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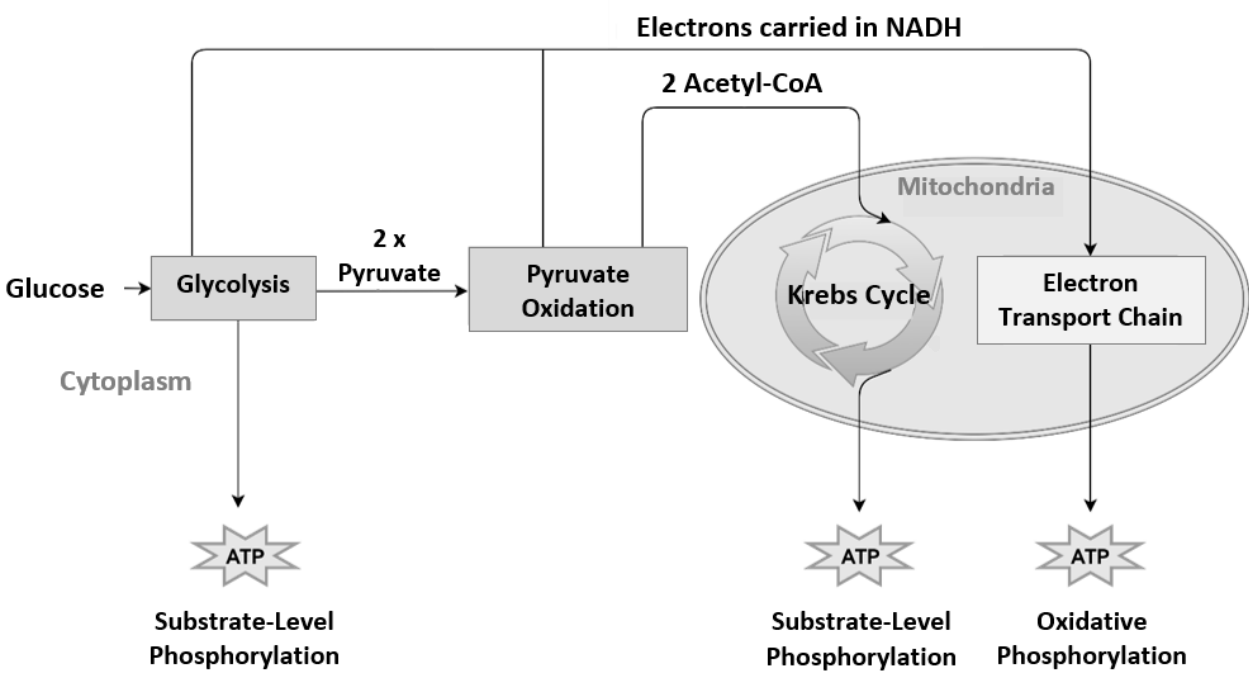
Cellular Respiration

Cellular respiration is the cell's primary method of creating adenosine triphosphate (ATP), an energy-rich molecule used to carry out many cellular processes. Glucose, a six-carbon sugar, is the primary input for cellular respiration in many living organisms. There are two types of respiration: anaerobic and aerobic. This handout will primarily focus on aerobic respiration, which is when oxygen is present. Cellular respiration involves four steps: glycolysis, pyruvate oxidation, Krebs cycle, and an electron transport chain (ETC). The first step, glycolysis, takes place outside the mitochondria, while the other three steps, pyruvate oxidation, Krebs cycle, and electron transport chain, take place inside the mitochondria. In the diagram below, a simplified form of the cellular respiration process can be seen with each of the steps involved.



