Eur. Phys. J. Special Topics **227**, 767–776 (2018)

https://doi.org/10.1140/epjst/e2018-700140-1

THE EUROPEAN PHYSICAL JOURNAL SPECIAL TOPICS

Regular Article

Effects of temperature and electromagnetic induction on action potential of Hodgkin–Huxley model

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Received 26 December 2017 / Received in final form 15 March 2018
Published online 19 October 2018

Abstract. Based on an improved the Hodgkin–Huxley (HH) neuron model which is driven by the electromagnetic induction, the effects of temperature and electromagnetic induction on the action potential of neuron are investigated by numerical computations. It is very interesting that, under the fixed condition of electromagnetic induction, there is a region for the electrical activity of neuron in the external current and temperature parameters plane, the region of electrical firing is similar to the Arnold' tongue-like structure, and the Arnold' tongue originates from the nonlinear variation of temperature with the increasing of threshold external current. The effects of temperature and electromagnetic induction on neuronic electrical activity are respectively discussed by using numerical simulations. Our results provide new insights into the roles of temperature in the improved HH neuron model, the existence of Arnold' tongue-like structure might give some insights for the treatment of neurological diseases such as the epilepsia.

1 Introduction

The electrical behaviors are playing an important role in the activities of neuron system. It is known that intrinsic mechanisms, such as the permeability, intrinsic noise, the distribution of ion channels, can lead to the electrical response, in addition, the effect of other external factors (such as the weak periodic signal, external current, various noises, environmental temperature) on neural activity have been surveyed in previous works [1–9].

As an unignorable factor in neural systems, temperature is known to modulate ion channel kinetics and hence generate the action potential. In previous works, these studies [10,11] of ion channels and biological membranes have been carried out at constant temperature, that is, $T = 6.3\,^{\circ}\mathrm{C}$. However, the environmental temperature, one of the most important factors to neural activities, affects the neuronal excitability by regulating the conductance and gating kinetics of ion channels [12,13]. Related

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theoretical work had been surveyed in previous works. For instance, the effects of temperature acclimation on a central neural circuit and its behavioral output was studied in reference [14]. The neuronal intrinsic excitability was studied when the neuron is subject to varying environmental temperatures in reference [15]. Temperature dependent conformational changes in a voltage gated potassium channel was investigated in reference [16]. Benndorf et al. [17] investigated sodium ion channel in myocardium under the different temperature, it was found that the opening time of the channel is greatly increased when the temperature is reduced by 15 °C. Furthermore, the experimental researches were outlined, the effect of temperature on the electrical activity of the giant axon of squid had been researched by Hodgkin and Katz [18] in previous work. Gorman et al. [19] examined the temperature dependence of the membrane potential of a molluscan giant neurone under conditions which block the electrogenic activity of the Na^+–K^+ exchange pump. Micheva and Smith [20] examined the effects of temperature on presynaptic function in primary cultures of rat hippocampal neurons, and these results showed that there are very substantial differences in synaptic vesicle recycling at physiological temperature as opposed to the common, lower experimental temperatures. Hyun et al. [21] performed experiments using Aplysia' neurons to identify the mechanism underlying the changes in the firing patterns in response to temperature changes. Some of works have been applied in the treatment of human diseases [22–27]. The researches of single neural and neural networks involve a wide range with many real physiological systems, for instance, the theoretical [28–34] and experimental [35–37] researches have been applied to the nervous systems or the biomedicine such as the treatment of neurological diseases.

In addition, as another nonnegligible factor, electromagnetic induction [38] is playing an important role in neuron system. As it can be known, the fluctuation or changes in action potentials in neurons can generate magnet field in the media. So electrical activity will be modulated by feedback effect in the neuron. That is, the fluctuation of membrane potential can alter the distribution of electromagnetic field in neuronic cell membrane. Therefore, the effect of electromagnetic induction on membrane potential should be considered in neuron system [39,40], then the related theoretical discussion had been investigated in subsequent works [41,42]. Here we introduce a related technology called transcranial magnetic stimulaton (TMS) [43], which operates on the principle of electromagnetic induction. TMS is a painless, non-invasive, green treatment, it use magnetic field to induce electric field, and generate electrovital currents in organization. This technology can change the action potential in cortical cell, which affects brain metabolism and neuronal activity [44,45]. The experimental results showed that TMS is effective in the treatment of depression, such as parkinson and epilepsy. This is the most favorable proof that electromagnetic induction is applied to the neuron experiments.

