A Biophysical Network Model Displaying the Role of Basal Ganglia Pathways in Action Selection

Cem Yucelgen, Berat Denizdurduran, Selin Metin,
Rahmi Elibol, N. Serap Sengor

Istanbul Technical University, Electronics and Communication Engineering
Dept.,Maslak 34469, Istanbul, Turkey
{yucelgenc,denizdurdu,smetin,rahmielibol,sengorn}@itu.edu.tr

Abstract. Basal ganglia circuits are known to have role in a wide range of behaviour spanning from movement initiation to high order cognitive processes as reward related learning. Here, the intention is to have a biophysically realistic model of basal ganglia circuit for voluntary motor action selection. The ultimate aim is to provide a framework for models which could help comprehension of complex processes. To fulfill this aim a model capable of simulating direct, indirect and hyperdirect pathways with modified Hodgkin-Huxley neuron model is proposed. This model considers more neural structures than the works similar in the literature and can simulate activity of neurons in the neural structures taking part in action selection. The model proposed is shown to be versatile as the simulation results obtained are similar to the neuron activity recordings of the considered neural structures published previously.[1,2]
Keywords: Basal ganglia, computational model, action selection.

1 Introduction

The aim of existing computational models is usually to handle Basal Ganglia (BG) as the primary and unique place that performs action selection [1, 2]. The advantage of such models is their functional effectivity which makes them feasible to use as they are and furthermore these models prepare the background to model other cognitive processes such as reward-related learning, goal-directed behaviour and reinforcement learning. However, these models also have disadvantages: even though they are biologically plausible, in the sense that these models consider connections between neural structures and the functional role of each structure; they are not biophysically realistic enough to give insight in understanding how the neural activation arises, how the dynamical behaviour of neurons in individual structures change and how the relevant stimuli is conveyed to initiate an action selection. So they run short in explaining the causes of deficits and neurodegenerative diseases as Parkinson's Disease (PD).

[1] The supplementary material can be obtained from yucelgenc@itu.edu.tr
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Our aim is to propose a biologically realistic model capable of simulating information flow in BG circuit during voluntary motor action selection. To obtain biologically realistic model each neural structure is modelled by Hodgkin-Huxley (HH) type neuron model modified with additional ion channels. Though the structure of BG circuit is considered and connection between different neural structures are demonstrated in the model to convey direct [2–4], indirect [2–4], and hyperdirect [12] pathways of BG circuit, a reductionist approach is taken and each neural structure is modeled with a single neuron. In the given model, the effect of neurotransmitters are considered as negatively or positively actualizing currents. Considering previously published works demonstrating the recordings of neuron activation in cortico-striato-thalamic circuits [13, 14] realistic synaptic activation of the considered structures are obtained with the model. The proposed model of BG circuit is able to demonstrate the reflection of the sensory stimulus of the higher cortical areas on the motor cortical areas.

There are some computational models of BG circuits, they either focus on the functional behavior and give a biologically plausible models [1, 2, 15] or focus on only one aspect and give a biologically realistic model [5–7]. The model proposed in this work actualize a functional behaviour which can be followed by neural activity through each structure considered in BG circuit. It is biologically realistic like [5–7], but not devoted to specific substructures in BG circuit as it comprises all pathways taking role in action selection. The work in [5, 6] is devoted to modelling specific structures especially considered for PD. The modulatory effect of Dopamine (DA) due to dopaminergic pathway through Substantia Nigra pars compacta (SNc) is also considered in the proposed model and the effect of both D1 and D2 type receptors are illustrated with simulation results. The effect of DA on striatal medium spiny neurons are considered in [7] and it is modelled as a multiplicative parameter effecting inwardly rectifying potassium current and L-type calcium current. The biophysically realistic model proposed here is novel in the sense that, it is capable of creating neuronal activity of each structure engaged in action selection. The main result of simulations is that they show the possibility of setting up a biophysically realistic model which has the capability of explaining ongoing dynamic activity during a functional behaviour.

