

Synchronization of Excitatory Neurons with Strongly Heterogeneous Phase Responses

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In many real-world oscillator systems, the phase response curves are highly heterogeneous. However, the dynamics of heterogeneous oscillator networks has not been seriously addressed. We propose a theoretical framework to analyze such a system by dealing explicitly with the heterogeneous phase response curves. We develop a method to solve the self-consistent equations for order parameters by using formal complex-valued phase variables, and apply our theory to networks of *in vitro* cortical neurons. We find a novel state transition that is not observed in previous oscillator network models.

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Synchronization phenomena are ubiquitous in nonlinear dynamical systems, such as Josephson junction arrays [1], laser arrays [2], and biological systems [3–5]. Synchronous firing of cortical neurons is considered to play an active role in cognitive functions [3] and is governed by the intrinsic properties of neurons as well as by the network connectivity. These properties include the phase response curve (PRC) [4–6], which describes how the timing of a succeeding output spike is shifted by an input spike [7–11]. In general, we can categorize the phase responses of cortical neurons into two types. Type-I PRC has only positive values (corresponding to phase advances), while type-II has both positive and negative values (corresponding to phase delays) depending on the phase at which a stimulus is applied [8]. Mutual synchronization of excitatory neurons may be easier with type-II PRC than with type-I PRC, if the PRCs of the neurons are homogeneous [8]. However, the PRCs recorded from various brain areas, which include the hippocampus [12], the entorhinal cortex [13], the somatosensory cortex [14], and the motor cortex [7,15], have revealed that the PRC type of pyramidal neurons is highly heterogeneous, especially if they belong to different cortical layers [15]. Even if two neurons have the same PRC type, the shape of PRC varies significantly from neuron to neuron (see Fig. 1).

In general, the heterogeneity of PRCs disturbs the stability of the synchronous state. However, the heterogeneity of PRCs can be compensated by other intrinsic properties that enhance synchronization. In this Letter, we explore how such compensation may occur in networks of heterogeneous oscillators. The population dynamics of the heterogeneous phase oscillators was first studied in the Kuramoto model [6], which demonstrated the emergence of transitions between synchronized and desynchronized states [16–19]. These studies transformed the heterogeneity of the PRC shapes into that of the natural frequencies, assuming that the heterogeneity is weak in both cases. Here, we develop an analytical method to explicitly deal with the heterogeneity since the PRC shapes of cortical neural oscillators are strongly heterogeneous. Unlike in the origi-

nal Kuramoto model, we can show that the order parameter of synchronization changes discontinuously in the neural population with heterogeneous PRCs. This implies that this type of heterogeneity creates a dramatic effect on networks of neural oscillators.

We first derive the interaction functions $\Gamma_j(\psi)$ [6] from a set of differential equations of the phase oscillators with a common frequency ω . These oscillators have heterogeneous PRCs, $Z_j(\theta)$, and are globally coupled with each other. The phase of the j th oscillator θ_j obeys the evolution equation,

$$\frac{d\theta_j}{dt} = \omega + \frac{\epsilon}{N} Z_j(\theta_j) \sum_{k=1}^N \sum_n \alpha(t - t_k^n). \quad (1)$$

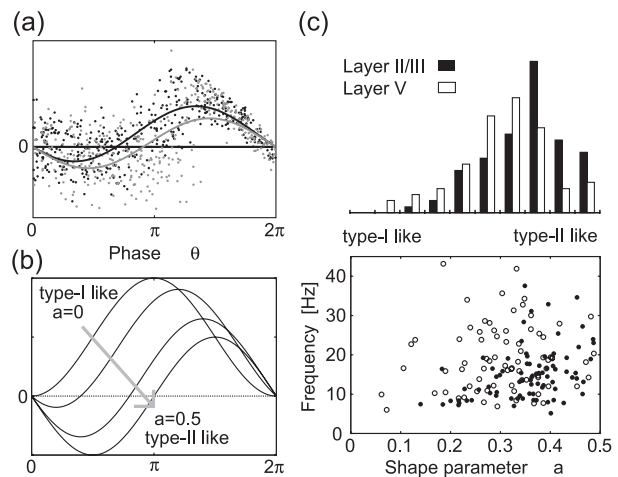


FIG. 1. Heterogeneity of the phase response curves (PRCs) of cortical neurons in our *in vitro* recording studies [15]. We performed the least-square-error fitting of the PRCs with $Z(\theta) = -\cos(\theta - a\pi) + \cos a\pi$ by changing the shape parameter a [see also Eq. (11)]. (a) Two typical examples of the estimated PRCs. (b) The dependence of the PRC shape on a . (c) The distributions of the estimated shape parameters (upper) and the intrinsic frequencies of neuronal oscillators (lower) in different cortical layers. The frequency was tuned in experiments by varying the amplitude of a dc injected current.

