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Dynamics of spike threshold in a two-compartment neuron with passive dendrite

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ABSTRACT

Here a two-compartment model is used to investigate how spike threshold depends on the rate of membrane depolarization leading to the action potential, i.e., dV_S/dt. The model is comprised of a soma and a passive dendrite, and incorporates a morphological parameter that describes the area proportion occupied by soma. The threshold potential of somatic chamber is determined within a range of dV_S/dt for different values of morphological parameter and internal coupling conductance. By analyzing the interactions of inward and outward membrane currents prior to spike initiation, the biophysical basis associated with each threshold dynamic has been identified. Based on the simulations, we conceptualize the threshold dynamics of neuron as the outward level of somatic net current at the perithreshold potentials. These results provide a detailed description about how the morphology and biophysics of neurons participate in their threshold dynamics, which could facilitate to interpret the modulatory mechanism of subthreshold electromagnetic fields as well as the biophysical basis of neural coding.

1. Introduction

Nowadays, weak electric or magnetic fields have been widely used to treat a number of neuropsychiatric and pain disorders as well as to study cognitive, plasticity and memory in healthy subjects [1–4], which indicates that they have the capability of modulating brain activity and function. The weak fields applied only polarize neuronal membrane by a small amount [5–7], which are traditionally categorized as subthreshold stimulation [1,8,9]. Although their magnitude is usually not sufficient to directly elicit action potentials, these subthreshold fields could influence the excitability level of active neuron, and modulate its spike timing and firing rate to additional inputs, especially the former. Experiments [6,8,10] have identified that the modulatory effects induced by weak fields are governed by neuronal morphology, which are also confirmed by our recent theoretical study with biophysical model [11]. However, the fundamental question that how subthreshold field interacts with the ongoing activity of active neuron is still unclear.

Neurons, as the basic unit for information processing in the central nervous system, could accurately represent various spatiotemporal patterns of sensory input. They use sequences of action potential or spike as the principal carrier to transmit and integrate signals [12,13]. The generation of spike train is not only dependent on presynaptic input, but also tightly related to the critical value of membrane potential, i.e., spike threshold. Only when membrane potential exceeds this threshold level, action potential can be initiated in the neuron. This special membrane potential is not fixed but dynamic [14–17], which varies with the firing history of neuron, especially the rate of membrane depolarization prior to spike initiation, i.e.,

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dV_S/dt. In many neurons, it is sensitive to the preceding dV_S/dt, and there is an inverse relationship between them [14–24]. Such dynamics of spike threshold is critically important in the process of encoding presynaptic inputs by a neuron [18], which allows it to filter out incoming signals and effectively contributes to the precise temporal coding to suprathreshold stimulus [17,25]. Then, investigating the mechanism that underlies the interaction between threshold dynamics and weak field is crucial for understanding how subthreshold field modulates the ongoing activity of active neuron. To address this problem, it requires the knowledge of threshold dynamics in the absence of weak field. Such as, how does spike threshold depend on dV_S/dt in different neurons? How does the morphology of neuron affect its threshold dynamic? What is the relevant biophysical mechanism?

There are two possible biophysical mechanisms that contribute to regulate the dynamics of spike threshold. One of them is the inactivation of inward Na^+ current [14–16,18,19,26], which is gradually accumulated during the upstroke of action potential. It is commonly considered as the fundamental mechanism of threshold modulation, since Na^+ inactivation specifically impacts spike initiation without affecting membrane potential [14]. The other one is the activation of outward K^+ currents, especially those activated at the subthreshold potentials [17,18,27–30]. Recent experiments [17,27–30] find that some low-threshold K^+ currents, such as Kv1 channels or D-current, prominently regulate spike threshold and further modulate neural excitability. Blocking them with α-DTX could result in a loss of the inverse relation between threshold and dV_S/dt in auditory brainstem [24] or layer 2/3 cortex pyramidal neurons [17].

