9.5: Oxidative Phosphorylation

Learning Objectives

- Understand parts 2 and 3 of the third stage of food catabolism, i.e., oxidative phosphorylation, and the basics of the redox chemistry of the molecules involved, including flavin mononucleotide, ubiquinone, and cytochrome c.
- Understand the electron transport process basics, including basic redox reactions and proton pumping in complexes I through IV.
- Understand the ATP synthesis process, accounting for the ATP yield, body heating, and reactive oxygen species produced.

What is oxidative phosphorylation?

In food catabolism up to this point, the energy is transferred from food to high-energy molecules, such as energetic electron carriers NADH and $\mathrm{FADH_2}$. Recall that these electron carrier molecules do not deliver elections alone; they deliver protons and electrons, i.e., $2\,\mathrm{H^+} + 2\,\mathrm{e^-}$. The electrons in NADH and FADH are transported through a series of enzymes located in the inner membrane of mitochondria, and ultimately, the $2\,\mathrm{H^+} + 2\,\mathrm{e^-}$ reduce O into $\mathrm{H_2O}$ by the reaction shown below.

$$4\,\mathrm{H^+} + 4\,\mathrm{e^-} + \mathrm{O_2} \longrightarrow 2\,\mathrm{H_2O}$$

In each step, the electrons are transferred from a substance with a higher reduction potential to one with a lower reduction potential. Energy is released in each step proportional to the difference in the reduction potential. The energy is converted to electrochemical potential energy by pumping protons ($\mathrm{H^+}$) from the matrix to intermembrane spaces through sets of enzymes called complexes I, III, & IV. The electrochemical energy is harnessed by ATP synthase, which allows protons to flow back from the intermembrane space to the matrix and couples the energy released to synthesize higher energy ATP by phosphorylating lower energy ADP with inorganic phosphate (Pi). These interconnected processes of electron transport and ATP synthesis are collectively called **oxidative phosphorylation**. It happens in the mitochondria of cells as illustrated in Figure $9.5.1$ and is explained in the following sections.

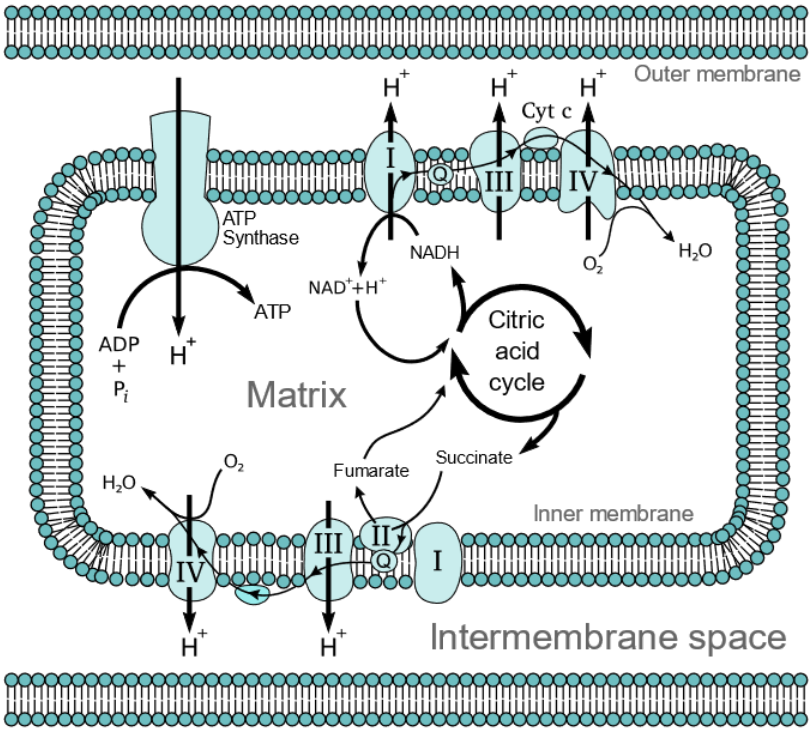
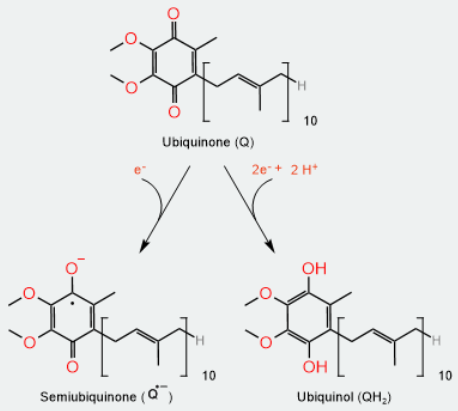
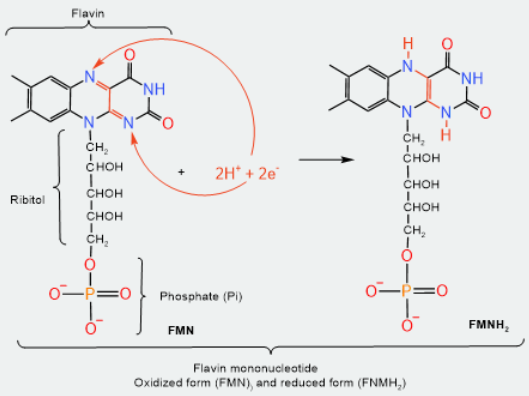


