Optimal design of minimum-power stimuli for phase models of neuron oscillators

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(Received 3 November 2010; revised manuscript received 15 February 2011; published 27 June 2011)

In this paper, we study optimal control problems of spiking neurons whose dynamics are described by a phase model. We design minimum-power current stimuli (controls) that lead to targeted spiking times. In particular, we consider bounded control amplitude and characterize the range of possible spiking times determined by the bound, which can be chosen sufficiently small within the range where the phase model is valid. We show that for a given bound the corresponding feasible spiking times are optimally achieved by piecewise continuous controls. We present analytic expressions with numerical simulations of the minimum-power stimuli for several phase models. We demonstrate the applicability of our method with an experimentally determined phase response curve.

DOI: 10.1103/PhysRevE.83.061916 PACS number(s): 87.19.lr, 87.19.ll, 02.30.Yy

I. INTRODUCTION

Control of neurons and hence the nervous system by external current stimuli (controls) has received increased scientific attention in recent years for its wide range of applications from deep brain stimulation to oscillatory neurocomputers [1–3]. Conventionally, neuron oscillators are represented by phase-reduced models, which form a standard nonlinear system [4,5]. Intensive studies using phase models have been carried out, for example, on the investigation of the patterns of synchrony that result from the type and architecture of coupling [6,7] and on the response of large groups of oscillators to external stimuli [8,9], where the inputs to the neuron systems were initially defined and the dynamics of neural populations were analyzed in detail.

Recently, control theoretic approaches have been employed to design external stimuli that drive neurons to behave in a desired way. For example, a multilinear feedback control technique has been used to control the individual phase relation between coupled oscillators [10] and geometric control theory has been adopted to study controllability and optimal control of a network of neurons with different natural oscillation frequencies [11]. There has been an increase in the demand for controlling not only the collective behavior of a network of oscillators but also the behavior of each individual oscillator. It is feasible to change the spiking periods of oscillators or tune the individual phase relationship between coupled oscillators by the use of electric stimuli [10,12]. Minimum-power stimuli that elicit spikes of a neuron at specified times close to the natural spiking time were analyzed [8]. Optimal wave forms for the entrainment of weakly forced oscillators that maximize the locking range have been calculated, where first and second harmonics were used to approximate the phase response curve (PRC) [13]. These optimal controls were found mainly based on the calculus of variations, which restricts the optimal solutions to the class of smooth controls, and the bound of the control amplitude was not taken into account.

In this paper, we apply techniques from optimal control theory to derive minimum-power controls that spike a neuron at desired time instants. We consider bounded control amplitude and fully characterize the range of feasible spiking times determined by the bound. In particular, our optimal control strategies are general so that the bound can be chosen sufficiently small within the range where the PRC is valid. The design of such minimum-power stimuli to elicit spikes of neuron oscillators is also of clinical importance, notably in deep brain stimulation therapy for Parkinson's disease and essential tremor [14], where mild stimulations are required. In addition, interest in reducing the energy consumption in neurological implants such as cardiac pacemakers makes such optimal designs imperative.

This paper is organized as follows. In Sec. II, we introduce the phase model for spiking neurons and formulate the related optimal control problem. In Sec. III, we derive minimum-power controls associated with specified spiking times in the absence and presence of control amplitude constraints, in which various phase models, including the sinusoidal PRC, SNIPER (saddle-node bifurcation of a fixed point on a periodic orbit) PRC, and Morris-Lecar PRC, are considered. In addition, we present examples and simulations to demonstrate the resulting optimal control strategies.

II. OPTIMAL CONTROL OF SPIKING NEURON OSCILLATORS

A periodically spiking or firing neuron can be considered as a periodic oscillator governed by a nonlinear dynamical equation of the form

$$\frac{d\theta}{dt} = f(\theta) + Z(\theta)I(t), \tag{1}$$

where θ is the phase of the oscillation, $f(\theta)$ and $Z(\theta)$ are real-valued functions giving the neuron's baseline dynamics and its phase response, respectively, and $I(t)$ is an external current stimulus [4]. This nonlinear dynamical system described in (1) is referred to as the phase model for the oscillation. The assumptions that $Z(\theta)$ vanishes only on isolated points and that $f(\theta) > 0$ are made so that a full revolution of the phase is possible. By convention, neuron spikes occur when $\theta = 2n\pi$, where $n \in \mathbb{N}$, e.g., $\theta = 0$ or 2π. In the absence of any input $I(t)$, the neuron spikes periodically at its natural frequency,

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while the spiking time can be advanced or delayed in a desired manner by an appropriate choice of $I(t)$.

In this paper, we study optimal design of neural inputs that lead to the spiking of neurons at a specified time T_1 after spiking at time $t = 0$. In particular, we find the bounded stimulus that fires a neuron with minimum power, which is formulated as the following optimal control problem:

$$\begin{aligned} &\min_{I(t)} \int_0^{T_1} I(t)^2\, dt \qquad (2)\\ &\text{subject to} \quad \dot{\theta} = f(\theta) + Z(\theta)I(t),\\ &\qquad \theta(0) = 0, \quad \theta(T_1) = 2\pi,\\ &\qquad |I(t)| \leqslant M, \qquad \forall\, t \in [0,T_1], \end{aligned}$$

where $M > 0$ is the amplitude bound of the current stimulus $I(t)$. Here, we consider both hyperpolarizing and depolarizing inputs, i.e., $I(t)$ can be positive or negative. Note that if T_1 is equal to the natural spiking time, then no input is needed. We first investigate the case when the control amplitude is unbounded, upon which the optimal control with bounded amplitude can be constructed.

III. MINIMUM-POWER STIMULUS FOR SPECIFIED FIRING TIME

We consider the minimum-power optimal control problem of spiking neurons as formulated in (2) for various phase models including both models for type I and type II neurons. Specifically, we examine the examples of the sinusoidal PRC, SNIPER PRC, and Morris-Lecar PRC.

A. Sinusoidal PRC

Consider the following dynamical system with sinusoidal PRC:

$$\dot{\theta} = \omega + z_d(\sin\theta)I(t), \qquad (3)$$

where ω is the natural oscillation frequency of the neuron and z_d is a model-dependent constant. The neuron described by this phase model spikes periodically with the period $T = 2\pi/\omega$ in the absence of any external input, i.e., $I(t) = 0$. Note that this type of PRC with both positive and negative regions can be obtained by periodic orbits near the supercritical Hopf bifurcation [4]. This type of bifurcation occurs for type II neuron models like the Fitzhugh-Nagumo model [15].

1. *Spiking neurons with unbounded control*

The optimal current profile can be derived by Pontryagin's maximum principle [16,17]. Given the optimal control problem as in (2), we form the control Hamiltonian

$$H = I^2 + \lambda[\omega + z_d(\sin\theta)I], \qquad (4)$$

where λ is the Lagrange multiplier. The necessary optimality conditions give

$$\dot{\lambda} = -\frac{\partial H}{\partial \theta} = -\lambda z_d I \cos\theta, \qquad (5)$$

and $\frac{\partial H}{\partial I} = 2I + \lambda z_d \sin\theta = 0$. Hence, the optimal current I satisfies

$$I = -\frac{1}{2}\lambda z_d \sin\theta. \qquad (6)$$

The optimal control problem is then transformed to a boundary value problem, which characterizes the optimal trajectories of $\theta(t)$ and $\lambda(t)$,

$$\dot{\theta} = \omega - \frac{z_d^2\lambda}{2}\sin^2\theta, \qquad (7)$$

$$\dot{\lambda} = \frac{z_d^2\lambda^2}{2}\sin\theta\cos\theta, \qquad (8)$$

with boundary conditions $\theta(0) = 0$ and $\theta(T_1) = 2\pi$ while $\lambda(0)$ and $\lambda(T_1)$ are unspecified.

