Mathematical Neuroscience

Organizer: Mary Pugh, University of Toronto

Dynamics in responses to auditory motion

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We are interested in the cellular mechanisms shaping the neuronal responses to auditory motion stimuli. In this framework, we study how the presence of biologically realistic features influences the performance of a periodically driven system. We show that the presence of the cellular mechanisms of firing rate adaptation and the post-inhibitory rebound is sufficient to account for experimentally observed phenomena, such as rebound responses, hysteresis and phase shift in response to periodic forcing. We quantify various physiologically relevant features of the response and make testable predictions. We also compare the performance of spiking and firing-rate-type models in the context of the auditory motion processing.

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Biophysical mechanisms for frequency encoding in a model sensory system

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It is well known that the passive membrane properties of neurons function as a low-pass filter for synaptic inputs. Current inputs arriving at low frequencies yield large voltage responses, but high frequency inputs are attenuated or blocked. Neurons can also exhibit bandpass filtering properties with large responses when driven by inputs near their resonant frequencies and smaller responses at other frequencies. This mechanism occurs due to the interactions between active and passive membrane properties. For example, currents that actively oppose changes in membrane voltage and also activate slowly relative to the membrane time constant will produce resonance. We examine the effects of morphology, passive membrane properties, and active channels on frequency tuning in a model sensory system. Theoretical studies and simulations show that the low-pass filtering observed in some neurons can be explained by the passive electrotonic structure of the dendritic arbor and the dynamic sensitivity of the spike initiation zone. In contrast, neurons that exhibit bandpass tuning at higher frequencies have dendritic structures with fewer branching structures and larger diameters that are more electrotonically compact. This morphology causes less attenuation of higher frequencies; however, ion channels that resonate in the desired frequency range are also required.

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Chaotic phase synchronization in systems with small phase diffusion

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The geometric theory of phase locking between periodic oscillators as proposed by Winfree and Kuramoto has been used with much success in the past. I will discuss extensions of this theory to phase coherent chaotic systems. This approach explains the qualitative features of phase locked chaotic systems and provides an analytical tool for a quantitative description of the phase locked states. Moreover, this geometric viewpoint allows for the identification of obstructions to phase locking even in systems with negligible phase diffusion, and provides sufficient conditions for phase locking to occur. These techniques were applied to the Rössler system and a phase coherent electronic circuit and good agreement was found between numerical results, experiments and theoretical predictions.

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Temporal synchronization of pyramidal cells by high-frequency, depressing inhibition

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The sharp wave-associated ripple is a high-frequency, extracellular recording observed in the rat hippocampus during periods of immobility. During the ripple, pyramidal cells synchronize over a short period of time despite the fact that these cells have sparse recurrent connections. The timing of synchronized pyramidal cell spiking is critical for encoding information that is passed onto post-hippocampal targets. Both the synchronization and precision of pyramidal cells is believed to be coordinated by inhibition provided by a vast array of interneurons. We consider a minimal model consisting of a single interneuron which synapses onto a network of uncoupled pyramidal cells. We show that fast decaying, high-frequency, depressing inhibition is capable of rapidly synchronizing the pyramidal cells and modulating spike timing. These mechanisms are robust in the presence of intracellular noise. We prove the existence and stability of synchronous, periodic solutions using geometric singular perturbation techniques. The effects of synaptic strength, synaptic recovery, and inhibition frequency are discussed. In contrast to prior work which suggests that the ripple is produced by homogeneous populations of either pyramidal cells or interneurons, our results suggest that cooperation between interneurons and pyramidal cells is necessary for ripple genesis.

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Stabilization of “bumps”by noise

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Spatially localized regions of active neurons (“bumps”) have been proposed as a mechanism for working memory, the head direction system, and feature selectivity in the visual system. Stationary bumps are ordinarily stable, but including spike frequency adaptation in the neural dynamics causes a stationary bump to become unstable to a moving bump through a supercritical pitchfork bifurcation in bump speed. Adding spatiotemporal noise to the network supporting the bump can cause the average speed of the bump to decrease to almost zero, reversing the effect of the adaptation and “restabilizing” the bump. This restabilizing can be understood by examining the effects of noise on the normal form of the pitchfork bifurcation where the variable involved in the bifurcation is bump speed. This noise–induced stabilization is a novel example in which moderate amounts of noise have a beneficial effect on a system, specifically, stabilizing a spatiotemporal pattern. Determining which aspects of our model system (integral rather than diffusive coupling, a slow variable, travelling structures that appear through a pitchfork bifurcation in speed) are necessary for this type of behavior remains an open problem.