Figure $9.5.1$: Schematic diagram of the mitochondrial electron transport chain comprising of complexes I through IV and production of ATP by ATP-synthase. (Copyright; Fvasconcellos 22:35, 9 September 2007 (UTC), Public domain, via Wikimedia Commons)

Electron and proton transport molecules

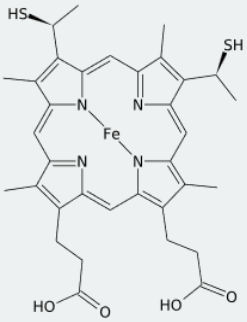


In addition to NAD^+ and FAD, the following molecules are involved in the transport of electrons and protons in the electron transport chain. The first electron acceptor from $NADH$ or $FADH_2$ in the electron transport chain is **flavin mononucleotide** which changes from its oxidized form represented as FMN to its reduced form represented as $FMNH_2$ as illustrated in the figure on the right. Structure of FMN comprises three parts, phosphate, ribitol, and flavin. It is the same as one of the two nucleotides in flavin adenine dinucleotide. Nitrogen atoms in flavin part of FMN take part in the redo process, as illustrated in the figure on the right. $FMNH_2$ pass on the electrons to iron-sulfur clusters, which include $[2\,Fe{-}2\,S]$ and $[4\,Fe{-}4\,S]$ clusters. The redox couple in iron-sulfur clusters is Fe^{3+}/Fe^{2+}, i.e., the following redox reaction:



$$Fe^{3+} + e^- \underset{Oxidation}{\overset{Reduction}{\rightleftharpoons}} Fe^{2+}.$$

Finally, the electrons are transferred to coenzyme-Q, which in oxidized form is ubiquinone represented as Q and in its reduced form is ubiquinol represented as QH_2, as illustrated in the figure above on the left. Coenzyme-Q is hydrophobic, i.e., lipid-soluble. Coenzyme-Q moves freely in the hydrophobic environment within the biliary inner membrane to pass on electrons from complex I and II to complex III. Coenzyme-Q not only can accept two electrons and two protons, but it can also accept one electron to become semiubiquinone, a resonance-stabilized radical anion.



Cytochrome c (Cyt c) is another electron carrier protein with a heme group attached. Heme group is illustrated in the figure on the right. Iron in the heme group of cytochrome c is the redox couple (Fe^{3+}/Fe^{2+}) as in the case of iron-sulfur clusters. Fe^{3+} changes to Fe^{2+} when an electron is added to it, and the reverse happens when an electron is removed. Cytochrome c is water soluble and travels between complex III and complex IV in the watery environment along the inner membrane's surface facing intermembrane space.

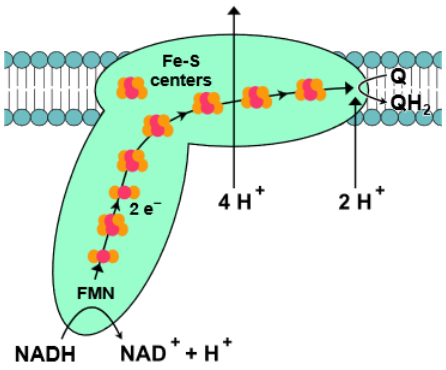
Electron transport chain

In this part 2 of stage 3, electrons are removed from $NADH$ and $FADH_2$ and passed on to reduce O_2 into H_2O through a series of enzyme complexes, i.e., complexes I through IV and mobile electron carriers like ubiquinone (Q) and cytochrome c ($Cyt\ c$) by a process called **electron transport chain**. At each step, electrons pass from a substance with a higher reduction potential to one with a lower one. Energy is released proportional to the difference in the reduction potentials.

The complex I, III, and IV extend from the matrix to the intermembrane space through the inner membrane, as illustrated in Figure $9.5.1$. These three complexes utilize the energy released to pump protons (H^+) from the matrix to the intermembrane space. Complex II extends to the matrix from the inner membrane but does not cross the membrane to intermembrane space. Therefore complex II transports electrons but does not pump protons. Coenzyme-Q (Q) is a hydrophobic electron carrier molecule that moves in a hydrophobic environment inside the lipid bilayer of the inner membrane from complexes I and II to complex III. Cytochrome c ($Cyt\ c$) is a hydrophilic electron carrier molecule that moves along the surface of the inner membrane facing the intermembrane space from complex III to complex IV. The enzyme complexes and the mobile electron carriers involved in the electron transport chain and ATP synthesis are described in the following sub-sections, where the chemical equations and figures are taken from the public domain source via Wikipedia.