Additionally, since the Hamiltonian is not explicitly dependent on time, the optimal triple (λ,θ,I) satisfies $H(\lambda,\theta,I) = c$, $\forall\, 0 \leqslant t \leqslant T_1$, where c is a constant. Together with (6), this yields

$$-\frac{z_d^2}{4}\sin^2\theta\lambda^2 + \omega\lambda = c. \qquad (9)$$

Since $\theta(0) = 0$, $c = \omega\lambda_0$, where $\lambda_0 = \lambda(0)$, which is undetermined. The optimal multiplier can be found by solving the above quadratic equation (9), which gives

$$\lambda = \frac{2\omega \pm 2\sqrt{\omega^2 - \omega\lambda_0 z_d^2 \sin^2\theta}}{z_d^2\sin^2\theta}, \qquad (10)$$

and then, from (7), the optimal trajectory of θ follows

$$\dot{\theta} = \mp\sqrt{\omega^2 - \omega\lambda_0 z_d^2\sin^2\theta}. \qquad (11)$$

Integrating Eq. (11), we find the spiking time T_1 in terms of the initial condition λ_0,

$$T_1 = \int_0^{2\pi} \frac{1}{\sqrt{\omega^2 - \omega\lambda_0 z_d^2\sin^2\theta}}\, d\theta. \qquad (12)$$

Note that we choose the positive sign in (11), which corresponds to forward phase evolution. Therefore, given a desired spiking time T_1 of the neuron, the initial value λ_0 corresponding to the optimal trajectory of the multiplier can be found via the one-to-one relation in (12). Consequently, the optimal trajectories of θ and λ can be easily computed by evolving (7) and (8) forward in time. Plugging (10) into (6), we obtain the optimal feedback law for spiking the neuron at time T_1 of the form

$$I^* = \frac{-\omega + \sqrt{\omega^2 - \omega\lambda_0 z_d^2\sin^2\theta}}{z_d\sin\theta}, \qquad (13)$$

where λ_0 is to be calculated according to (12).

The feasibility of spiking the neuron at a desired time T_1 largely depends on the initial value of the multiplier, λ_0. It is not feasible to have a 2π revolution if $\lambda_0 \geqslant \omega/z_d^2$. This fact can be seen from Fig. 1, where the system evolution defined by (7) and (8) for $z_d = 1$ rad/nC and $\omega = 1$ rad/ms with respect to different λ_0 values ($\theta = 0$ axis) is illustrated. When $\lambda_0 = 0$, the spiking period is equal to the natural spiking period $2\pi/\omega$, and no external stimulus needs to be applied, i.e., $I^*(t) = 0$,

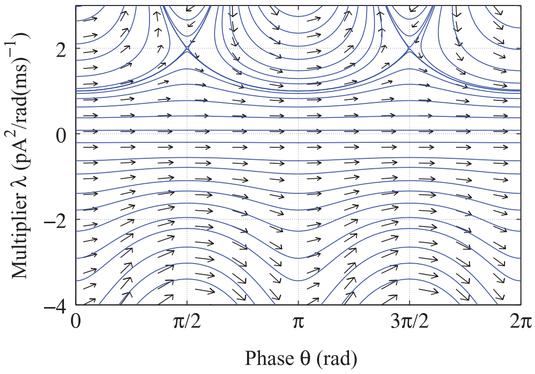


FIG. 1. (Color online) Extremals of sinusoidal PRC model with $z_d = 1$ rad/nC and $\omega = 1$ rad/ms.

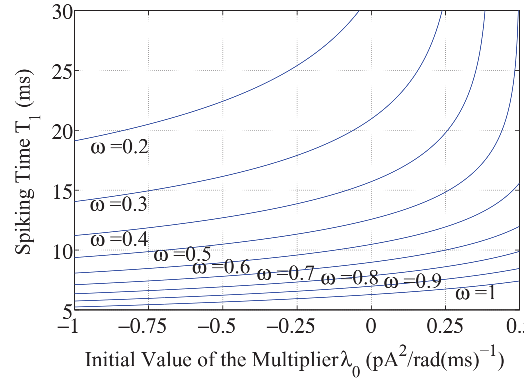


FIG. 2. (Color online) Variation of the spiking time T_1 with respect to the initial multiplier value λ_0 leading to optimal trajectories, with different values of ω (rad/ms) and $z_d = 1$ rad/nC for sinusoidal PRC model.

$\forall\ t \in [0,2\pi/\omega]$. T_1 is a monotonically increasing function of λ_0 for fixed ω and z_d and the average phase velocity decreases when λ_0 increases, the spiking time $T_1 > 2\pi/\omega$ for $\lambda_0 > 0$ and $T_1 < 2\pi/\omega$ for $\lambda_0 < 0$. Figure 2 shows variation of the spiking time T_1 with the λ_0 corresponding to the optimal trajectories for different ω values with $z_d = 1$ rad/nC.

The relation between the spiking time T_1 and required minimum energy $E = \min \int_0^{T_1} I^2(t)dt$ is evident via a simple sensitivity analysis [18]. Since a small change in the initial condition $d\theta$ and a small change in the initial time dt result in a small change in power according to $dE = \lambda(t)d\theta - H(t)dt$, it follows that $-\frac{\partial E}{\partial t} = H = c = \omega\lambda_0$ [18]. This implies that E increases with initial time t for $\lambda_0 < 0$ and decreases for $\lambda_0 > 0$. Since the increment of the initial time is equivalent to the decrement of spiking time T_1, $\partial E/\partial T_1 = \omega\lambda_0$. Since $\lambda_0 < 0$ ($\lambda_0 > 0$) corresponds to $T_1 < 2\pi/\omega$ ($T_1 > 2\pi/\omega$), we see that the required minimum energy increases if we move away from the natural spiking time.

The minimum-power stimulus I^* as in (13) plotted with respect to time and the phase for various spiking times $T_1 = 3,5,10,12$ ms with $\omega = 1$ rad/ms and $z_d = 1$ rad/nC are shown in Figs. 3(a) and 3(b), respectively. The respective optimal trajectories of $\lambda(\theta)$ and $\theta(t)$ for these spiking times are illustrated in Figs. 3(c) and 3(d).

