

BIOCHEMISTRY

CELLULAR METABOLISM

Consist of all the biochemical reactions and process with take place in the living cell. Metabolism involves the storage of energy in the form of chemical bonds, and the release of that energy when the bonds are broken. Metabolism may be described as consisting of two essentially opposite process which take place within each individually cell:

Catabolism : Biochemical process (metabolic pathways) which, through a series of chemical reactions, break larger molecules into smaller ones. The breaking of bonds releases cellular energy which may then used to drive other biochemical processes.

Anabolism : Biochemical process (metabolic pathways) which synthesize larger molecules by creating bonds to join smaller molecules together. The creation of these bonds requires the expenditure of cellular energy.

Cellular Energy is primarily stored in the form of a molecule called **ATP** (**A**denosine **t**riphosphate). Energy stored in high-energy bonds joining three phosphate groups in series to the adenosine molecule. Energy is stored when a bond joins a phosphate group to the molecule, and released when the phosphate bond is broken [see *Inorganic and Organic Compounds* handout for ATP structure] ATP is formed by adding one phosphate group to **ADP** (**a**denosine **d**iphosphate). Two other important energy storage molecules are **NAD⁺** (**n**icotinamide **a**denine **d**inucleotide) and **FAD** (**f**lavine **a**denine **d**inucleotide). These molecules store a smaller amount of energy by bonding to hydrogen atoms, forming **NADH** and **FADH₂**.

Synthesis is the construction of larger molecules from smaller ones. In the living systems, synthesis is termed **biosynthesis**. Anabolic processes are those which conduct biosynthesis.

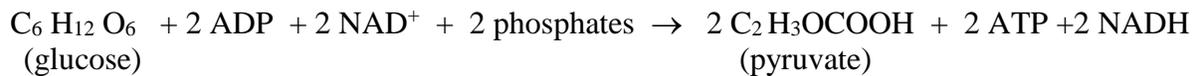
Assimilation is the process by which the body incorporates synthesized molecules into the body .

CELLULAR RESPIRATION involves the breakdown of organic food molecules in the cell, and using or storing the energy released. It involves two catabolic processes: 1) **glycolysis**, and 2) either **aerobic respiration** or **fermentation**. When aerobic respiration takes place, the simplified overall net reaction for cellular respiration(including glycolysis) theoretically is :



1. **Glycolysis**. This is the first process in cellular respiration . It occurs in the cytoplasm. It is an anaerobic process because it does not require oxygen for completion. A series of chemical reactions breaks down a 6-carbon molecule called **glucose** to a 3-carbon molecule, **pyruvic acid** (or **pyruvate**). ATP is used up to drive these reactions, but even more ATP is produced, so there is a net gain of 2ATPmolecules for each glucose broken down.

The net reaction can be represented as:

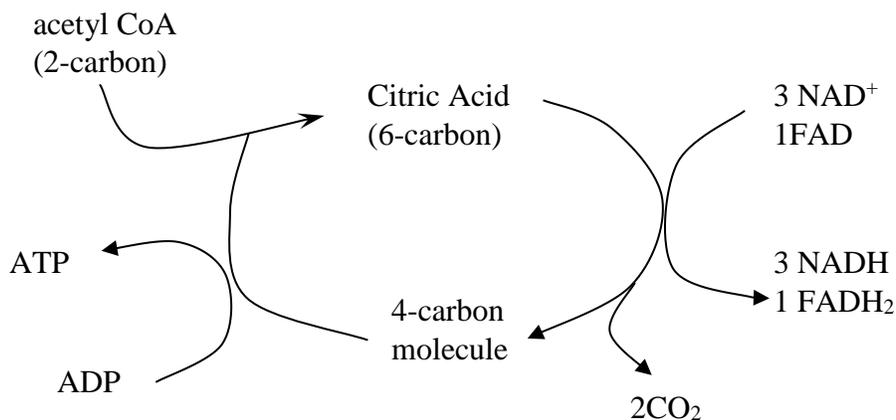


2. **Aerobic Respiration.** This process begins with the pyruvic acid (pyruvate) produced during glycolysis. It takes place on the cristae inside the mitochondria of cells. The three stages of aerobic respiration are:

