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, 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 novel 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, 4, 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, 5, 6], which describes how the timing of a succeeding output spike is shifted by an input spike [7, 8, 9, 10, 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 paper, 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, 17, 18, 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 original 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 $\omega$. These oscillators have heterogeneous PRCs, $Z_j(\theta)$, and are globally coupled with each other. The phase of the $j$th oscillator $\theta_j$ obeys the evo-

FIG. 1: Heterogeneity of the phase response curves (PRCs) of cortical neurons in our in vitro recording studies [12]. 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.
tion equation,
\[ \frac{d\theta_j}{dt} = \omega + \epsilon N \sum_{k=1}^{N} \alpha(t - t_k^j). \] (1)

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

The mutual interactions shift the frequency of the mean phase of these oscillators by \( \epsilon \Omega \) from the natural frequency \( \omega \). We define the relative phase \( \psi_j = \theta_j - \Phi \), where the phase \( \Phi = (\omega + \epsilon \Omega)t \). The relative phase \( \psi_j \) changes slowly compared with \( \theta_j \) and will hardly change during the oscillation period \( 2\pi/(\omega + \epsilon \Omega) \). Therefore, we can average Eq. (1) over one period keeping \( \psi_j \) constant. Using \( \omega = (\omega + \epsilon \Omega) \), and \( t_k^j = 2\pi n - \psi_k \), we can describe the dynamics of the relative phase \( \psi_j \) as
\[ \frac{1}{\epsilon} \frac{d\psi_j}{dt} = -\Omega + \frac{1}{2\pi N} \int_0^{2\pi} \sum_k \beta(\psi_k + \Phi) d\Phi, \] (2)

where \( \beta(\psi_k + \Phi) \) is the sum of the contributions of past inputs from the kth oscillator \( \sum_n \alpha((\psi_k + \Phi - 2\pi n)/(\omega + \epsilon \Omega)) \). In the limit of \( N \to \infty \), 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 \( \psi \). The functions \( Z, P, \beta \) and \( \beta \) are \( 2\pi \)-periodic, so we can expand them into Fourier series. The nth Fourier coefficient \( r_n^j e^{i\lambda_n^j} \) of a function \( f(\psi) \) is defined as \( r_n^j e^{i\lambda_n^j(j)} \equiv (2\pi)^{-1} \int_0^{2\pi} f(x)e^{-i\lambda_n x} dx \). Then, Eq. (2) becomes
\[ \frac{1}{\epsilon} \frac{d\psi_j}{dt} = \Gamma_j(\psi_j) \] (3)
\[ \equiv \omega_j - \Omega + \sum_{n=1}^{\infty} K_n^r R^n \cos \left( n\psi_j + \Delta_n^r + \lambda_n^r \right), \]

where \( \omega_j = r_0^j + \beta K_n^r \), \( K_n^r = 2r_n^j (Z_j^r) / r_n^j \) and \( \Delta_n^r = \lambda_n^r - \lambda_n^r \). The order parameters \( R^n = 2\pi r_n^r, \Omega, \) and \( \lambda_n^r \) in Eq. (3) describe the dynamics of neural oscillators.

Below, we focus on non-trivial 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, \( \mathcal{O}_d^n \). Given the phase distribution function of the ‘synchronized’ oscillators, \( P_s \), we can represent \( \mathcal{O}_s^n \) as
\[ \mathcal{O}_s^n = \int_0^{2\pi} P_s(\psi) e^{-i\psi_j} d\psi = \frac{1}{N} \sum_{j \in D} e^{-i\psi_j}, \] (4)

where \( D \) refers to the indices of the ‘synchronized’ oscillators and \( \psi_j \) is a real-valued solution to \( \Gamma(\psi_j) = 0 \) satisfying \( \Gamma'(\psi_j) < 0 \). In general, the equation 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 \( \mathcal{O}_d^n \) is given as
\[ \mathcal{O}_d^n = \int_0^{2\pi} P_d(\psi) e^{-i\psi_j} d\psi = \frac{1}{N} \sum_{j \in D} e^{-i\psi_j}, \] (5)

where \( \bar{D} \) is the set of the indices of the ‘desynchronized’ oscillators and \( P_d \) is their phase distribution function. We can calculate the above integral using the residue theory as
\[ \mathcal{O}_d^n = \frac{1}{N} \sum_{j \in \bar{D}} e^{-i\psi_j}. \] (6)

Here, \( e^{-i\psi_j} \equiv \left( e^{-i\psi_j}; \Gamma(\psi_j)^{-1} \right)_k \) with \( \psi_j \) being an imaginary solution to \( \Gamma(\psi_j) = 0 \). Im \( \psi_j \) < 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:
\[ R^n e^{i\lambda_n^P} = \frac{1}{N} \sum_j e^{-i\psi_j}. \] (7)

This equation means that the nth complex order parameters \( R^n e^{i\lambda_n^P} \) should be identical with the nth 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 \( \psi_j \) are given by
\[ e^{-i\psi_j} = \begin{cases} \left( -W_j + \sqrt{W_j^2 - 1} \right) e^{i\Delta_j^1} & (W_j \geq 1) \\ \left( -W_j - \sqrt{W_j^2 - 1} \right) e^{i\Delta_j^1} & (W_j < 1) \end{cases}, \] (8)

where \( W_j \equiv (\omega_j - \Omega)/K_1^n R^1 \). If a single variable \( a \) parameterizes the heterogeneity of the PRC shapes, we can
explicitly describe the phase distribution functions as

