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Effect of the Transient Voltage-Dependent Calcium Conductance Time Constant on Dynamical States in a Mathematical Model of Snail RPa1 Neurons

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Abstract

In this study, a numerical simulation was conducted to explore the sensitivity of dynamical states in a mathematical model representing snail RPa1 neurons, previously reported as a system of nonlinear ordinary differential equations, to specific system parameters: the maximum value (g_{Ca}) and time constant (τ_{Ca}) of transient voltage-dependent calcium conductance. Results of the numerical simulation with g_{Ca} set at its default value revealed that an increase in τ_{Ca} leads to the following dynamical state changes: a periodic low-frequency spiking state → a periodic bursting state → a depolarized steady state. In contrast, when g_{Ca} was set at twice the default value, an increase in τ_{Ca} induced the following dynamical state changes: a periodic bursting state → a periodic high-frequency spiking state → a depolarized steady state.

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Keywords: mathematical model, snail RPa1 neuron, time constant, transient voltage-dependent calcium conductance

1 Introduction

A mathematical model representing snail RPa1 neurons was previously developed as a system of nonlinear ordinary differential equations (ODEs) based on the Hodgkin–Huxley formalism [1]. Moreover, extensive research has explored how variations in parameters, such as the maximum value of ionic conductance, regulate dynamical states in this snail RPa1 neuron model (e.g., [1, 2]). However, a detailed study of how changes in the time constant of ionic conductance impact the model's dynamical state has been lacking. Previous studies on mathematical models of other excitable systems, including neuronal, endocrine, and cardiac cells, have highlighted the importance of the time constant of ionic conductance as a model parameter [3-8]. Our prior work focused on variations in the time constant of potassium conductance in the snail RPa1 neuron model, revealing its effect on the model's dynamical state [9]. However, the influence of variations in the time constant of other ionic conductances on the dynamical states of this model remains unexplored. Given that the maximum value of calcium conductance can regulate the dynamical state of the snail RPa1 neuron model [2], and that the time constant of the calcium conductance can regulate the dynamical state of other models [6, 7], it is hypothesized that the time constant of calcium conductance in the snail RPa1 neuron model similarly regulates its dynamical state. However, this hypothesis has yet to be tested. The periodic spiking state, a dynamical state observed in the snail RPa1 neuron model, is characterized by its sensitivity to variations in the maximum value of transient voltage-dependent calcium conductance. Specifically, a periodic low-frequency spiking state occurs at the default conductance value, whereas a periodic high-frequency spiking state manifests at values exceeding the default [2]. The present study numerically investigates how different types of periodic spiking states in the snail RPa1 neuron model are modulated by varying the time constant of the transient voltage-dependent calcium conductance.

2 Mathematical Model of Snail RPa1 Neurons

The mathematical model of snail RPa1 neurons is described by the following system of nonlinear ODEs (further details about the equations are provided in [1]):

$$\frac{dV}{dt} = \frac{1}{0.02}\left(-0.11\left(\frac{1}{1+e^{-0.2(V+45)}}\right)(V-40) - 0.1100 m_B h_B (V+58)\right.$$

$$-0.0231(V-40) - 0.25(V+70)$$

$$-400 m^3 h (V-40) - 10 n^4 (V+70)$$

$$-g_{Ca}m_{Ca}{}^{2}\left(V-150\right)-0.02\left(\frac{1}{1+e^{-0.06(V+45)}}\right)\left(\frac{1}{1+e^{15000([\mathrm{Ca}]-0.00004)}}\right)\left(V-150\right)\Bigg) \quad (1)$$

$$\frac{dm_B}{dt}=\frac{1}{0.05}\left(\frac{1}{1+e^{0.4(V+34)}}-m_B\right) \quad (2)$$

$$\frac{dh_B}{dt}=\frac{1}{1.5}\left(\frac{1}{1+e^{-0.55(V+43)}}-h_B\right) \quad (3)$$

$$\frac{dm}{dt}=\frac{1}{0.0005}\left(\frac{1}{1+e^{-0.4(V+31)}}-m\right) \quad (4)$$

$$\frac{dh}{dt}=\frac{1}{0.01}\left(\frac{1}{1+e^{0.25(V+45)}}-h\right) \quad (5)$$

$$\frac{dn}{dt}=\frac{1}{0.015}\left(\frac{1}{1+e^{-0.18(V+25)}}-n\right) \quad (6)$$

$$\frac{dm_{Ca}}{dt}=\frac{1}{\tau_{Ca}}\left(\frac{1}{1+e^{-0.2V}}-m_{Ca}\right) \quad (7)$$

$$\frac{d[\mathrm{Ca}]}{dt}=0.002\left(-\frac{g_{Ca}m_{Ca}{}^{2}\left(V-150\right)}{2F\left(\frac{4}{3}\pi 0.1^{3}\right)}-50[\mathrm{Ca}]\right) \quad (8)$$

