Collective phase response curves for heterogeneous coupled oscillators

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Phase response curves (PRCs) have become an indispensable tool in understanding the entrainment and synchronization of biological oscillators. However, biological oscillators are often found in large coupled heterogeneous systems and the variable of physiological importance is the collective rhythm resulting from an aggregation of the individual oscillations. To study this phenomena we consider phase resetting of the collective rhythm for large ensembles of globally coupled Sakaguchi-Kuramoto oscillators. Making use of Ott-Antonsen theory we derive an asymptotically valid analytic formula for the collective PRC. A result of this analysis is a characteristic scaling for the change in the amplitude and entrainment points for the collective PRC compared to the individual oscillator PRC. We support the analytical findings with numerical evidence and demonstrate the applicability of the theory to large ensembles of coupled neuronal oscillators.

I. INTRODUCTION

Many biological rhythms are produced in a collective manner by a large ensemble of coupled heterogeneous oscillators. For example, the mammalian circadian clock consists of approximately 20 000 coupled heterogeneous neuronal oscillators [1]. The collective oscillation produced by the ensemble of individual neurons drives the behavioral circadian rhythm [1]. Similar phenomena have been observed in the generation of brain rhythms, cardiac pacemaker cells, and many other biological systems [2–4].

For weakly coupled limit-cycle oscillators the dynamics of each oscillator may be reduced to a single phase variable and the collective properties of the system may be revealed through the study of the coupled phase equations [5–7]. One of the best characterized systems of coupled phase oscillators is the mean-field Sakaguchi-Kuramoto model [5,8]. In this model the oscillators are assumed to be all-to-all coupled through a sinusoidal coupling function. The existence, stability and phase distribution of the synchronized state in the Sakaguchi-Kuramoto equations has been the subject of extensive mathematical investigation [8,9]. In particular, several dimension-reduction techniques have been developed for this system which allow for analytical investigation [10–13].

The properties of oscillating systems are often studied both experimentally and theoretically by characterizing their response to perturbations applied at different phases in the oscillation [6,14]. Commonly, the effect of the perturbation is measured in terms of a phase shift and the resulting curve is termed a phase response curve (PRC).

For a single oscillator, the (microscopic) PRC is well defined both mathematically and experimentally and can provide insights into the stability, synchronization, and entrainment behaviors of the oscillator [15–17]. Of particular importance are the amplitude and zeros of the PRC. For entrainment by a weak resetting signal, the amplitude of the PRC determines the range of frequencies the oscillator can entrain to and the stable zeros give the phase difference between the entraining force and the oscillator [17].

Comparatively little is known about the (macroscopic) collective phase response curve. Here an external stimulus perturbs each individual oscillator which induces a phase shift according to the microscopic PRC. These microscopic shifts interact to produce a macroscopic shift in the collective rhythmicity of the population. The phase shift in the macroscopic phase gives the collective PRC for the ensemble of oscillators.

For a population of oscillators with identical phases the collective and microscopic phase PRCs will coincide. However, when the oscillator population has some variance in the phase distribution, the collective PRC will generally differ from the microscopic PRC [16]. A central question is how the collective and the microscopic PRCs may be related for a population of heterogeneous oscillators.

Mathematically, several factors have been identified which can lead to significant differences between the microscopic and collective PRCs. The nature of the coupling function as well as the connectivity between the individual oscillators is known to have important effects on how the collective PRC differs from the microscopic PRC [18]. The effect of a general network structure on the collective PRC is discussed in Ref. [18] for the case of small deviations from a global limit cycle attractor. Furthermore, the effect of a non-odd coupling function on collective phase shifts is examined in Ref. [19] using the Ott-Antonsen dimension reduction technique [10,20]. The effect of non-odd coupling functions is also examined in Ref. [21] using symmetry properties of the coupling function. Moreover, the phase distribution of the ensemble of oscillators is known to effect the shape of the collective PRC [16].

In this work, we consider an all-to-all coupled network and focus on the effect of the phase distribution and the coupling function in determining the collective PRC. We study a globally coupled system of Sakaguchi-Kuramoto oscillators with a non-odd sinusoidal coupling function. Each individual oscillator experiences an instantaneous phase shift according to a microscopic PRC where we make no assumptions on the form of the microscopic PRC. We analytically determine an asymptotic expansion for the collective phase response curve making use of the formalism developed in Ref. [19] based on the Ott-Antonsen reduction [10,20].

The resulting analytical formula reveals the effect of heterogeneity. The formula predicts that the collective PRC

differs from the microscopic PRC by an amplification of the first harmonic and dissipation of the higher harmonics. In addition, an important effect of coupling is shown to be a shift in the zeros of the collective PRC. Significantly, these results give a characteristic scaling for the amplitude and change in the zeros of the collective PRC as a function of the mean phase coherence of the system. We also derive the instantaneous amplitude response function for the coupled system which characterizes the transient effect of perturbations on the phase coherence of the system.

Our work builds upon that of Levnajić and Pikovsky [19] in that we consider general microscopic phase response curves and derive a characteristic scaling for the collective phase response curve. We also focus on the deterministic case, whereas in Refs. [22,23] they study a stochastic system.

This paper is organized as follows: In Sec. II we define the model to be studied, components of the collective phase response curve, and the Ott-Antonsen reduction approach. In Sec. III we derive an asymptotic formula for the collective phase response curve. In Sec. IV we test the analytical theory against numerical simulations for phase oscillators. In Sec. V we demonstrate the applicability of the theory to biological systems by studying a population of coupled neuronal oscillators. The results and conclusions are discussed in Sec. VI.

