Astrocytes organize neural associative memory

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Abstract. We investigate one aspect of the functional role played by astrocytes in neuron-astrocyte networks present in the mammal brain. To highlight the effect of neuron-astrocyte interaction, we consider simplified networks with bidirectional neuron-astrocyte communication and without any connections between neurons. We show that the fact, that astrocyte covers several neurons and a different time scale of calcium events in astrocyte, alone can lead to the appearance of neural associative memory. Without any doubt, this mechanism makes the neuron networks more flexible to learning, and, hence, may contribute to the explanation, why astrocytes have been evolutionary needed for the development of the mammal brain.

Keywords: astrocyte, associative memory, neural network.

1 Introduction

The functional role of astrocyte calcium signaling in brain information processing was intensely debated in recent decades. Astrocytes play crucial roles in brain homeostasis and are emerging as regulatory elements of neuronal and synaptic physiology by responding to neurotransmitters with Ca^{2+} elevations and releasing gliotransmitters that activate neuronal receptors [1]. The characteristic times of calcium signals (1-2 sec) are three orders of magnitude longer than the duration of spikes in neurons (1 msec). It was shown that astrocyte can act as temporal and spatial integrator, hence, detecting the level of spatio-temporal coherence in the activity of accompanying neuronal network. Currently actively discussed hypothesis is that the astrocytic calcium activity can induce spatial synchronization in neuronal circuits defined by the morphological territory of the astrocyte [2-4]. In other words one can draw an analogy with the Hopfield network. Calcium events in astrocytes that induce synchronization in surrounding neural ensembles work as a temporal Hopfield network, and, hence, can be interpreted as an associative memory model.

In this paper, we consider one of the simplest model of the neuron-astrocyte network (NAN), where we implement a kind of the Hopfield network with forgetting. There is just a few of previous works studying role of astrocyte in learning tasks. Porto-Pazos and collaborators investigated the performance of an astrocyte-inspired learning rule

to train deep learning networks in data classification and found that the neuron-astrocyte networks were able to outperform identical networks without astrocytes in all classification tasks they implemented [5-7]. In the presented studies they taken into account only temporal features of astrocytic modulation of the signal transmission in neural network. In contrast to this approach, we concentrate on the local spatial synchronization organized by astrocyte, which, due to its different time scale, work as a kind of neural associative memory.

2 Model and architecture of neuron-astrocyte network

The proposed neuron-astrocyte network consists of 2 layers, first layer of neurons with dimensions 40x40 and second layer of astrocytes with dimensions 13x13. To focus only on associative learning, the elements in each layer are not interconnected. We consider bidirectional neuron-astrocytic communication between layers. Each astrocyte interacts with neuronal ensemble dimensions of 4x4 with overlapping in one row (see Fig. 1). Experiments show that astrocytes and neurons communicate via a special mechanism modulated by neurotransmitters from both sides. The model is designed so that when the calcium level inside an astrocyte exceeds a threshold, the astrocyte releases neuromodulator (e.g., glutamate) that may affect the release probability (and thus a synaptic strength) at neighboring connections in a tissue volume. Single astrocyte can regulate the synaptic strength of several neighboring synapses.
The membrane potential of a single neuron is described by Izhikevich model and evolves according to the following equations [8]:

$$\begin{cases} \frac{dV}{dt} = 0.04V^2 + 5V + 140 - U + I_{app} + I_{astro}, \\ \frac{dU}{dt} = a(bV - U), \end{cases} \quad (1)$$

If $V \geq 30$ mV, then $V \rightarrow c$, $U \rightarrow U + d$.

