CAREER: Analysis and Simulation of Visual Cortex Network Dynamics

Project Summary

The primary visual cortex (V1) is the first region along the mammalian visual pathway where individual neurons have selective responses to elementary features of the visual scene (for instance, a pattern's orientation). It is properties similar to "orientation selectivity" that likely underlie important higher-level processing such as "contour completion" and "edge detection." This proposal describes research in the analysis and numerical simulation of large-scale neuronal networks to study the dynamics that underlie cortical response to visual stimuli and to understand the functional mechanisms behind visual processing. Mathematical analysis of network dynamics will be carried out using kinetic theory, stability and bifurcation analysis, and numerical simulations. The PI will develop large-scale neuronal network models of the visual cortex, spanning large cortical areas containing neurons that see both distinct and distant regions of the visual field. While these problems are motivated primarily by the response dynamics observed in V1 neurons, they are very similar to the dynamics of many other neuronal networks from the mathematical point of view.

Intellectual Merit: How visual processing occurs is one of the most challenging questions in neuroscience. V1 plays a central role in modern brain research because of its role a model system for cortical functions in other areas of the brain. The large-scale mathematical modeling proposed here is designed to study some of the cortical mechanisms in a systematic manner. Through analysis and simulations, the PI intends to identify general principles underlying neuronal network functions and propose experimentally testable hypotheses about their dynamical structures.

Broader Impact: This work is highly interdisciplinary, involving mathematical modeling, analysis and numerical simulation, and experimental and theoretical neuroscience. Research will be performed in close collaboration with experimentalists, and is therefore well positioned to enhance both applied mathematics and neuroscience. This is an area where numerical simulations and mathematical analysis, coupled to experimental observations, can have a major impact on an important area of the life sciences. Furthermore, the knowledge gained will be used in training graduate students. The PI will design and teach computational neuroscience and mathematical biology courses at NJIT. The PI will provide research opportunities for both graduate and undergraduate students to work on mathematical modeling and computational neuroscience. In this way, students will become competitive for positions in departments and centers for neuroscience, in addition to mathematics departments.

1 Results from Prior NSF Support

Results from prior NSF Support are outlined below. My research in orientation selectivity in mammalian primary visual cortex is supported by a currently active grant **DMS-0506396**. This work studies how intrinsic dynamic fluctuations in neuronal synaptic currents modify the effects of strong recurrent excitation, within a large-scale neuronal network model of macaque primary visual cortex. This builds upon earlier work [119, 179, 196] that shows a cortical model with strong network inhibition balanced with feedforward and recurrent excitation can reproduce many observed properties of simple and complex cells in V1. In [177], we show that a sparse network produces large, instrinsic fluctuations in the cortico-cortical conductances which can stabilize the network against runaway self-excitation. Furthermore, there is a critical level of fluctuations which allows strong cortical gain and the emergence of orientation selectivity within the model cortex. The resultant sparse network shows near contrast invariance in its selectivity, and, in agreement with recent experiments, has extracellular tuning properties that are similar in pinwheel center and iso-orientation regions, while intracellular conductances show positional dependencies [118, 163]. By varying the strength of synaptic fluctuations by adjusting the sparsity of network connectivity, we identify a transition between dynamics of bistability and no bistability.

The other area supported by **DMS-0506396** is the derivations of kinetic theory and population density methods. In [33], we presented a detailed theoretical framework for statistical descriptions of neuronal networks. We derived $(1 + 1)$-dimensional kinetic equations directly from conductance-based integrate-and-fire neuronal networks. We established accuracy of our kinetic theory by comparing its prediction with the full dynamical simulations of the original point-neuron networks. These kinetic equations are a system of nonlinear partial differential equations (PDE) on a bounded domain, with nonlinear boundary conditions that are themselves a functional of the present solution, and can be stiff in space and time. In [144], we presented numerical methods for efficiently and accurately solving these kinetic equations. First the system is discretized in time with an implicit Euler method within a spectral deferred correction framework. Therefore, the PDEs of the kinetic theory are reduced to a sequence, in time, of boundary value problems (BVPs) with nonlinear boundary conditions. Then, a set of auxiliary parameters is introduced to recast the original BVP with nonlinear boundary conditions as BVPs with linear boundary conditions. Finally, each BVP is solved using Newton's iteration and a fast spectral method [56].

Many of the computations in the work described above were performed on the NJIT Hydra, a Beowulf cluster obtained under NSF **MRI-0420590**.

2 Project Description

2.1 Introduction

My general research interest is to apply the methods of applied mathematics and scientific computation to the modeling, simulation and analysis of network dynamics in neuroscience. During the next few years, I plan to develop further the asymptotics and reduction techniques, that have been successful in my previous and on-going work in computational neuroscience. These techniques will be applied to large-scale visual cortex network dynamics and its role in elementary visual processing. In particular, I will use large-scale dynamical simulations and dimension reduction techniques in two related problems in visual neuroscience. The first is the emergence of the so-called γ-band oscillations $(25 - 90$ Hz) in mammalian primary visual cortex (area V1). Network oscillations and near synchronous neuronal populations are believed to play a fundamental role in sensory processing. A distinguishing feature of V1 oscillations is the recent observation that

γ-rhythms emerge when the visual stimulus is larger than a critical size, suggesting thet network connectivities and network dynamics play a critical role in the generation of these γ-oscillations. A quantitative framework to model these neuronal interactions can contribute greatly to the interpretation of neurophysiological data and show how to infer network architecture from the observation of its dynamics. The second related research area is the mathematical framework within which to study visual signal integration. Individual neurons "see" only a fraction of a degree of visual space. Therefore, visual information need to be incorporated from widely separated regions of the visual scene to create a global, unified visual percept. Dimension reduction and coarse-graining techniques applied towards establishing a modular mathematical framework consistent with experimental and simulational data will contribute immensely to our understanding of visual processing.

The mammalian primary visual cortex is of particular interest to systems neuroscientists owing to its fundamental role in visual processing and the belief that understanding cortical function in V1 will advance our understanding of cortical processing in other areas of the mammalian brain. V1 is the first area along the visual pathway where individual neurons are sensitive to elementary features of the visual scene (for instance, a pattern's orientation or its spatial location). Individual V1 neurons show *preference* to certain orientations of a visual pattern in terms of higher firing rates. V1 has a complex architecture that is several cm^2 in lateral area and $1-2$ mm thick, and is characterized by a layered structure with intralayer connections that are locally isotropic while specific feedforward and feedback pathways run between layers and to higher visual areas (e.g., V2, V3, MT, etc.). The layers are anatomically distinct and contain both excitatory and inhibitory neurons. Visual stimuli are processed by the retina and the lateral geniculate nucleus (LGN, in the thalamus) before evoking excitatory inputs in V1, primarily in the input layers 4Cα (part of the "magno pathway" carrying information for motion analysis) and 4Cβ (part of the "parvo pathway" carrying information for shape and color analysis).

Elementary feature selectivity is revealed through electrophysiological measurements of activity of individual neurons. For example, when an anesthetized animal is shown a simple visual pattern, such as a bar or a grating, the pattern's orientation (or location, contrast, size, etc.) is measured through neuronal activity. Steady-state orientation tuning curves can be constructed this way by finding the stimulus orientation, spatial frequency, and size that elicit the maximal response and then plotting the time-averaged firing rate of the neuron versus the orientation angle of the stimulus (with all other stimulus parameters fixed). Analogous tuning curves can be constructed for spatial and temporal frequency, stimulus size, and so on.