II. FORMULATION OF THE MODEL

A. Model definition

We consider an ensemble of N heterogeneous oscillators characterized by their natural frequencies ω_k and whose dynamical states may be described as phase variables ϕ_k, $k = 1, 2, \ldots, N$. Further we assume a Sakaguchi-Kuramoto-type sinusoidally coupled system where each individual oscillator responds to a instantaneous perturbation according to a microscopic phase response curve $Q(\phi)$:

$$\dot{\phi}_k = \omega_k + \frac{K_0}{N} \sum_{j=1}^{N} \sin(\phi_j - \phi_k + \beta) + \epsilon Q(\phi_k)\delta(t - t') \quad (1)$$

for $\beta \in (\frac{-\pi}{2}, \frac{\pi}{2})$. The ϵ parameter will be used to control the magnitude of the phase shifts. The collective dynamical state of the ensemble is described through the set of generalized Daido order parameters Z_n defined according to [24–26]

$$Z_n = \frac{1}{N} \sum_{k=1}^{N} e^{in\phi_k} \in \mathbb{C}. \quad (2)$$

When $n = 1$ we refer to $|Z_1| = R$ as the phase coherence of the system and $\text{Arg}(Z_1) = \psi$ as the mean or collective phase. The collective PRC will be expressed as a function of the mean phase ψ. In the limit as $N \to \infty$ we may convert Eq. (1) to a partial differential equation for the continuous density function $f(\omega, \phi, t)$ such that $f(\omega, \phi, t)d\phi d\omega$ gives the fraction of oscillators at phase ϕ with natural frequency ω at time t. The continuity equation as $N \to \infty$ is given by

$$\frac{\partial f}{\partial t} + \frac{\partial}{\partial \phi}[f(\omega, \phi, t)v] = 0,$$

$$v = \omega + K_0 \text{Im}[e^{i\beta} e^{i\phi} Z] + \epsilon Q(\phi)\delta(t). \quad (3)$$

The generalized Daido order parameter Z_n for a continuous density function is given by

$$Z_n(t) = \int_{-\pi}^{\pi} \int_{-\infty}^{\infty} f(\omega, \phi, t) e^{in\phi} d\omega d\phi \in \mathbb{C}. \quad (4)$$

Finally, we assume the distribution of natural frequencies follows a Lorentzian distribution with mean ω_0 and dispersion parameter γ,

$$g(\omega) = \frac{1}{\pi} \frac{\gamma}{(\omega - \omega_0)^2 + \gamma^2}. \quad (5)$$

B. Components of the phase response curve

The shift induced on the collective phase in this system may be separated into two components: (1) the prompt phase shift induced on the system at $t = t'$ governed by the microscopic phase response curve and (2) the slower-acting phase shift mediated by the coupling function as the ensemble returns to its asymptotic state [19] (see Fig. 1). Assume that just before the perturbation occurs the order parameter is given by Z_0 and the mean phase ψ_0. Barred quantities refer to the system after the perturbation has occurred.

Definition 1 (pPRC Δ_0). Let us define the *prompt phase response curve* as the phase shift of the mean phase just after the perturbation $t = t'$:

$$\Delta_0(\psi_0) = \bar{\psi} - \psi_0 = \text{Arg} \frac{\bar{Z}}{Z_0}.$$

Definition 2 (fPRC Δ_∞). Let us define the final ($t \to \infty$) phase resetting value as the *final phase response curve* where

$$\Delta_\infty(\psi_0) = \lim_{t \to \infty}[\bar{\psi}(t) - \psi(t)] = \lim_{t \to \infty} \text{Arg} \frac{\bar{Z}(t)}{Z(t)}.$$

In the long-time limit the dynamics of Eq. (3) for heterogeneous oscillators collapses to the so-called Ott-Antonsen manifold [10]. Within the Ott-Antonsen manifold the dynamics of Z are described by a two-dimensional system for the phase coherence R and the mean phase ψ:

$$\dot{R} = \frac{K_0 \cos(\beta)}{2} R(1 - R^2) - \gamma R, \quad (6a)$$

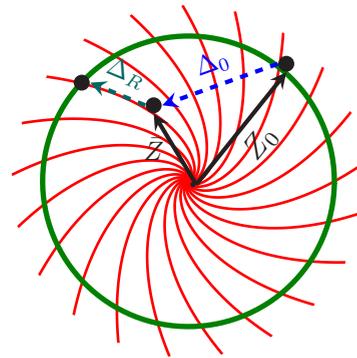$$\dot{\psi} = w_0 + \frac{K_0 \sin(\beta)}{2}(1 + R^2). \quad (6b)$$

FIG. 1. (Color online) The order parameter just before the perturbation is at Z_0. Just after the perturbation it is shifted to $\bar{Z}$. Δ_0 tracks the shift in the mean phase that occurs in the movement from Z_0 to $\bar{Z}$ and Δ_R gives the relaxation phase shift of the collective oscillator. The isochrons here show the case where $\beta = -\frac{1}{2}$.

These equations are solved analytically in Ref. [19] to give a prediction for the final phase shift as

$$\Delta_\infty = \text{Arg}\left[\frac{\bar{Z}}{Z_0}\right] + \tan(\beta)\ln\left|\frac{\bar{Z}}{Z_0}\right|, \tag{7a}$$

$$= \Delta_0 + \Delta_R. \tag{7b}$$

Here we define Δ_R as the "reset phase shift" or the phase shift induced by the relaxation of the system to equilibrium. The dynamics of the order parameter only collapse to two dimensions [Eq. (6)] for continuous density functions which lie strictly within the Ott-Antonsen manifold [10,27]. However, as demonstrated in Ref. [19] numerically and further validated in this work, we expect Eq. (7) to provide a good approximation for sufficiently small deviations off the manifold.

Using the Ott-Antonsen reduced system [Eq. (6)] we can analyze the isochrons of the collective oscillator for states lying within the OA manifold. When $\beta = 0$ the coupling function is odd and the isochrons of the collective oscillator are radial. For radial isochrons a change in the phase coherence will not affect the phase and $\Delta_R = 0$ meaning $\Delta_\infty = \Delta_0$. However, when $\beta \neq 0$ the collective oscillator [Eq. (6)] has spiral isochrons and a change in the phase coherence will induce an additional rotation (Fig. 1).

From Eq. (7) we can see the collective PRC (Δ_∞) is determined by the mapping $Z_0 \to \bar{Z}$ at the instant the perturbation is applied (Fig. 1). We will now show that the nature of this mapping depends on the Fourier decomposition of the microscopic PRC $Q(\phi)$.

