Masters’ research projects

1. Adapting Granger causality for use on EEG data.

**Background.** Granger causality is a concept introduced in the field of economy to determine which variables influence, or cause, other variables. The basic idea is that in order for a variable x to cause y, the prediction of future values based on just the past values of y has to be improved when information about the past of x is also included. This has been quantified by assuming the future response can be fitted by a linear autoregressive (AR) model, and determining the change in prediction error when the past of x is included. Recent studies have extended Granger causality in two different directions: First, into the nonlinear realm using the concept of transfer entropy (Schreiber, *Phys Rev Lett* (2000)). Second, by making it non-parametric through the use of spectral methods rather than using an AR model (Ding and coworkers, *Phys Rev Lett* (2008)). Applying Granger causality to EEG data may yield important insights into the pathologies underlying schizophrenia.

The **overall goal** of this project is to explore how Granger causality, and its two extensions, can be useful in characterizing causal relationships between EEG signals recorded on different electrodes and identifying the underlying neural sources.

**Learning goals** are to: (1) obtain familiarity with real-life features of electrophysiological data and (2) design statistical models to account for these; (3) learn how to fit AR models using a Matlab toolbox; (4) gain familiarity with the underlying numerical linear algebra techniques and (5) multi-taper spectral analysis techniques.

This project has a number of open-ended components that could lead to publications. The underlying assumption of AR methods is that the time-series are normally distributed, which is typically not the case for electrophysiological data. It is therefore of interest to characterize the appropriate distribution and to adapt the AR maximum-likelihood fitting procedure to this distribution, for instance by nonlinear rescaling of the measurements. Data from various sources (laminar probes from rat hippocampus; scalp EEG from schizophrenia patients etc) can be analyzed, which may lead to new insights that are publishable.
2. Study the functional role of interneuron activity in stimulus competition using firing rate models.

**Background:** The receptive field of a visual neuron is the area in the visual field where it responds to presentation of visual stimuli by firing spikes. The receptive fields of neurons in intermediate cortical areas are large enough to fit multiple stimuli. Preferred stimuli (P) strongly activate the neuron, whereas nonpreferred (NP) stimuli activate the neurons to a lesser degree. Stimulus competition refers to the situation when the simultaneous presentation of a P and NP stimulus, contrary to expectations, results in a firing rate in between the response to NP and P stimulus presented singly. Recent experiments suggest that this effect depends on stimulus contrast (Ghose & Maunsell *J Neurosci* 2008), whereas models suggest that the activity of interneurons may be important (Buia & Tiesinga *J. Neurophysiol* (2008). Firing rate models have so far only focused on the role of excitatory neurons. Understanding the mechanism for stimulus competition at the cellular level is important because it may help understand pathologies of the process of selective attention such as occur during attention deficit disorder.

The overall goal of the project is to build a firing rate model comprised of two cortical columns each with inhibitory and excitatory neurons, in order to quantify the contrast dependence of stimulus competition and determine the role of interneurons.

**Learning goals** are to (1) gain familiarity with the literature on stimulus competition; (2) learn how to implement a firing rate model of a cortical column; (3) explore, using phase-plane analysis, the dynamics of the coupled differential equations representing the columns, with a focus on oscillatory solutions; (4) fit and compare the model responses to published experimental data.

This project has a number of open-ended components that could lead to publications. First, the model of the cortical column can be extended to include multiple cortical layers. Second, the model can be extended to include multiple types of interneurons. The model responses then predict correlations between different groups of neurons that could be measured during experiment.
3. **Study the mechanism for modulating the relative phase between networks of spiking neurons.**

**Background.** The local field potential (LFP) often contains oscillating components in the gamma frequency range (30-80 Hz), which makes it possibly to define a neuron’s spiking phase relative to this oscillation. Experiments suggest that the communication between two neurons is best, as quantified in terms of correlations between firing rate fluctuations, when their phase difference has a specific value (the “good-phase hypothesis”, Womelsdorf et al, *Science* 2007). The question is how can the phase difference between two networks be set to reflect behavioral goals? A recently proposed hypothesis holds that depolarizing interneurons is effective in changing the relative phase between excitatory and inhibitory neurons (Buia & Tiesinga, *J Comput Neurosci* 2006). Exploring this hypothesis is important because it may yield insight into the mechanisms underlying selective communication between different brain areas.

