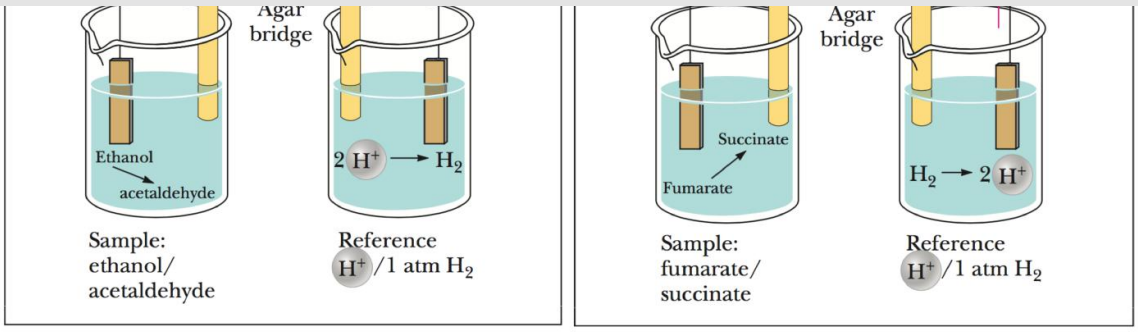
**Bioenergetics of Cellular Respiration**

Bioenergetics behind ETC allows us to understand how the proteins and prosthetic groups of the complexes were arranged. First, consider the most fundamental idea of redox reactions and aply it in the context of a simple voltaic cell as shown in Figure XX. The solution that contains an acidic solution, wherein protons or hydrogen ions are present is used as a reference. Take note that when hydrogen ions encounter electrons, they are reduced to form hydrogen gas, while the reverse process occurs during oxidation. The entire setup is



Moreover, the two test solutions are connected by an agar bridge and electron flow from either side of the cell is monitored through a potentiometer. When ethanol is added on the beaker for test solution, the potentiometer will provide a negative reading (-_). This suggests that electrons were produced during ethanol oxidation which turns it into acetaldehyde. Those electrons flow towards the other side of the cell and cause the hydrogen ions to be reduced to form hydrogen gas. This is evident as the reference solution forms bubbles. An opposite observation is obtained when succinctness-fumarole mixture is used as a test solution. The potentiometer provides a positive reading, indicative of electrons flowing from the reference solution towards the test solution. This suggests that the succinctness has been oxidized to form fumarate by acquiring electrons, and such electrons were provided through oxidation of Hydrogen gas into hydrogen ions and free electrons. To sum it up, test solutions with positive values of reduction potential are ore likely to be reduced (gain electrons) than those with lower (negative) reduction potential.

## Table 20.1

### Standard Reduction Potentials for Several Biological Reduction Half Reactions

| Reduction Half Reaction | $E^{\circ\prime}$ (V) |
|---|---|
| $\frac{1}{2}O_2 + 2H^+ + 2e^- \rightarrow H_2O$ | 0.816 |
| $Fe^{3+} + e^- \rightarrow Fe^{2+}$ | 0.771 |
| Cytochrome $a_3(Fe^{3+}) + e^-$ | 350 |
| Cytochrome $a(Fe^{3+}) + e^-$ | 290 |
| Cytochrome $c(Fe^{3+}) + e^-$ | 254 |
| Cytochrome $c_1(Fe^{3+}) + e^-$ | 220 |
| $CoQH^\bullet + H^+ + e^- \rightarrow CoQH$ | 190 |
| $CoQ + 2H^+ + 2e^- \rightarrow CoQH$ | 060 |
| Cytochrome $b_H(Fe^{3+}) + e^-$ | 050 |
| Fumarate + $2H^+ + 2e^- \rightarrow$ S | 031 |
| $CoQ + H^+ + e^- \rightarrow CoQH^\bullet$ | 030 |
| [FAD] + $2H^+ + 2e^- \rightarrow$ [FAI | 003–0.091* |
| Cytochrome $b_L(Fe^{3+}) + e^-$ | .100 |
| Oxaloacetate + $2H^+ + 2e^-$ | .166 |
| Pyruvate + $2H^+ + 2e^- \rightarrow$ La | .185 |
| Acetaldehyde + $2H^+ + 2e^-$ | .197 |
| FMN + $2H^+ + 2e^- \rightarrow$ FMNH | .219 |
| FAD + $2H^+ + 2e^- \rightarrow$ $FADH_2$ | .219 |
| 1,3-*bis*phosphoglycerate + | |
| Glyceraldehyde-3-phospha | .290 |
| $NAD^+ + 2H^+ + 2e^- \rightarrow$ NADH | .320 |
| $NADP^+ + 2H^+ + 2e^- \rightarrow NADPH + H^+$ | –0.320 |
| α-Ketoglutarate + $CO_2 + 2H^+ + 2e^- \rightarrow$ Isocitrate | –0.380 |
| Succinate + $CO_2 + 2H^+ + 2e^- \rightarrow$ α-Ketoglutarate + $H_2O$ | –0.670 |

*Typical values for reduction of bound FAD in flavoproteins such as succinate dehydrogenase.

