

SOME Important Points About Cellular Energetics

by Dr. Ty C.M. Hoffman

An Introduction to Metabolism

- Most biochemical processes occur as biochemical pathways, each individual reaction of which is catalyzed by its own enzyme.
- Energy is the capacity to do work, and it can be classified as potential energy ("stored") or kinetic energy ("in use").
- The first law of thermodynamics states that energy can be neither created nor destroyed; however, it can be transferred and transformed.
- The second law of thermodynamics states that, in every chemical reaction, some energy is lost as heat, and the total amount of entropy (disorder) in the universe is always increasing.
- Gibbs free energy (G) represents the potential energy of a system. The change in free energy (ΔG) of a system that has undergone a change is defined as the final value of G minus the initial value of G ($\Delta G = G_f - G_i$).
- A chemical reaction with a negative ΔG is spontaneous and exergonic; one with a positive ΔG is non-spontaneous and endergonic.
- Under appropriate conditions some of the energy released by an exergonic reaction can be harnessed by a cell to do some cellular work or to phosphorylate ADP into ATP.
- An ATP molecule is rich in energy because of its phosphate bonds. When an ATP is hydrolyzed, a phosphate is removed, creating ADP and inorganic phosphate. The energy released can be put to use for cellular work.
- Cellular work can be transport work, in which particles are transported through membranes, or mechanical work, in which motor proteins carry vesicles along the cytoskeleton.
- ATP is the link between exergonic biochemical reactions and endergonic biochemical reactions. Energy released from exergonic reactions can be used to phosphorylate ADP into ATP. That ATP can then be hydrolyzed (dephosphorylated), and the energy released can be used to drive endergonic reactions.
- In general, anabolic reactions are endergonic, and catabolic reactions are exergonic.
- Any reaction features an activation energy that must be supplied for that reaction to proceed. Enzymes operate by decreasing the activation energy. Enzymes never change the value of ΔG .
- A reactant that can temporarily bind to an enzyme is called that enzyme's substrate. Enzymes are specific for substrates. When the substrate binds, the enzyme-substrate complex is formed, and the substrate is converted into product. The product is then released, leaving the enzyme intact.
- Any given enzyme has an optimal pH and an optimal temperature at which it works best.

- A noncompetitive inhibitor is a non-substrate particle that binds to an enzyme somewhere other than on its active site, resulting in a change in the shape of the active site such that the normal substrate cannot bind.
- A competitive inhibitor is a particle that can bind to the active site, thereby blocking the active site and disallowing the normal substrate from binding.
- Allosteric regulation is either the activation or the inhibition of a multi-subunit enzyme when a regulator (non-substrate) particle binds to the enzyme away from the active sites, causing a change in the active sites.
- Many biochemical pathways are regulated by feedback inhibition using noncompetitive or allosteric inhibition of one of the enzymes of the pathway.

Cellular Respiration

- The summary reactions for cellular respiration and photosynthesis are reverses of each other. The inputs for cellular respiration are sugar and oxygen (which are the outputs of photosynthesis). The outputs of cellular respiration are carbon dioxide, water, and energy (which are the inputs into photosynthesis).
- Oxidation is the removal of electrons from a particle; reduction is the gain of electrons by a particle. Oxidation and reduction always occur together (never individually). Reactions that feature oxidation and reduction are redox reactions.
- In a redox reaction, the reducing agent is the particle that becomes oxidized; the oxidizing agent is the particle that becomes reduced.
- Dehydrogenase is an enzyme that can strip two hydrogen atoms from an organic fuel molecule, converting NAD^+ to $\text{NADH} + \text{H}^+$. This oxidizes the organic fuel and reduces the NAD^+ .
- Nicotinamide adenine dinucleotide (NAD^+) is an energy-carrying molecule that carries energy in the form of electrons from one molecule to another in a cell. The energized (reduced) form is $\text{NADH} + \text{H}^+$; the de-energized (oxidized) form is NAD^+ .
- Cellular respiration is able to capture some of the energy released by the combustion of organic fuel (e.g., glucose) by carrying out the reaction in many steps, each of which releases a small, manageable amount of energy. The captured energy is then either transferred directly to ATP or transferred to $\text{NADH} + \text{H}^+$ or FADH_2 . Energy that is transferred to $\text{NADH} + \text{H}^+$ or FADH_2 will eventually be transferred to ATP, the ultimate energetic product of cellular respiration.
- Cellular respiration, the complete oxidation of glucose, occurs in four primary phases: glycolysis, conversion of pyruvate into acetyl coenzyme A, the citric acid cycle, and oxidative phosphorylation.
- ATP is produced in three of the four phases of cellular respiration. Glycolysis and the citric acid cycle produce ATP via substrate-level phosphorylation. Oxidative phosphorylation produces ATP via electron transport and chemiosmosis.
- In substrate-level phosphorylation, a substrate carries a phosphate to an enzyme, and the enzyme transfers the phosphate to ADP to make ATP.

