

Highlights Catalytic Mechanisms II

1. Many other proteases and other enzymes share similarities with the mechanism used by serine proteases. Other proteases include cysteine proteases (use cysteine and histidine in the active site), aspartyl proteases (use aspartic acids and water in the active site) metalloproteases (use a metal ion - usually zinc - and water in the active site).
2. I discussed in the lecture the implications of the exact ways in which they worked as to how they differed from serine proteases and how they were similar. You should be familiar with these.
3. Cysteine proteases use an ion of the sulfhydryl group of cysteine to act as a nucleophile to attached the carbonyl peptide bond and facilitate breakage of the peptide bond.
4. Aspartyl proteases use two aspartic acid side chains to hold water in place and use an ion of it to act as a nucleophile to attack the peptide bond.
5. Metalloproteases use a metal ion to hold water in place so it can be ionized to act as a nucleophile to attack the peptide bond.
6. Carbonic anhydrase is an enzyme that catalyzes the joining of carbon dioxide and water to form carbonic acid.
7. A zinc ion (held in place by three histidines in the active site of carbonic anhydrase) plays an important role in the catalysis of the enzyme by binding a water molecule. A subsequent loss of a proton by water is necessary for catalysis. Notably, the enzyme has maximal activity at a high pH (where protons are easily removed) and a lower activity in an acidic pH (6.0).
8. The limiting step in the action of carbonic anhydrase is the abstraction of the proton from water. Buffers and/or bases help facilitate this and thus speed the reaction.
9. Restriction enzymes are bacterial enzymes that can cleave DNA by breaking phosphodiester bonds between adjacent nucleotides in the molecule.
10. They act at specific nucleotide sequences. When these bind in the enzyme, it changes shape and this shape change causes a bend in the DNA. The bend provides a "pocket" for a water molecule and magnesium ion to be positioned properly so that the water can be activated to be a nucleophile to attack the phosphodiester bond between nucleotides to cleave it.