

Discrete Modeling of Multi-transmitter Neural Networks with Neuronal Competition

Nikolay Bazenkov^{1(✉)}, Varvara Dyakonova², Oleg Kuznetsov¹,
Dmitri Sakharov², Dmitry Vorontsov², and Liudmila Zhilyakova¹

¹ Trapeznikov Institute of Control Sciences of RAS,
Moscow, Russian Federation
n.bazenkov@yandex.ru

² Koltzov Institute of Developmental Biology of RAS,
Moscow, Russian Federation

Abstract. We propose a novel discrete model of central pattern generators (CPG), neuronal ensembles generating rhythmic activity. The model emphasizes the role of nonsynaptic interactions and the diversity of electrical properties in nervous systems. Neurons in the model release different neurotransmitters into the shared extracellular space (ECS) so each neuron with the appropriate set of receptors can receive signals from other neurons. We consider neurons, differing in their electrical activity, represented as finite-state machines functioning in discrete time steps. Discrete modeling is aimed to provide a computationally tractable and compact explanation of rhythmic pattern generation in nervous systems. The important feature of the model is the introduced mechanism of neuronal competition which is shown to be responsible for the generation of proper rhythms. The model is illustrated with an example of the well-studied feeding network of a pond snail. Future research will focus on the neuromodulatory effects ubiquitous in CPG networks and the whole nervous systems.

Keywords: Discrete dynamics · Multitransmitter neuronal system · Neurotransmitters · Neuromodulation · Central Pattern Generator

1 Introduction

The neurotransmitter diversity is common to nearly all nervous systems, including the most primitive ones. This similarity indicates a fundamental role played by the neuronal heterogeneity. Functional significance and evolutionary origins of multiple neuronal phenotypes have been discussed in a number of papers [4, 11, 13].

We propose a formal model called a *multitransmitter neuronal system*. The model introduces several key features. First, the neurons produce endogenous activity like tonic spiking or oscillatory bursting. Second, the neurons interact not by synaptic wirings but via the extracellular space (ECS), which is shared by all neurons present in the circuit. One of the main objectives of the study is to show that a model based on pure non-synaptic interactions could produce the same patterns of neuronal activity as synaptic, “wired”, models. As a proof-of-concept example we provide a simplified model of a snail feeding network [15]. The extended paper can be found in [1].

2 Related Work

Continuous models. These models describe biological neurons and their membrane processes by differential equations [14]. In [15] a two-compartment neuron-axon model based on Hodgkin–Huxley equations [7] is created for modeling of the snail feeding circuit. The model of bursting neurons, was used in [5] to construct the interaction of interneurons in CPG and motor neurons in the locomotor system of insects.

The main advantage of continuous models is their high degree of accuracy. But this leads to some drawbacks: lack of robustness to slight perturbations of parameters, significant computational complexity and poor scalability. Therefore, continuous models were applied only to networks with small numbers of neurons.

Discrete models. In contrast to continuous models, discrete models tend to formalize neuronal processes as simple as possible. The most common type of discrete models is the formal neurons [10] and artificial neural networks (ANN) [6].

Another class of discrete models, called “complex networks” [8], considers the nervous system as a large complex network – “connectome” [3]. However, it is shown that a complete connectome is not sufficient for understanding the behavior [2].

One more type of models is represented in [12] where an automata-based language is used for the description of neurons with several types of endogenous activity.

Biological background. The empirical generalizations which the model is based on are mostly derived from small neural networks that produce motor outputs, so called Central Pattern Generators [2, 9]. The given paper focuses mostly on heterogeneity of neuronal phenotypes and non-synaptic organization of phasic activity, leaving other properties for further research.

3 Multitransmitter Neural System

3.1 Main Definitions

A multi-transmitter neuronal system is a triple $\mathbf{S} = \langle \mathbf{N}, \mathbf{X}, \mathbf{C} \rangle$, where \mathbf{N} is a set of neurons, \mathbf{X} – extracellular space (ECS) and \mathbf{C} is a set of neurotransmitters.

Neural inputs. Each neuronal input is characterized by a weight $w_{ij} \in \mathbb{R}$ where $i \in \mathbf{N}$, $j \in \mathbf{C}$. If $w_{ij} > 0$ then transmitter j excites neuron i and $w_{ij} < 0$ denotes that transmitter j inhibits neuron i . Neuronal inputs are represented as a matrix $W = (w_{ij})_{n \times m}$.

Neural outputs. The model functions in discrete times t . Neuronal activity is denoted as $y_i(t) \in \{0, 1\}$, $y_i(t) = 1$ if neuron i is active at time t . After an activation, a neuron

releases some amount of one or several neurotransmitters represented in a matrix $D = (d_{ij})_{n \times m}$ where $d_{ij} \geq 0$ is the amount of transmitter j released by neuron i .

