EVOLUTION IN ACTION

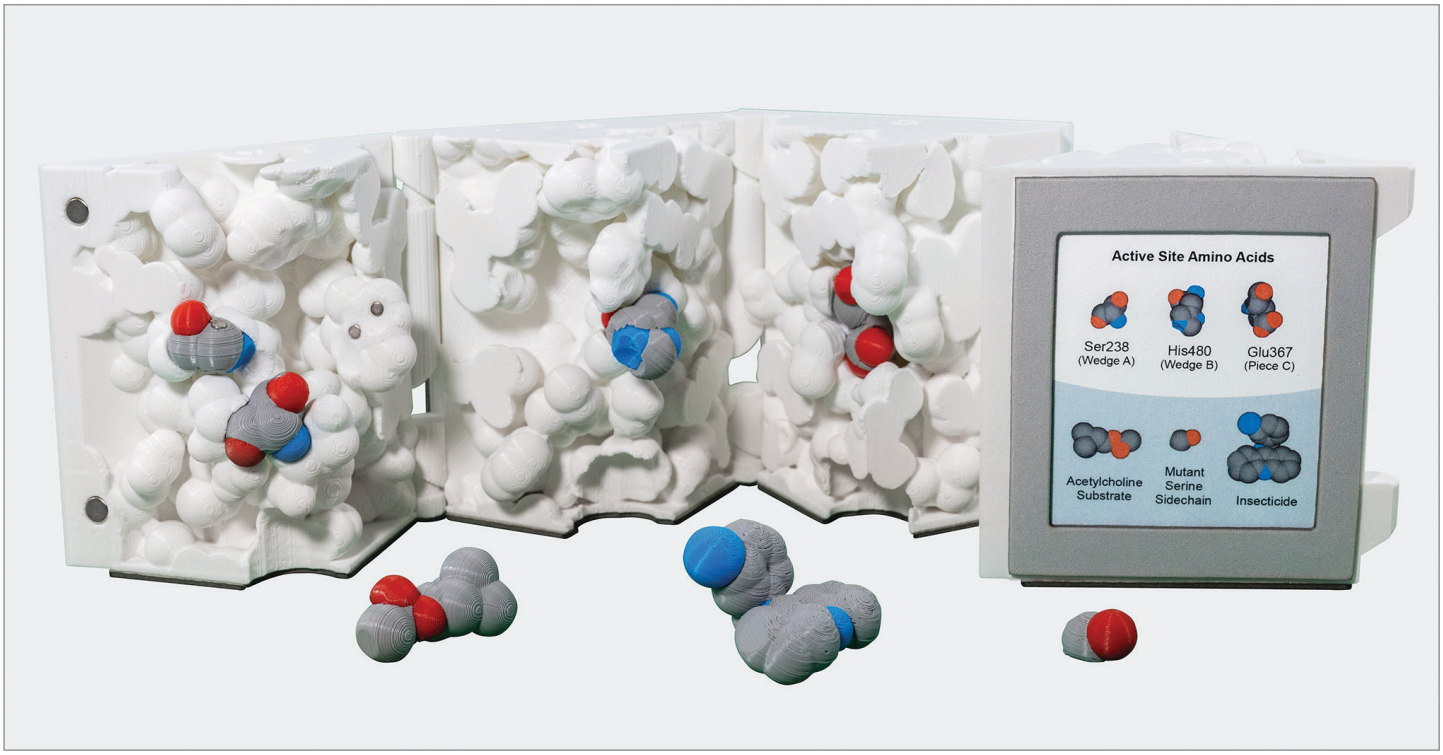
Emerging Insecticide Resistance in Mosquitoes

Many insecticides are used to control mosquito populations in regions with high malaria infection rates. These insecticides, typically organophosphates, target the enzyme **acetylcholinesterase (ACHE)**, which normally cleaves the neurotransmitter **acetylcholine,** terminating synaptic transmission.

A study by Weill et al. (Nature, 423, pp. 136-137, 2003) describes the molecular basis of **insecticide resistance,** which arises from a **glycine-to-serine mutation at position 119 (G119S).** Due to the tightly packed nature of ACHE, visualizing the enzyme's **substrate-inhibitor-active site** interactions is challenging.

This **3D model** unfolds to reveal the **catalytic triad** of active-site residues: **Ser238, His480, and Glu367.** The acetylcholine substrate or the insecticide inhibitor can be docked within the active site at any one time. The addition of the **serine side chain at position 119** demonstrates how this mutation blocks insecticide binding while still allowing acetylcholine to bind, conferring resistance.

This model is based on **PDB coordinates from 1QON.**



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