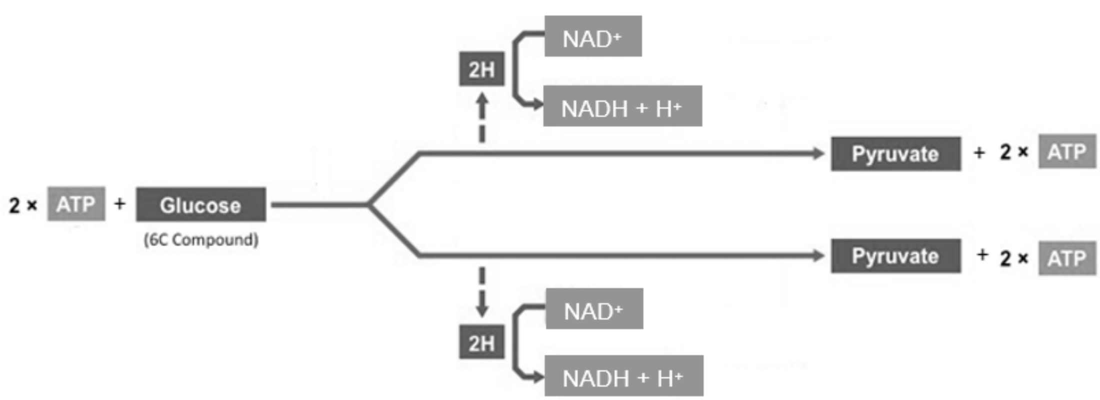
Oxidation and Reduction

Before viewing the individual steps of cellular respiration, it is important to understand the core concept of oxidation and reduction (redox), as it plays a critical role in the overall process. Most of the metabolites in cellular respiration undergo a redox reaction, which involves oxidation of one molecule and the reduction of another. Oxidation is the process of losing electrons while reduction is the process of gaining electrons. A good way to remember which molecule is being oxidized or reduced is to use the acronym "OIL RIG" – **O**xidation **I**s **L**osing, **R**eduction **I**s **G**aining. In this acronym "gaining" and "losing" refer to electrons being transferred. The oxidation and reduction reactions are coupled since, as one compound gains electrons, another must give them up. In cellular respiration, glucose and its intermediates are always oxidized. The energy within glucose is converted to ATP, with some energy being lost as heat.

For further information on oxidation and reduction, please refer to the Oxidation-Reduction Reactions handout.

Glycolysis

Glycolysis is the first step of cellular respiration. This step refers to the breakdown, or lysing, of glucose. This process starts with one glucose molecule and involves investing two ATP molecules to break down glucose into two pyruvate molecules, a three-carbon intermediate. This process also produces four ATP molecules through substrate-level phosphorylation, which is a method of producing ATP by an enzyme adding a phosphate group to ADP. Since two ATP molecules were invested in breaking down the glucose, glycolysis has a net production of two ATP molecules. Furthermore, glycolysis also produces two NADH, a reduced form of the coenzyme NAD^+, which holds onto electrons for later use. The diagram below shows glucose being split to produce two molecules of pyruvate.



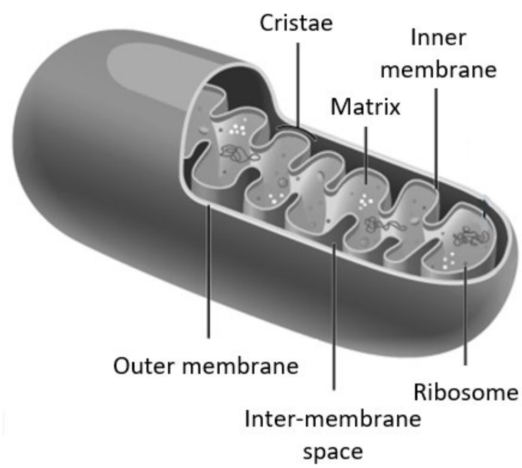
Net Gain:	2 ATP	2 x NADH + H^+	2 x pyruvate

Source: https://ib.bioninja.com.au/higher-level/topic-8-metabolism-cell/untitled/glycolysis.html#previous-photo

Depending on the concentration of oxygen present, pyruvate can undergo different reactions. In the presence of oxygen, pyruvate will go through pyruvate oxidation and follow the steps of cellular respiration; however, in low concentrations of oxygen, pyruvate goes through fermentation, which will be covered later in the handout.

Structure of the Mitochondria

After glycolysis, the remaining steps of respiration occur inside energy-producing organelles, called mitochondria. A distinctive characteristic of the mitochondria is that it has a double membrane with a space between these two membranes, called the intermembrane space. The inner membrane has many folds to increase its surface area. These folds are called cristae and can be seen in the diagram below.



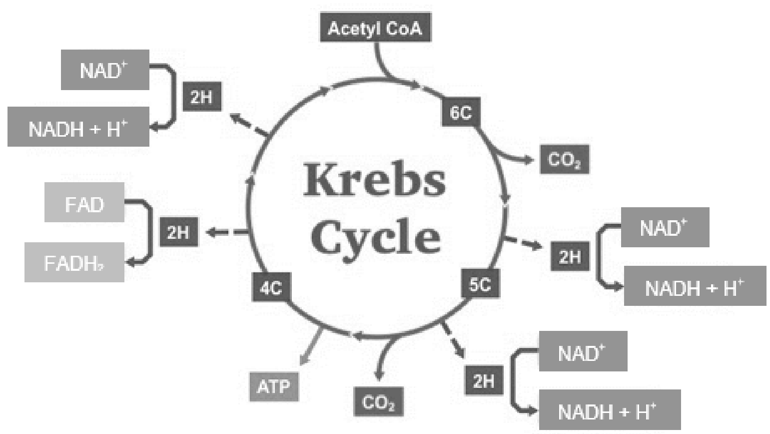
Source: https://flexbooks.ck12.org/cbook/ck-12-biology-flexbook-2.0/section/2.25/primary/lesson/cellular-respiration-bio/

Preparatory Reaction (Pyruvate Oxidation)

As aerobic respiration continues, the two molecules of pyruvate are oxidized to produce acetyl CoA, a two-carbon molecule attached to Coenzyme A. This intermediate is what goes into the next step, the Krebs cycle. While pyruvate is being oxidized into acetyl CoA, NAD^+ is being reduced to produce NADH. This occurs twice since the step occurs once for each pyruvate molecule, thus producing two NADH. Two CO_2 molecules are produced in this step.

