Synchronous phase clustering in a network of neurons with spatially decaying excitatory coupling

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Abstract

Synchronization is studied in a spatially-distributed network of weekly-coupled, excitatory neurons of Hodgkin-Huxley type. All neurons are coupled to each other synaptically with a fixed time delay and a coupling strength inversely proportional to the distance between two neurons. We found that a robust, noise-resistant phase clustering state occurred regardless of the initial phase distribution. This has not been shown in previous studies where similar clustering states were found only when the coupling was inhibitory. The spatial distribution of neurons in each synchronous cluster is determined by the spatial distribution of the coupling strength. Phase-interaction properties of the model neurons in the network are used to explain why can such a clustering state be robust.

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Synchronization of coupled neural networks has attracted much interest. In many parts of the central nervous system (CNS), synchronous oscillations have been observed and are assumed to be correlated to specific behaviors, cognitive tasks as well as pathological states [1]. Synchronization in coupled neural networks has been studied theoretically by using various neuronal models [2]. It is generally assumed that neurons in the network are pulse coupled since real neurons interact with each other only when they generate spikes of action potentials. The occurrence of synchrony in a network of neurons is largely determined by: (1) the phase-response nature of each neuron, (2) the nature of coupling (e.g. excitatory or inhibitory) between neurons, (3) the time delay involved in the coupling. Furthermore, the presence of noise can also influence the stability of synchronized states. The fact that neurons distributed across a wide spatial range can still synchronize [3] poses an important question as to what makes it possible. Many studies have indicated that synchronous states can be observed when time-delayed synaptic coupling is predominantly inhibitory [4,5]. The influence of other important features such heterogeneity and sparseness in the coupling have also been investigated [6]. However, conditions for the occurrence of robust, fully or partially synchronized states in a network of synaptically coupled excitatory neurons have not been fully investigated.

In this Letter, we address this problem with a large network of excitatory neurons that are organized in a two dimensional square lattice in space. We found that, in the presence of independent local noise, a robust synchronous clustering state can occur regardless of the initial phase distribution. This state is characterized by the clustering of neurons into 15 synchronized clusters that fire consecutively at a fixed time interval that is one 15th of their intrinsic period [4,5]. In previous studies, similar clustering states were found robust only with inhibitory mean-field coupling [4,5]. It is known that excitatory coupling usually causes instability to synchronized state. The occurrence of robust synchronized clusters in the network of excitatory neurons seems to contradict this well established fact. Our analysis provides an intuitive explanation of how this is possible.

Figure 1 is a schematic diagram of the network consisting of an array of 30 by 30 neurons.
This network was originally proposed in an attempt to model the network of an array of electoreceptor cells that are distributed on the rostrum of the paddlefish, *Polydon Daphnia*. The distance between nearest neighbors is taken as the unit length. The coupling strength between any pair of neurons is inversely proportional to the distance $R$ between them [9]. The neurons are all identical and are coupled to each other through excitatory synapses modeled by an alpha function with a fixed time delay. The model that we use to describe each neuron in the network was previously developed for the electoreceptor cells in the paddlefish [10], [11], and [12]. It is a modified Hodgkin-Huxley type model involving four ionic currents and a leak current.

$$C_M \frac{dV}{dt} = -I_{\text{leak}} - I_{\text{Na-spike}} - I_{\text{K-spike}} - I_{\text{Na-slow}} - I_{\text{K-slow}} + I_{\text{syn}} + \sqrt{2D}\eta(t) \quad (1)$$

where all the ion currents are expressed in terms of ohm’s law $I_x = g_x(V - V_x)$ (subscript “x” specifies each specific ion current involved). Detailed expressions for $g_x$, the gating equations, and the parameter values can be found in [10], [11], and [12]. Independent Gaussian white noise was added to each neurons with uniform intensity $D$ as described by the last term in Eq. (1). Synaptic coupling was excitatory and was modeled by an $\alpha$ function [13] given in the following expression.

$$I_{\text{syn}} = \sum_{j=1}^{N} \frac{W}{R_{ij}} \int_0^{\infty} (s/\tau^2) \exp(-s/\tau) S_j(t-s) ds \quad (2)$$

where $S_j(t) = \sum_k \delta(t - t_k)$ represents the output spike train from the $j$th neuron firing at times $t_k$. The delay between the peak time of the presynaptic pulse and that of the postsynaptic current is fixed at $\tau = 7$ ms. $R_{ij}$ denotes the distance between the $i$th and the $j$th neuron (Fig. 1). $W(>0)$ is a constant denoting the coupling strength. For the parameter values used in this model [11], each uncoupled neuron exhibits a stable limit cycle oscillation.

