Stochastic dynamics of small networks of neurons

organized by
Victoria Booth, Priscilla Greenwood, and Rachel Kuske

Workshop Summary

The idea for this workshop was that single stochastic neuron models, about which we have new, interesting information, should be put together into models of a small number of interacting neurons, and questions asked about the relation of input to output for these simple assemblies. There has been much effort to simulate the behavior of large networks of neurons, but without much attention to the question of how their behavior depends of the single neuron model used. Each single neuron component has usually been modeled as a rather simple agent. This workshop was intended to focus the attention of a variety of experts and new researchers on this gap between single neuron modeling and the construction of large networks. In fact, the question came out of a workshop at SAMSI in the spring of 2010 where 4 of our AIM participants were present.

Before the workshop, in addition to gathering files of participants' papers, AIM circulated a compilation of participant contributions containing their background, relevant research interests and proposed workshop research questions. Looking back, now, over this lead-in material, one can see how the workshop has amalgomated these various viewpoints and enthusiasms, and how specific new research directions have emerged.

After introductory talks Monday morning, we used the afternoon to list questions. Many questions came in on stick-it notes, several individuals requesting definitions of terms, questions arising in the morning's talks, topics suggested by the speakers (Laura Sacerdote, Lawrence Ward). All these were formulated and typed up by co-organizer Victoria Booth, copies made by AIM, and circulated Tuesday morning, when we had additional background talks (by Farzan Nadim and Brent Doiron) and additional topics suggested. During Tuesday lunch break the organizers recast the long topics list into four topics, combining several associated ones. The participants quickly formed working groups around three of these topics:

(1) Deterministic and stochastic features in small networks: what is the role of fixed point and bifurcation structure?
(2) Synchronization mechanisms in small networks and noise effects on synchroinization.
(3) What behavior of single units survives in small networks?

Each group would choose a particular example to focus on and would refine the topic further.

At the end of Tuesday afternoon, after a few shifts, the group membership became:

Group 1: Andrea Barreiro, Katarina Bodova, Victoria Booth, Badal Joshi, Jung Eun Kim, Erin Munro, Jasmin Nirody.

Group 2: Antonio Di Crescenzo, Luis Gordillo, Jaine Mancilla, Sashi Marella, Hermann Riecke, Lawrence Ward.

Group 3: Brent Doiron, Priscilla Greenwood, Xiangying Meng, Farzan Nadim, Duane Nykamp, Jonathan Rubin, Laura Sacerdote.

Each group spent the remainder of the workshop working with great devotion and enthusiasm, all break times, lunch and happy hour being increasingly delayed. Additional relevant talks were given Wednesday morning by Duane Nykamp and Jonathan Rubin. Starting Wed afternoon we were joined by John Rinzel, a wonderful source of wisdom on neuron modeling. On Friday there were summary talks from the three groups. There follows a synopsis of progress from each of the three groups.

Group 1 chose to investigate the influences and interactions of deterministic and stochastic features in the smallest neuronal network we could think of, a single neuron receiving variable inhibitory synaptic input from a single, periodically firing pre-synaptic neuron. We consentrated on quantifying phase-locked firing dynamics. In the deterministic case, this simple network can display a variety of firing patterns as the periods of the pre- and post-synaptic cells are varied. If the periods of each cell are relatively close, phase-locked firing in a 1-1 anti-phase pattern is obtained. By increasing the period of the pre-synaptic cell, dynamics transition between intervals where phase-locking is lost and intervals of m:1 phase-locked firing in which the post synapticcell fires m spikes for every 1 spike of the pre-synaptic cel. One way to visualize these changes in firing dynamics is the Devil's Staircase, a plot of the rotation or winding number of the post-synaptic cell relative to the pre-synaptic cell as a function of the period of the pre-synaptic cell (which can be normalized by the period of the post-snyaptic cell). We decided to incorporate variability into the network by setting the amplitude of each synaptic input to a random value drawn from a binomial distribution, B(n,p), where n can be varied to represent the number of post-synaptic receptors available at the synapse and p represents the probability of receptor activation. We are numerically investigating the effect of this variability on phase-locked firing and the Devil's Staircase in three different neuronal models: the theta neuron model, the leaky integrate-and-fire (LIF) model, and the Morris-Lecar model.

An anylytical method used to investigate phase-locked firing in small deterministic neuronal networks is to utilize the phase response curve to create a map for successive firing times. Phase-locked firing corresponds to a fixed point of the map. For the LIF and theta neuron models, the phase response curve can be explicitly quantified and thus the map can be analytically solved to determine the phase-locking regions. We have constructed nd solved these maps for the deterministic network, and work is continuing to analyze the effects of variable synaptic input.

Group 2 's topic was the influence of noise on small neural network generation of oscillations and synchronization. We decided to focus on some data one of our members had collected from slice preparations. He recorded the spikes and post-synaptic inhibitory potentials (IPSPs) from two inhibitory interneurons that were connected by chemical synapses, showing that for low driving frequencies they fired in anti-phase whereas for high driving frequencies they fired synchronously. We decided to model this system, determine the influence of the in-phase and anti-phase firing on downstream excitatory neurons (including possibly oscillatory behaviour induced by feedback loops), and examine the influence of noise on the functioning of this system. We decided that we would construct a realistic model of synaptic noise as a part of this exercise. After examining several extant models of synaptic noise we adopted a synthesis of them for simulation and also proceeded to solve one of them, a system of three differential equations, analytically. During the workshop, we simulated, using implementations of Izhikevich model neurons, the inhibitory interactions giving rise to the in-phase and anti-phase behaviour of the interneurons, and determined the influence of synaptic noise on this process. We also obtained preliminary analytic solutions of the deterministic form of the synaptic transmission model. Since the end of the workshop we have continued to work on both analytic and numerical approaches. Additional simulations have confirmed our initial results, and additional analytic work has suggested a new approach to modeling the noisy synaptic activity. A Gillespie-type (exact) stochastic simulation of one non-spiking cycle in the new approach has confirmed the analytic results. Our group is continuing to work on these problems and to interact. We are setting up a Skype meeting to decide how to proceed from here, probably to a paper. We have talked about applying for a Squares grant to continue the work.

Group 3, under the topic What single neuron properties survive in a network?, chose the focus: effect of adaptation on variability as neasured by the Fano factor. The topic is related to Brent Dorion's talk of Tuesday morning. A prediction was that, whereas adaptation will decrease variability in a single neuron, it will increase variability in a two-cell mutually inhibitory coupled network. The Italian motto L'Union fa la forze, (union makes strength) was adopted. Part of the group did prelinary work by simulations using leaky integrate and fire (IF) models, and others of us used simulations of Morris Lecar (ML) models. We calibrated parameters so that the output of the two models for single units with adaptation looked roughly similar. Very preliminary results are that both for IF and ML uncoupled and coupled models, fast adaptation decreases the Fano factor. However we defined a more gradually applied version of adaptation, which we called slow adaptation and found that for the uncoupled ML neuron,adaptation INCREASES the Fano factor, whereas for the coupled ML neurons, adptation DECREASES the Fano factor. Group 3 is continuing to work together to verify and further explore these effects, to quantify them and to understand the effects in terms of analysis of the stochastic dynamics involved.