Metabolism - Part 1
Glycolysis & Respiration

Cells harvest chemical energy from foodstuffs in a series of exergonic reactions. The harvested energy can then be used to power energy demanding processes including endergonic reactions.
**Metabolism** - the sum of all chemical processes carried out by living cells

**Catabolism** - the chemical reactions that break larger molecules into smaller molecules. It is usually an exergonic process.

**Anabolism** - the chemical reactions that form larger molecules from smaller molecules. It is usually an endergonic process.

**Autotroph** - an organism that obtains its energy from sunlight or inorganic chemicals. Plants, photosynthetic protists, and photosynthetic prokaryotes are autotrophs.

**Heterotroph** - an organism that obtains its energy by consuming and degrading organic molecules. Some eat other organisms, some parasitize, some degrade the remains of once-living organisms. Animals, Fungi, many protists and most prokaryotes are heterotrophs.
Glucose is the preferred energy source of all organisms and it is the principal product of photosynthesis.

Glucose is made and used in complementary processes

**Photosynthesis** makes glucose:

\[
6 \text{CO}_2 + 12 \text{H}_2\text{O} + \text{light energy} \rightarrow \text{C}_6\text{H}_{12}\text{O}_6 + 6 \text{H}_2\text{O} + 6 \text{O}_2
\]

**Glycolysis and Respiration** use glucose and yield energy:

\[
\text{C}_6\text{H}_{12}\text{O}_6 + 6 \text{O}_2 + 6 \text{H}_2\text{O} \rightarrow 6 \text{CO}_2 + 12 \text{H}_2\text{O} + \text{chemical energy}
\]
Glucose breakdown can be aerobic (using oxygen) or anaerobic (without oxygen). Anaerobic metabolism of glucose is also known as **anaerobic glycolysis** or **fermentation**. Aerobic metabolism of glucose is known as **glycolysis and respiration**.

Complete aerobic metabolism of glucose produces water and carbon dioxide as products.

\[ \text{C}_6\text{H}_{12}\text{O}_6 + 6 \text{O}_2 \rightarrow 6 \text{CO}_2 + 6 \text{H}_2\text{O} \]

Energy is released in this process. The overall \( \Delta G \) of glucose breakdown in cells is -720 kcal/mole. Normally about 32% of the energy released is captured through the formation of ATP. The remainder is released as heat.
Aerobic breakdown of glucose consists of four stages

1. **Glycolysis** - a 10 step biochemical pathway where a glucose molecule (6 C) is split into 2 molecules of pyruvate (3 C). To begin the process 2 ATP must be invested. Energy released from the reactions is captured in the form of 4 molecules of ATP molecules and high energy electrons are trapped in the reduction of 2 molecules NAD to NADH.

The remaining steps are collectively called **Respiration**.

2. **Pyruvate oxidation** - In a single step a carbon is removed from pyruvate (3 C) as CO₂, leaving 2 of the original carbons attached to Coenzyme-A. The complex is called Acetyl Co-A. In this process one NADH molecule is produced.

3. **Krebs cycle** - A 9 step biochemical pathway that converts all of the remaining carbons from the original glucose into CO₂, and yields 1 ATP, and traps high energy electrons in 3 NADH, and 1 FADH per Acetyl Co-A.
4. **Electron Transport Chain** - the high energy electrons trapped in NADH and FADH in glycolysis, pyruvate oxidation, and the Krebs cycle are used to produce ATP through chemiosmosis. \( O_2 \) is the final acceptor of high energy electrons.

In eukaryotes, glycolysis occurs in the cytoplasm, pyruvate oxidation, the Krebs cycle and the Electron Transport System occur in the mitochondrion.

In prokaryotes all steps occur in the cytoplasm.
Energy tally - starting with glucose and following all carbons

**Glycolysis:** Glucose $\rightarrow$ 2 pyruvate + 2 ATP (net) + 2 NADH

**Pyruvate oxidation:** 2 pyruvate $\rightarrow$ 2 Acetyl Co-A + 2CO$_2$ + 2 NADH

**Krebs Cycle:**
2 Acetyl Co-A $\rightarrow$ 4 CO$_2$ + 2 ATP + 6 NADH + 2 FADH

**Electron transport system (ETS):**
2 NADH from glycolysis allow production of $3^e$ or $5^p$ ATP
2 NADH from pyruvate oxidation allow production of 5 ATP
6 NADH from the Krebs cycle allow the production of 15 ATP
2 FADH from Krebs cycle allow the production of 3 ATP

e – eukaryotes, p - prokaryotes
2 ATP are produced in glycolysis and 2 ATP are produced in the Krebs cycle.

High energy electrons carried by NADH and FADH are used to produce ATP in the electron transport system.