The input to the j th oscillator from the k th is given as $\epsilon N^{-1} \sum_n \alpha(t - t_k^n)$, where ϵ is a weak coupling constant, N the number of oscillators, $\alpha(t)$ a causal coupling function, and the n th firing time of the k th oscillator t_k^n defined as $\theta_k(t_k^n) = 2\pi n$.

The mutual interactions shift the frequency of the mean phase of these oscillators by $\epsilon\Omega$ from the natural frequency ω . We define the relative phase $\psi_j = \theta_j - \Phi$, where the phase $\Phi = (\omega + \epsilon\Omega)t$. The relative phase ψ_j changes slowly compared with θ_j and will hardly change during the oscillation period $2\pi/(\omega + \epsilon\Omega)$. Therefore, we can average Eq. (1) over one period keeping ψ_j constant. Using $(\omega + \epsilon\Omega)t_k^n = 2\pi n - \psi_k$, we can describe the dynamics of the relative phase ψ_j as

$$\frac{1}{\epsilon} \frac{d\psi_j}{dt} = -\Omega + \frac{1}{2\pi N} \int_0^{2\pi} Z_j(\psi_j + \Phi) \sum_k \beta(\psi_k + \Phi) d\Phi, \quad (2)$$

where $\beta(\psi_k + \Phi)$ is the sum of the contributions of past inputs from the k th oscillator $\sum_n \alpha[(\psi_k + \Phi - 2\pi n)/(\omega + \epsilon\Omega)]$. In the limit of $N \rightarrow \infty$, we can apply the mean-field approximation, $N^{-1} \sum_k \beta(\psi_k + \Phi) \sim \int_0^{2\pi} \beta(\psi + \Phi) P(\psi) d\psi$, where $P(\psi)$ is the distribution function of the relative phase ψ . The functions Z , P , and β are 2π -periodic, so we can expand them into Fourier series. The n th Fourier coefficient $r_n^{(f)} e^{i\lambda_n^{(f)}}$ of a function $f(\psi)$ is defined as $r_n^{(f)} e^{i\lambda_n^{(f)}} \equiv (2\pi)^{-1} \int_0^{2\pi} f(x) e^{-inx} dx$. Then, Eq. (2) becomes,

$$\begin{aligned} \frac{1}{\epsilon} \frac{d\psi_j}{dt} &= \Gamma_j(\psi_j) \\ &\equiv \tilde{\omega}_j - \Omega + \sum_{n=1}^{\infty} K_j^n R^n \cos(n\psi_j + \Delta_j^n + \lambda_n^{(P)}), \end{aligned} \quad (3)$$

where $\tilde{\omega}_j = r_0^{(Z_j)} r_0^{(\beta)}$, $K_j^n = 2 r_n^{(Z_j)} r_n^{(\beta)}$, and $\Delta_j^n = \lambda_n^{(Z_j)} - \lambda_n^{(\beta)}$. The order parameters $R^n = 2\pi r_n^{(P)}$, Ω and $\lambda_n^{(P)}$ in Eq. (3) describe the dynamics of neural oscillators.

Below, we focus on nontrivial solutions ($R^n \neq 0$) to Eq. (3) other than the trivial one $R^n = 0$. Each oscillator exhibits two dynamical modes, ‘‘synchronized’’ or ‘‘desynchronized,’’ according to the shape of the PRC or the interaction function $\Gamma_j(\psi)$. In the synchronized mode, the oscillator is trapped at a stable fixed point of Eq. (3). In the desynchronized mode, Eq. (3) has no stable fixed point, so the oscillator cannot be locked at any relative phase and drifts at a period of $T_j = \epsilon^{-1} \int_0^{2\pi} |\Gamma_j(\psi)|^{-1} d\psi$. To derive the order-parameter equations, we introduce complex order parameters $R^n e^{i\lambda_n^{(P)}}$, and divide them into the contributions of the synchronized population, \mathcal{O}_s^n , and those of the desynchronized population, \mathcal{O}_{ds}^n . Given the phase distribution function of the synchronized oscillators, P_s , we can represent \mathcal{O}_s^n as

