Glycolysis: Process and Explanation

The first metabolic pathway is *glycolysis,* an ancient pathway employed by a host of organisms. *Glycolysis is the sequence of reactions that metabolizes one molecule of glucose to two molecules of pyruvate with the concomitant net production of two molecules of ATP*. This process is anaerobic (i.e., it does not require O_2). Pyruvate can be further processed anaerobically to lactate (*lactic acid fermentation*) or ethanol (*alcoholic fermentation*). Under aerobic conditions, pyruvate can be completely oxidized to CO_2 generating much more ATP.
To honour the major contributions in the field made by Gustav Embeden, Otto Meyerhof and Jacob Parnas, it is also known as *Embden Meyerhof Parnas pathway*.

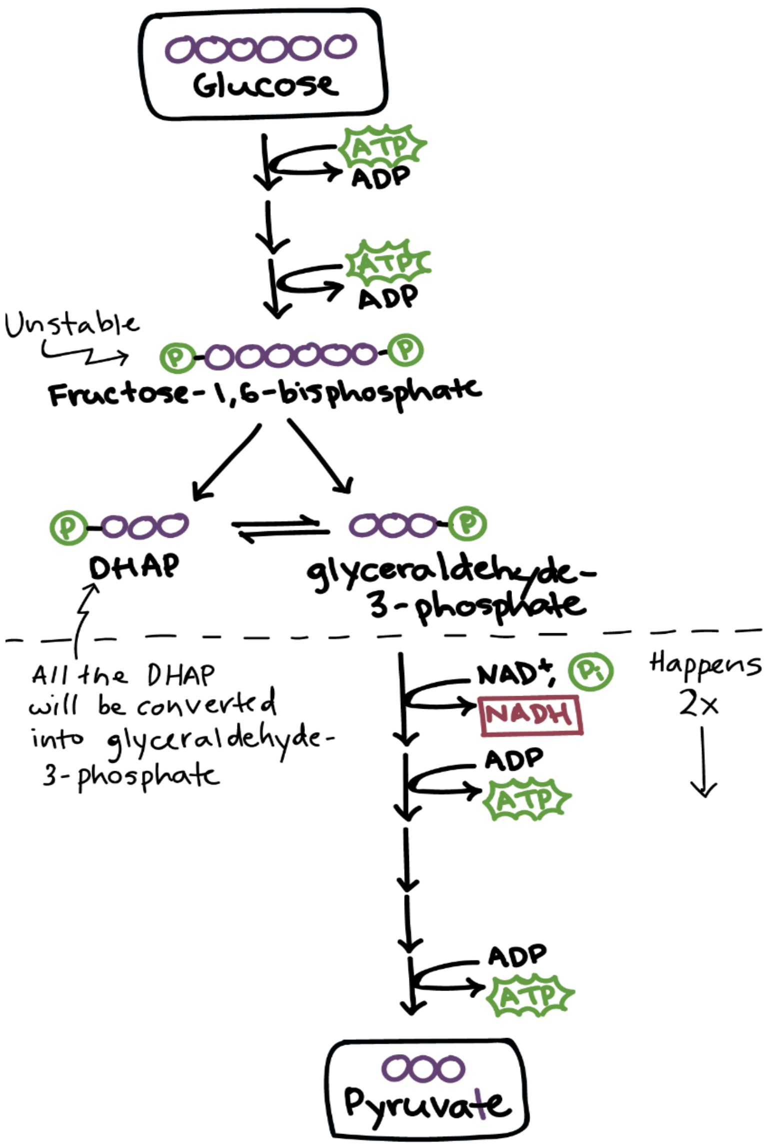
Important points - glycolysis
Glycolysis takes place in the **cytosol of a cell**, and it can be broken down into two main phases: the energy-requiring phase, (above the dotted line in the image below,) and the energy-releasing phase, (below the dotted line).

- **Energy-requiring phase.** In this phase, the starting molecule of glucose gets rearranged, and two phosphate groups are attached to it. The phosphate groups make the modified sugar—now called fructose-1,6-bisphosphate that is unstable, allowing it to split in half and form two phosphate-bearing three-carbon sugars. Because the phosphates used in these steps come from ATP, two ATP molecules get used up.

The three-carbon sugars formed when the unstable sugar breaks down are different from each other. Only one—glyceraldehyde-3-phosphate—can enter the following step. However, the unfavorable sugar, DHAP can be easily converted into the favorable one, so both finish the pathway in the end.

- **Energy-releasing phase.** In this phase, each three-carbon sugar is converted into another three-carbon molecule, pyruvate, through a series of reactions. In these reactions, two ATP molecules and one NADH molecule are made. Because this phase takes place twice, once for each of the two three-carbon sugars, it makes four ATP and two NADH overall.

Each reaction in glycolysis is catalyzed by its own enzyme. The most important enzyme for regulation of glycolysis is **phosphofructokinase**, which catalyzes formation of the unstable, two-phosphate sugar molecule, fructose-1,6-bisphosphate. Phosphofructokinase speeds up or slows down glycolysis in response to the energy needs of the cell.

