

Biophysicists Describe New Gating Action of Acetylcholine Receptor

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Biophysicist Anthony Auerbach has described a formerly unknown action of the acetylcholine receptor channel in a paper in *Nature*.

A formerly unknown action of the acetylcholine receptor channel, a protein that regulates the electrical activity of nerve and muscle cells, is described by biophysicists at the University at Buffalo in the April 19 issue of the journal *Nature*.

Acetylcholine is a neurotransmitter that carries chemical messages

across certain brain synapses and across all human nerve-muscle synapses. Acetylcholine receptors bind the neurotransmitter and set in motion a cascade of molecular activity that ultimately results in thought or motion.

"The acetylcholine receptor channel is a molecule-sized valve that opens and closes to regulate the flow of electricity in nerve and muscle cells," said Anthony L. Auerbach, Ph.D., UB professor of physiology and biophysics in the UB School of Medicine and Biomedical Sciences and senior author on the study.

"Before our work, most scientists thought that this protein had a small number of moving parts, perhaps even just one. Also, they thought that these parts moved, between closed and open, smoothly and nearly instantaneously. Our work has shown that the receptor is made up of a much larger number of moving parts, maybe 20 or so, and that these parts jiggle about when they move."

Prasad G. Purohit, Ph.D., postdoctoral associate working with Auerbach, is first author on the paper. Ananya Mitra, a doctoral student in the laboratory, also contributed to the study.

The researchers use a technique called single-molecule kinetic analysis to probe the transition state of the receptor's "gating mechanism," and to estimate the timing of motions within the protein's opening process.

"Perhaps this newfound understanding of how a protein machine works, how it changes shape in order to carry out its appointed task, will someday lead to better protein engineering and drug design," said Auerbach. "If you want to build a better protein, or to modify its function, an important first step is to understand the ones nature has given us."

Auerbach has conducted research for 18 years into the molecular processes involved in protein activity in the nervous system and on how synaptic receptors are activated by their transmitters. He and scientists working in his laboratory now are studying how the subunits that form the receptor work together, and how the protein limits its receptiveness to signaling mechanisms.

Source: University at Buffalo

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