Stochastic synaptic integration in a spatial neuron with voltage-activated currents

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Background

The computational power of the neocortex, the most recent part of the brain in evolutionary terms, 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 their axis normal to the cortical surface. Because the cell is extended it cannot be assumed to have a homogeneous membrane voltage but has rather 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, though the firing rate of individual neurons is low (around 0-5Hz) neurons are subject to a massive bombardment of stochastic synaptic current.

Though equation (1) provides a fairly detailed account of the dynamics of membrane voltage in dendrites, 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

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

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 Monte-Carlo simulation numerics (no risk) to mathematical reductions strategies such as two-compartment approximations to the continuum dendrite or mode analysis. Depending on progress, a voltage-dependent Calcium current with a spatially-dependent concentration gradient $\gamma(x)m(x,t)(E_{Ca} - v)$ can also be added allowing for the modelling of dendritic calcium spikes. This important feature of pyramidal cell integration has not yet been combined with a stochastic model of synaptic input.

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. The developent of a mathematically tractable model of pyramidal cells that capture their active properties and spatially separated synaptic drive would be a strategic contribution to the field of theoretical neuroscience.

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)

• Step-wise repolarization from Ca2+ plateaus in neocortical pyramidal cells. Reuveni et al. J Neurosci 13 4609-4612 (1993)