Advanced Studies in Theoretical Physics
Vol. 15, 2021, no. 3, 123 - 129
HIKARI Ltd, www.m-hikari.com
https://doi.org/10.12988/astp.2021.91545

Calcium Conductances Can Modulate Burst Duration in a Mathematical Model of Snail RPa1 Neurons

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Abstract

A mathematical model of snail RPa1 neurons described by a system of nonlinear ordinary differential equations can exhibit a chaotic bursting state under a particular default condition. Here, a numerical simulation of the model was conducted to study the sensitivity of a chaotic bursting state under the default condition to an increase or decrease in two system parameters: transient voltage-dependent calcium conductance and stationary calcium-inhibited calcium conductance. The simulation results indicate that when the former conductance is increased, a periodic bursting state can appear in which the duration of each burst is much shorter than in the default condition. In contrast, when the latter conductance is decreased, a periodic bursting state can appear in which each burst duration is much shorter than in the default condition.

Mathematics Subject Classification: 37N25, 92C20
PACS: 05.45.-a, 87.19.ll
Keywords: A mathematical model of snail RPa1 neurons, chaotic bursting state, transient voltage-dependent calcium conductance, stationary calcium-inhibited calcium conductance, burst duration

1 Introduction

It is important to determine how the membrane potential of excitable cells such as muscle and nerve is regulated by various ionic conductances [1, 2]. A previous study of a mathematical model of mouse urinary bladder smooth muscle reported, for example, that the action potential could be regulated by calcium conductance [1]. Another study of a mathematical model of snail RPa1 neurons described by a system of nonlinear ordinary differential equations (ODEs) based on the Hodgkin-Huxley formalism found that bursting involving more complex dynamics than action potential could also be regulated by calcium conductance [3]. Specifically, that study concluded that the burst frequency of the model was differently regulated by two types of calcium conductance (i.e., transient voltage-dependent calcium conductance and stationary calcium-inhibited calcium conductance), a conclusion obtained by investigating the sensitivity of a periodic bursting state to variation of the above two types of calcium conductance. The mathematical model of snail RPa1 neurons can exhibit a bursting state that is more complex than a periodic bursting state (i.e., chaotic bursting state) under a specific condition [2]. It is crucial to investigate the sensitivity of a periodic bursting state to variation of calcium conductance and the sensitivity of a chaotic bursting state to conductance variation to understand better the sensitivity of a bursting state to variation of calcium conductance. Although the former case was clarified in the previous study [3], the latter case was not. Therefore, we performed a numerical simulation of the model to reveal a chaotic bursting state's sensitivity to variation of the two types of calcium conductance.

2 The Mathematical Model

The sensitivity of a chaotic bursting state to variation of two system parameters [i.e., transient voltage-dependent calcium conductance (g_{Ca}) and stationary calcium-inhibited calcium conductance (g_{CaCa})] was investigated by numerical simulation of a mathematical model of snail RPa1 neurons [2] described by a system of ODEs:

$$\begin{aligned}\frac{dV}{dt} = \frac{1}{0.02}\Bigg(& -0.13\left(\frac{1}{1+e^{-0.2(V+45)}}\right)(V-40) - 0.18 m_B h_B (V+58) \\ & -0.02(V-40) - 0.25(V+70) \\ & -400 m^3 h (V-40) - 10 n^4 (V+70) \\ & - g_{Ca} m_{Ca}{}^2 (V-150) - g_{CaCa}\left(\frac{1}{1+e^{-0.06(V+45)}}\right)\left(\frac{1}{1+e^{15000([\mathrm{Ca}]-0.00004)}}\right)(V-150)\Bigg)\end{aligned} \tag{1}$$

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

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

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

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

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

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

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

, in which V (mV) describes the membrane potential of snail RPa1 neurons, m_B, h_B, m, h, n, and m_{Ca} describe the gating variables, and [Ca] (mM) describes the concentration of intracellular calcium (the state variables); t (s) is time, and F is a Faraday constant. Equations (1)–(8) were numerically solved using the free, open-source software Scilab (http://www.scilab.org/).