- **Pyruvate oxidation** (also known as the **transition reaction**)
- **Krebs Cycle** (also known as the **Citric Acid** or **TriCarboxylic Acid [TCA] Cycle**)
- **Electron Transport Chain [ETC]** (also known as the Electron Transport System, the **Respiratory Chain**, and the **Cytochrome System**) and **Chemiosmosis**

a. **Pyruvate Oxidation.** Pyruvate is broken down into CO₂, hydrogen, and a 2-carbon acetyl group. The acetyl group is then combined with Coenzyme A to form **acetyl CoA** (acetyl Coenzyme A, also known as **active acetate**), which in turn is used in the Krebs cycle. Two molecules of NADH are produced during the formation of acetyl CoA, which later be used in the ETC.

b. **Krebs Cycle.** The Krebs cycle is a series of reactions that involves many enzymes and coenzymes found in the mitochondria. It begins by combining the acetyl group from acetyl CoA with another molecule (oxaloacetate) to form new citric acid (hence the alternate name Citric Acid Cycle). Coenzyme A is release to form new acetyl CoA, and the citric acid enters into the series of reactions. The series of reactions is referred to as a cycle because it eventually produces oxaloacetate, which reacts with more acetyl CoA to form more citric acid, and so begins the process all over again. The end products of the Krebs Cycle are CO₂, ATP, NADH, and FADH₂. One turn of the Krebs Cycle produced 2 molecules of CO₂ as an end product, and converts one ADP to ATP, three NAD⁺ to NADH, and one FAD to FADH₂. The cycle is illustrated below:



Since glycolysis produces 2 pyruvate molecules from each glucose molecule, both of which are then converted to acetyl CoA, one glucose molecule will drive two turns of the Krebs Cycle, producing a total of 2 ATP, 6 NADH, and 2 FADH₂. So far, cellular respiration has produced from one glucose molecule a net total of 4 ATP (two from glycolysis, and two from the Krebs Cycle).

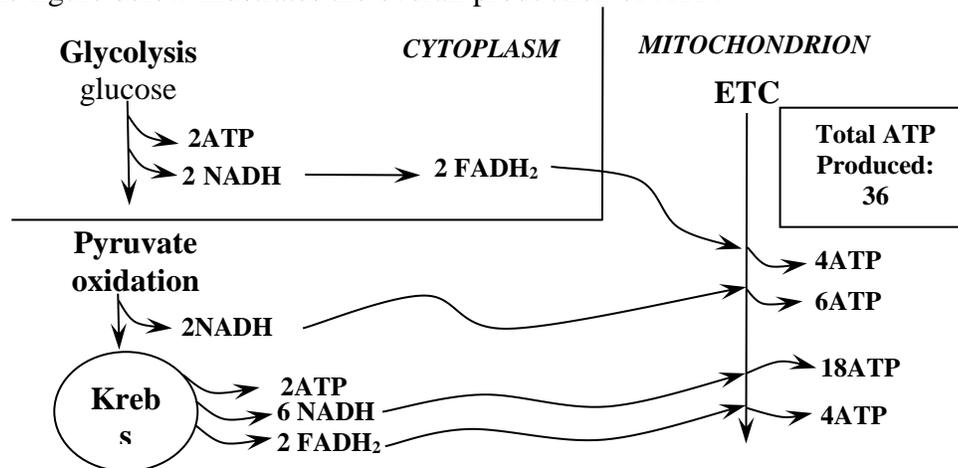
- c. ***Electron Transport Chain and Chemiosmosis.*** The remaining energy (not yet stored in ATP) from the glucose molecule is stored in the hydrogen atoms attached to NADH and FADH₂. This actually represents most of the energy. The ETC will transfer these hydrogen atoms (actually, electrons from atoms) to a series of pigment molecules called **cytochromes**. Each time a transfer is made, some energy is released. The energy released from the electrons as they move down the ETC is used to create a hydrogen ion (proton) gradient. This gradient along with chemiosmosis is used to form ATP. The electrons and hydrogen ions ultimately end up on oxygen (O₂) to form water. In aerobic respiration, oxygen serves as the final electron acceptor.