III. ANALYTICAL APPROXIMATION OF $\bar{Z}$

As $N \to \infty$ we may replace Eq. (1) with the continuity equation [Eq. (3)] describing the time evolution of $f(w,\phi,t)$ the continuous density function. To ease the notation in this section we set the time of the perturbation $t' = 0$.

As $t \to \infty$ the continuous density function $f(\omega,\phi,t)$ will collapse to the Ott-Antonsen manifold [10]. Within the Ott-Antonsen manifold the higher moments of Z may be expressed as powers of Z such that $Z_n = (Z)^n$ and $Z_{-n} = (Z^*)^n$ where $*$ denotes the complex conjugate. This property will be exploited to obtain the map from $Z_0 \to \bar{Z}$ for a general Q in closed form.

For times sufficiently close to the moment of the perturbation ($t = t' = 0$) the $\epsilon Q(\phi)$ term will dominate the velocity of f and the continuity equation can be approximated as

$$f_t + \frac{\partial}{\partial\phi}[\epsilon Q(\phi)f(w,\phi,t)\delta(t)] \approx 0. \tag{8}$$

Applying the method of characteristics to Eq. (8) yields the characteristic equations

$$\frac{d\phi}{dt} = \epsilon\delta(t)Q(\phi), \tag{9a}$$

$$\frac{dh}{dt} = -\epsilon\delta(t)Q'(\phi)h, \tag{9b}$$

where $h(t) = f(\omega,\phi,t)$. In order to obtain an analytical solution for Eq. (9) we assume ϵ is a small parameter and conduct a perturbation expansion. The expansion will be valid

for small changes in the mean phase ψ. To leading order in ϵ we find

$$\phi(t) = \phi_0 + \epsilon Q(\phi_0), \tag{10a}$$

$$h(t) = h_0 e^{-\epsilon Q'(\phi_0)}, \tag{10b}$$

for $t > 0$ where ϕ_0,h_0 indicate the quantities just prior to the perturbation.

Since $Q(\phi) = Q(\phi_0) + O(\epsilon)$ we approximate $\phi_0 \approx \phi - \epsilon Q(\phi)$. Thus, we approximate $\bar{f}(\omega,\phi)$ the distribution after the perturbation as

$$\bar{f}(\omega,\phi) = f[\omega,\phi - \epsilon Q(\phi)]e^{-\epsilon Q'[\phi - \epsilon Q(\phi)]} \tag{11}$$

to leading order in ϵ. We integrate out the ω dependence and define $\rho(\phi)$ which gives the fraction of oscillators at phase ϕ,

$$\rho(\phi) = \int_{-\infty}^{\infty} f(\omega,\phi)d\omega. \tag{12}$$

Therefore, we can write

$$\bar{\rho}(\phi) = \rho[\phi - \epsilon Q(\phi)]e^{-\epsilon Q'[\phi - \epsilon Q(\phi)]}. \tag{13}$$

Equation (13) gives an expression, valid for small ϵ, for the continuous phase distribution just after the perturbation $\bar{\rho}(\phi)$ in terms of the phase distribution prior to the perturbation $\rho(\phi)$. We now convert Eq. (13) into an expression for the order parameter and derive a form for the desired mapping $Z_0 \to \bar{Z}$. We expand Eq. (13) to leading order in ϵ, multiply by $e^{i\phi}$, and integrate to get an expression in terms of the order parameter Z:

$$\bar{Z} = Z_0 - \epsilon \int_{-\pi}^{\pi} \rho(\phi)Q'(\phi)e^{i\phi}d\phi - \epsilon \int_{-\pi}^{\pi} \rho_\phi Q(\phi)e^{i\phi}d\phi. \tag{14}$$

Integrating the second term by parts and simplifying gives

$$\bar{Z} = Z_0 + i\epsilon \int_{-\pi}^{\pi} \rho(\phi)Q(\phi)e^{i\phi}d\phi. \tag{15}$$

In order to express the integral in Eq. (15) in terms of powers of Z_0 we replace $Q(\phi)$ with its Fourier series representation,

$$Q(\phi) = \frac{A_0}{2} + \sum_{n=1}^{\infty} A_n e^{in\phi} + A_n^* e^{-in\phi}. \tag{16}$$

This gives the following expression:

$$\bar{Z} = Z_0 + i\epsilon\left[\frac{A_0}{2}Z_0 + \sum_{n=1}^{\infty} \int_{-\pi}^{\pi} A_n \rho e^{i(n+1)\phi} + A_n^* \rho e^{i(1-n)\phi}\right]. \tag{17}$$

Since $\rho(\phi)$ describes a system on the Ott-Antonsen manifold we have the special property

$$\int_{-\pi}^{\pi} \rho(\phi)e^{in\phi}d\phi = (Z_0)^n \int_{-\pi}^{\pi} \rho(\phi)e^{-in\phi}d\phi = (Z_0^*)^n. \tag{18}$$

Applying this moment closure allows us to close Eq. (17),

$$\bar{Z} = Z_0 + i\epsilon\left[\frac{A_0}{2}Z_0 + \sum_{n=1}^{\infty} A_n Z_0^{n+1} + A_n^*(Z_0^*)^{n-1}\right].$$

This can be rearranged to give

$$\bar{Z} = Z_0[1 + i\epsilon \hat{Q}(\psi)], \tag{19a}$$

$$\hat{Q}(\psi) = \frac{A_0}{2} + \sum_{n=1}^{\infty} R^{n-1}\left(RA_n e^{in\psi} + \frac{A_n^*}{R} e^{-in\psi} \right). \tag{19b}$$

Equation (19) give an expression for $\bar{Z}$ in terms of Z_0 valid for small values of ϵ in terms of the Fourier series for the microscopic PRC.

Notice that $\hat{Q}(\psi)$ is closely related to the microscopic phase response curve $Q(\phi)$. For values of the phase coherence ≈ 1 the spread of the phase distribution is small and $\hat{Q}(\psi) \approx Q(\psi)$. However, as the phase coherence decreases, $\hat{Q}(\psi)$ diverges from the microscopic phase response curve.

In addition, we note the Ott-Antonsen reduction has only been applied as a moment closure in this derivation. In particular the integral equation Eq. (15) may be used for cases for which the Ott-Antonsen reduction cannot be applied and be adapted to moment-closure schemes which close the moments at a higher order.

