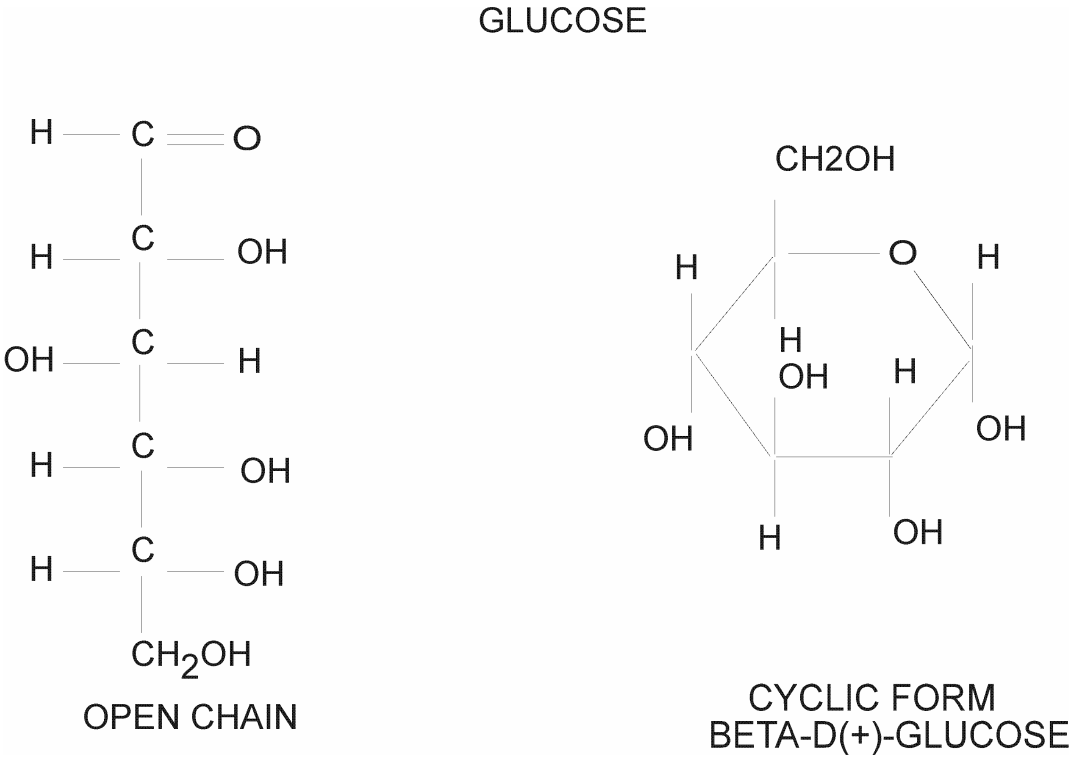
CHAPTER THREE

FIRST STAGE OF GLYCOLYSIS AND ENZYME INHIBITION

Draw the structure of glucose in its straight chain and cyclic forms.



There are not many chemical structures that you have to be able to draw - but glucose is one of them.

What does the word glycolysis mean ?

Glycolysis means "splitting glucose". One of the first things discovered about glucose metabolism was that the six carbon structure was "split" into two three carbon structures (hence the name). Glycolysis is also called the Ebdemen-Meyerhoff pathway.

How many steps are there in the first stage of glycolysis ?

Four.

What is the first step in the first stage of glycolysis ?

Conversion of glucose into glucose-6-phosphate.

What enzymes catalyze this reaction ?

Hexokinase in muscle and glucokinase in the liver.

What other molecule is required in this reaction ?

ATP.

Does the answer to the last question strike you as odd ?

Yes, because glucose catabolism is supposed to make ATP and instead this first step uses ATP. However, you must use some ATP to "activate" the glucose before you can extract the energy from it.

What is the second step in glycolysis ?

Glucose-6-phosphate is converted into fructose-6-phosphate.

What is the third step in glycolysis ?

The conversion of fructose-6-phosphate to fructose-1,6-bisphosphate. ***This is an important step***.

What other molecule is required for this step ?

This step also uses a molecule of ATP.

What enzyme catalyzes this step ?

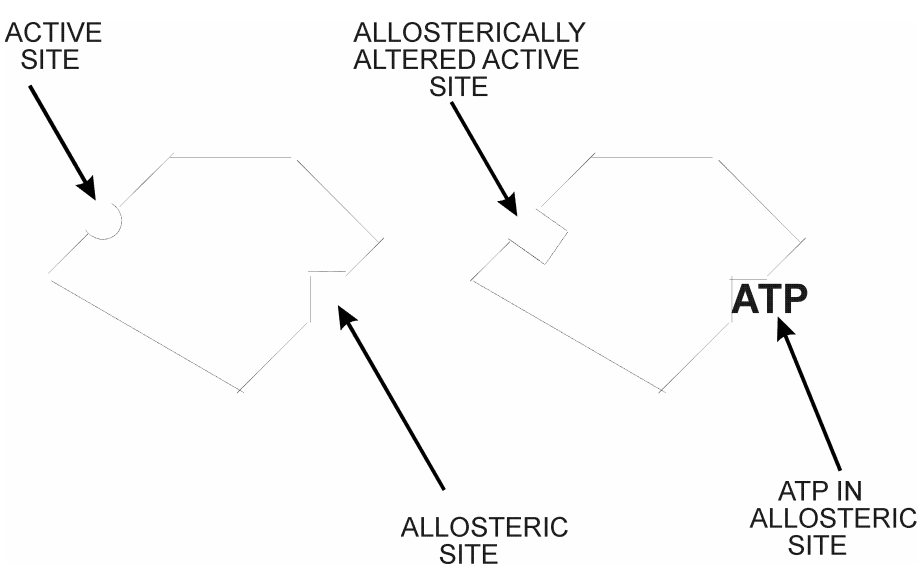
Phosphofructokinase (PFK) which is the rate limiting enzyme of glycolysis (and hence of ATP synthesis from glucose). Glycolysis as a whole will only proceed as fast as this enzyme can catalyze the formation of its product fructose-1,6-bisphosphate. (It's like a toll booth on a road. The number of cars entering and passing along the road is determined by the rate at which cars can get through the toll booth).

