



Mechanistic modeling of the retinogeniculate circuit in cat

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Abstract

An early version of a biologically realistic spike-based model for the X-on pathway of the retinogeniculate circuit is presented. The model comprises feed-forward retinal connections to the lateral geniculate nucleus as well as intrageniculate inhibitory actions from dendro-dendritic structures (triads) and axonal output of interneurons. Neurons are modeled as leaky integrate-and-fire-or-burst neurons. A network model comprising some 100 neurons was implemented using the SYNOD neural network simulator and tested with circular-spot stimuli. Our example simulations were able to reproduce corresponding experimental data. © 2002 Elsevier Science B.V. All rights reserved.

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1. Introduction

A central aim of neuroscience is to understand how individual neurons integrate to form a network, a brain, 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

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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 an early version of a biologically realistic model using spiking neurons of the retinogeniculate circuit in mammals.

2. Model

The current model comprises only the feed-forward connections from retina to the lateral geniculate nucleus (LGN), and is constricted to one pathway, namely the X-on pathway. This is certainly a simplification since it, for example, neglects the feedback from the thalamic reticular nucleus (TRN) and cortex. Still it provides for a model of considerable complexity. We believe that much can be learned from such a simple model before moving on to more realistic systems.

The input layer of our network is a hexagonal grid of retinal ganglion cells [11], which are implemented as stochastic spike-train generators. Each retinal ganglion cell projects to one geniculate relay cell via a triadic synapse [7], i.e., we assume an equal number of ganglion and relay cells (see Fig. 1). Our model also includes thalamic interneurons; in accordance with experimental evidence, we chose the number of interneurons to be one-third as large as the number of relay cells [7]. Each interneuron is thus “surrounded” by three next-neighbor and three second-next-neighbor relay cells. Each interneuron receives excitatory input through conventional synapses from axon collaterals of the retinal ganglion cells at next-neighbor locations, as well as through the triadic synapses at the next-neighbor geniculate relay cells. Interneurons provide inhibitory input to relay cells through normal synapses to both next and second-next-neighbors. In addition, they effect shunting inhibition of excitatory input to the relay cells within the triadic synapses.

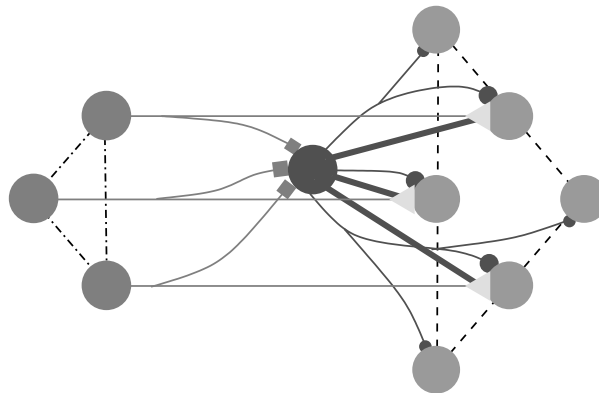


Fig. 1. Structure of the retinogeniculate circuit. Retinal ganglion cells are to the left, geniculate relay cells to the right, with one interneuron in the center. Squares mark excitatory, circle inhibitory synapses, and triangles triads. The thick lines from the triads to the interneuron are dendrites (for details, see text).

The neurons are connected by two types of synapses. Conventional synapses are modeled as injecting a β -function post-synaptic current (PSC) into the target cell. The synaptic current

$$I_{\text{PSC}}(t) = wc(e^{-t/\tau_d} - e^{-t/\tau_r}) \quad (1)$$

is characterized by the rise and decay time constants τ_r and τ_d , and the synaptic weight w . The constant $c = c(\tau_d, \tau_r)$ normalizes the PSC amplitude such that $w = 1$ pA leads to a peak PSC amplitude of 1 pA.

A peculiarity of LGN circuitry are triadic synapses in the X-on pathway [7]. In these triads, excitatory synapses from the ganglion-cell axon to both relay-cell and interneuron dendrite are combined with a dendro-dendritic inhibitory synapse from interneuron to relay cell. The latter effectively shunts the excitatory input to the relay cell [3]. The net input to the relay cell can thus be modeled as

$$I_{\text{triad}}(t) = wcte^{-t/\tau}[1 - s(t - \Delta)]_+, \quad s(t) = s_{\text{max}}(e^{-t/\check{\tau}_d} - e^{-t/\check{\tau}_r}). \quad (2)$$

Here, w and c are again weight and normalization constants, while $\check{\tau}_r$, $\check{\tau}_d$, and τ are, respectively, the rise and decay time constants of the shunting, and the excitatory current decay time; Δ is the shunting delay, and $[x]_+ = (x + |x|)/2$. The effect of triadic excitatory input on the interneuron is modeled via a slow standard synapse, Eq. (1), as this inhibition appears to be mediated by metabotropic receptors [6].

