An Introduction to Metabolism
by Dr. Ty C.M. Hoffman

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Much of the transfer of materials that occurs between objects within an ecosystem stems from the reciprocal relationship between two important cellular processes:

- Photosynthesis is a set of biochemical pathways that take in inorganic carbon (in the form of carbon dioxide) and water to produce organic compounds (carbohydrates) and oxygen. Overall, this is an anabolic and endergonic process that is powered by the energy of sunlight entering the ecosystem.
- Cellular respiration is a set of biochemical pathways that take in organic compounds (as fuel) and oxygen to produce carbon dioxide and water. Overall, this is a catabolic and exergonic process, and some of the energy that is released is used to phosphorylate ADP molecules into ATP molecules.

The individual reactions within these two processes are thermodynamically inefficient, so much of the energy entering as sunlight is lost as heat that passes through the ecosystem.

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A reduction-oxidation (or redox) reaction is one that involves a transfer of electrons. The substance losing the electron becomes oxidized, and the substance gaining the electron becomes reduced.

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In a redox reaction, the substance that becomes reduced is called the oxidizing agent (because it oxidizes the other substances). The substance that becomes oxidized is called the reducing agent (because it reduces the other substance).

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A combustion reaction is a redox reaction in which a fuel (usually containing carbon and hydrogen atoms) reacts with oxygen to produce carbon dioxide and water. The fuel becomes oxidized and the oxygen becomes reduced. A combustion reaction is exergonic, because the rearrangement of electrons results in electrons becoming closer to atomic nuclei than before the reaction occurred. Thus, the free energy (G) is decreased, and energy is released. Cells combust fuels to release energy that can be used to build ATP molecules. The ATP molecules store energy that can then be released (by dephosphorylating the ATP) to power endergonic processes within the cell.

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Glucose ($C_6H_{12}O_6$) is the predominant fuel in all cells. The complete oxidation (combustion) of glucose occurs within cells in many steps, but these steps can be summarized by the single reaction that converts glucose and oxygen into carbon dioxide and water, accompanied by the release of energy.

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Whether a cell is using glucose or some other substance as a fuel, the fuel molecule contains hydrogen atoms. Oxidizing a fuel consists of dehydrogenating the fuel (removing hydrogen atoms). So the oxidation of a cellular fuel involves not just removal of electrons, but removal of protons as well (a hydrogen atom is made up of a proton and an electron). The oxidation of fuels is catalyzed by a class of enzymes called dehydrogenases. When the hydrogens (protons and electrons) are removed from the fuel, they are transferred to energy-carrying coenzyme molecules. The predominant coenzyme used in the oxidation of fuels is NAD (nicotinamide adenine dinucleotide), which exists in oxidized form (NAD^+) and reduced form ($NADH+H^+$). When NAD^+ receives electrons and protons from the fuel, NAD^+ gets reduced into $NADH+H^+$, which now carries energy that the fuel has just released.

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Nicotinamide is a nitrogenous base, as is adenine. NAD^+ is a dinucleotide, because it is formed by linking two nucleotides, one with nicotinamide as its nitrogenous base, the other with adenine as its nitrogenous base.

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When hydrogen reacts with oxygen in a single step, there is a large, explosive release of energy (heat and light). This explosive release of energy is not manageable to a cell, so cells react hydrogen (from fuels) with oxygen in a stepwise fashion, releasing the energy in small parcels that can be harnessed by the cell to do the work of producing ATP. The stepwise release of energy involves an electron transport chain. Electrons from the hydrogen are passed down the chain and received at the other end by oxygen, which also receives the protons from the hydrogen. The combination of electrons and protons (hydrogen) and oxygen results in the formation of water.

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The cellular combustion (or complete oxidation) of glucose occurs in two major phases:

- Glycolysis is the biochemical pathway that breaks glucose (a six-carbon compound) into two pyruvate molecules (each pyruvate is a three-carbon compound). The hydrogens that get stripped from the fuel in the process are transferred to NAD^+, reducing it into $NADH+H^+$. This represents some of the energy that used to be in the glucose molecule. Additionally, some energy released by the fuel is used to make ATP, and some energy is lost as heat. Glycolysis occurs in the cytoplasm.
- Cellular respiration begins where glycolysis ends. Pyruvate still contains useful energy (it is only partially spent fuel). Cellular respiration extracts as much of the useable energy as possible from the remaining fuel (pyruvate), thereby maximizing the production of ATP. Cellular respiration occurs in mitochondria.