Name one way in which the activity of PFK can be controlled *?*

A high level of ATP will inhibit this enzyme. This makes sense because if there is lots of ATP around you do not need to be making more ATP.

How does ATP inhibit the enzyme PFK ?

It binds to a site on the enzyme called an allosteric site and this leads to *a change in the conformation* of the enzyme protein. This alters the shape of the active site (where the actual reaction takes place) which alters the activity of the enzyme which, in turn, alters the rate at which the reaction takes place. *This concept of allosteric control is an important on*e.



What is the inhibition of PFK by ATP an example of ?

It is an example of *feedback inhibition*, because a downstream product of an enzyme in a reaction chain "feeds back" to alter the activity of one of the enzymes in that reaction chain.

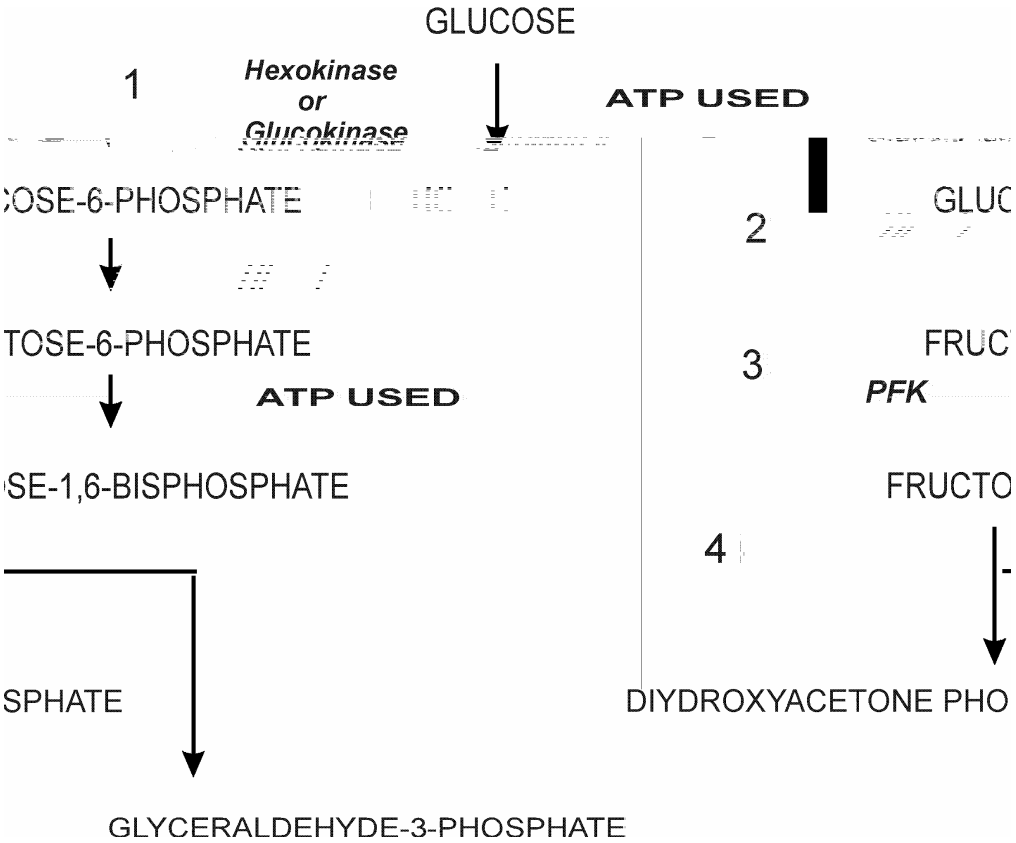
What is the fourth and final step in the first stage of glycolysis ?

The conversion of the six carbon fructose-1,6-bisphosphate into dihydroxyacetone phosphate (DHAP) and glyceraldehyde-3-phosphate (G-3-P). This reaction is catalyzed by the enzyme aldolase.

How many carbons do the products of this step have ?

DHAP and G-3-P are both three carbon compounds.

Draw a diagram of the first stage of the glycolysis pathway with the names of the important intermediates, enzymes and the sites where ATP is used.



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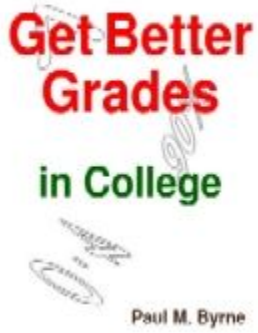

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