Type-II phase resetting curve is optimal for stochastic synchrony

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(Received 12 February 2009; published 16 July 2009)

The phase-resetting curve (PRC) describes the response of a neural oscillator to small perturbations in membrane potential. Its usefulness for predicting the dynamics of weakly coupled deterministic networks has been well characterized. However, the inputs to real neurons may often be more accurately described as barrages of synaptic noise. Effective connectivity between cells may thus arise in the form of correlations between the noisy input streams. We use constrained optimization and perturbation methods to prove that the PRC shape determines susceptibility to synchrony among otherwise uncoupled noise-driven neural oscillators. PRCs can be placed into two general categories: type-I PRCs are non-negative, while type-II PRCs have a large negative region. Here we show that oscillators with type-II PRCs receiving common noisy input synchronize more readily than those with type-I PRCs.

DOI: 10.1103/PhysRevE.80.011911 PACS number(s): 87.19.lc, 87.19.lm, 87.19.ln, 05.45.Xt

I. INTRODUCTION

Synchronous oscillations are found in many brain areas and are responsible for macroscopic electrical responses of the brain including field potentials and EEG signals. Within a single brain area, synchronization of neuronal activity serves to amplify signals to upstream regions [1], while synchronization across different areas may allow activity to be selectively routed.

Considerable theoretical interest has recently emerged in the generation of synchrony by correlated noisy inputs to uncoupled oscillators [2–5], a phenomenon we will refer to as stochastic synchrony. In the brain, stochastic synchrony may account for observations such as long-range synchronization [6,7], which are difficult to explain by the presence of synaptic connectivity alone. Moreover, noisy inputs have been shown to synchronize real neurons *in vitro* [8].

The key component in the study of noisy oscillators is the phase-resetting curve (PRC). This curve characterizes how inputs to an oscillator shift its timing or phase. In the context of neurons, spike times are believed to play an important role in coding and in the propagation of information across brain regions. Thus, the PRC provides a quantitative characterization of how inputs to neural oscillators alter the timing of spikes.

The theory of deterministic oscillators has shown that the type of bifurcation from steady state to periodic behavior determines the shape of the PRC. Weak-coupling theory shows that the form of the interaction between oscillators together with their intrinsic response (the PRC) provide sufficient information about the ability of the coupling to synchronize (or desynchronize) the oscillations. For very fast excitatory synaptic interactions, type-II oscillators characterized by the Hopf bifurcation synchronize more readily than type-I oscillators characterized by the saddle-node-on-an-invariant-circle (SNIC) bifurcation [9–12]. This difference in ability to synchronize with excitatory coupling is a consequence of the shape of the PRC occurring near the two different bifurcations. A PRC which contains both negative and positive lobes can allow inputs to both slow down the oscillator which is ahead and speed up the oscillator which is behind. In contrast, a non-negative PRC can only speed up the timing of both oscillators so that synchronization becomes more difficult. Several authors [10,13,14] have shown that the PRC near a SNIC is non-negative and approximately proportional to $1-\cos t$, while the PRC near a Hopf is proportional to $\sin(t+\alpha)$. Thus, type-II PRCs have a large negative lobe, whereas type-I PRCs are strictly positive.

Two recent papers have shown that type-II PRCs are better than type-I PRCs at synchronizing uncoupled oscillators with correlated input [15,16]. That is, for a given input correlation of the noisy stimulus, the output correlation of the oscillators is higher with type-II than with type-I PRCs. In these two papers, specific functions for PRCs were checked [namely, $\sin(t)$ and $1-\cos(t)$], and the correlations and degree of synchrony were analytically and numerically computed. However, it is not known whether there are other PRC shapes that might produce even stronger stochastic synchronization.

The easiest way to quantify stochastic synchrony is to examine the Lyapunov exponent, the rate at which two oscillators receiving identical inputs converge to synchrony. In this paper we will explore how this quantity depends on the shape of the PRC. In particular, we find that type-II PRCs lead to faster convergence than type-I PRCs, and we use variational principles to determine the optimal shape of the PRC to maximize this convergence.

First in Sec. I we introduce the phase reduction of a stochastically driven neural oscillator using the Itô change of variables, and in Sec. II we derive the Lyapunov exponent for two such oscillators receiving common noise. Next we use the Fokker-Planck equation in Sec. III to obtain the probability distribution of the phase of a noise-driven neural oscillator. The Euler-Lagrange method for constrained optimization allows us in Sec. IV to find the PRC that minimizes the Lyapunov exponent. This leads to a fourth-order system of nonlinear differential equations, which we approximate to an arbitrary order of accuracy using regular perturbations in Sec. V. The resulting approximation shows that a type-II PRC achieves the minimal Lyapunov exponent, hence producing more robust convergence to synchrony than a type-I PRC. Several interesting cases that arise as a function of the constraint parameters are discussed in Sec. VI. Finally in

Sec. VII we show that numerical solution of the fourth-order system agrees with the perturbation-derived approximation.

