Optimal Control of Neuronal Activity

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We investigate the optimal control of neuronal spiking activity for neurons receiving a class of random synaptic inputs, characterized by a positive parameter α. Optimal control signals and optimal variances are found exactly for the diffusion process approximating an integrate and fire model. When synaptic inputs are "sub-Poisson" ($\alpha < 0.5$), we find that the optimal synaptic input is a delta function (corresponding to bang-bang control) and the optimal signal is not unique. Poisson synaptic input is the critical case: The control signal is unique, but the control signal is still a delta function. For "supra-Poisson" ($\alpha > 0.5$) inputs, the optimal control is smooth and unique. The optimal variance obtained in the current paper sets the lowest possible bound in controlling the stochasticity of neuronal activity. We also discuss how to implement the optimal control signal for certain model neurons.

Introduction.—The effective control of neuronal activity and, hence, that of nervous system function is one of the most exciting topics in theoretical neuroscience (Chapter 12 in [1], Chapter 17 in [2]) with great potential for applications in health care [3]. An extremely successful example is the current treatment of Parkinson's disease [4]. In basic neuroscience, mammalian and other nervous systems must have developed in such a way as to enable the effective control of neuronal activity in order to achieve optimal performance. A dilemma concerning the achievement of optimal control of neuronal activity lies in the fact that most neurons in the central nervous system seem to receive synaptic input stochastically and as a consequence fire randomly [2,5]. Nevertheless, it is clear that an accurate control is performed in some sense. How the nervous system tunes its activity so that an animal or human can precisely and promptly respond to its environment is still an unknown and challenging problem, and doubtless involves synaptic plasticity. In the current Letter, we theoretically investigate how to optimally control a given neuron's spiking activity, in the case that it is driven by stochastic synaptic inputs. Optimal control is defined as the stochastic input which minimizes the variance of the interspike interval for a given mean interval and, hence, firing rate of the neuron.

The actual technique we use here to tackle the problem is transparent, but the conclusions are interesting and clear-cut. In the model presented below, a neuron's behavior depends on a property of the input, which may be temporally nonhomogeneous or homogeneous. The input and, hence, the behavior is characterized by a parameter $\alpha > 0$, such that, when $\alpha = 1/2$, the synaptic input corresponds to Poisson processes; when $\alpha < 1/2$, it is called sub-Poisson input; when $\alpha > 1/2$, it is supra-Poisson (see below for more details).

We find that when $\alpha < 1/2$ the optimal control signal is a delta function and the optimal output variance is then zero. When $\alpha = 1/2$, the Poisson input case, the optimal control signal is a delta function at the starting point of the control and the optimal variance is positive. When $\alpha > 1/2$, the optimal variance is positive and exact expressions for the optimal control signal and the variance are obtained. It is interesting to note that, when $\alpha \geq 1/2$, the optimal variance is in agreement with the empirical Fitt's law: The longer the time an action is required, the smaller the variance [6].

The optimal variance obtained here exhibits some interesting phenomena. When $\alpha = 1/2$, the optimal variance is not continuous and, when $\alpha = 1$, the derivative of the optimal variance is not continuous. Furthermore, when $\alpha = 1$, the optimal variance may attain a local minimum. The theoretically obtained optimal variance sets the lowest bound for the control problem. Finally, we also discuss how to actually implement the optimal control signal for certain model neurons.

The Model.—The model neuron we use here is the classical integrate-and-fire model [7]. When the membrane potential $V(t)$ is below the threshold V_{thre}, it is determined by $dV(t) = -\{[V(t) - V_{\text{rest}}]/\gamma\}dt + dI_{\text{syn}}(t)$ $t > 0$ with $V(0) = V_{\text{rest}} < V_{\text{thre}}$, where γ is the decay time constant and V_{rest} is the resting potential. The synaptic input current is $I_{\text{syn}}(t) = \sum_{i=1}^{p} a_i E_i(t) - \sum_{j=1}^{q} b_i I_j(t)$ with $E_i = \{E_i(t), t \geq 0\}, I_j = \{I_j(t), t \geq 0\}$ as independent and nonhomogeneous point processes with rates $\lambda_{E,i}(t)$ and $\lambda_{I,j}(t)$, respectively [5], $a_i > 0$, $b_i > 0$ are the magnitudes of each EPSP (excitatory postsynaptic potential) and inhibitory postsynaptic potential, and p and q are the total number of active excitatory and inhibitory synapses. Once $V(t)$ crosses V_{thre} from below a spike is generated and V is reset to V_{rest}. This model is termed the leaky integrate and fire (IF) model. The interspike interval of

efferent spikes is the random variable $T = \inf\{t : V(t) \geq V_{\text{thre}} | V(0) = V_{\text{rest}}\}$ i.e., the first time when $V(t)$ crosses the threshold V_{thre}.

