Chapter 8

8.1 Cellular Respiration

1. Cellular respiration involves various metabolic pathways that break down carbohydrates and other metabolites with the concomitant buildup of ATP.
2. **Cellular respiration** consumes oxygen and produces CO_2; because oxygen is required, cellular respiration is **aerobic**.
3. Cellular respiration usually involves the complete breakdown of glucose into CO_2 and H_2O.
4. The net equation for glucose breakdown is: $C_6H_{12}O_6 + 6\ O_2\ = 6\ CO_2 + 6\ H_2O$ + energy
5. Glucose is a high-energy molecule; CO_2 and H_2O are low-energy molecules; cellular respiration is thus *exergonic* because it releases energy.
6. Electrons are removed from substrates and received by oxygen, which combines with H^+ to become water.
7. Glucose is oxidized and O_2 is reduced.
8. The reactions of cellular respiration allow energy in glucose to be released slowly; therefore ATP is produced gradually.
9. In contrast, if glucose were broken down rapidly, most of its energy would be lost as non-usable heat.
10. The breakdown of glucose yields synthesis of 36 or 38 ATP (depending on certain conditions); this preserves about 39% of the energy available in glucose.
11. This is relatively efficient compared to, for example, the 25% efficiency of a car burning gasoline.

A. NAD^+ and FAD

1. Each metabolic reaction in cellular respiration is catalyzed by a specific enzyme.
2. As a metabolite is oxidized, **NAD^+** (nicotinamide adenine dinucleotide) accepts two electrons and a hydrogen ion (H^+); this results in NADH + H^+.
3. Electrons received by NAD^+ and FAD are high-energy electrons and are usually carried to the electron transport chain.
4. NAD^+ is a coenzyme of oxidation-reduction since it both accepts and gives up electrons; thus, NAD^+ is sometimes called a *redox coenzyme*
5. Only a small amount of NAD^+ is needed in cells because each NAD^+ molecule is used repeatedly.
6. FAD coenzyme of oxidation-reduction can replace NAD^+; FAD accepts two electrons and two hydrogen ions to become $FADH_2$.

B. Phases of Cellular Respiration

1. Cellular respiration includes four phases:
   a. **Glycolysis** is the breakdown of glucose in the cytoplasm into two molecules of pyruvate.
      1) Enough energy is released for an immediate yield of two ATP.
      2) Glycolysis takes place outside the mitochondria and does not utilize oxygen; it is therefore an **anaerobic** process.

b. In the **preparatory (prep) reaction**, pyruvate enters a mitochondrion and is oxidized to a two-carbon acetyl group and CO_2 is removed; this reaction occurs twice per glucose molecule.
c. The **citric acid cycle**:
   1) occurs in the matrix of the mitochondrion and produces NADH and $FADH_2$;
   2) is a series of reactions that gives off CO_2 and produces one ATP;
   3) turns twice because two acetyl-CoA molecules enter the cycle per glucose molecule;
   4) produces two immediate ATP molecules per glucose molecule.
d. The **electron transport chain**:
   1) is a series of carriers in the inner mitochondrial membrane that accept electrons from glucose--electrons are passed from carrier to carrier until received by oxygen;
   2) passes electrons from higher to lower energy states, allowing energy to be released and stored for ATP production;

8.2 Outside the Mitochondria: Glycolysis

1. **Glycolysis** occurs in the cytoplasm outside the mitochondria.
2. Glycolysis is the breakdown of glucose into two pyruvate molecules.
3. Glycolysis is universally found in organisms; therefore, it likely evolved before the citric acid cycle and electron transport chain.
4. Thycolosis can be divided into the energy-investment steps where ATP is used to "jump start" glycolosis, and the energy-harvesting steps, where more ATP is made than used.

A. Energy-Investment Steps
   1. Glycolysis begins with the activation of glucose with two ATP; the glucose splits into two C_3 molecules known as G3P, each of which carries a phosphate group.