II. ITÔ PHASE REDUCTION

Consider a neural oscillator with additive white noise described by the stochastic differential equation

$$dX = F(X)dt + \sigma M dW, \tag{1}$$

where $F(X)$ represents the deterministic equations of motion, σ is the amplitude of the noise, M is a constant matrix, and dW is a vector of Gaussian white noise. Note that for a general limit-cycle oscillator, there need be no constraints on the entries of M. For neural models however, the noise typically occurs in current felt by the neuron, and this current appears only in the voltage component of the deterministic model. Without loss of generality, we take the voltage to be the first component. Thus, we will assume here that M has all zero entries except for the (1,1) element, which is identically 1.

The phase reduction method [2] applied to Eq. (1) gives a stochastic differential equation for the evolution of the oscillator's phase:

$$d\theta = dt + \sigma\Delta(\theta)dW, \tag{2}$$

where we have assumed without loss of generality that the intrinsic frequency of the oscillator is $\omega=1$, and dW is now a scalar white noise process. Here Δ is the infinitesimal phase response curve defined by

$$\Delta(\theta) \coloneqq \nabla_X \theta|_{X=X_0(\theta)},$$

where $X_0(\theta)$ is the unperturbed limit-cycle solution of the deterministic equation $\dot{X}=F(X)$. See Kuramoto [17], pages 26 and 27.

It is now important to note that the usual phase reduction method uses the conventional change of variables so Eq. (2) must be regarded as a Stratonovich differential equation [2,18]. To eliminate the correlation between θ and the white noise $\xi=dW$, we must apply Itô's lemma to obtain an equivalent but analytically more convenient formulation

$$d\theta = \left[1 + \frac{\sigma^2}{2}\Delta'(\theta)\Delta(\theta)\right]dt + \sigma\Delta(\theta)dW, \tag{3}$$

where $'$ denotes $\frac{\partial}{\partial\theta}$. In a recent paper, Yoshimura and Arai [19] show that Eq. (3) is incomplete and that another term must be added in the case where the noise is strictly white. However, more recently (in preparation) we show that the correct reduction is more subtle, and under some reasonable circumstances the additional term can be made arbitrarily small. Thus we will stay with the conventional phase-reduced model as first proposed by Teramae and Tanaka [2].

III. LYAPUNOV EXPONENT

As a standard measure of susceptibility to synchrony, we will now derive the Lyapunov exponent for two identical uncoupled neural oscillators receiving common additive white noise. The resulting analysis, however, applies equally well to an arbitrary number of identical noninteracting oscillators.

This approach is made possible by the pioneering work of Oseledec [20], who showed that Lyapunov theory applies in the stochastic setting. For a survey of the results, see [21,22].

Let us define the phase difference $\phi \coloneqq \theta_2 - \theta_1$, where θ_1 and θ_2 each obey Eq. (3). Linearizing around the synchronous state $\phi=0$, we obtain as in [2]

$$d\phi = \frac{\sigma^2}{2}[(\Delta'\Delta)'(\theta)\phi]dt + \sigma[\Delta'(\theta)\phi]dW,$$

where θ obeys Eq. (3) as well. Since the Lyapunov exponent is defined as $\lambda \coloneqq \lim_{t\to\infty}\frac{\log[\phi(t)]}{t}$, let us make the change of variables $y \coloneqq \log(\phi)$. Once again we invoke Itô's lemma, and after simplification we find that y satisfies the stochastic differential equation

$$dy = \frac{\sigma^2}{2}[\Delta''\Delta]dt + \sigma\Delta' dW.$$

Next we integrate, divide by t, and take the limit as $t\to\infty$ to obtain an expression for λ,

$$\begin{aligned}\lambda &= \lim_{t\to\infty}\frac{y(t)}{t}\\ &= \lim_{t\to\infty}\frac{\sigma^2}{2t}\int_0^t \Delta''[\theta(s)]\Delta[\theta(s)]ds + \frac{\sigma}{t}\int_0^t \Delta'[\theta(s)]dW(s).\end{aligned}$$

Assuming the system is ergodic, we can replace the long time average on the right-hand side with the spatial or ensemble average. Due to the Itô change of variables, the last term drops out leaving

$$\lambda = \frac{\sigma^2}{2}\int_0^1 \Delta''(\theta)\Delta(\theta)P(\theta)d\theta, \tag{4}$$

where $P(\theta)$ is the steady-state distribution of the phase.

Note that Teramae and Tanaka derive an expression for λ in [2] by making the approximation $P(\theta)=1$. Substituting this value into Eq. (4) and performing integration by parts, they obtain

$$\lambda \approx -\frac{\sigma^2}{2}\int_0^1 [\Delta'(\theta)]^2 d\theta.$$

In this paper, however, we wish to retain the generality of $P(\theta)$ as discussed below.

IV. STEADY-STATE PHASE DISTRIBUTION

In order to evaluate the Lyapunov exponent, we need to obtain the stationary density of the phase when perturbed by noise. Series expansion of the stationary density was originally developed by Khasminskii [23]; for discussion see also [21,22]. In a recent paper, Teramae and Tanaka [2] treated the density as uniform, which is correct for weak noise. However our subsequent perturbation analysis will require higher-order terms, so we will need to derive a more accurate value for the steady-state phase distribution.