We use the following parameter values: $a = 0.1$, $b = 0.25$, $c = -65$, $d = 2$. The applied currents Iapp simulating input signal $I_{app} = 5$ if input signal is presented. The astrocytic modulation of the synaptic activity is modeled by current I_{astro}, which has a value $I_{astro} = 30$, if Ca^{2+} level in astrocyte exceeds 0.15 μM and more than 50% of neurons, corresponding to this astrocyte, are activated.
Calcium dynamics in astrocyte is described by the Li-Rinzel model. State variables of each cell include IP_3 concentration IP_3, Ca^{2+} concentration Ca, and the fraction of activated IP_3 receptors h. They evolve according to the following equations [9]:

$$\begin{cases} \frac{dCa}{dt} = I_{er} - I_{pump} + I_{leak}, \\ \frac{dh}{dt} = \frac{H-h}{\tau_n}, \\ \frac{dIP_3}{dt} = (IP_{3s} - IP_3)\tau_r + I_{plc} + I_{neuro}, \end{cases} \quad (2)$$

$$I_{er} = c_1 v_1 \left(\frac{IP_3}{IP_3+d_1}\right)^3 \left(\frac{Ca}{Ca+d_5}\right)^3 h^3 \left(\frac{c_0-Ca}{c_1} - Ca\right),$$

$$I_{leak} = c_1 v_2 \left(\frac{c_0-Ca}{c_1} - Ca\right),$$

$$I_{pump} = v_3 \frac{Ca^2}{Ca^2+k_3^2},$$

$$H = \left(d_2 \frac{IP_3+d_1}{IP_3+d_3}\right) / \left(d_2 \frac{IP_3+d_1}{IP_3+d_3} + Ca\right),$$

$\tau_n = 1/(a_2(d_2 \frac{IP_3+d_1}{IP_3+d_3} + Ca))$,
$I_{plc} = v_4 \frac{Ca+(1-\alpha)k_4}{Ca+k_4}$.

Biophysical meaning of all parameters in Eqs. (2) and their values determined experimentally can be found in Refs. [6]. For our purpose we use the following parameter values $c_0 = 2.0\mu$M, $c_1 = 0.185$, $v1 = 6$ s^{-1}, $v_2 = 0.11$ s^{-1}, $v_3 = 2.2$ μMs^{-1}, $v_5 = 0.025$ μMs^{-1}, $v_6 = 0.2$ μMs^{-1}, $k_1 = 0.5$ s^{-1}, $k_2 = 1.0$ μM, $k_3 = 0.1$ μM, $a_2 = 0.14\mu$M^{-1}s^{-1}, $d_1 = 0.13$ μM, $d_2 = 1.049$ μM, $d_3 = 0.9434$ μM, $d_5 = 0.082$ μM, $\alpha = 0.8$, $\tau_0 = 7.143$ s, $IP_3 = 0.16$ μM, $k_4 = 1.1$ μM [6].

The current I_{neuro} describes production of IP_3 due to the synaptic activity of nearbour neurons. The current I_{neuro} is modeled by rectangular pulse signal with amplitude 5 μM and duration 60 msec. $I_{neuro} \neq 0$ if more than 50% of neurons, interacting with this astrocyte, are activated.

Note that the time unit in the neuronal model Eqs. (1) is 1 msec. Due to a slower timescale, in the astrocytic model Eqs. (2) all empirical constants are indicated using seconds as time units. When integrating the joint system of differential equations, the astrocytic model time is rescaled so that the units in both models match up.

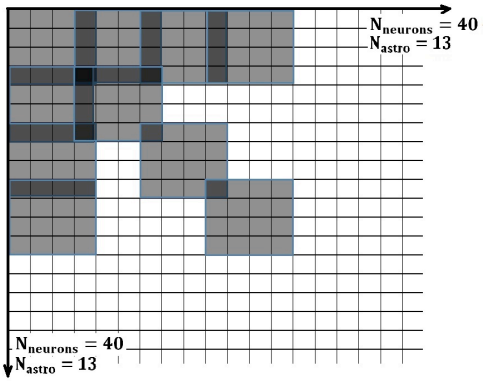


Fig. 1. A network structure. Input images 40x40 pixels size fed into the neuronal network containing 40x40 neurons. Gray fields correspond to the astrocyte, which overlap by one neuron wide layer.