2 Modelling The Neural Activation

Before introducing the network model of BG pathways, we will first give how each neuronal structure is modeled with modified HH neuron models. HH model is inadequate in defining all neuron dynamics thus, the model for each neural structure, except SNc, is extended to include more types of ion currents in order to reflect the relevant neurodynamics for that structure. To produce bursting dynamics calcium current I_{Ca} is added to the neuron voltage equation [5]. Unless otherwise mentioned, I_{Ca} and afterhyperpolarization potassium current I_{AHP} currents modeling the Ca processes are taken from [5]. Also, interior calcium ion concentration ($[Ca^{2+}]$) and rapid activation channel dynamics are also taken from [5]. The gate and time constant expressions we use for HH model are

slightly different than the original model [9]. These and all the other necessary parameters and functions are available as supplementary material.

Table 1. Currents required for neuron models. In the upper part, plus signs denote the existence of relevant ion currents in the structure considered. In the lower part, the currents define the afferent connections to the structure considered.

Ion Currents	$-I_L$	$-I_K$	$-I_{Na}$	$-I_{L_{Ca}}$	$-I_{AHP}$	$-I_{Ca}$	$-I_{Kv1}$	$-I_T$
AC	+	+	+	+	+	+	-	-
MC	+	+	+	+	+	+	-	-
SNc	+	+	+	-	-	-	-	-
Striatum D1	+	+	+	+	+	+	+	-
Striatum D2	+	+	+	+	+	+	+	-
GPe	+	+	+	-	+	+	-	+
GPi	+	+	+	-	+	+	-	+
STN	+	+	+	-	+	+	-	+
Thl	+	+	+	-	+	-	-	+

	$I_{Network\ Connections}$
AC	I_{app}
MC	I_{Thl-MC}
SNc	I_{SNc}
Striatum D1	$I_{AC-Str_{D1}},\ I_{SNc-Str_{D1}},\ I_{MC-Str_{D1}}$
Striatum D1	$I_{AC-Str_{D2}},\ I_{SNc-Str_{D2}},\ I_{MC-Str_{D2}}$
GPe	$I_{Str_{D2}-GPe}$
GPi	$I_{Str_{D1}-GPi},\ I_{GPe-GPi},\ I_{STN-GPi}$
STN	$I_{GPe-STN},\ I_{MC-STN}$
Thl	$I_{GPi-Thl}$

Here, only the equations for motor cortex (MC) will be given explicitly due to space limitations and the ion currents added for each structure will be explained. Ion currents that are considered in each neural structure is given in Table 1.

Cortex neurons: The cortex neuron dynamics are designed using the models in [5, 10]. The membrane potential dynamics of MC neuron is given in Eq.1:

$$C_m \dot{v_{MC}} = -I_L - I_K - I_{Na} - I_{L_{Ca}} - I_{AHP} - I_{Ca} + I_{Thl-MC} \tag{1}$$

In Eq.1, the first three currents I_L, I_K, I_{Na} correspond to ion channels considered in HH equations, the next three $I_{L_{Ca}}, I_{AHP}, I_{Ca}$ correspond to high threshold calcium current, after hyperpolarization calcium current and calcium current, respectively. High threshold calcium current ($I_{L_{Ca}}$) is defined by Goldman-Hodgkin-Katz equation [7, 10] and decreases the excitability of the neuron. The formulation of I_{AHP} is based on [5, 10]. The last current I_{Thl-MC} denotes the network connections between thalamus (Thl) and MC. The equations for each current mentioned above are given as follows:

$$I_L = g_L(v_{MC} - V_L), \quad I_K = g_K n^4 (v_{MC} - V_K)$$

$$I_{Na} = g_{Na} m^3 h (v_{MC} - V_{Na}), \quad I_{Ca} = g_{Ca} s_\infty^2 (v_{MC} - V_{Ca})$$

