Module 18 / 
# Electron Transport and Oxidative Phosphorylation

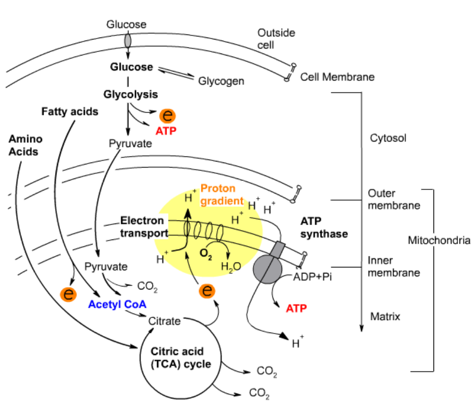


| | | |
|---|---|---|
| Explain the role of the four complexes, coenzyme Q, and cytochrome C in electron transport. | Identify the pathway of the electrons from NADH to oxygen resulting in the formation of water. | Identify the pathway of the electrons from $FADH_2$ to oxygen resulting in the formation of water. |
| Explain what happens when electrons transport through complexes I, III, and IV. | Predict whether the free energy stored in the non-equilibrium hydrogen ion gradient is sufficient to sythesize ATP from the transport of 3 protons. | Explain ATP synthase and the effects of allosteric changes during proton translocation. |

The production of ATP from "high-energy" electrons on NADH and $FADH_2$ occurs in two steps, electron transport followed by ATP synthesis. The energy obtained from electron transport is stored as a pH gradient across the inner mitochondrial membrane. The combination of a concentration difference of hydrogen ions and a voltage difference accross this membrane is often referred to as an **electrochemical gradient**. The electrochemical gradient is a form of potential energy that is utilized by the enzyme ATP synthase to convert ADP to ATP. The coupling between the proton gradient and the chemical synthesis of ATP, was originally proposed by Dr. Peter Michell in 1961 as the **chemiosmotic hypothesis**. His theory proved to be true, leading to a Nobel prize for his work in 1978.

## Electron Transport

The electron transport chain consists of **four multi-protein complexes** that are contained within the **inner mitochondrial membrane**. These complexes remove electrons from NADH or $FADH_2$ molecules that were generated by oxidative processes in glycolysis and the TCA cycle. These high energy compounds ultimately deposit their electrons on oxygen, forming water. The energy that is released by electron transport is stored as a proton gradient across the inner mitochondrial membrane. This proton gradient is used to drive the synthesis of ATP.




The hilighted region focusing in on the **Electron Transport Chain**, part of the complex process of metabolism.

The highlighted region focusing in on the **Electron Transport Chain**, part of the complex process of metabolism.

Various compounds are used by the electron transport chain to carry electrons. These components include:

- **FAD/FADH$_2$**, is a cofactor that is tightly bound to the enzymes in the electron transport complexes.
- **Iron-sulfur** centers in the electron transport complexes shuttle electrons by alternating between $Fe^{+2}$ and $Fe^{+3}$.
- **Coenzyme Q** is an organic non-polar electron carrier that is dissolved within the membrane lipids of the inner mitochondrial membrane. It carries electrons between complex I and III and complex II and III.
- **Cytochrome C** is a heme containing protein that is very similar in structure to myoglobin. It is a water soluble protein found in the inter-membrane space. Cytochrome C carries one electron at a time from complex III to complex IV.

The organization of the four complexes and electron carriers in the electron transport chain are illustrated in the following diagram:

Flash Player needed! Please click here to install Flash Player.

The electron transport chain is contained within the inner membrane of the mitochondria. In addition to the four protein complexes, the location of electron carriers coenzymeQ and cytochrome C are also indicated. Complex I accepts electrons from NADH and complex II accepts electrons from succinate. Complex IV is responsible for transferring the electrons to the final electron acceptor, oxygen. **Selecting the button labeled NADH** will show the flow of electrons from **NADH to complex IV**. The button labeled **FADH$_2$** will show the path of electrons from **succinate to FADH$_2$ in complex II** (succinate dehydrogenase), followed by movement of these electrons to complex IV.

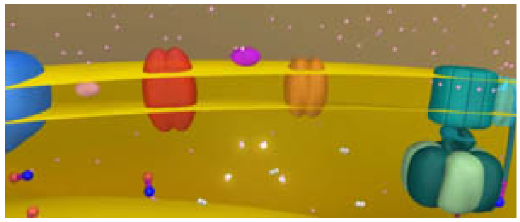
**NADH** is oxidized by the electron transport chain by the transfer of the two electrons from NADH to complex I. These electrons are then transferred to coenzyme Q, followed by transfer to complex III. The electrons are then carried by cytochrome C to complex IV, where the electrons are used to reduce oxygen to water. The energy that is released by the transfer of electrons from NADH to water is used to transport a total of 10 protons across the inner membrane. For every pair of electrons, four protons are transported by complex I, four by complex II and two by complex IV.

The electrons from **FADH$_2$** are first processed by complex II. Complex II is actually succinate dehydrogenase from the TCA cycle. The electron acceptor for succinate, FAD, is tightly bound to the enzyme. Consequently, it is more correct to consider that complex II processes the electrons from succinate, first passing them to FAD and then via iron-sulfur centers to coenzyme Q. The two electrons then follow the same path as those from NADH$_2$, from coenzyme Q to complex III, and then to complex IV via cytochrome C, finally to oxygen to produce water. Since electron transport through complex II does not result in the transport of protons only a total of 6 protons/2 electrons are transported across the inner membrane when succinate is the initial electron donor.

