Synchronization properties of slow cortical oscillations

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During slow-wave sleep, the brain shows slow oscillatory activity with remarkable long-range synchrony. Intracellular recordings show that the slow oscillation consists of two phases: an \textit{up} state and a \textit{down} state. Deriving the phase-response function of simplified neuronal systems, we examine the synchronization properties on slow oscillations between the \textit{up} state and the \textit{down} state. As a result, the strange interaction functions are found in some parameter ranges. These functions indicate that the states with the smaller phase lag than a critical value are all stable.

\section{Introduction}

The corticothalamic system is a complex network that generates various oscillatory patterns. Specifically, the slow, neocortical (0.1–0.5 Hz) oscillatory activities affect the synchronized activities over wide regions of the brain.\textsuperscript{1} With multi-site, simultaneous intracellular recordings, the synchronized slow activities were observed in the corticothalamic network\textsuperscript{2,3}. Recently, spontaneous activity similar to the slow oscillations recorded \textit{in vivo} has been described in an \textit{in vitro} slice preparation of cerebral cortex\textsuperscript{4}, and a large-scale biological network model was proposed.\textsuperscript{5} The interplay between spontaneous neuronal firing amplified by recurrent excitation, and the negative feedback due to slow intrinsic ionic currents provide the basic mechanism for the emergence of the oscillatory activity in the network model.\textsuperscript{5} In order to examine the synchronization properties of the slow oscillatory activity, we consider a reduced model in which recurrent synaptic input is replaced with self-feedback synaptic connections (see Fig. 1). These feedback inputs effectively represent the average activity of population of synchronized cortical neurons.

\section{Method}

The neuron model used here is the Hodgkin-Huxley type model,\textsuperscript{6} and the details of each current are described in 5). The time development for the membrane potential of the soma ($V_s$) and of the dendrite ($V_d$) are described by the following equations:\textsuperscript{5}

\begin{equation}
C_m A_s \frac{dV_{s,i}}{dt} = -A_s I_{I,s,i} - g_{\text{ad}} (V_{s,i} - V_{d,i}),
\end{equation}

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where $C_m$ is the membrane capacitance, and $g_{sd}$ is the coupling conductance between soma and dendrite. $A_s$ and $A_d$ are the areas of the soma and dendrite, respectively.

\[
I_s = I_L + I_{Na} + I_K + I_A + I_M + I_{KNa} \quad \text{and} \quad I_d = I_{NaP} + I_{AR} + I_{Ca} + I_{KCa}
\]

are intrinsic current experienced by the soma and the dendrite, respectively. Synaptic current consists of AMPA and NMDA type currents:

\[
I_{syn,ji} = s_{AMPA,ji}(t)I_{AMPA}(V_{d,i}) + s_{NMDA,ji}(t)I_{NMDA}(V_{d,i}).
\]

It is well known that a network of oscillatory units can be reduced to a simpler system of phase oscillators if each unit exhibits a limit cycle behavior, and the interaction between the units is weak.\(^7\) This technique has been applied to spiking neurons and its synchronization properties studied.\(^8\) Here, we apply the phase reduction approach to the slow oscillations.

§3. Results

Depending on the strength of the synaptic conductance and the intrinsic membrane properties, this model exhibits various firing patterns including a slow oscillatory activity. If the conductance of the excitatory synapse $g_{syn,ii}$ is small, the model generates regular spikes, firing with a frequency of around 0.2–0.5 Hz. An increase in synaptic conductance leads to a slow oscillatory activity with an up and a down state. Sequential action potentials with 5–10 Hz (up state) are generated by the excitatory recurrent synaptic current $I_{syn,ii}$ and suppressed by the intrinsic $Ca^{2+}$ current ($I_{KCa}$) and Na$^+$-activated K$^+$ current ($I_{KNa}$). $A$-current ($I_A$) leads to prolonged hyper-polarization (down-state).

In simulations involving coupled neurons, two neurons that are generating slow oscillations come into an in-phase synchronized state. However, at some parameter range, the various phase lags (ranging from 0 to a few hundred msec) can be realized in the asymptotic state depending on initial conditions (see Fig. 2). When the synaptic current $I_{syn,ji}$ increases, the oscillation around the 0 of the phase lag is often observed. The up state of one neuron precedes the up state of the other for a certain time, and this order reverses itself iteratively (data not shown).