A. Prompt phase response curve Δ_0

With an analytical expression for the order parameter after the perturbation is applied [Eq. (19)] we may derive an expression for the prompt phase resetting curve Δ_0.

$$\Delta_0 = \text{Arg}\left[\frac{\bar{Z}}{Z_0}\right] = \text{Arg}\left\{\frac{Z_0[1 + i\epsilon \hat{Q}(\psi)]}{Z_0}\right\}$$

$$= \arctan\left(\frac{\epsilon \text{Re}[\hat{Q}(\psi)]}{1 - \epsilon \text{Im}[\hat{Q}(\psi)]}\right) \approx \epsilon \text{Re}[\hat{Q}(\psi)] + O(\epsilon^2).$$

Taking the real part of $\hat{Q}(\psi)$ yields

$$\Delta_0(\epsilon, R, \psi) = \frac{\epsilon}{2}\left\{A_0 + \sum_{n=1}^{\infty} R^{n-1}\left(R + \frac{1}{R}\right)[a_n \sin(n\psi) \right.$$

$$\left. + b_n \cos(n\psi)]\right\}, \tag{20}$$

which is an asymptotic expansion valid as $\epsilon \to 0$ for the prompt phase resetting curve as a function of the Fourier series for the microscopic phase response curve and the phase coherence (R) of the system. Lower phase coherence values affect the Fourier modes of the microscopic phase response curves differently.

Specifically, Eq. (20) predicts a scaling for the amplitude of the collective PRC. In particular, for microscopic PRCs which are dominated by their first harmonic the amplitude of the collective PRC should scale like $R + \frac{1}{R}$ and for a microscopic PRC whose principal Fourier coefficient is of order N the amplitude of the collective PRC should scale like $R^N + R^{N-2}$. For microscopic PRCs composed of several modes we expect the first harmonic to be amplified and higher harmonics to be damped in the collective PRC, resulting in a change in shape of the PRC (Fig. 2).
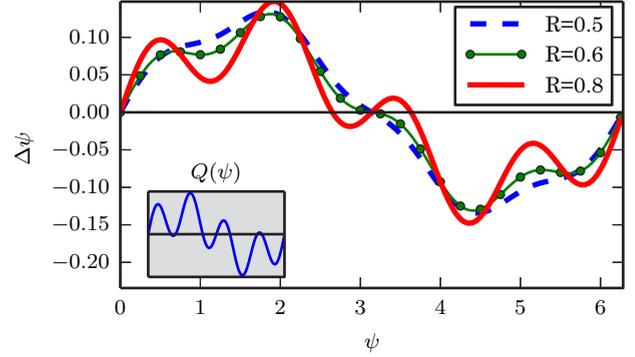

FIG. 2. (Color online) A representative plot of the prompt phase response curve Δ_0 for various values of R and $Q(\psi) = \sin(\psi) + \sin(4\psi)$ with $\epsilon = 0.1$. The first harmonic is amplified and higher harmonics are dissipated in the collective PRC.

B. Amplitude response curve

The formalism developed here allows us to predict not only the phase shift of the collective phase but also how perturbations of individual oscillators affect the phase coherence of the population. Since we are operating within the Ott-Antonsen framework we expect that after a perturbation the system will return to its equilibrium R value for long times. However, it is interesting to consider how the phase coherence is transiently altered by perturbations. To study this we introduce the amplitude response curve $\Lambda(\psi, R, \epsilon)$ where Λ is defined as the ratio of the phase coherence after the perturbation to the phase coherence prior to the perturbation.

$$\Lambda_0(\psi, R, \epsilon) = \left|\frac{\bar{Z}}{Z_0}\right| \approx \left|\frac{Z_0 + \epsilon i Z_0 \hat{Q}(\psi)}{Z_0}\right|$$

$$= \sqrt{1 - 2\epsilon \text{Im}[\hat{Q}] + \epsilon^2(\text{Re}[\hat{Q}]^2 + \text{Im}[\hat{Q}]^2)}$$

$$= 1 - \epsilon \text{Im}[\hat{Q}] + O(\epsilon^2).$$

Therefore using that $\text{Im}[z] = \frac{z - z^*}{2i}$ we have that

$$\text{Im}[\hat{Q}] = \sum_{n=1}^{\infty} R^{n-1}\left(\frac{1}{R} - R\right)\text{Im}[A_n^* e^{-in\psi}],$$

$$\text{Im}[\hat{Q}] = \frac{1}{2}\sum_{n=1}^{\infty} R^{n-1}\left(\frac{1}{R} - R\right)[a_n \cos(n\psi) - b_n \sin(n\psi)],$$

where a_n is the nth sine coefficient and b_n is the nth cosine coefficient in the Fourier series of $Q(\psi)$. This gives the following expression for Λ_0:

$$\Lambda_0(\psi, R, \epsilon) \approx 1 + \frac{\epsilon}{2}\sum_{n=1}^{\infty} R^{n-1}\left(\frac{1}{R} - R\right)$$

$$\times [b_n \sin(n\psi) - a_n \cos(n\psi)]. \tag{21}$$

Notice that

$$b_n \sin(n\psi) - a_n \cos(n\psi) \propto -\frac{dQ}{d\psi},$$

so we expect the amplitude shifts to be greatest around the zeros of the microscopic phase response curve, with increases
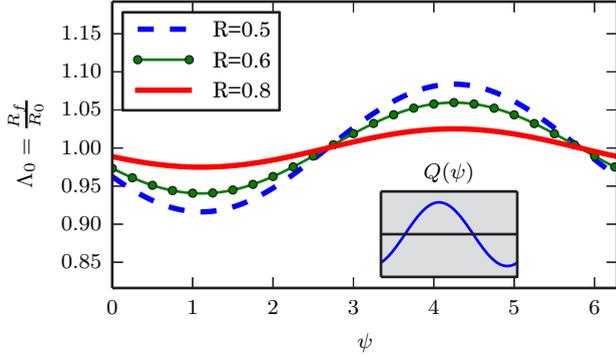
FIG. 3. (Color online) A representative plot of the amplitude response curve Λ for various values of the phase coherence with $Q(\psi) = \frac{1}{2}\sin(\psi) - \cos(\psi)$ and $\epsilon = 0.1$. Perturbations around stable fixed points of $Q(\psi)$ give transient increases in the phase coherence and perturbations about unstable fixed points of $Q(\psi)$ give decreases in the phase coherence.

in R around stable points and decreases around unstable points (Fig. 3).

