Competitive, Uncompetitive and Noncompetitive Inhibition

- In order to function effectively, biological systems must be able to regulate the activity of enzymes. Special agents called inhibitors can bind onto enzymes and inhibit or block their activity.

Irreversible Inhibition

- Some inhibitors will bind to enzymes very tightly, either by covalent or non-covalent means. Once bound, they will not dissociate very easily from the enzyme. These inhibitors are called irreversible inhibitors; they have a high affinity for the enzyme.

$$E + I \rightleftharpoons EI$$ Equilibrium lies for to the right

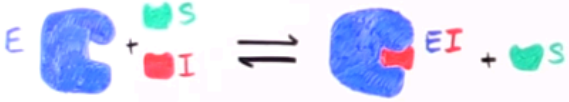
- Some examples of irreversible inhibitors are nerve gas, penicillin and aspirin.

Reversible Inhibition

- The defining property of reversible inhibition is the ease with which the inhibitors can dissociate from the enzyme under certain conditions.

① Competitive Inhibition

- In this inhibition, the inhibitor molecule typically resembles the substrate and can therefore bind directly to the active site of the enzyme. Once bound, the inhibitor prevents the substrate from occupying the active site.



- Competitive inhibitors typically have a much higher affinity for the active site than the natural substrate. However, if we increase the concentration of the substrate, the additional substrate can outcompete the inhibitor for the active site! Thus increasing substrate concentration can remove the effect of the competitive inhibitor.

- Methotrexate is a competitive inhibitor of dihydrofolate reductase.

② Uncompetitive Inhibition

- In some instances, the binding of the substrate to the active site changes the conformation of the enzyme and creates an allosteric site that was not previously there. Now, a certain inhibitor can bind to the enzyme-substrate complex and block its activity.

- Uncompetitive inhibitors cannot be overcome by ↑ concentration of substrate.

③ Non-competitive Inhibition

- Some enzymes have a permanent allosteric site that can bind inhibitors. These inhibitors, called non-competitive inhibitors because they do not compete for the active site, can bind to enzyme regardless of whether the substrate is bound or not. These inhibitors block enzymatic activity by decreasing the turnover number k_{cat}.