In summary:

In summary:

- Electrons from NADH and $FADH_2$ are transferred to oxygen, generating water.
- Electron transport is spontaneous and releases energy. This energy is stored by transporting protons across the inner membrane.
- Oxidation of NADH results in 10 protons transported across the inner membrane.
- Oxidation of $FADH_2$ results in 6 protons transported across the inner membrane.



This link will take you to a movie providing an alternate representation of the electron transport process.

## ATP Synthesis

The energy that has been stored in the proton gradient across the inner mitochondrial membrane cannot be easily utilized by other processes in the cell. It must be converted to a more usable source, such as ATP. The enzyme ATP synthase is responsible for converting the energy stored in the proton gradient to ATP. This enzyme is found in the inner mitochondrial membrane and it projects into the matrix.

The mechanism of ATP synthase is such that the enzyme generates one ATP molecule every time 3 protons are transferred back to the matrix from the inter-membrane space. Since the standard energy for the formation of ATP from ADP and Pi is +30 kJ/mol the transport of three protons must release at least 30kJ/mol in order to provide enough energy to synthesize ATP. The amount of energy that is stored in the protein gradient can be obtained by calculating the Gibbs free energy. If the products are defined as the protons that have been transported to the matrix, the formula is:

$$\Delta G = RT\ \ ln\,\frac{[H^+]_{IN}}{[H^+]_{OUT}} + ZF\Delta\Psi$$

where Z is the change on the transported particle, F is Faraday's constant (96,494 Coulomb/mol) and $\Delta\Psi$ is the voltage difference across the membrane:

$$\Delta\Psi = V_{IN} - V_{OUT}$$

The Gibbs free energy consists of two terms. The first indicates the energy change due to the difference of proton concentration across the membrane. Its form is analogous to the formula give for the transport of glucose across the membrane in glycolysis. The second term accounts for the fact that the energy of a charged particle depends on the voltage. If there is a voltage difference across the membrane then the energy of the proton will depend on its location.

Typical proton concentration differences across the inner membrane are approximately 10 fold, with the outside being more acidic. In addition to the concentration difference, there is also an approximately 100 mV voltage difference across the membrane, with the inside being more negative. Therefore, the Gibbs free energy change under these conditions at 300 K is:

$$\Delta G = R(300)\,ln\,\frac{1}{\ldots} + 1 \times 96494 \times (-0.1)$$

$$\Delta G = R(300)\, ln \frac{\ }{10} + 1 \times 96494 \times (-0.1)$$
$$= -5.7 - 9.6\ kJ/mol$$
$$= -15.3\ kJ/mol$$

Therefore the transport of 3 protons will release 45.9 kJ/mol, which is more than sufficient to generate a single ATP.

## Mechanism of ATP Synthase

The synthesis of ATP utilizing the proton gradient as a source of energy is an example of direct coupling. The energy released as the protons flow through the enzyme cause a conformational change in the protein that causes the formation of ATP from bound ADP and inorganic phosphate.

The enzyme consists of two separable subunits. The $F_o$ subunit is within the membrane and is responsible for the transfer of protons through the membrane. The $F_1$ subunit extends into the mitochondrial matrix and is responsible for the synthesis of ATP. The $F_1$ subunit is composed of three $\alpha$ subunits and three $\beta$ subunits. These six subunits from a spherical structure where the $\alpha$ and $\beta$ subunits alternate. The $\gamma$ subunit extends from the $F_o$ domain through the center of the $\alpha$-$\beta$ sphere. The $\gamma$ subunit rotates 120 degrees every time three protons flows through the $F_o$ domain. The $\alpha$-$\beta$ sphere is prevented from rotating along with the $\gamma$ subunit by the b-subunit, which anchors the $\alpha$-$\beta$ sphere to the membrane.

The conformation of the $\alpha$-$\beta$ subunits is affected by the relative position of the $\gamma$ subunit. Since the gamma subunit rotates $120^o$, there are three possible conformations of the $\alpha$-$\beta$ subunits:

- A conformation that has low affinity of nucleotides, i.e. neither ATP or ADP bind.
- A conformation that has high affinity for ADP plus inorganic phosphate.
- A conformation that has high affinity for ATP, i.e. ATP is more stable in this conformation than ADP.

The cycle of ATP synthesis is as follows:

1. ADP and inorganic phosphate bind to the subunits that have high affinity for these compounds.
2. A three protons flow through the $F_o$ domain, causing a $120^o$ rotation of the $\gamma$-subunit.
3. The rotation of the $\gamma$-subunit causes a conformational change in the $\alpha$-$\beta$ subunits.
4. ATP is more stable in the new conformation of the $\alpha$-$\beta$ subunits, consequently the bound ADP and inorganic phosphate is spontaneously converted to ATP.
5. Another three protons flow through the $F_o$ domain, causing another $120^o$ rotation of the $\gamma$ subunit.
6. This rotation causes an additional conformational change of the $\alpha$-$\beta$ subunits, generating the conformation that has low affinity for ATP and ADP, thus the newly synthesized ATP is released.
7. A three additional protons flows through the $F_o$ domain, causing another rotation of $\gamma$ subunits. This restores the system to the starting conditions.

Complete rotation of the $\gamma$ subunit requires the transfer of 9 protons across the membrane. This generates a total of 3 ATP molecules since there are three ADP/ATP binding sites on the $F_1$ domain, one associated with each $\alpha$-$\beta$ subunit. Consequently, only three protons are required to synthesize one ATP.

Click the green arrow or PLAY button to play the animation.

## did I get this

The movement of electrons down the electron transport chain performs work. The work is used to

- synthesize AcetylCoA
- hydrolyze ATP
- pump protons
- synthesize ATP

NEXT » Reset this Activity

88