

ELECTRON TRANSPORT CHAIN

Electron Transport Chain Components/ Electron Carriers:

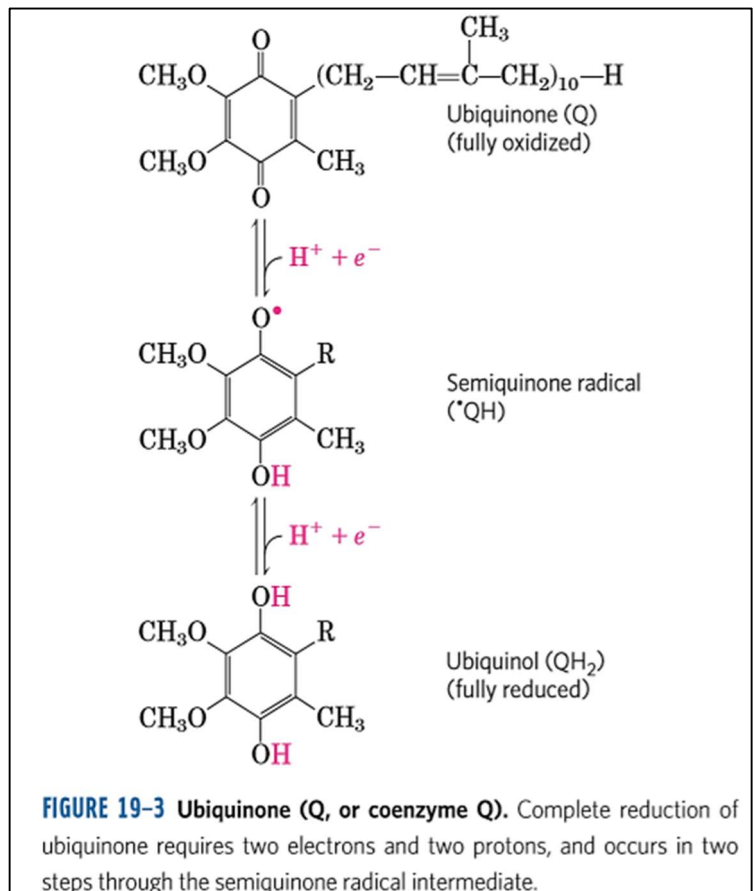
The mitochondrial respiratory chain consists of a series of sequentially acting electron carriers, most of which are integral proteins with prosthetic groups capable of accepting and donating either one or two electrons.

TABLE 19-3 The Protein Components of the Mitochondrial Electron-Transfer Chain

Enzyme complex/protein	Mass (kDa)	Number of subunits*	Prosthetic group(s)
I NADH dehydrogenase	850	43 (14)	FMN, Fe-S
II Succinate dehydrogenase	140	4	FAD, Fe-S
III Ubiquinone:cytochrome <i>c</i> oxidoreductase	250	11	Hemes, Fe-S
Cytochrome <i>c</i> [†]	13	1	Heme
IV Cytochrome oxidase	160	13 (3-4)	Hemes; Cu _A , Cu _B

- **NADH (Nicotinamide Adenine Dinucleotide):** A high-energy, water-soluble electron carrier derived from vitamin B3 (niacin). Acts as the primary electron donor for the ETC, feeding electrons directly into Complex I.
- **FAD / FADH₂ (Flavin Adenine Dinucleotide):** A riboflavin-derived (vitamin B2) coenzyme covalently bound as a prosthetic group to Complex II. Acts as a lower-energy electron donor that bypasses Complex I, entering the ETC directly at Complex II (succinate dehydrogenase).

