

Chapter 9 – Cellular Respiration and Fermentation*

*Lecture notes are to be used as a **study guide** only and *do not* represent the comprehensive information you will need to know for the exams.

Overview : Life Is Work

Living cells need energy to perform their tasks, such as creating polymers (Figure 9.1). The ultimate energy for life comes from the sun. Energy flows into an ecosystem as sunlight and exists as heat (Figure 9.2). Cells harvest chemical energy stored in organic molecules and use it to generate ATP. There are three (3) key pathways of respiration: 1) glycolysis, 2) the citric acid cycle, and 3) oxidative phosphorylation. Another important pathway is fermentation.

Concept 9.1 : Catabolic pathways yield energy by oxidizing organic fuels

Catabolic pathways release stored energy by breaking down complex organic molecules. Electron transfer is important in these pathways.

Catabolic Pathways and Production of ATP

Using enzymes, cells can extract the potential energy stored in organic compounds during exergonic reactions. The energy taken out can be used to do work, and the rest is given off as heat.

One catabolic process is called **fermentation** which is a partial oxidation of organic molecules, and it occurs without oxygen. **Aerobic respiration** is the complete oxidation of organic compounds, like sugar, with the participation of oxygen in the process. Food provides the “fuel” for the cells, and mixed with oxygen, energy is extracted. The final products of this reaction are CO₂, H₂O and energy.

Glucose (C₆H₁₂O₆) is commonly used as the representative organic molecule to understand aerobic respiration since most cells use glucose as a fuel source. The breakdown of glucose is exergonic ($\Delta G = -686$ kcal/mol). This reaction can happen spontaneously, without any input of energy. ATP is critical in allowing the cell to do work, like pumping solutes across the cell membrane. It is important to understand the chemical process of oxidation and reduction.

The Principle of Redox The transfer of electrons (e⁻) is a process called oxidation – reduction, or **redox reactions**. The loss of electrons is called **oxidation**, and the gain of electrons is called **reduction** (see diagram reaction page 164, and Figure 9.3). A **reducing agent** is the one that will give up its electron; the **oxidizing agent** is one that will accept the electrons.

Oxidation of Organic Fuel Molecules During Cellular Respiration As biologists, we are more interested in the energy-yielding redox process of respiration – the oxidation of glucose. Glucose is oxidized, and oxygen is reduced. In this process hydrogen is transferred, and in the process energy is produced, ATP. The enzymes in cells lowers the energy barrier to allow glucose to be oxidized in a series of steps.

Stepwise Energy Harvest via NAD^+ and the Electron Transport Chain In the cell glucose is broken down in a series of steps to release energy, and each step is catalyzed by an enzyme. The hydrogen atoms (H^+ and its e^-), are passed to an electron carrier called **NAD^+** , a derivative of niacin vitamin. NAD^+ cycles between NAD^+ and NADH. Enzymes called dehydrogenases remove a pair of hydrogen atoms from the substrate. The enzyme delivers the electrons to NAD^+ (Figure 9.4). NADH represents stored energy that can be used to make ATP.

Respiration uses a step-wise process, called the electron transport chain, to break the fall of electrons to oxygen in several energy releasing steps, called the **electron transport chain** (Figure 9.5b). The proteins involved in the electron transport chain are located in the inner membrane of mitochondria in eukaryotic cells. The electrons travel “down” the electron transport chain, until they reach oxygen.

The Stages of Cellular Respiration: A Preview

There are three (3) metabolic stages to harvest energy from glucose:

1. **Glycolysis**
2. **Pyruvate oxidation / citric acid cycle**
3. **Oxidative phosphorylation**

The overall pathway of cellular respiration is in Figure 9.6. **Glycolysis** is the first set of biochemical reactions, and occurs in the cell cytoplasm – glucose is split into two pyruvate molecules. Pyruvate enters the mitochondrion and combines with acetyl-CoA to initiate the **citric acid cycle**. As the citric acid cycle is proceeding, glucose is oxidized to CO_2 . During the steps of glycolysis and the citric acid cycle, NADH is produced. In the third stage of cellular respiration, NADH removes its H ($\text{H}^+ + \text{e}^-$), and the electron travels down the electron transport chain where it complexes with H^+ and O_2 to form water.

ATP is produced by two mechanisms: 1) **oxidative phosphorylation** – H^+ that were pumped out along the electron transport chain are used by the enzyme ATP synthase to generate ATP; 2) **substrate-level phosphorylation** – the intermediates of the glycolysis and citric acid cycle pathways are used to generate ATP (Figure 9.7).

Concept 9.2 : Glycolysis harvests chemical energy by oxidizing glucose to pyruvate

Glycolysis is the splitting of one glucose molecule to form two pyruvate molecules. Glycolysis is divided into two phases: 1) an energy investment phase, and 2) an energy payoff phase (Figure 9.8). During glycolysis ATP is generated by substrate-level phosphorylation, and NADH is produced (Figure 9.9)

Concept 9.3 : After pyruvate is oxidized, the citric acid cycle completes the energy-yielding oxidation of organic molecules

The oxidation of glucose to pyruvate only yields a small portion of the energy stored in glucose. Further oxidation of glucose in the citric acid cycle yields more energy.