3 Results

We have used as input signals the black and white images of digit 0 or 1, with size 40x40 pixels as shown in Figure 2. The training set included 10 samples for each image with 10% of salt and pepper noise added to every sample fed into the NAN (see Fig.3a).

Fig. 2. Patterns for network training.

A 40 × 40 pixel input is processed by a 40 × 40 neuron layer (1600 neurons), obtaining the applied currents, I_{app}, in Eq. (1) for each input which will be further converted into spikes. The neural response, shown in Figure 3 b, is the membrane potential map, further converted into spike trains. Each sample was presented to the network during 4 msec with period between samples 40 msec. In Figure 4, the membrane potential change is shown. During the training, each astrocyte monitored activity associated with it 16 neurons in time window of 400 msec. If more than 8 neurons were spiking and spiking frequency was more than 17.5 sec^{-1}, astrocyte received an input signal, I_{neuro} (see Eq. (2)), inducing an increase in intracellular calcium concentration (see Fig. 3c).

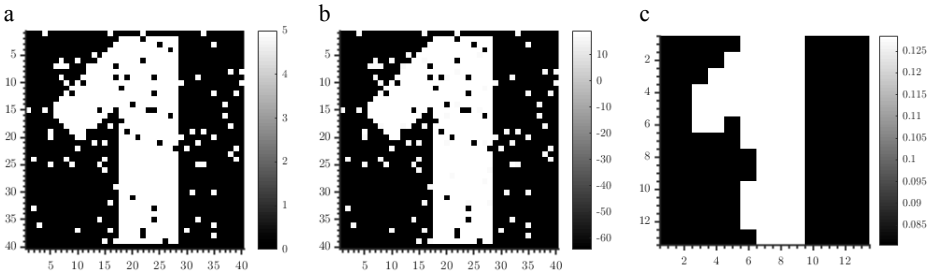


Fig. 3. (a) The training sample with 10% of salt and pepper noise. (b) The response of the neuronal network. The values of the membrane potentials are shown. (c) The intracellular Ca^{2+} concentrations in astrocytic layer.

After training, our neuron-astrocyte network remembers the pattern for a period of time that is determined by the duration of the calcium pulse in astrocyte. Testing sample was presented to the network for 20 msec. While Ca^{2+} concentration in astrocyte exceeded the threshold in 0.15 μM and more than 8 neurons were still active, a feedback from astrocytes to neurons is turned on. This feedback is determined by biophysical mechanisms of astrocytic modulation of synaptic transmission and modeled as additional current I_{astro} in Eq. (1). Example of this test is shown in the Figure 5.

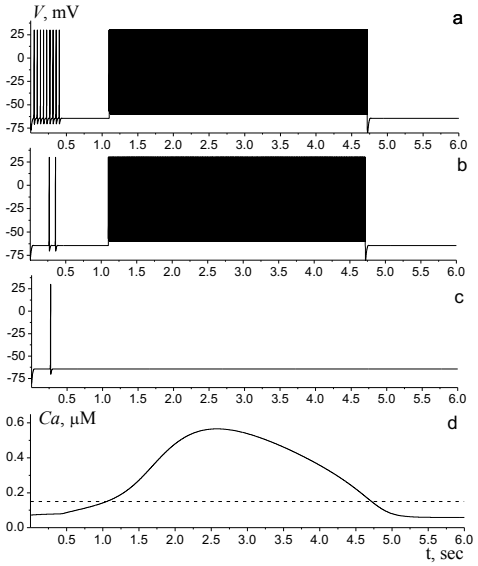


Fig. 4. (a-c) Membrane potentials of neurons during and after training. (a) Neuron in target pattern interacted with active astrocyte. (b) Neuron, which are not in target pattern, interacted with active astrocyte. (c) Neuron not in target pattern interacted with quiet astrocyte. (d) The intracellular Ca^{2+} concentration in active astrocyte.