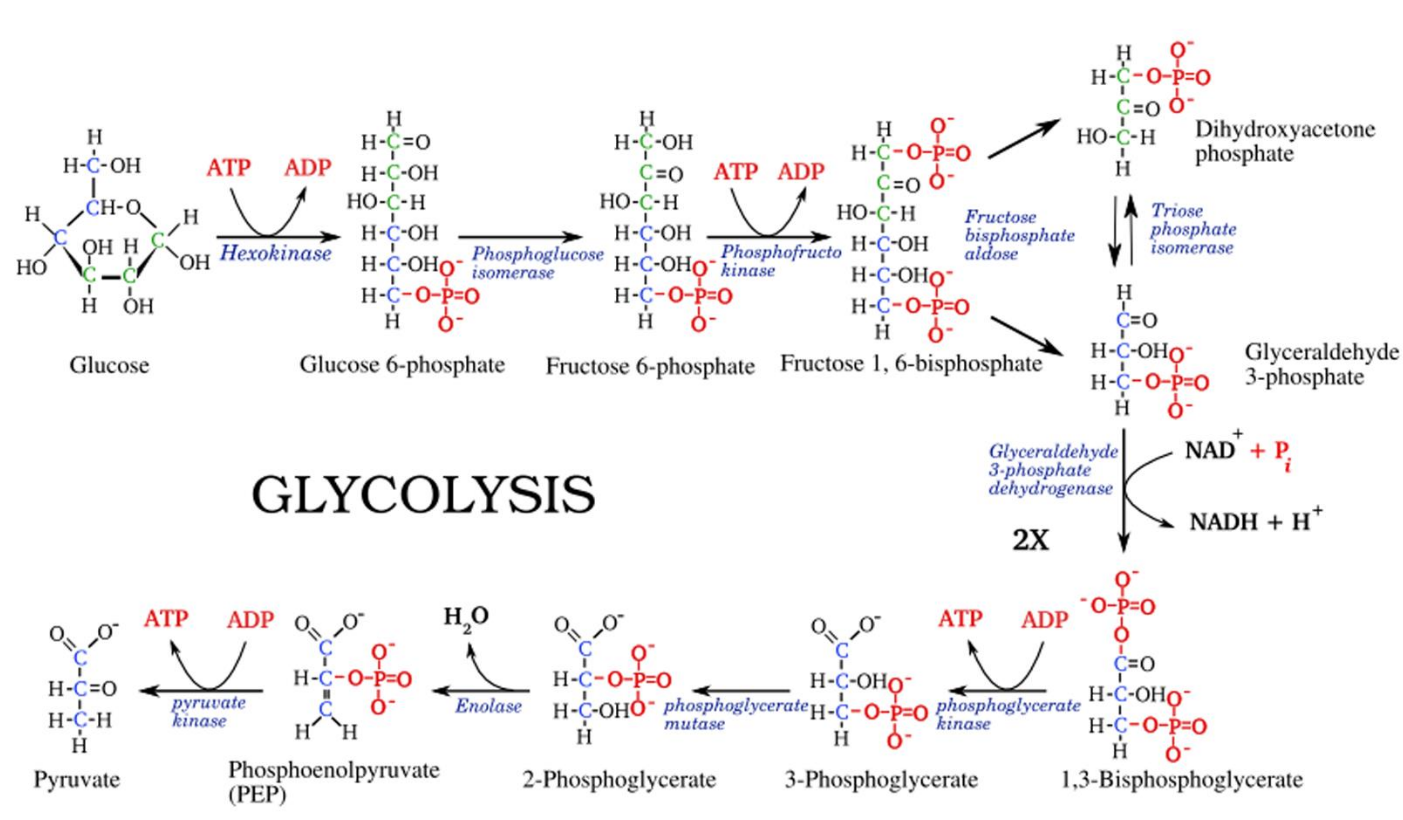


Overall, glycolysis converts one six-carbon molecule of glucose into two three-carbon molecules of pyruvate. The net products of this process are two molecules of ATP produced, 2 ATP used up and two molecules of NADH.

Detailed steps: Energy-requiring phase

During the energy-requiring phase of glycolysis, two ATP are spent to form an unstable sugar with two phosphate groups, which then splits to form two three-carbon molecules that are isomers of each other.

Each step is catalyzed by its own **specific enzyme**, which plays a very important role in catalyzing the reactions (indicated in blue below the reaction arrow in the diagram below).



From the above figure, - The reactions from the lysis of compound Glucose till the formation of Glyceraldehyde 3-phosphate (1-5) shows steps under Energy Requiring Reactions

Step 1. Phosphorylation of glucose: This step is catalyzed by the enzyme *hexokinase* and phosphate group is transferred from ATP to glucose, making glucose-6-phosphate. Glucose-6-phosphate is more reactive than glucose, and the addition of the phosphate also traps glucose inside the cell since glucose with a phosphate can't readily cross the membrane.

Step 2. ***Isomerization****:* Glucose-6-phosphate is converted into its isomer, fructose-6-phosphate.