By applying the Fokker-Planck equation to Eq. (3), we obtain after simplification a partial differential equation for the probability distribution $P(\theta,t)$:

$$\frac{\partial P}{\partial t}=-\frac{\partial P}{\partial \theta}+\frac{\sigma^2}{2}\frac{\partial}{\partial \theta}\left[\Delta\frac{\partial(\Delta P)}{\partial \theta}\right].$$

Now we may set $\frac{\partial P}{\partial t}=0$ to find the steady state, then integrate once with respect to θ to obtain

$$-J=-P+\frac{\sigma^2}{2}\left[\Delta\frac{\partial(\Delta P)}{\partial \theta}\right], \tag{5}$$

where $-J$ is a constant of integration. We require that $P(0)=P(1)$ and that the solution be normalized, namely, $\int_0^1 P(\theta)d\theta=1$. Note that the equations are singular since $\Delta(\theta)$ generally vanishes at several places, in particular at $\theta=0,1$. In the Appendix below, we prove the existence of the stationary density by directly solving the linear equations and taking appropriate limits.

In the remainder of this section, we use regular perturbation theory to approximate the stationary density for small noise, $0<\sigma\ll 1$. To approximate both J and P we substitute

$$J=1+\sigma^2 J_1+\sigma^4 J_2+\cdots,$$

$$P(\theta)=1+\sigma^2 P_1(\theta)+\sigma^4 P_2(\theta)+\cdots$$

into Eq. (5). Equating like powers of σ gives

$$-J_1=-P_1(\theta)+\frac{1}{2}\Delta(\theta)\Delta'(\theta).$$

Integrating both sides over [0,1] leaves the constant on the left-hand side unchanged. For the right-hand side, note that $\int_0^1 P(\theta)d\theta=1$, and hence $\int_0^1 P_1(\theta)d\theta=0$. Furthermore, $\Delta\Delta'=\frac{1}{2}\frac{d}{d\theta}(\Delta^2)$ so that

$$J_1=-\frac{1}{4}[\Delta(1)^2-\Delta(0)^2]=0$$

since Δ is periodic. Thus we have $P_1(\theta)=\frac{1}{2}\Delta(\theta)\Delta'(\theta)$.

Similarly,

$$-J_2=-P_2(\theta)+\frac{1}{2}\Delta(\theta)^2\Delta'(\theta)^2+\frac{1}{4}\Delta(\theta)^3\Delta''(\theta).$$

Since $\int_0^1 P_2(\theta)d\theta=0$ as well, we can integrate both sides as above and use integration by parts to obtain

$$J_2=\frac{1}{4}\int_0^1[\Delta(\theta)\Delta'(\theta)]^2 d\theta,$$

$$P_2(\theta)=\frac{1}{2}\Delta(\theta)^2\Delta'(\theta)^2+\frac{1}{4}\Delta(\theta)^3\Delta''(\theta)+\frac{1}{4}\int_0^1[\Delta(\theta)\Delta'(\theta)]^2 d\theta.$$

In summary,

$$J=1+\frac{\sigma^4}{4}\int_0^1[\Delta(\theta)\Delta'(\theta)]^2 d\theta,$$

$$P(\theta)=1+\frac{\sigma^2}{2}\Delta(\theta)\Delta'(\theta)+\frac{\sigma^4}{4}\Big\{2\Delta(\theta)^2\Delta'(\theta)^2+\Delta(\theta)^3\Delta''(\theta)+\int_0^1[\Delta(\theta)\Delta'(\theta)]^2 d\theta\Big\}. \tag{6}$$

For the perturbation expansions in the next section, it will suffice to write $J=1$. We will use Eq. (6) in Sec. VI and for the numerical verifications in Sec. VII.

V. CONSTRAINED OPTIMIZATION

The Euler-Lagrange variational technique provides a method for determining the phase resetting curve Δ that minimizes the Lyapunov exponent, subject to appropriate constraints. To ensure smooth solutions and to eliminate uninformative and biologically implausible higher harmonics of the optimal solution, we begin by imposing the general constraint

$$\int_0^1 a[\Delta(\theta)]^2+b[\Delta'(\theta)]^2+c[\Delta''(\theta)]^2 d\theta=1, \tag{7}$$

where a, b, and c are free parameters. A standard normalization has $a=1$, $b=0$, and $c=0$. However, nonzero values of b and c endow solutions with additional smoothness observed in naturally occurring PRCs. Constraints on higher derivatives also impose a bound on the amplitude of potentially optimal solutions. (See Fig. 3.) Otherwise, an arbitrarily large PRC could produce an arbitrarily negative Lyapunov exponent. Below we will explore the cases that arise from specific choices of the constraint parameters.

We proceed by placing Eqs. (4), (5), and (7) together with the approximation $J=1$ into the Euler-Lagrange formula to obtain the functional

$$\int_0^1 \Delta''\Delta P+\nu_1[a\Delta^2+b(\Delta')^2+c(\Delta'')^2-1]+\nu_2(\theta)\left[1-P+\frac{\sigma^2}{2}\Delta(\Delta P)'\right]d\theta=0, \tag{8}$$

where ν_1 is a free parameter and $\nu_2(\theta)$ represents a continuum of free parameters.

