

Dendritic Effects in Networks of Fast-Spiking Interneurons Connected by Inhibition and Electrical Coupling

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Abstract:

Experimental and theoretical studies suggest that local inhibitory interneurons play critical roles in generating and maintaining coordinated rhythmic cortical activity. How the intrinsic cellular dynamics and connectivity properties interact to produce this behavior is poorly understood.

Fast-spiking interneurons in the cortex are connected by both mutual inhibitory synapses and direct electrical coupling. Recently, we studied phase-locking in single-compartment model neurons connected by both inhibition and electrical coupling. These single-compartment models neglect spatial aspects of dendrites that can affect phase-locking dynamics.

In the present study, we replace the single-compartment model neurons by a two-compartment model, consisting of a somatic compartment and a dendritic compartment. We show that the location of electrical and inhibitory coupling can substantially change the phase-locking structure.

Introduction

Recently, direct electrical coupling has been found to be widespread in networks of cortical inhibitory interneurons. The effects of electrical coupling between cortical interneurons has been the focus of much experimental and theoretical work, however the functional role that electrical coupling plays in cortical networks remains unclear. Evidence suggests that electrical coupling can help coordinate synchronous oscillatory behavior in inhibitory networks, which has been hypothesized to be important for sensory and cognitive processes.

Previous studies have systematically examined synchronization patterns between single-compartment neurons coupled by electrical coupling alone [4, 10, 9], as well as combined electrical and inhibitory coupling [10]. Whether or not these studies are applicable to dynamics in cortical interneuronal networks depends on, among other things, whether or not a single-compartment description is a sufficient model of cortical interneurons.

If neurons are not electrotonically compact, then a single-compartment model is not sufficient in most circumstances. In this case, the response properties of neurons can be highly dependent on the site of the applied or synaptic input [3, 5, 11]. Similarly, the location of electrical coupling can have substantial effects on phase-locking [1].

Using electron microscopy, Tamas *et al* [12] found gap junctions located on the somata and proximal dendrites of cortical fast-spiking (FS) interneurons. On the other hand, using paired-cell recordings, Amitai *et al* [2] showed putative direct electrical connections between neurons up to 200 microns away from one another. This suggests gap junctions can also be located between distal dendrites.

In this summary, we address the issue of effects of dendrites on network dynamics. We add a passive dendritic compartment to a single-compartment model for FS interneurons and systematically examine the effects of the location of electrical coupling on phase-locking in networks of neurons. Because FS interneurons are connected by inhibition as well, we will also examine the effects of combined electrical and inhibitory coupling; this, however, is not included in this summary.

The Two-Compartment FS Model: Single Cell

Model description

We take a single model neuron to consist of an active somatic compartment and a passive dendritic compartment. The governing equations are

$$\begin{aligned} C \frac{dV_s}{dt} &= -I_{ionic}(V_s, m, h, n_1, n_3) + I_{applied} + g(V_d - V_s) \\ C \frac{dV_d}{dt} &= -g_{lk}(V_d - E_{lk}) + \gamma g(V_s - V_d) \end{aligned}, \quad (1)$$

where V_s and V_d are the transmembrane potentials of the somatic and dendritic compartments, g is the electrotonic coupling strength between the compartments, $I_{applied}$ is the bias current applied to the soma, g_{lk} and E_{lk} are the conductance and reversal potentials of the dendritic leakage current, and γ is the ratio of the membrane surface area of the dendritic compartment to that of the somatic compartment. I_{ionic} is given by a conductance-based model for cortical FS interneurons proposed by Erisir and coworkers [6]. All parameters are the same as those in the original Erisir *et al* model except for the leak conductance for which we use $g_l = 0.25 \text{ mS/cm}^2$ (instead of 1.25 mS/cm^2).