- Ubiquinone (Q, or coenzyme Q):** In its fully oxidized state, ubiquinone (Q) features a quinone ring structure attached to a long, hydrophobic isoprenoid tail. The reduction process begins when ubiquinone accepts a single proton (H^+) and a single electron (e^-), transforming it into a semiquinone radical ($\cdot QH$), which is a highly reactive intermediate state. In the second step, this intermediate accepts another proton and electron, completing the transformation into ubiquinol (QH_2), the fully

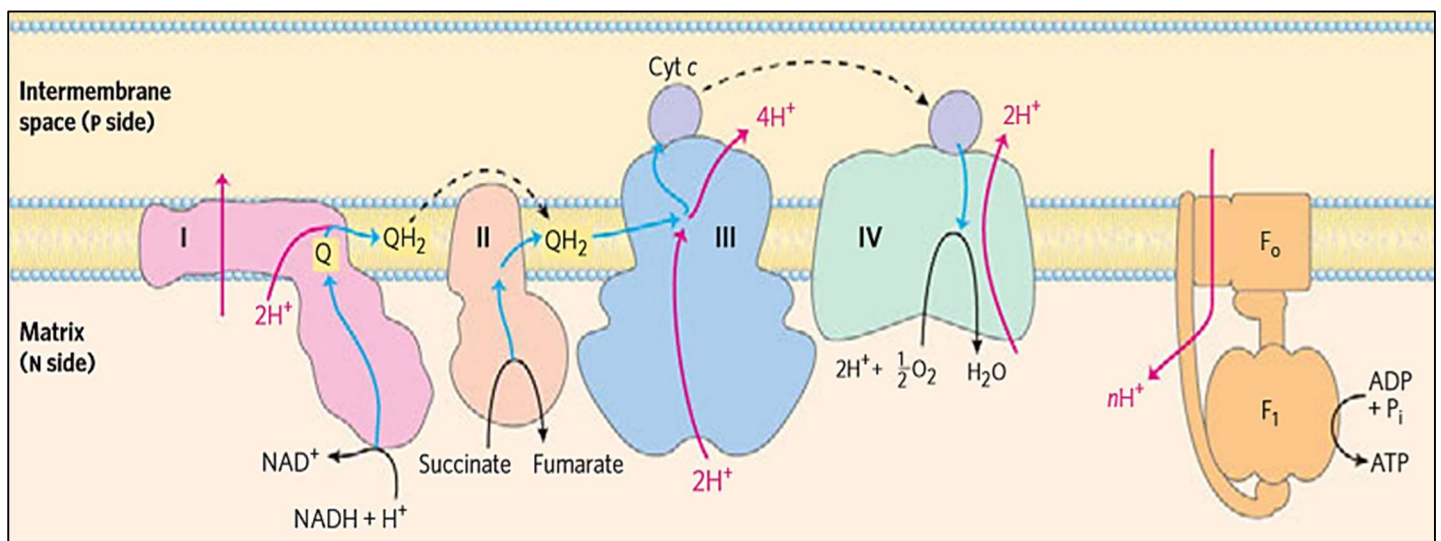


- reduced form. Because it can alternate between these oxidized, radical, and reduced states, coenzyme Q functions as a mobile electron shuttle within the inner mitochondrial membrane, effectively bridging the transfer of electrons between different complexes in the respiratory chain.
- Cytochromes:** A class of membrane-bound proteins containing a characteristic iron-containing heme prosthetic group. Functions as sequential single-electron carriers (such as Cytochrome c, b, and a_3) moving electrons between Complex III, Complex IV, and eventually to oxygen. Transfers one electron at a time via the reversible oxidation-reduction of the iron atom ($Fe^{2+} \rightleftharpoons Fe^{3+}$).
- Electrons in the chain are transferred from substrate to oxygen through a series of electron carriers.

- Prosthetic groups in the ETC are non-protein, tightly bound cofactors (FMN, FAD, FeS clusters, hemes and copper) that facilitate electron transfer within complexes I – IV.
- Complexes I and II catalyze electron transfer to ubiquinone from two different electron donors: NADH (Complex I) and succinate (Complex II). Complex III carries electrons from reduced ubiquinone to cytochrome c, and Complex IV completes the sequence by transferring electrons from cytochrome c to O₂.

ELECTRON TRANSPORT CHAIN:

The electron transport chain is a series of protein complexes and organic molecules embedded in a cell membrane. It transfers electrons from donors like NADH and FADH₂ to a final acceptor through redox reactions. This movement pumps protons across the membrane to create an electrochemical gradient that drives ATP synthesis.