- Glycolysis (the breakdown of glucose) is a pathway that involves an energy-investment phase (in which two ATP must be "spent") and an energy-payoff phase (in which four ATP are produced). This results in a net gain of two ATP per glucose molecule.
- Glycolysis occurs in the cytosol, and it converts one molecule of glucose into two molecules of pyruvate.
- Pyruvate (the end product of glycolysis) is transported into the mitochondrion, where the aerobic part of cellular respiration takes place. In the process of being transported into the mitochondrial matrix, pyruvate is oxidized, converting it into carbon dioxide and acetyl CoA. Some of the energy released by this reaction is used to reduce NAD^+ into $\text{NADH} + \text{H}^+$.
- A coenzyme is a molecule that carries a particle to an enzyme. Coenzyme A (CoA) carries acetyl to the first enzyme of the citric acid cycle.
- The citric acid cycle receives acetyl (a two-carbon compound) and combines it with oxaloacetate (a four-carbon compound) to produce citrate (a six-carbon compound). This six carbon compound is then broken down into oxaloacetate, releasing two carbon dioxide molecules (spent fuel). The cycle then repeats, using a new acetyl. Some of the energy released by breaking down citrate is used to produce $\text{NADH} + \text{H}^+$ and FADH_2 .
- The function of the citric acid cycle is to complete the oxidation (breakdown) of what is left of the fuel. After the citric acid cycle, the fuel is completely spent, but most of the useable energy that was originally in the glucose (fuel) molecule is at this point being carried by $\text{NADH} + \text{H}^+$ and FADH_2 .
- The final phase of cellular respiration (oxidative phosphorylation) involves two sub-phases: the electron transport chain and chemiosmosis.
- The electron transport chain is a group of proteins and other particles embedded in the inner mitochondrial membrane. The chain has two functions: 1. to receive electrons from the energy-carrying molecules ($\text{NADH} + \text{H}^+$ and FADH_2) and pass them along, step-by-step, to oxygen; and 2. to use the energy released by the transfer of electrons to power the pumping of the protons (hydrogen ions) from the mitochondrial matrix, through the inner membrane, and into the intermembrane space.
- The pumping of protons by the electron transport chain produces a gradient across the membrane. That gradient is a form of potential energy, and it can therefore perform some work for the cell. That work is the phosphorylation of ADP into ATP via chemiosmosis, the second sub-phase of oxidative phosphorylation.
- In chemiosmosis, protons that have been pumped (by the electron transport chain) into the intermembrane space of the mitochondrion diffuse back through the inner membrane into the mitochondrial matrix. The only places in the membrane at which the protons are allowed back through the membrane are at proteins called ATP synthase molecules. When protons pass through an ATP synthase, the ATP synthase spins, and this allows phosphate to be added to ADP, creating ATP. This is oxidative phosphorylation.