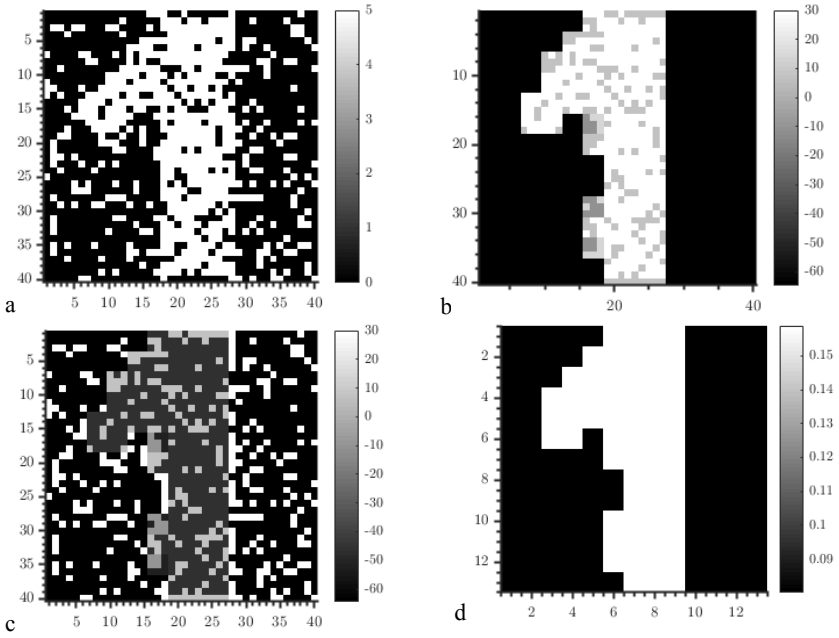


Fig. 5. The testing sample with 40% of salt and pepper noise. (a) The response of the neuronal network after an input with 4,4 (b) and 11,6 (c) msec duration. (d) The

intracellular Ca^{2+} concentrations in astrocytic layer.

Tests showed that the network can not only clean noise inside the target pattern (Fig. 5b) as expected but also can separate in time the pattern and noise around (Fig. 5c). The latter is due to the fact that neuronal spiking frequency is proportional to value of applied current.

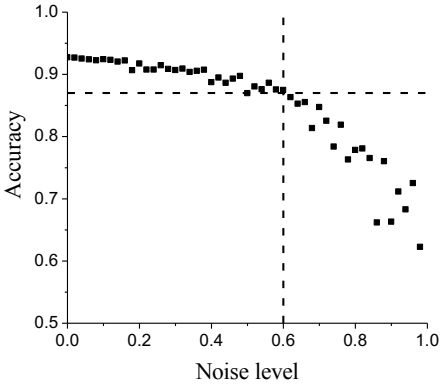
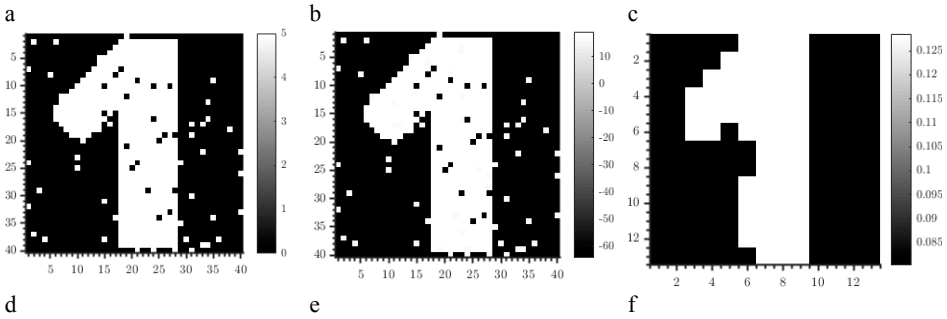


Fig. 6. The dependences of the accuracy on noise level. Red dotted line corresponds to manual selected threshold of accuracy.