Optical imaging experiments show that orientation preference is distributed across the cortex in a regular way: Pinwheel-like *hypercolumns* tile the cortical surface [13–15, 61, 113, 189] (see Fig. 1). Neurons preferring similar orientation lie along the same spoke of a pinwheel with the preferred angle varying continuously around an apparent orientation singularity, located near the centers of ocular dominance columns and separated from each other by approximately 500μm.

Simple models of the responses of individual neurons are developed using the concept of the "receptive field." The receptive field is systematically measured by using simple visual stimuli (such as spots, bars, and gratings) and determining the part of the visual field that evokes spiking. However, different stimuli and methods yield different answers. For example, receptive fields measured using spots is usually smaller than measured with gratings or bars (see, e.g., [38, 123]). Furthermore, using grating patterns often reveals suppressed firing rates as the stimulus is expanded beyond a certain size (see, e.g., [154]). This is usually interpreted as an inhibitory "surround" that is activated as the stimulus becomes sufficiently large. Thus, at the single neuron level, responses to larger stimuli reflect the nonlinear interaction between excitation and inhibition that necessarily have different spatial structures.

While the "classical receptive field" is thought to represent local visual processing, experimental

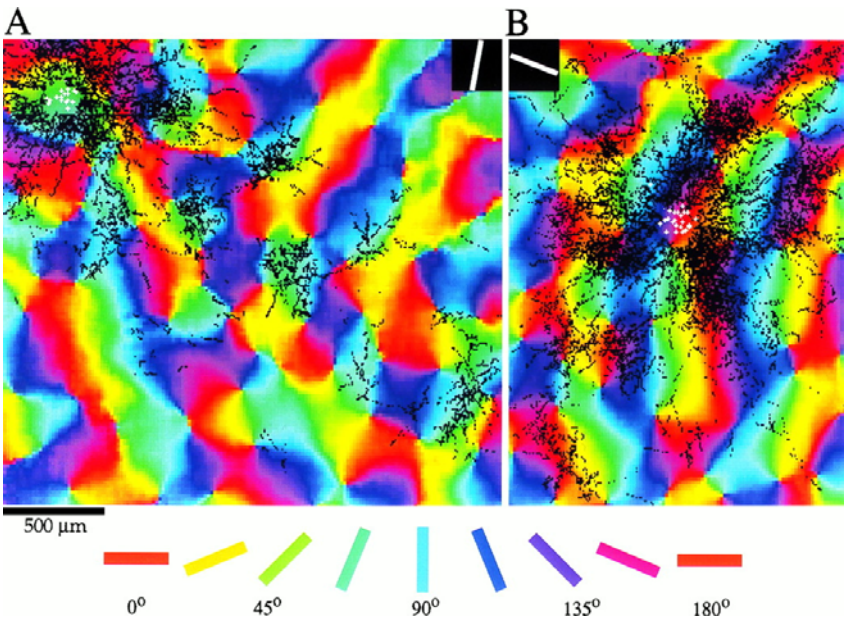

Figure 1: Optical imaging of orientation hypercolumns and long range connections: Fig. 4 of [21] showing the map of orientation preference in color and the distribution of connections in black. The orientation preference is color-coded to the oriented color bars below (e.g., the areas colored orange prefer gratings oriented at 0°). The white symbols indicate the sites of biocytin injection. Local to the injection site, the distribution of connectivities is nearly isotropic. However, at distances larger than a hypercolumn, the connections are between neurons that have similar orientation preferences.

evidence suggests that neurons in V1 receive signal from regions much larger than the classical receptive field (see, e.g., [2, 12, 38, 39, 50, 72, 87, 100, 126, 192]). Anatomical studies show that the local, sub-hypercolumn scale, synaptic connections are dense and isotropic [35, 36, 63, 107], while the longer range ($> 500\mu$m) connections tend to couple neurons that prefer similar orientations [20, 21, 71, 95, 112, 147]. (See Fig. 1.) It is this anatomical substrate that likely underlies global signal integration. The goal of the research outlined in this proposal is to unveil how this long-distance integration occurs. I propose to use a recurrent network of integrate-and-fire (I&F) point neurons to study the visual integration.

2.2 Detailed large-scale cortical model

In recent work [119, 177, 179, 196], my collaborators and I have developed a computational model of a small, local patch of layer $4C\alpha$, which is the primary input layer in macaque V1. Here, I describe the biological detail it incorporates, and to set the stage for its idealizations and multi-hypercolumn extensions, which I will use in the proposed research.

The cortical model contains four orientation hypercolumns with pinwheel centers within a 1 mm^2 patch of V1 4Cα. For simplicity, the boundary conditions are taken to be periodic. Individual neurons are modeled as conductance-based, linear I&F point neurons [99] (i.e., all spatial effects within a cell are neglected). Between "spike times," the intra-cellular potentials v^j are described by the linear differential equation:

$$\frac{dv_P^j}{dt} = -g_L \left(v_P^j - V_R\right) - g_{PE}^j(t) \left(v_P^j - V_E\right) - g_{PI}^j(t) \left(v_P^j - V_I\right), \quad P = E, I. \tag{1}$$

The m^{th} spike time, t_m^j, of the j^{th} model neuron, is determined by $v_P^j(t_m^{j-}) = V_T$; $v_P^j(t_m^j + \tau_{ref}) = V_R$ where τ_{ref} is an absolute refractory period. Here the membrane potentials of the excitatory (E) (inhibitory (I)) neurons are denoted by v_E^j (v_I^j) where the superscript j indexes the spatial location of the neuron within the network. g_L, g_{PE}, and g_{PI} are the leak, excitatory, and inhibitory conductances, respectively. The various synaptic potentials are ordered, $V_I < V_L < V_T < V_E$, and therefore, the term $-g_E^j(t)\left[v^j - V_E\right]$ drives the voltage up and is "excitatory," while $-g_I^j(t)\left[v^j - V_I\right]$ drives the voltage down and is "inhibitory." We take $\tau_{ref} = 3$ ms (1 ms) for excitatory (inhibitory) neurons.

The **time-dependent** postsynaptic conductances arise due to visual stimulation and from the cortical network activity of the excitatory and inhibitory populations. The distinguishing features of the local model that are based on biological data are that the local lateral connectivities are *nonspecific* and *isotropic*, and that lateral monosynaptic inhibition acts on shorter length-scales than excitation. Both excitation and inhibition have local length-scales that are shorter than the length-scale of a single orientation hypercolumn [35, 36, 63, 107].

Results from this model show that orientation selectivity of cells in such a model of $4C\alpha$ is greatly enhanced by lateral cortico-cortical interactions [119, 177]. The model cortex acts like the biological cortex and produces very large conductances resulting from network activity that is dominated by inhibition [162, 196] (as observed in experimental measurements [16, 17, 54, 136, 149–152, 161]). Furthermore, this class of models operates mostly in a "fluctuation-driven" regime. This means that the time-average of the membrane potential is below the firing threshold, even under high contrast stimulation. Only membrane potential fluctuations that reach threshold cause spiking (see, e.g., [34]). This is consistent with several experimental studies, both *in-vivo* [3, 190, 191] and *in-vitro* [111, 130, 165, 176]. I believe that this model can serve as the basis for analysis and extended modeling, which I now describe.