Apart from above experiments, there are also theoretical investigations of spike threshold with computational models. In earlier studies [31–35], researchers mainly focus on the connection between voltage threshold and neuronal excitability, while do not involve the threshold dynamics dependent on dV_S/dt. Recently, Wester and Contreras [18] use a three-compartment biophysical model to systematically investigate the role of K^+ and Na^+ current (i.e., voltage-dependency or kinetics) in regulating spike threshold as a function of dV_S/dt. They find that Na^+ inactivation is sufficient to produce dynamic threshold provided it occurs at hyperpolarized voltages combined with slow kinetics; alternatively, hyperpolarizing K^+ activation voltage, even in the absence of Na^+ inactivation, is also sufficient to produce a dynamic threshold sensitive to the preceding dV_S/dt. With a Morris–Lecar like single-compartment model, we have recently investigated the threshold dynamics in Type I and Type II neurons [36]. It is found that Type II threshold is more depolarized and more sensitive to dV_S/dt than Type I, which arises from the different activations of outward K^+ current at the subthreshold potentials. Moreover, we have also characterized the input–output relation and energy efficiency associated with different threshold dynamics [37]. However, there are still no experimental or modeling studies with regard to how the morphological feature of neuron affects its threshold dynamics.

Here we adopt a reduced two-compartment model with passive dendrite to solve this problem. The model is first proposed in our previous study [11,38] to explore the neuromodulatory effects of extracellular electric field, which incorporates a morphological parameter that describes the area proportion occupied by soma. With this reduced model, we have found that the modulations of spike timing and firing rate with subthreshold fields are dependent on morphological parameter and internal coupling conductance [11]. Thus, in the following we mainly investigate how these two parameters affect the threshold dynamics of neuron in the case of saddle-node on invariant cycle (SNIC) or Hopf bifurcation. Further, their relevant biophysical basis is also identified by analyzing the interactions of inward and outward membrane currents at the perithreshold potentials.

2. Model and methods

2.1. Two-compartment neuron model

A schematic representation of our reduced two-compartment neuron [11,38] is shown in Fig. 1(a). The model is comprised of a somatic and a dendritic compartment, which are connected by an internal coupling conductance g_c. Their membrane potential V_S and V_D are governed by the following current-balance equations [11]

$$\begin{aligned} C\frac{dV_S}{dt} &= \frac{I_S}{p} - \frac{I_{SD}}{p} - I_{Na} - I_K - I_{SL} \\ C\frac{dV_D}{dt} &= \frac{I_D}{1-p} + \frac{I_{SD}}{1-p} - I_{DL} \end{aligned} \tag{1}$$

where $C = 2\ \mu F/cm^2$ is the membrane capacitance. The somatic chamber contains three ionic currents, i.e., inward Na^+ current $I_{Na} = \bar{g}_{Na} m_\infty(V_S)(V_S - E_{Na})$, outward K^+ current $I_K = \bar{g}_K w(V_S - E_K)$, as well as outward leakage current $I_{SL} = g_{SL}(V_S - E_{SL})$. The former two active currents, i.e., Na^+ and K^+, are necessary to reproduce somatic action potentials. There is only a passive leakage current $I_{DL} = g_{DL}(V_D - E_{DL})$ in dendrite. $I_{SD} = g_c(V_S - V_D)$ is the internal current flowing from soma to dendrite, which couples two chambers. I_S and I_D are stimulus current injected into each compartment. $E_{Na} = 50$ mV and $E_K = -100$ mV are the reversal potentials of Na^+ and K^+ currents on somatic membrane, $E_{SL} = -70$ mV and $E_{DL} = -70$ mV are the reversal potentials of somatic and dendritic leakage currents. $\bar{g}_{Na} = 20\ mS/cm^2$, $\bar{g}_K = 20\ mS/cm^2$, $g_{SL} = 2\ mS/cm^2$ and $g_{DL} = 2\ mS/cm^2$ are their corresponding maximum conductance. p and $1 - p$ are morphological parameters that respectively describe the area proportion of soma and dendrite in the neuron.