Define the operator

$$\mathcal{L}(\Delta):=\Delta''\Delta P+\nu_1[a\Delta^2+b(\Delta')^2+c(\Delta'')^2-1]+\nu_2(\theta)\left[1-P+\frac{\sigma^2}{2}\Delta(\Delta P)'\right].$$

The optimal Δ we seek will satisfy the two equations

$$\frac{\partial\mathcal{L}}{\partial\Delta}-\frac{d}{d\theta}\frac{\partial\mathcal{L}}{\partial\Delta'}+\frac{d^2}{d\theta^2}\frac{\partial L}{\partial\Delta''}=0, \tag{9}$$

$$\frac{\partial\mathcal{L}}{\partial P}-\frac{d}{d\theta}\frac{\partial\mathcal{L}}{\partial P'}=0. \tag{10}$$

Note that we can write two more Euler-Lagrange equations, but $\frac{\partial\mathcal{L}}{\partial\nu_1}=0$ simply restates Eq. (7), and $\frac{\partial\mathcal{L}}{\partial\nu_2}=0$ returns Eq. (5) governing P.

Assuming the parameter c is nonzero, we obtain from Eqs. (9) and (10) a fourth-order system of ordinary differential equations:

$$P''\Delta + 2(P'\Delta' + P\Delta'' + a\Delta\nu_1 - b\Delta''\nu_1 + c\Delta^{(4)}\nu_1) + \frac{1}{2}\Delta(P'\nu_2 - P\nu_2')\sigma^2 = 0, \tag{11}$$

$$\Delta\Delta'' - \nu_2 - \frac{1}{2}\Delta(\Delta'\nu_2 + \Delta\nu_2')\sigma^2 = 0. \tag{12}$$

If $c=0$, we will have instead the second-order system which obtains by setting $c=0$ in Eq. (11). When we examine the effects of varying the constraint parameters in Sec. VI, we will see that the main result remains the same in this case as well.

VI. PERTURBATION APPROXIMATION

Let us first consider the fourth-order case where the parameter c is nonzero.

Assuming the noise amplitude σ is sufficiently small, we write the following expansions:

$$P(\theta) = P_0(\theta) + \sigma^2 P_1(\theta) + \cdots,$$

$$\Delta(\theta) = \Delta_0(\theta) + \sigma^2\Delta_1(\theta) + \cdots,$$

$$\nu_1 = \nu_{1,0} + \sigma^2\nu_{1,1} + \cdots,$$

$$\nu_2(\theta) = \nu_{2,0}(\theta) + \sigma^2\nu_{2,1}(\theta) + \cdots. \tag{13}$$

Substituting these into Eqs. (11) and (12) and equating like powers of σ gives to lowest order: $P_0(\theta)=1$, $\nu_{2,0}(\theta)=\Delta_0(\theta)\Delta_0''(\theta)$, and the fourth-order homogeneous equation

$$a\nu_{1,0}\Delta_0 + (1 - b\nu_{1,0})\Delta_0'' + c\nu_{1,0}\Delta_0^{(4)} = 0. \tag{14}$$

For convenience let us define the differential operator

$$\mathcal{J} = a\nu_{1,0} + (1 - b\nu_{1,0})\frac{\partial^2}{\partial\theta^2} + c\nu_{1,0}\frac{\partial^4}{\partial\theta^4}.$$

Thus Eq. (14) becomes $\mathcal{J}(\Delta_0)=0$, and the first-order correction Δ_1 obeys the inhomogeneous equation

$$\mathcal{J}(\Delta_1) = (\Delta_0')^3 - b\nu_{1,1}\Delta_0'' + \Delta_0(a\nu_{1,1} + 3\Delta_0'\Delta_0'') + c\nu_{1,1}\Delta_0^{(4)}. \tag{15}$$

Furthermore, substituting expansions (13) into Eq. (7) gives the corresponding constraints:

$$\int_0^1 a\Delta_0^2 + b(\Delta_0')^2 + c(\Delta_0'')^2 = 1, \tag{16}$$

$$\int_0^1 a\Delta_0\Delta_1 + b\Delta_0'\Delta_1' + c\Delta_0''\Delta_1'' = 0. \tag{17}$$

Before solving Eq. (14), we must first determine the unknown parameter $\nu_{1,0}$. Since we seek only periodic solutions, we can impose a condition on the characteristic equation of Eq. (14):

$$a\nu_{1,0} + (1 - b\nu_{1,0})y^2 + c\nu_{1,0}y^4 = 0. \tag{18}$$

Specifically, by requiring that the roots of this polynomial satisfy $y=2\pi i$, we determine that

$$\nu_{1,0} = \frac{4\pi^2}{a + 4b\pi^2 + 16c\pi^4}.$$

Now we are ready to impose periodic boundary conditions, and we find that the solution of Eq. (14) is just $\Delta_0(\theta)=C_0\sin(2\pi\theta)$. The constant of integration C_0 is determined from constraint (16) so that

$$C_0 = \pm\frac{\sqrt{2}}{\sqrt{a + 4b\pi^2 + 16c\pi^4}}.$$

While both values of C_0 will give the same minimal value of the Lyapunov exponent, we choose the negative value for biological plausibility. Hence to lowest order we find that the optimal phase resetting curve is type II:

$$\Delta_0(\theta) = -\frac{\sqrt{2}\sin(2\pi\theta)}{\sqrt{a + 4b\pi^2 + 16c\pi^4}}. \tag{19}$$

The next order correction does not appreciably change this result. To obtain the σ^2 term, we must solve Eq. (15) subject to Eq. (17). By the Fredholm alternative, a solution to the inhomogeneous problem exists if and only if (iff) the right-hand side of Eq. (15), call it $r(\theta)$, is orthogonal to the null space of $\mathcal{J}^*$. However, since $\mathcal{J}$ is self-adjoint we simply solve for the value of $\nu_{1,1}$ such that

$$\int_0^1 \sin(2\pi\theta)r(\theta)d\theta = 0,$$

namely, $\nu_{1,1}=0$.