In addition, notice this derivation contains two expected limits for this system: as $\epsilon \to 0$ we expect the ratio of phase coherences to go to one (no change in R, due to the perturbation), as $R \to 1$ we expect the change in R values to go to zero as well.

C. Reset phase response curve Δ_R

We now consider the case where the system [Eq. (1)] evolves with a non-odd coupling function $\beta \neq 0$. In this case we expect the reset phase shift (Δ_R) to be nonzero. If the deviation off the Ott-Antonsen manifold is small enough we expect that Eq. (7) will provide a good estimate for Δ_R:

$$\Delta_R = \tan(\beta)\ln\left(\left|\frac{\bar{Z}}{Z}\right|\right) = \tan(\beta)\ln[\Lambda_0(R,\psi,\epsilon)].$$

Therefore, the reset phase shift depends on the logarithm of the amplitude response curve. Expanding this system to leading order in ϵ we get:

$$\Delta_R = \frac{\epsilon}{2}\tan(\beta)\sum_{n=1}^{\infty} R^{n-1}\left(\frac{1}{R} - R\right)[b_n\sin(n\psi) - a_n\cos(n\psi)],$$

$$(22)$$

where a_n is the nth sine coefficient and b_n is the nth cosine coefficient in the Fourier series for $Q(\psi)$. Once again, as the phase coherence goes to 1 the reset phase shift goes to zero. Also, we expect the effect of the reset phase shift to be strongest around the zeros of the microscopic phase response curve $Q(\psi)$ because the amplitude response curve is maximal at those points (Fig. 3).

Therefore, for systems with $\beta \neq 0$ we expect the collective PRC to have shifted zeros compared to the microscopic phase response curve. Moreover, this shift will become more exaggerated when the microscopic phase response curve is dominated by low harmonics and the ensemble has a small phase coherence.

D. Collective phase response curve Δ_∞

Having computed the prompt phase response curve Δ_0 and the resetting curve Δ_R we can now write down an expression for the collective phase response curve Δ_∞ valid for small ϵ:

$$\Delta_\infty = \Delta_0 + \Delta_R, \tag{23a}$$

$$\Delta_0 = \frac{\epsilon}{2}\left\{A_0 + \sum_{n=1}^{\infty} R^{n-1}\left(R + \frac{1}{R}\right)\right.$$

$$\left. \times [a_n\sin(n\psi) + b_n\cos(n\psi)]\right\}, \tag{23b}$$

$$\Delta_R = \frac{\epsilon}{2}\tan(\beta)\sum_{n=1}^{\infty} R^{n-1}\left(\frac{1}{R} - R\right)[b_n\sin(n\psi) - a_n\cos(n\psi)]. \tag{23c}$$

Therefore we have expressed the collective phase response function in terms of the Fourier coefficients of the microscopic phase response function and the phase coherence of the equilibrium state.

We may now find an approximation for the shift in zeros for the collective phase response curve. If $\Delta_\infty(\psi_0) = 0$, then we have $\Delta_0(\psi_0) = -\Delta_R(\psi_0)$. Let $Q(\psi)$ be a microscopic PRC which is dominated by its nth harmonic; then, applying Eq. (23), we get that

$$\tan(n\psi_0) = \tan(\beta)\left(\frac{2}{1 + R^2} - 1\right). \tag{24}$$

Let ψ^* be the zero of the microscopic PRC $Q(\psi^*) = \Delta_0(\psi^*) = 0$ and let $\Delta\psi_z = \psi_0 - \psi^*$ be the shift in the zero for the collective PRC. We expand Eq. (24) about ψ^* to get an expression for the shift in the zero $\Delta\psi_z$,

$$\Delta\psi_z = \frac{1}{n}\left(\frac{2}{R^2 + 1} - 1\right)\tan(\beta). \tag{25}$$

Thus, the shift in the zeros of the collective phase response curve relative to the microscopic PRC will increase like $\frac{1}{R^2+1}$ for smaller values of the phase coherence and will be attenuated like $\frac{1}{n}$ when the microscopic phase response curve is dominated by higher harmonics.

In summary, Eq. (23) make the following predictions concerning the difference between the microscopic phase response curve Q and the collective PRC for sinusoidally coupled heterogeneous phase oscillators:

(1) The amplitude of the nth harmonic in the collective PRC should scale like $R^{n-1}(R + \frac{1}{R})$ relative to the microscopic PRC.

(2) For non-odd coupling functions ($\beta \neq 0$) the zeros of the collective PRC should be shifted in a manner that scales with $\frac{2}{R^2+1} - 1$ relative to the microscopic PRC.

We now test these predictions numerically for coupled phase oscillators and for a model of electrically coupled neurons.

IV. NUMERICAL RESULTS

In this section we present numerical results in order to test the theoretical findings from the previous section. For each simulation we set $N = 10^4$ oscillators and numerically

integrate [Eq. (1)] to find the stationary phase distribution. The natural frequencies of the oscillators were drawn from a Lorentzian distribution [Eq. (5)] with dispersion parameter $\gamma = 0.5$ and mean $w_0 = 0.0$. In order to generate phase distributions with differing phase coherence (R) values the strength of the coupling constant K_0 in Eq. (1) was varied. Ott-Antonsen theory predicts and numerics validate that the equilibrium phase coherence and coupling constant are related by, $K_0 = \frac{2\gamma}{(1-R^2)\cos(\beta)}$. A stationary phase distribution was generated by numerically integrating Eq. (1) for long times.

A stimulus was applied to the stationary phase distribution at a sampling of mean phase values $\psi \in [0, 2\pi)$ and the order parameter was recorded just after the application of the stimulus. The system was numerically integrated for a long-time until a steady-state phase shift in the mean phase was recovered relative to the unperturbed system. These numerical collective PRCs were compared against the theoretical predictions from Sec. III.