2.3 Long-Range Connectivities and Network Oscillations

2.3.1 Experimental Background

Experiments of [6, 20, 21] show intriguing patterns of cortico-cortical connections on the scale of several orientation hypercolumns. Anatomically, the lateral connections are patchy and anisotropic. Physiologically, the long-range lateral connections appear to be specific for orientation preference [20, 21, 95, 147]: Connections tend to occur between neurons that prefer similar orientations (see Fig. 1). These anatomical connections were not accounted for in the local versions of the I&F model; however, they will have important consequences for the modeling.

The main motivation for this part of my studies comes from recent and ongoing experimental work by Henrie and Shapley [83, 84] and Henrie and Ringach on ensemble activity of neurons in V1. The emergence of γ-band oscillations in this activity and the parametric dependence of these oscillations was studied via the simultaneous measurement of the local field potentials (LFPs) and the spiking of individual neurons. To determine the LFPs, the extracellular potential was measured, and the signal was denoised and filtered, so that only frequencies of ≤ 300 Hz remained. (This is the part of the signal known as the LFP.) In [83, 84], the dependence of the LFPs and the extracellular spiking rates of single neurons on contrast, orientation, and size of the presented drifting grating stimuli were investigated.

The physical source of the LFPs is the dendro-somatic currents of nearby neurons [10, 52, 65, 86, 106, 120, 128, 129, 131, 143]. Due to the nonlinear conductive properties of brain tissue and the decay of voltage with distance from its origin as well as frequency [10], the LFP observed at a single electrode location is a weighted sum of signals from a nearby population of neurons within a radius

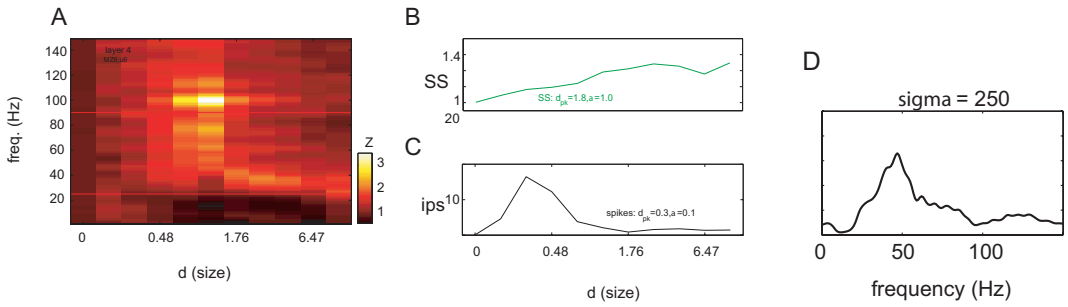

Figure 2: *Left*: Properties of the measured LFP spectrum [84] as a function of the receptive field 40 Hz as the receptive field increases in size. *Right*: Computed model spectra from [84]: B is the LFP power, C is the spike power, D is a sample LFP fluctuation spectrum from our simulations, showing a peak at 50 Hz.

of 0.5–3 mm [90, 106, 121], containing hundreds of neurons [85]. Therefore, the LFP fluctuations can be thought of as the average of the intracellular voltage fluctuations over this population, which was confirmed by the high correlation between the simultaneous recordings of LFPs and intracellular voltages of individual neurons [45, 91, 96, 137, 173–175]. In turn, intracellular voltage fluctuations in single neurons give an estimate of the summed local network activity [53, 150]. This is due to the large number of active synapses on V1 neurons [11, 53, 136, 161] and a "high" conductance state [16, 17, 54, 136, 149–152, 161, 162]. Therefore, the LFP fluctuations provide an indirect but easily measurable estimate of summed network activity [138]. Studies that have used LFPs as the measurement of neural activity in various parts of the brain include [22, 49, 124, 125, 138, 153].

The orientation tuning of LFPs, in particular of γ-band oscillations, was investigated in [66, 74, 75, 93, 94, 164, 168, 190, 191]. These papers show that the LFP activity is tuned to the same stimulus orientation as the local neuronal spiking rates; however, the LFP is more broadly tuned than the spiking rates. At the same time, the γ-oscillations in the voltage fluctuations increase neuronal firing rates, while the time average of the membrane potential in any given neuron remains constant [190, 191]. Both *in-vivo* studies [3] and *in-vitro* studies [111, 130, 165, 176] suggest that cortical firing rates are controlled mostly by the membrane potential fluctuations rather than its mean. Taken together, these experimental results give credence to our claim that V1 neural activity is fluctuation-driven, as our local V1 model suggests [34, 119, 162, 177].

Furthermore, γ-band power in the LFP in cat V1 increased with stimulus size, while the firing rates decreased or reached a plateau after the stimulus size exceeded the size of the receptive field [9]. Long-range γ-band oscillations appear to be synchronized over distances ~ 5 mm between pairs of neurons with non-overlapping receptive fields [58, 76, 77, 82, 104, 114, 158, 168, 187, 188]. Neurons with similar orientation preferences were seen to synchronize much more readily. This synchronization is also more likely if the two neurons are stimulated simultaneously by a single contour [58, 77]. This points to the role that long-range cortical connections may play in synchronizing the γ-band oscillations at longer distances. Finally, intracellular measurements of the membrane potential show pronounced fluctuations in the γ-band even though the spiking activity of single neurons show little or no oscillation in the γ-band [67, 105, 190, 191].

In [83], it was shown that with all the other parameters at their optimal values, as stimulus contrast increases, the LFP develops a spectral power peak at 25–90 Hz in the γ-band. (At the same time, the power content of the very low frequencies, which contain the most power, and reflect the modulations of the membrane potentials due to the drifting-grating stimulus [191],

hardly changes at all.) This increase in γ-band power of the LFP is similar to the increase in the simultaneously recorded spike rate; however, single neuron spiking activity shows little or no oscillatory behavior. In addition to the contrast dependence of the LFP spectra reported in [83], in [84], their dependence on the stimulus orientation and size was reported. As the stimulus orientation approached an optimum, a growing γ-band spectral peak developed at frequencies around 50 Hz. There was a significant variation in the tuning properties of this peak, which parallels the diversity in the orientation tuning of the firing rates of V1 cells [145]. The LFP orientation tuning is less pronounced than the spike-rate tuning due to the high level of the overall LFP activity. Finally, as the size of the stimulus was increased, the prominence of the spectral peak of the LFP increased with it, while firing rates only increased up to the optimal stimulus size and then decreased. (This is because the LFP measures the summed network activity, that is, the sum of both excitatory and inhibitory synaptic currents which are both large, while the firing rates are suppressed by inhibition.) In addition, the spectral peak moved from about 90 Hz at the stimulus size where it first became prominent to about 40 Hz at large stimulus sizes. (See Fig. 2 A.)

