Integration of parallel information streams in pyramidal neurons

Dr Magnus Richardson[1] and Dr Yulia Timofeeva[2]
[1]Warwick Systems Biology Centre, [2]Centre for Complexity Science

Background. The computational power of the neocortex arises from a combination of the rich response properties of neurons and the highly complex networks they form. The principal cells of the neocortex - pyramidal cells - are highly elongated with dendrites up to 1mm long. Because the cell is extended it cannot be assumed to have a homogeneous membrane voltage but rather has a voltage described by a diffusion-like cable equation

$$\tau \frac{\partial v}{\partial t} = -v + \lambda^2 \frac{\partial^2 v}{\partial x^2} + I_{syn}(x,t) \tag{1}$$

where τ and λ are the time and space constants of the neuronal dendrite and I_{syn} is a spatially inhomogeneous synaptic drive. Each cortical neuron can receive as many as 10,000 synapses - so even though the firing rate of individual neurons is low neurons are subject to a massive synaptic bombardment. Equation (1) provides a fairly detailed account of the dynamics of membrane voltage in dendrites; however, the spatial term is often neglected yielding a one-dimensional equation for a homogeneous voltage. This equation is combined with a white noise $\xi(t)$ model of synaptic drive with strength σ to yield an Ornstein-Uhlenbeck process for the homogeneous voltage

$$\tau \frac{\partial v}{\partial t} = -v + \sigma\sqrt{2\tau}\xi(t). \tag{2}$$

The spiking mechanism is then implemented through a threshold-reset: if the voltage v is above some threshold value v_{th} a spike is registered and the voltage reset at v_{re} from which the dynamics continue.

Project aim. The goal will be to combine equations (1) and (2) to create a biophysically reasonable model of spatially-distributed stochastic synaptic input in pyramidal cells. A number of approaches are possible from simulational numerics to mathematical reduction strategies. Depending on progress, a voltage-dependent Calcium current with a spatially-dependent concentration gradient $\gamma(x)m(x,t)(E_{Ca} - v)$ can be added allowing for the modelling of dendritic calcium spikes. We might also consider how a cellular frequency preference called subthreshold resonance interacts with the synaptic drive which can be incorporated through a second variable w.

$$\tau \frac{\partial v}{\partial t} = \kappa w - v + \lambda^2 \frac{\partial^2 v}{\partial x^2} + I_{syn}(x,t) \quad \text{where} \quad \tau_w \frac{dw}{dt} = v - w. \tag{3}$$

Extension to a PhD. The effects of dendritic geometry in pyramidal neurons have not been analysed in combined models of stochastic synaptic drive and active dendrites. There is, however, a wealth of experimental data available for the construction of biophysically detailed models and a number of experimental groups have already been identified that would be interested to collaborate. There is also potential for external partners in the pharmaceutical industry and in the AI industry through the link with neuromorphic models of intelligence. Both will be pursued before the PhD deadline.

Skills required. Good mathematical and/or programming skills and an interest in applying theoretical approaches to understanding biological data.

Additional reading.
• Travelling waves in a model of quasi-active dendrites with active spines. Timofeeva Y. Physica D (2010). http://dx.doi.org/10.1016/j.physd.2010.01.004.
• Dynamics of populations and networks of neurons with voltage-activated and calcium-activated currents Richardson MJE. Physical Review E 80: article-no 021928 (2009)