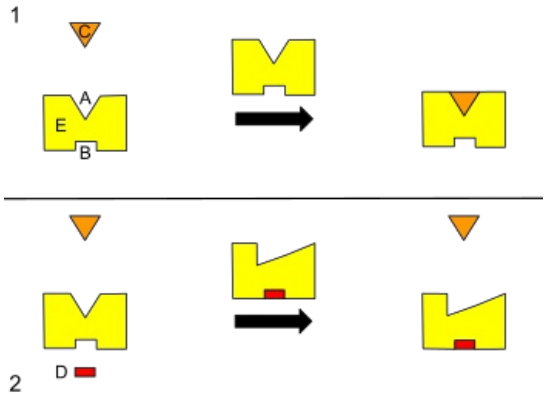
Allosteric regulation of enzyme reaction

Many regulatory enzymes that limit the rate of metabolic pathways (so-called *rate-limiting enzymes*) are **allosteric** enzymes. Allosteric regulation of their activity is one of the most important forms of regulation of metabolic pathways.



Binding of the inhibitor on the enzyme molecule: A - Active site; B - Allosteric site; C - Substrate; D - Inhibitor; E - Enzyme

An **allosteric enzyme** has on its surface, in addition to the active site, another site, the so-called allosteric *(Greek αλλος - other)*, through which it can be influenced by **modulators** (activators or inhibitors). The Binding of an allosteric modulator causes a **conformational change** of the enzyme molecule. This change leads to different affinities for the substrate and other ligands. Most allosteric enzymes are **oligomeric** (composed of subunits). The binding of a modulator to one subunit will affect the activity of the other subunits through a conformational change. There are two basic types of allosteric regulation:

1. **Homotropic** - The modulator is also the substrate for the enzyme. A well-known example is O_2, which is a homotropic allosteric modulator of hemoglobin.
2. **Heterotropic** - The modulator and the substrate are different molecules. In reference to the previous example, CO_2 would be a heterotropic allosteric modulator of hemoglobin.

Allosteric enzymes display sigmoidal kinetics

As an example, we will use a reaction affected by a homotropically active allosteric activator. At low substrate concentrations, the reaction proceeds slowly because few enzyme molecules are occupied. If the substrate binds to at least one subunit of the enzyme, this will increase the affinity of the other subunits. This is reflected in the graph by a sharp rise in the reaction rate. The more subunits an enzyme molecule contains, the more abrupt the onset of the effect of increasing the substrate concentration.

The enzyme works on an **all-or-none** basis. Before a certain substrate concentration is reached, the reaction almost does not run, but above a given substrate concentration it quickly reaches V_{max}. At this point, all binding sites of the enzyme subunits are already occupied.

This property of allosteric enzymes is very useful in the regulation of metabolic pathways, as it allows them to quickly switch off or on the course of the reaction and thus the whole metabolic pathway.