18/SCI03/008

Biochemistry

MCB 202

Describe the mechanism in aerobic respiration.

Aerobic respiration is the aerobic catabolism of nutrients to carbon dioxide, water, and energy, and involves an electron transport system in which molecular oxygen is the final electron acceptor. Most eukaryotes and prokaryotes use aerobic respiration to obtain energy from glucose. The overall reaction is:

C6H12O6+6O2→6CO2 + 6H2O

Note that glucose (C6H12O6) is oxidized to produce carbon dioxide (CO2) and oxygen (O2) is reduced to produce water (H2O). This reaction is a strongly driven reactions and "releases" energy as ATP molecules. This type of ATP production is seen in aerobes and facultative anaerobes. Obligate aerobes are organisms that require molecular oxygen because they produce ATP only by aerobic respiration. Facultative anaerobes, on the other hand are capable of aerobic respiration but can switch to fermentation, an anaerobic ATP-producing process, if oxygen is unavailable.

Aerobic respiration involves four stages:

* Glycolysis,
* A transition reaction that forms acetyl coenzyme A,
* The citric acid (Krebs) cycle, and an electron transport chain and
* Chemiosmosis.

1. Glycolysis: Glycolysis is a partial breakdown of a six-carbon glucose molecule into two, three-carbon molecules of pyruvate, 2NADH +2H+, and 2 net ATP as a result of substrate-level phosphorylation. Glycolysis occurs in the cytoplasm of the cell. The overall reaction is:

Glucose (2C)+2NAD+2ADP+2inorganic phosphates(Pi) glucose→2pyruvate (3C)+2NADH+2H++2ATP

Glycolysis also produces a number of key precursor metabolites. Glycolysis does not require oxygen and can occur under aerobic and anaerobic conditions. However, during aerobic respiration, the two reduced NADH molecules transfer protons and electrons to the electron transport chain to generate additional ATPs by way of oxidative phosphorylation. The glycolysis pathway involves 9 distinct steps, each catalyzed by a unique enzyme.

Step 1: To initiate glycolysis in eukaryotic cells, a molecule of ATP is hydrolyzed to transfer a phosphate group to the number 6 carbon of glucose to produce glucose 6-phosphate. In prokaryotes, the conversion of phosphoenolpyruvate (PEP) to pyruvate provides the energy to transport glucose across the cytoplasmic membrane and, in the process, adds a phosphate group to glucose producing glucose 6-phosphate.

Step 2: The glucose 6-phosphate is rearranged to an isomeric form called fructose 6-phosphate.

Step 3: A second molecule of ATP is hydrolyzed to transfer a phosphate group to the number 1 carbon of fructose 6-phosphate to produce fructose 1, 6-biphosphate.

Step 4: The 6-carbon fructose 1, 6 biphosphate is split to form two, 3-carbon molecules: glyceraldehyde 3-phosphate and dihydroxyacetone phosphate. The dihydroxyacetone phosphate is then converted into a second molecule of glyceraldehyde 3-phosphate. Two molecules of glyceraldehyde 3-phosphate will now go through each of the remaining steps in glycolysis producing two molecules of each product.

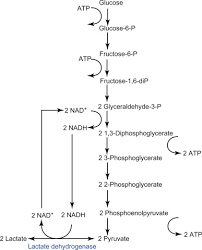
Step 5: As each of the two molecules of glyceraldehyde 3-phosphate are oxidized, the energy released is used to add an inorganic phosphate group to form two molecules of 1, 3-biphosphoglycerate, each containing a high-energy phosphate bond. During these oxidations, two molecules of NAD+ are reduced to form 2NADH + 2H+. During aerobic respiration, the 2NADH + 2H+ carry protons and electrons to the electron transport chain to generate additional ATP by oxidative phosphorylation.

Step 6: As each of the two molecules of 1, 3-biphosphoglycerate is converted to 3-phosphoglycerate, the high-energy phosphate group is added to ADP producing 2 ATP by substrate-level phosphorylation.