In this paper, based on the Hodgkin–Huxley (HH) neuron model, the effects of temperature on action potential are investigated in single neuron when the electromagnetic induction are considered. In order to study the effects of temperature on the neuron system under electromagnetic induction, we consider the effects of both temperature and electromagnetic induction by computing the mean inters-pike interval (ISI) and the mean duration of spikes.

2 Models and methods

The HH model describes the spiking behavior and especial properties of real neurons [46,47]. According to electromagnetic induction, frequent discharge and fluctuation in membrane potentials can generate distribution of electromagnetic field. Therefore, based on the mean field theory and application of memristor, a modified HH neuronal model was proposed [48,49]. The membrane equation of the improved HH neuron model that was introduced additive variable as magnet flux is described as follow:

$$\frac{dV_m}{dt} = \frac{1}{C_m}\Big[g_K n^4(V_K - V_m) + g_{Na}m^3h(V_{Na} - V_m) + g_L(V_L - V_m) \\ -k\rho(\varphi)V_m + I_{\text{ext}}\Big], \tag{1}$$

$$\frac{dy}{dt} = \alpha_y(1-y) - \beta_y y, \quad (y = n, m, h), \tag{2}$$

$$\frac{d\varphi}{dt} = k_1 V_m - k_2\varphi. \tag{3}$$

In fact, the dynamics of membrane potential is driven by five nonlinear coupled equations, including one for the membrane potential V_m, three for gating variables (n, m, h), and the last one for magnetic flux φ. Where magnetic flux φ is used to describe the effect of electromagnetic induction, k_1V_m, and $k_2\varphi$ describe the membrane potential-induced change on magnet flux and leakage of magnet flux, respectively. The term $k\rho(\varphi)V_m$ is the feedback current on the membrane potential induced by electromagnetic induction

$$k\rho(\varphi)V_m = i' = dq/dt, \quad \rho(\varphi) = a + 3b\varphi^2, \tag{4}$$

the parameters are selected as $a = 0.4$, $b = 0.02$, and $k_2 = 0.01$. Parameter k is feedback gain associated with the media, C_m is capacitance of membrane. Here we want to underline two parameters (k, k_1), the intensity of electromagnetic induction rest on the value of these parameters.

Different from previous studies, we consider that the electrical activity is not only manipulated by changing the electromagnetic induction, but also depend on the variation of temperature of the environment in which neurons are located. Thus the temperature factor is lead into the open and closing rate of ion channel:

$$\alpha_n = \frac{0.01\phi(T)(V_m + 55)}{1 - \exp[-(V_m + 55)/10]}, \tag{5}$$

$$\beta_n = 0.125\phi(T)\exp[-(V_m + 65)/80], \tag{6}$$

$$\alpha_m = \frac{0.1\phi(T)(V_m + 40)}{1 - \exp[-(V_m + 40)/10]}, \tag{7}$$

$$\beta_m = 4\phi(T)\exp[-(V_m + 65)/18], \tag{8}$$

$$\alpha_h = 0.07\phi(T)\exp[-(V_m + 65)/20], \tag{9}$$

$$\beta_h = \frac{\phi(T)}{1 + \exp[-(V_m + 35)/10]}, \tag{10}$$

with

$$\phi(T) = 3^{(T-6.3\,^\circ\mathrm{C})/10\,^\circ\mathrm{C}}, \tag{11}$$

and α_n and β_n are the opening and closing rates of K^+ channel, α_m and β_m are the opening and closing rates for the activation gates of Na^+ channel, α_h and β_h are the opening and closing rates for the inactivation gates of Na^+ channel, respectively.