We define the vector $\bar{X}(t) = (V_s(t), m(t), h(t), n_1(t), n_3(t), V_d(t))$ to denote the complete state of the single cell. For this work, we take $\gamma = 1$. Also, the conductance and reversal potential in the dendritic compartment is chosen to be the same as those in the somatic compartment. The electrotonic coupling strength g between the compartments is taken to be half of the leakage conductance.

Periodic oscillations

Given sufficiently large input current $I_{applied}$, the two-compartment cell can exhibit intrinsic oscillatory behavior. Examples of this periodic activity are seen in the top panels of figures 1 and 2. An attracting limit cycle, $X_{LC}(t)$, underlies the stable periodic activity of the single cell. $X_{LC}(t)$ depends on all of the single-cell parameters including $I_{applied}$.

Electrically Coupled Oscillating Cells

Now let us consider a pair of cells. We add the subscript i to denote the variables for the i^{th} cell. The complete state of each cell is given by $\bar{X}_i(t)$, $i = 1, 2$.

Coupling description

Electrical coupling between cells is modeled as an ohmic resistance. If coupling is between somata of cells i and j , then the right-hand side of the differential equation for $V_{s,i}$ will have the additional term $I_{coup,ij} = g_c(V_{s,j} - V_{s,i})$. That is, $I_{coup,ij}$ is the coupling current and g_c is the electrical coupling conductance. If coupling is between dendrites of cells i and j , then the right-hand side of the differential equation for $V_{d,i}$ will have the additional term $I_{coup,ij} = g_c(V_{d,j} - V_{d,i})$. There are several other combinations of coupling that one could study, but for now we limit the study to either somato-somatic coupling or dendro-dendritic coupling.

Weak coupling and phase models

When coupling is sufficiently weak, the complete state of the cells can be well-approximated by the relative phase of the cell ϕ_i on the intrinsic limit cycle, $\bar{X}_{LC}(t - \phi_i)$. The theory of weakly coupled oscillators [8, 7] derives equations that describe the slow rate of change in the relative phases of the cells

$$\frac{d\phi_i}{dt} = H(\phi_i - \phi_j) = \frac{1}{T} \int_0^T \bar{Z}(\tilde{t}) \cdot \bar{I}_{coup,ij}(\bar{X}_{LC}(\tilde{t}), \bar{X}_{LC}(\tilde{t} + (\phi_i - \phi_j))) d\tilde{t}.$$

where T is period of the intrinsic single-cell oscillation. $\bar{Z}(t)$ is called the infinitesimal phase response curve (iPRC) or phase-dependent sensitivity function. In general, $\bar{Z}(t)$ and $\bar{I}_{coup,ij}$ are vectors, but if the coupling is between only somata or only the dendritic compartments, they reduce to scalars: $\bar{Z}(t) \rightarrow Z_s(t)$ for somatic coupling and $\bar{Z}(t) \rightarrow Z_d(t)$ for dendritic coupling. $Z_s(t)$ ($Z_d(t)$) is proportional to the phase-shift due to a small charge rapidly delivered to the somatic (dendritic) compartment at a time $t \in [0, T)$ in the oscillation.

Note that, because H only depends on the difference in relative phase, a single equation for the phase difference between cells can be obtained

$$\frac{d\phi}{dt} = H(-\phi) - H(\phi) = G(\phi).$$

Phase-locked states with phase difference ϕ^* are determined simply by $G(\phi^*) = 0$ (i.e. $\frac{d\phi}{dt} = 0$). The states are stable (unstable) if $G'(\phi^*) < 0$ ($G'(\phi^*) > 0$).

Phase-Locking in Electrically Coupled Oscillating Cells

For conductance-based models like the one we consider here, the periodic orbit $\bar{X}_{LC}(t)$ and iPRC $\bar{Z}(t)$ must be found numerically for each set of parameters describing the dynamics of the single cell. $\bar{X}_{LC}(t)$ is found by straight-forward numerical simulations; $\bar{Z}(t)$ can be found by linearizing the system around $\bar{X}_{LC}(t)$ and solving the adjoint equation.

