A computational platform to assess the metabolic-electrophysiological behaviour of neurons cultured in monolayers

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In vitro models of neural tissues are invaluable tools for the study of the human brain. However, they are associated with high costs and poorly reproducible results. In this scenario, computational model-based solutions can support a better characterization of neural behavior *in vitro*. However, current *in silico* models of neurons and neuron networks do not consider oxygen concentration, which is a crucial parameter for *in vitro* constructs since they lack vascularization. Here we present a computational platform where an oxygen-dependent model of neuron firing is implemented. It allows modelling *in vitro* monolayers of neurons reproducing their spatial arrangement and connections. Oxygen diffuses through the aqueous medium over the monolayer and is consumed by the cells, for sustaining both neuron firing and cell functions not directly related to electrophysiological activities. Input conditions are cell density, medium height, spatial arrangement of neurons and boundary oxygen concentration. The outputs of the simulation are the neuron membrane potential and the oxygen concentration at the cell level over time.

To validate the platform, we implemented *in silico* networks reproducing those observed *in vitro* and monitored via commercial micro electrode arrays and simulated their firing. To emphasize the crucial role of oxygen, the same networks were also simulated without considering oxygen dynamics. The outputs of both the models were compared with experimental data. The results highlight statistically significant differences with the oxygen-independent model, while the outcomes of the experimental data and the oxygen-dependent model are similar. These results suggest that our platform more accurately replicates the electrophysiological behavior of neuronal monolayers and that oxygen is a key variable to be considered for describing their firing dynamics. The computational platform represents a powerful tool useful to optimize - or even replace - *in vitro* experiments.

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