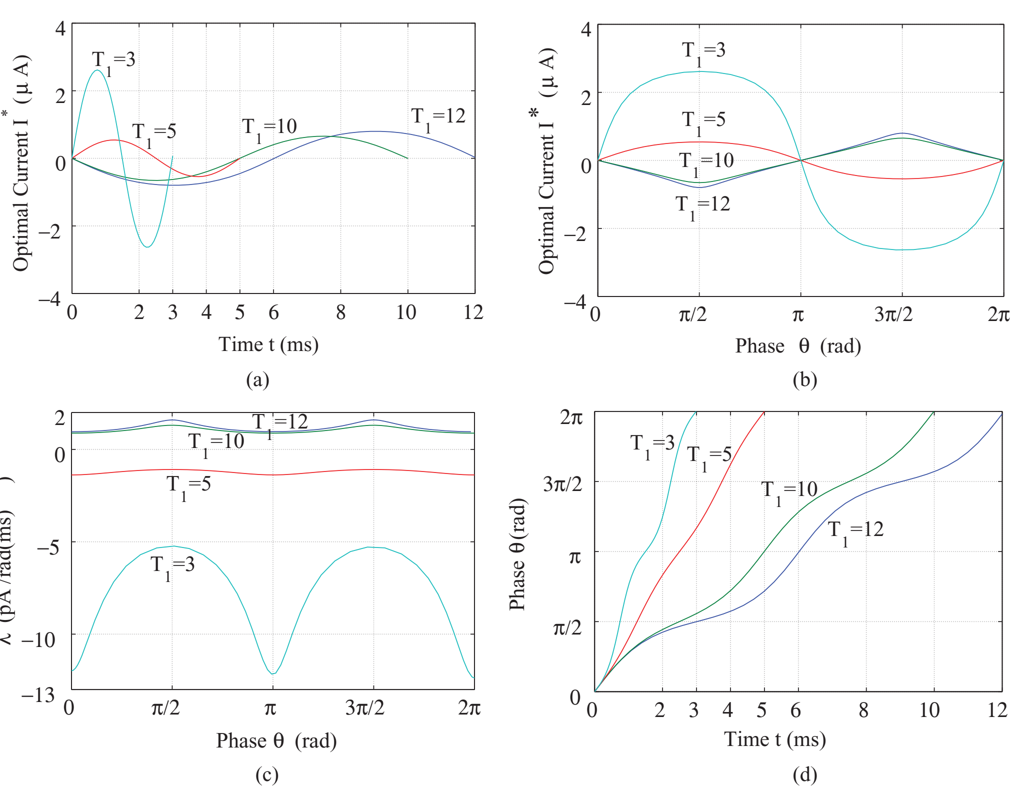


FIG. 3. (Color online) Optimal solutions for various spiking times $T_1 = 3,5,10,12$ ms for sinusoidal PRC model with $z_d = 1$ rad/nC and $\omega = 1$ rad/ms. (a) The minimum-power control I^*. (b) Variation of I^* with phase θ. (c) Variation of the optimal multiplier λ with θ. (d) Optimal phase trajectories following I^*.

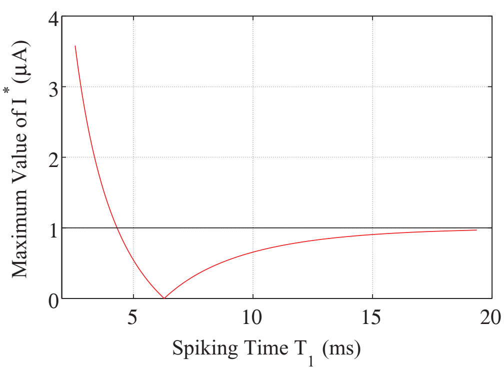


FIG. 4. (Color online) Variation of the maximum value of I^* with spiking time T_1 for sinusoidal PRC model with $\omega = 1$ rad/ms and $z_d = 1$ rad/nC.

2. Spiking neurons with bounded control

In practice, the amplitudes of stimuli in physical systems are limited and phase models are valid for weak inputs; hence we consider spiking the sinusoidal neuron with bounded control amplitude, namely, in the optimal control problem (2), $|I(t)| \leqslant M < \infty$ for all $t \in [0,T_1]$, where T_1 is the desired spiking time. In this case, there exists a range in which the neuron can be spiked, depending on the value of M, in contrast to the previous case where any desired spiking time is feasible. We first observe that, given this bound M, the minimum time it takes to spike a neuron can be achieved by choosing the control that keeps the phase velocity $\dot{\theta}$ maximum over $t \in [0,T_1]$. Such a time-optimal control, for $z_d > 0$, can be characterized by a switching, i.e.,

$$I^*_{T\,\min} = \begin{cases} M & \text{for} \quad 0 \leqslant \theta < \pi, \\ -M & \text{for} \quad \pi \leqslant \theta < 2\pi. \end{cases} \tag{14}$$

Consequently, the spiking time with $I^*_{T\,\min}$ for $\omega \neq z_d M$ can be computed using (3) and (14), which yields

$$T^M_{\min} = 2\pi\sqrt{\frac{1}{-z_d^2M^2+\omega^2}} - \frac{4\tan^{-1}\left\{z_dM/\sqrt{-z_d^2M^2+\omega^2}\right\}}{\sqrt{-z_d^2M^2+\omega^2}}. \tag{15}$$

It follows that I^*, given in (13), is the minimum-power stimulus that spikes the neuron at a desired spiking time T_1 if $|I^*| \leqslant M$ for all $t \in [0,T_1]$. However, there exists a shortest possible spiking time by I^* given the bound M, that is (see Appendix A),

$$T^{I^*}_{\min} = \int_0^{2\pi} \frac{1}{\sqrt{\omega^2 + z_d M(z_d M + 2\omega)\sin^2(\theta)}}\, d\theta. \tag{16}$$

Note that $T^M_{\min} < T^{I^*}_{\min}$. According to (3) when $M \geqslant \omega/z_d$, arbitrarily large spiking times can be achieved by making $\dot{\theta}$ arbitrary close to zero. Therefore we consider two cases for $M \geqslant \omega/z_d$ and $M < \omega/z_d$.

Case I: $M \geqslant \omega/z_d$. Since $|I^*| < \omega/z_d \leqslant M$ for $\lambda_0 > 0$, I^* is the minimum-power control for any desired spiking time $T_1 > 2\pi/\omega$, and hence for any spiking time $T_1 \geqslant T^{I^*}_{\min}$. Variation of the maximum value of the control I^* with spiking time T_1 for $\omega = 1$ rad/ms and $z_d = 1$ rad/nC is depicted in Fig. 4. Shorter spiking times $T_1 \in [T^M_{\min}, T^{I^*}_{\min})$ are feasible but, due to the bound M, cannot be achieved by I^* since it requires a control with amplitude greater than M for some $t \in [0,T_1]$. However, these spiking times can be optimally achieved by applying controls switching between I^* and $I^*_{T\,\min}$.

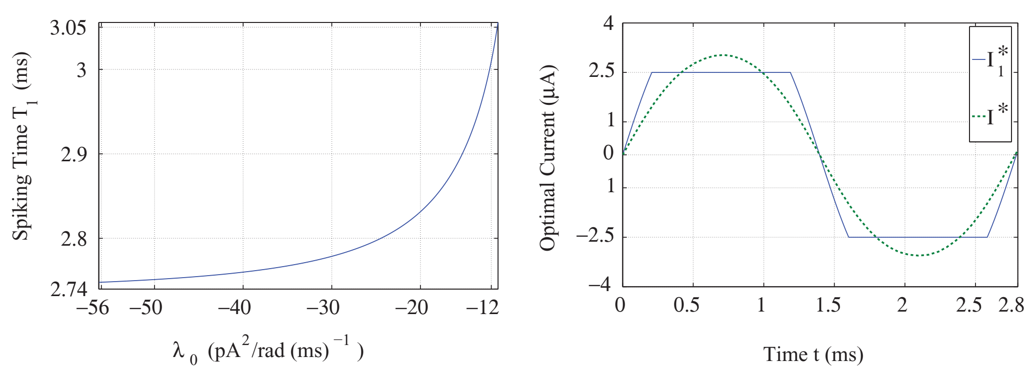
The minimum-power optimal control that spikes the neuron at $T_1 \in [T^M_{\min}, T^{I^*}_{\min})$ is characterized by four switchings between I^* and M, i.e.,

$$I^*_1 = \begin{cases} I^*, & 0 \leqslant \theta < \theta_1, \\ M, & \theta_1 \leqslant \theta \leqslant \theta_2, \\ I^*, & \theta_2 < \theta < \theta_3, \\ -M, & \theta_3 \leqslant \theta \leqslant \theta_4, \\ I^*, & \theta_4 < \theta \leqslant 2\pi, \end{cases} \tag{17}$$

in which $\theta_1 = \sin^{-1}[-2M\omega/(z_dM^2 + z_d\omega\lambda_0)]$ and $\theta_2 = \pi - \theta_1$ are the phases where I^* meets the bound M, $\theta_3 = \pi + \theta_1$, and $\theta_4 = 2\pi - \theta_1$. The initial value of the multiplier, λ_0, resulting in the optimal trajectory, can then be found according to the desired $T_1 \in [T^M_{\min}, T^{I^*}_{\min})$ through the relation

$$T_1 = \int_0^{\theta_1} \frac{4}{\sqrt{\omega^2 - \omega\lambda_0 z_d^2\sin^2\theta}}\, d\theta + \int_{\theta_1}^{\pi/2} \frac{4}{\omega + z_d M\sin(\theta)}\, d\theta.$$

