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Theoretical Analyzing the Spatial Variability of Pre-Synaptic Vesicle Locations and Its Effect on ATP Concentration Gradients Within the Excitatory Axon Varicosity

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ABSTRACT

It is widely recognized that neurons are highly responsive to fluctuations in oxidative phosphorylation and ATP concentrations. Variations in these factors may contribute to the molecular basis of neurodegenerative diseases. The level of ATP is essential for the process in which neuromediators are loaded into pre-synaptic vesicles, because the creation of a H^+-gradient by V-ATPases allows antiporters to transport materials into the vesicles using the secondary active transport. Variations in the amount and positioning of vesicles may contribute to the changes observed in ATP levels within a neuron. To estimate his process, the 3D digital model of an exciatory mouse axon varicosity has been created on the base of experimental data [1]. The present study focuses on three distinct locations where pre-synaptic vesicles can be found. The activity of ATP synthase for a single protein was assessed based on a model that has been previously described. Additionally, the ATPase activities were considered for V-ATPases, Na^+, K^+-ATPases and cytoplasmic/matrix processes. The rate of adenosine translocator (ANT) was also included as a function of a membrane potential. ATP/ADP concentration gradients were evaluated using the final element method (FEM) in COMSOL Multiphisics Software ver. 5.5. It was found that the location of pre-synaptic vesicles impacts the distribution of ATP levels within a localized area of the neuron.

Keywords: convectional reaction-diffusion, mathematical modelling, pre-synaptic vesicles, axon, mitochondria, ATP

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