Complex I

Complex I, also known as NADH-coenzyme Q oxidoreductase or NADH dehydrogenase, is the first enzyme complex in the electron transport chain. Complex I is illustrated in the figure on the right. The electron transport begins when an NADH binds with and donates two electrons to complex I. The electrons are received by flavin mononucleotide (FMN) attached to the complex, which is reduced to $FMNH_2$ form. Then the electrons are transferred through a series of iron-sulfur clusters within complex I to coenzyme-Q (Q) that, in turn, reduces to its reduced form QH_2. QH_2 travels through the lipid bilayer to and delivers the electrons to complex III.



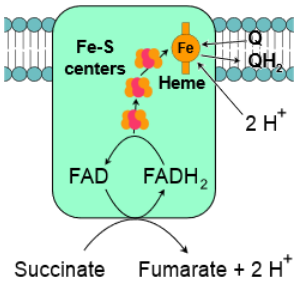
As the electrons move through complex I and release part of their energy, four protons ($4\,H^+$) are pumped from the matrix to intermembrane space by utilizing the energy released. It generated polarity across the inner membrane, with the positive side (P-side) facing the intermembrane area and the negative side (N-side) facing the matrix. The exact mechanics of proton pumping is not yet clearly understood. Still, the research indicates that it happens through conformational changes in complex I such that the protein bind protons on the N-side and releases them on the P-side of the membrane. The overall redox reaction in complex I is the following.

$$NADH + Q + 5\,H^+_{matrix} \longrightarrow NAD^+ + QH_2 + 4\,H^+_{intermembrane}$$

NAD^+ liberated in this reaction becomes available to oxidize more substrates in the metabolic pathways.

Complex II

Complex II, also known as succinate-Q oxidoreductase or succinate dehydrogenase, is a second entry point to the electron transport chain. It is part of the citric acid cycle and the electron transport chain. It contains protein subunits bonded with flavin adenine dinucleotide FAD, iron-sulfur clusters, and a heme group, as illustrated in the figure on the right. Succinate is oxidized to fumarate in the citric acid cycle at the expense of oxidation of FAD to $FADH_2$ in complex II. The electrons and protons transfer from $FADH_2$ through iron-sulfur clusters to coenzyme-Q in complex II by the following overall reaction.



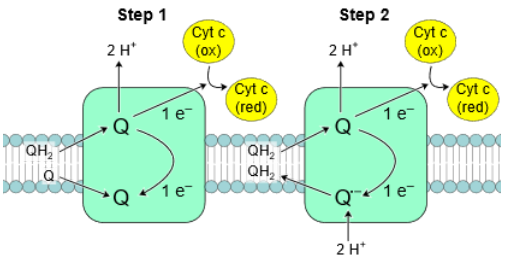
$$Succinate + Q \longrightarrow Fumarate + QH_2$$

Coenzyme-Q passes on the electrons from complex II to complex III as from complex I to complex III.

Recall that (\ce{FADH2}\) is less energetic than (\ce{NADH}\). Since oxidation $FADH_2$ to FAD at complex II releases less energy than oxidation of $NADH$ to NAD^+ at complex I, complex II do not pump protons from matrix to intermembrane space. The energy released by electron transport is utilized to pump protons in complex III and IV, as described in the next section.

Complex III

Complex III, also known as cytochrome C reductase or cytochrome bc_1 complex, contains protein subunits, an iron-sulfur cluster, and cytochromes. A cytochrome is a protein with at least one heme group that transfers one electron by accepting and releasing an electron based on the following reaction:



$$Fe^{3+} + e^- \rightleftharpoons Fe^{2+}$$

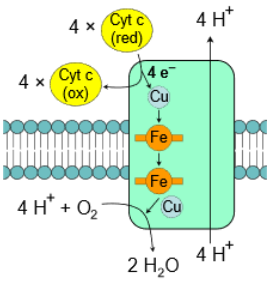
Complex III passes on electrons from coenzyme-Q (QH_2) to cytochrome c ($Cyt\ c$). Since QH_2 delivers two electrons (e^-) while $Cyt\ c$ can accept only one, the process happens in two steps, as illustrated in the figure on the right. In the first step, QH_2 transfers one e^- to $Cyt\ c$ and one to another coenzyme-Q in quinone (Q) form and releases $2\,H^+$. Q converts to a semiubiquinone ($Q^{\bullet -}$). In the second step, another QH_2 transfers one electron to a second $Cyt\ c$ and one to $Q^{\bullet -}$ converting it to Q which is released from the complex and repeats the above two steps. This way, two electrons are transferred from a Q to two $Cyt\ c$ and $4\,H^+$ are pumped out into intermembrane space by complex III as shown in the following reaction.

$$QH_2 + 2\,Cyt\ c_{ox} + 2\,H^+_{matrix} \longrightarrow Q + 2\,Cyt\ c_{red} + 4\,H^+_{intermembrane}$$

$Cyt\ c$ carries the electron to complex IV.