More detailed derivations of the optimal solutions can be found in Appendix A. Figure 5(a) shows the relation between λ_0 and T_1 by I^*_1 for $M = 2.5\ \mu$A, $z_d = 1$ rad/nC, and $\omega = 1$ rad/ms. From (15) the minimum possible spiking time with



(a) (b)

FIG. 5. (Color online) (a) Variation of the spiking time $T_1 \in [T^M_{\min}, T^{I^*}_{\min})$ for sinusoidal PRC model with respect to the initial multiplier value λ_0 for $M = 2.5\ \mu$A. (b) Unbounded and bounded ($M = 2.5\ \mu$A) minimum-power controls of sinusoidal PRC model for $T_1 = 2.8$ ms, $z_d = 1$ rad/nC, and $\omega = 1$ rad/ms.

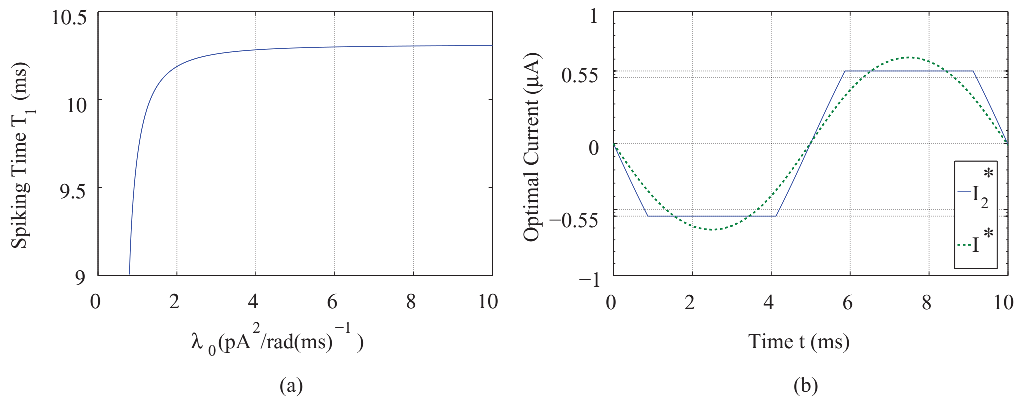


FIG. 6. (Color online)(a) Variation of the spiking time $T_1 \in (T_{max}^{I^*}, T_{max}^{M}]$ with respect to the initial multiplier value, λ_0, for sinusoidal PRC model when $M = 0.55$ μA. (b) Unbounded and bounded ($M = 0.55$ μA) minimum-power controls for sinusoidal PRC model with $T_1 = 10$ ms, $z_d = 1$ rad/nC, and $\omega = 1$ rad/ms.

this control bound $M = 2.5$ μA is $T_{\min}^{M} = 2.735$ ms and from (16) the minimum spiking time by I^* is $T_{\min}^{I^*} = 3.056$ ms. Thus, in this example, any desired spiking time $T_1 > 3.056$ ms can be optimally achieved by I^* whereas any $T_1 \in [2.735, 3.056)$ ms can be optimally obtained by I_1^* as in (17). Figure 5(b) illustrates the bounded and unbounded optimal controls that fire the neuron at $T_1 = 2.8$ ms, where I^* is the minimum-power stimulus when the control amplitude is not limited and I_1^* is the minimum-power stimulus when the bound $M = 2.5$ μA. I^* drives the neuron from $\theta(0) = 0$ to $\theta(2.8) = 2\pi$ with 4.836 pW of power whereas I_1^* requires 5.046 pW.

Case II: $M < \omega/z_d$. In contrast with case I in the previous section, achieving arbitrarily large spiking times is not feasible with a bound $M < \omega/z_d$. In this case, the longest possible spiking time is achieved by

$$I_{T\max}^* = \begin{cases} -M & \text{for} \quad 0 \leqslant \theta < \pi, \\ M & \text{for} \quad \pi \leqslant \theta < 2\pi. \end{cases}$$

The spiking time of the neuron under this control is

$$T_{\max}^{M} = 2\pi\sqrt{\frac{1}{-z_d^2M^2+\omega^2}} + \frac{4\tan^{-1}\left\{z_dM/\sqrt{-z_d^2M^2+\omega^2}\right\}}{\sqrt{-z_d^2M^2+\omega^2}}, \quad (18)$$

and the longest spiking time feasible with control I^* is given by

$$T_{\max}^{I^*} = \int_0^{2\pi} \frac{1}{\sqrt{\omega^2 + z_dM(z_dM - 2\omega)\sin^2(\theta)}}d\theta. \quad (19)$$

Then, by similar analysis as for case I, any spiking time $T_1 \in [T_{\min}^{M}, T_{\min}^{I^*})$ for a given $M < \omega/z_d$ can be achieved with the minimum-power control I_1^* as given in (17), any $T_1 \in [T_{\min}^{I^*}, T_{\max}^{I^*}]$ can be achieved with minimum power by I^* in (13), and moreover any $T_1 \in (T_{\max}^{I^*}, T_{\max}^{M}]$ can be obtained by switching between I^* and $I_{\max}^*$. The corresponding switching angles are $\theta_5 = \sin^{-1}[2M\omega/(z_dM^2 + z_d\omega\lambda_0)]$, $\theta_6 = \pi - \theta_5$, $\theta_7 = \pi + \theta_5$, and $\theta_8 = 2\pi - \theta_5$, and the minimum-power optimal control for $T_1 \in (T_{\max}^{I^*}, T_{\max}^{M}]$ is characterized by

$$I_2^* = \begin{cases} I^*, & 0 \leqslant \theta < \theta_5, \\ -M, & \theta_5 \leqslant \theta \leqslant \theta_6, \\ I^*, & \theta_6 < \theta < \theta_7, \\ M, & \theta_7 \leqslant \theta \leqslant \theta_8, \\ I^*, & \theta_8 < \theta \leqslant 2\pi. \end{cases}$$

The λ_0 resulting in the optimal trajectory by I_2^* can be calculated according to the given $T_1 \in (T_{\max}^{I^*}, T_{\max}^{M}]$ via the relation

$$T_1 = \int_0^{\theta_5} \frac{4}{\sqrt{\omega^2 - \omega\lambda_0 z_d^2 \sin^2\theta}}d\theta + \int_{\theta_5}^{\pi/2} \frac{4}{\omega - z_dM\sin\theta}d\theta.$$

Figure 6(a) shows the relation between λ_0 and T_1 by I_2^* for $M = 0.55$ μA, $z_d = 1$ rad/nC, and $\omega = 1$ rad/ms. From (18) the maximum possible spiking time with $M = 0.55$ μA is $T_{\max}^{M} = 10.312$ ms and from (19) the maximum spiking time feasible by I^* is $T_{\max}^{I^*} = 9.006$ ms. Therefore, in this example, any desired spiking time $T_1 \in (9.006, 10.312]$ ms can be obtained with minimum power by the use of I_2^*. Figure 6(b) illustrates the bounded and unbounded optimal controls that spike the neuron at $T_1 = 10$ ms, where I^* is the minimum-power stimulus when the control amplitude is not

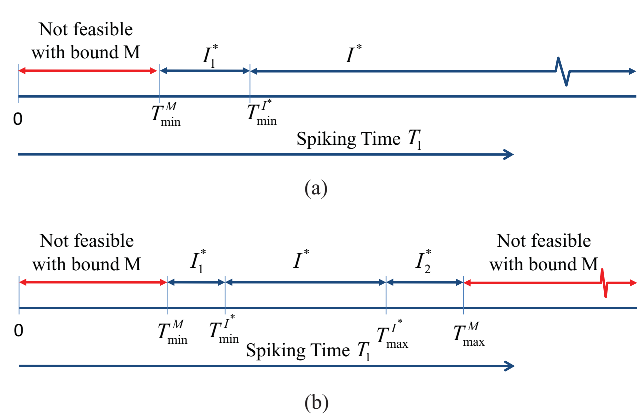


FIG. 7. (Color online) A summary of the optimal control strategies for the sinusoidal PRC model for (a) $M \geqslant \omega/z_d$ and (b) $M < \omega/z_d$.