3 Numerical Results

First, we performed a numerical simulation by varying the value of g_{Ca}. The default value of g_{Ca} is 1.0 μS. We illustrate in Figure 1 the time courses of the membrane potential of the snail RPa1 neuron model under the following circumstances for g_{Ca}: smaller than (Figures 1a, 1b, and 1c), equal to (Figure 1d), and larger than that of the default condition (Figures 1e, 1f, and 1g). The model indicates the appearance of a chaotic bursting state under the default g_{Ca} condition—various types of bursting indicated as “d1,” “d2,” “d3,” “d4,” and “d5” (Figure 1d). Similarly, when the g_{Ca} value is smaller than the default value, the model also shows a chaotic bursting state—various types of bursting indicated as “a1,” “a2,” “a3,” “a4,” “a5,” and “a6” (Figure 1a) and as “b1,” “b2,” “b3,” “b4,” and “b5” (Figure 1b). However, when the g_{Ca} value is slightly smaller than the default value (i.e., g_{Ca} is 99%), the model shows a periodic bursting state—after the first bursting indicated as “c1,” bursting indicated as “c2” periodically appears (Figure 1c). When the g_{Ca} value is slightly larger than the default value (i.e., g_{Ca} is 101%), the model shows a periodic bursting state—the first bursting indicated as “e1,” followed by that indicated as “e2” (Figure 1e). Similarly, when g_{Ca} is further increased, the model also shows a periodic bursting state, designated as “f1” and “g1” (Figure 1f and 1g). Additionally, the burst duration of a periodic bursting state (“e2” in Figure 1e, “f1” in Figure 1f, and “g1” in Figure 1g) is much smaller than that of a chaotic bursting state under the default g_{Ca} condition (Figure 1d).

Second, we performed a numerical simulation by varying g_{CaCa}. The g_{CaCa} is 0.01 μS under the default condition. We illustrate in Figure 2 the time courses of the membrane potential of the snail RPa1 neuron model when the g_{CaCa} value is smaller than (Figure 2a, 2b, and 2c), equal to (Figure 2d), and larger than that of the default condition (Figure 2e, 2f, and 2g). Under the default g_{CaCa} condition, the model shows a chaotic bursting state—various types of bursting indicated as “d1,” “d2,” “d3,” “d4,” and “d5” appear (Figure 2d). The model shows a periodic bursting state (Figure 2a and 2c) or a chaotic bursting state (Figure 2b) when the g_{CaCa} value is smaller than the default value. Bursting indicated as “a2” periodically appears after the first bursting designated as “a1” (Figure 2a) when g_{CaCa} is 97%. In particular, the burst duration of a periodic bursting state (“a2” in Figure 2a) is much smaller than that of a chaotic bursting state under the default g_{CaCa} condition (Figure 2d). Similarly, when the value of g_{CaCa} is 99%, bursting indicated as “c1” periodically appears (Figure 2c). In contrast, bursting types indicated as “b1,” “b2,” “b3,” and “b4” (Figure 2b) appear when the g_{CaCa} value is 98%. The model shows a chaotic bursting state—various types of bursting indicated as “f1,” “f2,” “f3,” and “f4” (Figure 2f) and as “g1,” “g2,” “g3,” “g4,” “g5,” and “g6” (Figure 2g) appear when the g_{CaCa} value is larger than the default value. However, when the g_{CaCa} value is slightly larger than the default value (i.e., g_{CaCa} is 101%), the model shows a periodic bursting state—bursting indicated as “e1” periodically appears (Figure 2e).

4 Conclusion

The present study reveals how a chaotic bursting state of the snail RPa1 neuron model changes according to specific ionic conductance parameters (i.e., g_{Ca} and g_{CaCa}). Previous studies reported that changes in different ionic conductance parameters in the snail RPa1 neuron model were capable of generating a chaotic bursting state [4, 5]. However, how this state is produced by variation of ionic conductance is dependent on the type of ionic conductance. In one case, a change of the spike-generating sodium conductance changes the dynamical state of the model such that a periodic bursting state → a chaotic bursting state → a periodic bursting state [4]; in another instance, a change of the voltage-independent potassium conductance produces a periodic spiking state → a chaotic spiking state → a chaotic bursting state → a periodic bursting state [5]. Therefore, it is important to determine how a chaotic bursting state generated by changes of calcium conductance influences classification as the former or the latter. Based on the present results (Figures 1c, 1d, and 1e, and Figures 2c, 2d, and 2e), a chaotic bursting state generated by calcium conductance change is classified as the former case. A previous study of a bursting mathematical model that differed from the snail RPa1 neuron model also reported that the above two cases generated a chaotic bursting state [6]. However, that model is a three-dimensional dynamical system [6]. The snail RPa1 neuron model used here is a much higher dimensional dynamical system (i.e., an eight-dimensional dynamical system). A previous study investigated how a periodic bursting state of the snail RPa1 neuron model was modulated by variation of calcium conductance and reported that the bursting frequency was modulated by variation of these ionic conductances [3]. However, how a chaotic bursting state of the snail RPa1 neuron model is modulated by variation of calcium conductance was not clarified by that study. Importantly, the present study clearly indicates that variation of calcium conductance results in the chaotic bursting state under the default condition being changed to a periodic bursting state in which the burst duration is much shorter.