$$\mathcal{O}_s^n \equiv \int_0^{2\pi} P_s(\psi) e^{-in\psi} d\psi = \frac{1}{N} \sum_{j \in D} e^{-in\psi_j^\dagger}, \quad (4)$$

where D refers to the indices of the synchronized oscillators and ψ_j^\dagger is a real-valued solution to $\Gamma(\psi_j^\dagger) = 0$ satisfying $\Gamma'(\psi_j^\dagger) < 0$. In general, Eq. (4) has more than one solution. However, Eq. (4) can uniquely be defined in the limit of weak noise since the noise excludes solutions other than the most stable one.

The contribution of the desynchronized oscillators \mathcal{O}_{ds}^n is given as

$$\begin{aligned} \mathcal{O}_{ds}^n &\equiv \int_0^{2\pi} P_{ds}(\psi) e^{-in\psi} d\psi \\ &= \frac{1}{N} \sum_{j \in \bar{D}} \int_0^{2\pi} d\psi \frac{1}{T_j |\Gamma_j(\psi)|} e^{-in\psi}, \end{aligned} \quad (5)$$

where \bar{D} is the set of the indices of the desynchronized oscillators and P_{ds} is their phase distribution function. We can calculate the above integral using the residue theory as

$$\mathcal{O}_{ds}^n = \frac{1}{N} \sum_{j \in \bar{D}} e^{-in\psi_j^\dagger}. \quad (6)$$

Here, $e^{-in\psi_j^\dagger} = \langle e^{-in\psi_j^{(k)}}; [\Gamma'(\psi_j^{(k)})]^{-1} \rangle_k$, with $\psi_j^{(k)}$ being an imaginary solution to $\Gamma(\psi_j^{(k)}) = 0$ satisfying $\text{Im}\psi_j^{(k)} < 0$ and the weighted average $\langle f(x_k); g(x_k) \rangle_k$ defined as $\langle f(x_k); g(x_k) \rangle_k \equiv \sum_k g(x_k) f(x_k) / \sum_k g(x_k)$. We find that the formal expressions of the contributions of the desynchronized and synchronized populations are identical. Thus, we finally obtain the following self-consistent equation:

$$R^n e^{i\lambda_n^{(P)}} = \frac{1}{N} \sum_j e^{-in\psi_j^\dagger}. \quad (7)$$

This equation means that the n th complex order parameters $R^n e^{i\lambda_n^{(P)}}$ should be identical with the n th circular moment of the complex solutions to $\Gamma_j(\psi) = 0$.

To obtain the explicit formula for the fixed points, we hereafter truncate $\Gamma(\psi)$ up to the first Fourier mode of Eq. (3). Then, the complex solutions ψ^\dagger are given by

$$e^{-i\psi_j^\dagger} = \begin{cases} (-W_j + \sqrt{W_j^2 - 1}) e^{i\Delta_j^1} & (W_j \geq 1) \\ (-W_j - \sqrt{W_j^2 - 1}) e^{i\Delta_j^1} & (W_j < 1) \end{cases}, \quad (8)$$

where $W_j \equiv (\tilde{\omega}_j - \Omega)/K_j^1 R^1$. If a single variable a parameterizes the heterogeneity of the PRC shapes, we can explicitly describe the phase distribution functions as

$$P_s(\psi) = g[a(\psi)] \left| \frac{\partial \log W}{\partial a} \frac{W}{\sqrt{1 - W^2}} - \frac{\partial \Delta^1}{\partial a} \right|^{-1}, \quad (9)$$

$$P_{ds}(\psi) = \frac{1}{2\pi} \int_{D_{ds}} \frac{g(a) \sqrt{W^2 - 1}}{|W + \cos(\psi + \Delta^1)|} da, \quad (10)$$

where $g(a)$ is the distribution of the parameter values over the oscillator population. As mentioned previously, $\Gamma(\psi, a) = 0$ has no real solution in the parameter range D_{ds} . It is noted that merely finding the equilibrium values of the order parameters does not require the explicit expressions of $P_{s,ds}(\psi)$ in the present analysis.

