Heterogeneous Spiking Neurons Connected by Both Inhibitory and Electrical Coupling

Timothy J Lewis
Center for Neural Science and Courant Institute for Mathematical Science, New York University, New York, New York 10003
tl14@nyu.edu

Sharon Crook
Department of Mathematics and Statistics, University of Maine, Orono, Maine 04469
crook@math.umaine.edu

John Rinzel
Center for Neural Science and Courant Institute for Mathematical Science, New York University, New York, New York 10003
rinzel@cns.nyu.edu

Abstract

Fast-spiking interneurons in the cortex are connected by both inhibitory chemical synapses and gap junctions, however it remains unclear how combinations of these two coupling modes affect dynamics in networks of fast-spiking neurons. To address this issue, we have recently examined synchronization patterns in model networks of identical oscillating cells (described by either the leaky integrate-and-fire model or a conductance-based model). We studied the influence of intrinsic cellular properties and coupling parameters, including the strengths of electrical and inhibitory coupling. Here, we extend this work by investigating the effects of heterogeneity in cells' intrinsic firing frequency on network synchronization patterns.

Introduction

There is a great deal of interest in the synchronous oscillatory activity observed in populations of cortical neurons and the possible role of this activity in cognition and sensory information processing. Experimental work suggests that inhibitory chemical synapses are critically involved in creating synchronous activity in some populations of neurons[1]. This is consistent with theoretical studies that demonstrate that inhibitory coupling can produce synchronized activity of oscillatory neurons under certain conditions[6,10]. However, modeling work has demonstrated that mild heterogeneity in oscillatory frequencies can sometimes destroy the ability of inhibition to produce synchronous activity[11,12]. Recent *in vitro* investigations have shown that a number local subpopulations of interneurons also display electrical coupling through gap junctions[4]. Experimental results show that electrical coupling seems to contribute to synchronous activity in some isolated networks of cortical interneurons, e.g.[13]; however, weak electrical coupling can foster anti-synchronous activity as well[2,8].

Networks of fast-spiking (FS) cortical interneurons are extensively connected by both inhibitory and electrical coupling[5]. It has been suggested that the presence of gap junctions could add robustness to inhibition-induced synchrony[12] and that a combination of electrical and inhibitory coupling acts synergistically to enhance synchronization[9]. In this work, we will extend previous results that examine the dynamics of cell pairs coupled with both inhibitory and electrical coupling [7]. We will study the influence of intrinsic firing frequency and coupling parameters on cell pair dynamics in the case of heterogeneous firing frequencies.

Homogeneous Cells

In order to construct a theoretical framework for understanding dynamics of identical neurons coupled with both electrical and inhibitory chemical synapses, Lewis et al [7] use a leaky integrate-and-fire model (LIF) to examine the behavior of coupled cell pairs in the case of weak coupling. In this work, electrical coupling between cells is modeled by a weak ohmic conductance, and inhibitory coupling is modeled by spike-triggered alpha-function current injection. The intrinsic frequency of the cells is set by the amount of constant current (I) injected into the cells, where frequency increases with I.

When performing theoretical studies involving weak coupling for either electrical coupling or inhibition alone, the coupling strengths g_c (electrical) and g_s (inhibitory) do not affect the phase-locked states or the stability of these states. However, in the case of combined coupling, changing the relative coupling can have substantial effects. To study these effects, we represent the fraction of coupling due to electrical coupling with the parameter $\rho = g_c/(g_c + g_s)$.

It was found that, below a certain critical value of I, cells can evolve either to a synchronous state or an anti-synchronous state, whereas above this value only the synchronous state exists. For parameters set to mimic the behavior of FS cells *in vitro* (relatively fast inhibitory synapses and large spikes), the critical value of I for electrical coupling alone (I_c) is less than that for inhibition alone (I_s). The critical input current for a combination of electrical and inhibitory (I_{sc}) is always between I_s and I_c, and it increases monotonically with ρ.