Complex IV

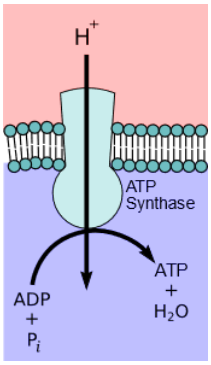
Complex IV, also known as cytochrome c oxidase, is the final complex in the electron transport chain. It contains several subunits, two heme groups, and several metal ion cofactors, including three atoms of copper, one magnesium, and one zinc. Complex IV reduces oxygen into water at the expense of oxidation of Cyt c and pumps $4\,H^+$ from matrix to intermembrane space as illustrated in the figure on the right and shown in the following overall reaction.

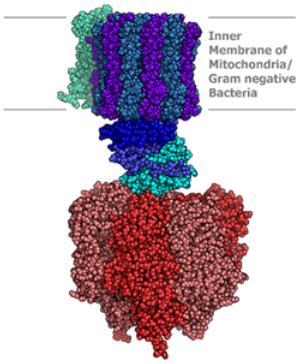


$$4\,\text{Cyt c}_{\text{red}} + O_2 + 8\,H^+_{\text{matrix}} \longrightarrow 4\,\text{Cyt c}_{\text{ox}} + 2\,H_2O + 4\,H^+_{\text{intermembrane}}$$

ATP-synthase

ATP-synthase, also known as complex V is the final complex in the oxidative phosphorylation process, i.e., part 3 of stage 3 of food catabolism. It comprises two parts in the shape of a mushroom, as illustrated in the figure on the left. The first part, F_O, is the hydrophobic part embedded in the inner membrane (a blue and purple region in the model image on the right (*Copyright; Alex. X, CC BY-SA 3.0, via Wikimedia Commons*). The F_O acts as a pore for the flow of protons (H^+) across the membrane. The second part is F_1 which is hydrophilic and spheroidal and protrudes into the matrix (red area in the image on the right). ATP synthesis takes place in the F_1 part of ATP-synthase. It operates on the principle of chemiosmosis, which is described below.





Chemiosmosis

Water movement from the direction of higher to lower concentration across a semipermeable membrane is called **osmosis.** When protons (H^+) are pumped from the matrix to intermembrane space by complex I, III, & IV, a proton concentration gradient is developed across the membrane. Since protons are positive charge ions (H^+), there is also an electrical gradient; collectively, it is called an electrochemical gradient. **Chemiosmosis** is the flow of ions (H^+) across a semipermeable membrane down their electrochemical gradient.

An electrochemical gradient developed due to protons (H^+) is a form of electrochemical potential energy. ATP-Synthase harnesses the electrochemical potential energy to synthesize ATP as the protons flow through it, just as electricity is generated as water from a dam flows through a turbine. The higher energy ATP is synthesized by condensing lower energy ADP and phosphate P_i in a process called **oxidative phosphorylation**. It takes three to four H^+ to synthesize one ATP by the following overall reaction.

$$ADP + P_i + 4\,H^+_{\text{intermembrane}} \rightleftharpoons ATP + H_2O + 4\,H^+_{\text{matrix}}$$

This is an equilibrium reaction, i.e., when the electrochemical gradient is low, ATP-synthase consumes ATP and returns protons from the matrix to the intermembrane space.

Structure and mechanisms of operation of ATP-synthase

ATP-synthase comprises several protein sub-units. It is in the shape of a mushroom with two major parts: a stem-like part which is a hydrophobic portion embedded in the inner membrane, is called $\mathbf{F_O}$, and a mushroom head-like part that protrudes into the matrix, is called $\mathbf{F_1}$, as illustrated in Figure 9.5.2 a. Note: the subscript in F_O is the letter O, not the number zero.

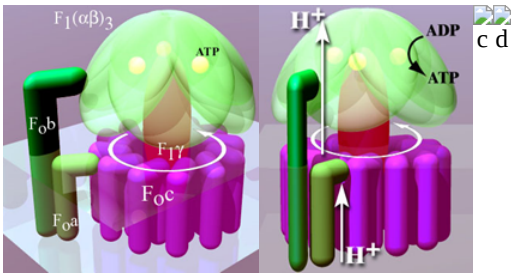


Figure 9.5.2: **a)** Simplified model of ATP-synthase (Copyright; Asw-hamburg, CC BY-SA 2.5, via Wikimedia commons), **b)** illustration proton flow in ATP-synthase (Copyright; Asw-hamburg at German Wikipedia., CC BY-SA 3.0, via Wikimedia Commons), **c)** Mechainsm of rotation of F_0c ring of ATP-synthase (Copyright: Asw-hamburg at German Wikipedia., CC BY-SA 3.0, via Wikimedia Commons), and **d)** Mechanism of ATP production in $F_1\beta$ subunits of ATP synthase. ATP is shown in red, ADP and phosphate in pink and the rotating γ subunit in black (Copyright; By US gov - US gov, Public Domain, https://commons.wikimedia.org/w/inde...?curid=3588598)

F_O portion of \(\ce{ATP}-synthase

F_O part consists of six c subunits (F_Oc) arranged in a ring shape with proton channels between them that make the rotor part of this molecular machinery, as illustrated in Figure 9.5.2 a & b. The b subunit (F_Ob) connects to the F_1 portion and prevents it from rotating. The subunit F_Oa connects F_Ob to the F_Oc ring. F_Oc part is embedded in the membrane and couples the energy released as the protons flow through the channels to kinetic energy in the form of rotation of the F_Oc ring, like a turbine moves by water in a hydroelectric dam. Other subunits are not described here.