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

\[ P_{ds}(\psi) = \frac{1}{2\pi} \int_{D_{ds}} g(a) \frac{\sqrt{W^2 - 1}}{|W + \cos(\psi + \Delta^1)|} da. \tag{10} \]

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 \( P_e, ds \) 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:

\[ Z(\theta) = -\cos(\theta - a\pi) + \cos a\pi. \tag{11} \]

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 \( \tau \): \( \alpha(t) = \tau^{-1}\Theta(t)e^{-t/\tau} \), 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

\[ \frac{1}{\epsilon K_1^2 R^1} \frac{d\psi_j}{dt} = W(a) - \cos(\psi_j - a\pi + \arctan(\tau\omega)) \]

\[ W(a) = \frac{\cos a\pi - 2\pi\Omega/\omega}{\sqrt{R^1}} \tag{12} \]

where \( K_1^2 = \omega/(2\pi \sqrt{1 + (\tau\omega)^2}) \).

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. When Eq. (13) has a non-trivial solution, neurons are either partially synchronized (PaS) or perfectly synchronized (PfS). 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.

The entire population of oscillators is perfectly desynchronized (PfD) if the self-consistent equation,

\[ R^1 = \frac{1}{N} \sum_j e^{-j\psi_j} \tag{13} \]

has no non-trivial \( R^1 \neq 0 \) solutions in the allowed range of \( a \)-value. 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. Figure 2(c)-(e) displays the raster plots of the neural oscillators in the PfS, PaS, and PfD states designated in Figure 2(a), respectively. In Figure 2(c) or (e), the population comprises only type II-like or type I-like neurons showing perfect synchronization or perfect desynchronization, respectively. In Figure 2(d), only sub-population of strongly type II-like neurons with \( a > a_c \) are synchronized.

![Figure 2](image1.png)

**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 PfD 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 \( \psi_j \) of 100 neural oscillators in the PFS (c), PaS (d), and PfD (e) states.

The necessary condition for getting a non-trivial solution to Eq. (13) is that the imaginary part of its right hand should vanish. While the original Kuramoto model always satisfies this condition due to its symmetry, this is not the case in the present example. Therefore, this model and the Kuramoto model exhibit qualitatively different transitions from the PfD to the PaS state. In this model, the order parameter \( R^1 \), which vanishes in the PfD state, jumps discontinuously to a non-zero value at the transition point (Fig. 3(b)). In contrast, the transition is continuous in the Kuramoto model. Therefore,
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 transition-like behaviors of oscillator networks.

We apply our theory to the data recorded from excitatory neurons in cortical layers II/III and V. The PRC shapes exhibited a remarkable layer dependence when the firing frequency $\omega$ is in a range of 20-45 Hz, which is within the $\gamma$-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 $\omega$ as well as the decay time constant of excitatory synapses. As $\omega$ 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 $\alpha$.

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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[1] P. Hadley, M.R. Beasley, and K. Wiesenfeld, Phys. Rev. B 38, 8712 (1988); S. Watanabe and S.H. Strogatz, Phys. Rev. Lett. 70, 2391 (1993).
[2] S.S. Wang and H.G. Winful, Appl. Phys. Lett. 52, 1774 (1998).
[3] D. Ploenz and S.T. Kitai, J. Neurophysiol. 76, 4180 (1996); S.F. Farmer, J. Physiol. 209, 3 (1998); P. Fries, J.H. Schroder, P.R. Roelfsema, W. Singer, and A.K. Engel, J. Neurosci. 22, 3739 (2002); C.S. Herrmann, M.H. Munk, and A.K. Engel, Trends Cogn. Sci. 8, 347 (2004); D. Lee, J. Neurosci. 24, 4453 (2004).
[4] A.T. Winfree, J. Theor. Biol. 16, 15 (1967).
[5] A.T. Winfree, The Geometry of Biological Time (Springer, New York, 1980).
[6] Y. Kuramoto, Chemical Oscillations, Waves, and Turbulence (Springer-Verlag, Berlin, 1984).
[7] D. Reyes and E.E. Fetz, J. Neurophysiol. 69, 1661 (1993); A.D. Reyes and E.E. Fetz, J. Neurophysiol. 69, 1673 (1993).
[8] D. Hansel, G. Mato, and C. Meunier, Neural Comput. 7, 307 (1995).
[9] B. Ermentrout, Neural Comput. 8, 979 (1996).
[10] R.F. Galan, G.B. Ermentrout, and N.N. Urban, Phys. Rev. Lett. 94, 158101 (2005).
[11] A.J. Preyer and R.J. Butera, Phys. Rev. Lett. 95, 138103 (2005).
[12] M. Lengyel, J. Kwag, O. Paulsen, and P. Dayan, Nat. Neurosci. 8, 1667 (2005).
[13] T.I. Netoff, M.I. Banks, A.D. Dorval, C.D. Acker, J.S. Haas, N. Kopell, and J.A. White, J. Neurophysiol. 93, 1197 (2005).
[14] T. Tateno, and H.P. Robinson, Biophys. J. 92, 683 (2007).
[15] Y. Tsubo, M. Takada, A.D. Reyes, and T. Fukai, Eur. J. Neurosci. 25, 3429 (2007).
[16] H. Sakaguchi and Y. Kuramoto, Prog. Theor. Phys. 76, 576 (1986).
[17] T. Shimokawa, S. Shinomoto, Phys. Rev. E. 73, 066221 (2006).
[18] H. Haas, N. Kopell, and J.A. White, J. Neurophysiol. 93, 1197 (2005).
[19] J. Teramae and D. Tanaka, Prog. Theor. Phys. Supp. 161, 360 (2006).