In the absence of noise, the system can evolve into a state of multiple clusters with carefully selected initial phase distributions. For example, if the initial phase distribution was uniform, a synchronous phase clustering state of 16 clusters can occur. The stroboscopic
picture of phases for all 900 neurons in Fig. 2(a) shows how the clusters emerge as time evolves. Each neuron fires periodically while the 16 clusters fire consecutively at a fixed phase difference. This makes the cycling frequency of the averaged electrical activity of the network 16 times the frequency of each neuron.

In the presence of weak noise ($D = 10^{-5}$), a robust phase clustering state with 15 clusters was obtained. Furthermore, the same 15-cluster state was always obtained regardless of the initial phase distribution [14]. All other clustering states that occurred in the absence of noise with selected initial phase distributions are no longer robust when noise was introduced. With noise, the same initial phase distribution as in Fig. 2(a) evolved into a clustering state of 15 clusters (Fig. 2(b)). Simulations further indicated that this 15-cluster state was robust in the presence of weak noise. Starting with a fully in-phase-synchronized initial state where each neuron fires simultaneously (Fig. 2(c), the synchronization was rapidly destroyed and the 15-cluster state eventually emerged. Had there been no noise, this fully in-phase-synchronized state would have remained unchanged for the same time duration. Similarly, when the system was initiated at a 2-cluster state (Fig. 2(d)) which would persisted in the absence of noise was destroyed by the noise and eventually evolved into the 15-cluster state, although a longer evolution time was required. We tried many different initial phase distributions and found that the same 15-cluster state emerged all the time, although the transients and the detailed distribution of neurons in each cluster were different.

A typical pattern of spatial distribution of neurons in each cluster is shown in Fig. 3 that corresponds to the 15-cluster state reached in Fig. 2(b). Three important features of such distributions were found: (1) the number of neurons in each cluster was approximately the same, i.e. about 60 ($=900/15$); (2) neurons in each synchronized cluster were almost evenly distributed in space; (3) the even distribution of neurons in each cluster also indicated that the average inter-cluster distance between neurons is similar between different clusters.

The results presented here are different from previous studies in networks with mean-field type excitatory coupling where phase clustering states cannot persist in the presence of week noise (see Fig. 7 in Ref. [3] and [15]). Our network differs from the mean-field type
of coupling because the coupling strength is inversely proportional to the distance between two neurons. The question is how this difference makes the robust, noise-resistant clustering state possible. Furthermore, why is the 15-cluster state the asymptotically stable one? What is special about the fixed phase difference $1/15 \approx 0.067$? Here are the conclusions reached by the following analysis: the fixed phase difference and the number of clusters are determined by the phase-interaction properties between two neurons while the robustness of the clustering state is achieved because the neurons in the network self-organizes into clusters in such way that the stabilizing inter-cluster interactions are stronger than the destabilizing intra-cluster interactions.

Several important features of the 15-cluster state can be explained by the phase-interaction properties between two neurons. Phase-interaction between two neurons depends on how the neurons are coupled to each other and how each neuron responds to interactions between them. These properties are characterized mathematically by the so-called interaction function that is defined as the convolution between the synaptic current $i_{syn}(t) = \frac{R}{W}I_{syn}(t)$ and the adjoint or the phase-response function $Z(t)$ over one oscillation period.