The somatic and dendritic membrane potentials, the iPRCs and the G -functions for $I_{applied} = 7\mu\text{A}/\text{cm}^2$ are shown in figure 1. As explained above, the existence and stability of phase-locked states is easily determined by the G -functions. $G_s(\phi)$ in the bottom panel of figure 1 indicates that, for $I_{applied} = 7\mu\text{A}/\text{cm}^2$, synchronous and anti-phase phase-locked states exist when cells are electrically coupled via the somata, but only the synchronous state is stable. $G_d(\phi)$ shows that the same result holds for dendritic electrical coupling.

Somatic and dendritic coupling do not always lead to the same phase-locking structure. Figure 2 shows the membrane potentials, the iPRCs and the G -functions for $I_{applied} = 11\mu\text{A}/\text{cm}^2$. Despite the fact that the membrane potentials and the iPRCs look qualitatively similar to those for $I_{applied} = 7\mu\text{A}/\text{cm}^2$, they combine to produce a different effect for dendritic coupling. $G_s(\phi)$ in figure 2 shows that the phase-locking for somatic coupling is similar to that described above: synchronous activity is stable, and anti-phase activity exists but is unstable. On the other hand, $G_d(\phi)$ indicates that dendritic coupling leads to stable anti-phase activity, and although synchronous activity exists, it is unstable.

Figure 3 depicts bifurcation diagrams that plot the phase-difference of phase-locked states as a function of constant current applied to the soma $I_{applied}$. The bifurcation diagram for somatic electrical coupling is qualitatively the same as that for the single compartment FS model. Synchronous activity is stable over the entire frequency (i.e. applied current) range studied, $20 - 160\text{Hz}$. An anti-phase state exists over this full range as well. It is unstable for intermediate to high frequencies, however at low frequencies (below $\sim 25\text{Hz}$), it is stable.

The bifurcation diagram for dendritic coupling shows that only synchronous activity is stable at low frequencies and only anti-phase activity is stable at high frequencies. There is an intermediate frequency range ($55 - 65\text{Hz}$) where neither synchrony nor anti-phase activity is stable. Instead, there is an asynchronous but not anti-phase stable phase-locked state.

The results presented in this summary demonstrate that, when neurons are not electrotonically compact, the location of electrical coupling can have substantial effects on synchronization patterns. Understanding these results could be important for understanding synchronous oscillations observed in experiments.

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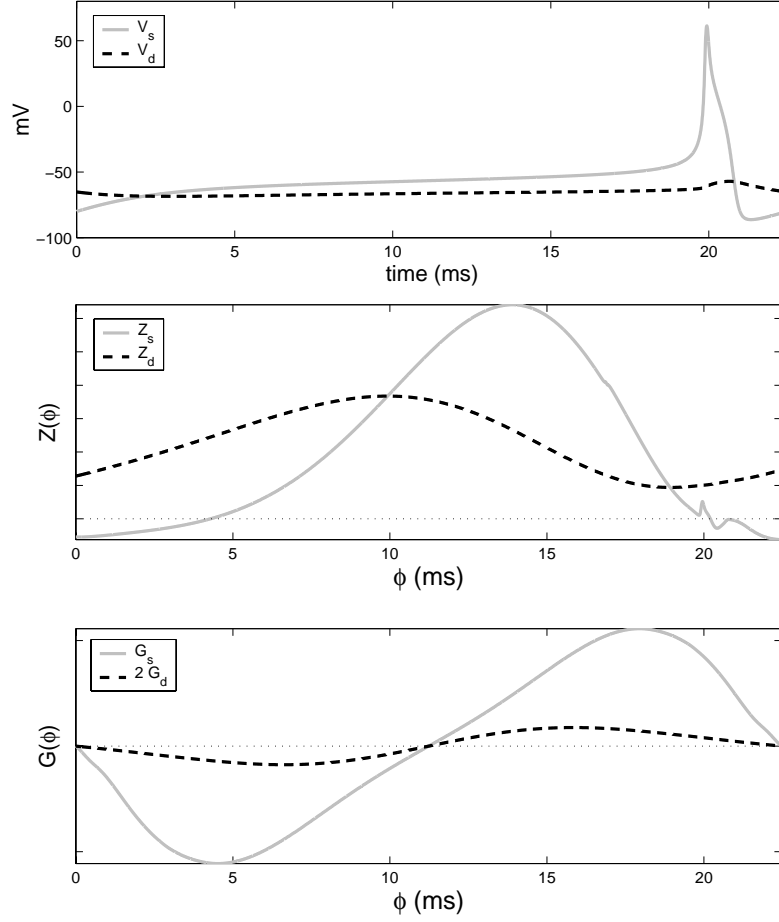