To test robustness to noise of the proposed network we calculated the dependencies of the accuracy on noise level (see Fig. 6). Here the accuracy was not equal to 100% in ideal sample without noise because of the fact, that resolution of our system have been determined by the interaction radius astrocytes with neurons. Capacity of the proposed network is determined by orthogonality of images, number of astrocytes, and the radius of overlap between the territories of the astrocyte. In the Figure 7 we presented the example of the training proposed network to 2 patterns, represented by digits 1 and 0.



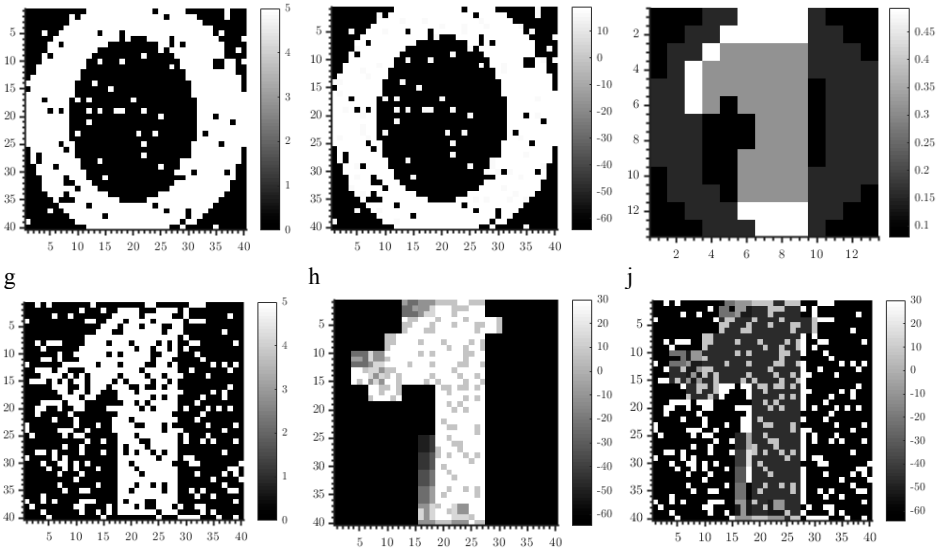


Fig. 7. (a) and (d) The training sample with 10% of salt and pepper noise. (b) and (e) The response of the neuronal network. The values of the membrane potentials are shown. (c) and (f) The intracellular Ca^{2+} concentrations in astrocytic layer. (g) The testing sample with 40% of salt and pepper noise. The response of the neuronal network after the 4,4 (h) and 11,6 (j) msec input.

4 Conclusions

In this paper, we describe a simple neuron-astrocyte network architecture having the capabilities for associative memory. The proposed neuron-astrocyte network works as a temporal Hopfield network. The effect considered occurs because of the local spatial synchronization organized by the astrocyte and working on a different time scale. No links between cells have been required. Astrocytic modulation of the activity of nearby neurons during elevation of calcium concentration imitates Hebbian temporary synapse. In the future, the proposed neuron-astrocyte network will be developed by incorporation of the Hebbian learning algorithm.

As we know from working with artificial intelligence algorithms, the flexibility of learning strongly depends on the complexity of the network. As we have demonstrated, astrocytes increases the complexity of the neural network by the coordination induce by calcium events, and this mechanism alone can lead to the organization of the neural associative memory. Without any doubt, it would be extremely interesting to investigate how this learning mechanism will work together with deep learning.

Another important direction of the future research will include identification of conceptual markers of malfunction associated either with age-related disease or grows disorders. In both these situation, the brain loses ability to learn properly, hence, the question arises whether we could model these processes without simple conceptual

model, and, probably, shed light on the methodology how to identify pathology markers in real medical applications.

This work was supported by the Ministry of Science and Education of Russian Federation (Grant No. 075-15-2019-1192 (MK-1940.2019.4)).

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