2.3.2 Modeling Background

Computational models of γ-oscillations, both transient and persistent, have been investigated by several groups. Studies of γ-oscillations involving large-scale, multi-compartmental, computational models include [182–185]. In minimal network models, γ-oscillations that involve only inhibitory interneurons were investigated in [42, 109, 110, 180, 193–195]. These works discuss mechanisms underlying the creation of the oscillations, dependence of the oscillation period on the decay rate of the inhibition (and/or axonal transmission delay [110]), and loss of synchrony in heterogeneous networks. Studies of γ-oscillations that involve both excitatory and inhibitory neurons include [18, 19, 29–31, 79, 181–183, 185]. The work in [18, 19] describes how sparseness and inhomogeneity of network connectivity may result in imperfectly synchronized oscillations, and presents an argument that, except in very carefully tuned parameter regimes, noise destroys oscillations with frequencies lower than those in the γ-range. The papers [29–31, 180] address the question of network oscillations produced with low and intermittent spike discharges of excitatory and inhibitory neurons. Experimental evidence points to excitatory-cell spiking rates being much lower than the LFP oscillation frequency [47, 48]. Even when the LFP signal is clearly oscillatory, the single-neuron spike trains tend to appear irregular and show no clear-cut oscillation [67, 105, 190, 191]. In [31], it is shown how to derive the oscillation frequency quantitatively in a randomly connected network of leaky I&F neurons with realistic synaptic parameters. Two mechanisms for oscillations are proposed. In a noisy network that only includes inhibitory neurons, the oscillation frequency is shown to depend largely on the shortest synaptic time constants, that is, delay and rise times ~ 200 Hz. In a noisy network composed of both excitatory and inhibitory neurons, the oscillation frequency arises from the competition of two mechanisms: the fast interaction among the inhibitory neurons, and the slower feedback loop between the excitatory and the inhibitory neurons. Having faster excitation than inhibition or having increased relative strength of excitatory favors the second mechanism, resulting in slower, typically γ-band oscillations.

The inclusion of orientation preference and long-range, intra-layer cortical connections [4, 6, 21, 108, 167] in V1 models and their influence on stationary cortical pattern formation and stability was addressed in [23–27]. Somers et al. [171] examined their influence within an I&F computational model with an idealized architecture. A one-dimensional model of very slow (< 1 Hz) cortical oscillations, (associated with sleep and anesthesia) that includes long-range cortical connections, was developed in [44]. The neuronal membrane potential is shown to oscillate slowly between an up-state and a down-state. The mechanism maintaining the up-state is strong recurrent excitation

balanced by inhibition, while the mechanism for the transition from the up-state to the down-state is a slow ionic current.

Preliminary analysis of our neuronal network model reveals features consistent with the LFP measurements of Henrie and Shapley: Ensembles of model neurons display γ-band specific modulation which become more apparent as ensemble size increases (poster presented at the Society for Neuroscience Annual Meeting in 2004 [178]). Furthermore, the network model displays various steady-state orientation selectivities as measured with drifting sinusoidal gratings in a manner consistent with spectral analysis of the LFP in V1. In particular, some recording sites, at which very orientation selective neurons are found, also have quite selective ensemble responses. At other sites, where the ensemble responses may not be very selective, single neuron responses at the same recording site can be highly selective. In the model, these two extremes in the relationship between the ensemble and single-unit orientation selectivity correspond to locations near iso-orientation domains, and pinwheel centers, respectively, and can be attributed to differing effective length-scales of cortical coupling in angular coordinates.

2.3.3 Proposed Work

I **propose** to investigate γ-oscillations in V1 using the extended computational model, which includes the addition of long-range, intercolumnar connections. In order to be able to model the γ-band oscillations and their associated properties in the experimentally relevant regime, the large-scale model ([119, 162, 177, 179, 196], and those described above) must be augmented in two ways. In previous models, the computational domain covered an area of four orientation pinwheels. Retinotopy has been ignored so far; in other words, it was assumed that all neurons look at precisely the same receptive-field center, which makes it impossible to vary stimulus size. Therefore, first, I will increase the size of the computational domain to cover at least 20×20 pinwheels, and incorporate in the model the long-range cortico-cortical connections. Second, I will include a retinotopic map [156, 157]. These two additions to the model will allow me to vary the size of the stimulus. In particular, I will activate the central part of the computational domain, while leaving the surround without external input. Furthermore, I will develop parallel versions of the code for the NJIT Beowulf cluster.

I describe here what I believe to be a plausible biological scenario for the γ-oscillation phenomena in V1, as characterized in the experimental literature quoted above. For small stimuli (up to the classical receptive field size), the network fires slowly and asynchronously with individual neuron firing rates of 5-10 spikes/sec [154, 155]. The network dynamics is driven by voltage fluctuations, i.e., that the time-average of the membrane potential is below the firing threshold and only membrane potential fluctuations reach threshold to cause spiking. As the stimulus size is increased beyond the minimum receptive field size, longer-range circuitry is activated as populations in nearby hypercolumns become active. The long-range connections are excitatory and connect neurons preferring similar orientations [4, 6, 21, 108, 167]. Because the long-range connections are orientation specific, if γ-oscillations are induced by these larger-size stimuli, then they are likely to show a corresponding orientation selectivity. Finally, at the largest stimulus sizes, long-range excitation acting on local inhibitory cells makes inhibition strong enough that local neuronal spiking becomes suppressed relative to the stimuli that drive only the classical receptive field. Moreover, since inhibition becomes more active for a larger stimulus, it shuts off the excitation for longer and longer periods before the inhibition shuts itself off as well, resulting in a longer silent phase. This creates the shift of the γ-oscillation peak to lower frequencies with increasing stimulus size.

In recent preliminary work, I have carried out part of the above model extension. A drifting grating stimulus is repeatedly shown at the same orientation, and for a selected neuron, the activity

of nearby cortical neurons is summed up. While the activity varies from trial to trial, the γ-frequency oscillation is evident in the spectrum. (See Fig. 2 D.) Using this extended model, I **propose** to investigate the following questions:

(1) Does the above scenario provide a plausible mechanism for generating γ-oscillations in the primary visual cortex? If so, what is its precise connection to the mechanisms of [18, 19] and [31]? Since in V1, γ-oscillations are observed for large stimuli, I believe it is the inhibition triggered by long-range excitation that slows down the network.

(2) How does one use the experimental data to constrain model parameters? How strongly does the orientation tuning of the model ensemble activity depend on parameters such as the strength or anistropy of long-range connections?

(3) How do the single-unit spiking activities sum up to the γ-frequency oscillations in the LFP? Experimentally, single units (presumably excitatory neurons) fire randomly. In the model, are individual cells of both excitatory and inhibitory populations firing randomly? Are the oscillations apparent in the spike trains of inhibitory cells? Do excitatory-inhibitory loops produce the oscillations? How are such loops maintained spatially?

(4) Are the γ-oscillations in V1 a signature of long-range coupling? In the experiments of [83, 84], the γ-band peak in the LFP spectra only appears when the stimulus size is sufficiently large. The effects of a recurrent excitatory-inhibitory feedback loop on synchrony and oscillations have been analyzed in all-to-all coupled networks [31], random networks with heterogeneous couplings [18, 19], and one-dimensional networks with homogeneous or heterogeneous spatial structure [44]. How γ-frequency oscillations can be sustained in networks that are heterogeneously coupled and driven on many different spatial scales is an open question.

(5) Why is the power in the γ-band orientation selective? Since γ-frequency oscillations appear to be a byproduct of long-range connectivity, their orientation selectivity seems consistent with the observation that these connections are orientation specific. In particular, the long range connections have different anisotropies in different species. For instance, the lateral connections are more anisotropic in the tree shrew than in the macaque. Will these different anisotropies be reflected in the orientation selectivity of the γ-band oscillations?

