[Re] Multiple dynamical modes of thalamic relay neurons: rhythmic bursting and intermittent phase-locking

Georgios Detorakis[1]

1 Department of Cognitive Sciences, UC Irvine, CA, USA

gdetorak@uci.edu

Editor
Name Surname

Reviewers
Name Surname
Name Surname

Received Sep, 1, 2015
Accepted Sep, 1, 2015
Published Sep, 1, 2015

Competing Interests:
The authors have declared that no competing interests exist.

Article repository

Code repository

A reference implementation of

→ *Multiple dynamical modes of thalamic relay neurons: rhythmic bursting and intermittent phase-locking*, Wang, X-J, Neuroscience, 59(1), pg. 21–31, 1994.

Introduction

This work introduces a reference implementation of a neuron model for thalamocortical relay neurons, [3] proposed by X-J Wang. The model is conductance-based and takes advantage of an interplay between a T-type calcium current and a non-specific cation sag current and thus it is able to generate spindle and delta rhythms. Another feature of this model is the presence of an intermittent phase-locking phenomenon where action potentials of sodium take place in a non-periodic manner, despite the fact that they are phase-locked to the periodic input current. Finally, the model is capable of generating tonic spike patterns. The reference implementation in this work, does not aim to reproduce all the results of the original article, but some of them in order to test if the model can be easily reproduced and at what degree the original results are reproducible. The source code of reference implementation is written in Python (Numpy, Scipy and Matplotlib).

Methods

The model is described in this section following the paradigm of Nordlie et al, [2]. Therefore, a brief description of the model, equations, parameters and inputs are given in the form of tables.

Table 1 provides a description of the model and Table 2 gives a glimpse of the input used during simulations. Table 3 introduces the equations of the model. The neuron model is conductance-based consisting in four differential equations describing the dynamics of membrane potential and the kinetics of a T-Type calcium current, a Sag current channel and a Potassium channel. The rest currents are described by algebraic equations. Finally, all simulations parameters are given in Table 5 and the simulations times can be found in Table 2.

The reference implementation has been done in a Python class (Python 3.5.1) along with Numpy (version 1.10.4), Scipy (version 0.17.0) and Matplotlib (1.5.1). The numerical integration has been done by the *ode* method of Scipy *integrate* package taking advantage of the BDF multistep method [1]. This is a diversion from the original implementation, since in [3], the author has numerically integrated the system of the four ODEs by using a fifth-order adaptive size Runge-Kutta method. This could cause some of the numerical deviations we noticed during the implementation of the model. The values for the input current must be slightly elevated in order to achieve exactly the same results as in the original implementation.

All the simulations ran on a Dell OptiPlex 7040, equipped with a sixth generation i7 processor, 8GB of physical memory and running Arch Linux as operating system. The total execution time of simulations is 38.76 seconds and the total consumed memory is 66MB. Table 3, shows all the parameters we used in order to produce our results (see Results). No any other implementation of this model found by the authors in order to make any further comparison with.

Model Summary	
Populations	No population – one neuron model
Topology	–
Connectivity	–
Neuron Model	Hodgkin-Huxley conductance-based
Channel Models	
Synapse Model	–
Plasticity	–
Input	Constant current or periodic rectangular pulses
Measurements	Membrane potential, channels activation, phase plane

Table 1: Summary of the model

Simulation Time		
Figure	Simulation Time (ms)	Integration Step (ms)
1	6000	0.05
2	2000	0.05
3	6000	0.05

Table 2: Simulations Time.

Input					
Figure	Type	Form	Frequency ($\frac{1}{P_0}$, Hz)	Duration (p, ms)	Amplitude ($\mu A/cm^2$)
Figure 1	Periodic		5, 8, 10	10, 40, 75, 120	-1.0
Figure 2	Constant		–	–	$+3.0$ 0.0 -0.5 -0.55 -0.6 -0.8 -1.3 -2.1
Figure 3	Constant		–	–	-0.95