The difference between prokaryotes and eukaryotes will be explained later.
Glycolysis Overview

1. 6-carbon glucose (Starting material) → 2 ATP
   → 6-carbon sugar diphosphate

2. Cleavage reactions. Then, the six-carbon molecule with two phosphates is split into two, forming two three-carbon sugar phosphates.

3. Energy-harvesting reactions. Finally, in a series of reactions, each of the two three-carbon sugar phosphates is converted to pyruvate. In the process, an energy-rich hydrogen is harvested as NADH, and two ATP molecules are formed.

Priming reactions. Glycolysis begins with addition of energy. Two high-energy phosphates from two molecules of ATP are added to the six-carbon molecule glucose, producing a six-carbon molecule with two phosphates.
Respiration - pyruvate oxidation, the Krebs cycle, and the ETS

Pyruvate, a 3 carbon molecule is oxidized to acetate (producing CO$_2$ and NADH) and combined with Coenzyme-A to form Acetyl Co-A in preparation for sending the remaining carbons of acetate into the Krebs cycle.

In eukaryotes, all steps of respiration occur in the mitochondrion.
The Krebs cycle occurs in the cytoplasm of prokaryotes and in the matrix of the mitochondrion in eukaryotes.
In eukaryotes, the Electron Transport System is located within the inner mitochondrial membrane. High energy electrons passed through the ETS are used to pump protons from the matrix into the intermembrane space. Oxygen is required as the final electron acceptor. Without oxygen, there is no place for NADH and FADH to donate their electrons and no energy can be harvested. 10 protons are pumped for each NADH and 6 protons for each FADH. When the ETS is active, the intermembrane space has a lower pH than the matrix.12
The protons pumped out of the matrix produce a proton gradient between the intermembrane space and the matrix. The proton gradient is used to produce ATP. This is the **Chemiosmotic Theory**.

ATP synthase couples ATP production to proton flow.

This production of ATP is called **oxidative phosphorylation** because it requires oxygen. It does not directly involve substrates.
ATP synthase is a large enzyme that acts as a rotary motor.

The ETS creates a proton gradient. Proton flow causes the rotary motor to spin and the mechanical energy of the spinning motor is captured by combining ADP and P_i to form ATP.
ATP production in the mitochondrion (a summary of respiration):

1. Electrons are harvested and carried to the transport system.

2. Electrons provide energy to pump protons across the membrane.

3. Oxygen joins with protons to form water.

4. Protons diffuse back in, driving the synthesis of ATP.
Q: Why do prokaryotes make 2 more ATP than eukaryotes?

A: In eukaryotes, the NADH produced from glycolysis must be transported into the mitochondrion before they can be used to make ATP.

It costs 1 ATP to transport each NADH made in glycolysis. So, for the 2 NADH that prokaryotes can use to make 5 ATP, eukaryotes can only harvest a net of 3.
A: The electrons carried by FADH have less energy than the electrons carried by NADH. FADH electrons can be used to pump fewer protons than the electrons from NADH.
Metabolizing glucose without oxygen: **Anaerobic glycolysis** or **fermentation**

Many organisms live in environments completely devoid of oxygen and still metabolize glucose. Some organisms can switch between metabolizing glucose aerobically and anaerobically depending on oxygen availability. Our own muscles must metabolize glucose anaerobically when we work them vigorously because they deplete oxygen faster than the circulatory system can supply it.

Relatively little ATP can be obtained from fermentation of a single molecule of glucose, but the process is very quick. So, many glucose molecules can be broken down to provide a large amount of ATP very quickly. If there is no oxygen available, fermentation is the only option for cells to harvest energy.
Yeast (a fungus), and some prokaryotes, can metabolize glucose anaerobically, harvesting 2 ATP. Since the ETS can’t be used without oxygen, the NADH can’t be used to generate more ATP. Without oxygen the pyruvate can’t be metabolized either because its metabolism depends on NADH being oxidized in the ETS.

Without a mechanism to recycle NADH back to NAD, glycolysis would stop. NADH is recycled to NAD through the production of ethanol from pyruvate.

Ethanol and CO₂ are metabolic by-products of the anaerobic metabolism of glucose.
Our muscle cells and some microorganisms can metabolize glucose anaerobically in a slightly different process. To recycle the NADH they produce lactic acid. The regenerated NAD can be used to keep glycolysis and ATP production going even when oxygen is absent.

Lactic acid produced during activity must be reconverted into pyruvate by reducing NAD to NADH when oxygen is available to remove it. The NADH ultimately donates electrons to O$_2$ in the ETS.

Accumulated lactic acid is called **oxygen debt** because oxygen must be used to metabolize it after exercise has stopped.
All organic molecules metabolized as a source of energy are converted to one of the intermediates of glycolysis or respiration.