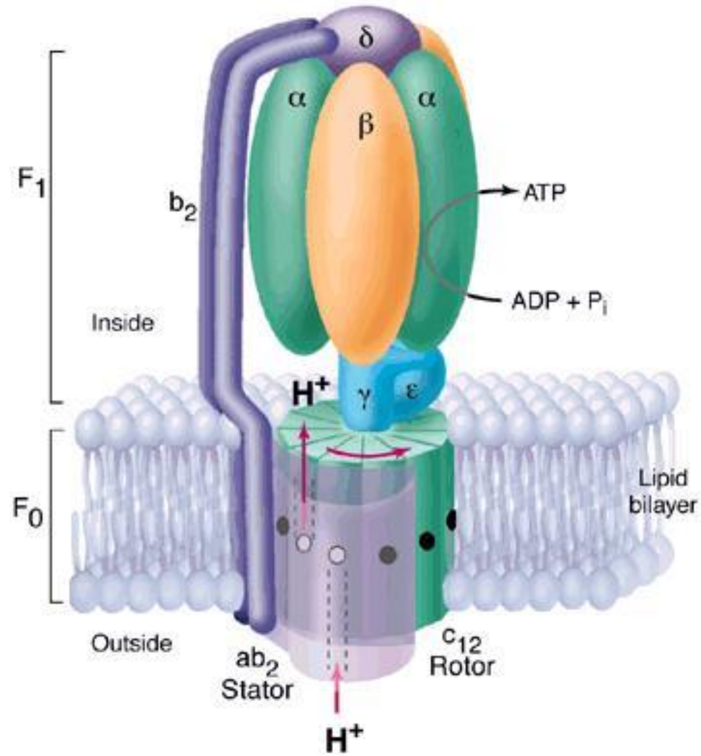
- It consists of 5 subunits (α, β, γ, δ, and ε).



Oxidative phosphorylation (cont.)

ATP synthase (cont.):

- As protons flow through F_o (from the intermembrane space back to the mitochondrial matrix) the energy released is used to drive the rotation of a rotor subunit (γ axel) within ATP synthase.
- This rotational motion of the rotor causes conformational changes in F_1, which promote the synthesis of ATP from ADP and Pi.
- Approximately one molecule of ATP is produced by every three protons pass through the ATP synthase channel.

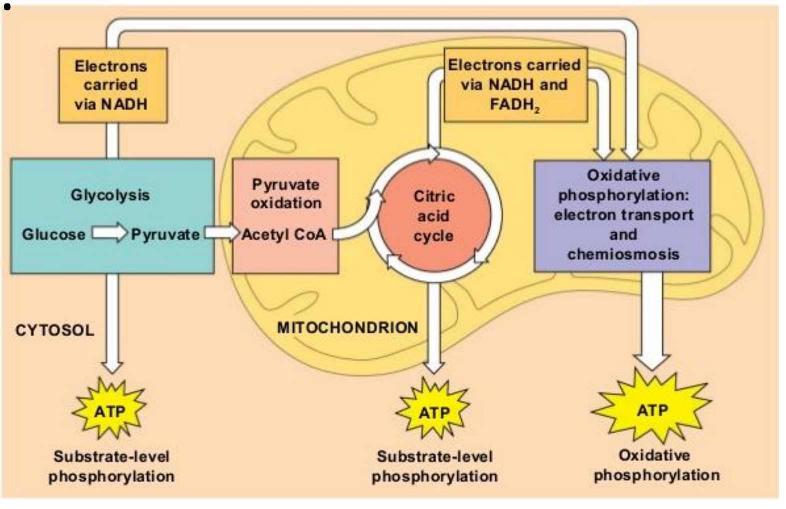


https://youtu.be/k_DQ1FjFuYM?si=xVMceGeR1S3CciBb

Oxidative phosphorylation (cont.)

ATP yield:

- Out of the 38 molecules of ATP generated from the complete oxidation of one molecule of glucose in aerobic conditions:
  - Only 3 ATP molecules are generated from substrate-level phosphorylation (two ATP in glycolysis and one ATP (GTP) in TCA cycle).
  - The majority of ATP molecules (34 ATP) are generated by the ETC and oxidative phosphorylation.



Oxidative phosphorylation (cont.)

ATP yield (cont.):

NADH:

- NADH generated during glycolysis and the Krebs cycle produces ATP through oxidative phosphorylation.
- For each NADH molecule oxidized by the ETC, approximately 3 ATP molecules are synthesized.