As a first case, we consider a simple microscopic PRC $Q(\psi) = \sin(\psi)$ (Fig. 4). This provides validation that the first harmonic is amplified like $R + \frac{1}{R}$ in the collective PRC and the zeros of the microscopic PRC are shifted proportional to $\tan(\beta)(\frac{1}{R} - R)$ in the collective PRC (Fig. 4).

In Fig. 5 we consider more general microscopic PRCs and once again see good agreement between the theoretical prediction [Eq. (23)] and numerical simulations. As can be seen in Fig. 5 the collective PRC can deviate significantly from the microscopic PRC and these differences can largely

be understood as an amplification of the first harmonic and dissipation of higher harmonics.

When the microscopic PRC is composed of several harmonics this change in amplitude of the harmonics can induce a significant change in shape from the microscopic to the collective PRC [Fig. 5(d)]. For example, in Fig. 5(d) the collective PRC has a phase delay region which is not present in the microscopic PRC. Moreover, the collective PRC in Fig. 5(d) has a stable entrainment point where the microscopic PRC has only a neutrally stable region ($\psi > \pi$).

V. APPLICATIONS

A. Application to a neuronal model

In order to investigate the broader application of this theory, we considered a system of coupled neurons modeled by the Morris-Lecar model. The Morris-Lecar model is a two-dimensional conductance-based neuronal firing model which is commonly used as a general neural model [28]. For model details and parameter values see Ref. [29].

We consider an all-to-all connected system of Morris-Lecar neurons with electrical coupling between the neurons. Specifically, the coupling term in the current balance equation for neuron i is $\sum_j g_{\text{syn}}(V_j - V_i)$, where j sums over all other neurons in the network. The population of neurons is set to fire with heterogeneous frequencies distributed in a Lorentzian manner. The Morris-Lecar model is capable of producing both Type I and Type II microscopic phase response
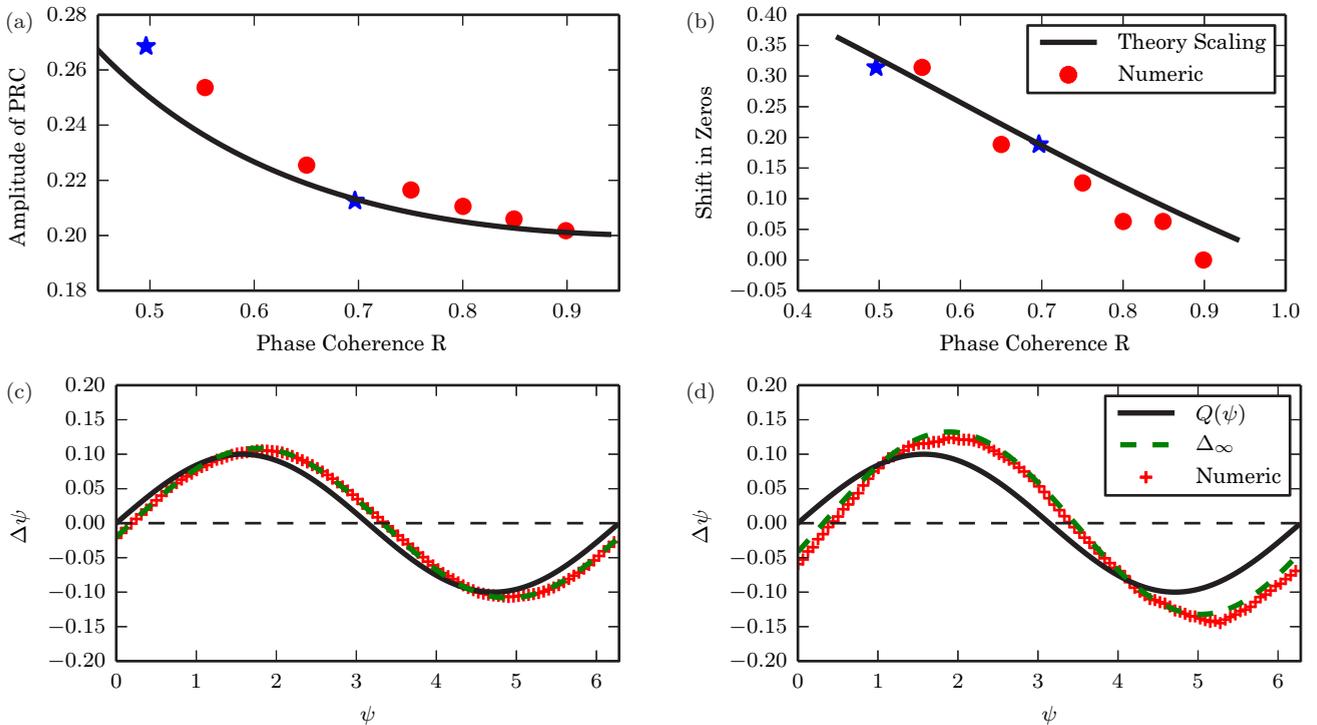