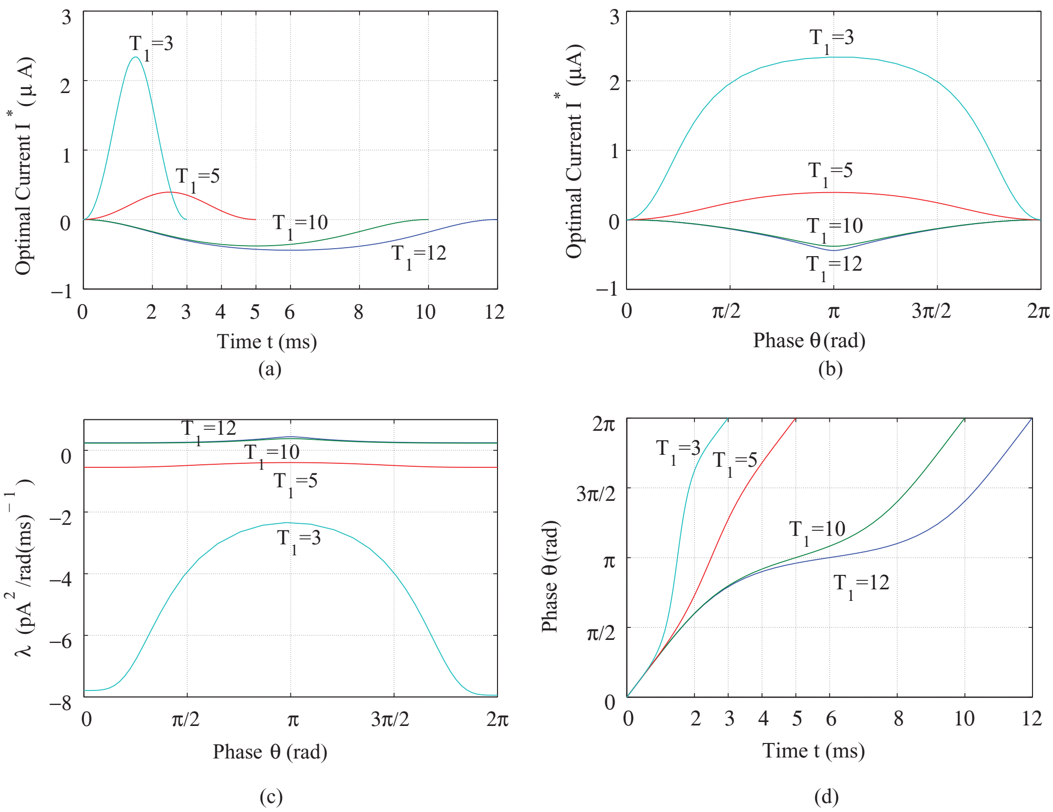


FIG. 8. (Color online) Optimal solutions for various spiking times $T_1 = 3,5,10,12$ ms for SNIPER PRC model with $z_d = 1$ rad/nC and $\omega = 1$ rad/ms. (a) The minimum-power control I^*. (b) Variation of I^* with phase θ. (c) Variation of the optimal multiplier, λ, with θ. (d) Optimal phase trajectories following I^*.

limited and I_2^* is the minimum-power stimulus when $M = 0.55\ \mu$A. I^* drives the neuron from $\theta(0) = 0$ to $\theta(10) = 2\pi$ with 0.219 pW of power whereas I_2^* requires 0.233 pW.

A summary of the optimal (minimum-power) spiking scenarios for a prescribed spiking time of the neuron governed by the sinusoidal phase model (3) is illustrated in Fig. 7. Note that repeated application of optimal controls with period T_1, as in (13), (17), and (20), leads to 1:1 phase locking.

B. SNIPER PRC

We now consider the SNIPER PRC model in which $f(\theta) = \omega$ and $Z(\theta) = z_d(1 - \cos\theta)$, where $z_d > 0$ and $\omega > 0$. That is,

$$\dot{\theta} = \omega + z_d(1 - \cos\theta)I(t). \tag{20}$$

The SNIPER PRC is derived for neuron models near a SNIPER bifurcation (i.e., a saddle-node bifurcation of a fixed point on a periodic orbit) which is found for type I neurons [19] like the Hindmarsh-Rose model [20]. The minimum-power stimuli for spiking neurons modeled by this phase model can be easily derived with analysis analogous to those described previously in Secs. III A 1 and III A 2.

1. Spiking neurons with unbounded control

Employing the maximum principle as in Sec. III A 1, the minimum-power stimulus that spikes the SNIPER neuron at a desired time T_1 can be derived and given by

$$I^* = \frac{-\omega + \sqrt{\omega^2 - \omega\lambda_0 z_d^2(1 - \cos\theta)^2}}{z_d(1 - \cos\theta)}, \tag{21}$$

where λ_0 corresponding to the optimal trajectory is determined through the integral relation with T_1,

$$T_1 = \int_0^{2\pi} \frac{1}{\sqrt{\omega^2 - \omega\lambda_0 z_d^2(1 - \cos\theta)^2}} d\theta.$$

The minimum-power stimuli I^* plotted with respect to time and phase for various spiking times $T_1 = 3,5,10,12$ ms with parameter values $z_d = 1$ rad/nC and $\omega = 1$ rad/ms are illustrated in Figs. 8(a) and 8(b), respectively. The corresponding optimal trajectories of $\lambda(\theta)$ and $\theta(t)$ for these spiking times are displayed in Figs. 8(c) and 8(d).

2. Spiking neurons with bounded control

When the amplitude of the available stimulus is limited, i.e., $|I(t)| \leqslant M$, the control that achieves the shortest spiking time for the SNIPER phase model is given by $I^*_{T\,\min} = M > 0$ for $0 \leqslant \theta \leqslant 2\pi$, since $1 - \cos\theta \geqslant 0$ for all $\theta \in [0,2\pi]$. As a result, the shortest possible spiking time with this control is $T^M_{\min} = 2\pi/\sqrt{\omega^2 + 2z_d\omega M}$. Also, the shortest spiking time achieved by the control I^* in (21) given the bound M is given by

$$T^{I^*}_{\min} = \int_0^{2\pi} \frac{1}{\sqrt{\omega^2 + z_d M(z_d M + \omega)(1 - \cos\theta)^2}} d\theta. \tag{22}$$