F_1 portion of \(\ce{ATP}-synthase

F_1 portion has a set of three α and thee β subunits arranged alternately like carpels of an orange ($F_1(\alpha\beta)_3$) with $F_1\gamma$ in the middle. The $F_1\gamma$ is like an axil connected with the rotary F_Oc, as shown in Figure 9.5.2 a. The $F_1(\alpha\beta)_3$ is prevented from rotating by the F_Ob subunit, but $F_1\gamma$ rotates along with the rotor F_Oc ring. The rotation of $F_1\gamma$ within $F_1(\alpha\beta)_3$ causes conformation changes in the β subunits, as illustrated in the video that will play by clicking this link. The conformational changes in the β subunits are linked to the mechanism of ATP synthesis. Other subunits of the F_1 portion are not described here.

Mechanism of F_Oc ring rotation in \(\ce{ATP}-synthase

The steps of the rotation of the F_Oc ring are illustrated below.

Steps in the rotation mechanism of F_Oc ring in ATP-synthase (Copyright; Asw-hamburg at German Wikipedia., CC BY-SA 3.0, via Wikimedia Commons)

Step a: F_Oc subunits are arranged in a circle. All of them have an amino acid asp residue with an acidic side chain but in neutral ($\text{peptide}-\text{COOH}$) form except one (labeled #1 in step a), which, being near a cation group ($\text{peptide}-\text{NH}_3^+$ of arg residue of F_Ob subunit, is an anion, i.e., $\text{peptide}-\text{COO}^-$. Electrostatic interaction between opposite charges builds mechanical tension in the F_Oc ring like a spiral spring.

1. Step b: A H^+ from outside (intermembrance space) neutralizes the anion ($\text{peptide}-\text{COO}^- + \text{H}^+ \longrightarrow \text{peptide}-\text{COOH}$).
2. Step c: The strained structure relaxes as the electrostatic tension is removed, causing the peptide to rotate.
3. Step d: Twisting motion bring F_Oc#1 back to the other side of the stator F_Ob $\text{peptide}-\text{NH}_3^+$ group causing the rotor F_Oc to rotate by 30^o.
4. Step e: F_Oc#1 subunit is neutral like other subunits in the ring.
5. Step f: The rotor F_Oc is rotated by 30^o, and F_Oc#2 is under the spell of the positive charge of F_Ob $\text{peptide}-\text{NH}_3^+$ group.
6. Step g: The asp residue of F_Oc#2 ionizes the \(\ce{-COOH) ($\text{peptide}-\text{COOH} \longrightarrow \text{peptide}-\text{COO}^- + \text{H}^+$) and the spring comes under tension again.
7. Step h: The asp residue releases the H^+ that moves inside (the matrix).
8. Step i: The initial position of step a is restored and the following has happed in the process:

1. F_Oc#2 has taken the place of F_Oc#1,
2. electrochemical energy of one H^+ movement transferred to kinetic energy through 30° rotation of the rotor, and
3. one H^+ is smuggled from the intermembrane space to the matrix.

The simulation of the movement described above is illustrated in Figure 9.5.2 c.

Mechanism of catalysis of ATP synthesis in $F_1(\alpha\beta)_3$ complex

The $F_1(\alpha\beta)_3$ complex catalyzes ATP synthesis. It has three α and three β subunits arranged alternately as three $\alpha\beta$ dimers in the shape of carpels in an orange. It is the β subunits that catalyze the ATP synthesis. Rotation of $F_1\gamma$ subunit inside the $F_1(\alpha\beta)_3$ complex causes conformational changes in the $F_1\beta$ subunits that are linked with the mechanism of ATP synthesis.

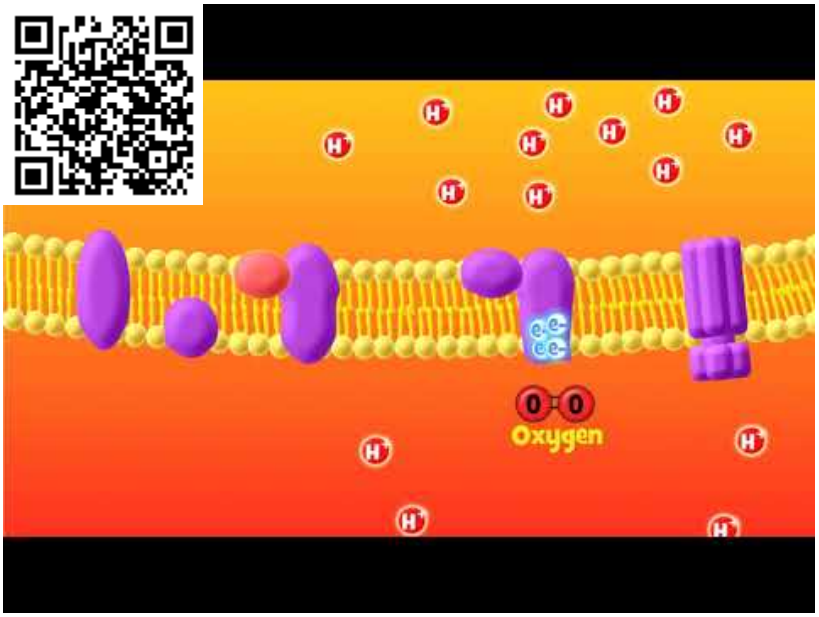
$F_1\beta$ switched between three states with each 360° rotation of $F_1\gamma$ subunit inside the $F_1(\alpha\beta)_3$ complex, as illustrated in Figure 9.5.2 d.