In the following, we further assume that $V_{\text{rest}} = 0$, $p = q$, $a = a_i = b_i$, $i = 1, \ldots, p$, and use diffusion approximations to approximate synaptic inputs [7]. However, the assumption of equal strengths for the excitatory and inhibitory synaptic drives may be easily relaxed. Thus, we put $dI_{\text{syn}}(t) = a(1 - r)\lambda(t)dt + a\sqrt{1 + r^{2\alpha}}\lambda^{\alpha}(t)dB(t)$, where $\lambda(t) = p\lambda_{E,i} = p\lambda_{E,1}$, the *total* synaptic input rate, and $\lambda_{I,i} = r\lambda_{E,i}$ for $i = 1, \ldots, p$ with r as the ratio between inhibitory and excitatory inputs, $B = \{B(t), t \geq 0\}$ is standard (mean zero, variance t at time t) Brownian motion and $\alpha > 0$. In the sequel, we confine ourselves to the case of $r = 0$ and all results can be easily generalized to the case of $r \neq 1$. When $\alpha = 1/2$, the input is derived from a Poisson process and the *index of dispersion* of the input (variance/mean) is 1. When $\alpha > 1/2$, the index of dispersion is $\lambda^{2\alpha-1}$, we call it supra-Poisson input and, when $\alpha < 1/2$, it is termed sub-Poisson input. The larger the value of α, the more randomness there is in the synaptic inputs. If $\alpha < 1/2$, the variance is less than that of a Poisson input and, when $\alpha > 1/2$, the variance is greater than in the Poisson case when $\lambda(t) > 1$. For a more detailed discussion on the relationship between the parameter α and renewal processes, we refer the reader to [7], in particular, Eqs. (10.16) and (10.17).

For a fixed time T_f ms, let us define $I(\lambda) = \text{var}[V(T_f)]$, i.e., $I(\lambda)$ is the variance at the end point T_f of the membrane potential with the input signal $\lambda(t)$. Here is the problem we are going to address in the current paper.

Control problem: To find a synaptic input $\lambda^*(s)$ satisfying

$$\langle V(T_f) \rangle = V_{\text{thre}}, \tag{1}$$

$$I(\lambda^*) = \min_{\lambda} I(\lambda). \tag{2}$$

The meaning of the optimal control problem is as follows. Suppose that we intend to drive a neuron to fire with a fixed frequency, say $1000/T_f$ Hz so that we can fix the time T_f. Equation (1) satisfies the requirement. The second requirement Eq. (2) indicates that we intend to determine an optimal (control) signal so that the variance of the membrane potential at time T_f attains its minimum value, among all possible control signals. Here all possible control signals $[\lambda(t)]$ mean all possible nonnegative function of time t since $\lambda(t)$ is the total firing rates of input neurons. The more difficult mathematically and indeed more realistic problem is to insist that with a stochastic input $E[T] = T_f$ and seek to minimize $I_1(\lambda) = \text{var}[T]$. Although minimizing the variance of the membrane potential is not the same as minimizing the variance of the interspike interval, it is usually the case that the relationship between them is monotonic [see, for example, Eq. (9.106) in [7]]. Hence, we proceed on the

reasonable assumption that, when the variance of the membrane potential reaches its minimum value, the corresponding variance of interspike intervals attains its minimum as well. We will consider the more general problem in a later article.

We fix a few parameters in the simulations: $\gamma = 20$ ms, $a = 0.5$ mV, $V_{\text{rest}} = 0$ mV, and $V_{\text{thre}} = 20$ mV, these values being appropriate for some pyramidal neurons in the mammalian neocortex [8]. In the simulations, 2000 spikes are generated to estimate various quantities.

Optimal control.—For the optimal control problem posed in the previous section, fortunately we are able to find a complete and analytical answer.

Theorem 1 (Optimal Control Signal)
For $\alpha > 1/2$, the unique optimal control signal $\lambda^*(s)$ is

$$\lambda^*(s) = \frac{(2\alpha - 2)V_{\text{thre}}}{(2\alpha - 1)a\gamma\left[1 - \exp\left(-\frac{T_f(2\alpha-2)}{\gamma(2\alpha-1)}\right)\right]}$$
$$\times \exp\left(\frac{T_f - s}{(2\alpha - 1)\gamma}\right). \tag{3}$$

In particular, when $\alpha = 1$, we have $\lambda^*(s) = [V_{\text{thre}}/(aT_f)]\exp[(T_f - s)/\gamma]$.

For $\alpha = 1/2$, the unique optimal control signal $\lambda^*(s) = \delta_0(s)$, the delta function at time zero.

For $\alpha < 1/2$, the optimal control signal $\lambda^*(s) = \delta_y(s)$, the delta function at $y \in [0, T_f]$. Hence, the solution is not unique.