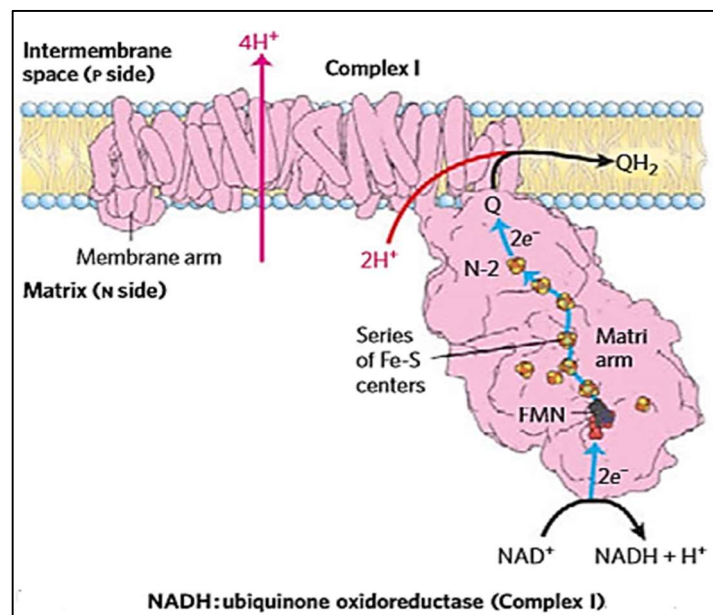
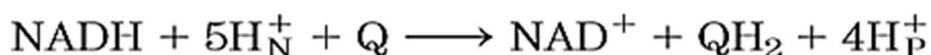
Electron Transport Chain Complexes:

A chain of four enzyme complexes is present in the electron transport chain that catalyzes the transfer of electrons through different electron carriers to the molecular oxygen. Complexes I and II catalyze electron transfer to ubiquinone from two different electron donors: NADH (Complex I) and succinate (Complex II). Complex III carries electrons from reduced ubiquinone to cytochrome c, and Complex IV completes the sequence by transferring electrons from cytochrome c to O₂.

Complex I: NADH: Ubiquinone Oxidoreductase or

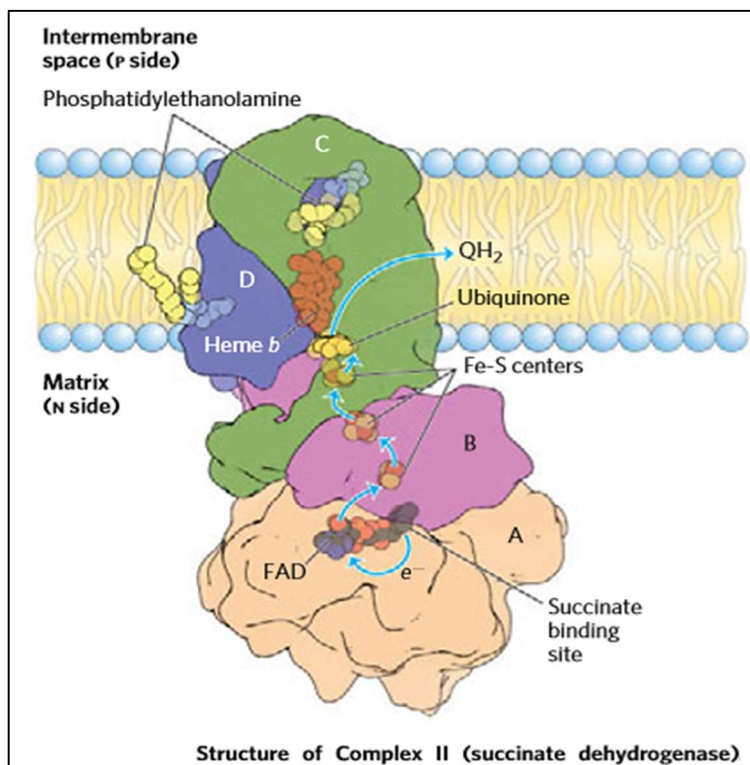
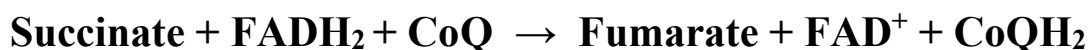
NADH Dehydrogenase