1. First is the **open-state**, shown in brown, where ADP and P_i enter the active state.
2. Second is the **loose-state** in which the $F_1\beta$ closes up around the substrate ADP and P_i binding them loosely, shown in red.
3. Third, is the **tight-state** in which $F_1\beta$ tightens around the substrate ADP and P_i forcing them to condense into an ATP product.
4. Finally, $F_1\beta$ reverts to an open-state that releases the ATP and binds ADP and P_i to repeat the process.

Since one H^+ cause a 30° turn, a complete (360°) turn of $F_1\gamma$ subunit inside $F_1(\alpha\beta)_3$ complex needs 12 H^+ and produces three ATP′s from three $F_1\beta$ subunits in it, that gives the following overall reaction.

$$ADP + P_i + 4\,H^+_{intermembrane} \rightleftharpoons ATP + H_2O + 4\,H^+_{matrix}$$

The next video presents the oxidative phosphorylation of glucose in a summary form.



Heating the body

NADH is reduced in the electron transport chain at the expense of reduction of O_2 by the following overall reaction.

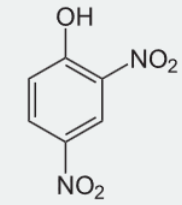
$$\tfrac{1}{2}O_2 + NADH + H^+ \longrightarrow H_2O + NAD^+$$

The potential difference between these redox pairs is 1.14 volts, equivalent to -218 kJ/mol. Reduction of one NADH can produce three ATP. Production of ATP costs 30.5 kJ/mole, which is equivalent to 30.5 kJ/mole x 3 = 91.5 kJ/mole of NADH. So the percentage of energy conserved as ATP, i.e., the **energy efficiency** is: $\frac{91.5}{218} \times 100 = 42\%$. The remaining 58% of energy ends up heating the body.

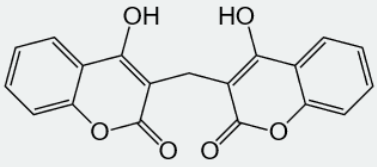
Some compounds, known as **uncouplers**, uncouple electron transport from ATP synthase, i.e., the electron transport pumps H^+ as usual but H^+ return to the matrix without producing ATP′s. So, all energy released during the electron transport

process becomes heat energy. Examples of uncouplers are 2,4-dinitrophenol and dicumarol that combine with H^+ and, being hydrophobic, carry them through the inner membrane. Some compounds, like oligomycin A prevent ATP synthesis by blocking H^+-channels in ATP synthase. Salicylic acid (aspirin), if taken in extreme excess, also blocks H^+-channels in ATP synthase. When the electron transport chain operates without ATP synthesis, all of the electron transport energy is used as heat.

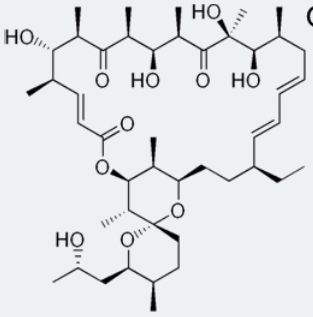
Certain animals adapted to the cold environment have developed uncoupling systems to generate more heat for heating their body. They contain a large amount of **brown fat,** a tissue with many mitochondria, and are brown due to iron in the cytochrome in the mitochondria. The electron transport works in the brown fat. Still, the mitochondria have certain proteins embedded in the inner membrane that allow H^+ to return to the matrix without ATP production. The body of newborn babies loses more heat per unit mass because of the larger surface area to mass ratio. Newborn babies have brown fat deposits on arteries that heat the blood circulating in their bodies. Adults usually do not have brown fat except those who live and work in a cold climate.



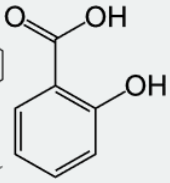
2,4-Dinitrophoenol



Dicumarol



Oligo
mycin A



Salicylic acid

Reactive oxygen species

The electron transport chain uses four electrons and four protons to reduce oxygen by the following overall reaction,

$$O_2 + 4\,e^- + 4\,H^+ \longrightarrow 2\,H_2O\ .$$

However, some electrons, particularly during the reduction of coenzyme-Q in the complex-III, leak and cause the following reaction.