To show the validity of our theoretical treatment and to get a novel insight into the dynamics of heterogeneous-oscillator networks, we now apply it to coupled oscillators having the following heterogeneous PRCs:

$$Z(\theta) = -\cos(\theta - a\pi) + \cos a\pi. \quad (11)$$

The value of the shape parameter a is distributed uniformly in the range ($a_{\min} \leq a \leq a_{\max}$). A large or a small value of a corresponds to type-II- or type-I-like PRC, respectively. The coupling function $\alpha(\psi)$ is an exponential function with a decay constant of τ : $\alpha(t) = \tau^{-1}\Theta(t)e^{-t/\tau}$, where $\Theta(x)$ is Heaviside function: $\Theta(x) = 1$ if $x > 0$ or 0 if $x < 0$. Neurons synchronize easier with type-II-like PRCs than with type-I-like PRCs. Using Eq. (11), we can rewrite Eq. (3) as

$$\frac{1}{\epsilon K_j^1 R^1} \frac{d\psi_j}{dt} = W(a) - \cos[\psi_j - a\pi + \arctan(\tau\omega)] \quad (12)$$

$$W(a) = \frac{\cos a\pi - 2\pi\Omega/\omega}{R^1/\sqrt{1 + (\tau\omega)^2}}$$

where $K_j^1 = \omega/[2\pi\sqrt{1 + (\tau\omega)^2}]$.

Using these results, we can study different dynamical states of the oscillator network. Figure 2(a) summarizes the phase diagram in the (a_{\min} , a_{\max}) half plane. Neurons are either partially synchronized (PaS) or perfectly synchronized (PFS) if the self-consistent equation,

$$R^1 = \frac{1}{N} \sum_j e^{-i\psi_j^\dagger} \quad (13)$$

has a nontrivial ($R^1 \neq 0$) solution. The border between the two states by can be determined by a critical value a_c , which is a solution to $|W(a_c)| = 1$. Since neurons with $a > a_c$ are synchronized and those with $a < a_c$ are desynchronized, the PFS state requires $a_{\min} > a_c$. Otherwise, neurons are only partially synchronized. If a_{\min} is sufficiently large, all neurons may be type-II-like. We note that even in such a case, a strong heterogeneity (i.e., a sufficiently large $a_{\max} - a_{\min}$) may disable the perfect synchronization of oscillators.

When Eq. (13) has no nontrivial solutions in the allowed range of a -value, the entire population of oscillators is perfectly desynchronized (PFD). Thus, the border between the PaS and PFD states is determined from the condition that a solution with $R^1 \neq 0$ exists. At $a_{\min} = a_{\max}$, the self-consistent equation has a stable fixed point if $a > \pi^{-1} \arctan(\tau\omega)$ and the system exhibits the PFS state (point Q). The PFS-PaS and PaS-PFD borders should merge at this

point. Figures 2(c)–2(e) display the raster plots of the neural oscillators in the PFS, PaS, and PFD states designated in Fig. 2(a), respectively. In Fig. 2(c) or 2(e), the population comprises only type-II-like or type-I-like neurons showing perfect synchronization or perfect desynchronization, respectively. In Fig. 2(d), only subpopulation of strongly type-II-like neurons with $a > a_c$ are synchronized.

The order parameter Eq. (13) consists of the amplitude condition $R^1 = N^{-1}|\sum_j e^{-i\psi_j^\dagger}|$ and the phase condition $0 = N^{-1} \arg(\sum_j e^{-i\psi_j^\dagger})$. It is relatively easy for neurons to satisfy the amplitude condition by tuning the number of neurons that are synchronized. By contrast, the phase condition enforces the synchronized neurons to take a specific configuration of the relative phases, which in general is difficult to achieve in the heterogeneous neural population. In fact, the phase condition induces a discontinuous change in the macroscopic state at the onset of the PaS state, as indicated by the jump in R^1 [Fig. 2(b)]. We note that the original Kuramoto model always satisfies the phase condition due to its highly symmetric structure. Thus, at the critical point, the model can easily fulfill the amplitude condition by adding an infinitesimal fraction of neurons to the synchronized population, raising R^1 contin-

