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*Understanding Allosteric Modulation of Pentameric Ligand-Gated Ion Channels by Fatty Acids*

**Abstract**

Pentameric Ligand-Gated Ion Channels (pLGICs), with famous members including nicotinic acetylcholine receptor and GABA receptor, are central to ultrafast synaptic signal transmission. These channels have a central role in many physiologic processes, including sleep, cognition, and muscle function, making them excellent potential targets for many pharmacotherapies. Despite many decades of research, however, it remains unclear how changes in the functional state of the protein affect binding of small molecule drugs. Through previous research efforts, we have determined that docosahexaenoic acid (DHA), a polyunsaturated fatty acid, inhibits ELIC, a bacterial pLGIC homolog, in a state-dependent manner. DHA, can therefore, serve as a model for understanding state-dependent small molecule binding and function, which will aid in the development of state-specific drugs to limit side effects. In this project, we will utilize state-of-the-art molecular dynamics (MD) computational simulation to examine how DHA binds to and stabilizes certain functional states. In addition we will utilize novel information theory approaches to better characterize and understand how the signal of DHA binding to ELIC is transmitted to a distant activation site, opening new avenues of drug discovery.