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In substrate-level phosphorylation, an enzyme is used to transfer phosphate directly from a substrate to ADP, forming ATP. Substrate-level phosphorylation occurs in glycolysis and in the citric acid cycle (a part of cellular respiration).

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Though glycolysis is a pathway consisting of ten reactions, it is useful to break glycolysis into two phases:

- In the energy-investment phase, ATP is required and spent to allow the reactions to proceed.
- In the energy-payoff phase, energy released by reactions is used to produce ATP by substrate-level phosphorylation. For each glucose molecule that enters glycolysis, two ATP are spent in the investment phase, but four ATP are produced in the payoff phase, so glycolysis results in a net gain of ATP.

In addition to energy in the form of ATP, glycolysis transfers energy from glucose to $NADH+H^+$. Some energy is lost as heat.

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The energy-investment phase of glycolysis requires two ATP and results in the production of two phosphorylated, three-carbon compounds (G3P).

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The energy-payoff phase releases enough energy to phosphorylate four ADP into ATP (two for each G3P), as well as reduce two NAD+ into $NADH+H^+$. Some energy is lost as heat.

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The first phase of cellular respiration is the oxidation of pyruvate. In the process, pyruvate (from glycolysis) is transported from the cytosol into the mitochondrial matrix, and it is stripped of one of its three carbons (along with two oxygens). The atoms that are removed are released as carbon dioxide. The remaining two-carbon particle (acetyl) is carried by a coenzyme (CoA) to the next step in the process. The combination of the acetyl group and coenzyme A is called acetyl coenzyme A, or acetyl CoA. Energy (in the form of hydrogen) released by the oxidation of pyruvate allows for the reduction of NAD+ into $NADH+H^+$.

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The second phase of cellular respiration is the citric acid cycle (also called the tricarboxylic acid cycle or the Krebs cycle). The citric acid cycle is the cyclic pathway that completes the oxidation of the fuel. Coenzyme A delivers acetyl (the remaining fuel) to the citric acid cycle, and the two-carbon skeleton of acetyl is dismantled into one-carbon compounds (CO_2). Some of the energy released in this process is used to produce ATP via substrate level phosphorylation, some energy is put into reducing NAD^+ into $NADH+H^+$ (and into reducing a related coenzyme, FAD, into $FADH_2$), and some energy is lost as heat.

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The component reactions of the citric acid cycle are shown. Some of those reactions release enough energy either to phosphorylate ADP into ATP or to reduce a coenzyme (NAD^+ or FAD).

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The final phase of cellular respiration is oxidative phosphorylation, which is subdivided into two parts (electron transport and chemiosmosis). An electron transport chain is shown here. It consists of several particles (including proteins complexes) that are embedded in the inner mitochondrial membrane. An electron transport chain operates by receiving electrons from reduced coenzymes ($NADH+H^+$ and $FADH_2$) and passing those electrons from particle to particle along the chain. Thus, operation of an electron transport chain is a series of redox reactions. In each transfer of an electron from one particle to the next, the electron becomes more stable (by ending up closer to an atomic nucleus), so each transfer releases a small amount of energy. Some of the energy released by electron transport is put to use in actively transporting hydrogen ions from the matrix to the intermembrane space. Three of the protein complexes in the chain have the additional function of serving as pumps to accomplish this active transport. The last member of the electron transport chain transfers electrons to oxygen, which serves as the final electron acceptor. This frees up the chain to accept more electrons, thereby continuing to pump protons.