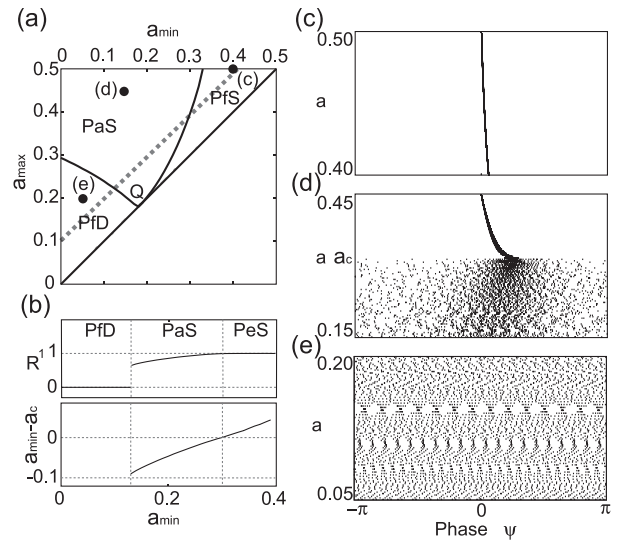


FIG. 2. Three different states in our coupled oscillator model with the PRCs represented by Eq. (11). The parameters were set as $\tau = 0.005$, $\omega = 40\pi$, and $\epsilon = 0.01$. (a) Phase diagram of this model, where the shape parameter a is distributed uniformly in $a_{\min} \leq a \leq a_{\max}$. The abbreviations mean perfectly synchronized (PFS), partially synchronized (PaS), and perfectly desynchronized (PFD) states. (b) The order parameters R^1 and $a_{\min} - a_c$ are shown along the line $a_{\max} - a_{\min} = 0.1$ [dashed line in (a)]. The PFD state corresponds to $R^1 = 0$, while the PaS or the PFS state is defined with $R^1 \neq 0$ and with $a_{\min} - a_c < 0$ or $a_{\min} - a_c > 0$, respectively. (c)–(e) Raster plots of the relative phases ψ_j of 100 neural oscillators in the PFS (c), PaS (d), and PFD (e) states.

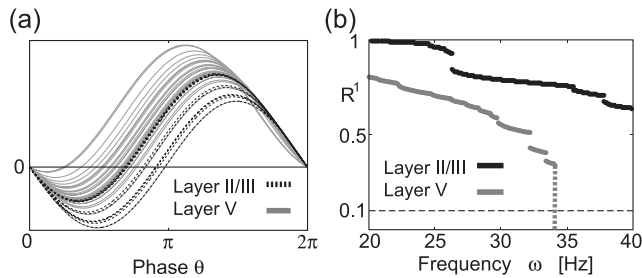


FIG. 3. The layer dependences of the PRCs of cortical neurons in the γ -frequency range and the order parameter R^1 . (a) The PRCs recorded in [15] were fitted by Eq. (11). PRCs were superimposed for 10 layer-II/III neurons (broken black lines) and 25 layer-V neurons (solid gray lines). (b) The order parameter R^1 depends differentially on the frequency ω of neuronal firing for layer-II/III (black) and layer-V (gray) neurons. Here, $\tau = 0.005$. Equation (13) in general has multiple solutions when the summation is taken over a finite number of oscillators. Here, we plotted the largest R^1 , or plotted nothing if $R^1 < 0.1$. Dashed line indicates a discontinuous transition of the network state. Other discontinuous points of the curves appeared due to the finite-size effect.

uously from 0. Therefore, the heterogeneous model and the original Kuramoto model exhibit qualitatively different transitions from the PfD to the PaS state, and the network state switches very sharply in the present model. Our quantitative results reveal that the different types of the heterogeneity can result in qualitatively different phase transitionlike behaviors of oscillator networks.

We apply our theory to the data recorded from excitatory neurons in cortical layers II/III and V [15]. The PRC shapes exhibited a remarkable layer dependence when the firing frequency ω is in a range of 20–45 Hz, which is within the γ -frequency range [Fig. 3(a)]. To demonstrate the effect of this layer dependence on the population dynamics of cortical neurons, we analyze coupled systems of layer-II/III or layer-V neurons separately. The synchronizing property in general depends on the frequency ω as well as the decay time constant of excitatory synapses. As ω is increased, layer-V neurons display an abrupt transition from the PaS to PfD state, as represented by a discontinuous jump in R^1 (dashed line). This transition can also be found in the simpler model shown previously in Fig. 2 with a uniform distribution of a .

These results may have considerable implications for exploring computational functions of local cortical circuits. Furthermore, in most real-world oscillator systems, the phase response curves are highly heterogeneous, so our theoretical method can be naturally applied to these systems. Our results provide a way to make quantitative predictions about the dynamics of general heterogeneous-

oscillator networks, indicating the existence of a clear-cut border between the PaS and PfD states with a discontinuous jump in the order parameter.

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