- The vast majority (about 90%) of the ATP produced during cellular respiration is produced via oxidative phosphorylation, which occurs after the fuel has been completely spent by the previous three phases.
- In the absence of oxygen (or in cells that do not have mitochondria), glycolysis is the only process available to produce ATP from the energy in glucose. This is called anaerobic metabolism.
- If glycolysis proceeds anaerobically (without oxygen), it must be coupled to some type of fermentation.
- Fermentation converts pyruvate (the product of glycolysis) into some other molecule. In the process of this conversion, the $\text{NADH}+\text{H}^+$ (the reduced form) that is produced by glycolysis is re-oxidized into NAD^+ . NAD^+ can then return to glycolysis, allowing glycolysis to continue.
- There are many different kinds of fermentation processes used by different organisms. Two examples are ethanol fermentation (occurring in yeast) and lactic acid fermentation (occurring in mammals). Ethanol fermentation converts pyruvate into carbon-dioxide and ethanol. Lactic acid fermentation converts pyruvate into lactic acid.
- The monomers that are produced when nutrient macromolecules are broken down can serve as fuel by feeding into the cellular respiration pathway at various points.
- Through negative feedback, cellular respiration is homeostatically slowed down by a buildup of ATP, and cellular respiration is homeostatically sped up by a buildup of AMP.

Photosynthesis

- Photosynthesis occurs in some eukaryotes and some prokaryotes. Photosynthetic eukaryotes are the only organisms with chloroplasts (because no prokaryotes have membrane-bounded organelles).
- Plants exchange carbon-dioxide, oxygen, and water vapor with the environment through small openings in leaves called stomata.
- Photosynthesis is the process by which light energy is captured and used to drive the conversion of carbon dioxide and water into sugar and oxygen.
- Photosynthesis occurs in two primary phases: the light-dependent reactions and the light-independent reactions (also called the Calvin cycle). These occur in the chloroplast (in photosynthetic eukaryotes).
- A chloroplast is a doubly membrane-bounded organelle containing disk-like thylakoids occurring in stacks called grana. The thylakoid membrane forms a barrier between the thylakoid space (inside the thylakoids) and the stroma (the fluid interior of the chloroplast).
- The light-dependent reactions are functionally linked to the light-independent reactions by two energy-carrying molecules: ADP/ATP and $\text{NADP}^++\text{H}^+/\text{NADPH}$. The light-dependent reactions require ADP and NADP^++H^+ (the de-energized or oxidized forms), and they produce ATP and NADPH (the energized or reduced forms). The light-independent reactions require ATP and NADPH , and they produce ADP and NADP^++H^+ .

- Light is electromagnetic energy, which has both wavelike properties and particle-like properties. When considered as waves, light can differ in its wavelength and frequency, which determine the "type" of light. Humanly visible light is just a small portion of the overall electromagnetic spectrum. When considered as particles, light occurs in tiny packets of energy (with no mass) called photons.
- When a photon encounters a particle, that photon can be either absorbed, transmitted, or reflected. Pigments are substances that are able to absorb photons of certain wavelengths.
- The principle pigments found in photosynthetic organisms are chlorophyll *a*, chlorophyll *b*, and carotenoids. These pigments absorb light well in the blue and red ranges, but not in the green range.
- When a photon is absorbed, that photon ceases to exist, and the energy of that photon is transferred to the particle that absorbed the photon. When a pigment (like chlorophyll) is not part of an organism, and it absorbs a photon, the energy of the photon excites an electron, causing it to move to a higher energy level (farther from the nucleus). The electron quickly returns to the lower energy level, and this creates a new photon that is emitted by the particle. This is fluorescence, and no useable energy is captured in fluorescence.
- A plant is able to capture useable energy from photons, because the plant's chlorophyll molecules occur in special structures called photosystems, which are embedded in the thylakoid membrane within a chloroplast.
- The structures that are responsible for the light-dependent reactions are two kinds of photosystems and two kinds of electron transport chains.
- A photosystem is a combination of pigment molecules, proteins, and other particles. It is arranged as a core (called the reaction center complex) surrounded by several light-harvesting complexes. The reaction center contains a special pair of chlorophyll *a* molecules and a primary electron acceptor. The light-harvesting complexes contain pigment molecules (mostly chlorophyll).
- When a photon strikes a photosystem, the photon is absorbed by one of the chlorophyll molecules of the light-harvesting complexes. That excited chlorophyll molecule then excites a nearby chlorophyll molecule (via resonance energy transfer), and so on, until the energy is transferred to the chlorophyll of the reaction center complex.
- When the chlorophyll of the reaction center complex becomes excited, it fully loses an electron, and that electron is transferred to the primary electron acceptor. The primary electron acceptor is thus reduced.
- There are two types of photosystems (photosystem II and photosystem I), and they are functionally linked by an electron transport chain. A second electron transport chain is associated with only the second photosystem (which is photosystem I). Both types of photosystems and both types of electron transport chains are embedded in the thylakoid membrane.