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The second step of oxidative phosphorylation is chemiosmosis. This is the part of cellular respiration that produces by far the most ATP. Chemiosmosis involves the diffusion of protons (also known as hydrogen ions, H^+). The pumping of protons by the electron transport chains establishes a proton gradient, which is a form of potential energy. The proton gradient represents the remaining useful portion of the energy that was originally in the glucose molecule. The potential energy of the proton gradient can be put to use if the protons are allowed to diffuse back into the matrix (through the inner membrane). Since protons are fully charged, they do not easily pass directly through the phospholipid bilayer of the inner mitochondrial membrane. But the protons are able to diffuse back into the matrix by going through special transmembrane proteins called ATP synthase. Each ATP synthase molecule includes a rotor (which can spin) and a stator (which remains stationary). Protons diffuse through ATP synthase to get back into the matrix, and this causes the rotor to spin with respect to the stator. The spinning of the rotor allows ATP synthase to function as an enzyme, phosphorylating ADP into ATP. Because this type of ATP production involves the redox reactions of the electron transport chains, it is called oxidative phosphorylation.

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Oxidative phosphorylation requires the coordination of electron transport chains (which pump protons to establish and maintain the gradient) and chemiosmosis (which allows protons to diffuse through ATP synthase to power the phosphorylation of ADP into ATP). A continuous supply of oxygen is required, because without oxygen, the electron transport chains will fill up with electrons, making them incapable of receiving additional electrons. That would stop the pumping of protons, and oxidative phosphorylation would cease.

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The complete oxidation (combustion) of glucose is shown. Some ATP is produced in glycolysis and in the citric acid cycle, but most of the useable energy from the glucose molecule is transferred to reduced coenzymes ($NADH+H^+$ and $FADH_2$). The huge payoff of ATP occurs when the coenzymes transfer electrons to electron transport chains, allowing for oxidative phosphorylation.

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When cellular respiration is unable to occur (either because oxygen is absent or because the cell is not capable of cellular respiration), glycolysis must still be allowed to occur to produce ATP using energy from glucose. However, because glycolysis involves the reduction of NAD^+ into $NADH+H^+$, glycolysis requires a continuous source of NAD^+ (oxidized coenzymes). There is a finite supply of coenzyme molecules, so if there is not a mechanism to convert (oxidize) $NADH+H^+$ back into NAD^+, then eventually all available coenzyme molecules will be in the reduced form and unable to receive electrons from glycolysis. Cellular respiration provides a mechanism to reoxidize $NADH+H^+$ into NAD^+, allowing glycolysis to continue to occur. But when cellular respiration is not occurring, an alternative mechanism for reoxidizing $NADH+H^+$ into NAD^+ is required. That alternative mechanism is called fermentation. There are many types of fermentation that occur in various organisms, but two types are especially important to humans:

- In alcohol fermentation (which occurs in yeast cells, for example), the pyruvate produced by glycolysis gets converted to acetaldehyde, releasing carbon dioxide in the process. The acetaldehyde then gets reduced by the $NADH+H^+$ that was produced in glycolysis. This reoxidizes $NADH+H^+$ into NAD^+, so it can become reduced again in glycolysis, allowing further glycolysis. When acetaldehyde receives the electrons and protons, ethanol is produced. This is how beer, wine, spirits and bread are made.
- In lactic acid fermentation, pyruvate from glycolysis directly receives the electrons from $NADH+H^+$, so no carbon dioxide is produced. Pyruvate get converted to lactic acid. Human cells undergo this type of fermentation.

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The end of glycolysis (the production of pyruvate) presents a eukaryotic cell with a metabolic crossroads. If oxygen is available, the pyruvate will automatically be processed by cellular respiration in a mitochondrion. This will maximize the ATP yield. If oxygen is not available, the cell is forced to undergo fermentation, in which case no further ATP (other than the two ATP already produced by glycolysis) will be produced from energy in that glucose.

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Glycolysis and cellular respiration constitute the central metabolic pathways in eukaryotic cells. However, fuels other than glucose can be fed into those central pathways at different points, depending on the fuel.

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The central metabolic pathways operate under the homeostatic control of feedback. When ATP is present in great abundance, it allosterically inhibits one of the glycolytic enzymes, shutting down the process until ATP is needed again. An excess of citrate can also operate via feedback inhibition. AMP (adenosine monophosphate) is usually in the cell at very low levels, but it can rise in concentration when ADP molecules are used for energy, turning them into AMP. This happens only when ATP is in severely short supply, so a buildup of AMP signals the cell to increase the rate at which the central pathways operate. This increases glucose catabolism, returning ATP to normal levels.