In this system, the state variables include V (mV) (the membrane potential of snail RPa1 neurons), m_{B}, h_{B}, m, h, n, and m_{Ca} (the gating variables of ionic conductance), in addition to [Ca] (mM) (the intracellular calcium concentration). Time is denoted as t (s), and the system parameters are the maximum value [g_{Ca} (μS)] and time constant [τ_{Ca} (s)] of transient voltage-dependent calcium conductance. F represents the Faraday constant. The numerical solutions of equations of (1)–(8) were obtained using the free and open source software Scilab (http://www.scilab.org/).

3 Numerical Results

A previous investigation highlighted the dependency of the periodic spiking state frequency in the snail RPa1 neuron model on g_{Ca}: a periodic low-frequency (<5 Hz) spiking state emerged under conditions where g_{Ca} was set to the default value (1.5 μS), whereas a periodic high-frequency (~10 Hz) spiking state manifested under conditions where g_{Ca} was set to twice the default value [2].

Initially, we investigated the modulation of a periodic low-frequency spiking state in the snail RPa1 neuron model by varying τ_{Ca} (with the default τ_{Ca} value set as 0.01 s) (Figure 1). Figure 1 shows the temporal progression of V under various τ_{Ca} conditions when g_{Ca} was set at 100%. At τ_{Ca} values of 80%, the model exhibited a periodic low-frequency spiking state, characterized by a low-frequency (<5 Hz) membrane potential oscillation (Figure 1a). At τ_{Ca} values of 90% and 100%, the model sustained a periodic low-frequency spiking state, with a slight frequency decrease attributed to an increase in τ_{Ca} (Figure 1b and c). At a τ_{Ca} value of 110%, the model transitioned to a periodic bursting state, marked by periodic resting and spiking phases (Figure 1d). At a τ_{Ca} value of 120%, the model exhibited a depolarized steady state, with V maintaining a constant value between 0 and −50 mV irrespective of time (Figure 1e).

Second, we investigated the modulation of a periodic high-frequency spiking state in the snail RPa1 neuron model by varying τ_{Ca} (Figure 2). Figure 2 shows the temporal profiles of V under different τ_{Ca} conditions when g_{Ca} was set at 200%. At τ_{Ca} values of 80% and 90%, the model showed a periodic bursting state (Figure 2a and b). At a τ_{Ca} value of 100%, the model transitioned to a periodic high-frequency spiking state, characterized by a high-frequency (~10 Hz) membrane potential oscillation (Figure 2c). At τ_{Ca} values of 110% and 120%, the model assumed a depolarized steady state, with V maintaining a constant value between 0 and −50 mV regardless of time (Figure 2d and e).

4 Conclusion

This study revealed how periodic low- and high-frequency spiking states in the snail RPa1 neuron model are modulated by varying τ_{Ca}. Numerical simulation results indicated that τ_{Ca} can regulate the dynamical states of the model. Moreover, the τ_{Ca} range supporting a periodic low-frequency spiking state is wider than that supporting a periodic high-frequency spiking state. The time constant of ionic conductance has also proven influential in regulating the dynamical states of other mathematical models of excitable systems. For example, in endocrine and neuronal cell models, *a decrease but not an increase* in the time constant of *potassium* conductance induces the transition from a spiking state to a bursting state [3-5]. This aligns with findings from a previous study on the snail RPa1 neuron model [9]. Interestingly, in contrast to this prior research, the present study indicated that *not only a decrease but also an increase* in the time constant of *calcium* conductance (i.e., τ_{Ca}) can induce the transition from a spiking state to a bursting state in the snail RPa1 neuron model. Specifically, a decrease in τ_{Ca} induces the transition from a periodic high-frequency spiking state to a periodic bursting state (Figure 2), whereas an increase in τ_{Ca} induces the transition from a periodic low-frequency spiking state to a periodic bursting state (Figure 1).