B. Energy-Harvesting Steps
   1. Oxidation of G3P occurs by removal of electrons and hydrogen ions.
   2. Two electrons and one hydrogen ion are accepted by NAD^+, resulting in two NADH; later, when the NADH molecules pass two electrons to the electron transport chain, they become NAD^+ again.
   3. The oxidation of G3P and subsequent substrates results in four high-energy phosphate groups, which are used to synthesize four ATP molecules; this process is called **substrate-level phosphorylation**.
   4. Two of four ATP molecules produced are required to replace two ATP molecules used in the initial phosphorylation of glucose; therefore there is a *net* gain of two ATP from glycolysis.
   5. Pyruvate enters a mitochondrion (if oxygen is available) and cellular respiration ensues.
   6. If oxygen is not available, *fermentation occurs* and pyruvate undergoes reduction.

8.3 Fermentation

1. **Fermentation** is an *anaerobic* (i.e., occurs in the absence of oxygen) process which consists of glycolysis

plus reduction of pyruvate to either lactate or to alcohol and CO_2 (depending on the organism).

2. Animal cell fermentation results in lactate.
3. Bacteria can produce an organic acid like lactate, or an alcohol and CO_2.
4. Yeasts produce ethyl alcohol and CO_2.
5. NADH passes its electrons to pyruvate instead of to an electron transport chain; NAD^+ is then free to return and pick up more electrons during earlier reactions of glycolysis.

A. Advantages and Disadvantages of Fermentation

1. Despite a low yield of two ATP molecules, fermentation provides a quick burst of ATP energy for muscular activity.
2. Fermentation products are toxic to cells.
    a. When blood cannot remove all lactate from muscles, lactate changes pH and causes muscles to fatigue.
    b. The individual is in **oxygen debt** because oxygen is needed to restore ATP levels and rid the body of lactate.
    c. Recovery occurs after lactate is sent to the liver where it is converted into pyruvate; some pyruvate is then respired or converted back into glucose.

B. Efficiency of Fermentation

1. Two ATP produced per glucose molecule during fermentation is equivalent to 14.6 kcal.
2. Complete glucose breakdown to CO_2 and H_2O during cellular respiration represents a potential yield of 686 kcal per molecule.
3. Efficiency of fermentation is 14.6/686 or about 2.1%, far less efficient than complete breakdown of glucose.

C. Fermentation Helps Produce Numerous Food Products (*Science Focus box*)

1. Yeast Fermentation
    a. Baker's yeast, *Saccharomyces cerevisiae*, is added to bread for leavening. The dough rises when yeasts give off CO_2.
    b. Yeasts ferment the carbohydrates of fruit to produce ethyl alcohol in wine, and ferment grains to produce ethyl alcohol in beer.
    c. The acetic acid bacteria, *Acetobacter aceti*, spoil wine, and convert the alcohol to acetic acide to produce vinegar.
2. Bacterial Fermentation
    a. Lactic acid bacteria cause milk to sour and produce yogurt, sour cream, and cheese.
    b. Brine cucumber pickles, sauerkraut, and kimchi are pickled vegetables produced by acid producing fermenting bacteria.
3. Soy Sauce Production
    a. Yeast and fermenting bacteria are added to soy beans and wheat to produce soy sauce.

8.4 Inside the Mitochondria

1. The next reactions of cellular respiration involve the **preparatory reaction**, the **citric acid cycle**, and the **electron transport chain**.
2. These reactions occur in the mitochondria.

3. A **mitochondrion** has a double membrane with an intermembrane space (between the outer and inner membrane).
4. *Cristae* are the inner folds of membrane that jut into the *matrix*, the innermost compartment of a mitochondrion that is filled with a gel-like fluid.
5. The prep reaction and citric acid cycle enzymes are in the matrix; the electron transport chain is in the cristae.
6. Most of the ATP produced in cellular respiration is produced in the mitochondria; therefore, mitochondria are often called the "powerhouses" of the cell.