Thalamic neurons respond to tonic input with vigorous bursts of spikes after a period of hyperpolarization, while firing tonically when not hyperpolarized [7]. This feature, which is due to slow, low-threshold Ca^{2+} currents, is implemented compactly in the leaky integrate, fire and burst model (LIFB) due to Rinzel and collaborators [8]. In this model, the membrane potential evolves according to a standard integrator equation which is amended by a T-current term, effecting low-threshold calcium bursts:

$$C\dot{V}(t) = g_{\text{leak}}(V(t) - V_{\text{leak}}) + g_T m_{\infty} h(t) \mathcal{H}(V - V_h)(V(t) - V_T) + I_{\text{in}}(t), \quad (3)$$

where $\mathcal{H}(V - V_h)$ is the Heaviside step function. Activation and inactivation of the T-current are governed by the second state variable $h(t)$, which evolves as

$$\dot{h}(t) = -h/\tau_h^- \quad (V \geq V_h) \quad \text{and} \quad \dot{h}(t) = (1 - h)/\tau_h^+ \quad (V < V_h). \quad (4)$$

When the firing threshold $V(t) = V_{\text{th}}$ is reached, a spike is recorded and the membrane potential reset, $V(t) \rightarrow V_{\text{reset}}$. $I_{\text{in}}(t)$ includes synaptic and external current input. Note that upon firing a spike, only the membrane potential was reset, but neither the slow Ca^{2+} -dynamics described by $h(t)$, nor the synaptic input currents.

3. In silicio experiments

The network model was implemented using the SYNOD neural network simulator [1]. To test the model, we performed in silicio experiments where the network was stimulated with circular spots of light, concentric to the receptive field of the central neuron in the network. In our simulations, the retinal ganglion and the thalamic relay

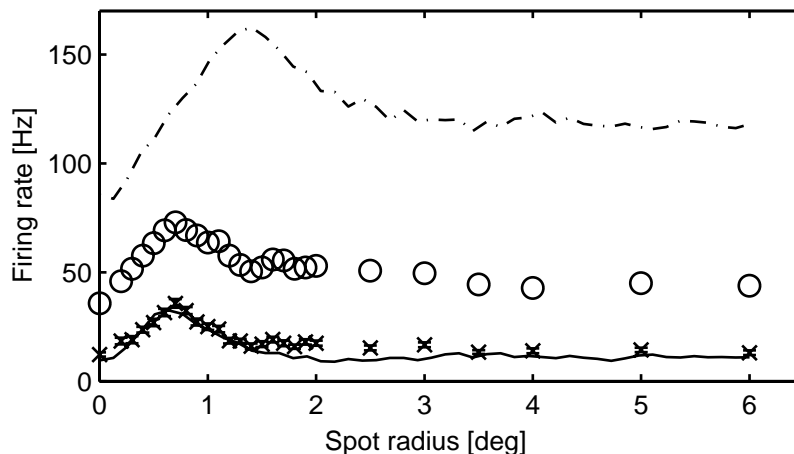


Fig. 2. Response of a geniculate relay cell to concentric light spots of varying diameter. Crosses mark experimental data as described in Ref. [5], the solid line simulation results. Circles show activity of the corresponding retinal ganglion cell (experimental data, error smaller than symbols). The dash-dotted line shows the activity of the central interneuron in the simulation; no corresponding experimental data is available.

cell layers each included 43 neurons, while the interneuron layer contained 9 cells. Ganglion-cell activity was modeled as a I -process with firing rates estimated from a rate-based, linear model [2,10]. Responses of the central neuron in the network were fit to responses measured extracellularly in X-on cells of cat LGN, as shown in Fig. 2. The fit is a least-mean squares fit obtained using the Nelder–Mead algorithm [9]. The model is thus able to reasonably reproduce these *in vivo* experimental data; see Ref. [5] for a detailed description of the experimental data and procedures.

4. Discussion

The model presented here is in an early stage of development, but our example results shown in Fig. 2 demonstrate its ability to reproduce *in vivo* extracellular relay-cell recordings in cat following stimulations with spot stimuli. The model—with the present choice of parameter values—also accounts for the experimentally observed larger interneuron receptive field size, i.e., the spot radius for which the interneuron firing rate is maximal in Fig. 2, as discussed in Ref. [2]. The observed higher interneuron firing rate, as compared to relay cells, is in qualitative agreement with experimental findings [4] (even though this effect appears exaggerated with the current model parameters).

Model simulations are technically straightforward thanks to the SYNOD network simulator. Biological realism is far more difficult to attain, and the major challenge is to constrain the structure and ranges of parameter values using available experimental findings. Among the problems and refinements we intend to pursue are: (i) The exact hexagonal symmetry imposed on neuronal connections is implausible; better models will require more detailed knowledge of wiring patterns in the LGN, in particular those

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