Heterogeneous Cells

In the work presented here, we examine the behavior of the LIF model in the case of heterogeneous firing frequencies. The synchronous and anti-synchronous phase-locked states discussed above are 1:1 rhythms. Here, we study the effect of weak heterogeneity on the existence of these states; i.e. we ask how robust the states are to heterogeneity. For sufficiently large heterogeneity, no 1:1 phase locked state exists. In this case, activity in the system consists of either higher order phase-locking, quasi-periodic behavior or irregular behavior, but the exact behavior remains to be determined. Note that when a 1:1 phase locked state exists in the presence of heterogeneity, the synchronous and anti-synchronous states will (usually) become almost synchronous and almost anti-synchronous, but we will refer to them simply as synchronous and anti-synchronous states.

For inhibitory coupling only (see $\rho=0$ in figure 1), extremely weak heterogeneity will destroy the synchronous state at low current input. Also, for any given level of heterogeneity, there is a finite range of frequencies over which the synchronous state exists, and the size of the range decreases with increasing level of heterogeneity. This agrees with results from numerical simulations of activity in large networks of interneurons (White et al 1998; Wang and Buzsaki 1996). Sufficiently below the critical input current, the anti-synchronous state is much more robust to heterogeneity than the synchronous state.

With the addition of electrical coupling (an increase in ρ), the synchronous state is more robust, especially at low values of I (compare $\rho=0$ to $\rho=0.5$ and $\rho=1$ in figure 1). This results in an increase in the range of I over which the synchronous state exists. The range of I over which the anti-synchronous state exists decreases. In general, as the relative strength of the electrical coupling (ρ) increases, the robustness of the synchronous state increases and, when it exists, the robustness of the anti-synchronous state decreases (see dashed and solid line respectively in bottom row of figure 1). These relationships produce a potentially interesting result: Combinations of electrical and inhibitory coupling appear to promote co-existence of the synchronous and anti-synchronous state (compare size of AS/S region for $\rho=0.5$ to that of $\rho=0$ and $\rho=1$ in figure 1).

Additional work

Lewis et al [7] also perform studies on identical cell pairs using a conductance-based model for FS interneurons developed by Erisir et al [3] in order to compare the results for the LIF model to those for a biophysical model. The results obtained for the FS model were very similar to those obtained for the LIF model. We will examine the effects of heterogeneity in this conductance-based model as well. In addition, we will compare the results from the theoretical studies presented here with simulations of activity in large networks composed of LIF and conductance-based model cells that do not rely on a weak-coupling analysis.