Step 7: The two molecules of 3-phosphoglycerate is rearranged to form two molecules of 2-phosphoglycerate.

Step 8: Water is removed from each of the two molecules of 2-phosphoglycerate converting the phosphate bonds to a high-energy phosphate bonds as two molecules of phosphoenolpyruvate are produced.

Step 9: As the two molecules of phosphoenolpyruvate are converted to two molecules of pyruvate, the high-energy phosphate groups are added to ADP producing 2 ATP by substrate-level phosphorylation.

 glycolysis pathway

1. A transition reaction that forms acetyl Co-A: The transition reaction connects [glycolysis](https://bio.libretexts.org/Bookshelves/Microbiology/Book%3A_Microbiology_(Kaiser)/Unit_7%3A_Microbial_Genetics_and_Microbial_Metabolism/18%3A_Microbial_Metabolism/18.3%3A_Aerobic_Respiration/18.3A%3A_Glycolysis" \o "18.3A: Glycolysis)to the [citric acid (Krebs) cycle](https://bio.libretexts.org/Bookshelves/Microbiology/Book%3A_Microbiology_(Kaiser)/Unit_7%3A_Microbial_Genetics_and_Microbial_Metabolism/18%3A_Microbial_Metabolism/18.3%3A_Aerobic_Respiration/18.3C%3A_Citric_Acid_(Krebs)_Cycle). Through a process called oxidative decarboxylation, the transition reaction converts the two molecules of the 3-carbon pyruvate from glycolysis (and other pathways) into two molecules of the 2-carbon molecule acetyl Coenzyme A (acetyl-CoA) and 2 molecules of carbon dioxide. First, a carboxyl group of each pyruvate is removed as carbon dioxide and then the remaining acetyl group combines with coenzyme A (CoA) to form acetyl-CoA. As the two pyruvates undergo oxidative decarboxylation, two molecules of NAD+ become reduced to 2NADH + 2H+. The 2NADH + 2H+ carry protons and electrons to the electron transport chain to generate additional ATP by [oxidative phosphorylation](https://bio.libretexts.org/Bookshelves/Introductory_and_General_Biology/Book%3A_General_Biology_(OpenStax)/2%3A_The_Cell/07%3A_Cellular_Respiration/7.4%3A_Oxidative_Phosphorylation).

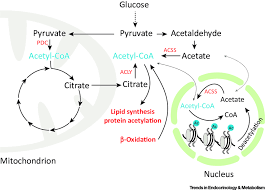
The two molecules of acetyl-CoA then enter the [citric acid cycle](https://bio.libretexts.org/Bookshelves/Microbiology/Book%3A_Microbiology_(Kaiser)/Unit_7%3A_Microbial_Genetics_and_Microbial_Metabolism/18%3A_Microbial_Metabolism/18.3%3A_Aerobic_Respiration/18.3C%3A_Citric_Acid_(Krebs)_Cycle). The 2NADH molecules that are produced carry electrons to the electron transport system for further production of ATPs by oxidative phosphorylation.

The overall reaction for the transition reaction is:

2 pyruvate + 2 NAD+ + 2 coenzyme A→2 acetyl-CoA + 2 NADH + 2 H+ + 2 CO2

In [prokaryotic cells](https://bio.libretexts.org/Bookshelves/Microbiology/Book%3A_Microbiology_(Kaiser)/Unit_1%3A_Introduction_to_Microbiology_and_Prokaryotic_Cell_Anatomy/1%3A_Fundamentals_of_Microbiology/1.2%3A_Cellular_Organization_-_Prokaryotic_and_Eukaryotic_Cells), the transition step occurs in the cytoplasm; in eukaryotic cells the pyruvates must first enter the mitochondria because the transition reaction and the citric acid cycle take place in the matrix of the mitochondria.

The two molecules of acetyl-CoA can now enter the citric acid cycle. Acetyl-CoA is also a **precursor metabolite** for fatty acid synthesis.



