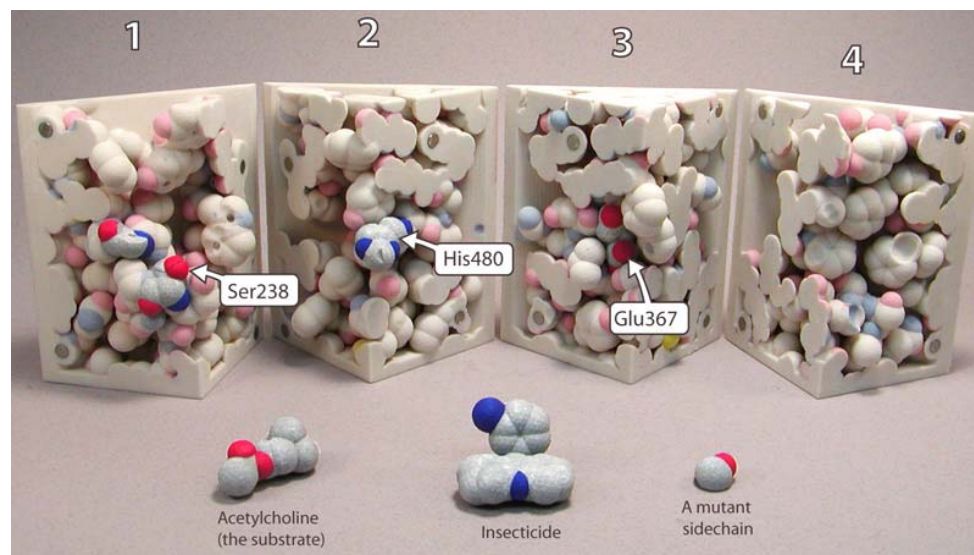


Evolution In Action

Emerging Insecticide Resistance in Mosquitoes

A three-dimensional molecular story about the acetylcholinesterase active site

Organophosphate insecticides are routinely used to control mosquito populations in areas where malaria is endemic. Many of these insecticides target the enzyme acetylcholinesterase --- which normally cleaves the acetylcholine neurotransmitter, and terminates synaptic transmission. A recent report by Weil et. al. (Nature, 423, pp136-137, 2003) described the molecular basis for this insecticide resistance -- a Gly119Ser mutation. Because it is difficult to communicate the close-packed nature of an enzyme active site, and the specific interactions between active site residues and the substrate/inhibitor with 2D illustrations and computer graphics, we have constructed a physical model of this enzyme active site. This space-filled model of the active site “unfolds” to reveal the catalytic triad of active site residues Ser238, His480 and Glu367. The substrate and inhibitor can be alternatively docked into the active site. Replacement of the normal Gly119 sidechain with a serine sidechain blocks the binding of the insecticide, without interfering with substrate binding. This physical model is based on coordinates from 1qon.pdb.



This model can be borrowed from the MSOE Model Lending Library.