Extracellular space. Neurons in the model communicate over the common extracellular space which contains the transmitters that have been released at time t . A state of ECS is represented as a vector $X(t) = (x_1(t), \dots, x_m(t))$, where $x_j(t)$ denotes the amount of neurotransmitter j present in the ECS at time t .

3.2 Excitation and Inhibition

Every neuron is influenced by all transmitters to which it possesses receptors. Each neuron has excitation and inhibition thresholds P_{1i} and P_{0i} , $P_{0i} < 0 < P_{1i}$. The excitation function $z_{1i}(t)$ indicates that neuron i is excited at time t :

$$z_{1i}(t) = I\left(\sum_{j=1}^m w_{ij}x_j(t) \geq P_{1i}\right). \quad (1)$$

The inhibition function $z_{0i}(t)$, which indicates that a neuron is inhibited, is similar:

$$z_{0i}(t) = I\left(\sum_{j=1}^m w_{ij}x_j(t) \leq P_{0i}\right). \quad (2)$$

Here $I(\cdot)$ is the indicator function, $x_j(t)$ – the components of the ECS state at time t .

3.3 Neuronal Types

We consider three types of neurons which represent different firing behavior properties: oscillatory, tonic and passive follower. Each neuron is represented as a finite automaton with two inputs. The activity at time t is described by the output function:

$$y_i(t) = F_{\theta(i)}(z_{1i}(t-1), z_{0i}(t), s_i(t-1)). \quad (3)$$

Here $\theta(i)$ is a type of neuron i , $z_{1i}(t-1)$ is the excitation at the previous time, $z_{0i}(t)$ is the inhibition at time t and $s_i(t-1)$ is the internal state at the previous time.

Endogenous oscillator. An endogenous oscillator produces bursts of spikes every T_i times if not inhibited by other neurons. If an oscillator is inhibited it will be active after the inhibition disappears. If an oscillatory neuron is excited then it will become active at the next time immediately. The internal structure and the output function of an oscillatory neuron are provided in the Table 1.

Tonic neuron. Neurons of this type are active as long as they are not inhibited:

$$y_i(t) = \neg z_{0i}(t). \quad (4)$$

Table 1. State transitions and outputs of an oscillatory neuron

State	Inputs (z_0, z_1)		
	$(z_0 = 0, z_1 = 0)$	$(z_0 = 0, z_1 = 1)$	$(z_0 = 1, z_1 \in \{0,1\})$
s_0	$s_1, y = 0$	$s_0, y = 1$	$s_1, y = 0$
\dots	\dots	\dots	\dots
s_k	$s_{k+1}, y = 0$	$s_0, y = 1$	$s_{k+1}, y = 0$
\dots	\dots	\dots	\dots
s_T	$s_0, y = 1$	$s_0, y = 1$	$s_T, y = 0$

Follower neuron is active only after being excited by others so the output function takes the following form:

$$y_i(t) = \neg z_{0i}(t) z_{1i}(t - 1). \quad (5)$$

Post-inhibitory rebound (PIR). It is a gain coefficient that increases the output of a neuron that was inhibited at the previous time by the PIR gain coefficient $k_i^{PIR} \geq 1$.

3.4 Neuronal Competition and Model Dynamics

The main principle of the model's dynamics is a competition between neurons for the opportunity to be active during the next time step. The competition algorithm doesn't mimic functioning of biological CPGs but provides a conflict resolution rule so the model can generate rhythms similar to those observed in biological circuits. Figure 1 shows an example from [15] where the competition plays a crucial.

This algorithm determines which neurons will be active during the next time t .

Algorithm 1. Neuronal competition

1. *Initialization of ECS.* Set the state of ECS to zero $x_j(t)=0, j=1, \dots, m$
2. *Initialization of neurons.* $y_i(t)=F_i(z_{1i}(x(t-1))), 0, s_i(t-1))$.
3. *Update ECS.*

$$x_j(t) = \sum_{i=1}^n (1 + k^{PIR} z_{0i}(t - 1)) d_{ij} y_i(t)$$

4. *Conflict resolution.*
 - a. Compute inhibition $z_{0i}(t)$ for each neuron
 - b. If for each neuron $i \in N$ $z_{0i}(t)=0$ then go to step 5.
 - c. Else find a neuron k such that the value $\sum w_{ij} x_j(t) - P_{0i}$ is minimal among the neurons with $z_{0i}(t)=1$
 - d. Set $y_k(t)=0$. This neuron cannot be active at time t . Go to step 3.
5. *Finish.* Vectors $x(t), y(t)$ is the states of the ECS and the neurons at time t .