Note that we have shown a number of components of the electron transport chain individually. We are going to see them again as part of complexes. We have also included values for a number of reactions we saw in earlier chapters.

As can be seen on the Table X, the reduction of NAD+ into NADH has a reduction potential of -0.320. As of what is currently known about the ETC, NADH is generated through glycolysis and Krebs cycle, and it carries electrons to the CI of ETC. Therefore, the equation in Table X can be reversed for this purpose together with the sign of the reduction potential for the reaction. On a related note, oxygen is the final electron acceptor in the ETC, wherein it is reduced to form water. The electrons ultimately come from oxidation of NADH. In Table X, it can be seen that reduction of Oxygen to glucose has the highest reduction potential (0.816). this suggests that it has the highest propensity to accept electrons. So when the reactions that gives off electrons and the one that accepts them are paired, we get:

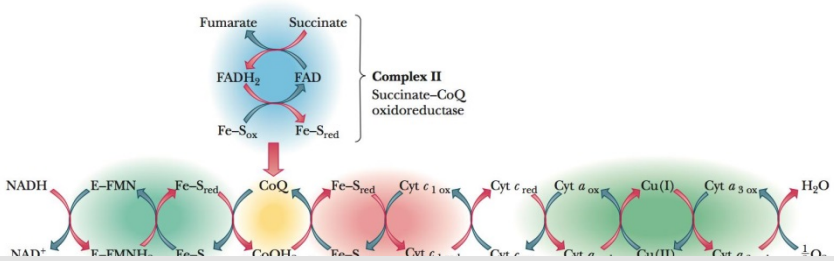
| | | |
|---|---|---|
| | $NADH + H^+ \rightarrow NAD^+ + 2H^+ + 2e^-$ | 0.320 |
| | $\frac{1}{2}O_2 + 2H^+ + 2e^- \rightarrow H_2O$ | 0.816 |
| Sum | $NADH + \frac{1}{2}O_2 + H^+ \rightarrow NAD^+ + H_2O$ | 1.136 |

This reflects that total transfer of electrons from the donor (NADH) to its final acceptor (Oxygen) has a net electron potential of 1.136. After obtaining this value, the amount of energy that is released could be calculated by:

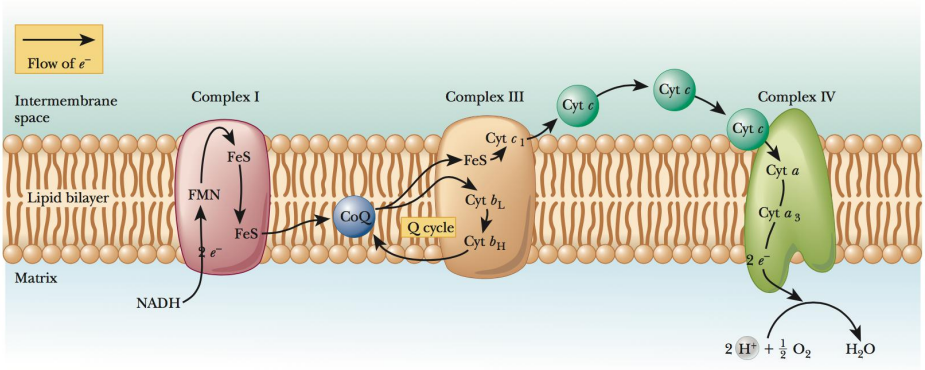
$$\Delta G^{\circ} = -nF\,\Delta E^{\circ\prime}$$

$$\Delta G^{\circ} = -(2)\,(96.485\ \text{kJ V}^{-1}\ \text{mol}^{-1})\,(1.136\ \text{V}) = -219\ \text{kJ mol}^{-1}$$

Thus, a tremendous amount of energy is liberated through this reaction. This is the main reason why ETC exists. The large amount of energy release through NADH oxidation with concomitant reduction of Oxygen gas to water could potentially harm the cells. The main objective is to gradually decrease the potential energy of the electron by allowing to be transferred from one complex to another, until such time that if could be safely lodged to an oxygen atom and combine with hydrogen ions to form water.



