Mathematical modeling of calcium-mediated exosomal dynamics in neural cells

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Abstract. An exosome-mediated drug delivery system has received significant attention for the treatment of neurological disorders, such as Parkinson's disease. In this contribution, we report a more realistic mathematical model for capturing the calcium (Ca^{2+})-mediated exosomal release in the neural stem cells. We use the modified Hodgkin-Huxley neuronal model to describe the electrical activity of a depolarized neuron via membrane potential for initiation and propagation of action potentials. The intracellular Ca^{2+} dynamics have been modeled by coupling the neuronal electrical activity and Ca^{2+}-mediated exocytosis, taking into account the high-voltage (L-type) and low-voltage (T-type) activated Ca^{2+} channels, plasma membrane, bulk cytosol and endoplasmic reticulum. A comparative analysis has been further conducted to quantify the effect of temperature on the Ca^{2+}-mediated exosomal release in the neurons. It is expected that the proposed model would provide a more comprehensive understanding of the key mechanisms underlying the dynamics of various brain diseases.

Introduction

Exosomes are naturally occurring nanosized vesicles comprising of natural lipid bilayers with the abundance of adhesive proteins that readily interact with cellular membranes [1]. Studies have revealed that exosomes derived from the central nervous system occur in the body fluids such as cerebrospinal fluid and plasma, and their contents are altered during disease, making them an appealing target for biomarker development of multiple neurodegenerative diseases, viz., Alzheimer, Parkinson, Huntington and Creutzfeldt-Jacob [2-3]. It has also been reported in the literature that specific types of Ca^{2+} channels in differentiated neurons are activated upon cell depolarization leading to the increased intracellular Ca^{2+} concentration levels which, in turn, interact with mobilization of multivesicular bodies and exosomal release [3].

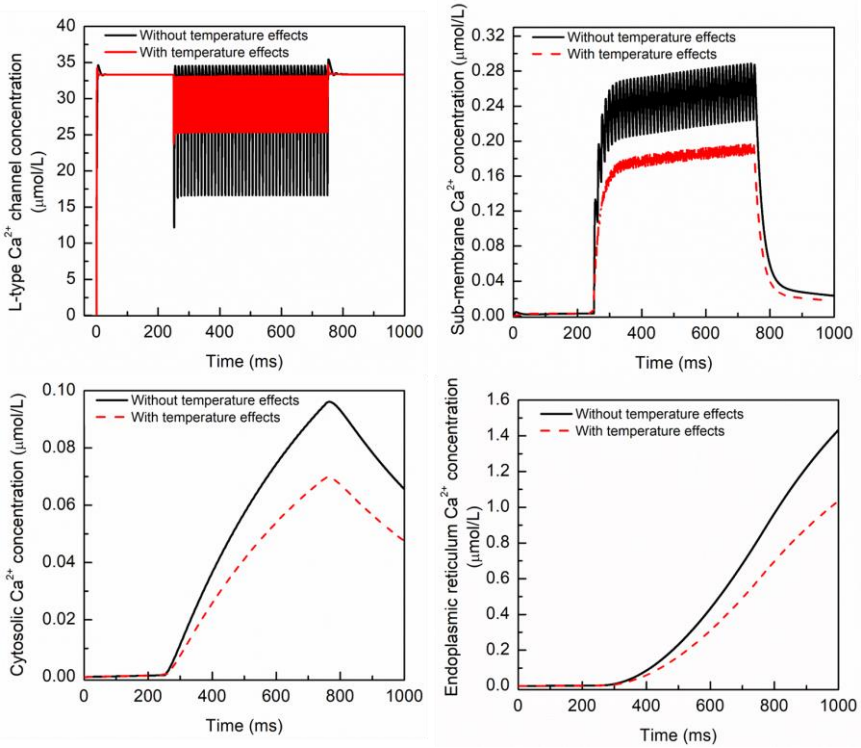

Figure 1: Microdomain Ca^{2+} concentrations corresponding to induced current pulses of 20 μA/cm^2 amplitude and 500 ms duration.

Results and discussion

The results obtained from the developed model for different compartments of Ca^{2+} microdomain have been presented in Figure 1, with and without considering the temperature effects. As evident, significant variation prevails in the intracellular Ca^{2+} concentration levels among the two considered cases.

References

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