Module 16 / Glycolysis

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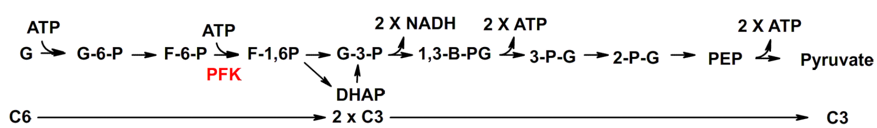
Define glycolysis and identify its cellular location.	Explain what happens when glucose is metabolized through glycolysis.	Describe how energy released by oxidation is stored.
Distinguish how direct and indirect coupling are used to make glycolysis spontaneous.	Describe anaerobic metabolism and how it effects glycolysis.	

Glycolysis is the first pathway that occurs in the metabolism of carbohydrates. This pathway occurs in the cytosol of all cells, i.e. it is a highly conserved and ubiquitous pathway. Although many different disaccharides are broken down into monosaccharides and enter the glycolysis, we will focus on how glucose is metabolized in this section. The entry points of other sugars will be discussed in the module on **integrated metabolism**.

An overall summary of glycolysis is depicted below:



An overview of glycolysis. The intermediates in the pathway are shown near the top of the figure, along with a summary of energy consumption and production by the pathway. The molecular structure of these compounds can be seen in the learn-by-doing exercise below. ADP and NAD^+ have been omitted in this diagram for clarity. The lower part of the figure shows the change in the carbon skeleton in the pathway. The step following F-1,6-P splits the 6 carbon fructose into two three carbon compounds, both of which proceed down the pathway to form pyruvate. The key regulatory step, the enzyme phosphofructose kinase, is indicated as PFK.

Key features of Glycolysis:

1. Glucose, a six carbon hexose, is the input compound.
2. Pyruvate, a three carbon keto-acid is the output. There is no loss of carbon in glycolysis, so two pyruvates are produced/glucose. Pyruvate is further oxidized in the TCA cycle.
3. Two ATP molecules are produced/glucose. Note that the energy content of two ATP molecules is required to initiate the pathway. Four ATP (2/pyruvate) are produced later in the pathway. Consequently, the net yield is two ATP.
4. Two NADH molecules are produced. A single oxidation step produces one molecule of NADH/pyruvate. The energy stored in NADH is extracted during electron transport.
5. The key regulatory step is the addition of the second phosphate to fructose, by the enzyme **phosphofructose kinase**

Capture of Glucose by the Cell

Glucose from the outside of the cell is transported across the cell membrane by a multi-subunit protein called the glucose transporter. This enzyme catalyzes the diffusion of glucose across the membrane without the input of energy. Consequently, spontaneous flow of glucose into the cell can only occur if the concentration of glucose is lower in the cell than outside the cell. The Gibbs free energy for the transport of glucose is:

$$\Delta G = RT\ ln \frac{[glucose]_{IN}}{[glucose]_{OUT}}$$

Although this expression for the Gibbs free energy appears different than previous expressions, it is really the same equation. The "product" of the reaction is glucose inside the cell and the "reactant" is glucose outside the cell. The difference in standard free energy, ΔG^o, is zero because the reactants and products are the same compound, differing only in their location. If the concentration of glucose outside the cell is higher than the concentration inside the cell, then the Gibbs free energy is negative (the ln of a number less than one is negative) and glucose will spontaneously enter the cell. If the glucose concentration in both compartments are the same, then Δ=0 and there is no net movement of glucose across the membrane. If the concentration of glucose inside the cell exceeds the concentration outside then Δ>0 and the reverse reaction, the net movement of glucose out of the cell, will be spontaneous.

The levels of glucose in the blood vary considerably at times. We will discuss how glucose levels are regulated in the section on integrated metabolism. The focus here is to understand how the entry of glucose into the cell is spontaneous, even when the levels of glucose in the blood can drop to low values. How is it possible to maintain a negative Gibbs free energy for glucose transport into the cell, even if there are low levels of glucose outside the cell?

Question: Use the tutorial below to discover how glucose spontaneously enters the cell, even if the intracelluar concentration exceeds the concentration outside the cell.

Flash Player needed! Please click here to install Flash Player.

Glucose Transporter

Instructions: Compare the behavior of the two simulations to see how the Hexose Kinase molecule changes the concentration of glucose inside and outside of the cell.

The Glucose molecules in this example are too large to freely pass through the membrane. This Glucose Transporter allows them through the specific channel through the protein.

The Hexose Kinase molecule binds with the glucose to make glucose 6-P which is too large to return through the transporter.

Glycolysis

The following learn-by-doing activity allows you to investigate the chemical and energetic changes that occur in glycolysis. Once you open up the page, explore it using the embedded questions to prepare you for the self-assessment at the end of this module.

> **Question:** As you move through the glycolysis pathway, determine which steps become spontaneous by direct coupling, which by indirect coupling, and how energy is captured from steps that release large amounts of energy.

Energy Changes in Glycolysis

Instructions: The left panel shows the energy changes that occur for each of the ten steps in glycolysis in the **absence** of coupling. The right panel shows the actual energy changes during the normal operation of glycolysis. These energy changes include contributions from both direct and indirect coupling. **Click on any of the red labeled steps on the left to see the details of that step in the glycolysis pathway.** You may also explore this activity in a separate larger window

did I get this

Non-spontaneous reactions in glycolysis become spontaneous due to ______ the reaction to ______.

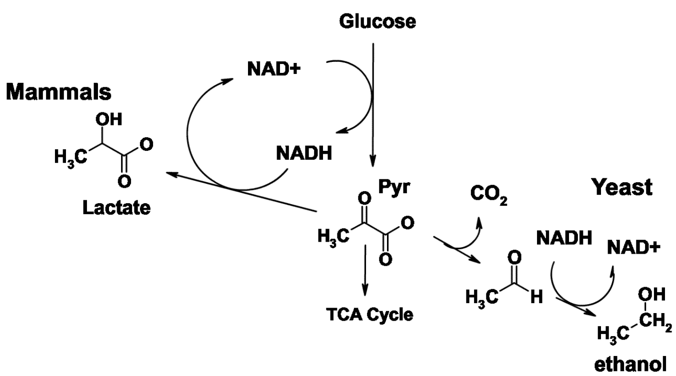
- indirect coupling, ATP hydrolysis
- direct coupling, ATP hydrolysis
- direct coupling, NADH oxidation

Reset this Activity

Anaerobic Glycolysis

Under anaerobic (oxygen limited) conditions, which occurs in the muscle tissue during vigorous activity, the NADH produced in glycolysis cannot be reoxidized to NAD^+ by electron transport because there is insufficient oxygen to accept electrons. Under these conditions, the cell runs out of NAD^+ and glycolysis will halt and the cell can no longer produce ATP.

The levels of NAD^+ can be restored by using pyruvate as the electron acceptor. In mammals, lactate is the product of this reaction. In yeast, it is alcohol and the process of anaerobic glycolysis is referred to as **fermentation**. The reduction of pyruvate will oxidize NADH to NAD^+, allowing glycolysis to resume.



Anaerobic metabolism. Pyruvate can serve as the electron acceptor for NADH. The reduction of pyruvate to lactate in mammals, or ethanol in yeast, regenerates the NAD^+ required for glycolysis to operate.

The lactate that is produced by active muscle tissue is transported to the liver. When oxygen becomes available, the lactate is reoxidized to pyruvate and it can then be used for the synthesis of glucose.

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Glycolysis takes place in

- mitochondria
- lysozomes
- cytosol
- nucleus

NEXT »

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