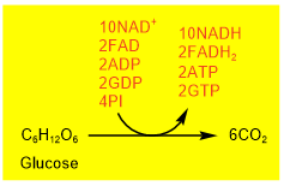
$$O_2 \xrightarrow{e^-} \underset{\text{Superoxide}}{O_2^{\bullet -}} \xrightarrow{e^-} \underset{\text{Peroxide}}{O_2^{2-}}$$

Species like superoxide ($O_2^{\bullet -}$), peroxide (O_2^{2-}) and their product hydroxyl radical ($HO^{\bullet}$) are called **reactive oxygen species** which are harmful. They damage proteins, cause mutations by reacting with DNA, and are responsible for aging, as illustrated in the figure on the right (*taken from* *https://www.hiclipart.com/free-trans...-clipart-npvtr*). The body has mechanisms to suppress the production of reactive species and destroy them if formed. Production of reactive oxygen species increases with an increase in the inter-member potential. The reactive oxygen species, oxidants, activate uncoupling proteins that reduce the membrane potential. Some substances in the body, e.g., vitamins C, E and antioxidant enzymes, react with and destroy the reactive oxygen species.

Summary of glucose catabolism

Aerobic catabolism of a glucose molecule converts a 6 C′s glucose molecule to six carbon dioxide along with ATP′s, GTP′s, and reduced coenzyme NADH′s, and $FADH_2$′s, as shown in the figure on the right.

Glucose first goes through glycolysis that produces two pyruvate and overall two ATP and two NADH. Two pyruvates go through oxidative decarboxylation producing two acetyl-CoA and two NADH. Each acetyl-CoA goes through one turn of the citric acid cycle. So, the two turns of the citric acid cycles convert two acetyl-CoA into four CO_2, six NADH, two $FADH_2$, and two GDP. These steps are summarized in Figure 9.5.3 and Figure 9.5.4 shown below.



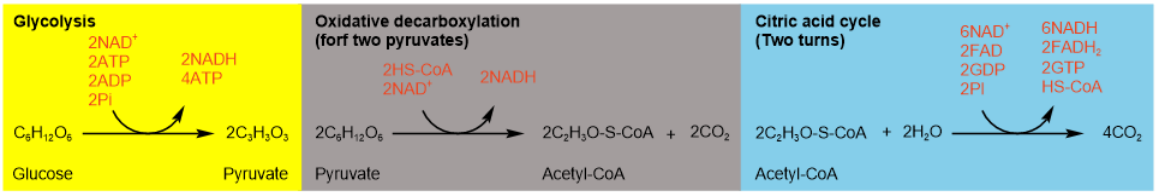


Figure 9.5.3 illustrates the summary of aerobic catabolism of glucose and production of ATP′s, GTP′s, and reduced coenzyme NADH′s, and $FADH_2$′s at different stages.

