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Regulation of Periodic Spiking by Different Types of Calcium Conductance in a Mathematical Model of Snail RPa1 Neurons

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Abstract

This study focuses on a mathematical model of snail RPa1 neurons, which was previously described via a system of nonlinear ordinary differential equations, and numerically investigates how the periodic spiking state of the model is regulated by variations in two types of calcium conductance parameters (i.e., transient voltage-dependent calcium conductance and stationary calcium-inhibited calcium conductance). Numerical simulation results indicate that the two calcium conductances affect the periodic spiking state differently. According to the results, an increase in the transient voltage-dependent calcium conductance changes the dynamic state of the model such that a depolarized steady state → a periodic spiking state → a periodic bursting state → a periodic spiking state → a depolarized steady state. However, an increase in the stationary calcium-inhibited calcium conductance changes the dynamic state of the model such that a hyperpolarized steady state → a periodic bursting state → a periodic spiking state → a depolarized steady state.

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Keywords: A mathematical model of snail RPa1 neurons, periodic spiking, calcium conductance

1 Introduction

Electrophysiological experiments indicate that the membrane potential of snail RPa1 neurons can show interesting nonlinear behavior, such as spiking or bursting oscillations. In addition, a mathematical model that mimics these oscillatory states has previously been described using a system of nonlinear ordinary differential equations (ODEs) based on Hodgkin–Huxley formalism [1]. A previous study investigated how the periodic bursting state of this snail RPa1 neuron model was modulated by changing two types of calcium conductance parameters (i.e., the transient voltage-dependent calcium conductance and the stationary calcium-inhibited calcium conductance), and clarified that the two calcium conductance parameters had different effects on the periodic bursting frequency—a decrease in the former conductance increased the bursting frequency, whereas a decrease in the latter conductance decreased it [2]. In addition, a previous study investigated how changing the chemosensitive conductance parameter modulates the spiking state of the snail RPa1 neuron model and found that changing this parameter changed the model's dynamic state from spiking to bursting [1]. However, how the calcium conductance parameters modulate the spiking state of the snail RPa1 neuron model has not yet been clarified. Given that calcium conductance parameters are crucial for the spiking state of excitable systems (e.g., neurons and cardiac cells) [3–5], they can also modulate the spiking state of the snail RPa1 neuron model. According to a previous study, the spiking state of the snail RPa1 neuron model was classified into several subtypes (i.e., a period-1 spiking state, a period-2 spiking state, a period-4 spiking state, and a chaotic spiking state) [1]. For simplicity, this study focuses on a period-1 spiking state, which is called a periodic spiking state in this study, and numerically investigates how changing the two calcium conductance parameters modulates a periodic spiking state.

2 The Mathematical Model of Snail RPa1 Neurons

In this study, a system of eight coupled nonlinear ODEs was used to study the snail RPa1 neuron model numerically:

$$\begin{aligned}\frac{dV}{dt} = \frac{1}{0.02}\Bigg(& -0.11\left(\frac{1}{1+e^{-0.2(V+45)}}\right)(V-40) - 0.1100 m_B h_B (V+58) \\ & -0.0231(V-40) - 0.25(V+70) \\ & -400 m^3 h (V-40) - 10 n^4 (V+70) \\ & - g_{Ca} {m_{Ca}}^2 (V-150) - g_{CaCa}\left(\frac{1}{1+e^{-0.06(V+45)}}\right)\left(\frac{1}{1+e^{15000([\mathrm{Ca}]-0.00004)}}\right)(V-150)\Bigg), \end{aligned} \quad (1)$$

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

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

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

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

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

$$\frac{dm_{Ca}}{dt} = \frac{1}{0.01}\left(\frac{1}{1+e^{-0.2V}} - m_{Ca}\right), \tag{7}$$

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

where V (mV) (the membrane potential of snail RPa1 neurons); m_B, h_B, m, h, n, and m_{Ca} (the gating variables of ionic conductances); and [Ca] (mM) (the intracellular calcium concentration) are state variables; t (s) is time; the transient voltage-dependent calcium conductance g_{Ca} (μS) and the stationary calcium-inhibited calcium conductance g_{CaCa} (μS) are system parameters; and F is a Faraday constant. The free and open-source software Scilab (http://www.scilab.org/) was used to numerically solve equations (1)–(8), which are explained in detail in [1].

