

Characterization of the Kinetic Properties of Tetraethylammonium (TEA)-Sensitive Potassium Conductance in a Mathematical Model of Snail Neurons

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Abstract

A mathematical model of snail RPa1 neurons has previously been proposed using a system of nonlinear ordinary differential equations. In the present study, we described a numerical simulation analysis of this model. We investigated the effects of changes to a parameter reflecting the time constant of activation of tetraethylammonium (TEA)-sensitive potassium conductance (τ_n) in the model. Simulation results suggested that an increase in the parameter τ_n changes the dynamic state of the model such that a depolarized steady state leads to a regular bursting state, which produces a chaotic bursting state, then a regular bursting state, leading in turn to a repetitive spiking state.

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1 Introduction

A dynamic state such as a bursting state, which is characterized by alterations between repetitive spiking and quiescent states, can be observed in mathematical models of excitable cells such as neurons [1] and endocrine cells [2, 3]. All of these models are constructed based on the Hodgkin-Huxley theory, and can be described using a system of nonlinear ordinary differential equations (ODEs). An important question with respect to a bursting state is the way in which the bursting state is influenced by changes in parameter values. A previous study using a mathematical model of snail RPa1 neurons revealed the sensitivity of a bursting state to variations of a parameter describing the ionic conductance (e.g., in this case the chemosensitive sodium conductance), which changed the dynamical state of the model such that a regular bursting state \rightarrow a chaotic spiking state \rightarrow a repetitive spiking state [1]. However, the sensitivity of a bursting state to other parameter variations is not well understood. For example, we do not understand whether a bursting state is modulated by the time constant of the ionic conductance in the snail RPa1 neuron model. Previous studies have reported the sensitivity of a bursting state to variations in the time constant of the ionic conductance. For example, an increase in the time constant of activation of the fast-activating voltage- and calcium-dependent potassium (BK) conductance has been shown to change the dynamic state of a mathematical model of pituitary lactotroph cells from a bursting state to a repetitive spiking state [2]. An increase in the time constant of activation of delayed-rectifier potassium conductance changes the dynamical state of a mathematical model of pituitary corticotroph cells such that a depolarized steady state leads to a regular bursting state, which in turn leads to a repetitive spiking state [3]. Combining the results of these two pituitary cell models, the time constant of potassium conductance is hypothesized to play an important role in regulating the dynamic state of the snail RPa1 neuron model, but the way in which the time constant influences the model is not clear [1]. In the study described here, we perform a numerical simulation of the snail RPa1 neuron model in which we investigated the effects of variation of the time constant of activation on the tetraethylammonium (TEA)-sensitive potassium conductance on the model.

2 The Mathematical Model

We used a system of nonlinear ODEs describing the dynamics of snail RPa1 neurons. The state variables of the ODEs are V (mV) describing the membrane potential of snail RPa1 neurons, m_B , h_B , m , h , n , and m_{Ca} describing gating variables, and $[Ca]$ (mM) describing the concentration of intracellular calcium. A system parameter τ_n describes the time constant of activation of TEA-sensitive potassium conductance. The dynamics of the state variables can be represented as:

$$\begin{aligned} \frac{dV}{dt} = & \frac{1}{0.02} \left(-0.13 \left(\frac{1}{1 + e^{-0.2(V+45)}} \right) (V - 40) - 0.18 m_B h_B (V + 58) \right. \\ & - 0.02(V - 40) - 0.25(V + 70) \\ & - 400 m^3 h (V - 40) - 10 n^4 (V + 70) \\ & \left. - m_{Ca}^2 (V - 150) - 0.01 \left(\frac{1}{1 + e^{-0.06(V+45)}} \right) \left(\frac{1}{1 + e^{15000([Ca] - 0.00004)}} \right) (V - 150) \right) \end{aligned} \quad (1)$$

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

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

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

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

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

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

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

, in which F is a Faraday constant. The initial conditions were taken from [4], and detailed explanations of the equations are provided in [1]. Numerical simulations were performed using the free open source software Scilab (<http://www.scilab.org/>).

3 Numerical Results

In this study we investigated the effects of changes in the parameter τ_n on the snail RPa1 neuron model. The value of τ_n value was varied from 97% to 103% of its default value of 0.015 s. The time courses of the membrane potential of the model under different τ_n conditions are illustrated in Figure 1. When τ_n is 97%, the model shows a depolarized steady state: after a single spike, as indicated by “a1” in Figure 1a, the membrane potential converges to a depolarized steady state potential. When τ_n is 98% or 99%, the model shows a regular bursting state; a single type of bursting, indicated in “b1” and “c1” in Figure 1b and 1c respectively, appears periodically. When τ_n is 100%, the dynamical state of the