Step 3. Phosphorylation: A phosphate group is transferred from ATP to fructose-6-phosphate, producing fructose-1,6-bisphosphate. This step is catalyzed by the enzyme phosphofructokinase, which can be regulated to speed up or slow down the glycolysis pathway.

Step 4. Cleavage: Fructose-1,6-bisphosphate splits to form two essentially similar three-carbon sugars: dihydroxyacetone phosphate (DHAP) and glyceraldehyde-3-phosphate. They are isomers of each other, (interconvertible by means of an isomerizing reaction, catalyzed by the enzyme *phosphotriose isomerase*) but only one—glyceraldehyde-3-phosphate—can directly continue through the next steps of glycolysis.

Step 5. DHAP is converted into glyceraldehyde-3-phosphate, as glyceraldehyde-3-phosphate is used up, all of the DHAP is eventually converted.

Detailed steps: Energy-releasing phase

In the second half of glycolysis, the three-carbon sugars formed in the first half of the process go through a series of additional transformations, ultimately turning into pyruvate. In the process, four ATP molecules are produced, along with two molecules of NADH.

Here, when we see in detail, the reactions happens twice for each glucose molecule since a glucose splits into two three-carbon molecules, both of which will eventually proceed through the pathway.

Step 6. Oxidation: Two half reactions occur simultaneously: 1) Glyceraldehyde-3-phosphate (one of the three-carbon sugars formed in the initial phase) is oxidized, and 2) NAD+ is reduced to NADH and H+. The overall reaction is exergonic, releasing energy that is then used to phosphorylate the molecule, forming 1,3-bisphosphoglycerate.

Step 7. 1, 3-bisphosphoglycerate donates one of its phosphate groups to ADP, making a molecule of ATP and turning into 3-phosphoglycerate in the process.

Step 8. 3-phosphoglycerate is converted into its isomer, 2-phosphoglycerate.

Step 9. 2-phosphoglycerate loses a molecule of water, becoming phosphoenolpyruvate. PEP is an unstable molecule, ready to lose its phosphate group in the final step of glycolysis.

Step 10. PEP readily donates its phosphate group to ADP making a second molecule of ATP. As it loses its phosphate, PEP is converted to pyruvate, the end product of glycolysis.

The following equation represents the overall result of glycolysis in animal cells, e.g. muscles:

$$\textbf{Glucose (6C)} + 2NAD^{+} + 2ADP + 2Pi \longrightarrow \textbf{2pyruvate (3C)} + 2NADH + 2H^{+} + \textbf{2net ATP}$$

What happens to pyruvate and NADH?

At the end of glycolysis, we're left with two ATP, two NADH, and two pyruvate molecules. If oxygen is available, the pyruvate can be broken down (oxidized) all the way to carbon dioxide in cellular respiration, making many molecules of ATP. (Study Krebs cycle, Oxidative Phosphorylation)

What happens to the NADH?

It cannot keep accumulating around in the cell, piling up. That's because cells have only a certain number of NAD+ molecules, which cycle back and forth between oxidized (NAD+) and reduced (NADH) states:

$$NAD^+ + 2e^- + 2H^+ \rightleftharpoons NADH + H^+$$

Glycolysis needs NAD+ to accept electrons as part of a specific reaction. If there's no NAD^+ around (because it's all stuck in its NADH form), this reaction can't happen and glycolysis will come to a halt. So, all cells need a way to turn NADH back into NAD^+ to keep glycolysis going.

There are two basic ways of accomplishing this. When oxygen is present, NADH can pass its electrons into the electron transport chain, regenerating NAD^+ for use in glycolysis.

When oxygen is absent, cells may use other, simpler pathways to regenerate NAD. In these pathways, NADH donates its electrons to an acceptor molecule in a reaction that doesn't make ATP but does regenerate NAD^+ so glycolysis can continue. This process is called **fermentation**.

Fermentation is a primary metabolic strategy for lots of bacteria, including *Lactobacillus acidophilus*, even some cells in the body, such as red blood cells, rely on fermentation to make their ATP.

Pyruvic acid to Lactic acid: in the case of inadequacy of oxygen, (e.g. skeletal muscles, during muscle exercise), pyruvic acid is converted into lactic acid by an oxidation-reduction in which DPNH reduces *pyruvic acid* to *lactic acid* in the presence of the specific enzyme, *lactic acid dehydrogenase*, this releases very less energy.

References:

- Berg, Jeremy M., John L. Tymoczsko, and Lubert Stryer. "The Glycolytic Pathway Is Tightly Controlled." In *Biochemistry*. 8th ed. New York: W. H. Freeman, 2015.
- http://www.ncbi.nlm.nih.gov/books/NBK22395/(Opens in a new window)(Opens in a new window).
- modified derivative of "Glycolysis(Opens in a new window)(Opens in a new window)(Opens in a new window)" by OpenStax Biology, CC BY 3.0. Download the original article for free at http://cnx.org/contents/185cbf87-c72e-48f5-b51e-f14f21b5eabd@9.85:35/Glycolysis.
- H.R. Singh, "Animal Physiology and Related Biochemistry", S.Chand & Co., India