A. Preparatory Reaction
   1. The preparatory reaction connects glycolysis to the citric acid cycle.
   2. In this reaction, pyruvate is converted to a two-carbon acetyl group, and is attached to *coenzyme A*, resulting in the compound **acetyl-CoA**.
   3. This redox reaction removes electrons from pyruvate by a dehydrogenase enzyme, using NAD^+ as a coenzyme.
   4. This reaction occurs twice for each glucose molecule.
   5. CoA carry the acetyl group to the citric acid cycle.
   6. The two NADH carry to electrons to the electron transport chain.
   7. The CO_2 diffuses out of animal cells into blood, transported to lungs, and exhaled.

B. Citric Acid Cycle
   1. The citric acid cycle occurs in the matrix of mitochondria.
   2. The cycle is sometimes called the Krebs cycle, named for Sir Hans Krebs, who described the fundamentals of the reactions in the 1930s.
   3. The cycle begins by the addition of a two-carbon acetyl group to a four-carbon molecule, forming a six-carbon citrate (citric acid) molecule.
   4. In the subsequent reactions, at three different times two electrons and one hydrogen ion are accepted by NAD^+, forming NADH.
   5. At one time, two electrons and one hydrogen ion are accepted by FAD, forming $FADH_2$.
   6. NADH and $FADH_2$ carry these electrons to the electron transport chain.
   7. Some energy is released and is used to synthesize ATP by *substrate-level phosphorylation*.
   8. One high-energy metabolite accepts a phosphate group and transfers it to convert ADP to ATP.
   9. The citric acid cycle turns twice for each original glucose molecule.
   10. The products of the citric acid cycle (per glucose molecule) are 4 CO_2, 2 ATP, 6 NADH and 2 $FADH_2$.
   11. Production of CO_2
       a. The six carbon atoms in the glucose molecule have now become the carbon atoms of six CO_2 molecules, two from the prep reaction and four from the citric acid cycle.

C. The Electron Transport Chain
   1. The electron transport chain is located in the cristae of mitochondria and consists of carriers that pass electrons successively from one to another.
   2. NADH and $FADH_2$ carry the electrons to the electron transport system.

3. Members of the Chain
    a. NADH gives up its electrons and becomes NAD^+; the next carrier then gains electrons and is thereby reduced.
    b. At each sequential redox reaction, energy is released to form ATP molecules.
    c. Some of the protein carriers are **cytochrome** molecules, complex carbon rings with a heme (iron) group in the center.
4. Cycling of Carriers
    a. By the time electrons are received by O_2, *three* ATP have been made.
    b. When $FADH_2$ delivers electrons to the electron transport system, *two* ATP are formed by the time the electrons are received by O_2.
    c. Oxygen serves as the terminal electron acceptor and combines with hydrogen ions to form water.
5. The Cristae of a Mitochondrion and Chemiosmosis
    a. The electron transport chain consists of three protein complexes and two protein mobile carriers that transport electrons.
    b. The three protein complexes include *NADH-Q reductase complex*, the *cytochrome reductase complex*, and the *cytochrome oxidase complex*; the two protein mobile carriers are *coenzyme Q* and *cytochrome c*.
    c. Energy released from the flow of electrons down the electron transport chain is used to pump H^+ ions, which are carried by NADH and $FADH_2$, into intermembrane space.
    d. Accumulation of H^+ ions in this intermembrane space creates a strong electrochemical gradient.
    e. **ATP synthase complexes** are channel proteins that serve as enzymes for ATP synthesis.
    f. As H^+ ions flow from high to low concentration, ATP synthase synthesizes ATP by the reaction: ADP + P = ATP.
    g. **Chemiosmosis** is the term used for ATP production tied to an electrochemical (H^+) gradient across a membrane.
    h. Once formed, ATP molecules diffuse out of the mitochondrial matrix through channel proteins.
    i. ATP is the energy currency for all living things; all organisms must continuously produce high levels of ATP to survive.