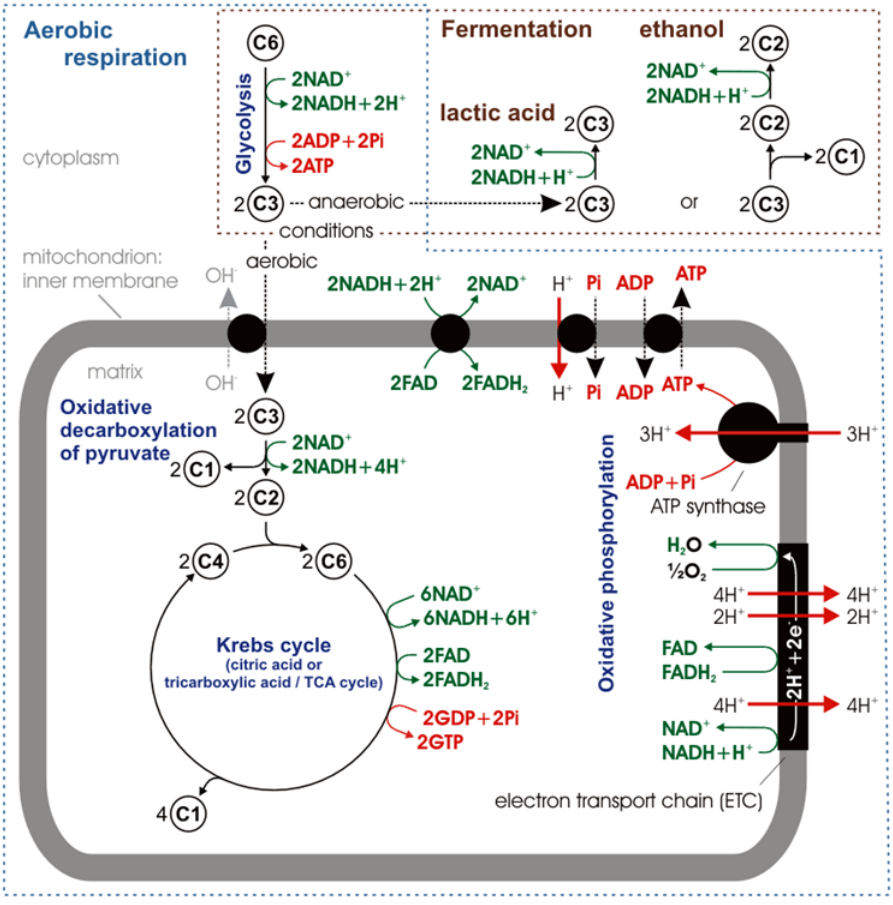


Figure 9.5.4: Stoichiometry of aerobic respiration and most known fermentation types in the eucaryotic cell. Numbers in circles indicate counts of carbon atoms in molecules; C6 is glucose $C_6H_{12}O_6$, and C1 carbon dioxide CO_2. The mitochondrial outer membrane is omitted. (Copyright; Darekk2, CC BY-SA 3.0, via Wikimedia Commons)

Insulin -the blood glucose-regulating hormone

Insulin is a hormone that regulates blood glucose levels. The glucose level increases after a meal, and the insulin promotes its absorption into the liver, fat, and muscle cells, converting it into glycogen or fats. High levels of insulin also inhibit the production of glucose by the liver. Low insulin levels have the opposite effects, which happen when a person has diabetes.

Comparison of ATP yield in aerobic and anaerobic catabolism of glucose

Anaerobic catabolism, i.e., the two forms of fermentation shown in Figure 9.5.3 yields a net two ATP′s from a glucose molecule.

Aerobic catabolism yields about thirty ATP′s. Two ATP′s are produced before the citric acid cycle and two GTP′s, ten NADH′s, and two $FADH_2$′s are produced during citric acid cycle. GTP′s later convert to ATP′s. the reduced coenzymes, i.e., NADH′s and $FADH_2$′s enter the electron transport chain and produce heat and ATP′s as explained in the next section.

Account of ATP production from complete oxidation of glucose

Two ATP′s are produced before the citric acid cycle along with four NADH. The citric acid cycle yields GTP′s, six NADH′s, and two $FADH_2$′s. GTP′s convert to ATP′s, i.e., one GTP is equivalent to one ATP. NADH′s and $FADH_2$′s enter the electron transport chain and produce heat and ATP′s. Recall that NADH is more energetic and pumps more proton through complex I, III, and IV than $FADH_2$ which is less energetic and pumps less protons through complex III and IV only. Therefore, NADH yields more ATP′s than $FADH_2$. Earlier books state that one NADH′s is equivalent to three ATP′s, but currently accepted average values are the following.

$$\mathrm{GTP} \approx 1\mathrm{ATP}$$

$$\mathrm{NADH} \approx 2.5\mathrm{ATP}$$

$$\mathrm{FADH_2} \approx 1.5\mathrm{ATP}$$

Based on these conversions, complete aerobic respiration of glucose produces approximately 32 ATP′s, as shown in the following equation and detailed in Table 1.

$$\underbrace{\mathrm{C_6H_{12}O_6}}_{\text{Glucose}} + 6\,\mathrm{O_2} + 10\,\mathrm{NAD^+} + 2\,\mathrm{FAD} + +2\,\mathrm{GTP} + 2\,\mathrm{ADP} + 4\,\mathrm{Pi} \longrightarrow 6\,\mathrm{CO_2} + 6\,\mathrm{H_2O} + 10\,\mathrm{NADH} + 2\,\mathrm{FADH_2}$$
$$+ 2\,\mathrm{GTP} + 2\,\mathrm{ATP}$$

$$\underbrace{\mathrm{C_6H_{12}O_6}}_{\text{Glucose}} + 6\,\mathrm{O_2} + 32\,\mathrm{ADP} + 32\,\mathrm{Pi} \longrightarrow 6\,\mathrm{CO_2} + 6\,\mathrm{H_2O} + 32\,\mathrm{ATP}$$

Table 1: ATP Production from complete aerobic catabolism of one glucose molecule.

Reaction	ATP or reduced coenzymes	Total ATP′s output
Glycolysis		
glucose → glucose-6-phosphate		-1
fructose 6-phosphate → fructose 1,6-bisphosphate		-1
2 glyceraldehyde-3-phosphate → 2 1,3-bisphosphoglycerat	2 NADH	5
2 1,3-bisphosphoglycerate → 2 3-phosphoglycerate	2 ATP	2
2 phosphoenolpyruvate → 2 pyruvate	2 ATP	2
Oxidative phosphorylation of two pyruvate		
2 pyruvate → 2 acetyl-CoA	2 NADH	5
Two turns citric acid cycles to consume to 2 acetyl-CoA		
2 isocitrate → 2 α-ketoglutarate	2 NADH	5
2 α-ketoglutarate → 2 succinyl-CoA	2 NADH	5
2 succinyl-CoA → 2 succinate	2 GTP	2
2 succinate → 2 fumarate	2 $FADH_2$	3

Reaction	ATP or reduced coenzymes	Total ATP′s output
2 malate → 2 oxaloacetate	2 NADH	5
Total		**32**