(6) Why does the spectral peak in the γ-band shift to lower frequencies at large stimulus size? What is the precise interaction mechanism between excitation and inhibition that causes this shift? As the stimulus size increases, a larger number of V1 neurons will be activated, but their spiking rates will be suppressed [83, 84]. Given that the extracellular single electrode measurements mostly record the spike rates of excitatory neurons, does this mean that the LFP mainly represents inhibitory contributions? How is the power in the γ-band of the LFP maintained even as spike rates are suppressed at the largest stimulus sizes?

2.4 Reduced Descriptions of Neuronal Network Dynamics and Application to Global Visual Processing

2.4.1 Theoretical Framework

A major theoretical challenge in neuroscience modeling is to develop reduced descriptions of the dynamics of large-scale neuronal networks. In recent work, my collaborators and I have undertaken the theoretical task to construct reduced representations of fluctuation-driven networks. These reductions are necessary to "scale-up" computational models to large regions of the cortex, and to allow further mathematical understanding of networks structure and mechanisms. For a simple network of integrate-and-fire neurons coupled via AMPA connections, we have derived reduced dynamical equations to capture the statistical behavior of the many neurons within the coarse-

grained patch. This representation is achieved via a kinetic theory, accomplished by a novel closure (For earlier probabilistic representations, see, e.g., [1, 8, 30, 40, 64, 69, 81, 98, 132, 133, 135, 139, 186, 197].)

As described in [33, 34], the coarse-grained kinetic theory begins with the derivation of time-dynamics of the probability density function (pdf). For a single all-to-all coupled, coarse-grained population containing N_E excitatory and N_I inhibitory neurons,

$$\bar{\rho}_{\mathrm{P}}(v, g_E, g_I; t) \equiv \mathbb{E}\left[\frac{1}{N_{\mathrm{P}}}\sum_{i=1}^{N_{\mathrm{P}}}\left\{\delta[v - V_i^{\mathrm{P}}(t)]\delta[g_E - G_i^{\mathrm{P}E}(t)]\delta[g_I - G_i^{\mathrm{P}I}(t)]\right\}\right],$$

where the expectation $\mathbb{E}$ is taken over all realizations of incoming Poisson spike trains from the external drive, and over all possible random initial conditions. $\mathrm{P} = E, I$ labels the excitatory and inhibitory population, respectively. Define the marginal and conditional moments:

$$\rho_{\mathrm{P}}(v;t) \equiv \int_0^\infty \bar{\rho}_{\mathrm{P}}(v, g_E, g_I; t) dg_E dg_I, \quad \mu_{\mathrm{PP}'}(v) \equiv \int_0^\infty g_{\mathrm{P}'}\bar{\rho}_{\mathrm{P}}(g_E, g_I|v, t) dg_E dg_I, \tag{2}$$

where $\bar{\rho}_{\mathrm{P}}(g_E, g_I|v, t)$ is the conditional pdf, i.e., $\bar{\rho}_{\mathrm{P}}(v, g_E, g_I; t) = \bar{\rho}_{\mathrm{P}}(g_E, g_I|v, t)\rho_{\mathrm{P}}(v, t)$, and $\mathrm{P}' = E, I$. The assumptions underlying the derivation of our particular kinetic equations are the following: (1) the number of neurons is large, $N_E \gg 1, N_I \gg 1$; (2) the summed spike train into a single neuron is Poisson; (3) the time-course of both excitatory and inhibitory postsynaptic conductances are single exponentials; (4) the closure condition: conditional variances of conductances are independent of the voltage, v, and are set to be the instantaneous conductance variances. Upon closure assumptions [34], this coarse-grained kinetic theory of the integrate-and-fire dynamics reduces to a closed system of PDEs for $\rho_{\mathrm{P}}(v, t), \mu_{\mathrm{P}E}(v)$ and $\mu_{\mathrm{P}I}(v)$:

$$\begin{aligned}
\frac{\partial}{\partial t}\rho_{\mathrm{P}}(v) &= \frac{\partial}{\partial v}\{U(v)\rho_{\mathrm{P}}(v)\} \\
\frac{\partial}{\partial t}\mu_{\mathrm{P}E}(v) &= -\frac{1}{\sigma_E}[\mu_{\mathrm{P}E}(v) - \bar{g}_{\mathrm{P}E}(t)] + U(v)\frac{\partial}{\partial v}\mu_{\mathrm{P}E}(v) + \frac{\sigma_{\mathrm{P}E}^2}{\rho_{\mathrm{P}}(v)}\frac{\partial}{\partial v}\left[\left(\frac{v - V_E}{\tau}\right)\rho_{\mathrm{P}}(v)\right] \\
\frac{\partial}{\partial t}\mu_{\mathrm{P}I}(v) &= -\frac{1}{\sigma_I}[\mu_{\mathrm{P}I}(v) - \bar{g}_{\mathrm{P}I}(t)] + U(v)\frac{\partial}{\partial v}\mu_{\mathrm{P}I}(v) + \frac{\sigma_{\mathrm{P}I}^2}{\rho_{\mathrm{P}}(v)}\frac{\partial}{\partial v}\left[\left(\frac{v - V_I}{\tau}\right)\rho_{\mathrm{P}}(v)\right]
\end{aligned} \tag{3a}$$

where

$$U(v) \equiv \left(\frac{v - V_R}{\tau}\right) + \mu_{\mathrm{P}E}(v)\left(\frac{v - V_E}{\tau}\right) + \mu_{\mathrm{P}I}(v)\left(\frac{v - V_I}{\tau}\right)$$

and

$$\bar{g}_{\mathrm{PP}'}(t) \equiv \nu_{0\mathrm{P}'}(t) f_{\mathrm{P}'} + S_{\mathrm{PP}'} m_{\mathrm{P}'}(t), \quad \sigma_{\mathrm{PP}'}^2 \equiv \frac{1}{2\sigma_{\mathrm{P}'}}\left[f_{\mathrm{P}'}^2 \nu_{0\mathrm{P}'}(t) + \frac{S_{\mathrm{PP}'}^2}{N^{\mathrm{P}'}} m_{\mathrm{P}'}(t)\right] \tag{4}$$

$\bar{g}_{\mathrm{PP}'}(t)$ and $\sigma_{\mathrm{PP}'}^2$ are the mean excitatory and inhibitory conductances and variances. $S_{\mathrm{P}E}$, $S_{\mathrm{P}I}$ are the cortico-cortical excitatory and inhibitory coupling strengths, respectively, f_E is the strength of a single LGN (or feedforward) postsynaptic conductance, and σ_E and σ_I are the excitatory and inhibitory synaptic time-scales. The feedforward drive has firing rate $\nu_{0E}(t)$ whereas $m_{E,I}(t)$ are the average population firing rates per neuron for the excitatory (inhibitory) population in this coarse-grained patch. With $J_{\mathrm{P}}(v, t) \equiv -U(v, \mu_{\mathrm{P}E}(v), \mu_{\mathrm{P}I}(v))\rho_{\mathrm{P}}(v)$, the flux along v, the firing rate of the population is given by the flux at threshold V_T: $m_{E,I}(t) = J_{E,I}(V_T; t)$. This set of equations (3) is further specified by imposing the appropriate flux boundary conditions, derived by demanding that the flux across the firing threshold V_T be equal to the flux at the reset potential V_R together with vanishing flux at $v = V_I$. Generalization to multiple patches with spatial interactions

can achieved by allowing positional dependences in the mean conductances and variances: $\bar{g}_{\mathrm{PP}'}(\mathbf{x},t)$ and $\sigma^2_{\mathrm{PP}'}(\mathbf{x},t)$.