The values of other parameters are $C_m = 1\,\mu$ F/cm^2, $V_K = -77$ mV, $g_K = 36$ mS/cm^2, $V_{Na} = 50$ mV, $g_{Na} = 120$ mS/cm^2, $V_L = -54$ mV, $g_L = 0.3$ mS/cm^2, the detailed meanings of these parameters can be found in reference [50]. In addition, nonlinear coupled equations are integrated by using a fourth-order Runge–Kutta algorithm with a time step of 0.001. In each calculation the time evolution of the system lasted 100 000 time units after transient behaviour was discarded.

3 Numerical results and discussions

3.1 The effects of temperature on neuronic electrical activity

In this section, the effects of temperature on neuronic electrical activity are investigated, the results show that under confirmed electromagnetic induction, electrical activities of neuron appear an obvious boundary with different external currents and temperatures. In order to study the response of neuron to external stimuli, we consider the compositive effects of the external current and temperature on the neuron system. Figure 1 shows mean inters-pike interval in external current I_{ext} and temperature parameter T plane.

From Figure 1, when the intensity of electromagnetic induction is fixed, it is found that electrical activities of neuron appear an obvious boundary with different external currents and temperatures. The mean inters-pike interval of black areas is zero. When the external current I_{ext} is less than 5.20 mA, the discharge state of electrical activity has not a correlation with the temperature. Between $I_{\mathrm{ext}} = 5.20$ mA and 29.0 mA, threshold external current I_{ext} which change the neuron condition from quiescent state to spiking state will increase nonlinearly with the increasing of temperature. However, when I_{ext} is between 29.0 mA and 70.0 mA, the mean inters-spike intervals show different behavior: threshold external current I_{ext} will reduce nonlinearly with the increasing of temperature. It is very interesting that the region of electrical firing is similar to Arnold' tongue. The Arnold' tongues were generally found in coupled nonlinear oscillators such as the model of intercellular calcium oscillations in hepatocytes [51,52].

In order to observe this phenomena in Figure 1 clearly, the detailed depicts of different parameters (threshold I_{ext} vs. different temperature; different temperature vs. threshold I_{ext}) are plotted in Figure 2. The curved line is drawn as a guide to discriminate the different states approximately on the boundary between quiescent state and spiking state. It can be found that the Arnold' tongue-like structure as shown in Figure 1 comes from the variation of temperature with the increasing of threshold external current.

According to the data simulation and analysis, we know that the temperature plays an important role in neuron electrical activity. In order to observe the effects of different temperatures on neuron temporal evolution, our samples ($T = 0.3, 10.3, 16.3, 22.3\,^\circ$C) were plotted in Figure 3. With increasing of the temperature, temporal evolution of membrane potentials appear an obvious transformation: the amplitude decrease greatly, the frequency increase substantially.

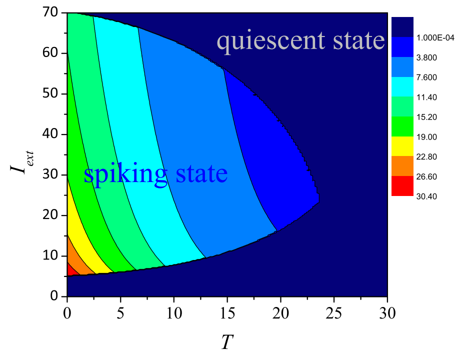

Fig. 1. The modes of action potential of neuron driven by electromagnetic induction ($k = 0.01$ and $k_1 = 0.001$) in the external current I_{ext} and temperature parameter T plane.

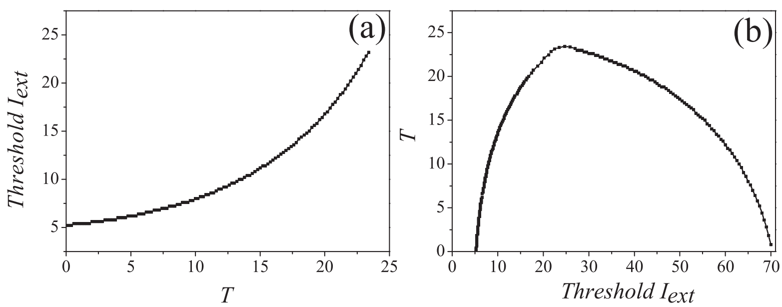

Fig. 2. (a) Threshold I_{ext} vs. different temperature and (b) temperature vs. different threshold I_{ext}. $k = 0.01$ and $k_1 = 0.001$.

