

## Acetylcholinesterase Video

by Frank Deis

This video shows the action of the enzyme Acetylcholinesterase. The synapse is discussed briefly in Chapter 13 of Berg and Stryer, 5th Edition. Acetylcholine (ACh) floods the synaptic cleft in response to pre-synaptic nerve impulses (Fig 13.4, p. 355) and activates the pentameric Acetylcholine receptor (Fig 13.17 p. 356), causing depolarization of the post-synaptic neuron. Acetylcholinesterase (AChase) then is responsible for removing a huge amount of transmitter in a very short time. Stryer says, on p. 296 of the 4<sup>th</sup> edition:

"Acetylcholinesterase has a very high turnover number (25,000 s<sup>-1</sup>). Indeed, acetylcholinesterase has attained kinetic perfection (p. 195), as indicated by its  $k_{\text{cat}}/K_M$  value of  $2 \times 10^8 \text{ M}^{-1}\text{s}^{-1}$ . The catalytic prowess of acetylcholinesterase enables synapses to transmit action potentials at high frequency."

The video helps us to understand how AChase can be as fast as it is. The molecule, Acetylcholine, carries a positive charge. When it has been hydrolyzed, the two halves are choline, which still carries a positive charge, and acetate, which bears a negative charge. The active site is located in a "tunnel" through the enzyme, and the charge structure of the molecule basically converts this into a "wind tunnel" through which ACh is sucked in a motion quite similar to a vacuum cleaner. The film shows the negatively charged areas in red and the positively charged areas in green, and shows the small ACh molecules sweeping through and the products of hydrolysis sweeping out. It is certainly easier to visualize how an enzyme could be so fast and efficient after seeing this video.

Inhibitors of Acetylcholinesterase are used as lethal "nerve gases" -- these include Tabun, Sarin, and Parathion (see Homework 13:2 p. 367). AChase has a serine residue at the active site that participates in hydrolysis, so it can be inactivated by reagents like DIPF (see Fig 8.19 p. 211, and Fig 9.2 p. 230).