$$I_{L_{Ca}} = g_{L_{Ca}} m_{L_{Ca}}^2 \frac{v_{MC} z^2 F^2}{RT} \frac{[Ca^{2+}]_e e^{-\frac{v_{MC} zF}{RT}} - [Ca^{2+}]_i}{1 - e^{-\frac{v_{MC} zF}{RT}}}$$

$$I_{AHP} = \frac{g_{AHP}(v_{MC} - V_K)[Ca^{2+}]_i}{[Ca^{2+}]_i + k_L}$$

$$I_{Thl-MC} = g_{Thl-MC} s_{Thl-MC} (v_{MC} - V_{Thl-MC})$$

Here $c_x : m, n, h$ and $m_{L_{Ca}}$ denote the gate dynamics given by following differential equation where $c_{x_\infty} : m_\infty, n_\infty, h_\infty, m_{L_{Ca}\infty}$:

$$\dot{c}_x = \frac{c_{x_\infty} - c_x}{\tau_{c_x}}, \quad s_\infty(v_{MC}) = \frac{1}{1 + e^{-(v_{MC} - \Theta_s)/\sigma_s}}$$

The gate dynamics related to calcium ions are as follows:

$$[\dot{Ca}^{2+}]_i = I_{L_{Ca}} - I_{Ca} - k_{Ca}[Ca^{2+}]_i$$

The dynamics of the network connection s_{Thl-MC} is as follows:

$$\dot{s}_{Thl-MC} = \alpha_{Thl-MC} H_\infty (v_{MC} - \varphi_{Thl-MC})(1 - s_{Thl-MC}) - \beta_{Thl-MC} s_{Thl-MC}$$

As it can be followed from Table 1 the dynamics of association cortex (AC) is similar.

Striatum: The medium spiny neuron dynamics constructed with ion channels given in Table 1 enables the bursting activity which is characteristic of medium spiny neurons. To demonstrate the difference between D1 and D2 type receptors, these are modeled using different conductance coefficients. Kv1 channel dynamics is defined as in [11].

$$I_{Kv1} = g_K m^2 h (v_{Str} - V_K)$$

GPe and GPi: Cell membrane dynamics are expressed as in [5, 6]. The ion currents and connections for GPe and GPi neurons are given in Table 1. Low threshold T-type calcium current I_T modeling the Ca processes are as in [5].

$$I_T = g_T a_\infty^3 r (v_{GPe} - V_{Ca})$$

STN: Low-threshold T-type calcium current I_T is as in [6].

$$I_T = g_T a_\infty^3 b_\infty^2 (v_{STN} - V_{Ca})$$

Thl: Low threshold T-type calcium current I_T is as defined above. The ion channels defining Thl dynamics given in Table 1 enables the production of rebound spikes. Though both STN and Thl have same I_T, the difference between ion channels defining their dynamics the dynamic behaviour of them are not same.

3 Simulation Results for the Proposed Model

The biophysical network model of BG pathways proposed for the dorsal striatal action selection circuit is given in Figure 1a,b for two different cases. In Figure 1a there is no attended stimuli at AC, in Figure 1b there is an attended stimuli. The excitatory connections are glutamate (Glu) and the inhibitory connection is GABA. The connections between structures are depicted as currents from the source neural structure to the target and they are given in Section 2. The proposed network model is realized using in-house MATLAB codes. Figure 1c,d show the simulation results of the cases in Figure 1a,b, respectively.

