A biophysical model of AMPA receptor dynamics

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The α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptor plays a critical role in excitatory glutamatergic neurotransmission. Traditionally viewed as the fastest form of neurotransmission, it has recently been shown that the transmission rate can vary significantly. Specifically, transmembrane AMPA receptor regulatory protein (TARP) molecules can change the speed at which the receptor channels open and close, and in turn modulate the speed of synaptic transmission (Carbone, A., Plested, A, 2016). Previous models of neural dynamics assume a simple phenomenological model of synaptic transmission in the form of exponential or alpha functions. We study the 8-state receptor model of Milstein et al (2007), with the goal of coupling this model to the voltage dynamics.

We first convert the Monte Carlo kinetic scheme of Milstein et al. to a system of ordinary differential equations and confirm that the evolution of state probabilities match (see Fig. 1 of the supplementary information). Next, we study a "two pulse protocol" to examine the recovery rate of the AMPA receptor. Adjusting the pulse parameters and the transition rate from the desensitised state we found a good match with the experimental data of Bowie and Lange (2002) (see Fig. 2 of the supplementary information). Now that we have an accurate description of the receptor dynamics, we integrate the model into a network of spiking neurons, replacing the phenomenological exponential or alpha-type synaptic response with our biologically realistic model. With the inclusion of realistic synaptic dynamics, we can study how the network dynamics are affected and the impact that varying levels of TARPs has on a system. e.g. in the stargazer mutant mouse, it is seen that a lack of TARPS-gamma-2 results in absence epilepsy and ataxia (Payne 2013).

The long-term goal of this project is to perform a mean-field reduction on this network of spiking neurons with realistic synaptic dynamics, most likely resulting in an extended version of the next generation neural mass model. To reach this goal, it may be necessary to simplify the receptor model somewhat. However, once this is complete we will be able to study how certain neurological disorders could arise from pathological synaptic transmission.

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