Non-random connectivity and the response properties of neocortical networks
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Background The neocortex is the part of the mammalian brain where high-level functions take place – from integration of sensory input to complex motor planning output. The tissue is a folded sheet-like structure featuring 5-6 layers. The principal recurrent neuronal networks are found in layers 3 (40% connectivity) and layers 5 (20% connectivity). Both of these networks feature non-random higher-order connectivity; the probability that neuron A is connected onto neuron B is much more likely if it is known that B is connected onto A. The synapses between neurons in each of these layers show synaptic depression, meaning that they become weaker with use over short time scales with recovery over longer timescales. This dynamic weakening is much stronger in the highly connected layer-3 network than in the more sparsely connected layer-5 networks.

Aim The project involves the construction (analytical and computational) of models of networks of excitatory neocortical neurons featuring measured non-random connectivity and synaptic dynamics. A great deal is known about the steady state rate, first-order response properties (susceptibility) and cross-correlations in all-to-all or sparse-random connected networks with static synapses. The goal will be to test the validity of these predictions when more realistic connectivity (particularly the increased rate of reciprocal connections) and synapses are included, using the latest available experimental data.

Techniques The computational techniques to be used will be Monte-Carlo simulations of coupled stochastic differential equations. This will require the student to become familiar with evolving coupled neurons subject to Gaussian white noise. Analytical techniques to be used involve the Fokker-Planck framework for networks of neurons and level-crossing methods for Gaussian processes. The computational approach is low risk, the level crossing methods low-to-medium risk and a full analytical solution to the problem high risk.

Deliverables and beneficiaries Neocortical networks are currently subject to an intense international research effort, but current modeling approaches lag behind experimental data. We are in a unique position in that we have access to the latest (and currently unpublished) data on neocortical connectivity. Incorporating these latest data into more realistic models of the neocortex is key to uncovering the natural computational processes taking place in tissue. More realistic models would be rapidly taken up and be of direct benefit to both the modeling and experimental communities.

Potential for a follow on PhD project The tools required to analyse the dynamics of activity in non-random neocortical networks are yet to be fully developed. The quality of the data now available makes this an urgent priority for theoreticians and it would provide an excellent thesis subject for a mathematically competent student. The current project could also be extended to take into account inter-layer connectivity and the effects of inhibitory interneurons. A wealth of data is available from collaborators at the Karolinska (Stockholm), Brain Mind Institute (Lausanne) and Life Sciences (Warwick).

Reading material

Highly Nonrandom Features of Synaptic Connectivity in Local Cortical Circuits.
Song et al (2005*)* PLoS Biol 3(3): e68. doi:10.1371/journal.pbio.0030068

Firing-rate response of linear and nonlinear integrate-and-fire neurons to modulated current-based and conductance-based synaptic drive
Richardson MJE (2007) Physical Review E 76: article-no 021919