How Does Metabolism Influence Neural Activity? A Comparative Analysis of Brain Neuron Models Integrating Metabolism

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Abstract
Schizophrenia has been linked to metabolic changes in the nervous system. Yet, due to the heterogeneity of this disorder, it remains challenging to predict the effects of specific perturbations and to design targeted treatments at the individual level. To overcome these limitations, computational models can be used to trace the effect of alterations in the metabolism and how they are related to measurable outcomes. However, the comparability of metabolic models and their compatibility with existing neuron models remain unclear. Here we present a comparative study of brain metabolism models and examine the behavior of a neuron model with integrated metabolic processes. We implemented three models of metabolism in the simulation environment NEURON RxD and compared them to the data reported in the original publications. The best model was added to a Hodgkin-Huxley neuron to study how metabolism changes the spiking pattern of the cell. Two of the three models replicated the BOLD signal reported in the original publications. Interestingly, the inclusion of a metabolic model to the neural model changed the action potential firing pattern from a stable firing to adaptative behavior. Sodium, oxygen and ATP concentrations follow neural activity, with a pathological higher-frequency activity depleting these species. The models follow the expected activity-metabolism behavior. Implementing the models in NEURON RxD also provides a scalable framework with potential applicability to disease-oriented studies. This work is a first step in the development of predictive computational models of metabolism associated brain disorders.

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