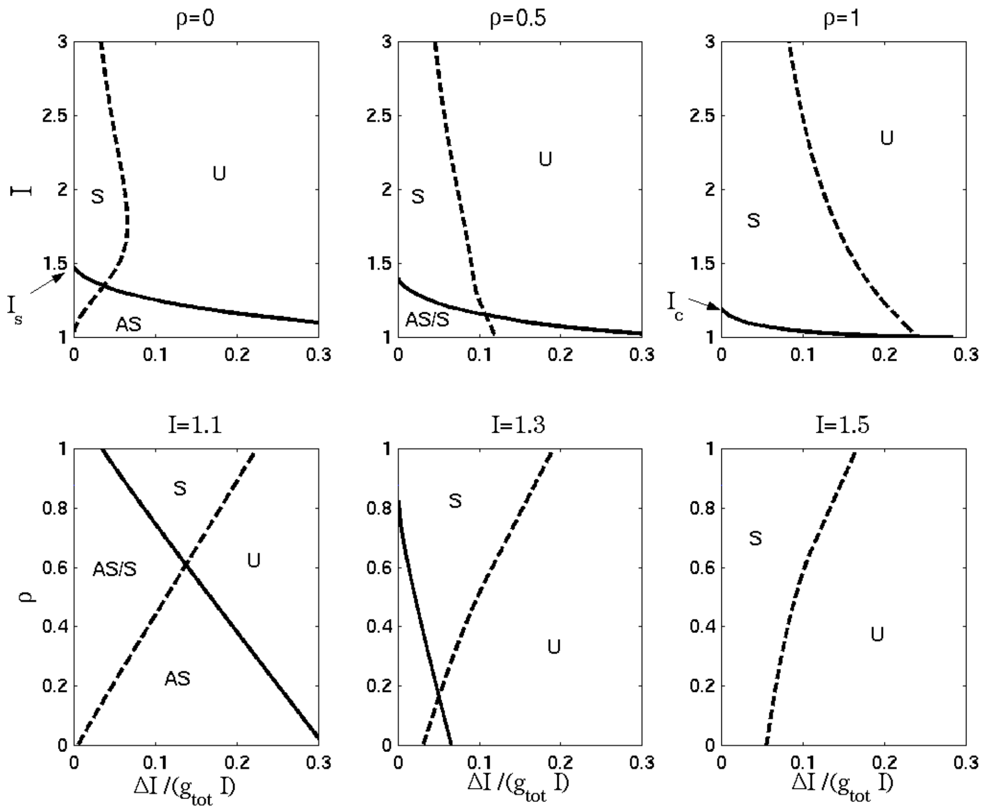

Figure 1: Two-parameter state diagrams: I (top row) and ρ (bottom row) vs $\Delta I/(g_{tot}I)$. Synchronous 1:1 phase-locked states (S) exist to the left of the dashed curves; anti-synchronous 1:1 phase-locked states exist below the solid lines. Behavior is undetermined (U) above the solid line and to the right of the dashed line.

Reference List

1. Buzsaki G. and Chrobak J.J. (1995) Temporal structure in spatially organized neuronal ensembles: a role for interneuronal networks. *Curr. Opin. Neurobiol.* 5, 504-510.

2. Chow C.C. and Kopell N. (2000) Dynamics of spiking neurons with electrical coupling. *Neural Comput.* 12, 1643-1678.

3. Erisir A., Lau D., Rudy B., and Leonard C.S. (1999) Function of specific K(+) channels in sustained high-frequency firing of fast-spiking neocortical interneurons. *J. Neurophysiol.* 82, 2476-2489.

4. Galarreta M. and Hestrin S. (2001) Electrical synapses between GABA-releasing interneurons. *Nat. Rev. Neurosci.* 2, 425-433.

5. Gibson J.R., Beierlein M., and Connors B.W. (1999) Two networks of electrically coupled inhibitory neurons in neocortex. *Nature* 402, 75-79.

6. Golomb D. and Rinzel J. (1993) Dynamics of globally coupled inhibitory neurons with heterogeneity. *Physical. Review. E.* 48, 4810-4814.

7. Lewis T.J., Gibson J.R., Connors B.W., and Rinzel J. Dynamics of spiking neurons connected by inhibitory and electrical synapses. Society for Neuroscience Abstracts 504.16. 2001.
   Ref Type: Abstract

8. Sherman A. and Rinzel J. (1992) Rhythmogenic effects of weak electrotonic coupling in neuronal models. *Proc. Natl. Acad. Sci. U. S. A* 89, 2471-2474.

9. Tamas G., Buhl E.H., Lorincz A., and Somogyi P. (2000) Proximally targeted GABAergic synapses and gap junctions synchronize cortical interneurons. *Nat. Neurosci.* 3, 366-371.

10. Van Vreeswijk C.A., Abbott L.F., and Ermentrout G.B. (1994) When inhibition not excitation synchronizes neural firing. *J. Comput. Neurosci.* 1, 313-321.

11. Wang X.J. and Buzsaki G. (1996) Gamma oscillation by synaptic inhibition in a hippocampal interneuronal network model. *J. Neurosci.* 16, 6402-6413.

12. White J.A., Chow C.C., Ritt J., Soto-Trevino C., and Kopell N. (1998) Synchronization and oscillatory dynamics in heterogeneous, mutually inhibited neurons. *J. Comput. Neurosci.* 5, 5-16.

13. Whittington M.A., Traub R.D., and Jefferys J.G. (1995) Synchronized oscillations in interneuron networks driven by metabotropic glutamate receptor activation. *Nature* 373, 612-615.