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The Relationship Between Mixed-Mode Oscillation and the Kinetics of Potassium Conductances in a Mathematical Model of Vibrissa Motoneurons

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Abstract

A mathematical model of vibrissa motoneurons (vMNs) is described by a system of ordinary nonlinear differential equations, based on the Hodgkin–Huxley concept, in a previous study. When a parameter describing the externally injected current (I_{app}) is increased, this model changes its dynamical state: subthreshold oscillation state → a mixed-mode oscillation state → a tonic firing state. In addition, this model contains two types of potassium conductances (i.e., the M-type K^+ and AHP-type K^+). The present study performs a numerical simulation analysis of the model to understand the relationship between mixed-mode oscillation and the kinetics of the two types of potassium conductances. By varying three system parameters of the model [i.e., I_{app} and the time constants of activation of the M-type K^+ (τ_z) and AHP-type K^+ conductances (τ_u)], the present study reveals that the I_{app} range, wherein the vMN model shows a mixed-mode oscillation state, is differently sensitive to variations in the time constant between τ_z and τ_u.

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Keywords: Mathematical model, vibrissa motoneurons, mixed-mode oscillation, potassium conductance, time constant

1 Introduction

The neuronal system is a highly nonlinear dynamical system; various types of dynamical states, such as quiescent, tonic firing, and bursting, have been observed (i.e., a mathematical model that describes the dynamics of electrosensory neurons shows these three dynamical states, and the effect of parameter changes on these dynamical states has been extensively studied [1, 2]). However, the dynamical neuronal system is not restricted to these three states. For example, a mathematical model of vibrissa motoneurons (vMNs) shows subthreshold and mixed-mode oscillation states [3, 4]. The vMN model is described as a system of ordinary nonlinear differential equations (ODEs) based on the Hodgkin–Huxley formalism, and a change in the value of a certain parameter (i.e., the externally injected current) alters the dynamical state of the vMN model: subthreshold oscillation state → a mixed-mode oscillation state → a tonic firing state [4]. Mixed-mode oscillation is an important topic of dynamical systems [5]. This type of oscillation corresponds to the switching between small-amplitude and relaxation oscillations.

The vMN model contains two types of potassium conductances (i.e., the M-type K^+ and AHP-type K^+); a previous study extensively investigated the characteristics of these conductances, and the effect of variations of the maximal value of these conductances on the vMN model was revealed [3]. However, the kinetics of these conductances was not studied in the previous study. Other studies have reported that the kinetics of potassium conductances can modulate the dynamical states of various mathematical models such as that for a neuron [6] and a pituitary cell [7, 8]. Considering this information, how the kinetics of the two potassium conductances affects the vMN model must be investigated. In the present study, a numerical simulation of the vMN model is performed to determine the relationship between the kinetics of the potassium conductances and mixed-mode oscillation. The effect of variations of three system parameters (i.e., the externally injected current and the time constants of activation of the M-type K^+ and AHP-type K^+ conductances) on the dynamical states of the vMN model, has been investigated.

2 Materials and Methods

A mathematical model of vMNs, which is numerically analyzed in the present study, is described by an ODE system wherein six state variables are included. These variables consist of the membrane potential of the vMN model [V (mV)] and five gating variables of ionic currents (z, u, h, n, and r). The time evolution of these state variables is described by equations (1)–(6):

$$\frac{dV}{dt} = I_{app} - z\ \left(V+90\right) - 10u\ \left(V+90\right)$$

$$-100\left(\frac{1}{1+e^{-(V+28)/7.8}}\right)^3 h\left(V-55\right) - 0.04\left(\frac{1}{1+e^{-(V+53)/5}}\right)\left(V-55\right) - 20n^4\left(V+90\right)$$

$$-0.05r\left(V+27.4\right)-0.12\left(V+70\right) \quad (1)$$

$$\frac{dz}{dt}=\frac{1}{\tau_z}\left(\frac{1}{1+e^{-(V+45)/4.25}}-z\right) \quad (2)$$

$$\frac{du}{dt}=\frac{1}{\tau_u}\left(\frac{1}{1+e^{-(V+25)/3}}-u\right) \quad (3)$$

$$\frac{dh}{dt}=\left(\frac{e^{(V+50)/15}+e^{-(V+50)/16}}{30}\right)\left(\frac{1}{1+e^{(V+50)/7}}-h\right) \quad (4)$$

$$\frac{dn}{dt}=\left(\frac{e^{(V+40)/40}+e^{-(V+40)/50}}{7}\right)\left(\frac{1}{1+e^{-(V+23)/15}}-n\right) \quad (5)$$

$$\frac{dr}{dt}=\left(\frac{e^{(V+140)/21.6}+e^{-(V+40)/22.7}}{6,000}\right)\left(\frac{1}{1+e^{(V+83.9)/7.4}}-r\right) \quad (6),$$

Here, I_{app} (μA/cm^2), τ_z (ms), and τ_u (ms) are system parameters of the present investigation: I_{app} is the externally injected current, and τ_z and τ_u are time constants of activation of the M-type K^+ and AHP-type K^+ conductances, respectively. Detailed explanations of the equations (1)–(6) are provided in [3, 4]. A simulation example is also described on the website: https://senselab.med.yale.edu/ModelDB/ShowModel.cshtml?model=127022.

