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A Spatial Stochastic Model of AMPAR Trafficking and Subunit Dynamics

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ABSTRACT

In excitatory neurons, the ability of a synaptic connection to strengthen or weaken is known as synaptic plasticity and is thought to be the cellular basis for learning and memory. Understanding the mechanism of synaptic plasticity is an important step towards understanding and developing treatment methods for learning and memory disorders. A key molecular process in synaptic plasticity for mammalian glutamatergic neurons is the exocytosis (delivery to the synapse) of AMPA-type glutamate receptors (AMPARs). While the protein signaling pathways responsible for exocytosis have long been investigated with experimental methods, it remains unreasonable to study the system in its full complexity via only in vitro and in vivo studies. A large number of protein interaction states are observed, creating a system both difficult to monitor and limited in spatiotemporal resolution in an experimental setting. Thus, a computational modeling approach could be employed to help elucidate the underlying protein interaction mechanisms. Here we develop a systematic model to investigate the spatiotemporal patterning of AMPARs. We replicate in silico two distinct mechanisms of AMPAR trafficking related to variation in AMPAR subunit functionality. This model is validated against current knowledge of AMPAR trafficking and used to explore spatial localization of AMPARs to specific synaptic sites, as well as to describe the differences in the spatiotemporal dynamics between the two interacting pathways. These findings help to explain how AMPAR trafficking occurs and can serve as a step towards understanding the role it plays in synaptic plasticity.

KEYWORDS

Learning and Memory, Synaptic Plasticity, AMPAR, Computational Neuroscience, Enzyme Kinetics