FIG. 4. (Color online) Change in the amplitude and entrainment points for a sinusoidal microscopic PRC. Here we set $Q(\psi) = \sin(\psi)$, $\epsilon = 0.1$, and $\beta = 0.5$. The coupling strength K_0 was varied to produce phase distributions with differing phase coherence (R) values in the synchronized state. Blue stars in (a) and (b) indicate the values of R which are plotted in (c) and (d). (a) The amplitude of the collective phase response curve scales like $R + \frac{1}{R}$ with the phase coherence. (b) The shift in the zero at $\psi = \pi$ scales like $\tan(\beta)(\frac{2}{R^2+1} - 1)$. (c) Microscopic, predicted collective PRC and numerical collective PRC for $R = 0.7$. (d) Microscopic, predicted collective PRC and numerical collective PRC when $R = 0.5$.
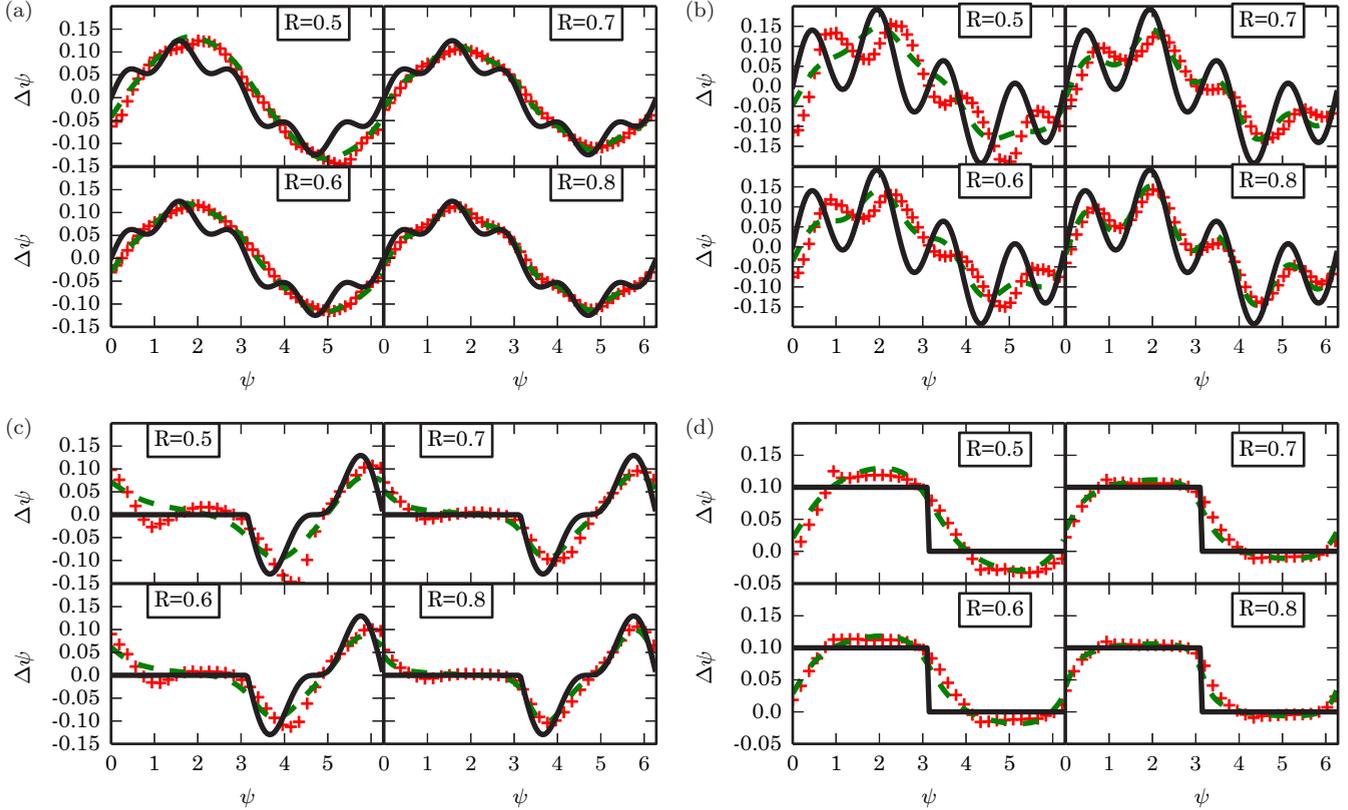
FIG. 5. (Color online) Comparing theoretical predictions against numerical results for the collective PRC for various microscopic PRC with $\epsilon = 0.1$ and $\beta = 0.5$. The coupling strength K_0 was varied to produce phase distributions with differing phase coherence (R) values in the synchronized state. Microscopic PRC (solid black), Δ_∞ (dashed green), numerical simulation (red "+"). Let $H(\psi)$ be the heaviside step function. (a) $Q(\psi) = \sin(\psi) + \frac{1}{4}\sin(5\psi)$; (b) $Q(\phi) = \sin(\psi) + \sin(4\psi)$; (c) $Q(\psi) = H(\psi - \pi)[-\sin(2\psi) - \sin(2\psi)\cos(2\psi)]$; (d) $Q(\psi) = H(-\psi - \pi)$.

curves for different parameter values [30]. This classification of neuronal PRCs distinguishes between two physiologically observed neuronal firing properties and is linked to the neural membrane properties and the bifurcation which births the oscillations. In a Type I neuronal system the PRC is characterized by having a large region of phase advances and a comparatively small region of phase delays in response to an applied current [30]. A Type II PRC is characterized by having regions of both phase advances and delays. In this context the distinction allows us to test the collective PRC theory for two qualitatively different and physiologically relevant microscopic phase response curves.

In order to evaluate the utility of the theoretical predictions of this work we computed the individual neuron phase response curves, the Ott-Antonsen predicted collective phase response function and the numerical collective phase response function in both the Type I and Type II parameter regimes. The numerical curves were produced using a short weak applied current pulse ($I_{\text{applied}} = 1.0 \frac{\mu A}{cm^2}$, $\Delta t = 1$ ms) to each individual neuron and then measuring the phase shift in the mean phase for an ensemble of $N = 10^3$ neurons. Ensembles of neurons with differing phase coherence (R) values in the equilibrium state were generated by varying the strength of the coupling through the g_{syn} parameter.

We first consider the Type I parameter regime for the Morris-Lecar model. We numerically determined the collec-

tive phase response curve for various values of the phase coherence. For $R \approx 1$ all oscillators are phase locked together and the microscopic, asymptotic Ott-Antonsen collective and numerical collective PRC agree. However, as R was decreased we observed several changes in the shape of the collective phase response curve. First, higher-harmonic Fourier terms in the microscopic PRC damped out quickly. Second, the amplitude of the first harmonic grew as R decreased and, finally, we saw a slight phase shift in the zeros of the curve. The asymptotic Ott-Antonsen procedure correctly predicted each of these qualitative changes (Fig. 6).

