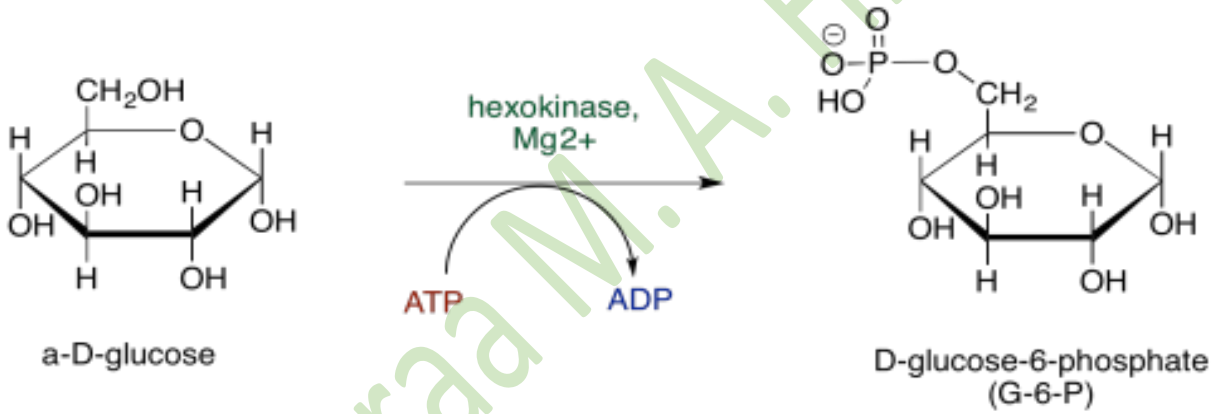
The Regulation of Enzyme Activity:

Regulation of enzyme activity is essential for the metabolism

1- Substrate-Level Control

The substrates and products of each enzyme-catalyzed reaction interact directly with the enzyme to regulate it.
kinetics study shows that increased substrate concentrations accelerate reactions until enzyme saturation.

As an example, consider the first step in glycolysis (see Chapter 13)—the phosphorylation of glucose to yield glucose-6-phosphate (G6P):



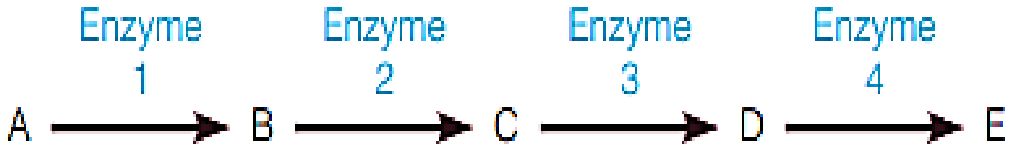
Hexokinase catalyzes this reaction and is inhibited by its product, glucose-6-phosphate (G6P). If subsequent steps in glycolysis are blocked for any reason, G6P will accumulate and bind to hexokinase. This results in the inhibition of hexokinase and slows down further production of G6P from glucose.

In many cases, the reaction product binds the active site for the enzyme and acts as a competitive inhibitor. Hexokinase is an interesting example because the product (G6P) can act as a competitive inhibitor (by binding to the active site for the enzyme) and an uncompetitive inhibitor (by binding at another place for the enzyme).

2- Feedback Control

Feedback control is important in the efficient regulation of complex metabolic pathways.

The metabolic pathways resemble assembly lines. The simplest metabolic assembly line looks like this:

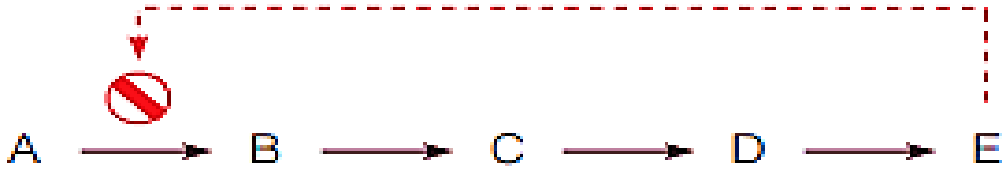


Where **A** represents the initial reactant or raw material (crud), **B**, **C**, and **D** represent intermediate products, and **E** represents the final product.

This pathway's end product **(E)** may be employed in another path, and **A** may be used in other processes. Consider that E's utilization slows. As previously pathway, E would accumulate, and A would be consumed. But this process is inefficient.

A more efficient process would solve this problem by closely monitoring the concentration of E and, when E accumulated, sending a signal back to prevent its production. The cell can control the generation of the final product through activation (⬆) or inhibition (⛔) of a critical step in the pathway.

It would be most efficient to slow the first step—converting A to B ($A \rightarrow B$) So, the "machine" should be regulated by the concentration of E.

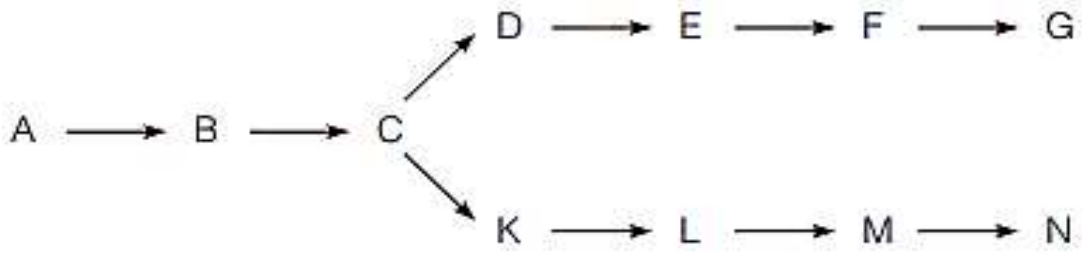


This type of feedback control is called feedback inhibition because an increase in the concentration of E leads to a decrease in its production rate.

Note that inhibiting the first step prevents unwanted utilization of A and accumulation of E.

3- Substrate fed into two pathways

Other metabolic situations require more complicated patterns in which activation and inhibition may be useful. For example, consider a slightly more complex case in which ***A is fed into two pathways***, which leads to two products needed in roughly equivalent amounts. Then, a scheme like the following emerges:



To control the pathways so that **G and N** keep in balance, high concentrations of G might inhibit the C → D enzyme or activate C → K enzyme. Conversely, high concentrations of N might inhibit C → K enzyme or activate the C → D enzyme.

An example of this kind of control is found in the synthesis of the purine and pyrimidine monomers that go into making DNA because approximately equal quantities of all four deoxyribonucleotides are required for DNA replication.