We refer the reader to [9] for detailed proofs.

Theorem 1 tells us that, when $\alpha > 1/2$, the optimal control signal is a smooth function of time but, when $\alpha \leq 1/2$, the optimal control signal is degenerate. It is easily seen from Eq. (3) that, when α decreases to $1/2$, the optimal control signal will gradually converge to the delta function at the original. When α increases to infinity, it will become flat.

As a direct consequence of Theorem 1, we have the following conclusions.

Theorem 2 (Optimal Variance)
For $\alpha > 1/2$,

$$I[\lambda^*(s)] = a^{2-2\alpha}V_{\text{thre}}^{2\alpha}\left|\frac{2\alpha - 2}{(2\alpha - 1)\gamma}\right|^{2\alpha-1}$$
$$\times \left|\left[1 - \exp\left(-\frac{T_f(2\alpha - 2)}{\gamma(2\alpha - 1)}\right)\right]\right|^{1-2\alpha}. \tag{4}$$

In particular, when $\alpha = 1$, we have

$$I[\lambda^*(s)] = \frac{V_{\text{thre}}^2}{T_f}. \tag{5}$$

For $\alpha = 1/2$, $I(\lambda^*) = aV_{\text{thre}}\exp[-(T_f/\gamma)]$.
For $\alpha < 1/2$, $I(\lambda^*) = 0$.

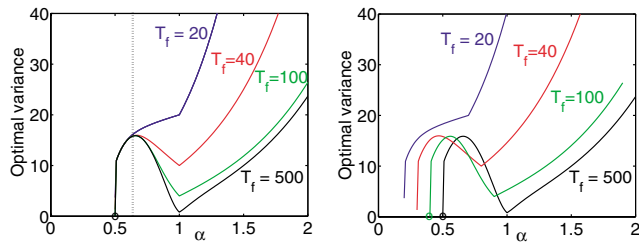From the numerical example plotted in Fig. 1, we conclude that when $T_f < 24$ the optimal variance is

FIG. 1 (color online). Optimal variance against α for $T_f =$ 20, 40, 100, 500. The right panel is the same as the left panel, but $T_f = 20$ is shifted towards left with 0.3 units, $T_f = 40$ with 0.2 units, and $T_f = 100$ with 0.1 units.

monotonic but, when $T_f > 24$, the optimal variance has another (local) minimum point at $\alpha = 1$.

The optimal variance exhibits two singular points. The second one is at $\alpha = 1$, where we see that the derivative of the optimal variance is not continuous, reminding us of a first order phase transition point. The first one is at $\alpha = 0.5$, as we have theoretically described in Theorem 2. When $\alpha < 0.5$, the optimal variance is zero but, when $\alpha \geq 0.5$, the optimal variance is positive. In Fig. 1, when $T_f = 20$, the optimal variance for $\alpha = 0.5$ is approximately 3. Hence, the variance is discontinuous.

If we think of α as an index of the randomness of synaptic inputs (the larger the α, the more randomness the input), Fig. 1 reveals another interesting phenomenon: multipoint stochastic resonance. The optimal variance is naturally a measurement of the quality of the output signal. The larger the variance, the worse the quality of the efferent signal. Figure 1 indicates that, at the points $\alpha < 0.5$ and $\alpha = 1$, the optimal variance attains its local minima. Although stochastic resonance has been extensively studied in the literature, to the best of our knowledge, the multipoint stochastic resonance as shown in Fig. 1 has not been reported before.

The results of Fig. 1 are also in accordance with Fitt's law [6], which implies that the shorter the time an action is required, the larger the variance of the action. Figure 1 clearly shows that the larger the T_f, the smaller the optimal variance. Our results, hence, provide neuronal level evidence for Fitt's law.

Another interesting phenomenon to be noted is that the variances are almost identical when α is between 0.5 and the thick dotted vertical line, although they are different at $\alpha = 0.5$ [see Fig. 1 (right)]. In particular, when $\alpha = 1$, the optimal variance is independent of the magnitude of EPSPs and the decay constant γ [see Eq. (5)]. In general, the optimal variance plotted in Fig. 1 gives the best accuracy we can achieve in the framework of our setup.

Neuronal implementations.—Having found the optimal control signals, we now turn our attention to how to implement them in neuronal models; that is, how to carry out the actual control of neuronal activity. We simulate the IF model, with synaptic inputs given by λ^* defined in Theorem 1.

