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Research paper

Minimum energy control for a two-compartment neuron to extracellular electric fields

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ABSTRACT

The energy optimization of extracellular electric field (EF) stimulus for a neuron is considered in this paper. We employ the optimal control theory to design a low energy EF input for a reduced two-compartment model. It works by driving the neuron to closely track a prescriptive spike train. A cost function is introduced to balance the contradictory objectives, i.e., tracking errors and EF stimulus energy. By using the calculus of variations, we transform the minimization of cost function to a six-dimensional two-point boundary value problem (BVP). Through solving the obtained BVP in the cases of three fundamental bifurcations, it is shown that the control method is able to provide an optimal EF stimulus of reduced energy for the neuron to effectively track a prescriptive spike train. Further, the feasibility of the adopted method is interpreted from the point of view of the biophysical basis of spike initiation. These investigations are conducive to designing stimulating dose for extracellular neural stimulation, which are also helpful to interpret the effects of extracellular field on neural activity.

1. Introduction

Extracellular neural stimulation [1–6] has been used in clinics for the treatment or rehabilitation of various neuropsychiatric disorders for decades. Meanwhile, it is also widely applied in fundamental researches to study the stimulus-dependent dynamics and plasticity of neuronal system. Common techniques include, but are not limited to, deep brain stimulation (DBS), cochlear implant, cardiac pacemaker, retinal implant, and spinal cord stimulation. One major advantage of them over medication or surgery is that they interfere with brain activities in a controlled manner and their effects are reversible. The precise effects of extracellular stimulation are controlled by its dose, such as, the applied waveform, intensity, frequency, polarity, and the electrode configuration parameter. Despite the widespread applications, the dose optimization is still a challenge for this kind of technique [1,6–10]. Without precision in dosing, the real progress in both understanding the mechanism of extracellular stimulation and improving this technique will be limited.

The basic principle of extracellular stimulation is that it generates an extracellular electrical field (EF) around its electrode to stimulate brain tissue and affect ultimate behaviors [5,6,9–13]. Then, identifying how the generated EFs interact with neural activity is crucial to interpret and predict the precise effects of different doses of stimulation. It is well known that the EF will cause a distributed perturbation on neuronal membrane, which results in local depolarization or hyperpolarization in different neuronal segments [13–15]. Such special interactions make it difficult to comprehend the effects of

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stimulation in experiments. To overcome the limitations in experimental approaches, various models are used to describe and predict the response of neuronal segments to extracellular stimulation [5,6,9–11,13]. Meanwhile, some novel strategies have been proposed with modeling approaches to set the stimulating dose (such as, waveform or intensity) to improve the outcomes of stimulation [16–19]. One major index used by them to design the strategies is the energy efficiency of stimulation, since it is directly related to the clinical benefits, the side effects, or the battery lifetime, especially for the implanted devices. The basic principle for choosing an optimal dose of stimulation is that it evokes appropriate neural response with minimal energy consumption and stimulation-induced tissue damage. However, their targets are mostly specific brain nucleus or neuronal populations, while rarely involving single cell. This is due to the lack of a satisfied model describing the complicated interactions between the generated EFs and the dynamics of single neuron.

In fact, investigating neuronal properties and functions from the point of view of energy efficiency has always been the hot issue of common concern in neuroscience. Some of them focus on identifying the metabolic energy consumed by neuronal spiking behaviors as well as their relationships to information coding [20–23]. Beyond that, there are also researches using different control strategies to improve the energy efficiency of stimulus. For instance, Moehlis et al. [24] and Danzl et al. [25] adopted optimization techniques to realize the spike timing control for a given phase-reduced neuron by using input currents with minimal integral of amplitude squared; Ullah and Schiff [26] used Kalman filter to develop a low energy controller, and then applied it to track and control the dynamics of Hodgkin–Huxley (HH) model; Danzl et al. [27] proposed an event-based feedback control to drive a reduced HH model to its phaseless set with a magnitude-constrained stimulus current in the minimum possible time; Ellinger et al. [28] and Koelling et al. [29] presented another optimal control method that enables HH-like models of different dimensions to track a preset reference membrane trajectory under an input current stimuli of low energy; Krouchev et al. [30] proposed a least-action principle to obtain the specific energy-efficient current waveform for a given neuron model; Nabi et al. [31,32] employed optimal control theory to design minimum energy control stimulus for desynchronizing coupled neurons or regulating neuronal inter-spike-intervals.

All above studies aim at the energy optimization of single-compartment neuron model with intracellular current stimuli, but using it to describe how extracellular stimulation interacts with single cell membrane is inappropriate. As already mentioned, the nature of extracellular stimulation is the EFs flowing through neuronal segments in the interested brain tissue. Unlike intracellular current stimuli, the EF has two opposite polarities that can induce spatial polarizations on neuronal membrane [14,15,33]. The membrane near cathode is depolarized and near anode is hyperpolarized. Experimental [14,15,34] and modeling [35–39] studies have shown that the spatial polarizations induced by EF are governed by the morphological features of neuron. These two crucial factors, i.e., spatial polarizations and neuronal morphology, are both missing in the single-compartment model with intracellular current stimulus. Thus, the optimization of stimulus energy for single neuron to extracellular EF is still an open question.

To address this challenge, we first introduce a reduced two-compartment neuron model [37,38] to describe how extracellular EF interacts with neuronal activities in present study. Then, we adopt the optimal control theory to accomplish the objective of driving the neuron to track a preselected spike train with low energy extracellular EF stimuli. The paper is organized as follows. In Section 2, we describe the reduced two-compartment model. Section 3 is used to introduce the optimal method, and Section 4 gives the simulation results. In Section 5, we summarize our results and give the conclusions.

2. Two-compartment neuron model

In vitro experiments [14,15,33,34] have demonstrated that applied EFs can induce spatial polarizations in neuron membrane, as shown in Fig. 1(a). The membrane potential close to EF anode is hyperpolarized, and close to cathode is depolarized. This special polarization depends on the direction of EF relative to somatic-dendritic axis as well as neuronal morphology/biophysics [14,15, 34–39]. The minimal neuronal structure that reflects field-induced polarizations should at least have two spatially separated chambers. Based on Pinsky–Rinzel model, we have proposed a reduced two-compartment model in our previous studies [37,38] to describe how extracellular EF interacts with neuronal activities, which is shown in Fig. 1(b). This reduced two-compartment model can represent EF-induced spatial polarizations, and simultaneously it involves a parameter p that describes neuronal morphology. Both of them are crucial factors for field-induced effects, which are missing in single-compartment neuron with intracellular current stimulus.

The two compartments in our model are dendrite and soma, and their dynamics are controlled by the following equations [37,38]

$$C\frac{dV_S}{dt} = \frac{I_S}{p} + \frac{I_{DS}}{p} - \bar{g}_{Na}m_\infty(V_S)(V_S - E_{Na}) - \bar{g}_K w(V_S - E_K) - g_{SL}(V_S - E_{SL}) \tag{1}$$

$$\frac{dw}{dt} = \varphi\frac{w_\infty(V_S) - w}{\tau_w(V_S)} \tag{2}$$

$$C\frac{dV_D}{dt} = \frac{I_D}{1-p} - \frac{I_{DS}}{1-p} - g_{DL}(V_D - E_{DL}) \tag{3}$$

where V_S and V_D, respectively represent somatic and dendritic membrane voltage. w is the activation variable for K^+ channel in somatic chamber, which characterizes the probability of its activation gate being in the open state. The five terms on