3 Numerical Results

First, we investigated how changing g_{Ca} with g_{CaCa} fixed at a default value modulates the periodic spiking state of the snail RPa1 neuron model (g_{Ca} and g_{CaCa} have default values of 1.5 and 0.02 μS, respectively, based on a previous study [1]). Furthermore, we numerically solved equations (1)–(8) and illustrated in Figure 1 the time courses of V under various g_{Ca} conditions. When g_{Ca} was 0%, the model showed a depolarized steady state: V is a certain constant value between 0 and −50 mV irrespective of time (Figure 1a). When g_{Ca} was 50%, the model showed a periodic spiking state—the periodic membrane potential oscilla-

tion was observed (Figure 1b). When g_{Ca} was 100%, the model showed a periodic spiking state similar to that shown in Figure 1b. However, the spiking frequency was lower than that observed in Figure 1b (Figure 1c). When g_{Ca} was 150%, the model showed a periodic bursting state—a periodic alternation of the resting and spiking phases was observed (Figure 1d). When g_{Ca} was 200%, the model showed a periodic spiking state, but the spiking frequency was much higher than that observed in Figures 1b and 1c (Figure 1e). When g_{Ca} was 250%, the model showed a depolarized steady state similar to that in Figure 1a (Figure 1f). When g_{Ca} was 1000%, the model again showed a depolarized steady state, but the value of V, which exists between 50 and 100 mV, was much larger than that observed in Figures 1a and 1f (Figure 1g).

Second, we investigated how changing g_{CaCa} with g_{Ca} fixed at a default value modulates the periodic spiking state of the snail RPa1 neuron model. We numerically solved equations (1)–(8) and illustrated in Figure 2 the time courses of V under various g_{CaCa} conditions. When g_{CaCa} was 0%, the model showed a hyperpolarized steady state: V is a certain constant value below −50 mV irrespective of time (Figure 2a). When g_{CaCa} was 50%, the model showed a periodic bursting state (Figure 2b). The model showed a periodic spiking state when g_{Ca} was between 100% and 250% (Figures 2c to 2f). In addition, an increase in g_{CaCa} increased the spiking frequency. When g_{CaCa} was 1000%, the model showed a depolarized steady state similar to Figure 1a (Figure 2g).

4 Conclusion

This study investigates the sensitivity of the periodic spiking state of the snail RPa1 neuron model to the variations in the two types of calcium conductance (i.e., g_{Ca} and g_{CaCa}) and reveals the effect of an increase in g_{Ca} and g_{CaCa} on the model. An increase in g_{Ca} changes the dynamic state such that a depolarized steady state → a periodic spiking state → a periodic bursting state → a periodic spiking state → a depolarized steady state. However, an increase in g_{CaCa} changes the dynamic state such that a hyperpolarized steady state → a periodic bursting state → a periodic spiking state → a depolarized steady state. Previous studies of mathematical models of other excitable systems, such as a dopaminergic neuron model and a cardiac cell model, investigated the relationship between spiking activity and calcium conductance [3, 5]. However, unlike this study, they did not investigate the relationship between the transition from a periodic spiking state to a periodic bursting state and the variation in calcium conductance. According to the computational neuroscience textbook, the standard route to a bursting state is understood such that increasing the excitability (e.g., increasing the externally injected current) induces a change in the dynamic state such that a hyperpolarized steady state → a bursting state → a spiking state [6]. This change is consistent with the present result of changing g_{CaCa} as well as with a previous study of the snail RPa1 model [2]. Interestingly, this study clarifies a different route to a bursting state: an increase in g_{Ca} changes the dynamic state such that a periodic spiking state → a periodic bursting state → a periodic spiking state.