FADH2. The protein complexes are arranged in increasing affinities to electrons (increasing reduction potentials), thus these charged particles are passed in a unidirectional manner. CI is also called NADH-CoQ oxidoreductase. The name implies that it oxidizes NADH into NAD+ and transfers the electrons in order to reduce Coenzyme Q (CoQ) into CoQH2. This complex contains a flavin cofactor, namely Flavin mononucleotide (FMN) as shown in Fig. X. The only difference between the FMN and FAD structure is the absence of adenosine in FMN structure. Complex I also has an Fe-S center wherein the electrons from and cause shifts from ferrous (Fe2+) to Ferric (Fe3+) states of Iron, and vice verse. The entire redox reactions in CI is exergonic, releasing -81kJ/mol of NADH (-19.4 kcal/mol), thus is sufficient to drive phosphorylation of ADP into ATP that only requires +30.5 kJ/mol (+7.3 kcal/mol). As a transmembrane protein, CI also pumps hydrogen ions from the mitochondrial matrix into the intermembrane space.



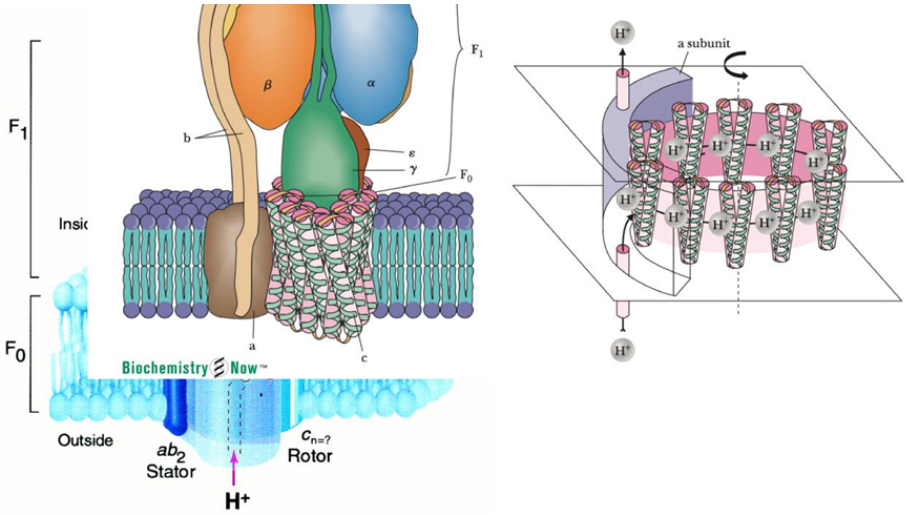
CII, also referred to as Succinate-CoQ oxidoreductase also the same enzyme as the Succinate dehydrogenase of the Krebs cycle. As it facilitates oxidation of Succinate into fumarate, electrons are transferred to FAD cofactor within CII which reduces it to FADH2. Electrons are then relayed to Fe-S centers and terminally to CoQ. Compared to CI, CII yields less energy, approximately -13.5 kJ/mol of NADH ((-3.2 kcal/mol), hence is not enough to generate an ATP. This complex also does not traverse the mitochondrial membrane, hence it cannot pump hydrogen ions into the intermembrane space. CIII or CoQH2-Cyt c



assemblies, approximately -110 kJ/mol or -26.3 kcal/mol of NADH. The main highlight of reactions in CIV is the formation of water through the reduction of oxygen gas which serves as the final electron acceptor of the ETC. As with CI, CIII and CIV also pump hydrogen ions into the intermembrane space.

Considering the processes that occur in the ETC, hydrogen ions accumulate in the intermembrane space, thus the pH

decreases. This difference in pH between the mitochondrial space and the matrix must be normalized. As hydrogen ions could not readily diffuse through the inner mitochondrial membrane, they pass through another protein transporter called the ATP synthase. The ATP synthase produces ATP and is




three types of subunits, namely a, b and c as shown in Fig. X. Furthermore, it also has a3, b3, y, d and e domains that serve as sites for ATP synthesis. The F1 portion is often described as a royalty motor wherein y and e domains are rotary shafts.

Together with domain c, these three parts comprise the rotary motor that moves around domains a3, b3, a and b to allow protons to enter the ATP synthase and synthesize ATP. On a more macroscopic view, the ATP synthase has three conformations, namely Open (O), Loose-binding (L) and Tight-binding (T). ADP and Pi enter the L site. Once hydrogen ions enter the synthase, the F1 rotates. This conformational change converts L conformation into T, thus the ADP and Pi are reacted together to form ATP. Further entry of hydrogen ions causes rotation of the

synthesized ATP molecules to be released and be used by the cell. It must be noted that A single ATP synthase has three subunits that alternately shift from L, T and O conformation, thus increasing its efficiency in generating ATP.