Imposing periodic boundary conditions on the resulting equation yields the solution

$$\Delta_1(\theta) = C_1\sin(2\pi\theta) + \frac{\sqrt{2}\pi\sin(2\pi\theta)\sin(4\pi\theta)}{(a - 144c\pi^4)\sqrt{a + 4b\pi^2 + 16c\pi^4}}.$$

As before, we use constraint (17) to obtain $C_1=0$. Hence to order σ^2 the optimal phase resetting curve is given by

$$\Delta(\theta) = -\frac{\sqrt{2}\sin(2\pi\theta)}{\sqrt{a + 4b\pi^2 + 16c\pi^4}} + \frac{\sigma^2}{2}\frac{\sqrt{2}\pi\sin(2\pi\theta)\sin(4\pi\theta)}{(a - 144c\pi^4)\sqrt{a + 4b\pi^2 + 16c\pi^4}}. \tag{20}$$

VII. CONSTRAINT PARAMETERS

Let us next explore the influence of the constraint parameters a, b, and c, which we will allow to take on the values of 0 or 1. Of the seven nontrivial combinations, one has no periodic solution at all and is thus inadmissible. Four parameter choices give rise to the same optimum already found in

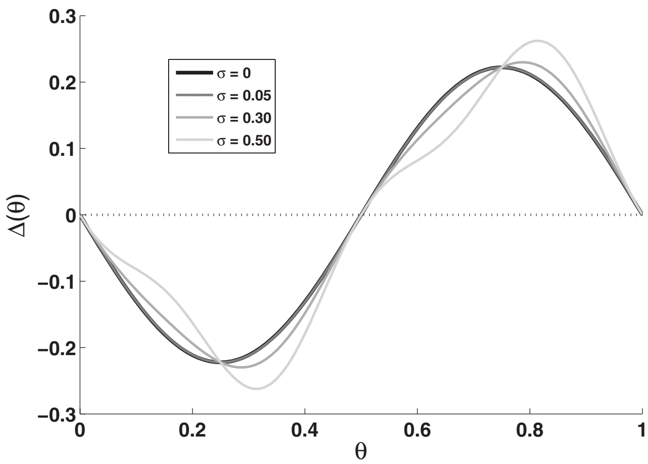

FIG. 1. In the case where the second derivative is left unconstrained, the optimal PRC deviates from a pure cosine function as the noise amplitude σ increases. Parameters are $a=1$, $b=1$, and $c=0$.

Eq. (20), and the two remaining parameter combinations do not produce a unique solution but instead yield a family of solutions ranging smoothly from type I to type II. In this case, we explicitly find the minimizer of λ among the family of solutions.

All of the cases can be analyzed by examining Eq. (18), the characteristic equation of $\mathcal{L}(\Delta)=0$. For example, the case $a=c=0$ and $b=1$ can have no periodic solution since the polynomial $(1-\nu_{1,0})y^2=0$ has no nontrivial roots.

The four parameter combinations that lead to Eq. (20) are those in which $a=1$. In these cases we have

$$\nu_{1,0}+(1-b\nu_{1,0})y^2+c\nu_{1,0}y^4=0.$$

If $c\neq 0$, the polynomial is fourth degree having four distinct roots; if $c=0$ the polynomial is quadratic with two distinct roots. In each case we can set $y=2\pi i$ and solve uniquely for $\nu_{1,0}$ as discussed above.

The case $c=0$ (while $a=1$) deserves further attention for another reason. In this regime, the optimal PRC becomes sensitive to the noise amplitude σ as illustrated in Fig. 1. To understand why the curve deforms, let us focus on the extrema of Eq. (20), which are given by the zeros of the derivative:

$$\Delta'(\theta)=-\frac{2\sqrt{2}\pi}{\sqrt{a+4b\pi^2+16c\pi^4}}\Bigg\{\cos(2\pi\theta)+\frac{\sigma^2\pi}{a-144c\pi^4}\times\left[\cos(4\pi\theta)\sin(2\pi\theta)+\frac{1}{2}\cos(2\pi\theta)\sin(4\pi\theta)\right]\Bigg\}.$$

In this form we clearly see that the unperturbed extrema (when $\sigma=0$) occur at $\theta=1/4$ and 3/4, while the deformation due to noise is on the order of $\sigma^2\pi/(a-144c\pi^4)$. More specifically, when $c\neq 0$ this quantity is $\mathcal{O}(\sigma^2 10^{-4})$ so that the weak noise in our model ($\sigma\ll 1$) has negligible effect. However when $c=0$, this quantity is $\mathcal{O}(\sigma^2)$ so that even relatively small magnitude noise can have a noticeable impact on the shape of the optimal PRC.