Network dynamics involves many components which may be impractical to simulate directly. It is natural to seek a reduced subsystem that would capture the qualitative dynamics. Part of the difficulty is that the statistical description is an asymptotic result which relies on a separation of space- and time-scales, which may not be available in certain regimes. Furthermore, the closure assumption can be shown to fail when cross-correlations between closely-coupled neurons are too strong. Therefore I propose to use a more empirical approach to find reduced descriptions by adopting dimension reduction and parametrization techniques which are used in turbulence modeling. In turbulence research, a reduced subsystem, involving low-dimensional projections of the flow field, can be obtained via principal component analysis techniques. What makes turbulence research challenging is that the unresolved modes of the system are often strongly coupled to the reduced subsystems, and usually a closure scheme is sought to represent effectively the influence of the neglected variables on the resolved modes.

A similiar difficulty arises in large-scale neuronal network modeling. I propose to develop lower-dimensional models, starting from very simple idealized networks (e.g., containing a single pinwheel) towards larger models including more realistic and complex components (containing multiple pinwheels, with anisotropic long range connections). These models will be developed through benchmarking with point-neuron network simulations. I propose to focus on a few different levels of description, each with its own range of validity and utility.

(1) *PDF* Representations: I will extend the pdf description to the situation where the closure condition fails. In strongly recurrent networks, when cross-correlation between nearby neurons becomes too strong, it is possible that the conditional variances of the conductances are no longer independent of the voltage. In these cases, the functional dependence is nearly quadratic, suggesting that a three variable parametrization may be sufficient to capture the dynamics. This new pdf description may be derived in two ways. One is a *direct derivation* from the integrate-and-fire equations, assuming a three-parameter family of conditional variances and a Galerkin truncation of the nonlinear terms. By benchmarking with point-neuron simulations, the importance of high-order terms can be assessed. Another is an empirical determination, from the point-neuron simulations themselves. Using time-periodic stimulation, a *principal components* decomposition will yield a scheme with three (or more) variable parametrization of the conditional variances. While principle components-based methods have been applied to optical imaging data to extract neuronal activity maps [60, 61, 68], how these techniques can be used to extract dynamics from numerical simulations will be interesting mathematically. I propose to examine these new sets of kinetic equations, through benchmarking with the point-neuron simulations, in regimes where the cross-correlations are sufficiently strong. This will provide further insight into the dynamics of strongly recurrent networks and an extension of our kinetic theory into the strong coupling regime. Starting from the simplest network models, I hope to arrive at a simple working model for the local network dynamics near pinwheels before extending to multiple pinwheels and long-range connections. I will explore to what extent the local model can be carried over to more global models and what modifications need to be introduced to maintain consistency with the point-neuron simulations.

(2) *Mean Firing Rate* Representations: To understand large-scale visual processing spanning many hypercolumns and cortical layers (and, ultimately, multiple cortical areas), a pdf description may still be too expensive computationally. A minimal model of "contour completion" should contain three layers (an input layer, 4Cα; an output layer, 4B; and a feedback layer, 6), with each layer containing a few hundred hypercolumns. Instead of keeping track of the pdfs, as described above, I will seek to parameterize the state of the network dynamics through the mean firing rate, mean voltages, and the mean conductances, by projecting the dynamical simulation onto the

appropriate subsystem. In this proposed modeling framework, I will explore how these statistical quantities will vary and may be concisely captured using a few parameters (e.g., distance to pinwheel centers; preferred orientation of the local patch; density and anisotropy of long-range connectivities; and so on). This reduced description will also be benchmarked against large-scale point-neuron simulations and pdf descriptions. Once the qualitative accuracy of this reduced description is validated for simple test cases, I will develop these models for large-scale cortical models, including multiple layers of sufficient lateral extent to capture simple perceptual phenomena, such as "contour completion."

(3) *Hybrid* Representations. To compare with new multi-mode experiments (combining simultaneously multi-electrode, LFP, and/or optical imaging techniques), firing rate information is not sufficient. One needs to obtain more detailed, and higher order statistical information of spike times, both from individual neurons or from an ensemble of neurons. To this end, my collaborators and I have developed a "hybrid" representation of network activity. In this framework, a sub-network of a small population of point neurons is embedding within a coarse-grained network, represented by a set of kinetic theory equations [32–34]. Each point neuron is coupled to other point neurons in the subnetwork and is driven by the coarse-grained network via Poisson spike trains, whose mean-rates are given by solutions of kinetic equations. By choosing a suitable averaging time-scale, feedback to the coarse-grained network from the embedded point neurons can be computed. Spike-times and various time-series are obtained directly from the small subset of embedded point-neurons. In [32], for very idealized networks, we showed that this approach is dynamically accurate and numerically efficient. Another advantage of this "hybrid" representation is that it is naturally modular. For example, instead of embedding integrate-and-fire point neurons, one can choose more realistic models, such as a Hodgkin-Huxley neuron, or neurons with multiple compartments. For the coarse-grained network, one can use either a pdf representation (see **(1)** above) or a representation built upon mean firing rates (and mean voltages and conductances) (such as detailed in **(2)** above).

2.4.2 Application to Global Cortical Modeling: Contextual Effects from Beyond the Classical Receptive Field

Experimental Background Long-range horizontal connections in V1 appear to be partly responsible for the nonlinear properties of spatial summation of stimuli whose size reaches beyond a given neuron's classical receptive field and the related center surround interactions [5, 59, 62, 70]. Recall that a neuron's classical receptive field can be measured in two ways. The first way is to measure it as the part of the visual field that elicits increased firing rate when stimulated by small bright and dark dots or bars [7, 80]. (Its extent can also be measured by reverse correlation techniques [51, 146].) Alternatively, a neuron's receptive field can be measured by stimulating the cell with increasing, optimally oriented drifting grating patches with optimal spatial and temporal frequencies; the size of the patch at which the neuron's firing rate stops increasing is the receptive field size [50, 100]. This is the spatial summation field (SSF).

Stimulation of the near surround in addition to the stimulation of the receptive field center elicits different effects, either facilitation or suppression, on the neuron's firing rate. The surround is tuned, although more broadly, to the stimulus parameter values close to those preferred by the receptive field center [50, 101]. Suppression and facilitation are likewise orientation-tuned: suppression tends to be maximal when both the center and surround stimuli are optimally oriented and minimal, or may even turn into facilitation, if the orientation of the surround stimulus is orthogonal [50, 92, 97, 100, 101, 140, 159, 160, 166, 192]. The same holds for facilitation [41, 89, 92, 97, 127, 140].

