In the ETC, electrons pass through a series of protein complexes and e⁻ carriers to O₂. Intermediate steps (instead of direct transfer to O₂) allow multiple opportunities for coupling e⁻ transfers with H⁺ translocations.
Each protein complex contains multiple redox cofactors used to transfer electrons.

Electrons move from cofactors of lower to higher reduction potential within each complex and from one complex or carrier to the next.

<table>
<thead>
<tr>
<th>Component</th>
<th>$E^{\circ'}$ (V)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NADH</td>
<td>−0.315</td>
</tr>
<tr>
<td>Complex I (NADH–CoQ oxidoreductase; ~900 kD, 46 subunits):</td>
<td></td>
</tr>
<tr>
<td>FMN</td>
<td>−0.340</td>
</tr>
<tr>
<td>[2Fe–2S]N1a</td>
<td>−0.380</td>
</tr>
<tr>
<td>[2Fe–2S]N1b</td>
<td>−0.250</td>
</tr>
<tr>
<td>[4Fe–4S]N3, 4, 5, 6a, 6b, 7</td>
<td>−0.250</td>
</tr>
<tr>
<td>[4Fe–4S]N2</td>
<td>−0.100</td>
</tr>
<tr>
<td>Succinate</td>
<td>0.031</td>
</tr>
<tr>
<td>Complex II (succinate–CoQ oxidoreductase; ~120 kD, 4 subunits):</td>
<td></td>
</tr>
<tr>
<td>FA D</td>
<td>−0.040</td>
</tr>
<tr>
<td>[2Fe–2S]</td>
<td>−0.030</td>
</tr>
<tr>
<td>[4Fe–4S]</td>
<td>−0.245</td>
</tr>
<tr>
<td>[3Fe–4S]</td>
<td>0.060</td>
</tr>
<tr>
<td>Heme $b_{560}$</td>
<td>−0.080</td>
</tr>
<tr>
<td>Coenzyme Q</td>
<td>0.045</td>
</tr>
</tbody>
</table>

| Complex III (CoQ–cytochrome c oxidoreductase; ~450 kD, 9–11 subunits): | |
| Heme $b_{H}$ ($b_{562}$) | 0.030 |
| Heme $b_{L}$ ($b_{566}$) | −0.030 |
| [2Fe–2S] | 0.280 |
| Heme $c_{1}$ | 0.215 |
| Cytochrome c | 0.235 |

| Complex IV (cytochrome c oxidase; ~410 kD, 8–13 subunits): | |
| Heme $a$ | 0.210 |
| Cu$_A$ | 0.245 |
| Cu$_B$ | 0.340 |
| Heme $a_{3}$ | 0.385 |
| O$_2$ | 0.815 |

Electrons enter the ETC (and are transferred to CoQ) through different enzymes.
Complex I (NADH-CoQ oxidoreductase) is a large, L-shaped protein complex.
Complex I uses three kinds of redox centers

**FMN**

Flavin nucleotides transfer one or two $e^-$ (and $H^+$) at a time

**2Fe-2S center**

Iron-sulfur clusters transfer only one $e^-$ at a time

**4Fe-4S center**

Iron-sulfur clusters transfer only one $e^-$ at a time
NADH transfers a hydride to FMN, then e- move one-by-one (via Fe-S centers) to CoQ
Coenzyme Q is a membrane-soluble, diffusible electron (and proton) carrier.
Complex I may translocate protons via proton jumping (involving aa sidechains)

4 protons are translocated for every two electrons transferred
Complex II (succinate-CoQ oxidoreductase) is succinate dehydrogenase from TCA cycle.

Electrons move one-at-a-time from FAD to CoQ (No protons are pumped)
Electron transport involves different kinds of hemes

Hemes transfer one electron at a time

Heme $a$
Heme $b$
Heme $c$

Complex IV
Complexes II and III
(and hemoglobin & myoglobin)
Complex III and Cytochrome C
Cytochromes (heme-containing redox proteins) are named by heme type.

Wavelength of $\alpha$-peak is used to distinguish different cytochromes:

<table>
<thead>
<tr>
<th>Cytochrome</th>
<th>$\gamma$</th>
<th>$\beta$</th>
<th>$\alpha$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytochrome $a$</td>
<td>439</td>
<td></td>
<td>600</td>
</tr>
<tr>
<td>Cytochrome $b$</td>
<td>429</td>
<td>532</td>
<td>563</td>
</tr>
<tr>
<td>Cytochrome $c$</td>
<td>415</td>
<td>521</td>
<td>550</td>
</tr>
<tr>
<td>Cytochrome $c_1$</td>
<td>418</td>
<td>524</td>
<td>554</td>
</tr>
</tbody>
</table>
Q is reduced to QH$_2$ near the membrane-matrix interface of Complex I or II.
Complex III (CoQ-cytochrome c oxidoreductase) pumps protons with the help of CoQ

“Q-cycling” allows for the release of 4 protons to the IM space (from QH₂) for every 2e⁻ transferred to Cytochrome c
Cytochrome c is a small peripheral mb protein that diffuses in the IM space

Since it has just one heme, cytochrome c is a 1e⁻ carrier

Lysine sidechains are involved in binding to Complex IV
Complex IV (Cytochrome c oxidase) transfers electrons to $O_2$ (reducing it to $H_2O$)
4 electrons (and 4 matrix protons) are used to reduce one molecule of O$_2$ to 2 H$_2$O.
2-electron transfers from NADH→O₂ result in 10H⁺ translocated; from FADH₂→O₂, 6H⁺
The electrochemical potential of the proton gradient is used to drive ATP synthesis.

To make ATP, $4H^+$ move back into the matrix;

$$10/4 = 2.5 \text{ ATP per } 2e^- \text{ from NADH};$$

$$6/4 = 1.5 \text{ ATP per } 2e^- \text{ from FADH}_2$$