1. Citric acid cycle: The citric acid cycle, also known as the tricarboxylic acid cycle and the Krebs cycle, completes the oxidation of glucose by taking the pyruvates from [glycolysis](https://bio.libretexts.org/Bookshelves/Introductory_and_General_Biology/Book%3A_Biology_(Kimball)/04%3A_Cell_Metabolism/4.04%3A_Glycolysis" \o "4.4: Glycolysis)(and other pathways), by way of the transition reaction mentioned previously, and completely breaking them down into CO2 molecules, H2O molecules, and generating additional ATP by oxidative phosphorylation. In prokaryotic cells, the citric acid cycle occurs in the cytoplasm; in eukaryotic cells the citric acid cycle takes place in the matrix of the mitochondria.

The overall reaction for the citric acid cycle is:

2 acetyl groups+6NAD++2FAD+2ADP+2Pi→4CO2+6NADH+6H++2FADH2+2ATP

The citric acid cycle provides a series of intermediate compounds that donate protons and electrons to the electron transport chain by way of the reduced coenzymes NADH and FADH2. The electron transport chain then generates additional ATPs by oxidative phosphorylation. The citric acid cycle also produces 2 ATP by substrate phosphorylation and plays an important role in the flow of carbon through the cell by supplying [precursor metabolites](http://faculty.ccbcmd.edu/courses/bio141/lecguide/unit7/metabolism/cellresp/fg3.html) for various biosynthetic pathways. The citric acid cycle involves 8 distinct steps, each catalyzed by a unique enzyme.

Step 1: The citric acid cycle begins when Coenzyme A transfers its 2-carbon acetyl group to the 4-carbon compound oxaloacetate to form the 6-carbon molecule citrate

Step 2: The citrate is rearranged to form an isomeric form, isocitrate

Step 3: The 6-carbon isocitrate is oxidized and a molecule of carbon dioxide is removed producing the 5-carbon molecule alpha-ketoglutarate. During this oxidation, NAD+ is reduced to NADH and H+

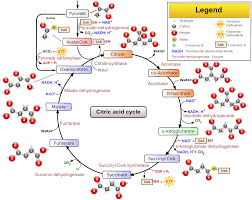
Step 4: Alpha-ketoglutarate is oxidized, carbon dioxide is removed, and coenzyme A is added to form the 4-carbon compound succinyl-CoA. During this oxidation, NAD+ is reduced to NADH + H+

Step 5: CoA is removed from succinyl-CoA to produce succinate. The energy released is used to make guanosine triphosphate (GTP) from guanosine diphosphate (GDP) and Pi by substrate-level phosphorylation. GTP can then be used to make ATP

Step 6: Succinate is oxidized to fumarate. During this oxidation, FAD is reduced to FADH2

Step 7: Water is added to fumarate to form malate

Step 8: Malate is oxidized to produce oxaloacetate, the starting compound of the citric acid cycle. During this oxidation, NAD+ is reduced to NADH + H+. The NADH + H+ and FADH2 carry protons and electrons to the electron transport chain to generate additional ATP by oxidative phosphorylation.

Citric acid cycle

1. Chemiosmosis: During various steps in glycolysis and the citric acid cycle, the oxidation of certain intermediate precursor molecules causes the reduction of NAD+ to NADH + H+ and FAD to FADH2. NADH and FADH2 then transfer protons and electrons to the electron transport chain to produce additional ATPs by oxidative phosphorylation .

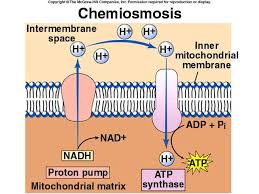
During the process of aerobic respiration, coupled oxidation-reduction reactions and electron carriers are often part of what is called an electron transport chain, a series of electron carriers that eventually transfers electrons from NADH and FADH2 to oxygen. The diffusible electron carriers NADH and FADH2 carry hydrogen atoms (protons and electrons) from substrates in exergonic catabolic pathways such as glycolysis and the citric acid cycle to other electron carriers that are embedded in membranes. These membrane-associated electron carriers include flavoproteins, iron-sulfur proteins, quinones, and cytochromes. The last electron carrier in the electron transport chain transfers the electrons to the terminal electron acceptor, oxygen. The chemiosmotic theory explains the functioning of electron transport chains. According to this theory, the transfer of electrons down an electron transport system through a series of oxidation-reduction reactions releases energy. This energy allows certain carriers in the chain to transport hydrogen ions (H+ or protons) across a membrane.