Figure 1: $I_{\text{applied}} = 7\mu\text{A}/\text{cm}^2$. **[top]** periodic activity in the two-compartment model FS neuron: transmembrane potential vs time for somatic compartment (V_s , grey solid line) and dendritic compartment (V_d , black dashed line). **[middle]** infinitesimal phase response curves (iPRCs) for perturbations to the somatic compartment (Z_s , grey solid line) and perturbations to the dendritic compartment (Z_d , black dashed line). **[bottom]** the resulting G -functions for somatic coupling (G_s , grey solid line) and dendritic coupling (G_d , black dashed line). The G -functions show that synchronous activity is stable and anti-phase activity is unstable for both somatic and dendritic electrical coupling.

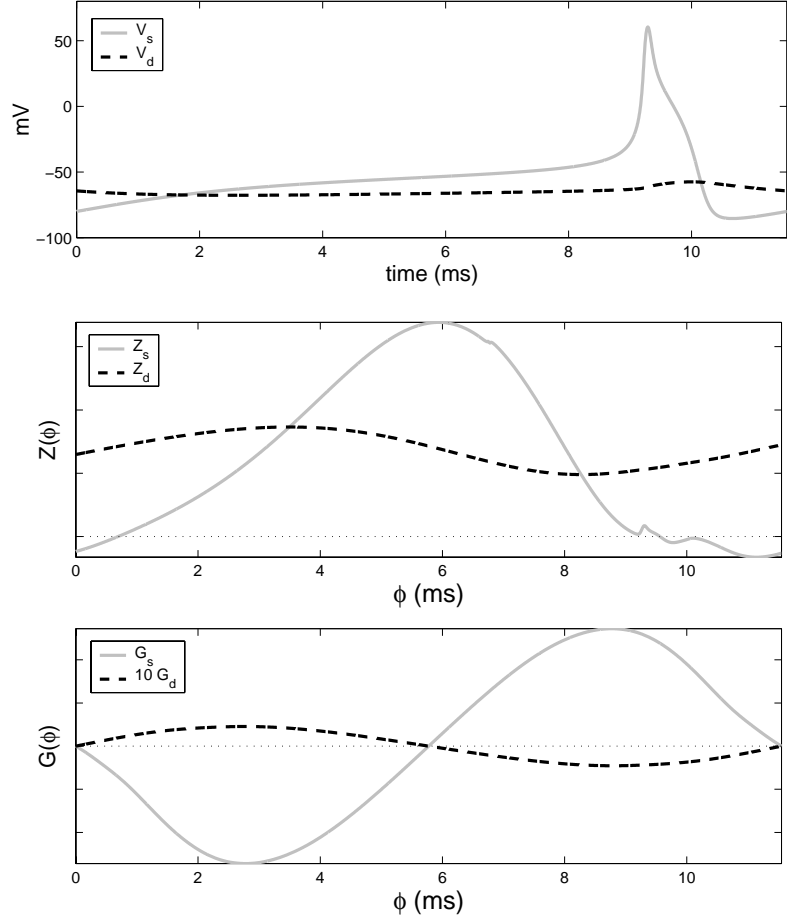