- When photosystem II is excited, and the chlorophyll loses its electron to the primary electron acceptor, that electron is passed on to the first electron transport chain. The chlorophyll must replace the electron that it has lost. That electron comes from a hydrogen atom that has been stripped from a water molecule. The stripping of hydrogen from water (leaving oxygen behind) is the reason water is an input of photosynthesis, and oxygen is an output.
- The electron that passes down the first electron transport chain releases energy that is used by the chain to pump protons (hydrogen ions) from the stroma, through the thylakoid membrane, and into the thylakoid space. Those protons then diffuse back into the stroma through ATP synthase molecules, producing ATP via oxidative phosphorylation.
- When photosystem I is excited (by a separate photon), the electron that is transferred from the chlorophyll to the primary electron acceptor is then transferred to the second electron transport chain. This leaves the chlorophyll of photosystem I in need of a replacement electron. The electron that is coming down the first electron transport chain (from photosystem II) replaces the electron lost by the chlorophyll of photosystem I.
- The electron that passes down the second electron transport chain is then transferred to $\text{NADP}^+ + \text{H}^+$, reducing it into NADPH.
- The function of the light-dependent reactions is to capture light energy so that electrons leave chlorophyll molecules and pass through transport chains. This provides energy to phosphorylate ADP into ATP and to reduce $\text{NADP}^+ + \text{H}^+$ into NADPH. The lost electron that must be replaced comes from a hydrogen of water, and that process forms oxygen.
- The light-dependent reactions are necessary, because the ATP and NADPH that are produced are required by the second phase of photosynthesis, the light-independent reactions.
- The light-independent reactions (the Calvin cycle) require both ATP and NADPH. However, more ATP is required than NADPH. To maximize efficiency, cyclic electron flow has evolved, in which the primary electron acceptor of photosystem I (which would normally pass that electron on to the second electron transport chain) cycles that electron back down the first electron transport chain. This has the effect of making ATP instead of NADPH. In this way, ATP and NADPH are produced by the light-dependent reactions in amounts that are appropriate for the needs of the light-independent reactions.
- The light-independent reactions use the energy carried by ATP and NADPH (produced by the light-dependent reactions) to convert carbon dioxide (an inorganic molecule) into sugar (an organic fuel for cells). The incorporation of carbon dioxide into the carbon skeleton of an organic molecule is called carbon fixation.
- The light-independent reactions occur as a cycle (the Calvin cycle) functionally divided into three phases: carbon fixation, reduction, and regeneration of the carbon dioxide acceptor.

- Ribulose biphosphate carboxylase oxygenase (RuBisCO) is an enzyme that fixes carbon dioxide (a one-carbon compound) by adding it to a molecule of ribulose biphosphate (RuBP, a five-carbon compound) to produce a six-carbon compound. This is what occurs in the carbon fixation phase of the light-independent reactions.
- The six-carbon compound produced by fixation is converted into various intermediates as the cycle proceeds. Some of the conversions require ATP. One of the steps requires electrons from NADPH. This is why the light-independent reactions use the energy-carrying molecules produced by the light-dependent reactions.
- The step that requires electrons from NADPH is the reduction phase (because the intermediate that receives the electrons is being reduced). The reduction phase produces a three-carbon sugar, glyceraldehyde-3-phosphate (G3P). Some of the G3P is the output of the light-independent reactions, and these three-carbon sugars can be combined to form glucose or other organic molecules. The rest of the G3P continues on through the cycle, being transformed into RuBP.
- The transformation of some of the G3P into RuBP is the final phase. This is the regeneration of the carbon dioxide acceptor, because RuBP functions as the acceptor of carbon dioxide. If more carbon dioxide is available, the RuBP will combine with carbon dioxide (under the catalytic action of RuBisCO), and the cycle will repeat, producing more and more sugar.