In Fig. 2, the histograms of interspike intervals (ISI) of an IF model are depicted. It is interesting to note that not every run of control is successful. It is easily seen from the results in the previous section that, if the neuron fails to fire within a time window, the probability of firing a spike becomes rare. We restart the simulation if $t \geq 50$ ms, i.e., the input signal is $\lambda^*(t)$ with $t \leq 50$. The ratio in Fig. 2 is defined as the number of successful runs divided by total runs. Two thousand runs are carried out for each histogram. For example, in Fig. 2 (right), we have 0.7265×2000 spikes. The mass of the histogram moves to the left when α decreases. This is in agreement with the optimal control signals in the previous section. Note that we intend to control the neuron to fire with a frequency around 40 Hz ($T_f +$ refractory period $=$ 25 ms) in Fig. 2. The output frequency in Fig. 2 is around 39, 41, and 37 Hz, respectively.

When $\alpha = 1/2$, it is easily seen that the model is not controllable. From the results in the previous section, we know that we have to inject a huge current at the beginning of the control. The current will drive the neuron to fire and so $T \sim 0$.

When $\alpha < 1/2$, the control signal is not unique. Hence, we can inject current at the end of the control period, i.e., at time T_f. For a network of spiking neurons, this can be achieved by synchronous bursting.

As we have mentioned before, α is a parameter which characterizes the variability in the synaptic input. Our
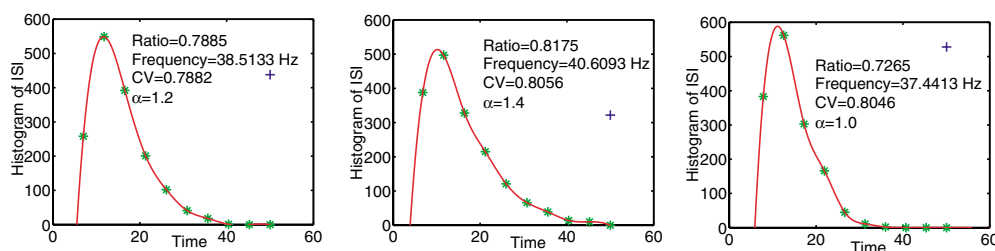

FIG. 2 (color online). Output interspike intervals histograms vs time (ms) for $\alpha = 1.2$, 1.4, and 1.0. Here 2000 runs are carried out for each α and ratio $=$ (number of successful runs)/2000. The number of unsuccessful runs are marked by "+". A refractory period of 5 ms is included in calculating the efferent firing rates (frequency). CV is the coefficient of variation of the ISI. The value of $T_f = 20$ ms.

conclusions above imply that, when the variability is low ($\alpha \leq 1/2$), the optimal output variance is zero, and the optimal control signal is degenerate. From data in [10], it seems that some motor neurons are sub-Poisson, with a CV (coefficient of variation, i.e., standard deviation/mean) of interspike intervals being less than 1. When the variability is high ($\alpha > 1/2$), we can actually control the neuronal activity and the optimal control signal is exactly given in Theorem 1. From data in [11], it seems that a neuron in the primary and inferior temporal visual cortices operates in the region of $\alpha > 1/2$, the supra-Poisson region (with a CV of interspike intervals being 1.91 and 1.84, respectively). Thus, results in Theorem 1 provide us with an explicit way to control neuronal activity.

Discussions.—We have presented a control theory for neuronal activity. Analytically, both the optimal control signal and the optimal variance are obtained. How to implement the optimal control in neuronal models was also discussed.

It is easily seen that we can implement the optimal control in a biologically realistic neuron as well. Of course, the optimal control signals might be totally different from the one we obtained here. In fact, for a biophysical model, we can expand the solution of it using, for example, the Volterra series. The optimal control problem is then similar to Eq. (3.6) in [9], but with a series of kernels. It is even reported in [12] that a single kernel can reproduce the Hodgkin-Huxley model behavior. Hence, our approach is generic and we can apply the similar technique developed here to biophysical models. On the other hand, we have seen a growing interest in the applications of spiking (IF) neurons and (IF) neuronal networks [1]. The theory developed here can be directly applied to controlling spiking neurons and neuronal networks composed of them.

Stochastic optimal control theory is a well-developed area [13]. Unfortunately, the theory usually leads to the Hamilton-Jacobi-Bellman equation [13] which is theoretically almost impossible to tackle. Furthermore, it is not applicable to our problem since the optimal control signals obtained here are degenerate in some cases (see, for example, Theorem 11.1 in [13]). As usual, a novel theory such as we have developed here can serve only to introduce more problems. For example, we have deliber-ately introduced 2 times here: T, the actual interspike interval, and T_f, an average time of intervals. We have then considered the control problem based upon the fluc-tuations of the membrane potential. It would be an illu-minating issue to consider how to control the fluctuations of T. Another issue is how to control the neuronal activity with reversal potentials [7]. Finally, we point out that it is disappointing that when $\alpha \leq 1/2$ the control problem is degenerate or uncontrollable, although it is theoretically interesting.

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