$$H(\phi) = \frac{1}{T} \int_0^T dt Z(t) \int_0^\infty (s/\tau^2) \exp(-s/\tau) \sum_{k=-\infty}^0 \delta(t - s + kT - \phi) ds.$$  \hspace{1cm} (3)

where $\phi$ is the phase difference between the two oscillators that satisfies

$$\frac{d\phi}{dt} = -wg(\phi)$$ \hspace{1cm} (4)

where $g(\phi) = H(\phi) - H(-\phi)$ is the odd part of $H(\phi)$ and $w = W/R$ is the coupling strength between the two neurons. Thus, the phase-lock solutions are the zeros of $g(\phi)$ and the stability is determined by the sign of $g'(\phi)$ (stable if $g' > 0$, unstable if $g' < 0$) \[17\]-\[18\]. The $g(\phi)$ and $g'(\phi)$ calculated with the model described by Eqs. (1-2) and the synaptic current given by Eq. (2) are shown in Fig. 4(a) for the $\tau$ value used in Figs. 2-3. There are 7 zeros in one complete period of which 3 pairs are symmetric. Thus only 4 possible phase-locking states are possible: in-phase ($\phi = 0$) that is unstable, anti-phase ($\phi = 0.5$) that is stable, a
fixed phase difference \( \phi \approx 0.062 \) that is stable, and an unstable phase-locking state. The \( g'(\phi) \) curve shows that the anti-phase solution is weekly stable but the phase-lock solution at \( \phi = 0.062 \) is strongly stable. Now we see that the number of clusters and this strongly stable phase-locking state is closely related since 0.062 is close to the actual phase difference (0.067) in the 15-cluster state. Fig. 4(b) shows that the locked phase difference of this phase-locking state increases as the synaptic time delay \( \tau \) increases. This implies that at larger values of \( \tau \), the number of clusters in the robust clustering state should decrease. However, this simple explanation does not answer how could the neurons in each synchronized cluster maintain their stability and why the 16-cluster state was not the asymptotic state although \( 1/0.062 \approx 16.13 \) is closer 16 or even 17 but not 15.

To further demonstrate the robustness of the 15-cluster state we need to study the stability of the clustering state based on the phase description of coupled neural network. With week coupling, each neuron can be approximately described by their respective phase variation \( \phi_i \) resulting from synaptic interactions with other neurons. Such interactions are characterized by the same interaction function \( H \) calculated in Eq. (3). Thus, the network can be described by the following 900 phase coupled equations.

\[
\frac{d\phi_i}{dt} = \frac{1}{N} \sum_{j=1(j\neq i)}^{N} w_{i,j} H(\phi_j - \phi_i).
\]

(5)

where \( w_{i,j} = w_{j,i} = \frac{W_{R_{i,j}}}{R_{i,j}} \) is the coupling strength between the \( i \)th and the \( j \)th neurons. It is hard to use these equations to determine all the possible solutions. However, they can be useful in determining the stability of a known solution. Instead of solving the eigenvalue problem of the huge Jacobian matrix, we here focus on the stability of the clustering state when the phase of a single neuron is perturbed. For simplicity, we assume that the average distances between two neurons within and between all clusters are identical (confirmed by our simulations), we can derive the equation that approximately describes the time evolution of the perturbation of any neuron \( \delta\phi = \phi_i - \Phi_i \) (where \( \Phi_i \) is the phase of all neurons in the cluster where neuron \( i \) belongs).
where the intra-cluster coupling strength, \( \bar{w}_0 = \frac{1}{n} \sum_{i=0}^{n-1} \frac{2}{n_i(n_i-1)} \sum_{i' \neq j} \sum_{j=1}^{n_i} \frac{W_{i',j}}{R_{i',j}} \), is the average coupling strength between two neurons within one cluster. The inter-cluster coupling strength, \( \bar{w}_1 = \frac{2}{n(n-1)} \sum_{i,j=1}^{n-1} \sum_{i' \neq j} \sum_{n_i=1}^{n} \sum_{j=1}^{n} \frac{W_{i',j'}}{R_{i',j'}} \), is the average coupling strength between two neurons in different clusters. In these expressions, \( n \) is the number of clusters and \( n_i \) is the number of neurons in the \( i \)-th cluster.