These conclusions carried through to the case of Type II neurons as well. However, for the Type II regime we did not see as prominent a phase shift between the collective and microscopic phase response curves. This can be explained by the β term in the Ott-Antonsen asymptotic method. The β term for both the Type I and II parameter regimes was computed numerically by truncating the Fourier series for the coupling function determined in the course of the phase reduction of the coupled Morris-Lecar system. For electrically coupled neurons with Type II microscopic PRCs $\beta = 0.25$ while for electrically coupled neurons with Type I microscopic PRCs $\beta = -0.65$. This implies that the Type II system isochrones are closer to radial so we see a smaller resetting shift (Δ_R) due to the perturbation.

In both of these cases we see that the Ott-Antonsen derived collective phase response curve gives a good approximation to
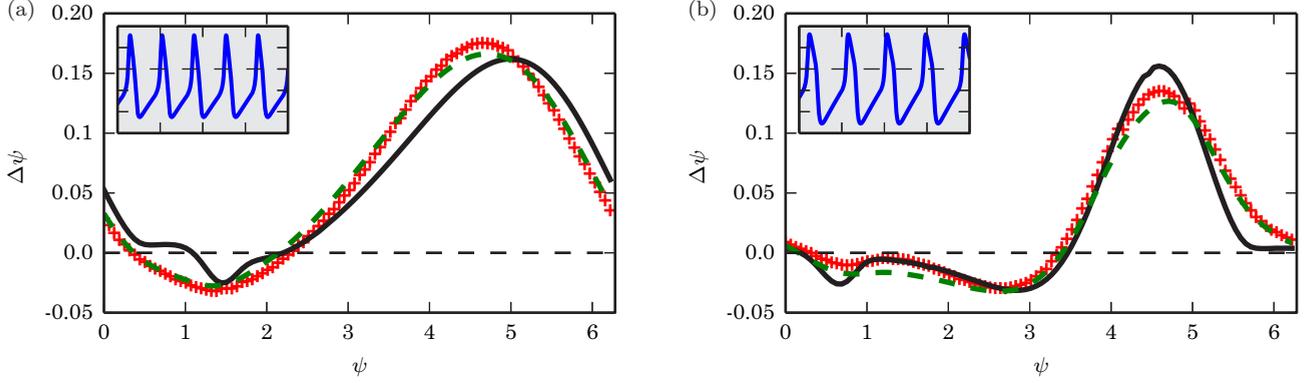
FIG. 6. (Color online) Comparing theoretical predictions against numerical results for the collective PRC of Morris-Lecar neurons. Inset plots show individual neurons action potentials (mV) for 400 ms in the synchronized state for the two parameter regimes. Microscopic PRC (solid black), Δ_∞ (dashed green), numerical simulation (red "+"). (a) Collective PRC for Type I Morris-Lecar neurons with $R = 0.67$ and mean applied current of 50.0 $\frac{\mu A}{cm^2}$. (b) Type II Morris-Lecar system with $R = 0.70$ and mean applied current of 95 $\frac{\mu A}{cm^2}$.

the numerical case and provides an accurate approximation for the shape, zeros, and amplitude of the collective phase response curve. We note the asymptotic procedure matches numerical simulations well despite a violation of the assumptions of the Ott-Antonsen reduction. In particular, the coupling functions for both the Type I and Type II parameter regimes have higher harmonic terms which violate a principal assumption of the Ott-Antonsen approach [27]. Finally, this theory makes the experimentally testable prediction that a coupled system of Type II neurons will be able to entrain to a smaller frequency range than the individual neurons with the opposite being true for coupled Type I neurons.

VI. CONCLUSIONS

We have constructed an asymptotically valid analytic formula for the collective phase response function in terms of the microscopic phase response curve for globally coupled Sakaguchi-Kuramoto phase oscillators interacting via an non-odd coupling function. Our analytic results extends the framework developed in Levnajić and Pikovsky [19] to consider a general microscopic PRC and derives a characteristic scaling for changes in the amplitude and zeros of the collective PRC relative to the microscopic PRC. These results were validated through comparison with numerical simulations for a variety of microscopic PRCs. By studying a system of coupled neurons we demonstrated the broader applicability of the theory to biological systems.

In particular, the theory predicts the amplitude and zeros of the collective PRC. For weakly forced system a larger amplitude PRC indicates a broader range of frequencies which can entrain the system and the zeros predict the phase offset between the entraining force and the mean phase of the population of oscillators. Therefore, a better understanding of how these properties may be altered by coupling between large ensembles of oscillators has direct application to many biological systems. For instance, in experimental studies of the mammalian circadian rhythm, it was found that weaker coupling between the neurons or a greater variance in the phase distribution of the oscillators decreased the entrainment time to light input and increased the entrainment range [31,32].

This suggests the collective PRC has a higher amplitude than the microscopic PRC in the circadian system.

Moreover, the collective PRC is shown to have a change in shape when the microscopic PRC is composed of several harmonics. The first harmonic is amplified and higher harmonics are dissipated as the phase coherence of the population is decreased. This can result in the introduction of advance-delay regions in the collective PRC which are not observed in the microscopic PRC and an overall smoothing of the curve.

The Ott-Antonsen dimension reduction is a key component allowing for an analytical investigation of the collective PRC presented in this work. The Ott-Antonsen reduction is strictly valid for sinusoidally coupled heterogenous Sakaguchi-Kuramoto phase oscillators. However, as demonstrated numerically, for a Morris-Lecar neuronal system here and for Stuart-Landau oscillators in Ref. [19], it provides a useful approximation even for systems which have not been shown to rigorously collapse to the Ott-Antonsen manifold. Moreover, additional dimension-reduction techniques have been developed which may be useful in studying the collective phase response curve in the future [11–13].

An important extension of these results is the generalization to complex networks. The prompt phase shift, Δ_0, can be estimated when the Ott-Antonsen moment closure cannot be applied using the integral equation Eq. (15) either numerically or analytically by using an appropriate higher-order moment closure.

However, in the absence of the Ott-Antonsen reduction the computation of the reset phase shift Δ_R presents a challenge. In this case we cannot assume the collective oscillator has simple spiral isochrons as exploited in Ref. [19] to derive Eq. (7). Therefore, the computation becomes much more difficult. In addition, the collective phase response curve for systems with a stochastic term has not been considered here and is of great interest in applications.

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