Recall that two NADH molecules were produced during glycolysis. The NADH is not able to pass through the mitochondrial membrane to deliver its hydrogen to the ETC, so the NADH is converted to FADH₂ (by transferring the hydrogens from each NADH to a FAD molecule). The two FADH₂ molecules then pass into a mitochondrion to take part in the ETC. The NADH and FADH₂ molecules produced by pyruvate oxidation and by the Krebs cycle also fed into the ETC.

The ETC produces 3 ATP molecules from each NADH molecule, and two ATPs from each FADH₂ molecule. Since cellular respiration has so far produced a total of 8 NADH and 4 FADH₂ to feed into the ETC, $(3 \times 8) + (2 \times 4) = 32$ ATPs produced from each molecule of glucose. This, plus the 2 ATPs produced during glycolysis, and the 2 more produced in the Krebs cycle, gives us a **grand total of 36 ATPs gained from each glucose molecule.**

WAIT! Didn't the definition and equation for aerobic respiration say up to 38 ATPs were produced from each glucose? Yes, theoretically, and that is the figure you will see in some text books, but that assumes that we will gain 6 ATPs from the two NADH molecules produced during glycolysis. But in reality, those NADH molecules must be converted to FADH₂ molecules before they can get into the mitochondrion to participate in the ETC. Since each FADH₂ molecule only produces 2 (instead of 3) ATPs in the ETC, we lost 2 ATPs from what we theoretically would expect to get. If you take a class covering biochemistry, your instructor should tell you which total he or she expects you to use.

The figure below illustrates the overall production of ATP:



3. **Fermentation.** This is a process where an organic molecule (in this case pyruvate), and not oxygen, is used as the final electron acceptor. Fermentation typically occurs in cells living where there is an inadequate supply of oxygen to conduct aerobic respiration. No additional energy is produced by this process, so there is a net gain of only 2 ATP from each glucose molecule (directly from glycolysis itself). Fermentation is obviously not a very efficient way of using the energy contained in a glucose molecule, and is adequate to supply the energy needs of only very small and simple organisms.

There are two main types of fermentation:

- Alcoholic Fermentation.** This takes place in simple organisms such as yeast. The pyruvate produced by glycolysis is reduced, and eventually broken down into ethyl alcohol (this is how alcoholic beverages are made) and CO₂.
- Lactic Acid Fermentation.** This occurs in some bacteria and in animal muscle tissues when there is not enough oxygen available to conduct aerobic respiration. Muscle tissue does not have the best blood supply in the body. When the pace of muscle exceeds the rate at which the can resupply it with oxygen, a type of fermentation takes place, reducing pyruvate to lactic acid. Although the amount of ATP produced is small and cannot sustain us for long, it can be produced very quickly, giving animal muscle a quick burst of energy when needed. There is a price to pay, however: the build-up of toxic lactic acid in the muscle tissues causes our muscles to ache the next day.

Both types of fermentation allow for the conversion (oxidation) of NADH back to NAD⁺, which allows for the continuation of glycolysis.

OTHER CATABOLIC PROCESSES. Glucose, of course, is not the body's only source of food energy. Through various enzymatic pathways, other types of food can also be used to make ATP.

1. **Other Carbohydrates.** Recall that all carbohydrates are composed of simple sugars. Through the use of different enzymes, all these other types of sugars can either be converted to glucose or broken into compounds which can be fed into one of the stages of glycolysis. So all carbohydrates eventually end up being broken down to pyruvate and fed into the Krebs cycle.
2. **Lipids (fats).** The breakdown of lipids produces products which can also be converted to acetyl CoA. Lipids are extremely rich forms of stored energy. Each triglyceride molecules can produce hundreds of ATPs (for example, the catabolism of a single 18-carbon fatty acid molecule produce 108 ATPs). Lipids are the most concentrated form of stored energy, containing by far the most calories per gram.
3. **Proteins.** Proteins can of course be broken down into their component amino acids. These amino acids can then either be converted into acetyl CoA, or converted into one of the intermediate products of the Krebs cycle. Either way, they can be used by the Krebs cycle to produce ATP. How much ATP is produced depends on which type of protein is broken down (due to different types of amino acids contained).
4. **Nucleic acids.** Nucleic acids in food are also broken down and the nucleotides are then used by the body, but they are a minor component of our food and are not a significant source of ATP energy.