The facilitative or suppressive nature of the near surround exhibits dependence on the combination of the relative stimulus contrast and the relative position of the stimuli. Collinear facilitation

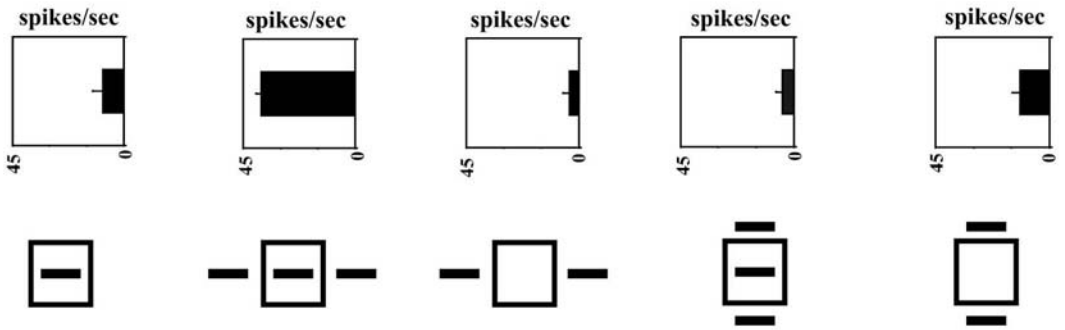

Figure 3: Responses for different stimulus configurations. The bottom panels indicate various stimulus configurations. The top panels show the corresponding neuronal responses in spikes/sec. Collinear configuration (second figure from left) show facilitation while other configurations show suppression. Figure taken from [92].

is generally observed (see Fig. 3).

Psychophysical experiments parallel the physiological findings. Human subjects find the apparent contrast of a high-contrast central grating embedded in iso-oriented surround grating lower than than without the surround grating [37, 43, 57, 134, 170, 199, 202]. Suppression is the strongest for like orientations and spatial frequencies of the two signals [37, 43]. It does not depend on the relative spatial phase of the stimuli, and increases with the contrast and size of the the surround stimulus [200]. Iso-oriented, collinear surround facilitates target detection in experiments measuring contrast detection threshold [89, 141, 142, 169, 198]. This facilitation decreases with decreasing collinearity and with increasing orientation difference and distance between the two stimuli [89, 141, 198, 201].

In [4] it is hypothesized that a visually-evoked subthreshold depolarizing field matching the size of the horizontal connections and SSF [28] may underlie facilitation or suppression of center stimuli by stimuli in the near surround. This hypothesis is strengthened by the fact that the speed of the activation wave generated by a restricted visual stimulus [78] appears to match the spreading speed of the depolarizing field [28] as well as the conduction speed of horizontal connections [73], and that these speeds agree with the response latency between center and near surround [88, 97, 102, 103, 148]. Additional evidence supporting the role of horizontal connections in mediating collinear facilitation was given in [46].

Not all center-surround interactions appear to be mediated by horizontal cconnections. In fact, the size of the far surround [155] and the reach of collinear facilitation [122], which both span up to about 12° in the visual space, seem to imply that at least some center-surround interactions may be mediated by feedback projections from higher cortical areas [4, 59, 155].

A theoretical study of the transition from suppression to facilitation with decreasing center stimulus contrast was performed in [171, 172]. Two different types of interplay between excitation and inhibition for high and low center stimulus contrasts provide an explanation for the transition. Facilitation for surround stimuli that are orthogonal to the center stimulus versus suppression for iso-oriented center and surround stimuli was studied theoretically in [55]. Facilitation for cross-oriented stimuli is explained by disinhibition of inhibitory neurons, while suppression for iso-oriented stimuli is accounted for by the excitation of local inhibitory neurons, which in turn suppress the local excitatory neurons. All these models contain $\sim 10^4$ cells, both excitatory and inhibitory, several hypercolumns, and both short-range and long-range connections within an idealized cortical architecture.

Proposed studies of contextual effects I believe that my reduced models of V1 is well-suited for investigating contextual effects inside the spatial summation field (SSF). In particular, the hybrid model of point-neurons coupled to mean rate models can be used to compare with experimental datasets. **I propose** to investigate the following questions:

(1) What is the cortical mechanism for the dependence of the spatial summation field size on the stimulus contrast? What, if any, is the role of short- and long-range horizontal connections? What are the roles of excitation and inhibition, and the interplay between the two?

(2) Same questions for the dependence of suppression and facilitation on stimulus parameters such as relative orientation, relative contrast, collinearity, and surround stimulus shape and size?

(3) What is the cortical mechanism for surround orientation tuning? Is it similar in nature to the mechanism for center orientation tuning, or are they distinct? How do the roles of excitation and inhibition, and short- and long-range horizontal connections, differ in the two mechanisms? How do various types of surround stimuli affect V1 neuronal orientation preference and tuning curves?

(4) What is the physiological mechanism for the orientation discrimination threshold phenomenon of [115–117], and what determines its dependence on the size, relative orientation, and contrast of the stimuli?

(5) How do we use the experimental data on contextual effects and the dynamics of orientation tuning curves to constrain model parameters?

3 Educational Plans

Since coming to NJIT, I have made a strong effort to incorporate my research interests, in particular my work in neuroscience modeling, into the curriculum. I have been involved in educational efforts in which my research experience has played a significant role. I have supervised three graduate students in summer reading courses on various mathematical aspects related to my work in computational neuroscience. Two of these students read papers on pattern formation in excitable systems. One of them (Hui Wu) will become my doctoral student. She will work on pattern formation in two-dimensional excitatory neuronal networks. The other (Yogesh Joshi) read papers on coupled oscillators and synchronization. One of my undergraduate students (Jasneet Kaur) has progressed beyond my introductory biomathematics class to become a part of our Undergraduate Biology and Mathematics Training Program (UBMTP). Two others undergraduates (from my freshman Honors Calculus class) have also applied to the UBMTP, with the goal of pursuing summer research projects in 2007. As NJIT is well known for the diversity of its student body, it will be easy to recruit diverse students to participate in my proposed research and educational programs.

NJIT's Mathematical Sciences Department offers a variety of special-topics courses both to the upper-level undergraduate and graduate students. For upper-level undergraduates, there are 3 semester-long courses on mathematical biology. For graduate students, there is an introductory course on mathematical biology (based on Keener and Sneyd's text). I plan to develop (1) a mathematical biology course at the senior undergraduate level that will introduce mathematical biology students to basic neuroscience modeling, and (2) a computational neuroscience course at the graduate level that would include the knowledge from my V1 modeling, emphasize applications to systems neuroscience by including examples from my own and my peers' research. In this way, I will add new components to the already broad research environment at NJIT's Mathematical Sciences Department. Furthermore, I will be an active part of the Howard Hughes Medical Institute Doctoral Training Grant in Quantitative Neuroscience at NJIT/Rutgers-Newark/UMDNJ. I am heavily involved in planning theoretical and modeling portions of the Quantitative Neuroscience

Curriculum and will initiate a course on Mathematical Tools in Theoretical Neuroscience and a course on Information Processing in Neural Systems. I expect my students, upon the completion of their doctoral work, to become competitive candidates for postdoctoral positions at departments and centers for neuroscience in addition to mathematics departments.

3.1 Undergraduate Curriculum Development

I have taught the first course in our undergraduate biomath sequence the last three year. Each year, I add more computational neuroscience examples to the curriculum. Last term, my students were able to calculate the oscillatory period of integrate-and-fire neurons. I plan on adding more examples, including coupled systems of two or three neurons, of both excitatory and inhibitory type. I have also introduced my students to some basic neuroscience, giving classes on visual pathway anatomy and physiology, to motivate them and expose them to contemporary research problems.