4 Example: Snail Feeding Rhythm

The feeding network of a pond snail *Lymnaea stagnalis* is a well-studied example of a CPG. As shown in the Fig. 1, the network consists of three interneurons responsible for separate phases of the feeding rhythm: protraction, rasp and swallow. A model proposed in [15] consists of 38-dimensional system of differential equations.

Here we propose a discrete model emphasizing the logic of the interactions and neuronal roles in the CPG. The network consists of three neurons N_1 , N_2 , N_3 , each produces its own transmitter: *ach*, *glu* and *xxx* because the third transmitter in the CPG remains unknown. The neuronal properties are shown in the Table 2.

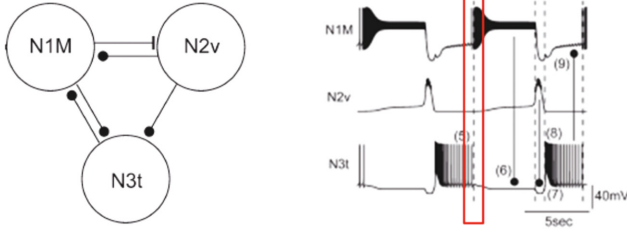


Fig. 1. A competition between oscillatory N1M and tonic N3t neurons in the feeding CPG [15]. The dominant neuron defines the current phase of the feeding cycle

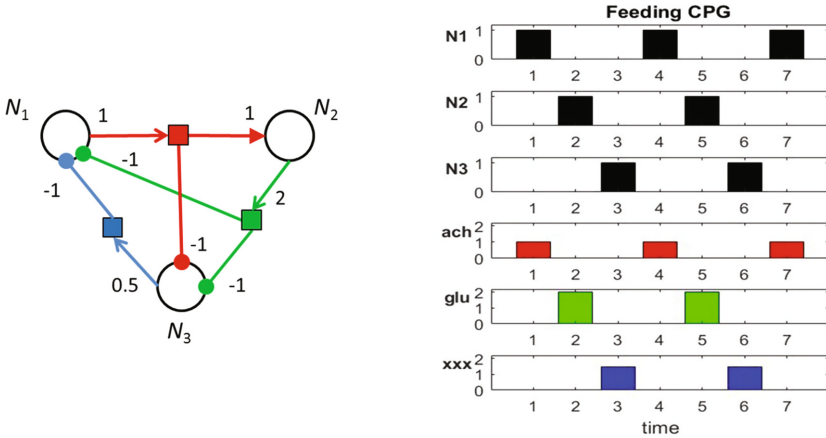


Fig. 2. Feeding CPG model: (left) structure of neuronal interactions; (right) the produced rhythm: neuronal activity (up) and concentrations of neurotransmitters (bottom)

The produced rhythm is shown in Fig. 2. The default output of N_3 is lower than that of N_1 so the first phase is won by N_1 . Then N_2 wins the competition because of its high output. After being inhibited N_3 is able to win and drives the third phase of the rhythm.

Then the effect of PIR disappears and N_1 wins the competition again. There are several combinations of model parameters that can produce the same rhythm. The question of how to choose the most efficient combination is left for further studies.

Table 2. Model of the feeding CPG

Neuron	Type	PIR	Input, W			Thresholds		Output, D			
P_{0i}	P_{1i}	ach			glu			xxx	ach	glu	xxx
N_1	Oscillator	1	-1	-	1	0	0	0	0	-1	-1
N_2	Follower	1	-1	1	0	2	0	1	0	0	0
N_3	Tonic	2	-1	-	0	0	0.5	-1	-1	0	0

5 Conclusion

We propose a formalized model of a multi-transmitter neural network where neurons interact via shared extracellular space without synaptic connections. Each neuron receives signals from the rest of the network by an individual set of receptors to a subset of the neurotransmitters which are released by other neurons. The model is intended to be a proof-of-concept example that some functional patterns of neural activity can in principle be implemented without synaptic wiring. In the model, we consider three various types of neurons differing in their electrical activity: tonic neurons, oscillators and followers. Oscillators and tonic neurons generate endogenous activity unless they are inhibited by other neurons. An algorithm of neuronal competition is introduced to resolve conflicts between those neurons that inhibits each other and are not allowed to be simultaneously active.

To illustrate the key features of the model we considered the well-known central pattern generator that is responsible for feeding behavior of a pond snail *Lymnaea stagnalis*. The model is able to produce rhythms similar to those observed experimentally and in continuous modeling and, despite its simplicity, proved to be capable of simulation and explanation of the phenomena taking place in living neural ensembles.

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Proceedings of the First International Early Research
Career Enhancement School on BICA and Cybersecurity
(FIERCES 2017)

Samsonovich, A.V.; Klimov, V.V. (Eds.)

2018, XIX, 358 p. 133 illus., Softcover

ISBN: 978-3-319-63939-0