БИОФИЗИКА КЛЕТОЧНЫХ ПРОЦЕССОВ И КЛЕТОЧНЫЕ ТЕХНОЛОГИИ

COMPETITIVE LEARNING IN NEURAL NETWORK UNDER NEUROMODULATORY INFLUENCES

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Brain and neural tissue have unique capabilities in learning, memory and information processing and require special tools and techniques for investigation. Studies of mechanisms underlying brain functioning have not only great scientific importance but also needed for development of modern therapies of brain diseases.

Basic elements of neural tissue are neurons which can communicate by means of action potentials via synaptic contacts. Efficacy of synaptic transmission can vary due to phenomenon called synaptic plasticity. Long-term forms of synaptic plasticity are considered as main phenomenona responsible for learning and memory in neural tissue. Properties of neurons and synapses can be altered by chemical factors – neuromodulators. Processes of neuromodulation are involved in regulation of neural activity and homeostasis, and many important neuropharmacological substances have neuromodulatory action used for therapeutical purposes.

One distinct form of synaptic plasticity – spike timing dependent synaptic plasticity (STDP) – has attracted special attention of investigators due to outstanding properties. In case of STDP synaptic changes depend on relative timing of activation of pre- and postsynaptic neurons in millisecond time scale.

Theoretical investigations showed that STDP based network processes, such as competitive learning and activity regulation, can substantially depend on fine tuning of STDP parameters. In neural tissue such tuning is implemented on the basis of the action of neuromodulators, and STDP properties are influenced by different neuromodulatory systems [1]. The analysis of neuromodulatory outcomes can be nontrivial because neural network as a complex system can demonstrate emergent phenomena which are difficult to predict on the basis

of the properties of individual neurons. Modern methods of computer simulation of biological neural networks can facilitate investigation of features of neural network functioning on the basis of the data about the action of neuroactive compound studied on the properties of individual neurons and synapses.

In our work we present the computer simulation based analysis of competitive learning process in simple STDP-based model in conditions of neuronal and synaptic properties modulation.

The model considered is based on the competitive learning model [2]. Additive STDP based synaptic changes depending on time interval between post- and presynaptic spikes Δt are described by the function

$$F(\Delta t) = \begin{cases} A_p e^{(-\Delta t / \tau_p)} & \Delta t \geq 0, \\ -A_n e^{(\Delta t / \tau_n)} & \Delta t < 0, \end{cases} \quad (1)$$

where A_p and A_n determine maximum positive and negative changes of synaptic weight, τ_p and τ_n are time constants of positive and negative branches of STDP function.

Initial distribution of synaptic weights is Gaussian, and as the result of the competitive learning process, initial distribution evolves into bimodal one when synaptic weights tending to have minimal and maximal values. We determine the final task of competitive learning as symmetrical bimodal weights distribution. Efficiency of the learning E is determined as

$$E = \frac{2 \min(N_{\min}, N_{\max})}{N} \quad (2)$$

where N_{min} and N_{max} are numbers of weights in the first and in the last bins of the histogram, N is total number of synapses. According to the equation (2), E reaches maximum in case of symmetric bimodal weights distribution. We also determine characteristic learning time T as a time required for E to reach the value equal to 0.1. Learning rate L is determined as $1/T$.

Synaptic modulation is modeled by alterations of the A_n value and neuronal modulation is modeled by alteration of the threshold V_t of action potential generation.

The dependencies of the learning efficiency E and the learning rate L on neuromodulation parameters are shown at Fig. 1*b* and Fig. 1*c* respectively.

There is a region in neuromodulation parameters space where E reaches maximal values. It is interesting to note that L reaches maximal values in another region of neuromodulation parameters which corresponds to higher postsynaptic frequency. This means that maximal learning efficiency is reached

when the neural network is in the mode with moderate learning rate. This phenomenon is explained by the fact that maximal positive weight changes occurs when groups of synapses cooperatively excite postsynaptic neuron and the postsynaptic frequencies are moderate in this mode of network functioning.

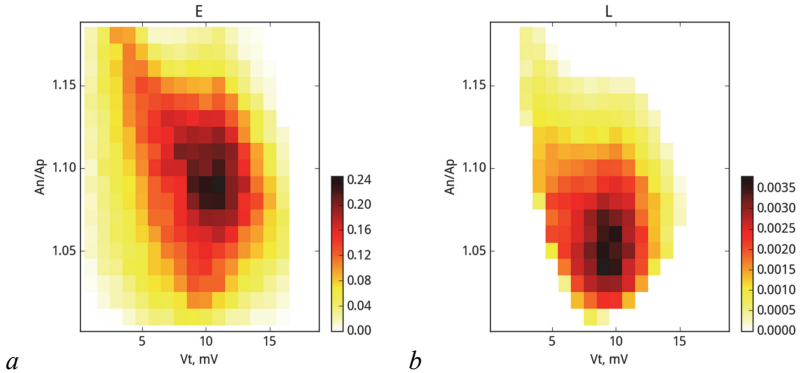

Fig. 1. Learning efficiency *E* (*b*) and learning rate *L* (*c*) depending on neuromodulation parameters

This simple model with relatively abstract learning task exhibit rather complex relations of efficiency and rate of the learning depending on neuromodulation parameters. More sophisticated neuromodulatory action can be embedded into the model, for example, dependence of number of postsynaptic spikes required for plasticity induction on the level of dopaminergic modulation [1] or involvement of other neuromodulatory systems. We are developing more complex neural network model corresponding to biological network formed by cultured neurons to investigate more sophisticated learning tasks under neuromodulatory action.

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References

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TROUT ERYTHROCYTE AS CELLULAR MODEL TO STUDY POLLUTANT TOXICITY

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Erythrocytes are a routinely used model to study the toxicity of new chemicals, in particular fish erythrocytes are useful simple models because they possess nuclei, mitochondria and other organelles typical of somatic cells. These cells are not thus simple contain hemoglobin but they are also able to maintain complex cellular processes, including protein synthesis and oxidative metabolism.

Contrary to mammals and birds, a multiplicity of hemoglobin components is present in fish erythrocytes. This multiplicity may be related to the fact that hemoglobins have to provide oxygen for different purposes, namely the metabolic demands and the operation of the swim bladder.

In the case of erythrocytes from *Salmo irideus trout,* there are four different hemoglobin components characterized by functional differences which have been correlated to a different physiological role. These hemoglobins are prone to oxidation, either as purified proteins or in the whole cell. This property permits, similarly to what occurs in subjects with unstable hemoglobin, to follow the autoxidation process over a relatively short time and to investigate the relationship between met-Hb formation and impairment of cellular structures in erythrocytes.

It is well to point out that hemoglobin auto-oxidation results in the liberation of superoxide anion, and thereby of products such as H_2O_2 or hydroxyl radicals, which can be derived from superoxide anion itself. Also it is possible to induce a condition of endogenous oxidative stress by promoting mitochondrial membrane depolarization and thus a decreased mitochondrial functionality. Thus these processes are of particular interest for studying the oxidative damage on different cellular compartments (cell membrane, nucleus etc.).