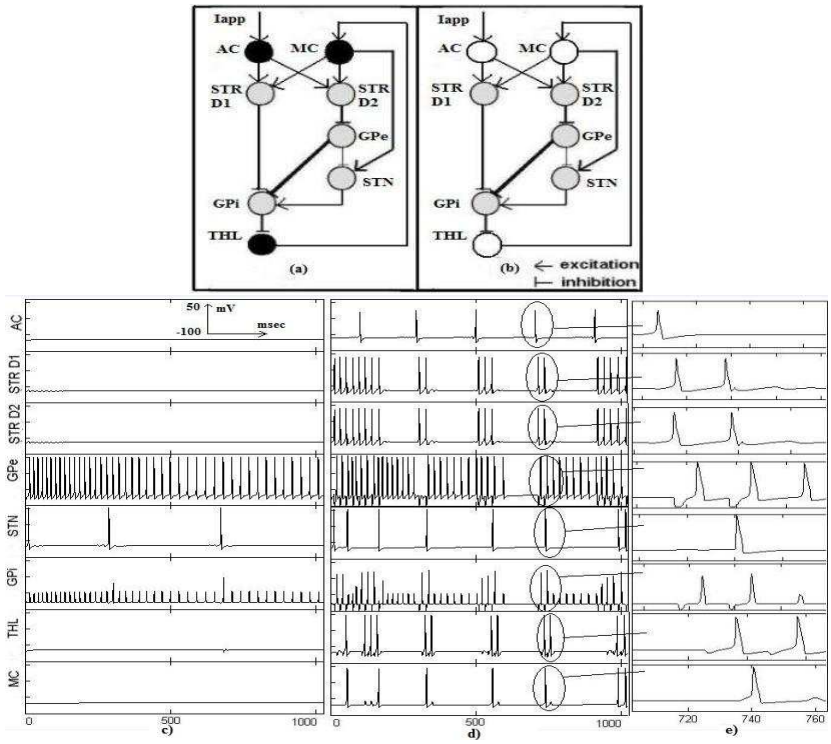

Fig. 1. The proposed model for action selection network (a) when there is no attended stimuli at AC (b) when there is an attended stimuli at AC. Black circles show the inactivity and white circles show the activity. Grey circles are BG nuclei. Simulation results of the network when (c) $I_{app} = 4pA$ and (d) $I_{app} = 16pA$ (e) in order to show clearly parts in circles are focused.

Figure 1c shows the case when there is no attended stimuli at AC. If the stimulus coming to the AC is below a certain threshold, AC will remain quiet. This means that the Str neurons (the pathway through Str D1 is the direct

pathway and the pathway through Str D2 is the indirect pathway) will also remain quiet since they are excited only by the AC. When Str neurons are quiet, GPi and GPe neurons are not inhibited so due to internal neuronal dynamics, these two neurons demonstrate a fast spiking sequence. Because of its internal neurodynamics, the STN neuron displays a slow spiking sequence (a single spike is generated each ∼500 msec at low frequencies). GPi neuron is expected to demonstrate a fast spiking behavior since it is not effected by STN or Str D1 neuron. However, the GABAergic projection from GPe stops all the activity in GPi. Since GPi is also quiet, no activity is seen in Thl. Due to the inactivity of Thl, MC is not stimulated and the quiescence of the AC is reflected to the MC.

The capability of the proposed model for action selection can be followed from Figure 1d where the activity due to the attended stimuli at AC is reflected to MC. Since the external stimulus is above a certain threshold, there is activity in AC and Str neurons are excited to produce bursting activity. Through GABAergic pathways, the bursting activity of Str neurons inhibit the fast spiking activity of GPe and GPi neurons and GPe produces arrays of bursts containing many spikes. GPe stops all the activity in GPi via the GABAergic projection. But GPi is not quiet at all: GPi neuron reacts to the inhibition from Str D1 as if it would produce a rebound spike. Since the neuron dynamics is not able to produce a rebound spike yet, the membrane potential increases above the post-inhibition equilibrium level of -65mV but does not go beyond the threshold level to produce a rebound spike. This means that although GPi seems quiet, Str D1 neuron activity is passed on to GPi with a similar frequency information. MC acts on the STN, which is unable to produce rebound spikes due to the low level inhibition from GPe, via the hyperdirect pathway the activity at MC is copied to the STN neuron with a small time shift. STN transfers cortical activity to the GPi via the glutamatergic pathway. Since Str D1 inhibition on GPi is not enough to produce a rebound spike but has increased GPi's subthreshold excitability, the excitatory signal from STN carries this increased activity over the threshold to form spikes. Therefore, GPi can reflect the cortical activity with the help of Str D1, GPe and STN neurons. At this stage, GPi has the frequency information of the AC and inhibits Thl via the GABAergic pathway. With a small time shift, Thl produces a rebound spike as it can be seen from Figure 1e and transfers this activity to the MC through the glutamatergic pathway. Hence the cortical activity is successfully reflected on the MC.

