

A NETWORK MODEL FOR STUDYING THE CONSEQUENCES OF LOCALIZED AND NON-LOCALIZED INHIBITION OF THALAMIC RELAY CELLS

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1. Introduction

A central aim of neuroscience is to understand how individual neurons integrate to form a network of singular signal processing capabilities. Neuroanatomical and -physiological research has unveiled a wide range of neuron types, synapses, and interconnection patterns, while providing only limited insight into the *how* of neuronal signal processing. A key problem is that hypotheses about the functional relevance of particular neuronal or synaptic properties are difficult to test experimentally.

These problems can be overcome using mechanistic models of neuronal networks, i.e., models that resemble network structures and neuron properties closely. In such models, properties of neurons and synapses, as well as connection patterns, can be changed at will, allowing one to test conjectures on the functional significance of neuronal properties.

The early visual pathway is particularly suited for mechanistic modeling, since it is well studied, so that models can be founded on solid experimental evidence. We present here a model of the retinogeniculate circuit in mammals designed to explore the functional significance of peculiarities of thalamic nuclei, namely (i) the ability of thalamic neurons to fire either in a burst or a tonic manner, and (ii) triadic synapses that connect axons of retinal ganglion cells with both a geniculate relay cell dendrite and an interneuron dendrite, and which include inhibitory dendro-dendritic synapses. Interneurons participating in such triads may provide either localized inhibition at the triads, or globally coupled inhibition via their axons, or both. The functional significance of this kind of localized and non-localized inhibition is as yet unclear.

2. Model Structure and Components

Our network model contains currently three types of neurons: retinal ganglion cells, which we take to be placed on a hexagonal grid; the same number of geniculate relay cells (X-cells); one third as many geniculate interneurons, each centered between three ganglion/relay cells. Each ganglion cell makes one triadic projection onto a relay cell, and a normal axo-dendritic connection to its nearest interneuron. Each interneuron thus receives input via normal synapses from three ganglion cells, and in addition receives triadic input from the same three ganglion cells. In turn, it inhibits via these triads the three corresponding relay cells. The interneuron furthermore provides normal axo-dendritic inhibitory input to its six nearest neighbor neurons. The resulting wiring scheme is shown in the Figure. This wiring scheme attempts to reflect current knowledge about neuronal connectivity in the X-pathway in lateral geniculate nucleus (Funke & Wörgötter, 1997; Sherman & Guillery, 2001; Steriade *et al*, 1997).

Both geniculate relay cells and interneurons are implemented using the leaky integrate, fire, and burst model derived by Rinzel and collaborators (Smith *et al*, 2000). This model compactly implements the most striking feature of thalamic neurons, namely the slow, low-threshold calcium currents, which give rise to burst of spikes in response to even weak input, if the neuron is in a hyperpolarized state.

Normal synapses between neurons are implemented as β -functions, with a rise and a decay time constant. These synapses are taken to be fast, ionotropic synapses with time constants on the order of 2-5ms. Our implementation of triadic synapses follows Koch (1985): the excitatory input from retinal ganglion cell to geniculate relay cell is modeled as a fast α -function, with shunting due to dendro-dendritic inhibition modeled as a multiplicative effect with β -function time course.

Model parameters are chosen to be compatible with the literature, and, in part, by fitting to experimental data.

3. Perspectives

Our model of the retinogeniculate circuit presented here is currently in an early stage of development towards a biologically realistic model of the early visual pathway. We hope to close many of the open issues concerning connectivity, especially of interneurons, the selection of realistic parameter values, interaction between X- and Y-pathways, and feedback from both the perigeniculate nucleus, and cortex, in the foreseeable future.

Once the model has been sufficiently validated against experimental findings, it will be an ideal system for *in silico* experiments exploring the role of particular properties of thalamic circuitry. A feature we consider particularly intriguing is the finding that cholinergic input to interneurons, arising from the brainstem, can shunt triadic input to interneurons (Zhu & Heggelund, 2001). The LGN may thus work in a regime of either localized or globally coupled inhibition to relay cells. We plan to investigate the functional significance of this finding once the model is well established.

References

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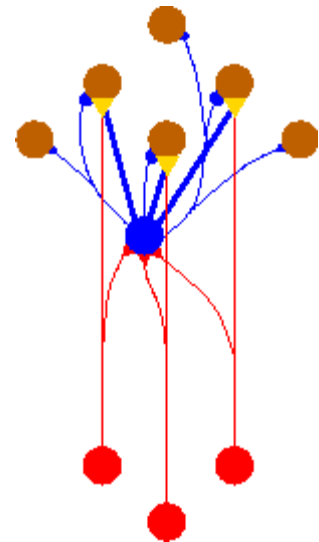


Figure: Network wiring scheme: retinal ganglion cells (red at the bottom) project to geniculate relay cells (brown, top) via triadic synapses (golden triangles), which also connect to interneuron dendrites (thick blue lines). Interneurons are excited by axonal projections from ganglion cells, and inhibit relay cells via axonal projections.