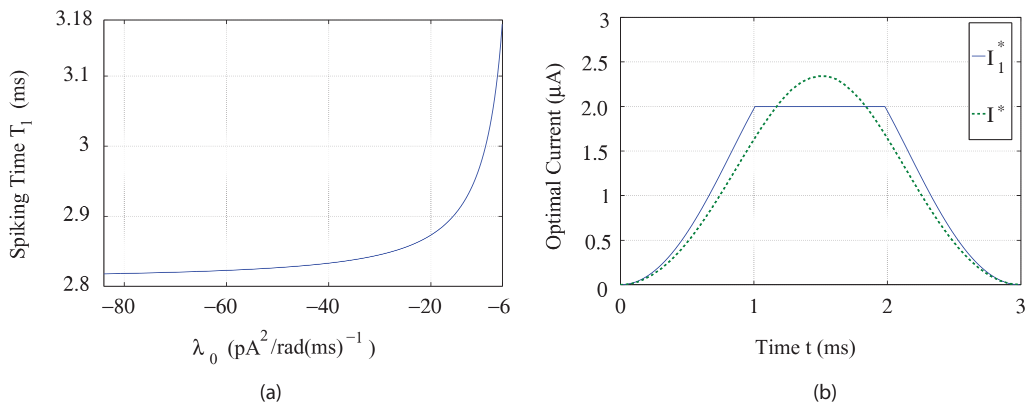


FIG. 9. (Color online) (a) Variation of the spiking time $T_1 \in [T_{\min}^M, T_{\min}^{I^*})$ with respect to the initial multiplier value λ_0 for SNIPER PRC model when $M = 2.0\ \mu$A. (b) Unbounded and bounded ($M = 2.0\ \mu$A) minimum-power controls for SNIPER PRC model with $T_1 = 3.0$ ms, $z_d = 1$ rad/nC, and $\omega = 1$ rad/ms.

Similarly to the sinusoidal PRC case, the longest possible spiking time of the neuron varies with the control bound M. If $M \geqslant \omega/(2z_d)$, an arbitrarily large spiking time is achievable; however, if $M < \omega/(2z_d)$ there exists a maximum spiking time.

Case I: $M \geqslant \omega/(2z_d)$. Any spiking time $T_1 \in [T_{\min}^{I^*}, \infty)$ is possible with control I^* but a shorter spiking time $T_1 \in [T_{\min}^M, T_{\min}^{I^*})$ requires switching between I^* and $I_{T\min}^*$, which is characterized by two switchings,

$$I_1^* = \begin{cases} I^*, & 0 \leqslant \theta < \theta_1, \\ M, & \theta_1 \leqslant \theta \leqslant 2\pi - \theta_1, \\ I^*, & 2\pi - \theta_1 < \theta \leqslant 2\pi, \end{cases} \tag{23}$$

where $\theta_1 = \cos^{-1}\left[1 + 2\omega M/(z_d M^2 + z_d \omega \lambda_0)\right]$. The initial value λ_0 that results in the optimal trajectory is given by

$$T_1 = \int_0^{\theta_1} \frac{2}{\sqrt{\omega^2 - \omega\lambda_0 z_d^2 (1-\cos\theta)^2}} d\theta + \int_{\theta_1}^{\pi} \frac{2}{\omega + z_d M(1-\cos\theta)} d\theta.$$

Figure 9(a) illustrates the relation between λ_0 and $T_1 \in [T_{\min}^M, T_{\min}^{I^*})$ by I_1^* for $M = 2.0\ \mu$A, $z_d = 1$ rad/nC, and $\omega =$ 1 rad/ms. In this case, the shortest feasible spiking time is $T_{\min}^M = 2.09$ ms and the shortest with the control I^* is $T_{\min}^{I^*} =$ 3.18 ms. Any spiking time in the interval [2.09,3.18) ms is achievable by I_1^* in (23) with minimum power. Figure 9(b) illustrates the unbounded and bounded, with $M = 2.0\ \mu$A, optimal stimuli that fire the neuron at $T_1 = 3$ ms with minimum power.

Case II: $M < \omega/(2z_d)$. In this case there exists a longest possible spiking time (i.e., $T_{\max}^M$) which is achieved by $I_{\max}^* = -M$ for all $\theta \in [0, 2\pi]$. $T_{\max}^M$ is given by $2\pi/\sqrt{\omega^2 - 2z_d\omega M}$. The longest spiking time feasible with the control I^* as in (21) is given by

$$T_{\max}^{I^*} = \int_0^{2\pi} \frac{1}{\sqrt{\omega^2 + z_d M(z_d M - 2\omega)(1-\cos\theta)^2}} d\theta.$$

Therefore, any spiking time $T_1 \in [T_{\min}^M, T_{\min}^{I^*})$ for a given $M < \omega/(2z_d)$ can be achieved with the minimum-power control I_1^* as given in (23), any $T_1 \in [T_{\min}^{I^*}, T_{\max}^{I^*}]$ can be achieved with minimum power by I^* in (21), and moreover any

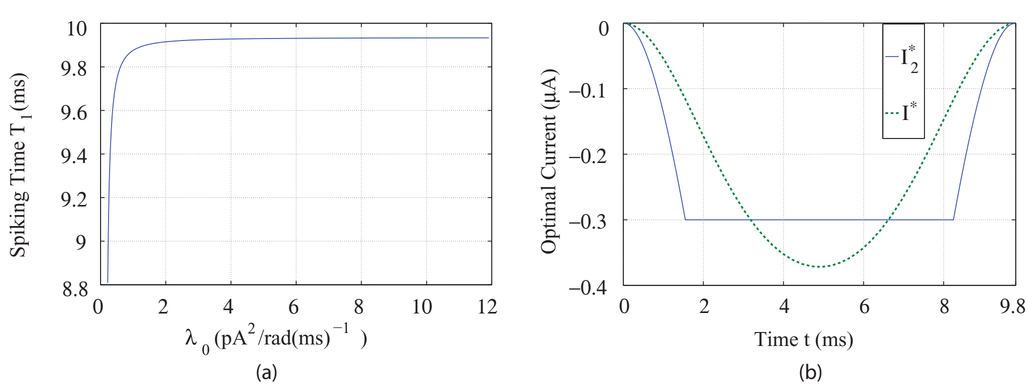


FIG. 10. (Color online) (a) Variation of the spiking time $T_1 \in (T_{\max}^{I^*}, T_{\max}^M]$ with respect to the initial multiplier value λ_0 for SNIPER PRC model when $M = 0.3\ \mu$A. (b) Unbounded and bounded ($M = 0.3\ \mu$A) minimum-power controls for SNIPER PRC model with $T_1 = 9.8$ ms, $z_d = 1$ rad/nC, and $\omega = 1$ rad/ms.

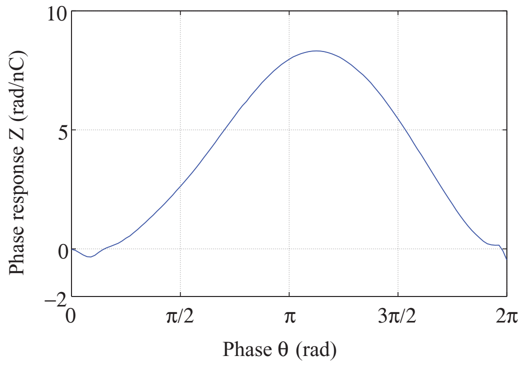


FIG. 11. (Color online) Morris-Lecar PRC.