Equations (1)–(6) are solved numerically using a free and open source software Scilab (http://www.scilab.org/) using the following initial conditions: $V = -65.84$ mV, z=0.00040176, u = 0.00040176, h = 0.92141213, n = 0.0497938, and r = 0.095137881.

3 Numerical Results

The present study focuses on three dynamical states of the vMN model: the subthreshold oscillation, mixed-mode oscillation, and tonic firing states. Figure 1 shows examples of the time course of the membrane potential of the vMN model. In the subthreshold oscillation state, the membrane potential oscillation of a small amplitude is observed (Figure 1A). In the mixed-mode oscillation state, the alternation of a large-amplitude spike and small-amplitude oscillations occurs (Figure 1B). The tonic firing state involves repetitive large-amplitude repetitive spiking (Figure 1C).

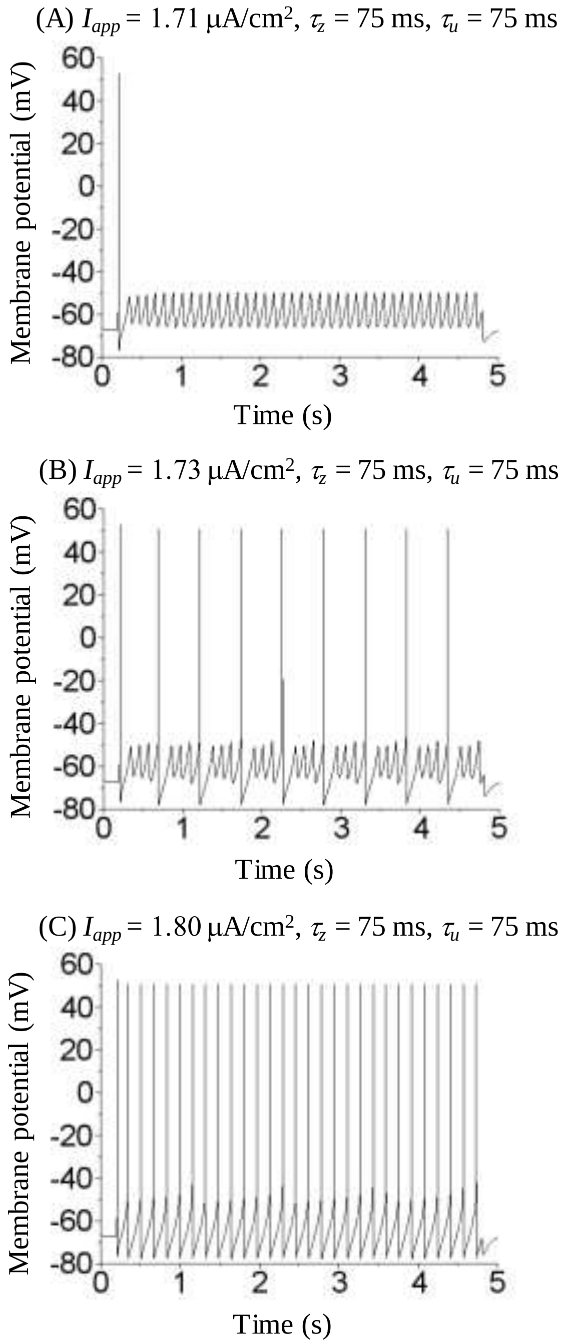

Figure 1. Time courses of the membrane potential of the vMN model. (A) I_{app} = 1.71 μA/cm^2, τ_z = 75 ms, and τ_u = 75 ms. (B) I_{app} = 1.73 μA/cm^2, τ_z = 75 ms, and τ_u = 75 ms. (C) I_{app} = 1.80 μA/cm^2, τ_z = 75 ms, and τ_u = 75 ms.

Next, we investigate how these dynamical states are regulated by system parameter changes. When τ_z is between 73 ms and 77 ms, an increase in I_{app}, with τ_z fixed at a specific value, changes the dynamical state of the vMN model: subthreshold oscillation state → a mixed-mode oscillation state → a tonic firing state (Figure 2A). In addition, an increase in the τ_z value induces a decrease in the upper and lower limits of I_{app}, wherein a mixed-mode oscillation state appears (i.e., the upper and lower limits decrease from 1.82 → 1.77 → 1.73 μA/cm^2 and 1.74 → 1.73 → 1.72 μA/cm^2, respectively). Given that the degree of the decrease in the upper limit is larger than that of the lower limit, the I_{app} range, in which a mixed-mode oscillation state appears, decreases with τ_z. When τ_u is between 73 ms and 77 ms, an increase in I_{app} with τ_u fixed at a specific value, changes the dynamical state of the vMN model: subthreshold oscillation state → a mixed-mode oscillation state → a tonic firing state (Figure 2B).