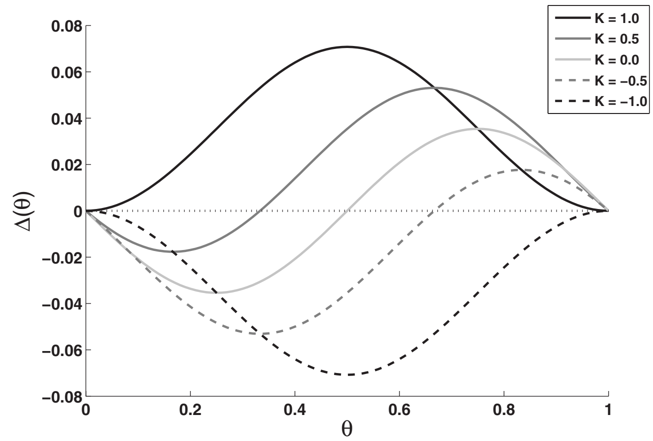

FIG. 2. When the first derivative is unconstrained while the second derivative is constrained, Euler-Lagrange optimization produces a family of candidates for the minimizer of the Lyapunov exponent ranging smoothly from type II to type I as the parameter K ranges from 0 to 1. For negative K (dashed), the curves do not represent biologically plausible PRCs. Parameters are $a=0$, $b=1$, and $c=1$.

Another interesting situation arises in the two cases where $a=0$, $c=1$, and b is arbitrary. Here the characteristic equation has a double root at $y=0$:

$$(1-b\nu_{1,0})y^2+\nu_{1,0}y^4=0.$$

After accounting for the boundary conditions, we have a superposition of two independent solutions

$$\Delta_0(\theta)=C_3[1-\cos(2\pi\theta)]+C_4\sin(2\pi\theta).$$

Constraint (16) eliminates only one degree of freedom, leaving a family of solutions as candidates for the optimum:

$$\Delta_0(\theta)=K\frac{1-\cos(2\pi\theta)}{\sqrt{2\pi^2(b+4\pi^2)}}-\sqrt{1-K^2}\frac{\sin(2\pi\theta)}{\sqrt{2\pi^2(b+4\pi^2)}}, \tag{21}$$

where the remaining degree of freedom K has been normalized to range between -1 and 1. See Fig. 2.

Combining Eq. (4) for the Lyapunov exponent with Eq. (6) for the steady-state phase distribution, we insert Eq. (21) to obtain the following expression:

$$\lambda=-\frac{1}{b+4\pi^2}+\frac{\sigma^4}{4}\frac{(4K^4+10K^2+1)}{4\pi^2(b+4\pi^2)^3},$$

where we have set $a=0$ and $c=1$. Note that we needed to carry out the expansion of λ to σ^4 in order to discover the dependence on K.

Since the derivative of λ with respect to K has only one real root at $K=0$, where a minimum occurs, the type-II curve remains the optimal PRC even in this case.

VIII. NUMERICAL VERIFICATION

We would like to independently verify the accuracy of the optimal PRC Eq. (20) derived via perturbation expansion by

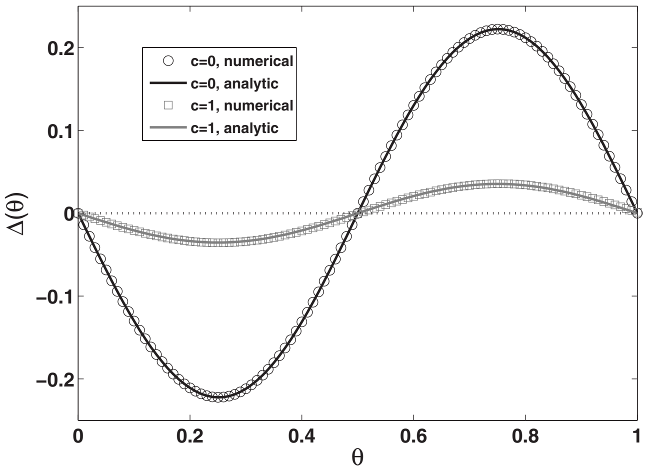

FIG. 3. The magnitude of the optimal PRC depends on the whether or not the second derivative is constrained. The numerical solution (open circles) and the analytic result (solid lines) coincide. Parameters are $a=1$, $b=1$, and $\sigma=0.05$.

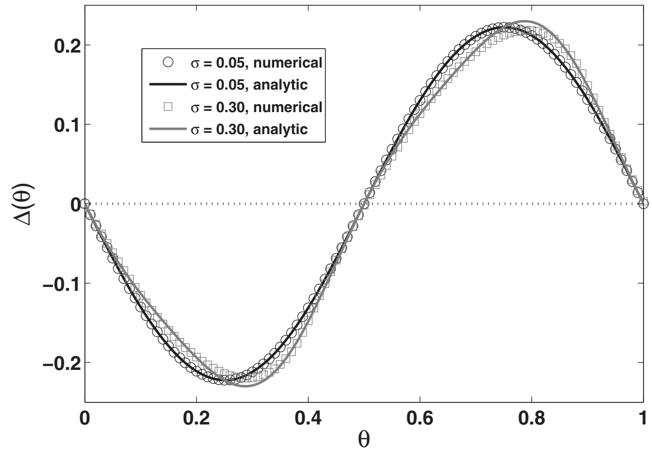

FIG. 4. When the second derivative is unconstrained, the optimal PRC shape deforms with increasing noise. The numerical solution (open circles) and the analytic result (solid lines) are in good agreement. Parameters are $a=1$, $b=0$, and $c=0$.