Table 3: Description of the applied current I_{app}

Neuron Model	
Name	Thalamocortical relay neuron
Type	Conductance-based neuron
Membrane Potential	$C_m \frac{dV(t)}{dt} = -I_T - I_h - I_{Na} - I_K - I_{Na(P)} - I_L + I_{\text{app}}$
T-Type Calcium Current (I_T)	$I_T = g_T \cdot s_\infty^3(V) \cdot h \cdot (V - V_{Ca})$ $s_\infty(V) = \frac{1}{1+\exp(-\frac{V+65}{7.8})}$ $\frac{dh(t)}{dt} = \phi_h \frac{h_\infty(V) - h}{\tau_h(V)}$ $h_\infty(V) = \frac{1}{1+\exp(\frac{V-\theta_h}{k_h})}$ $\tau_h(V) = h_\infty \exp(\frac{V+162.3}{17.8}) + 20$
Sag Current (I_h)	$I_h = g_h \cdot H^2 \cdot (V - V_h)$ $H_\infty(V) = \frac{1}{1+\exp(\frac{V+69}{7.1})}$ $\frac{dH(t)}{dt} = \phi_H \frac{H_\infty(V) - H}{\tau_H(V)}$
Hodgkin-Huxley Currents (I_K) and (I_{Na})	$I_K = g_K \cdot n^4 \cdot (V - V_K)$ $\frac{dn(t)}{dt} = \phi_n \frac{n_\infty(V) - n(t)}{\tau_n(V)}$ $n_\infty(\sigma_K, V) = \frac{\alpha_n(\sigma_K, V)}{\alpha_n(\sigma_K, V) + \beta_n(\sigma_K, V)}$ $\tau_n(\sigma_K, V) = \frac{1}{\alpha_n(\sigma_K, V) + \beta_n(\sigma_K, V)}$ $\alpha_n(\sigma_K, V) = \frac{-0.01(V + 45.7 - \sigma_K)}{\exp(-0.1(V + 45.7 - \sigma_K)) - 1}$ $\beta_n(\sigma_K, V) = 0.125 \exp(-\frac{V + 55.7 - \sigma_K}{80})$ $I_{Na} = g_{Na} \cdot m_\infty^3(\sigma_{Na}, V) \cdot (0.85 - n) \cdot (V - V_{Na})$ $m_\infty(V) = \frac{\alpha_m(\sigma_{Na}, V)}{\alpha_m(\sigma_{Na}, V) + \beta_m(\sigma_{Na}, V)}$ $\alpha_m(\sigma_{Na}, V) = -0.1 \frac{V + 29.7 - \sigma_{Na}}{\exp(-0.1(V + 54.7 - \sigma Na)) - 1}$ $\beta_m(\sigma_{Na}, V) = 4 \exp(-\frac{V + 54.7 - \sigma_{Na}}{18})$
Persistent Sodium Currents ($I_{Na(P)}$)	$I_{Na(P)} = g_{Na(P)} \cdot m_\infty^3(\sigma_{Na(P)}, V) \cdot (V - V_{Na})$
Leak Current (I_L)	$I_L = g_L \cdot (V - V_L)$

Table 4: Description of the neuron model

Model Parameters				
Currents Type	Common	Figure 1	Figure 2	Figure 3
Membrane Potential	$C_m = 1\mu F/cm^2$ $V_0 = -74mV$			
T-Type Calcium Current	$\phi_h = 2$ $V_{Ca} = 120mV$	$g_T = 1mS/cm^2$ $\theta_h = -81mV$ $k_h = 6.25mV^{-1}$	$g_T = 0.3mS/cm^2$ $\theta_h = -79mV$ $k_h = 5mV^{-1}$	$g_T = 0.3mS/cm^2$ $\theta_h = -75mV$ $k_h = 5mV^{-1}$
Sag Current	$\phi_H = 1$ $g_h = 0.04mS/cm^2$ $V_h = -40mV$			
Hodgkin-Huxley Currents	$g_K = 30mS/cm^2$ $V_K = -80mV$ $g_{Ca} = 42mS/cm^2$ $\phi_n = 28.5$ $V_{Ca} = 55mV$ $\sigma_K = 10$	$\sigma_{Na} = 3$	$\sigma_{Na} = 6$	$\sigma_{Na} = 6$
Persistent Sodium Currents	$V_{Na(P)} = 55mV$ $\sigma_{Na(P)} = -5$	$g_{Na(P)} = 9mS/cm^2$	$g_{Na(P)} = 9mS/cm^2$	$g_{Na(P)} = 9mS/cm^2$
Leak Current		$g_L = 0.1mS/cm^2$ $V_L = -72mV$	$g_L = 0.12mS/cm^2$ $V_L = -70mV$	$g_L = 0.08mS/cm^2$ $V_L = -70mV$