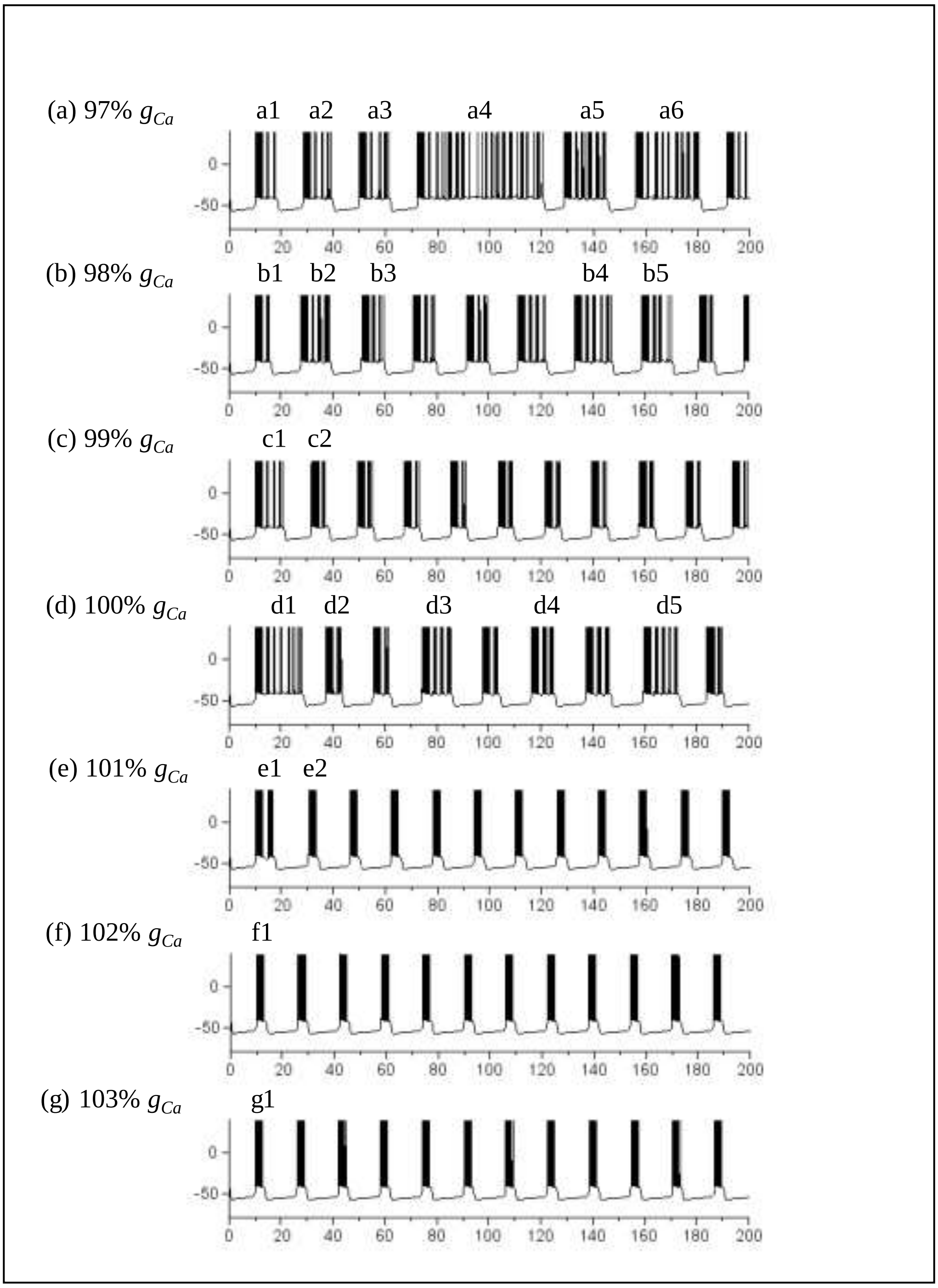

Figure 1. The time courses of the membrane potential of the snail RPa1 neuron model under variable g_{Ca} conditions: (a) 97% g_{Ca}, (b) 98% g_{Ca}, (c) 99% g_{Ca}, (d) 100% g_{Ca}, (e) 101% g_{Ca}, (f) 102% g_{Ca}, and (g) 103% g_{Ca}. The horizontal axis indicates t (s) and the vertical axis indicates V (mV) in all the panels. a1–a6, b1–b5, c1–c2, d1–d5, e1–e2, f1, and g1 denote bursting patterns observed in each g_{Ca} condition.