This phenomena show that electrical activity is largely attributed to the variations in temperature.

In the previous experiment of the effect of sodium ions on action potentials in the fiber of squid [53], it was demonstrated that the rise of temperature reduced the duration of spike of membrane potential. As seen from Figure 4a, we have plotted the mean duration of spikes as a function of temperature for $I_{\text{ext}} = 20.0$ mA under the fixed electromagnetic induction. Where the duration of spikes is defined as the time from the membrane potential exceeded 0 to -20 mV in a spike. Mean duration of spikes is decreased nonlinearly with the path temperature, which is consist with the experiment results. The behavior at $T = 24.0\,^{\circ}$C, there is a transition of electrical activity mode, and the mode change from the spiking state to quiescent state.

In addition, the bifurcation diagram of membrane potential under different temperature is plotted in Figure 4b. One can notice that this diagram shows the steady states and oscillatory solutions as well as their stabilities, with the increment of T, the neuron undergoes a Hopf bifurcation point at $T \approx 27.5\,^{\circ}$C. It is shown that the increase of temperature T level gives rise to membrane potential oscillations, and that the membrane potential is reduced with the temperature T stimulation level increasing.

3.2 The effects of electromagnetic induction on neuronic electrical activity

In this section, the effects of electromagnetic induction on neuronic electrical activity are investigated. The results show that electromagnetic induction can suppress neuronal firing behavior. Consider the influence of electromagnetic induction, this

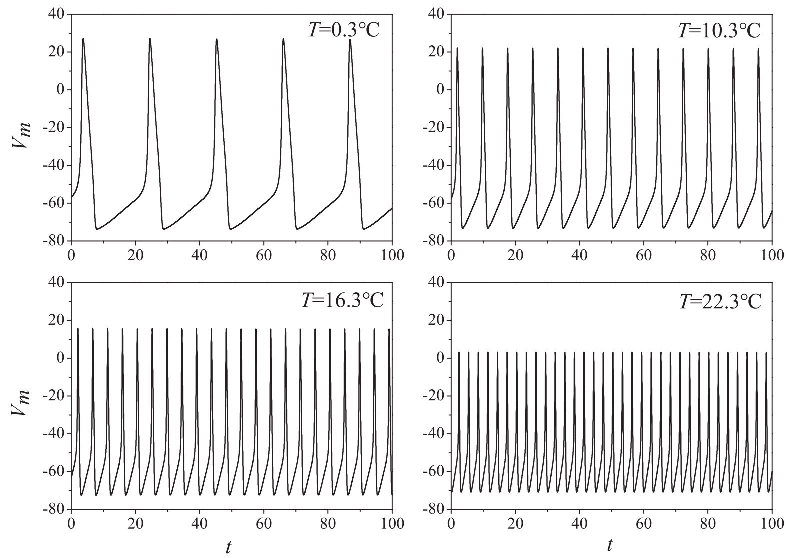

Fig. 3. Temporal evolution of transmembrane potentials for different temperature at $k = 0.01$, $k_1 = 0.001$, and $I_{\mathrm{ext}} = 20.0$ mA.

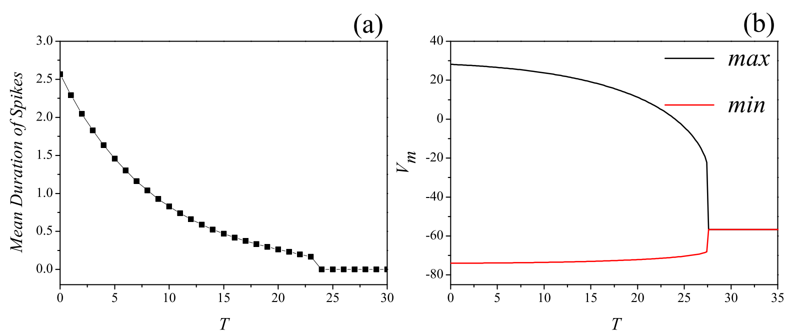

Fig. 4. The parameters is selected as $I_{\mathrm{ext}} = 20.0$ mA, $k = 0.01$, $k_1 = 0.001$. (a) Mean duration of spikes and (b) bifurcation diagram vs. different temperature T.