Krebs Cycle

The Krebs Cycle, also known as the citric acid cycle, is the next step in cellular respiration. This step occurs twice, once for each acetyl CoA molecule created in pyruvate oxidation. All steps in the Krebs cycle involve the oxidation of the carbon-based intermediate and reduction of NAD^+ and FAD to create NADH and $FADH_2$. FAD is another coenzyme similar to NAD^+ except that it has the capacity of holding two hydrogens and two electrons instead of NAD^+ only being able to hold one hydrogen with two electrons. One completion of the Krebs cycle produces three NADH, one $FADH_2$, and one ATP made through substrate-level phosphorylation. Since the Krebs cycle occurs twice, six NADH, two ATP, and two $FADH_2$ in total are produced. It is also important to note the majority of carbon dioxide produced in cellular respiration, four molecules, is produced in this step. The diagram below provides a simplified view of the Krebs cycle and its products.

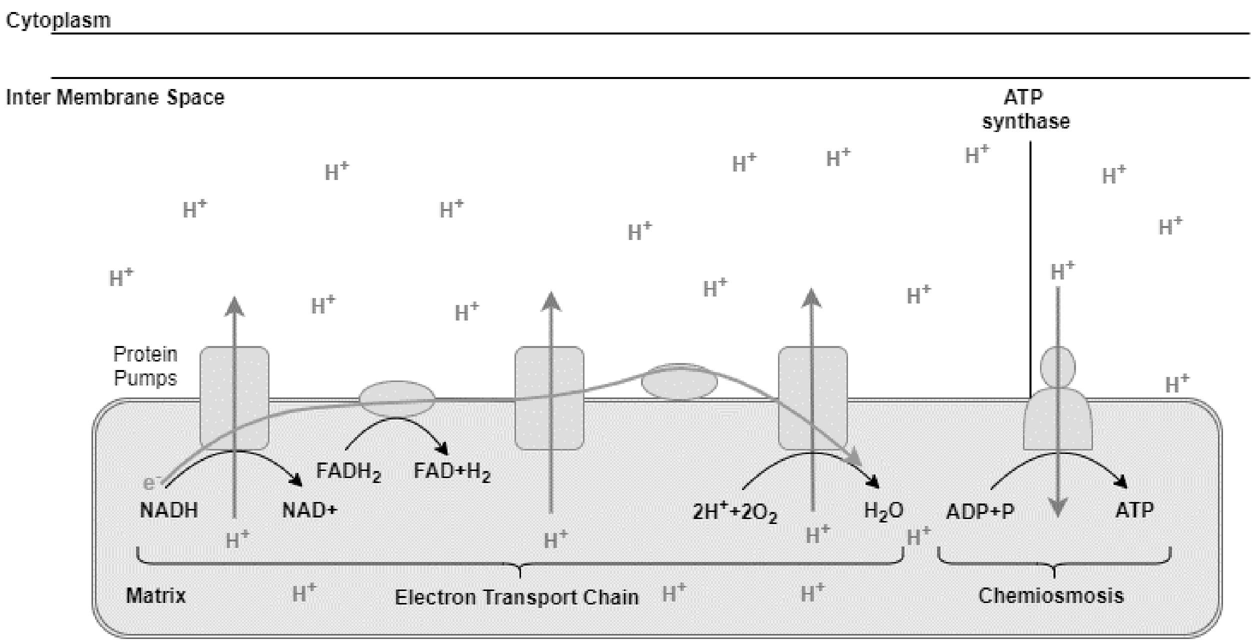


Single Cycle:	2 x CO_2	1 x ATP	1 x $FADH_2$	3 x NADH + H^+
Two Cycles:	4 x CO_2	2 x ATP	2 x $FADH_2$	6 x NADH + H^+