FADH2:

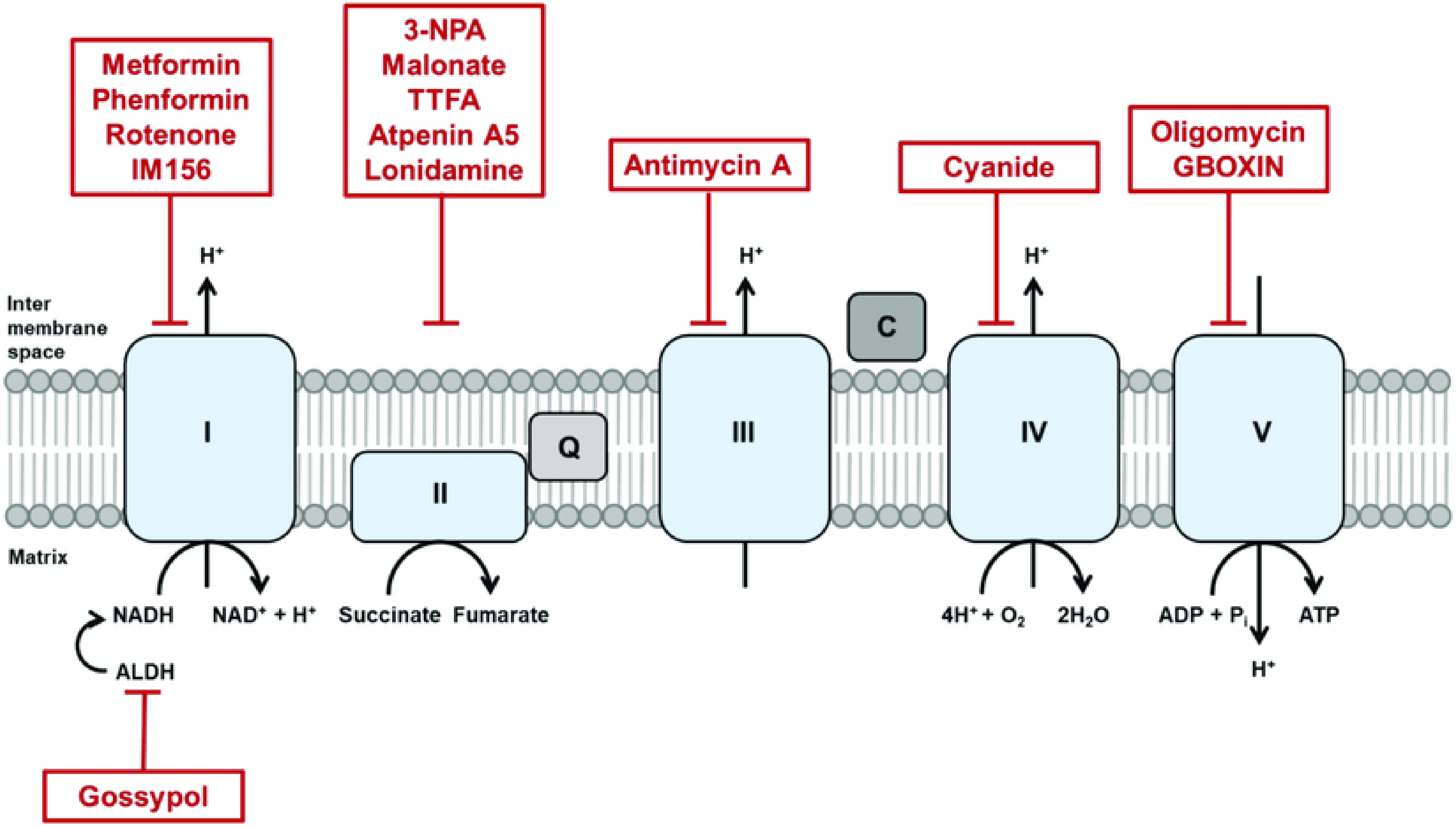
- FADH2 generated specifically in the Krebs cycle also contributes to ATP production.
- Each FADH2 molecule oxidized by the ETC produces approximately 2 ATP molecules.

Inhibition of respiratory chain

- Inhibition of the respiratory chain is the process by which the activity of one or more components of the ETC is impaired, leading to a decrease in the flow of electrons and ultimately affecting ATP synthesis (energy production).

- Several factors and substances can inhibit the respiratory chain, disrupting cellular energy metabolism. Some examples include:
  - **Rotenone:** inhibits Complex I (NADH dehydrogenase).
  - **Malonate:** inhibits Complex II (succinate dehydrogenase).
  - **Antimycin A**: inhibits Complex III (cytochrome bc1 complex).
  - **Cyanide and carbon monoxide:** both inhibit Complex IV (cytochrome c oxidase).
  - **Oligomycin:** inhibits Complex V (ATP synthase).

Inhibition of respiratory chain



Summary

- The ETC plays a crucial role in ATP production during cellular respiration.
- It efficiently converts the energy stored in NADH and FADH2 into ATP through the generation of a proton gradient and subsequent chemiosmotic synthesis of ATP.
- Oxidative phosphorylation (by the action of ATP synthase) generates a significant portion of the total ATP yield during cellular respiration.
- The ATP yield from oxidative phosphorylation provides cells with the energy required for various metabolic activities and physiological processes.