The **overall goal** of this project is to study how the relative phase between networks can be modulated by applying current pulses to specific groups of neurons.

The **learning goals** of this project are to: (1) gain familiarity with spiking neuron models for different types of neurons (pyramidal cells, fast spiking interneurons) developed by Izhikevich); (2) implement a model network of a 100-1000 of these neurons connected via synapses in matlab (or using C or python); (3) calculate the phase and frequency of the emerging network oscillations; (4) learn how to systematically perform a set of simulations to establish appropriate parameter ranges for which a certain effect occurs.

This project has a number of open-ended components that could lead to publications. First, a succinct characterization of how the relative phase could be modulated has not yet been performed and could be published. Second, it is interesting to extend the model to explicitly test the “good-phase” hypothesis and correlate effectiveness of communication between the model columns to the value of the relative phase. Third, the insights obtained from the modeling could be used to design new experiment using optogenetic techniques.
4. Characterizing the neural sensitivity to input correlations using multi compartment models.

Background. A layer 2/3 pyramidal cell receives synaptic inputs from a wide variety of sources, each with a distinct pattern of spatiotemporal coherence (Tiesinga et al, 2008). It is not fully understood how these patterns interact on the spatially extended dendritic tree and how their respective properties are reflected in the output spikes of the neuron. A very limited characterization is obtained by correlating the output spikes with the local field potential (LFP). From a functional standpoint one can identify feedforward inputs, representing stimulus-related information; recurrent inputs with emergent frequency content and top-down inputs, representing selective attention or behavioral goals, which modulate the transmission of feedforward information and putatively the coherence of recurrent inputs. A popular hypothesis is that top-down inputs cause gain modulation of the feedforward inputs. Computational models show that gain modulation can be achieved using numerous mechanisms (balanced synaptic inputs, Chance et al Neuron 2002; inhibitory synchrony, Tiesinga et al J. Physiol. 2004; nonlinearities, Murphy & Miller J. Neurosci 2003), but these have not yet been evaluated at the multi compartment level. Evaluating mechanisms for gain modulation is important because it will give insight at the cellular level into a common neural computation and will characterize the signature of this computation in terms of the spike-LFP correlation.

The overall goal of this project is determine how the feed-forward and topdown inputs interact at the level of the layer 2/3 pyramidal cell, whether top-down inputs can achieve gain modulation, and how this would be reflected in the LFP-spike correlation.

The learning goals of this project are to (1) gain a familiarity with the published electrophysiological properties of pyramidal cells; (2) learn how to run and design a multi compartment model using the software package neuron; (3) learn how to parameterize the statistical structure of the synaptic inputs to a cortical cell; (4) characterize the relation between the output spike train and the statistics of the input streams in terms of the gain and the LFP-spike correlation.

The results of these simulations are of current interest. Thus, a careful characterization of the interaction of topdown and feedforward inputs will likely lead to a publication.
5. Fisher information of heterogeneous spiking networks.

**Background.** Cells in the primary visual cortex are orientation selective, which means that the orientation of a stimulus can be inferred from their spiking activity as long as their preferred orientation is known. The Fisher information is a measure for the statistical efficiency of the orientation estimate: the higher the Fisher information the more precise the estimate. Another key concept is the tuning function, the firing rate as a function of stimulus orientation. The location of the peak of the tuning function indicates the neuron’s preferred orientation. Orientation selectivity can emerge in a feedforward way or as a result of recurrent cortical connections. It has been demonstrated that the correlations caused by recurrent connections reduce the Fisher information (Series et al Nat Neurosci 2004). In most computational studies the tuning functions of different neurons were identical except for the peak location. However, heterogeneity can be introduced by varying the peak amplitude and the shape of the tuning function across neurons. A recent paper holds that heterogeneity of tuning functions improves the Fisher information compared with a network with identical tuning functions (Chelaru & Dragoi, PNAS 2008). It is not clear what type of heterogeneity improves and what type of heterogeneity reduces the Fisher information, and by which correlations (spike count versus spike time) these changes are mediated.