numerically solving the Euler-Lagrange Eqs. (11) and (12) with periodic boundary conditions. Unfortunately, the resulting system is singular and therefore very difficult to solve numerically. Instead we substitute the approximation $P(\theta)=1+\frac{\sigma^2}{2}\Delta(\theta)\Delta'(\theta)$ into the Euler-Lagrange functional (8) to obtain a new functional

$$\int_0^1 \Delta''\Delta\left(1+\frac{\sigma^2}{2}\Delta(\theta)\Delta'(\theta)\right) + \nu_1[a\Delta^2+b(\Delta')^2+c(\Delta'')^2-1]d\theta=0,$$

which gives rise via Eq. (9) to the fourth-order boundary value problem

$$\Delta^{(4)}=\frac{-2\Delta''-2a\Delta\nu_1+2b\Delta''\nu_1-\Delta'^3 3\sigma^2-3\Delta\Delta'\Delta''\sigma^2}{2c\nu_1}.$$

When $c=0$, we similarly obtain a second-order boundary value problem.

Using the numerical integration package XPPAUT, we are able to achieve excellent agreement with our analytical approximation. Figure 3 illustrates numerical and analytic solutions in the case where $c=1$ and where $c=0$. Note that imposing a constraint on the second derivative of Δ results in an optimal PRC of much smaller magnitude.

In Fig. 4 we find good agreement between the analytic and numerical results even for the regime in which $a=1$, $c=0$, and PRC shape is sensitive to noise amplitude. The numerical simulation deforms with increasing σ just as the analytic approximation does.

IX. DISCUSSION

In this paper we have used perturbation theory and the calculus of variations to analyze the rate at which neurons can synchronize when subjected to common inputs. We treat the inputs as noise, that is, as if they are delta-correlated with no structure. Real neuronal inputs do have correlational structure, however, so that the expression for the rate of synchronization (the Lyapunov exponent) is more complex. Indeed, in previous work [15] we have shown that the temporal characteristics of the noise can also have an effect on how rapidly neurons synchronize. In that work, we asked the reverse question: given a particular PRC, what correlation time for the noise minimizes the Lyapunov exponent?

Suppose that we use some signal that is not white noise but still has zero mean and is stationary. Then the phase satisfies

$$\frac{d\theta}{dt}=1+\Delta(\theta)\xi(t),$$

where $\xi(t)$ is the input. The Lyapunov exponent is

$$\lambda := \lim_{T\to\infty}\frac{1}{T}\int_0^T \Delta'(\theta(t))\xi(t)dt.$$

By using an approximation of $\theta(t)$ as in [24] we may be able to obtain a functional for λ depending on $\xi(t)$ and Δ, and from this we may apply similar methods to estimate the optimal shape of the PRC given the statistics of the inputs.

Optimization has been applied to other aspects of neural oscillators. Moehlis *et al.* [25] asked the following question. Consider the scalar oscillator model

$$\frac{d\theta}{dt}=f(\theta)+\Delta(\theta)I(t).$$

[Note that if $f(\theta)=1$, we have Eq. (2), the case considered in this paper.] Suppose the neuron fired at $t=0$ and we desire it to fire again at time $T>0$. What is the minimum stimulus, $I(t)$ [which, say, minimizes $\int_0^T I(t)^2dt$] to do this? Moehlis *et al.* [25] write the Euler-Lagrange equations for this optimization problem and then assume that $I(t)$ is small in order to use perturbation methods. A related issue is the "optimal stimulus" [26] for producing a spike in a neuron, and for neural oscillators this has been answered in [27].

ACKNOWLEDGMENTS

The work was supported by the National Science Foundation, Contract No. NSF-DMS-0817131 and the National Science Foundation program for Collaborative Research in Computational Neuroscience, Contract No. R01MH079504.

APPENDIX: AN EXISTENCE PROOF

On the interval $[0,1]$, the phase resetting curve Δ is necessarily 0 at the end points and possibly at interior points as well. As a result, we have a singular equation for the steady-state distribution of phases P, derived earlier as Eq. (5) and repeated here:

$$-J = -P + \frac{\sigma^2}{2}\Delta(\Delta P)'. \tag{A1}$$

Existence of solutions for first-order linear ordinary differential equations with isolated singularities of the second kind are discussed in many classic references; see, for example, chapter 5 of [28]. For the reader unfamiliar with the general theory, we include the following direct proof that Eq. (A1) does indeed have a solution despite the singularities.

Suppose $\Delta(\theta)\neq 0$ in the open interval $(a,b)\subseteq[0,1]$, while $\Delta(a)=\Delta(b)=0$. In this way, we will be able to apply our proof to the entire domain $[0,1]$ in a piecewise fashion; for example, if $\Delta(x)=\sin(2\pi x)$, then $a=0$ and $b=1/2$ or $a=1/2$ and $b=1$. In the following we will assume, without loss of generality, that $\Delta(\theta)>0$ in (a,b).