- In Complex I, electrons first flow from NADH to FMN (flavin mononucleotide), then to an iron-sulfur (Fe-S) cluster, and finally to CoQ.
- At the same time, the complex translocates four H⁺ ions through the membrane, creating a proton gradient.
- The overall reaction catalyzed by this complex is:



Complex II: Succinate Dehydrogenase

- Succinate dehydrogenase, the enzyme that oxidizes a molecule of succinate to fumarate in the Krebs cycle.
- The released two electrons in conversion of succinate to fumarate are transferred from FADH₂ to Ubiquinone (Q). Electrons are transferred first to FAD (flavin adenine dinucleotide), then to Fe-S, and finally to CoQ.
- The overall reaction catalyzed by this complex is:

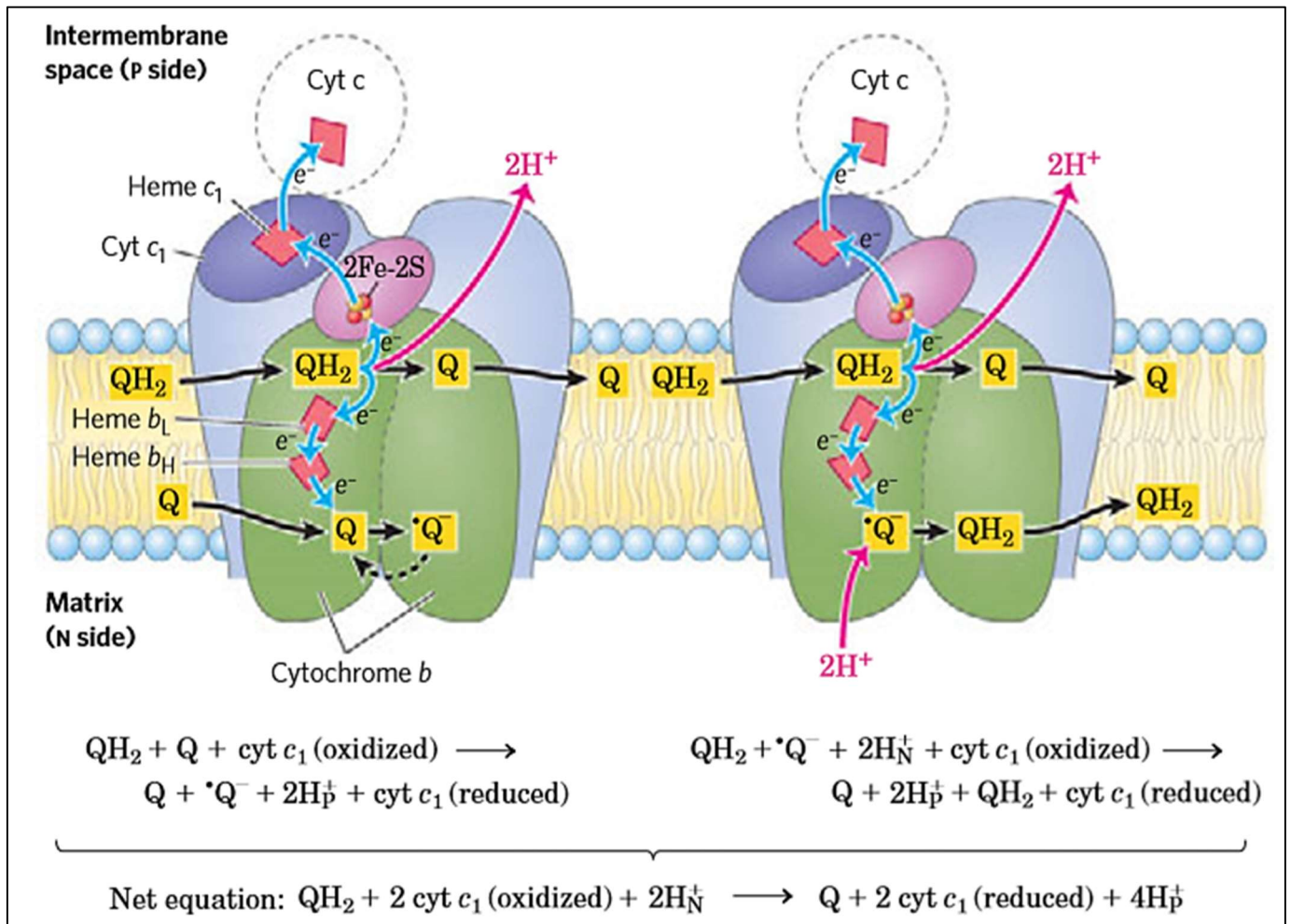


Coenzyme Q (CoQ)

- It is also called **ubiquinone**, is the only electron carrier in ETC that is not a protein bound prosthetic group.
- Receives electrons from both complex I and complex II, becoming reduced to ubiquinol (QH₂), and transfers them to complex III.
- Both CoQ and CoQH₂ are soluble in phospholipids and diffuse freely in the inner mitochondrial membrane.

Complex III: Cytochrome bc₁ Complex Or

Ubiquinone : Cytochrome c Oxidoreductase



- **The Q cycle mechanism within Complex III (Cytochrome bc₁ complex)** of the mitochondrial electron transport chain. It describes how electrons are

transferred from fat-soluble **ubiquinol (QH₂)** to water-soluble **cytochrome c (Cyt c)**, while simultaneously pumping protons across the inner mitochondrial membrane to drive ATP synthesis.

- The Q cycle, shown in two stages. In the first stage (left), a molecule of ubiquinol (**QH₂**) binds near the intermembrane space (P side). It is oxidized, releasing two protons (2H⁺) into the intermembrane space.
 - * Its two electrons split paths: one goes upward through the iron-sulfur center (2Fe-2S) and heme (c₁) to reduce a **cytochrome c** carrier.