section contemplates the effects of temperature on membrane potential under the different electromagnetic inductions. Mean ISI as a function of temperature for different electromagnetic inductions is surveyed in Figure 5, and the mean ISI is defined as the average of time intervals between adjacent peaks of the pulses when membrane potential exceed 0 mV. In Figure 5, the black line represents mean inter-spike interval without electromagnetic induction; the red line represents the one under the weak electromagnetic induction for $k = 0.01$ and $k_1 = 0.001$, and the blue line represent another one under the strong electromagnetic induction for $k = 0.3$ and $k_1 = 0.001$.

When the different electromagnetic inductions are imposed in the neuron, the oscillations show surprising behavior. With the increasing of temperature for each graph, it is apparent that, for small values of temperature, electrical activity of neuron is found in a spiking state and mean ISI reduced. After increasing temperature beyond some threshold value, mean ISI is zero, it means that the neuron is quiescent state. Therefore, the mode in electrical activities of neuron undergoes a transition from the spiking state to the quiescent one. That is, the mode in electrical activities of neuron undergoes a succession of two transitions (spiking state → quiescent state).

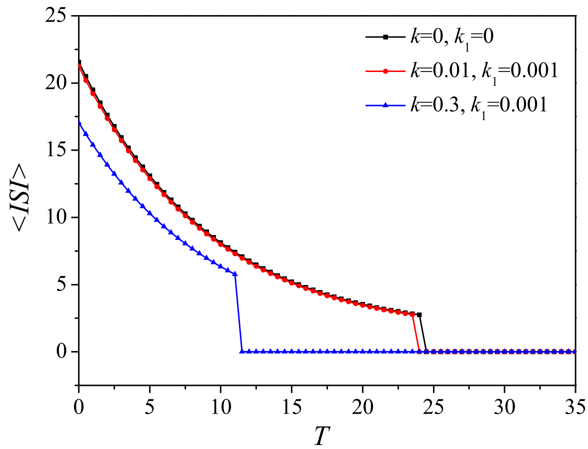

Fig. 5. Mean inter-spike interval (ISI) as a function of temperature T for different electromagnetic induction (k, k_1) at $I_{\mathrm{ext}} = 20.0$ mA.