Table 5: Simulations Parameters

Results

We simulated the model described in Table 4 using the parameters given in Table 5 and the corresponding input (see Table 3 for three different cases. First, we verified that the model is able to generate different types of burst responses such as in figure 1 of the original article. We did not reproduce the entire diagram, instead we picked up five different cases from the original article and we tested our implementation on these cases. Thus we applied a periodic current pulse of $-1\mu A/cm^2$ amplitude at three different frequencies (in the original article frequency is referred as $\frac{1}{P_0}$) $5Hz$, $8Hz$ and $10Hz$. The pulse is on for pms and the ratio $\frac{p}{P_0}$ is defined, accordingly. We chose the frequency and the on-duration of the pulse according to figure 1 of the original article and such that we have a different type of burst response for each ratio. The results are shown in Figure 1. It is apparent that the reference implementation can achieve the same behavior as the original implementation. In a second case, we used

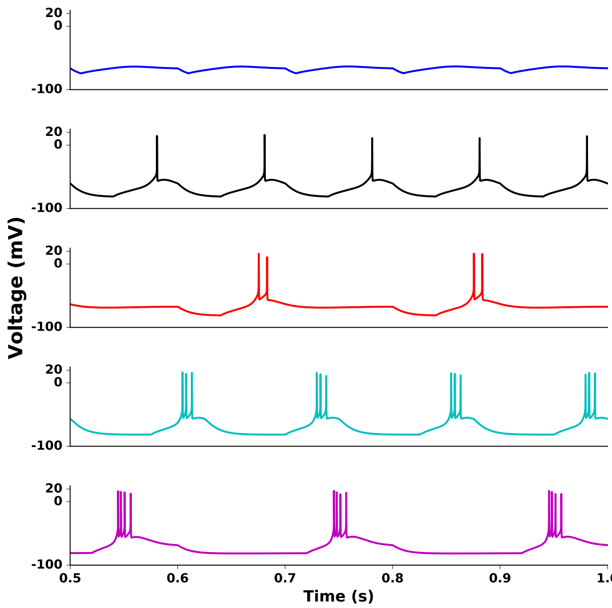

Figure 1: Responses to rhythmic hyperpolarizations. We stimulate the model with a periodic pulse with frequency $\frac{1}{P_0}$ and we record the response of the model. All the parameters for this simulation are given in Table 3. **Blue** indicates a frequency $\frac{1}{P_0} = 10Hz$ and a pulse duration $p = 10ms$. A resting state activity is generated. **Black** color shows the case where $\frac{1}{P_0} = 10Hz$ and $p = 40ms$. In this case we get a single spike periodically. **Red** color demonstrates a burst with two spikes, when the frequency of the periodic pulse is taken to be $\frac{1}{P_0} = 5Hz$ and $p = 40ms$. **Cyan** curve shows burst responses consist in three spikes. In this case $\frac{1}{P_0} = 8Hz$ and $p = 75ms$. **Magenta** curve indicates a burst periodical response of four spikes per period.

a steady current varying only its amplitude and keeping the rest parameters fixed. Hence, we used 8 different current amplitudes ($3, 0, -0.5, -0.55, -0.6, -0.8, -1.3$ and $-2.1\mu A/cm^2$) and Figure 2 illustrates the results of our simulations, which correspond to figure 3 of [3]. Again original results are reproducible and the model is capable of generating repetitive firing, resting state, subthreshold oscillation, $10Hz$ bursting, $3Hz$ bursting and hyperpolarized steady activity. However, the external current amplitudes used in this case are slightly different from the ones used in the original article. The last case we simulated is the one that corresponds to figure 6 of [3]. In this test-