Depending on the type of cell, the electron transport chain may be found in the cytoplasmic membrane or the inner membrane of mitochondria.

* In prokaryotic cells, the protons are transported from the cytoplasm of the bacterium across the cytoplasmic membrane to the periplasmic space located between the cytoplasmic membrane and the cell wall.
* In eukaryotic cells, protons are transported from the matrix of the mitochondria across the inner mitochondrial membrane to the intermembrane space located between the inner and outer mitochondrial membranes

As the hydrogen ions accumulate on one side of a membrane, the concentration of hydrogen ions creates an electrochemical gradient or potential difference (voltage) across the membrane. (The fluid on the side of the membrane where the protons accumulate acquires a positive charge; the fluid on the opposite side of the membrane is left with a negative charge.) The energized state of the membrane as a result of this charge separation is called proton motive force or PMF. This proton motive force provides the energy necessary for enzymes called ATP synthases (see Figure 3), also located in the membranes mentioned above, to catalyze the synthesis of ATP from ADP and phosphate. This generation of ATP occurs as the protons cross the membrane through the ATP synthase complexes and re-enter either the bacterial cytoplasm or the matrix of the mitochondria. As the protons move down the concentration gradient through the ATP synthase, the energy released causes the rotor and rod of the ATP synthase to rotate. The mechanical energy from this rotation is converted into chemical energy as phosphate is added to ADP to form ATP. Proton motive force is also used to transport substances across membranes during active transport and to rotate bacterial flagella.

At the end of the electron transport chain involved in aerobic respiration, the last electron carrier in the membrane transfers 2 electrons to half an oxygen molecule (an oxygen atom) that simultaneously combines with 2 protons from the surrounding medium to produce water as an end product.

Chemiosmosis

In addition to generating ATP by oxidative phosphorylation in prokaryotic cells, proton motive force is also used for functions such as transporting materials across membranes and rotating flagella. Also, some bacteria use different carriers in their electron transport chain than others and the carriers may vary in the number of protons they transport across the membrane. Furthermore, the number of ATP generated per reduced NADH or FADH2 is not always a whole number. For every pair of electrons transported to the electron transport chain by a molecule of NADH, between 2 and 3 ATP are generated. For each pair of electrons transferred by FADH2, between 1 and 2 ATP are generated. In eukaryotic cells, unlike prokaryotes, NADH generated in the cytoplasm during glycolysis must be transported across the mitochondrial membrane before it can transfer electrons to the electron transport chain and this requires energy. As a result, between 1 and 2 ATP are generated from these NADH.

One molecule of glucose oxidized by aerobic respiration in prokaryotes yields the following:

Glycolysis: 2 net ATP from substrate-level phosphorylation  
2 NADH yields 6 ATP (assuming 3 ATP per NADH) by oxidative phosphorylation.

Transition Reaction: 2 NADH yields 6 ATP (assuming 3 ATP per NADH) by oxidative phosphorylation.

Citric Acid Cycle: 2 ATP from substrate-level phosphorylation  
6 NADH yields 18 ATP (assuming 3 ATP per NADH) by oxidative phosphorylation  
2 FADH2 yields 4 ATP (assuming 2 ATP per FADH2) by oxidative phosphorylation.

Total Theoretical Maximum Number of ATP Generated per Glucose in Prokaryotes is 38 ATP, 4 from substrate-level phosphorylation; 34 from oxidative phosphorylation.

In eukaryotic cells, the theoretical maximum yield of ATP generated per glucose is 36 to 38, depending on how the 2 NADH generated in the cytoplasm during glycolysis enter the mitochondria and whether the resulting yield is 2 or 3 ATP per NADH.