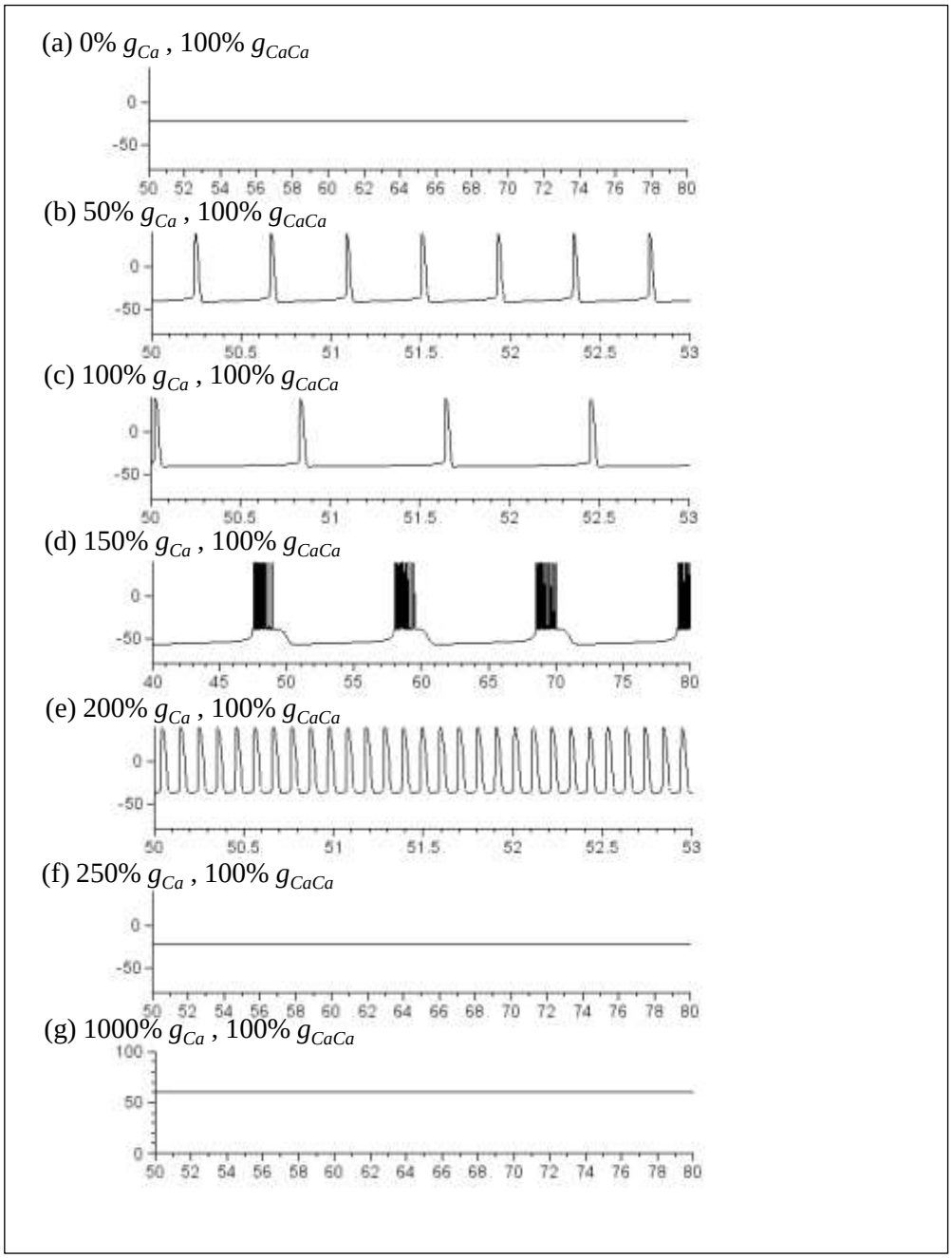

Figure 1. Time courses of the membrane potential of the snail RPa1 neuron model under variable g_{Ca} conditions with g_{CaCa} fixed as the default value. (a) 0% g_{Ca}, (b) 50% g_{Ca}, (c) 100% g_{Ca}, (d) 150% g_{Ca}, (e) 200% g_{Ca}, (f) 250% g_{Ca}, and (g) 1000% g_{Ca}. Across all panels, the horizontal axis indicates t (s) and the vertical axis indicates V (mV).