Oxidation of Pyruvate to Acetyl-CoA

When pyruvate enters the mitochondrion, it is converted to **acetyl-CoA** (Figure 9.10).

The Citric Acid Cycle

Other names for the cycle are: tricarboxylic acid cycle (TCA) and Krebs's cycle (Figure 9.11). CO₂ is generated, along with ATP from substrate-level phosphorylation. NADH and FADH₂ pick up the electrons they are released, and carry them to the electron transport chain. Here ATP is produced by oxidative phosphorylation (Figure 9.12).

Concept 9.4 : During oxidative phosphorylation, chemiosmosis couples electron transport to ATP synthesis

Some ATP is formed by substrate-level phosphorylation, but most of the ATP is generated from NADH and FADH₂ by the process called oxidative phosphorylation via the electron transport chain.

The Pathway of Electron Transport

The components of the electron transport chain reside in the inner membrane of the mitochondrion for eukaryotic cells. It is mainly comprised of protein complexes and various prosthetic groups (Figure 9.13). Initially, NADH has its electron removed at the first component. As the electron travels down the electron transport chain, each component (Complex I – IV) goes through a series of reduction (accepts the electron) and oxidation (the electron is removed) states. Proteins called **cytochromes** exist between ubiquinone and oxygen. The electron is then passed to oxygen, which picks up a pair of H^+ to form water. $FADH_2$ also contributes its electrons to the chain. The electron transport chain itself is not responsible for making ATP.

Chemiosmosis: The Energy-Coupling Mechanism

The enzyme **ATP synthase** is located on the inner membrane of the mitochondrion. This enzyme actually makes ATP from ADP and P_i (inorganic phosphate). ATP synthase uses the energy of a H^+ to make ATP. Energy stored in the form of a hydrogen ion gradient across the inner mitochondrial membrane is used to drive cellular work in a process called **chemiosmosis**.

ATP synthase is a multi-subunit enzyme. Protons move into the enzyme complex, causing it to spin, with the result being the formation of ATP (Figure 9.14). The electron transport chain establishes the H^+ proton gradient, called the **proton motive force** (Figure 9.15). The proton motive force is used by cells to do work.

An Accounting of ATP Production by Cellular Respiration

The overall function of cellular respiration is to harvest energy out of glucose in the form of ATP (Figure 9.16). As a result of the complete oxidation of glucose, ~ 30 – 32 ATP are made. The rest of the energy stored in glucose is released as heat.

Concept 9.5 : Fermentation and anaerobic respiration enable cells to produce ATP without the use of oxygen

Cells oxidize organic fuels and generate ATP *without* the use of oxygen – anaerobic respiration and fermentation. The electron transport chain is used in anaerobic respiration, but not fermentation. Anaerobic respiration is most often studied in prokaryotic microbes (bacteria). These organisms use sulfate ion (SO_4^{2-}) as the terminal electron acceptor, as an example.

Fermentation is essentially glycolysis with a few extra steps. ATP is produced by substrate-level phosphorylation, and fermentation products are produced to regenerate NAD^+ .

Types of Fermentation

Alcohol fermentation (Figure 9.17a), pyruvate is converted to ethanol, and NAD^+ is regenerated.

Lactic acid fermentation (Figure 9.17b), pyruvate is converted to lactate, and NAD^+ is regenerated.

Comparing Fermentation with Anaerobic and Aerobic Respiration

Fermentation, anaerobic respiration, and aerobic respiration are different pathways that produce ATP. All three pathways use NAD^+ as the oxidizing agent. The key difference is how NADH is regenerated back to NAD^+ .

Organisms can be classified based on their oxygen usage for respiration / fermentation. **Obligate anaerobes** carry out fermentation or anaerobic respiration. **Facultative anaerobes** can carry out aerobic and/or anaerobic respiration, and fermentation. In organisms that are facultative anaerobes, pyruvate is a critical intermediate in the pathway (Figure 9.18).

Concept 9.6 : Glycolysis and the citric acid cycle connect to many other metabolic pathways

Glycolysis and the citric acid cycle are the major intersection of the cell's catabolic and anabolic pathways.

The Versatility of Catabolism

Organic molecules other than glucose, such as fats, starch and proteins, can be used as organic fuel for the cell in cellular respiration (Figure 9.19). **Beta oxidation** is used to break down fatty acid chains.

Biosynthesis (Anabolic Pathways)

Organic monomers, and some intermediates of glycolysis can be used as the starting material to build polymer molecules.

Regulation of Cellular Respiration via Feedback Mechanisms

Control of the enzymes for cellular respiration is determined by the metabolic needs of the cell (Figure 9.20).