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Dynamics of neurons connected by inhibitory and electrical coupling

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Recent findings suggest that many inhibitory cell networks in the brain are connected through both inhibitory and electrical coupling. However, it is unclear how the interaction of these two coupling modes affects the dynamics of these networks. To begin addressing this issue, we use the theory of weakly coupled oscillators to study the influence of coupling parameters on synchronization patterns in a model of intrinsically oscillating cells connected by both inhibition and electrical coupling.

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Characterizing coupled neurons with white noise analysis

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We present an asymptotic analysis of two coupled linear-nonlinear neurons. By measuring the spike times of both neurons in response to a white noise stimulus, one can characterize the neurons’ properties and their mutual connections. The linear-nonlinear model used in the analysis is similar to a widely used phenomenological model of a neuron in response to sensory stimulation. Moreover, we demonstrate that the results of the analysis also work with more realistic neuron models. Thus, this analysis may help characterize neural circuitry in sensory brain regions.

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Phase plane analysis of neural decoding in the Rodent Whisker-Barrel System

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In the rodent whisker-to-barrel pathway, populations of thalamic neurons encode information from the periphery in terms of changes in the population firing rate. Correspondingly, cortical neurons respond preferentially to rapid changes in the rate of firing among input neurons from the thalamus. Previous computational models based on known features of cortical circuitry have captured this and other aspects of the thalamocorical response transformation in the rodent whisker system. In this presentation, I will examine these models using a modified version of phase plane analysis in order to understand the mechanisms that underlie cortical sensitivity to thalamic input timing. The analysis reveals that cortical processing in our model depends on strong inhibition that renders the net effect of cortical connections to be *damping.* This distinguishes it from previous models of cortical microcircuits, in which the net effect of cortical connections is *amplifying.* I will conclude with a brief comparison of the two proposed mechanisms of cortical processing and suggest a possible experimental means for distinguishing between them.

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Lateral inhibition is neither necessary nor sufficient for sustained, patterned activity

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Evidence suggests that sustained, localized neuronal activity, or bumps, may play a role in working memory or representation of internal states, such as head direction. Previous (and ongoing) theoretical work has demonstrated that a synaptic architecture featuring recurrent excitation and long-range inhibition, together known as lateral inhibition, can lead to activity bumps in neuronal network models. However, this architecture is absent in some areas of the brain where such activity may be relevant.Here we show how a rate-based integrodifferential equation model can support bump solutions without recurrent excitation. We also provide conditions under which no spatial patterns exist despite the presence of lateral inhibition.

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Modulating model inhibitory neuronal networks

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Synchronous oscillatory activity in networks of interneurons connected by inhibitory synapses play critical roles in brain function. Differences in the kinetics of the inhibitory response observed with anesthetics can affect this activity. We use theoretical insights to suggest a new mechanism of anesthesia. In particular, we suggest that the different behavioral effects of different anesthetic drugs might lie in the different ways in which these drugs modulate inhibitory network coherence.

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Dynamics of the visual cortex

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We present multivariate harmonic analysis methods for the analysis of dynamical optical imaging data; discuss the various components of the dynamical signal resulting from the harmonic analysis; and present an overall strategy for constructing a population model of visual cortex, with results from one functional component of the model.

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A neuronal network model of the macaque primary visual cortex

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Michael Shelly and **David McLaughlin**

Our objective is a realistic theory of the visual cortex that can explain the visual selectivity, dynamics, and the diversity of visual properties in cortical cell populations. To do this, we have studied a large-scale computational model of Macaque V1 [McLaughlin et al. 2000 PNAS] based on anatomy and physiology. Cells in the model are classified as Simple or Complex by the same index of linearity of spatial summation that has been used in physiology experiments. Previously we offered an explanation of how Simple cells could exist in the model despite the nonlinearity of the LGN input and of cortico-cortical excitation [Wielaard et al 2001 J. NS.] Now we report that Complex cells arise in the model by allowing for randomness in synaptic coupling strengths, which can increase the importance of network excitation, and randomness in the strength of LGN input. My

work suggests that the Simple-Complex classification reflect different synaptic balances within the same basic model circuit. Since the dichotomy of 'Simple' and 'Complex' behavior is seen in other areas of visual processing, the basic mechanism may be widely operating.

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Dynamical patterns in the basal ganglia and related neuronal networks

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A conductance-based network model was developed (in collaboration with J. Rubin, D. Terman, and C. Wilson) to describe neural interactions in the basal ganglia, with the aim of testing hypotheses on the origin of activity states associated with disorders such as Parkinson's disease. Computer simulations reveal that the system exhibits a variety of spatiotemporal patterns, including episodic synchronous oscillations, clustered rhythms, travelling waves, and irregular uncorrelated spiking. Using a dynamical systems approach, we analyze how synaptic coupling interacts with intrinsic neuronal properties to generate these types of behavior. We also investigate how transitions between patterns are effected as parameters are varied, and make comparisons with other similarly wired neuronal networks.

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