Equation (6) is valid for all neurons in the network. Therefore, the stability of a particular clustering state is achieved when \( \lambda = \bar{w}_0 g'(0) + \bar{w}_1 \sum_{j=1}^{n-1} g'(j/n) > 0 \) and the most robust clustering state is the one that maximizes \( \lambda \). \( g'(0) < 0 \) is generally true for excitatory coupling (see Fig. 4(a)). Thus intra-cluster interactions destabilize synchrony in each cluster, consistent with the known effect of excitatory coupling. However, the cluster can still be stable since \( g'(j/n) \) \( (j = 1, \cdots, n-1) \) can be positive (see Fig. 4(a)). For a given number of clusters \( n \), if \( g_n = \sum_{j=1}^{n-1} g'(j/n) > 0 \), the \( n \)-cluster state is stable if \( \bar{w}_1/\bar{w}_0 > |g'(0)|/g_n \) is satisfied. The most robust clustering state is the one with \( n^* \) clusters where \( n^* \) maximizes \( \lambda \). In the present network \( n^* = 15 \).

The analysis indicates that the stability of multi-cluster states with excitatory coupling is favored by two conditions: (1) \( g'(\phi) \) is strongly positive and/or positive for a larger part of the cycle (see Fig. 4(a)); (2) \( \bar{w}_1 > \bar{w}_0 \) (e.g. \( \bar{w}_1, \bar{w}_0 \approx 9.5e^{-4}, 9.1e^{-4} \) in Figs. 2-3), i.e. a larger average inter-cluster coupling than average intra-cluster coupling. Both conditions are met by our network. Fig. 4(a) shows that our \( g'(\phi) \) is indeed positive over a large part of the cycle and has two large positive peaks located at \( \phi = 0.062 \) and \( 1 - 0.062 \). The fact that \( |g'(0.062)| >> |g'(0)| \) not only explains why the asymptotic state has as many as 15 clusters but also indicates that this clustering state could still be robust even if condition (2) were not met. Spatial decay in coupling strength is crucial for the network to satisfy condition (2). It allows the network to minimize \( \bar{w}_0 \) by scattering the neurons in each cluster far apart from each other. This explains why neurons are evenly distributed in each cluster (Fig. 3).

This analysis shows that when the coupling strength is allowed to differ between different
neurons, robust clustering states can occur in networks of excitatory neurons. This result
is not model specific, although the number of clusters depends on specific features of the
model and some key parameters such as the delay time $\tau$. This results is further supported
by numerical studies of other neuronal models including the integrate-and-fire model (work
in progress), provided the conditions outlined above are satisfied.

The fact that distributed coupling strength can generate robust synchronous clusters may
have some relevance in understanding the dynamical variations of brain functions. First,
neurons can join different synchronized clusters depending on how the pattern of coupling
strength is modified. It is possible that these patterns can be mapped to the functional
states of the brain. The patterns of synchronized clusters may be used as codes in some
cognitive tasks. Second, associative memory patterns could be stored in the patterns of
coupling strength and the clustering patterns could be ‘selected’ by the coupling pattern.
Furthermore, these patterns could be modified during learning processes. Such memory
patterns can be retrieved once the clustering patterns are retrieved through dynamical evo-

cution. Finally, the large number of clusters ($n$) in the clustering states makes the average
electrical activity of the network oscillate with a frequency $n$ times the intrinsic frequency
of each individual neuron. It is worth noting that a high-frequency network oscillation
(200Hz, several times the spontaneous firing frequency of a single neuron) was reported in
experiments on pyramidal cells in the CA1 hippocampal region of rats [19].

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FIG. 1. Schematic diagram of a two-dimensional lattice of $30 \times 30$ modified HH neurons, with the black dots representing the neurons (1 to 900), where the coupling strength of the $i$th and $j$th neurons is $W/R_{ij}$ with $R_{ij}$ as the distance between neurons $i$ and $j$. 
FIG. 2. Typical spatial distribution of neurons in each cluster for the 15-cluster state in Fig. 2(b). The synchronized pattern labeled 1 to 15 appear consecutively as time evolves.
\[ g(\phi) \]

\[ g'(\phi) \]

\( \phi \)

\( \tau \text{ (msec)} \)
FIG. 3. (a) $g(\phi)$ (solid line) and $g'(\phi)$ (dashed line) plotted as a function of the phase $\phi$ when $\tau = 7ms$. The scale of $g(\phi)$ is shown on the left side of the figure and that for $g'(\phi)$ on the right side. (b) Phase difference of stable (solid) and unstable (dashed) states plotted as a function of $\tau$. 