Half-day CNS2008 workshop for morning of Thursday July 24th

Title*: Neuronal Gap Junctions: Modeling approaches, insights and possible roles*

Organizers: Frances Skinner (Toronto Western Research Institute and University of Toronto, Canada), Tim J. Lewis (University of California, Davis, USA)

Description:
Gap junctions are essential coupling components of neuronal networks in young and adult animals. They provide direct, fast electrical communication between cells, allowing current to flow down the electrical gradient between cells. For this reason, it is likely that they play a synchronizing role in neural systems. However, theoretical and modeling studies have shown that attributing only a synchronizing role to gap junctions neglects the richness of network dynamics that these protein molecules can support. The talks in this workshop will explore this rich behavior, which includes wave propagation, pattern formation and non-synchronous activities, thus elucidating the many possible roles that gap junctions can play in the nervous system.

Speakers (in alphabetical order): F. Gurel-Kazanci (Emory), T.J. Lewis (UC Davis), E. Munro (Tufts), F. Nadim (NJIT/Rutgers), F.K. Skinner (TWRI/Toronto)

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Talk abstracts:

Role of gap junctions in pattern formation in a network of weakly coupled neural oscillators

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Networks of coupled neural oscillators exhibit a variety of activity patterns according to the properties of the coupling. There is clear experimental evidence for the existence of electrical and chemical synapses in neocortical inhibitory networks . The effect of each type of coupling in isolation is well studied. Depending on the nature of the neural oscillation, inhibition can be either synchronizing or desynchronizing. In numerous computational and theoretical studies, it has been shown that electrical coupling can promote either synchrony or anti-synchrony depending on the shape of the action potential and the nature of the oscillator. Recently, the combined effects of these couplings have been an area of theoretical interest, however in these studies both the inhibition and the gap junctions encouraged synchronization. In a recent paper, we studied a spatially structured network of coupled neural oscillators in which there was local synchronizing coupling (mediated by electrical or gap junction coupling) and long range “desynchronizing” coupling mediated by synaptic inhibition [2]. The motivation for this work is the appearance of traveling waves and synchronous oscillations in the olfactory lobe of the garden slug [1]. The neurons which generate these patterns are coupled with both gap junctions and synaptic inhibition. Starting with a synchronous locally coupled network, we showed that the addition of global inhibitory coupling leads to a symmetry breaking bifurcation and ultimately to traveling waves. In another paper, we considered the same system (local synchronization and long-range desynchronization) from a different perspective. Starting with a globally coupled network of oscillators, we introduced local synchronizing coupling and asked what kinds of behaviors arise [4]. Our work for the inhibition only case is motivated by [3] where they show a heteroclinic connection between unstable two-cluster states for a different set of coupling functions. We used a slightly altered version of the coupling functions from our previous study to accommodate stable clustered states. With the addition of nearest neighbor synchronizing coupling , we studied the network behavior. Local coupling (as opposed to all-to-all) requires that we specify a geometry of the network; here we consider the simplest case, a one-dimensional ring of oscillators. We showed that for sufficiently strong gap junctions, there are stable traveling waves and that as the gap junction coupling decreases, there is a loss of stability of the traveling waves. For a structured network, the ordering of the oscillators matters and there are many arrangements for a clustered state. We showed that these have different stability behavior when local synchronizing coupling is added and that many new patterns bifurcate.

[1]B. Ermentrout, J. W. Wang, J. Flores, and A. Gelperin, Model for transition from waves to synchrony in the olfactory lobe of Limax, J. Comput. Neurosci., 17 (2004), pp. 365–383.

[2]F. Gurel Kazanci and B. Ermentrout, Pattern formation in an array of oscillators with electrical and chemical coupling,
SIAM J. Appl. Math. , 67 (2007), pp.512-529
[3]D. Hansel, G. Mato, and C. Meunier, Clustering and slow switching in globally coupled phase oscillators,
Phys. Rev. E, 48 (1993), pp. 3470–3477.
[4]F. Gurel Kazanci and B. Ermentrout, Wave formation through the interaction between clustered states and local coupling in array of neural oscillators, SIAM J. Applied Dynamical Systems, 7 (2008), pp. 491-509.