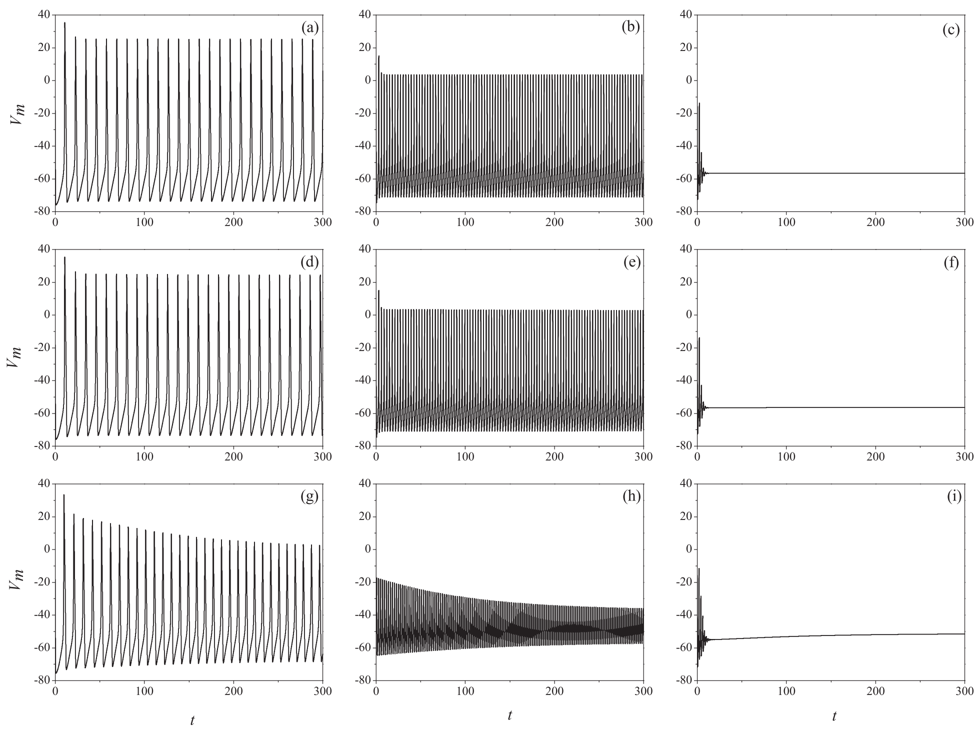

Fig. 6. Temporal evolution of transmembrane potentials for different temperature (from left to right: $T = 6.3$, 22.3, $28.3\,^{\circ}$C) and different electromagnetic inductions. Top row: $k = 0$ and $k_1 = 0$; middle row: $k = 0.01$ and $k_1 = 0.001$; bottom row: $k = 0.3$ and $k_1 = 0.001$.

In addition, the results surface that stronger electromagnetic induction will make the neuron transit from spiking state to quiescent state in a low temperature condition. The neuron without electromagnetic induction (black line), threshold T is $24.0\,^{\circ}$C; under the small electromagnetic induction (red line), threshold T is $23.5\,^{\circ}$C; under the big electromagnetic induction (red line), threshold T is $11.5\,^{\circ}$C. The small change of electromagnetic induction has great influence on threshold T, in addition,

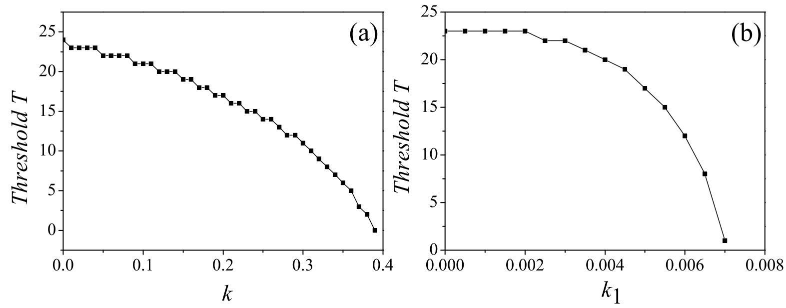

Fig. 7. The bifurcation diagram against different parameters at $I_{\text{ext}} = 20.0$ mA. (a) The bifurcation diagram vs. different feedback k in the induced current $k\rho(\varphi)V_m$ for $k_1 = 0.001$; (b) the bifurcation diagram vs. magnet flux k_1 in the membrane potential induced changes $k_1 V_m$ for $k = 0.01$.

if the feedback gain parameter k is bigger than 0.38, no matter how the temperature changes, the neuron is always at quiescent state. The threshold T is defined as the state transition point from spiking state to quiescent state. These data strongly imply that the mean inter-spike interval of membrane potential can be largely attributed to the electromagnetic induction.

In order to expound this phenomena in Figure 5, the temporal evolution of transmembrane potentials for different temperature is shown under the different electromagnetic inductions in Figure 6. Without electromagnetic induction, the electrical activity is spiking state under temperature is 6.3 and 22.3 °C, the electrical activity is quiescent state under $T = 28.3$ °C; when small electromagnetic induction is imposed in the neuron, the electrical activity is spiking state under temperature is 6.3 and 22.3 °C, another one is quiescent state under $T = 28.3$ °C; when big electromagnetic induction is imposed in the neuron, the electrical activity is spiking state under temperature is 6.3 °C, the membrane potential oscillate below threshold under $T = 22.3$ °C, and another one is quiescent state under $T = 28.3$ °C. These results are consistent with Figure 5.

To understand the effect of electromagnetic induction on membrane potential at different temperature, it is useful to examine the different state of electrical activity in more detail. Where we use the threshold T as a judgment sign to distinguish the different states, Figure 7 illustrates that, with the increasing of electromagnetic induction, threshold temperature which make neuron change from action potential to quiescent condition will reduce nonlinearly. The value of two parameters (k, k_1) represent the intensity of electromagnetic induction, the feedback gain k change from 0.0 to 0.4, and the magnet flux k_1 change from 0.0 to 0.008. It is found that the threshold T is decreased gradually with increasing of two parameters.