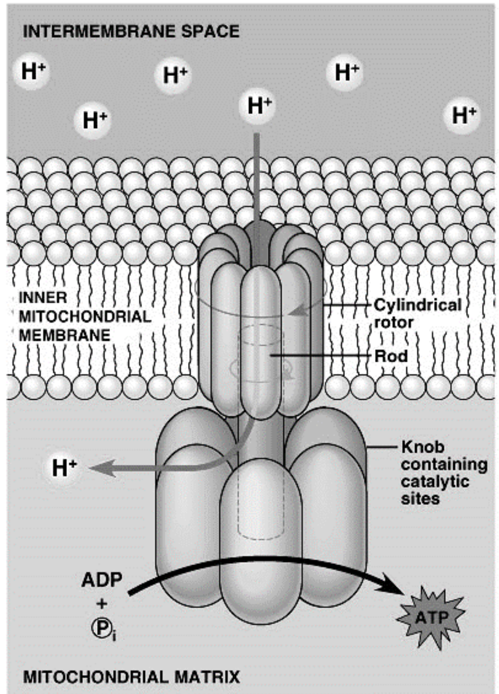
Source: https://ib.bioninja.com.au/higher-level/topic-8-metabolism-cell/untitled/krebs-cycle.html#previous-photo

Electron Transport Chain (ETC)

The final step of cellular respiration is the electron transport chain. This process takes place in the intermembrane, the space between the two membranes of the mitochondria. A concentration gradient is created by special proteins, called proton pumps. These proton pumps pull protons, hydrogen ions or H^+, off NADH and $FADH_2$ and push them into the intermembrane space. It is important to note that because H^+ are being pulled from NADH and $FADH_2$, both products, NAD^+ and FAD^+, are the oxidized form of the coenzyme. The oxygen later reacts with H^+ to form water. The diagram below depicts the electron transport chain, which includes the process of chemiosmosis.



The movement of H^+ into the intermembrane space creates a concentration gradient and a buildup of pressure. To release this pressure, the H^+ passes through ATP synthase. The kinetic energy of H^+ moving through the enzyme is captured and used to phosphorylate ADP to produce ATP. This type of ATP production is called oxidative phosphorylation and is responsible for about 90% of the total ATP produced in cellular respiration. When the H^+ go through the ATP synthase, they react with oxygen to produce water, H_2O. The diagram on the next page provides a visual reference of the ATP synthase at work.



Source: https://www2.southeastern.edu/Academics/Faculty/teperkins/151/ATP%20Synthase.html

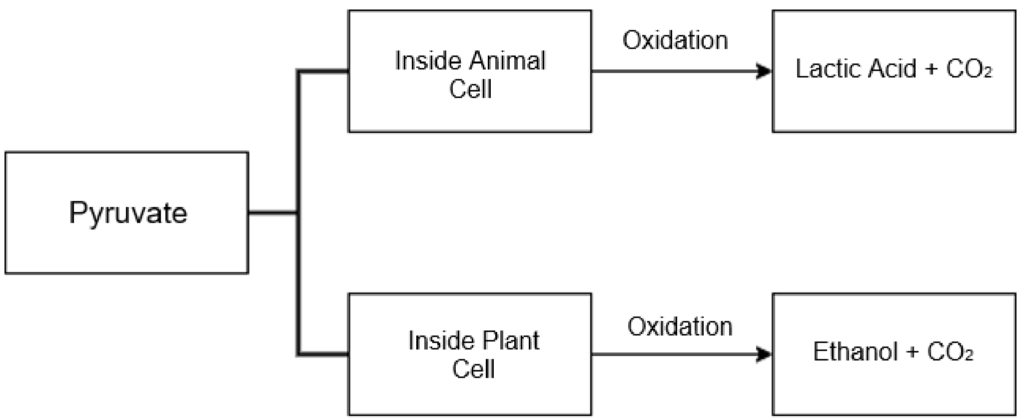
Products Produced in Each Stage

Products are made at different stages and in different quantities throughout cellular respiration. The chart below shows a summary of how much of each molecule is being produced during each stage.

Pathway	ATP Produced	NADH Produced	$FADH_2$ Produced
Glycolysis	4	2	0
Pyruvate Oxidation	0	2	0
Krebs Cycle	2	6	2
ETC	30-32	0	0
Total	36-38	10	2

Fermentation

Fermentation occurs after glycolysis when oxygen is in low concentration or not present, meaning that it is anaerobic respiration. No additional ATP is created through fermentation. There are two types of fermentation: ethanol fermentation, found in plants, and lactic acid fermentation, found in animals and bacteria. In ethanol fermentation, pyruvate is oxidized and turned into ethanol; carbon dioxide is also produced as a byproduct in the reaction. The other form of fermentation is lactic acid fermentation, which is similar to ethanol fermentation in that pyruvate is oxidized again, but this time the pyruvate is converted to lactic acid. The flow chart below shows the full anaerobic cellular respiration process.



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