The effects of rectifying gap junctions on phase-locking in neuronal networks

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with Donald French (2), Tamara J Schlichter (1),
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Gap junction mediated electrical coupling is ubiquitous in neuronal systems. Electrical coupling is almost always modeled as a linear ohmic resistance between cells, where the coupling current is proportional to the transjunctional potential. However, many gap junctions exhibit rectification with trans-junctional voltage (Bukauskas & Verselis, 2004). The rectification process can evolve at different time scales. Because gap junctional rectification alters the strength of coupling between cells in a way that depends on the intrinsic states of the cells, it can affect network dynamics in a significant and complicated manner. However, the effects of rectification are largely unstudied. In this talk, I will discuss our recent efforts to understand the effects of gap junction rectification on phase-locking in model neuronal networks.

The axonal plexus: A description of the behavior of a network of axons connected by gap junctions

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Gap junctions have been indicated in very fast oscillations (VFOs, >80 Hz) in the neocortex and hippocampus. Gap junctions among pyramidal axons have been identified in the hippocampus (Hamzei-Sichani et al. 2007), and are clearly indicated in VFOs within gamma oscillations in the hippocampus (Traub et al. 2003). Previous modeling studies have shown that an axonal plexus (network of axons connected by gap junctions) can produce a VFO (Traub et al. 1999), and that this VFO can be caused by expanding waves forming topological target patterns (Lewis and Rinzel 2000, Lewis and Rinzel 2001).

Using the axon of the model in Traub et al. 1999, we find that the axonal plexus can exhibit three different behaviors depending on the somatic voltage (V_S) and gap junction conductance (g_{gj}): (1) noisy non-oscillatory activity, (2) stimulus-driven VFOs as described in Lewis and Rinzel 2000, or (3) re-entrant VFOs where activity forms a spiral wave within the network. While stimulus-driven VFOs stop when external stimulation stops, re-entrant VFOs persist without external stimulation. Moreover, re-entrant VFOs occur for a wide range of V_S and g_{gj} in between the regions where we see noise and stimulus-driven VFOs. The behavior of the network is determined by the behavior of axons with the maximum number of connections (4-connected axons). These axons are key because (1) it is harder for them to fire when a neighbor fires relative to axons with fewer connections and (2) 4-connected axons are prevalent in the network. We see noise if 4-connected axons rarely fire, stimulus-driven VFOs if 4-connected axons always fire, and re-entrant VFOs if 4-connected axons fire most of the time but occasionally fail to propagate a spike. We discuss applications of this analysis for VFOs in gamma oscillations, slow-wave sleep, and seizure initiation.

The role of anatomical structure in determining activity in electrically-coupled neuronal networks

Farzan Nadim *NJIT/Rutgers*

Gap junctions are involved in transfer of ions and small molecules between cells in many tissues. Electrical signaling via gap junctions (electrical coupling) has been implicated in the generation of synchronous electrical activity. We show that signal transfer between electrically coupled neurons is maximized at an optimal diameter of the coupled processes. We then explore the ramifications of this optimal diameter for signaling in a network of electrically coupled model neurons.

Different roles for gap junctions in the dendrites of different inhibitory cell types?

Frances K. Skinner *Toronto Western Research Institute, University Health Network and University of Toronto*

There are several known subtypes of interneurons in hippocampus (McBain and Fisahn 2001). This diversity of interneurons likely has functional relevance as different interneuron subtypes fire at particular phases of *in vivo* theta and gamma rhythms, for example, suggesting distinct and specific contributions to behavioural patterning. Interestingly, gap junctions are known to be present on the dendrites of at least three different types of interneurons (Baude et al. 2007; Fukuda and Kosaka 2000). I will describe our use of phase response curves and weakly coupled oscillator theory to help understand the contribution of non-proximally located dendritic gap junctions in inhibitory networks with different intrinsic properties. In this way, different potential roles can be suggested.