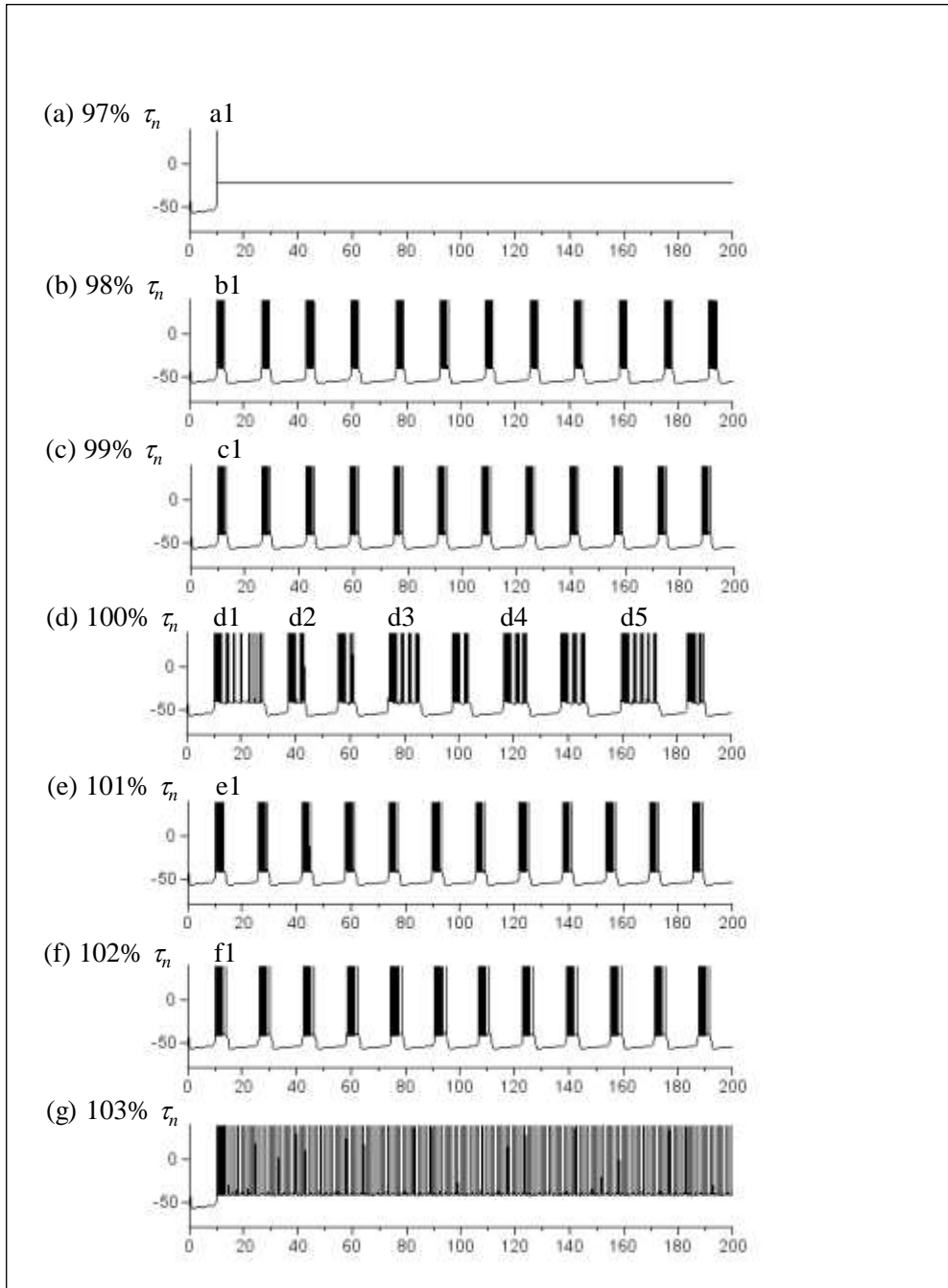


Figure 1. Time courses of the membrane potential of the snail RPa1 neuron model. (a) 97% τ_n , (b) 98% τ_n , (c) 99% τ_n , (d) 100% τ_n , (e) 101% τ_n , (f) 102% τ_n , and (g) 103% τ_n . In all panels, the horizontal axis indicates time in seconds and the vertical axis indicates the membrane potential in mV. a1 denotes a single spike, and b1, c1, d1, d2, d3, d4, d5, e1, and f1 denote bursting patterns observed in each τ_n condition.

model is a chaotic bursting state; various types of bursting, indicated by “d1,” “d2,” “d3,” “d4,” and “d5” appear in Figure 1d, all of which are different from “b1” and “c1”, and the appearance of each bursting pattern is very irregular. When τ_n is 101% or 102%, the dynamic state of the model is again a regular bursting state similar to Figure 1b and 1c; a regular bursting pattern, indicated by “e1” and “f1” in Figures 1e and 1f respectively, appears periodically. When τ_n is 103%, the dynamical state of the model is very different from that illustrated in Figures 1a-1f; the model shows a repetitive spiking state (Figure 1g).

4 Discussion and Conclusion

The present study clarifies the dependence of the dynamic state of the snail RPa1 neuron model on τ_n . An increase in the value of τ_n changes the dynamical state such that a depolarized steady state leads to a regular bursting state which in turn leads to a chaotic bursting state, which then generates a regular bursting state, which then produces a repetitive spiking state. A change in which a regular bursting state leads to a chaotic bursting state which then produces a regular bursting state can also be induced by variations in another parameter describing the spike-generating sodium conductance [$g_{Na(TTX)}$] of the snail RPa1 neuron model [4]. In both previous [4] and present studies, the regularity of bursting—regular or chaotic—is affected by only a 1% change in the parameter value. However, a comparison of the previous [4] and present studies reveals that the τ_n parameter range that supports a bursting state, irrespective of its regularity, is smaller than the $g_{Na(TTX)}$ parameter range that supports such a state. The transition of the dynamical state between a depolarized steady state and a regular bursting state has not been reported in previous studies [1, 4]. As with the present results, previous studies of mathematical models of pituitary cells have reported that the transition of dynamical states from a bursting state to a repetitive spiking state can be induced by an increase in the time constant of potassium conductance [2, 3]. However, in contrast to the present results, these two previous studies did not reveal whether or not variation in the time constant of potassium conductance is capable of inducing a chaotic bursting state. The present study clearly indicates that τ_n plays an important role in inducing a chaotic bursting state.

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