$T_1 \in (T^{I^*}_{\max}, T^M_{\max}]$ can be obtained by switching between I^* and $I^*_{\max}$, that is,

$$I^*_2 = \begin{cases} I^*, & 0 \leqslant \theta < \theta_2, \\ -M, & \theta_2 \leqslant \theta \leqslant 2\pi - \theta_2, \\ I^*, & 2\pi - \theta_2 < \theta < 2\pi, \end{cases}$$

where $\theta_2 = \cos^{-1}\left[1 - 2\omega M/(z_d M^2 + z_d \omega \lambda_0)\right]$. The λ_0 associated with the optimal trajectory is determined via the relation with the desired spiking time T_1,

$$T_1 = \int_0^{\theta_1} \frac{2}{\sqrt{\omega^2 - \omega\lambda_0 z_d^2 (1 - \cos\theta)^2}} d\theta + \int_{\theta_1}^{\pi} \frac{2}{\omega - z_d M(1 - \cos\theta)} d\theta.$$

Figure 10(a) illustrates the relation between λ_0 and $T_1 \in (T^{I^*}_{\max}, T^M_{\max}]$ by I^*_2 for $M = 0.3\ \mu$A, $z_d = 1$ rad/nC, and $\omega = 1$ rad/ms. In this case, the longest feasible spiking time is $T^M_{\max} = 9.935$ ms and the longest with the control I^* is $T^{I^*}_{\max} = 8.596$ ms. The unbounded and bounded, with $M = 0.3\ \mu$A, optimal stimuli that fire the neuron at $T_1 = 9.8$ ms with minimum power are illustrated in Fig. 10(b).

A summary of the optimal (minimum-power) spiking scenarios for a prescribed spiking time of the neuron governed by the SNIPER PRC model in (20) can be illustrated analogously to Figs. 7(a) and 7(b) for $M \geqslant \omega/(2z_d)$ and $M < \omega/(2z_d)$, respectively.

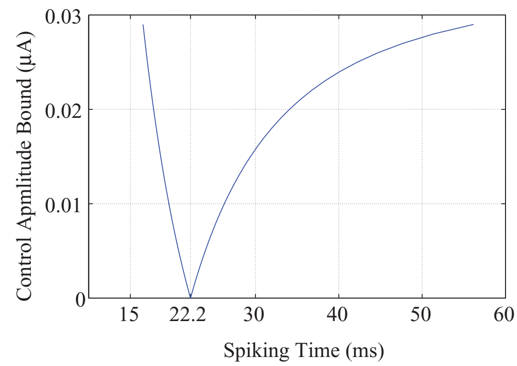


FIG. 13. (Color online) Variation of the minimum and maximum spiking times with respect to the control amplitude for Morris-Lecar PRC.

Many of the experimentally determined PRCs for real neurons are not of sinusoidal or SNIPER type, which are approximations arising from the study of mathematical models of neuron oscillators close to certain bifurcations. In the following, we apply the derived optimal control strategies to the Morris-Lecar PRC. Previous work has shown that the PRC for an Aplysia motoneuron, which can be experimentally observed, is extremely similar to that of a Morris-Lecar neuron [21]. As a result, we find minimum-power stimuli for the Morris-Lecar PRC to demonstrate the applicability and generality of our analytic method to practical PRCs.

C. Morris-Lecar PRC

The phase model of the Morris-Lecar neuron [22] is given by $\dot{\theta} = \omega + Z(\theta)I(t)$, where the PRC, $Z(\theta)$, for the system and parameters described in Appendix B is shown in Fig. 11, calculated by XPP [23]. It has the period $T = 22.211$ ms and natural frequency $\omega = 0.283$ rad/ms. We can calculate the optimal controls for different spiking times following the same procedure as we explained for sinusoidal PRCs. Figure 12 shows the optimal current stimuli without an amplitude constraint and the corresponding trajectories for various desired spiking times that are shorter than, close to, and longer than the natural spiking time.

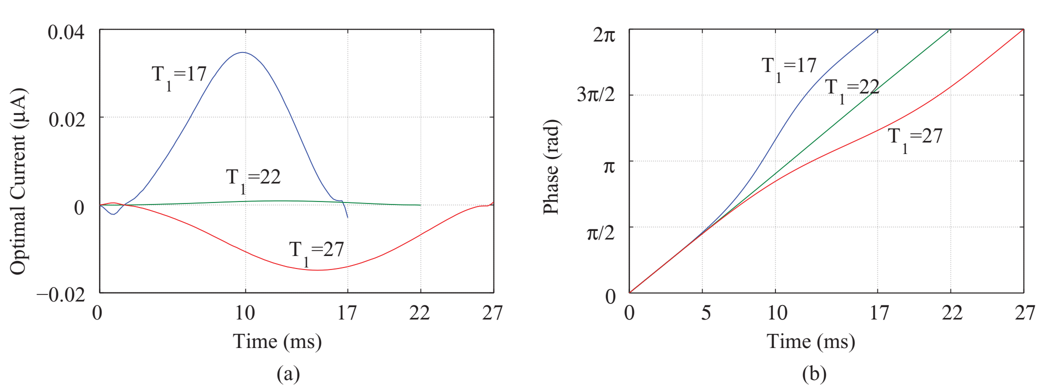


FIG. 12. (Color online) (a) Optimal currents for various spiking times $T_1 = 17,22,27$ ms for the Morris-Lecar PRC. (b) Phase trajectories under the optimal current stimuli.

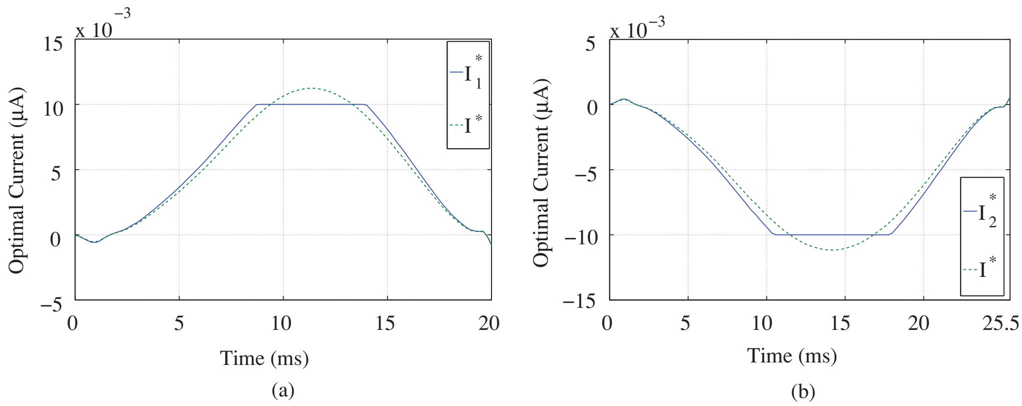


FIG. 14. (Color online) Unbounded and bounded minimum-power controls for the Morris-Lecar PRC for (a) $T_1 = 20.0$ ms and (b) $T_1 = 25.5$ ms, where $M = 0.01\mu$A.

With a bounded control amplitude, the feasible range of spiking times is limited, which is illustrated in Fig. 13. The spiking range with the bound $M = 0.01\ \mu$A is [19.623,26.268] ms. Figures 14(a) and 14(b) illustrate the unbound and bounded minimum-power controls for the spiking times $T_1 = 20$ ms and 25.5 ms that are shorter and longer than the natural spiking time, respectively.

IV. CONCLUSION AND DISCUSSION

In this paper, we studied various phase-reduced models that describe the dynamics of neuron systems. We considered the design of minimum-power stimuli for spiking a neuron at a specified time instant that is different from the natural spiking time. We formulated this as an optimal control problem and investigated both cases when the control amplitude is unbounded and bounded, for which we found analytic expressions of optimal feedback control laws. In particular for the bounded control case, we characterized the range of possible spiking times in terms of the control amplitude bound. The bound can be chosen sufficiently small within the range where the PRC of a neuron is valid. We illustrated that our method can be applied not only to ideal mathematical models of neuron oscillators but also to experimentally observed PRCs, such as that of an Aplysia motoneuron.

Moreover, minimum-power stimuli for steering any nonlinear oscillators of the form as in (1) between desired initial and target states can be derived following the steps presented in this paper. In addition, the charge-balanced constraint can be readily incorporated into this framework, which is of clinical importance as in deep brain stimulations for Parkinson's disease [24].