 - * The other electron travels downward through heme b_L and heme b_H to partially reduce a ubiquinone (Q) molecule at the matrix side (N side), forming a **semiquinone radical (·Q·)**.
- In the second stage (right), a second **QH₂** molecule undergoes the same oxidation at the P side, pumping two more protons (2H⁺) and reducing a second **cytochrome c**.
 - * The downward electron travels to the matrix side to finish reducing the waiting semiquinone radical (·Q·). This radical absorbs two protons (2H⁺) from the matrix, regenerating a fully reduced **QH₂** molecule.
- Ultimately, for every net ubiquinol molecule consumed, two cytochrome c molecules are reduced, two matrix protons are absorbed, and four protons are translocated into the intermembrane space.

Cytochromes c:

- Electron flow through the cytochromes occurs by oxidation and reduction of the Fe atom in the center of the heme molecule.



- In ETC, electrons move through the cytochromes in the following order: b, c₁, c, a, and a₃. Transfer electrons from complex III to complex IV.

Complex IV: Cytochrome c Oxidase

- This is final enzyme complex in the mitochondrial electron transport chain embedded within the inner membrane. The process begins on the intermembrane space (P side), where four reduced **cytochrome c** molecules sequentially deliver a total of four electrons ($4e^-$) to the copper center **Cu_A** in Subunit II.
- These electrons travel down through **Heme a** to the binuclear active site containing **Heme a₃** and **Cu_B** (the Fe-Cu center) in Subunit I.
- Here, the electrons reduce a single molecule of **molecular oxygen (O₂)** by binding it alongside four substrate protons ($4H^+$) extracted from the matrix (N side), ultimately generating two molecules of water ($2H_2O$).
- Concurrently, the free energy released by this highly exergonic reduction drives a conformational change that actively pumps four additional protons ($4H^+$) from the matrix into the intermembrane space.
- The overall reaction catalyzed by this complex is:

