Functional approach to modeling of neural-glial interactions.

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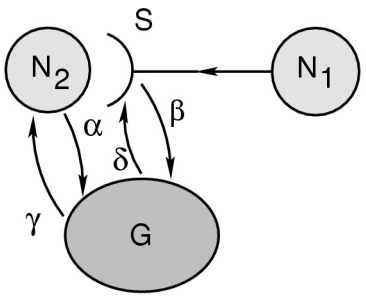
Neurons are the famous object for researchers. However, the glial cells, closely located or surrounding neurons also play an important role. In many cases the existing models of neural networks are not adequate to real structures because the presence and activity of glial cells are not taken into account. Often it is the glial cells control the neuronal activity and action potential propagation. It is believed, that neural-glial interaction serves as basement for processing, storing and retrieval of information. Thus, the study of interaction between the neurons and glial cells becomes one of important problems in neurophysiology and cell biophysics. It is shown, that neurons can control the operating regime (transmembrane potential, ion channels activity) of glial cell via the change of extracellular ions concentration. The glial response provides the feedback via the consumption of Ca^{2+} and K^{+} ions and neuromediators, and via the production of its own mediator. The modeling of neural-glial interaction can help to understand the transition between the normal and pathologic states.

The adequate mathematical model of neural-glial interaction should be obtained by taking into account all relevant ionic currents, the processes of production and propagation of neuromediators, etc. Such model inevitably will be high-dimentional with large number of control parameters. However, the more simple way to build qualitative model can be used exploiting the existing simplified models for each unit of such ensemble. We have developed the qualitative model, describing the two synaptically connected neurons and the glial cell (see Figure). Each of neurons N_1 and N_2 is described by the well-known FitzHugh-Nagumo model. For N_2 the second equation additionally contains the terms describing both the synaptic current and feedback from the glial cell G (factor γ in figure). The response of the glial cell is assumed to be governed by the calcium release from the internal stores. The above release is governed by the (i) activity of the synapse and (ii) firing of the second neuron, factors α and β, respectively. Synapse S is described with first-order nonlinear differential equation for synaptic variable. The activity of glial cell can reduce synaptic current applied to the second neuron. It is described with factor δ in figure. Generally, the above described model of neural-glial ensemble is expected to predict the specific effects arising due to dual nature of glial activation and response, combining slow and fast characteristic times.



The numeric simulation of model dynamics revealed the number of specific features. Because glial activity can change the strength of synaptic connection, the regime of subthreshold forcing of second neuron becomes typical. In this case, the individual properties of each neuron, as well as characteristic time of synapse play an important role. To understand the behavior of modeled ensemble, we first studied how two neurons can adjust its phases and firing frequencies at the vanishingly weak glial response. The most prominent result, that the firing rate of the second neuron does not follow monotonically the increasing frequency of first neuron spiking. We explain it in terms of resonator properties of FitzHugh-Nagumo neuron.

When glial cell response is increased by means of γ and / or δ factors, the threshold value for second neuron can be considerably reduced, but synaptic current weakened. It produces a variety of dynamical patterns including the changes of firing rate, adjusting of phase shift between neurons, quasiperiodic regimes, etc.

In conclusion, the model of neural-glial ensemble we consider does not provide the quantitative description of real processes of inter-cells communication, but able to reproduce at qualitative level the main types of response. It might be useful for modeling of larger similar structures.