The optimal control of a single neuron system investigated in this work illustrates the fundamental limit of spiking a neuron with external stimuli and provides a benchmark structure that enables us to study optimal control of spiking neuron populations. Our recent work showed that simultaneous spiking of a network of neurons with weak forcing is possible [11]; however, many of the related optimal control problems such as minimum-power or time-optimal controls for firing a neural network have not been studied. Although one-dimensional phase models are reasonably accurate to describe the dynamics of neurons, study of higher-dimensional models is essential for more accurate computation of optimal neural inputs.

APPENDIX A: SPIKING SINUSOIDAL NEURONS WITH BOUNDED CONTROL

Simple first- and second-order optimality conditions applied to (13) show that the maximum value of I^* occurs at $\theta = \pi/2$ for $\lambda_0 < 0$ and at $\theta = 3\pi/2$ for $\lambda_0 > 0$. Therefore, the λ_0 for the shortest spiking time with control I^* satisfying $|I^*(t)| \leqslant M$ can be calculated by substituting $I^* = M$ and $\theta = \pi/2$ into Eq. (13), and then from (12) we obtain this shortest spiking period in (16).

Since I^* takes the maximum value at $\theta = 3\pi/2$ for $\lambda_0 > 0$, we have $|I^*| \leqslant (\omega - \sqrt{\omega^2 - \omega\lambda_0 z_d^2})/z_d$, which leads to $|I^*| < \omega/z_d \leqslant M$ for $\lambda_0 > 0$. This implies that I^* is the minimum-power control for any desired spiking time $T_1 > 2\pi/\omega$ when $M \geqslant \omega/z_d$, and hence for any spiking time $T_1 \geqslant T_{\min}^{I^*}$. Shorter spiking times $T_1 \in [T_{\min}^M, T_{\min}^{I^*})$ are feasible but cannot be achieved by I^*. Let $T_1 \in [T_{\min}^M, T_{\min}^{I^*})$; then there exist two angles $\theta_1 = \sin^{-1}[-2M\omega/(z_d M^2 + z_d\omega\lambda_0)]$ and $\theta_2 = \pi - \theta_1$ where I^* meets the bound M. When $\theta \in (\theta_1,\theta_2)$, $I^* > M$ and we take $I(\theta) = M$ for $\theta \in [\theta_1,\theta_2]$. The Hamiltonian of the system when $\theta \in [\theta_1,\theta_2]$ is, from (4), $H = M^2 + \lambda(\omega + z_d \sin\theta\, M)$. If the triple (λ,θ,M) is optimal, then H is a constant, which gives $\lambda = (H - M^2)/(\omega + z_d M \sin\theta)$. This multiplier satisfies the adjoint equation (5), and therefore $I(\theta) = M$ is optimal for $\theta \in [\theta_1,\theta_2]$. Similarly, by symmetry, $I^* < -M$ when $\theta \in [\theta_3,\theta_4]$, where $\theta_3 = \pi + \theta_1$ and $\theta_4 = 2\pi - \theta_1$, if the desired spiking time $T \in [T_{\min}^M, T_{\min}^{I^*})$. It can be easily shown in the same fashion that $I(\theta) = -M$ is optimal in the interval $\theta \in [\theta_3,\theta_4]$. Therefore, the minimum-power optimal control that spikes the neuron at $T_1 \in [T_{\min}^M, T_{\min}^{I^*})$ can be characterized by four switchings between I^* and M as shown in (17).

APPENDIX B: DYNAMICS OF THE MORRIS-LECAR NEURON

The dynamics of the Morris-Lecar neuron is described by $C\dot{V} - (I^b + I) = g_{Ca} m_\infty (V_{Ca} - V) +$

$g_k w(V_k - V) + g_L(V_L - V)$ and $\dot{w} = \phi(\omega_\infty - w)/\tau_w(V)$, where $m_\infty = 0.5\{1 + \tanh[(V - V_1)/V_2]\}$, $\omega_\infty = 0.5\{1 + \tanh[(V - V_3)/V_4]\}$, $\tau_\omega = 1/\cosh[(V - V_3)/(2V_4)]$. We consider the following parameter values with the channel size of 1 cm^2,

$\phi = 0.5$, $I^b = 0.09\ \mu A/cm^2$, $V_1 = -0.01\ mV$, $V_2 = 0.15\ mV$, $V_3 = 0.1\ mV$, $V_4 = 0.145\ mV$, $g_{Ca} = 1\ mS/cm^2$, $V_k = -0.7\ mV$, $V_L = -0.5\ mV$, $g_k = 2\ mS/cm^2$, $g_L = 0.5\ mS/cm^2$, $C = 1\ \mu F/cm^2$, $V_{Ca} = 1 mV$.

[1] P. J. Uhlhaas and W. Singer, Neuron **52**, 155 (2006).

[2] G. V. Osipov, J. Kurths, and C. Zhou, *Synchronization in Oscillatory Networks* (Springer-Verlag, Berlin, 2007).

[3] F. C. Hoppensteadt and E. M. Izhikevich, Phys. Rev. Lett. **82**, 2983 (1999).

[4] E. Brown, J. Moehlis, and P. Holmes, Neural Comput. **16**, 673 (2004).

[5] A. Winfree, *The Geometry of Biological Time*, 2nd ed. (Springer, New York, 2001).

[6] P. Ashwin and J. Swift, J. Nonlinear Sci. **2**, 69 (1992).

[7] D. Taylor and P. Holmes, J. Math. Biol. **37**, 419 (1998).

[8] J. Moehlis, E. Shea-Brown, and H. Rabitz, J. Comput. Nonlinear Dynam. **1**, 358 (2006).

[9] P. A. Tass, *Phase Resetting in Medicine and Biology* (Springer, New York, 1999).

[10] T. Kano and S. Kinoshita, Phys. Rev. E **81**, 026206 (2010).

[11] J.-S. Li, in *Proceedings of the Eighth IFAC Symposium on Nonlinear Control Systems*, edited by L. Marconi, C. Rossi, and K. Schlacher (IFAC, Bologna, Italy, 2010).

[12] S. J. Schiff, K. Jerger, D. H. Duong, T. Chang, M. L. Spano, and W. L. Ditto, Nature (London) **370**, 615 (1994).

[13] T. Harada, H.-A. Tanaka, M. J. Hankins, and I. Z. Kiss, Phys. Rev. Lett. **105**, 088301 (2010).

[14] A. L. Benabid and P. Pollak, Lancet **337**, 403 (1991).

[15] J. Keener and J. Sneyd, *Mathematical Physiology* (Springer-Verlag, New York, 1998).

[16] L. S. Pontryagin, V. G. Boltyanskii, R. V. Gamkrelidze, and E. F. Mishchenko, *The Mathematical Theory of Optimal Processes* (John Wiley & Sons, New York, 1962).

[17] D. Stefanatos and J.-S. Li, Systems Control Lett. **59**, 601 (2010).

[18] A. E. Bryson Jr., and Y. C. Ho, *Applied Optimal Control* (Taylor & Francis Group, New York, 1975).

[19] G. Ermentrout, Neural Comput. **8**, 979 (1996).

[20] R. Rose and J. Haindmarsh, Proc. R. Soc. London, Ser. B **237**, 267 (1989).

[21] J. Foss and J. Milton, J. Neurophysiol. **84**, 975 (2000).

[22] C. Morris and H. Lecar, Biophys. J. **35**, 193 (1981).

[23] B. Ermentrout, *Stimulating, Analyzing, and Animating Dynamical Systems* (SIAM, Philadelphia, 2002).

[24] A. Nabi and J. Moehlis, in *Proceedings of the ASME Dynamic System and Control Conference*, edited by P. Meckl (ASME, New York, 2009), pp. 685–687.