A COMPUTATIONAL STUDY OF ASTROCYTIC CALCIUM HOMEOSTASIS IN THE SYNAPTIC CLEFT

Introduction:

Calcium (Ca^{2+}) contributes to long-term and short-term synaptic plasticity in many ways and Ca^{2+} concentrations within the synaptic cleft fluctuate drastically during neuronal activity. Delivery of Ca^{2+} to the synaptic cleft can be regulated by astrocytes through transporters in their peripheral processes, e.g. through NCX and PMCA. Therefore, astrocytes may affect synaptic plasticity through Ca^{2+} homeostasis in the synaptic cleft.

The main aim of this work is to develop a biophysically realistic computational model of how astrocytes contribute to synaptic plasticity through regulation of synaptic Ca^{2+} levels. This work builds on recent research [1] which shows that in thin astrocyte processes microdomains of sodium (Na^{+}) and potassium (K^{+}) forms at the perisynaptic cradle during neuronal excitation. The hypothesis that underpins this work is that elevated levels of Na^{+} at the cradle could potentially reverse the NCX extruder thereby producing a local supply of Ca^{2+}. Efflux of this Ca^{2+} via the PMCA would dictate Ca^{2+} homeostasis in the cleft thereby affecting synaptic plasticity. The proposed model will be used to capture this signalling pathway.

Preliminary results will be presented which demonstrates that neuronal excitation modulates Ca^{2+} concentration in the synaptic cleft.

Methods:

A biophysical model will be developed as a tool to investigate how the efflux of astrocytic Ca^{2+} effects Ca^{2+} homeostasis in the synaptic cleft and therefore plasticity. The model will consist of a mathematical framework which is constructed from existing biophysical models, including models for neuronal firing rates, synaptic transmission, astrocyte Ca^{2+} dynamics, probability of neurotransmitter release and synaptic plasticity.

Approach for statistical analysis:

In the first instance, model data will be analysed and graphically represented to help visualise how neuronal excitation modulates Ca^{2+} in the cleft. This approach will continue as more data emerges on the relationship between plasticity, probability of neurotransmitter release, neuronal excitations, postsynaptic potentiation and Ca^{2+}/Na^{+} levels in the perisynaptic cradle.

References:

[1] K. Breslin *et al.*, “Potassium and sodium microdomains in thin astroglial processes: A computational model study,” *PLOS Comput. Biol.*, vol. 14, no. 5, p. e1006151, May 2018.