Let us begin by rewriting the differential equation as an integral equation. Define $Q(x)\coloneqq\Delta(x)P(x)$. Then Eq. (A1) becomes

$$Q' - \frac{2Q}{\sigma^2\Delta^2} = \frac{-2J}{\sigma^2\Delta}. \tag{A2}$$

We now introduce an integrating factor; let

$$z(x) \coloneqq -\frac{2}{\sigma^2}\int_c^x \frac{ds}{\Delta^2(s)}, \tag{A3}$$

where $c\in(a,b)$ is fixed. Observe that, as x approaches a from above we eventually have $x<c$, and hence $z(x)$ approaches $+\infty$. Likewise, as x approaches b from below, $z(x)$ approaches $-\infty$.

Equation (A2) now becomes

$$(e^{z(x)}Q)' = -\frac{2J}{\sigma^2\Delta}e^{z(x)}.$$

Integrating both sides gives

$$Q(x) = \frac{2J}{\sigma^2}e^{-z(x)}\left(K - \int_c^x \frac{e^{z(t)}}{\Delta(t)}dt\right), \tag{A4}$$

where K is a constant of integration that will be determined below.

We see from Eq. (A1) that $P(a)=P(b)=J$. Therefore a solution exists iff $\lim_{x\to a^+} Q(x)/\Delta(x)=\lim_{x\to b^-} Q(x)/\Delta(x)=J$. Let us first consider the right end point and assume for now that the limit

$$\lim_{x\to b^-}\int_c^x \frac{e^{z(t)}}{\Delta(t)}dt = L \tag{A5}$$

exists. Let us compute

$$\lim_{x\to b^-}\frac{Q(x)}{\Delta(x)} = \frac{2J}{\sigma^2}\lim_{x\to b^-}\frac{K-\int_c^x \frac{e^{z(t)}}{\Delta(t)}dt}{\Delta(x)e^{z(x)}},$$

and note that when we set $K=L$, both numerator and denominator tend to 0 as $x\to b^-$. Thus we can use L'Hôpital's rule and definition (A3) to obtain

$$\lim_{x\to b^-}\frac{Q(x)}{\Delta(x)} = \frac{2J}{\sigma^2}\lim_{x\to b^-}\frac{-e^{z(x)}/\Delta(x)}{\Delta(x)z'(x)e^{z(x)}+\Delta'(x)e^{z(x)}} = J. \tag{A6}$$

Now let us return to the assumption we made and observe that the integral in Eq. (A5) is not improper after all. Rewriting the integrand of Eq. (A5) such that both numerator and denominator go to infinity, we can use L'Hôpital's rule again to see that the integrand goes to zero:

$$\lim_{t\to b^-}\frac{e^{z(t)}}{\Delta(t)} = \lim_{t\to b^-}\frac{1/\Delta(t)}{e^{-z(t)}} = \lim_{t\to b^-}\frac{-\Delta'(t)/\Delta(t)^2}{e^{-z(t)}/\Delta(t)^2} = 0.$$

The last equality follows since Δ' is bounded and $\lim_{x\to b^-} e^{z(t)}=0$. Hence our assumption was justified.

Now let us rewrite Eq. (A4), incorporating our knowledge from Eq. (A5), namely, that $K=L$:

$$Q(x) = \frac{2J}{\sigma^2}e^{-z(x)}\left(\int_c^b \frac{e^{z(t)}}{\Delta(t)}dt - \int_c^x \frac{e^{z(t)}}{\Delta(t)}dt\right)$$
$$= \frac{2J}{\sigma^2}e^{-z(x)}\int_x^b \frac{e^{z(t)}}{\Delta(t)}dt.$$

It remains to show that $\lim_{x\to a^+} Q(x)/\Delta(x)=J$. We will prepare to use L'Hôpital's rule once again by writing

$$\lim_{x\to a^+}\frac{Q(x)}{\Delta(x)} = \frac{2J}{\sigma^2}\lim_{x\to a^+}\frac{\int_x^b \frac{e^{z(t)}}{\Delta(t)}dt}{\Delta(x)e^{z(x)}}. \tag{A7}$$

Since $e^{z(t)}$ tends to infinity as x approaches a from above, by L'Hôpital's rule the denominator of Eq. (A7) also tends to infinity:

$$\lim_{x\to a^+}\frac{e^{z(x)}}{1/\Delta(x)} = -\frac{2}{\sigma^2}\lim_{x\to a^+}\frac{e^{z(x)}/\Delta(x)^2}{\Delta'(x)/\Delta(x)^2} = \infty.$$

The numerator of Eq. (A7) tends to infinity as well since

$$\int_x^b \frac{e^{z(t)}}{\Delta(t)}dt > \int_x^b \frac{e^{z(t)}}{M}dt,$$

when $M=\max\{\Delta(x):x\in[0,1]\}$, and the latter integral is clearly unbounded as x approaches a. Therefore we can apply to Eq. (A7) a similar calculation to that in Eq. (A6) and conclude that $\lim_{x\to a^+}Q(x)/\Delta(x)=J$ as desired.

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