The **overall goal** of this project is to study using a neural network how and in what way heterogeneity affects the Fisher information.

The **learning goals** for this project are to (1) gain a familiarity with the concept of Fisher information and learn how to calculate it analytically and numerically; (2) construct a coupled network of firing rate neurons using Matlab and obtain peaked tuning functions; (3) learn how to vary the degree and type of heterogeneity of the tuning functions obtained from the network; (4) determine the impact of tuning-function heterogeneity on the Fisher information.

The obvious extension of this project is to replace the firing rate neurons by spiking neurons, which will provide insight into the role of spike-to-spike correlations between neurons, which is topic of current interest.
6. Constructing and validating statistical models for spike patterns

**Background.** Half a century ago Hubel & Wiesel characterized the response properties of individual neurons in the visual cortex using a microelectrode. They found that cells were orientation-selective, for which they won the Nobel prize. Currently, the responses of multiple neurons are simultaneously recorded using multi-electrode arrays or two-photon microscopy. In order to understand these extremely complicated data sets it is necessary to develop statistical models. Recently two methods were proposed, one based on the Ising model of statistical physics (Scheidman et al *Nature* 2006) and one based on generalized linear models (Pillow et al *Nature* 2008). The Ising model is very powerful because it reduces the number of parameters, it fits the experimentally obtained cross correlation functions based on the principle of maximal entropy. The Ising model explains the data in terms of pair-wise coupling constants that could be interpreted as the presence of excitatory or inhibitory synapses for the pair in question.

The **overall goal** is determine how well pair-wise coupling constants represent the synaptic connectivity matrix under different states of the cortical network. This study will be conducted using model simulations of networks of spiking neurons and is relevant because it will help the interpretation of experimental results.

The **learning goals** are: (1) Gain familiarity with the Ising model for describing spike patterns; (2) Understand methods used to fit Ising models to experimental or simulation data; (3) Learn how to develop network models and simulate them using matlab, C or python; (4) Learn how to setup a simulations

There are a number of extensions that could lead to scientific publications. First, the Ising model is based on the optimization of the so called Shannon entropy, which is extensive – the question is whether there are other optimality principles that account better for the data. The Ising model presently does not include temporal interactions, but they could be included in a fairly straightforward way. The question in that case is whether including temporal interactions leads to a better description of the experimental data. Third, these techniques could be applied to real experimental data and lead to publishable insights.
7. Population models for motion sensitivity in the primary visual cortex of the Ferret

**Background.** The response of neurons in primary visual cortex (V1) can under certain circumstances be described as the output of a spatiotemporal energy (SE) filter, for instance as a space-time Gabor function (Basole et al *Nature* 2003; Mante & Carandini *J Neurophys* 2005). Our perception of the direction of motion is based on the population response in V1, which can thus be modeled as an array of SE filters. Because neurons are direction selective, the information about object motion is present in two types of responses: the preferred direction of motion of the neurons that are activated by the object and the change in time of the receptive field centers that are activated by it (position tracking). The waterfall illusion is a well known illusion: if you focus on a waterfall for a minute or so and then move your gaze to the rock wall next to the waterfall, the rock wall will appear to move upwards. Recent experiments in Ferret indicate that during a sudden shift in direction of motion of an object, certain aspects of the motion transition are misinterpreted perceptually (Wu et al, unpublished). Logic dictates that this shift could be due to either the adaptation of neurons (like for the waterfall illusion); short term plasticity of the synapses that connect them or specific features of the synaptic connectivity.

The **overall goal** is to construct a population model to account for the perceptual effects during a motion transition using a firing rate model with neurons that have a Gabor type receptive field and are connected through plastic synapses (meaning synapses with activity-dependent strength).

The **learning goals** are: (1) Learn how spatiotemporal energy filters extract stimulus features using Fourier space analysis; (2) Learn how to simulate in matlab the response of SE filter model to an arbitrary stimulus movie; (3) Design a network model with neurons that behave like SE filters and connected by plastic synapses; (4) Learn how to extract the direction of motion from the model response using either the motion selectivity or position tracking; (5) Compare these model results to experimental results obtained using voltage-sensitive dye imaging.

As there is presently no good model to account for these experimentally observed effects, a model-based explanation with clear predictions is publishable.