To demonstrate the effect of DA secretion on the action selection circuit, SNc is introduced to the model (Figure 2a) and it is stimulated by an external current, I_{SNc}. With this new component, while the previous explanations are still valid, the proposed model now demonstrates new dynamics. The simulation results given in Figure 2b and c show that with increase in DA secretion in D2 type receptors, attended stimulus is not selected at MC. SNc neuron projects to the Str via a dopaminergic pathway. DA has excitatory effects on Str D1 neuron and inhibitory effects on Str D2 neuron. When Str D1 has minor excitation but Str D2 is completely inhibited, the effect of Str D1 over GPi does not change, but Str D2 does not effect GPe anymore. Hence GPe has fast spiking activity.

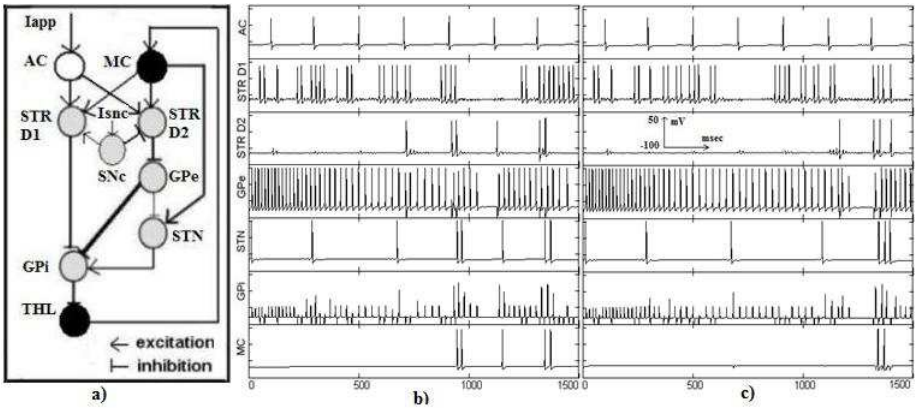

Fig. 2. (a) Dopamine effect on action selection. Simulation results when (b) $g_{D1} = 0.05nS/um^2$, $g_{D2} = 15nS/um^2$, $I_{app} = 16pA$ and (c) $g_{D1} = 0.1nS/um^2$, $g_{D2} = 20nS/um^2$, $I_{app} = 16pA$.

GPi is stimulated to a low threshold level becoming more excitable. However, since there is no inhibition on GPe, the inhibitory projections from GPe to GPi transfer all GPe activity to GPi, disrupting the excitable state of GPi. Although STN transfers its internal activity to GPi, STN stimulus does not increase GPi potential and GPi is quieted. As a result, MC does not reflect AC activity.

4 Conclusion

All of the striatal pathways taking part in action selection are realized with the proposed model. The novelty of this model lies in the fact that both direct and indirect basal ganglia pathways, as well as the hyper-direct pathway between MC and STN, are considered with a biophysically realistic conductance based model of neurons and their activity demonstrated through simulations is similar to neuron activation recordings in [13, 14]. The effect of DA in the action selection mechanism is also simulated, however SNc neuron features are not fully realized. As SNc utilizes pure HH equations and it should be more elaborately modeled for further development of the model. The model set up here, is a first step in obtaining a more comprehensive model which would be versatile in understanding the ongoing activity during information flow from somatosensory, association cortex to motor cortex. Thus it lacks some important aspects of action selection as inhibition of inappropriate actions. In order to model this feature the model should be enlarged to obtain more than one neuron in neuronal structures considered. Still, with such a reductionist approach the model illustrates the stimulation of motor cortex due to sensory information attended at associative cortex.

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