Figure 2: $I_{\text{applied}} = 11\mu\text{A}/\text{cm}^2$. **[top]** periodic activity in the two-compartment model FS neuron: transmembrane potential vs time for somatic compartment (V_s , grey solid line) and dendritic compartment (V_d , black dashed line). **[middle]** iPRCs for perturbations to the somatic compartment (Z_s , grey solid line) and perturbations to the dendritic compartment (Z_d , black dashed line). **[bottom]** the resulting G -functions for somatic coupling (G_s , grey solid line) and dendritic coupling (G_d , black dashed line). The G -functions show that synchronous activity is stable and anti-phase activity is unstable for somatic coupling, but the phase-locked activity for dendritic electrical coupling has the opposite stability.

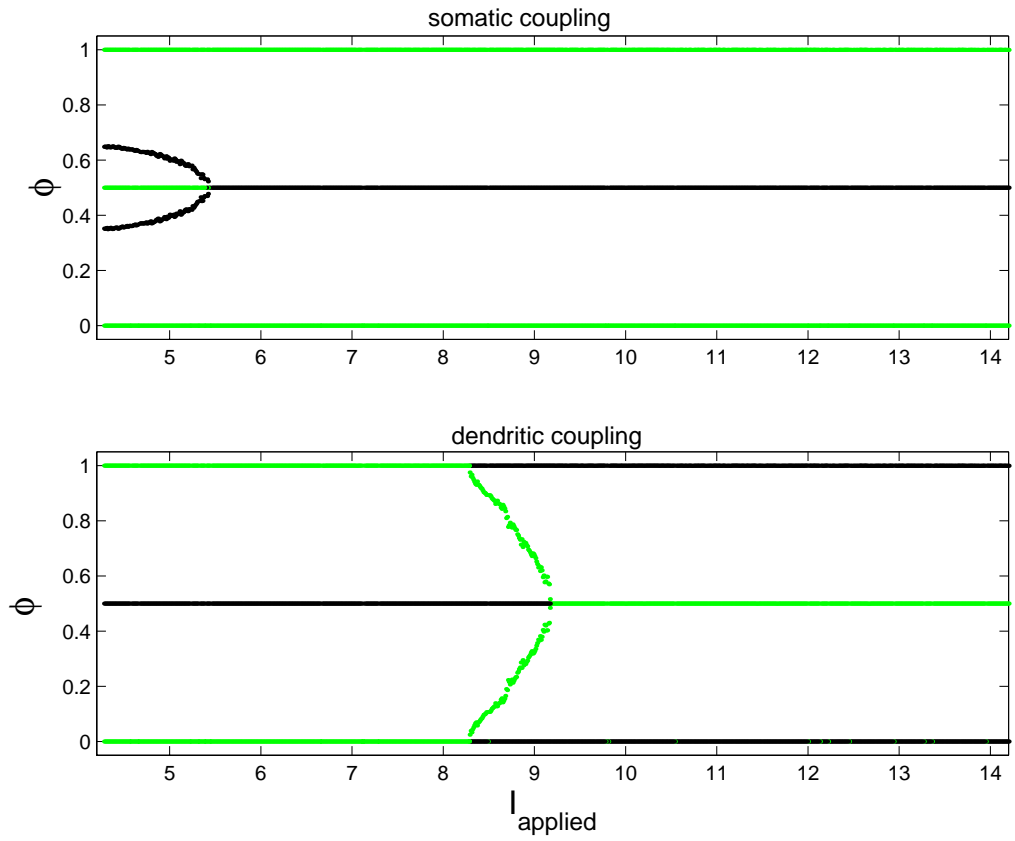


Figure 3: Bifurcation diagrams for somatic coupling (top) and dendritic compartment (bottom). Grey/green lines indicate phase-locked states that are stable; black lines indicate phase-locked states that are unstable.