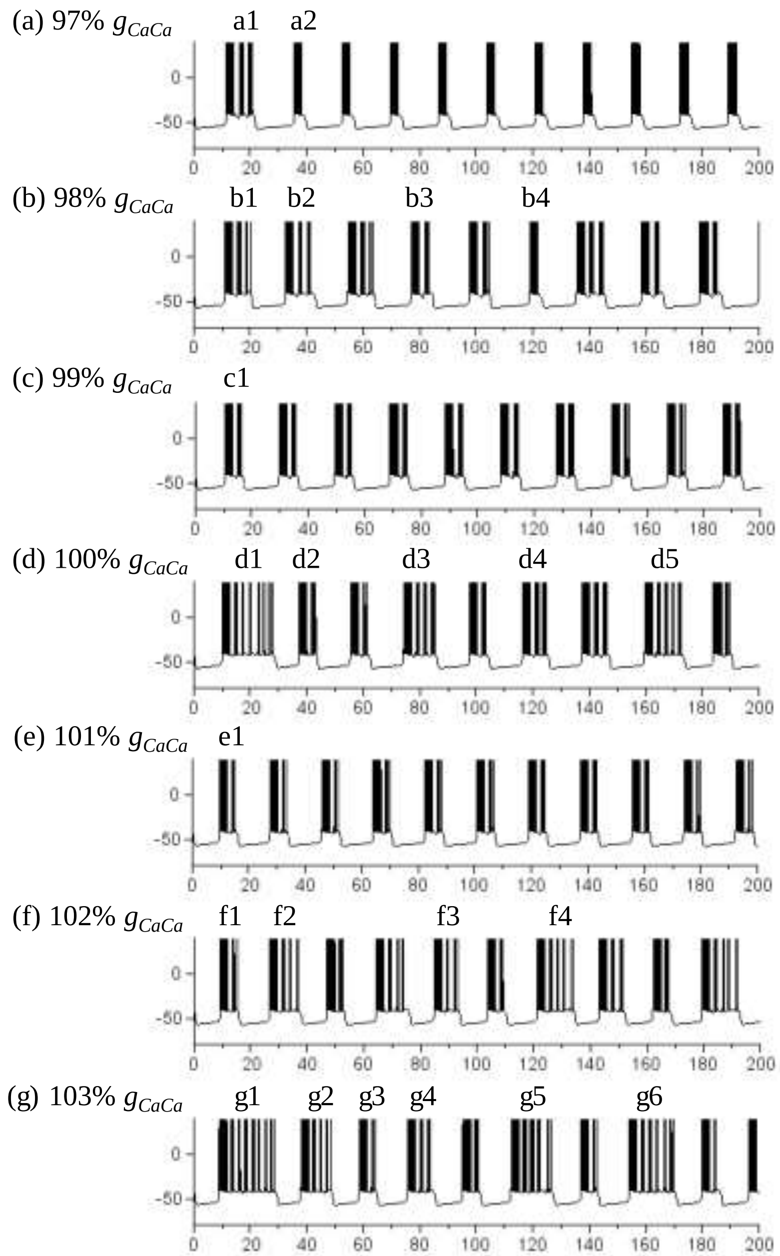

Figure 2. The time courses of the membrane potential of the snail RPa1 neuron model under variable g_{CaCa} conditions: (a) 97% g_{CaCa}, (b) 98% g_{CaCa}, (c) 99% g_{CaCa}, (d) 100% g_{CaCa}, (e) 101% g_{CaCa}, (f) 102% g_{CaCa}, and (g) 103% g_{CaCa}. The horizontal axis indicates t (s) and the vertical axis indicates V (mV) in all the panels. a1–a2, b1–b4, c1, d1–d5, e1, f1–f4, and g1–g6 denote bursting patterns observed in each g_{CaCa} condition.

Acknowledgements. The author would like to thank Enago (www.enago.jp) for the English language review.

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Received: March 31, 2021; Published: April 19, 2021, 20xx