

# Highlights Enzymes 4

1. Allosterism is only one way of controlling enzymes. Another powerful control over enzymes (for some enzymes) is covalent modification.
2. Covalent modification involves making or breaking covalent bonds within or to an enzyme. One common covalent modification is phosphorylation (putting on a phosphate) or dephosphorylation (taking off a phosphate). Only the hydroxylated amino acids (serine, threonine, or tyrosine) are typically phosphorylated.
3. Enzymes that put phosphates onto things are called kinases. Enzymes that take phosphates off are known as phosphatases.
4. The sodium-potassium ATPase is an example of a protein whose activity includes a transient step in which it is phosphorylated using phosphate from ATP. The phosphorylation/dephosphorylation cause the protein to either accept sodium ions or accept potassium ions, depending on which way it is pointed. The phosphor
5. A very common type of covalent modification is phosphorylation, as exhibited by Glycogen Phosphorylase. Phosphorylation converts glycogen phosphorylase b (less active) to glycogen phosphorylase a (more active). The kinase that puts the phosphates on is controlled by epinephrine (adrenalin) and the phosphatase that takes the phosphates off is controlled by insulin.
6. Another type of covalent modification is that which activates zymogens. Zymogens are enzymes made in an inactive form and then activated by cleavage of one or more peptide bonds in them. Chymotrypsinogen is a zymogen that gets activated by peptide cleavage to form chymotrypsin. It is made in the pancreas and normally activated in the digestive system. If it gets activated too soon, pancreatitis results from attack of the enzyme on the proteins in the pancreas.
7. Chymotrypsin is an enzyme that catalyzes a reaction in two phases - a slow phase and a fast phase. The fast phase occurs first. In this phase, the peptide bond is broken and the first peptide is released. As a result of this action, the other peptide is covalently linked to the enzyme transiently. The release of the second peptide from the enzyme is the slow phase and involves the action of water.
8. Chymotrypsin is a so-called serine protease, meaning that it uses the side chain of serine to catalyze proteolytic cleavage. The side chain of serine (hydroxyl group) is ionized in the reaction as a result of removal of its proton by a nearby histidine. This occurs when the substrate binds the active site, moving the histidine slightly closer to the serine.
9. In the catalytic mechanism of chymotrypsin, serine becomes covalently attached to one peptide when the other peptide is released. Release of the second peptide from serine requires the action of water.
10. Serine proteases act by creation of a reactive alkoxide ion. This is made by 1) binding of the proper substrate at the active site; 2) slight changes in shape that bring the catalytic triad (aspartic acid, histidine, and serine) closer together; 3) removal of a proton from the hydroxyl group of serine (creating the alkoxide ion).
11. The alkoxide ion is reactive and attacks the peptide bond in the active site, breaking it. One piece from the break is released and the other piece becomes transiently attached to the oxygen of the serine. Detachment of the attached peptide requires action of water in the active site. This is the slow step of the reaction.