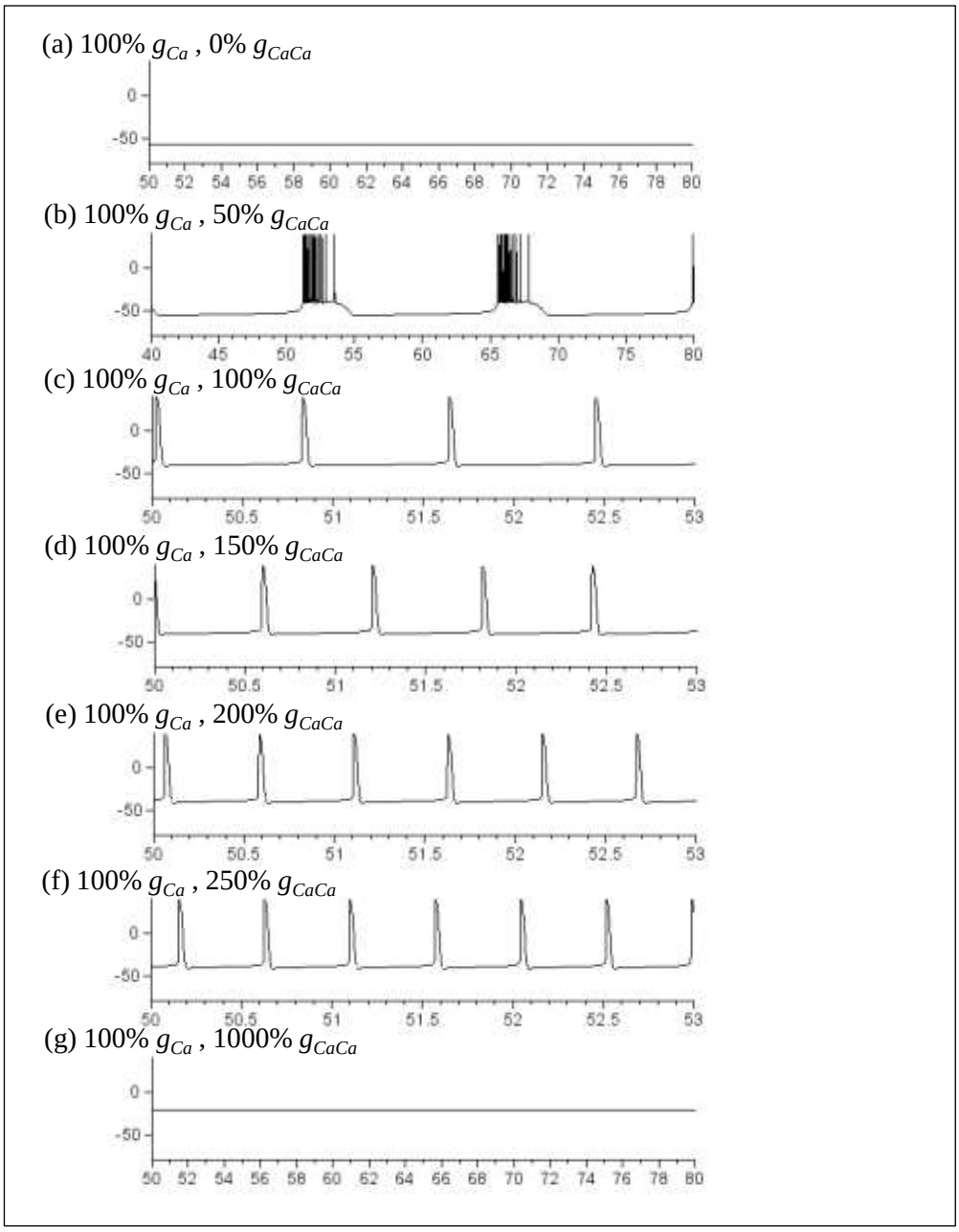

Figure 2. Time courses of the membrane potential of the snail RPa1 neuron model under variable g_{CaCa} conditions with g_{Ca} fixed as the default value. (a) 0% g_{CaCa}, (b) 50% g_{CaCa}, (c) 100% g_{CaCa}, (d) 150% g_{CaCa}, (e) 200% g_{CaCa}, (f) 250% g_{CaCa}, and (g) 1000% g_{CaCa}. Across all panels, the horizontal axis indicates t (s) and the vertical axis indicates V (mV).

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