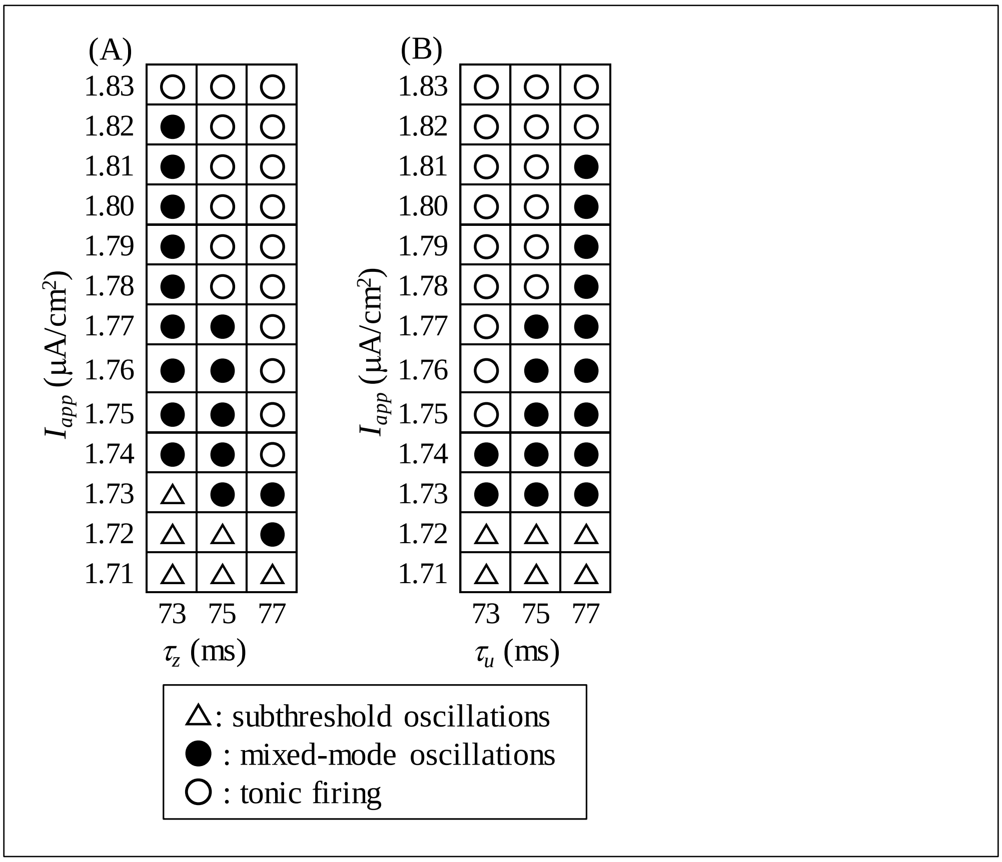

Figure 2. Dependence of the dynamical states of the vMN model on I_{app}, τ_z, and τ_u. (A) Dynamical states in the (I_{app}, τ_z) parameter space. (B) Dynamical states in the (I_{app}, τ_u) parameter space. △ indicates a subthreshold oscillation state, ●indicates a mixed-mode oscillation state, and ○ indicates a tonic firing state.

In addition, an increase in τ_u value increases the upper limit of I_{app} at which a mixed-mode oscillation state appears (i.e., the upper limit increases from 1.74 → 1.77 → 1.81 μA/cm^2), whereas it neither increases nor decreases the lower limit of I_{app}, at which a mixed-mode oscillation state emerges (i.e., the lower limit is 1.73 μA/cm^2, irrespective of the τ_u value). Therefore, the I_{app} range, wherein a mixed-mode oscillation state appears, increases with τ_u.

4 Conclusion

The present study reveals how the I_{app} range which the vMN model shows mixed-mode oscillation, is modulated by τ_z and τ_u. A previous study focused on the relationship between the I_{app} range and the characteristics of the ionic conductance of the vMN model. For example, an increase in the maximal value of the cationic h conductance increases the I_{app} range [4]. However, the previous study did not clarify whether the time constant of the ionic conductance of the vMN model affects the I_{app} range. An important contribution of the present investigation is that it can resolve this problem: an increase in the time constant values changes the I_{app} range (Figure 2). Another study focused on the difference between the M-type K^+ and AHP-type K^+ conductances. The difference was revealed by investigating the suprathreshold resonance response to sinusoidal inputs: changing the maximal value of the M-type K^+ conductance can modulate the maximal input frequency value for which the vMN model can spike, whereas changing the maximal value of the AHP-type K^+ conductance cannot modulate it [3]. However, the results of this study cannot answer whether changing the time constant values have an effect on the vMN model between τ_z and τ_u. Another important contribution of the present study is that it can determine why an increase in τ_z decreases the I_{app} range, whereas an increase in τ_u increases the I_{app} range (Figure 2). The results of the present study contribute to a better understanding of the relationship between the kinetics of potassium conductances and mixed-mode oscillation of the vMN model.

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