Furthermore, the bifurcation diagram of membrane potential as a function of different electromagnetic inductions is surveyed in Figure 7. One can notice that with the increment of feedback k, the neuron undergoes a Hopf bifurcation point at $k \approx 1.14$, meanwhile, the neuron undergoes a bifurcation at $k_1 \approx 0.0125$ with the increment of magnet flux k_1. It is evidence that the increase of parameters (k, k_1) level gives rise to membrane potential oscillations, and the membrane potential is reduced with the parameters (k, k_1) level increasing. In the meantime, this results indicate that the intensity of electromagnetic induction can affect the electrical activity in neuron under the fixed temperature $T = 15$ °C and external current $I_{\text{ext}} = 20.0$ mA. It is surprising that electromagnetic induction can suppress neuronal firing behavior, when the intensity of electromagnetic induction is larger than some threshold value, the membrane potential suspends oscillation and electric activity is at quiescent condition.

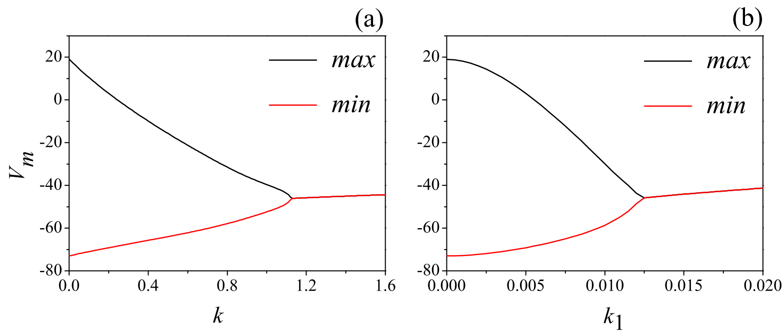

Fig. 8. The bifurcation diagram against different parameters at $I_{\text{ext}} = 20.0$ mA. (a) The bifurcation diagram vs. different feedback k in the induced current $k\rho(\varphi)V_m$ for $k_1 = 0.001$; (b) the bifurcation diagram vs. magnet flux k_1 in the membrane potential induced changes $k_1 V_m$ for $k = 0.01$.

4 Conclusions

In conclusion, under the fixed condition of electromagnetic induction, it is interesting to note that the above behaviour of neuron system for temperature and electromagnetic induction. Under the fixed condition of electromagnetic induction, it is found that there is a region for the electrical activity of neuron in the external current and temperature parameters plane, and the region of electrical firing is similar to the Arnold' tongue-like structure. The Arnold' tongue structure comes from the nonlinear variation of temperature with the increasing of threshold external current.

The effects of temperature on neuronic electrical activity are surveyed under the fixed electromagnetic induction, here the results show that electrical activities of neuron appear an obvious boundary with different external currents and temperatures. As the temperature increases, the amplitude and frequency of electrical activity have an obvious transformation, this phenomena show that electrical activity is largely attributed to the variations in temperature. Furthermore, the effects of electromagnetic induction on neuronic electrical activity are featured in this paper, the changes of membrane potential show a surprising behavior: under the fixed temperature, stronger electromagnetic induction will make the neuron transit from spiking state to quiescent state in a low temperature condition. It is surprising that electromagnetic induction can suppress neuronal firing behavior, when the intensity of electromagnetic induction is larger than some threshold value, the membrane potential suspends oscillation and electric activity is at quiescent condition. This theoretical analysis for the effects of temperature on nonlinear excitable system under electromagnetic induction provide further insights on the study of neurological diseases.

It is well known that hot weather can increase the incidence of epilepsy [54], reference above theory results, both the temperature and the electromagnetic induction effects might be used to reduce the morbidity. In addition, experiment circuit simulation might applied to this improved HH neuron model when the temperature and electromagnetic induction are considered. In order to simulate the temperature factor in the neuron, a miniature temperature regulating chamber could be built to control the temperature, one could consider the silica calefaction slice in the patch clamp, and obtain the effects of temperature on membrane potential by calculating and analysing the signal data.

This work was supported by the National Natural Science Foundation of China under Grant Nos. 11775091 and 11474117.

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