When your body needs energy, it first uses stored carbohydrates (in the form of glycogen). When there is not enough glycogen to meet the body's needs, it then starts to break down the fats. When your fat reserves are gone (as in case of starvation), as a last resort your body will turn to protein in your body's tissues as a source of energy. This robs your body of muscle tissue and enzymes, and your body will begin to waste away (if carried on long enough, the result will be fatal). Normally, the amino acids from the proteins we eat are used primarily to make others proteins our body needs, not to produce energy.

ANABOLIC PROCESSES. All of the processes involved in catabolism (the breakdown of carbohydrates, fats, and proteins) are **reversible** (i.e. can work either direction). By using the intermediate products of catabolism, the body can synthesize new or different proteins, lipids, and nucleotides, and can store carbohydrate energy as glycogen. Through biosynthesis the body can make almost anything it needs, regardless of our diets, with a few exceptions. We **MUST** obtain micronutrients (vitamins and minerals) and the nine essential amino acids in our diets, as our bodies cannot synthesize these products. Despite the body's manufacturing ability, a certain amount of all three of major food macromolecules (carbohydrates, lipids, and proteins) is still necessary to maintain good health. Eliminating any one of them from the diet *completely* (or even almost completely), as in some of the fad diets, can carry serious health consequences and can be extremely dangerous. Our bodies need *all three* in our diet to remain healthy.

Excess glucose molecules are first stored as glycogen for a “quick energy” source; further excesses are converted to fat by diverting their breakdown products from the Krebs cycle. Some intermediate products of the Krebs cycle can be converted to glycerol and fatty acids, and combined to form triglycerides or other lipids. These are used to build cell membranes and to store excess calories. This is way you can still get fat without eating fat - excess calories are stored as fat regardless of their source, and since fat is so rich in energy it is very hard to get rid of; a little goes along way. Other Krebs cycle intermediates can be converted to amino acids which must be obtained by digestion of dietary proteins containing them. Without all the essential amino acids, we will suffer proteins deficiencies. Although the essential amino acids can be obtained through a strictly vegetarian diet, it is a challenging task because some of them are present in only a few specific plants (like soy beans). A balanced omnivorous diet (containing a variety of fruits and vegetables, and moderate amount of animal protein) is the easiest and safest way to obtain all the essentials nutrients the body needs.

RESPIRATION VS. PHOTOSYNTHESIS

Photosynthesis is the process by which plants produce and store energy in their cells, and provides plants with the raw materials for anabolic processes (instead of eating and digestion food as animals do). It in some ways appears to be the opposite of respiration, and in fact, when there is not light to drive photosynthesis, plants will use respiration to live off the stored food made by photosynthesis. We will cover photosynthesis fully in another handout, but the chart below provides a brief comparison between the two processes.

	RESPIRATION	PHOTOSYNTHESIS
WHERE	in living cells	in cells containing chlorophyll
WHEN	all the time	only in the presence of light
INPUT	organic(carbon-containing) Compounds & oxygen	carbon dioxide & water
OUTPUT	ATP, carbon dioxide, and water	organic (carbon-containing) compounds, oxygen & water
ENERGY SOURCE	organic (carbon-containing)	light
ENERGY RESULTS	energy released in the form of 36-38 ATP molecules	energy stored in chemical bonds
CHEMICAL REATIONS	oxidation of organic compounds	reduction of organic compounds
CHEMICAL FORMULA	$C_6 H_{12} O_6 + 6O_2 \rightarrow 6CO_2 + 6 H_2O + \text{energy}$	$6CO_2 + 12 H_2O \rightarrow C_6 H_{12} O_6 + 6O_2 + 6 H_2O$

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