D. Energy Yield From Glucose Metabolism
1. Substrate-Level Phosphorylation
    a. Per glucose molecule, there is a net gain of two ATP from glycolysis in cytoplasm.
    b. The citric acid cycle in the matrix of the mitochondria produces two ATP per glucose.
    c. Thus, a total of four ATP are formed by substrate-level phosphorylation outside of the electron transport chain.
2. ETC and Chemiosmosis
    a. Most of the ATP is produced by the electron transport chain and chemiosmosis.

b. Per glucose, ten NADH and two $FADH_2$ molecules provide electrons and H^+ ions to the electron transport chain.
c. For each NADH formed within the mitochondrion, three ATP are produced.
d. For each $FADH_2$ formed by the citric acid cycle, two ATP are produced.
e. For each NADH formed outside mitochondria by glycolysis, two ATP are produced as electrons are shuttled across the mitochondrial membrane by an organic molecule and delivered to FAD.

3. Efficiency of Cellular Respiration
   a. The energy difference between total reactants (glucose and O_2) and products (CO_2 and H_2O) is 686 kcal.
   b. An ATP phosphate bond has an energy of 7.3 kcal; 36 to 38 ATP are produced during glucose breakdown for a total of at least 263 kcal.
   c. This efficiency is 263/686, or 39% of the available energy in glucose is transferred to ATP; the rest of the energy is lost as heat.

8.5 Metabolic Pool

1. In a **metabolic pool**, substrates serve as entry points for degeneration or synthesis of larger molecules.
2. Degradative reactions (**catabolism**) break down molecules; they tend to be exergonic.
3. Synthetic reactions (**anabolism**) build molecules; they tend to be endergonic.

A. Catabolism
   1. Just as glucose is broken down in cellular respiration, other molecules in the cell undergo catabolism.
   2. Fat breaks down into glycerol and three fatty acids.
      a. Glycerol is converted to G3P, a metabolite in glycolysis.
      b. An 18-carbon fatty acid is converted to nine acetyl-CoA molecules that enter the citric acid cycle.
      c. Respiration of fat products can produce 108 kcal in ATP molecules; fats are an efficient form of stored energy.
   3. Amino acids break down into carbon chains and amino groups.
      a. Hydrolysis of proteins results in amino acids.
      b. *R*-group size determines whether carbon chain is oxidized in glycolysis or the citric acid cycle.
      c. A carbon skeleton is produced in the liver by removal of the amino group, by the process of **deamination**.
      d. The amino group becomes ammonia (NH_3), which enters the urea cycle and ultimately becomes part of excreted urea.
      e. The size of the *R*-group determines the number of carbons left after deamination.

B. Anabolism
   1. ATP produced during catabolism drives anabolism.
   2. Substrates making up pathways can be used as starting materials for synthetic reactions.
   3. The molecules used for biosynthesis constitute the cell's metabolic pool.

4. Carbohydrates can result in fat synthesis: G3P converts to glycerol, acetyl groups join to form fatty acids.
5. Some metabolites can be converted to amino acids by *transamination*, the transfer of an amino acid group to an organic acid.
6. Plants synthesize all the amino acids they need; animals lack some enzymes needed to make some amino acids.
7. Humans synthesize 11 of 20 amino acids; the remaining 9 **essential amino acids** must be provided by the diet.

C. The Energy Organelles Revisited

1. Chloroplasts and mitochondria may be related based on their likeness, yet they carry out opposite processes.
   a. The inner membrane of the chloroplasts form the thylakoids of the grana. The inner membrane of the mitochondrion forms the convoluted cristae.
   b. In chloroplasts the electrons passed down the ETC have been energized by the sun. In mitochondria the electrons passed down the ETC have been removed from glucose products.
   c. In chloroplasts the stroma contains the enzymes of the Calvin cycle. In the mitochondria the matrix contains the enzymes of the citric acid cycle.
2. Flow Of Energy
   a. Energy flows through organisms. For example, the sun is the energy source for producing carbohydrates in chloroplasts. In the mitochondria, the carbohydrate energy is converted into ATP molecules during cellular respiration.
   b. Chemicals cycle throughout cells. Mitochondria use carbohydrates and oxygen produced in chloroplasts, and chloroplasts use carbon dioxide and water produced in the mitochondria.