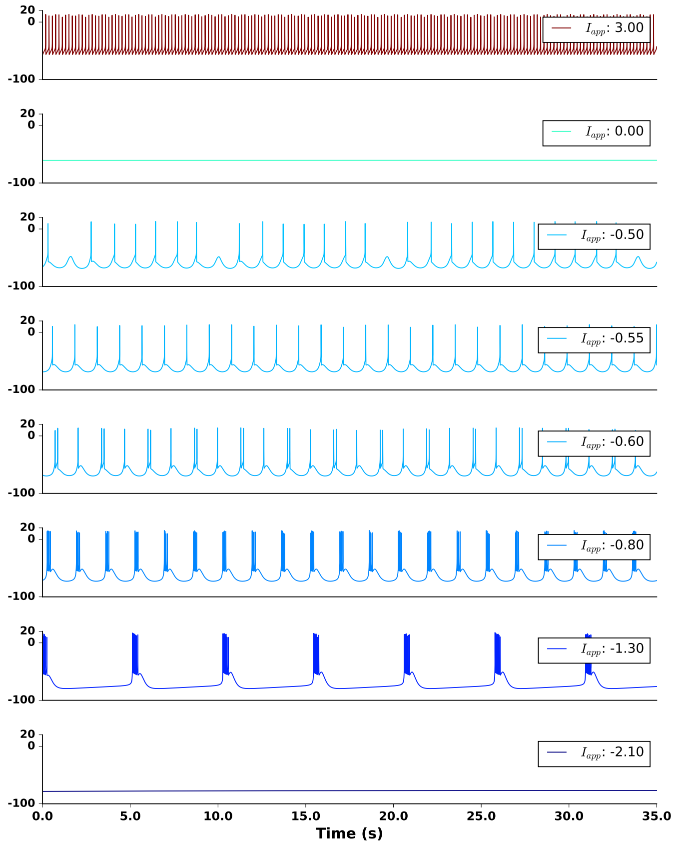

Figure 2: Dynamic behavior of neuron. Here we simulate the model with parameters given in Table 3. The only parameter that changes from panel to panel in this figure is the external current I_{app}. The jet colormap indicates the different current values. We observe that we get quite similar results as in the original article [3]. For isntance, we obtain, repetitive spiking when we apply a constant current at $3\mu A/cm^2$, or a periodic bursting response, when we apply an external current of $-1.3\mu A/cm^2$. These results correspond to Figure 3 of [3].

case the neuron receives a constant external current at $-0.95\frac{\mu A}{cm^2}$ and as Figure 3 points out "spiral chaos" is generated as in the original article. In addition, our results are quantitatively and qualitatively comparable with the ones provided by [3] pinpointing that the original model is fully reproducible apart from the point that we had to properly tune the amplitude of the external current. The parameters for this simulation are given in Table 4.

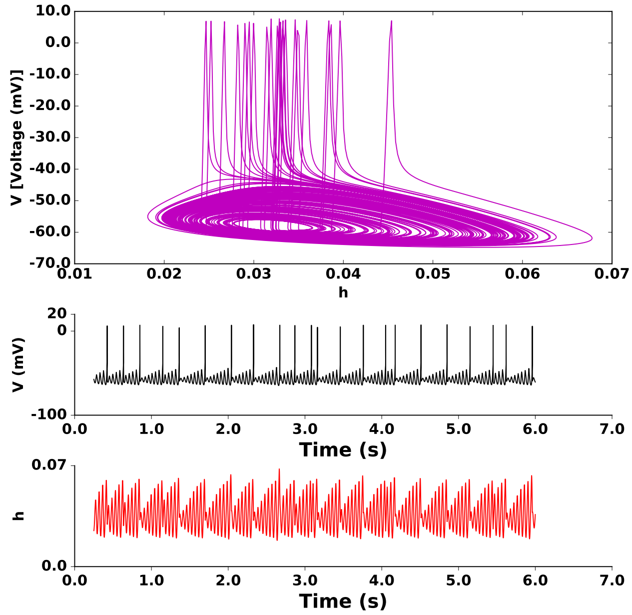

Figure 3: "Spiral Chaos". In this Figure we show that the model is capable of generating spiral chaos as it has been shown in Figure 6 [3]. Again all the parameters for this simulation are given in Table 3. The external current in this simulation is constant and we have traced the phase portrait of the membrane potential and of the Sag current (V vs h). The top panel illustrates the phase portrait, the middle panel shows the membrane potential (V) and the bottom panel depicts the h current over time. Our results are almost identical to the original ones rendering the model fully reproducible.

Conclusion

A conductance-based model for relay thalamocortical neurons proposed by [3] was implemented in Python. After a minor modification of the external current amplitude we were able to reproduce the results presented in [3]. The original model is easy to implement since all the equations, parameters and simulation details are given in [3]. All replicated figures are pretty much similar to the original ones rendering the new results quantitatively and qualitatively comparable to the original ones.

References

[1] Uri M Ascher and Linda R Petzold. *Computer methods for ordinary differential equations and differential-algebraic equations*. Vol. 61. Siam, 1998.

[2] Eilen Nordlie, Marc-Oliver Gewaltig, and Hans Ekkehard Plesser. "Towards reproducible descriptions of neuronal network models". In: *PLoS Comput Biol* 5.8 (2009), e1000456.

[3] X-J Wang. "Multiple dynamical modes of thalamic relay neurons: rhythmic bursting and intermittent phase-locking". In: *Neuroscience* 59.1 (1994), pp. 21–31.