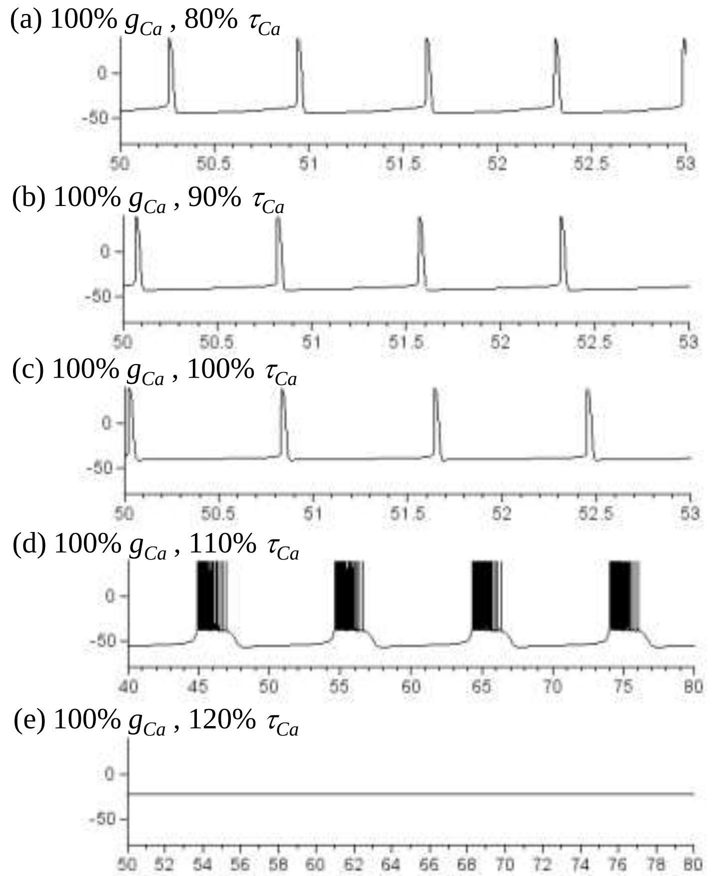

Figure 1. Time courses of membrane potential in the snail RPa1 neuron model under variable τ_{Ca} conditions with g_{Ca} set at 100% of the default value. Results with τ_{Ca} set at (a) 80%, (b) 90%, (c) 100%, (d) 110%, and (e) 120%. In all panels, the horizontal and vertical axes indicate t (s) and V (mV), respectively.

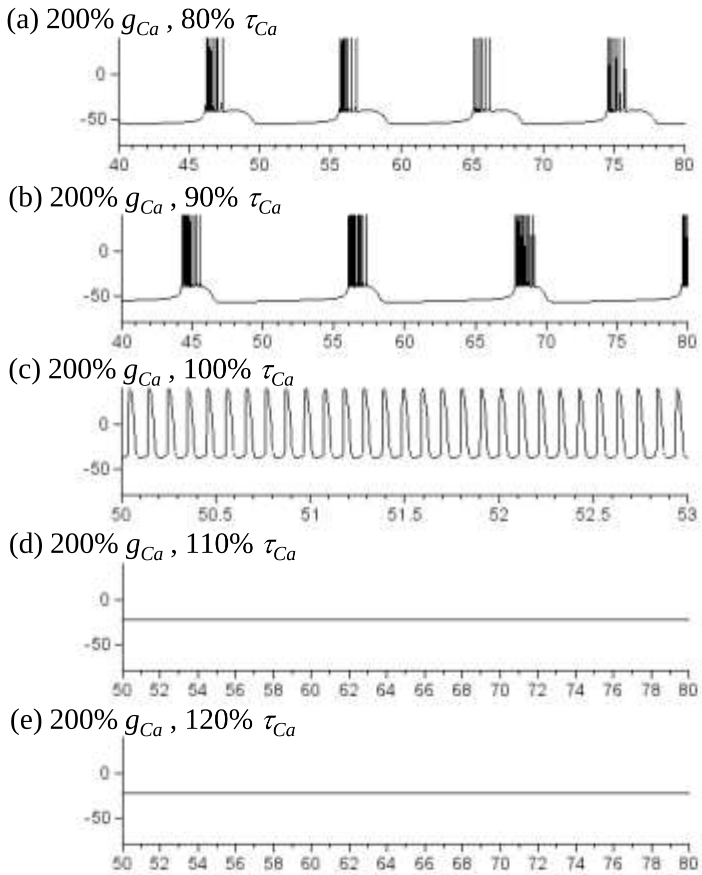

Figure 2. Time courses of membrane potential in the snail RPa1 neuron model under variable τ_{Ca} conditions with g_{Ca} set at 200% of the default value. Results with τ_{Ca} set at (a) 80%, (b) 90%, (c) 100%, (d) 110%, and (e) 120%. In all panels, the horizontal and vertical axes indicate t (s) and V (mV), respectively.

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