I plan to develop an undergraduate course on computational neuroscience, with the goal of introducing mathematical biology students to basic neuroscience modeling. This course will be aimed at senior mathematics major who have completed our sequence of introductory mathematical biology courses. This sequence of mathematical biology courses introduces our students to various ordinary differential equation models of mathematical biology (ranging from population biology to neuroscience), focusing on qualitative features and analytic solution techniques. Building upon this foundation, my proposed new course will focus on modeling and numerical solutions. This course will feature short programming projects. I will make versions of my code (in Fortran and in Matlab) accessible to student so that they can play and experiment with the codes and be exposed to hands-on experience. Students will be asked to present their results at the end of term. These programming projects will be posted on the web.

3.2 Graduate Curriculum Development

I plan to develop a graduate course on systems level modeling based on my work in V1. This course will be aimed at second year graduate students in Biomathematics, Applied Mathematics, Biomedical Engineering and Quantitative Neuroscience. Despite the mathematical coursework, few students are able to bridge the gap between their problem sets and research level modeling. This course will fill a niche in this regard. I will introduce students to visual pathway anatomy and physiology, while emphasizing possible coding schemes. I will pay special attention to the seminal papers on receptive field measurements and the role linear systems analysis techniques played. Then I will present the Hodgkin-Huxley model of action potential generation as a successful example of neurophysiological modeling and address the inadequacies of single neuron processing to motivate systems level modeling. I will expose the students to systems neuroscience through various models of orientation selectivity in visual cortex, accentuating the similarity and differences in both qualitative and quantitative ways. Finally, as final projects, students will be required to read and present recent systems level modeling papers, from topics such as central pattern generators, place cells, olfactory or somatosensory systems.

I will be involved in developing the theoretical portion of the HHMI Quantitative Neuroscience Doctoral Training Program. A Mathematical Tools in Neuroscience course will introduce first year graduate students to the basic mathematical techniques for analysis and modeling of neuroscientific data. I plan to cover topics that included Linear Systems, Fourier Analysis, Wiener-Hopf techniques, Bayesian Probability and Information Theory. Homework problems will be based in Matlab, and whenever possible, real data sets obtained from the labs of my colleagues will be used for illustration.

I also hope to develop a course on Information Processing in Neural Systems in addition to my systems level modeling course in the Math Department. I envision teaching these two courses in alternating years, emphasizing information theoretic concepts in one year and dynamical systems concepts in the other. In the Quantitative Neuroscience course, probabilistic and information theoretic concepts will be emphasized, and coding and decoding schemes will be discussed. I will focus on visual processing and the visual pathway with an aim to study vision from a systems analysis point of view. In the Mathematics course (see above), applied mathematical models will be the focus. Students will learn differential equation modeling and apply them to interpret neurophysiological datasets.

3.3 Advising and Seminars

I am currently advising two graduate students on their dissertation projects. Christina Lee (at RPI, jointly with Gregor Kovacic) and I have been working on coupled phase oscillators and synchronization. Hui Wu (NJIT Math) is just starting and will work on pattern formation in two-dimensional excitatory neuronal networks. I plan to attract one more student in the next two years.

Mathematical Biology Working Seminar Along with Drs. A. Bose, V. Matveev, and R. Miura, I have been leading a weekly meeting to train our mathematical biology graduate students. This is a forum where group members will present their research and/or seminal research papers in a series of informal meeting. Students will be encouraged to present their results, practice their presentations and seek advice on problems. Faculty members will present new ideas as well as recent research work.

Mathematical Biology Lecture Series Since arriving at NJIT, I have continued and extended a Mathematical Biology Seminar series started by Robert Miura. These seminars provided a forum for biophysics, biomedical engineering, and mathematical biology students to interact, and filled a niche in interdisciplinary focus between the various biomedical and neuroscientists at NJIT, Rutgers-Newark and UMDNJ. Partially supported by the Center for Applied Mathematics and Statistics at NJIT, these seminars featured a diverse group of speakers, trained in biophysics, computational neuroscience, biology and computer science and covered diverse topics ranging from cellular biophysics, cellular and systems neuroscience, mathematical modeling, bioinformatics and ecology. I also invited speakers from biotech industry and national laboratories in an effort to give students a glimpse of the breadth of possible careers in the biology and health sectors.

As these seminars were very well attended by mathematics students, as well as students from other departments, I plan to introduce a similar interdisciplinary vein into our weekly department colloquia. I am requesting funds to establish a new Lecture series, to be part of our colloquia, to feature prominent quantitative biologists and biomathematicians. Each speaker will present research seminars accessible to advanced undergraduates, in addition to the department colloquium. I plan to invite at least one speaker per term and will include student involvement to select the speakers and to provide further exposure to interdisciplinary research and career opportunities in quantitative biology.

4 Budget Justification

The budget request is mainly for two months of summer support for the principal investigator for four years (years 2-5), and for stipend and tuition for a graduate student for Years 2-5. The request for tuition appears in line G.6 as Other costs. Line G.6 also includes the request for funding speakers of a Mathematical Biology Lecture Series. There is a separate request in the budget for computer equipment and one for domestic travel. The requested equipment funds are to update a four-year old PC with a high-end PC in Year 1, to secure a laptop computer in Year 1, and to update the PC and laptop in year 4. The request for domestic travel funds is for the principal investigator and his student to attend and present results at conferences and to interact with collaborators. Conferences that will be attended include the annual Society for Neuroscience Meeting, the SIAM Life Sciences Conference, the SIAM Conference on the Application of Dynamical Systems, and the SIAM Conference on Nonlinear Waves and Coherent Structures. The funds for consultants are for speakers of a special Colloquium series focused on Mathematical Biology.

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Professional Experience

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1997–99 NSF Mathematical Sciences Postdoctoral Research Fellow, Astronomy Department, Columbia University.

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Education

Ph.D. University of Chicago, Physics, 1995.

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Publications Related to Proposed Project

[1] L. Tao, D. Cai, D. McLaughlin, R. Shapley and M. Shelley. Orientation selectivity in a fluctuation-driven neuronal network model of primary visual cortex. *Proc. Natl. Acad. Sci. (USA)*, in press.

[2] D. Cai, L. Tao, A. Rangan, and D. McLaughlin. Kinetic theory for neuronal network dynamics. *Comm. Math. Sci.*, 4:97-127, 2006.

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Other Significant Publications

[1] D. Cai, L. Tao, M. Shelley, and D.W. McLaughlin. An effective representation of fluctuation-driven neuronal networks with application to simple & complex cells in visual cortex. *Proc. Natl. Acad. Sci. (USA)*, 101:7757–7762, 2004.

[2] D. Cai, G. Kovacic, D.W. McLaughlin, R. Shapley, M.J. Shelley and L. Tao. On the role of nonlinear systems analysis in interpreting orientation tuning dynamics via reverse-time correlation. *In preparation.*

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Honors and Awards

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GAANN Fellowship of the University of Chicago, 1990-1993.

Recent Collaborators and Advisors

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Synergistic Activities

Organizer of computational neuroscience minisymposia at AIMS 6/04, SIAM Nonlinear Waves and Coherent Structure 10/04, SIAM Dynamical Systems 5/05, and SIAM Life Sciences 7/06.

Organizer of NYU Mathematical Neuroscience Seminar Series, 2000 - 2003.

Organizer of NJIT Mathematical Biology Seminar Series, 2003 - 2005.

Organizer of NJIT Mathematical Sciences Department Colloquia, 2005 - present.