Applying the phase reduction approach, the dynamics of the $i$-th neuron can be described by the phase variable $\phi_i$ and the reduced phase equations take the following general form:

\[
d\phi_i/dt = \omega + Z_{AMPA}(\phi_i) s_{AMPA}(\phi_j) + Z_{NMDA}(\phi_i) s_{NMDA}(\phi_j), \quad \text{where} \quad \omega \text{ is an intrinsic bursting (up state) frequency of an uncoupled neuron,} \quad Z_{AMPA}(\omega t) = Z_{V_{d}}(\omega t)(V_{d}(t) - E_{AMPA}) \quad \text{and} \quad Z_{NMDA}(\omega t) = Z_{V_{d}}(\omega t)B(V_{d}(t))(V_{d}(t) - E_{NMDA}) \quad \text{are the phase resetting curve for AMPA and NMDA synaptic input, respectively.} \quad B(V) \text{ represents the Mg}^{2+}-\text{block voltage dependency. The effective interaction function}
\]
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Fig. 2. The membrane potentials ($V_s$) of coupled neurons. The synchronized state and states with small lag are both stable.

$\pi$

$V_s$

$Z$

$V_d$

$\Gamma$

$\text{odd}$

$T = 6144$ msec

$663$ msec

$0$

$0$

$\pi$

$2\pi$

Fig. 3. Membrane potential, phase response curve and interaction function. The interaction function in the in-phase state $d\Gamma_{\text{odd}}/dt$ is almost zero.

of $T$ periodic repetitive bursting neurons is given as $d\phi_i/dt = \omega_i + \sum_j \Gamma(\phi_i - \phi_j)$, where $\Gamma(\phi) = \frac{1}{T} \int_0^T \sum_x \text{AMPA,NMDA} Z_x(\omega t) s_x(\omega t - \phi) dt$.

In two-neuron networks, we can rewrite the phase dynamics as $d\phi/dt = \Gamma_{\text{odd}}(\phi)$, where $\phi = \phi_1 - \phi_2$ and $\Gamma_{\text{odd}}(\phi) = \Gamma(\phi) - \Gamma(-\phi)$. Any phase-locking mode of this system corresponds to a solution to the equation $\Gamma_{\text{odd}}(\phi) = 0$. The stability of the solution $\phi$ can be determined by the condition $d\Gamma_{\text{odd}}/d\phi(\phi) < 0$. We derived the phase-response functions $Z$ and the interaction functions of coupled neurons $\Gamma_{\text{odd}}$ at various parameters. As shown in Fig. 3, for some parameter ranges, the interaction function $\Gamma_{\text{odd}}$ is almost 0 near 0 phase difference and the in-phase state is likely marginally stable. This indicates that the phase-lagging states are stable when the phase lags are smaller than some critical value. These results are consistent with coupled-neuron simulations.

Fig. 4 shows the effect of the synaptic conductance on the stability of the phase-locked states. Increasing maximal conductance of self-feedback NMDA currents, marginal stability comes to appear at $\phi = 0$ and $\pi$. It is notable that the phase response curve has a longer refractory period when the NMDA current is stronger and up-state spike frequency is higher. The $\phi$ range in which $\Gamma_{\text{odd}}$ is nearly 0 is widened by large synaptic delays (data not shown). As shown in Fig. 4, the synaptic intensity $s$ has a positive value during the up state. If $s(t)$ is approximated by $\delta(t - \Delta/2)$, where $\Delta$ is the midpoint-time of the up state, then the equation $\Gamma(\phi) = Z_V(\phi + \Delta/2)$ is derived. In Fig. 4(d), $Z_V$ is almost 0 during the up state; therefore the values of $\Gamma(\phi)$ in $-\Delta/2 < \phi < \Delta/2$ are also near 0. Finally interaction function $\Gamma_{\text{odd}}$ near $\phi = 0$ is nearly 0 and the system has the wide phase-lagging states.

In Fig. 4(a), spike frequency during bursting is low, and the phase response $Z_V$ has positive and negative peaks at each spike interval. Similar phase response with peaks during bursting is shown in the chattering neuron model. These responses during bursting cause strong in-phase stabilities in the chattering neuron model.
§4. Conclusion

We have evaluated the synchronization properties of slow oscillatory activities using a simplified network model. In this model, the wide-range stable phase-lagging states often manifest themselves in the simulations, and the phase reduction analysis support these results. In this paper, we only examined two-neuron networks. We are preliminarily studying a large-scale network of phase oscillators in which the neurons have different natural frequencies. In this case, the network makes one or two groups whose members are synchronized with each other. In these groups, each neuron pair does not synchronize entirely, and there is often a phase lag between them. Such an incomplete synchronization may cause a multiplicity of firing patterns in the network. Synchronization properties of networks that generate slow oscillatory activities will be reported in a forthcoming paper.

References

6) A. Hodgkin and A. Huxlay, J. Physiol. 117 (1952), 500.