Feed-forward inhibition in the visual thalamus

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Abstract

Based on recently available anatomical and physiological data, we propose a specific pattern of connectivity between relay and local interneuron cells in the lateral geniculate nucleus of the cat that can serve a more complex role in visual information processing than simply sharpen the receptive fields of relay cells. We treat a thalamic network composed of biophysical models of relay and interneuron cells receiving their input from partially overlapping retinal ON and OFF receptive field groups. A mechanism is proposed through which parallel processing and lateral inhibition in the forward direction can enhance spatial resolution at the thalamic level. © 2002 Elsevier Science B.V. All rights reserved.

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1. Introduction

The receptive field centers of retinal ganglion cells are defined from interactions between their dendritic tree and bipolar cell axons [1]. Therefore, although same type retinal ganglion cells are anatomically evenly spaced [17], their receptive fields overlap in various proportions. A coverage factor ranging between 7 and 10 was estimated for X ganglion cells, the cells responsible for high-acuity vision, in most parts of the cat retina. In the area centralis, the area of sharpest vision, this number increases up to 30 [16]. This extensive overlap gave rise to a recent debate between multineuronal coding [13] and individual cell coding theories [14]. In either case, given the topological organization of the retina, a “cross-talk” response from adjacent receptive fields would cause a loss of spatial resolution in the retinal output. Considering the dense tiling of X cells, such a response can result from the fact that receptive field surrounds, being wider, include receptive field centers of adjacent cells.

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The lamina A or A1 of the dorsal lateral geniculate nucleus (dLGN) in the thalamus, where almost all X retinal ganglion (RG) cells project to, is the next node of visual processing. Retinal axons provide the driving input to both intrageniculate cellular types, namely geniculate relay cells (RE) and local interneurons (LI). The pattern of connectivity between these cells remains unclear. Based on physiological and anatomical studies several models have been proposed [6,19,21,24]. It is now generally believed that local interneurons exert feed-forward inhibition on relay cells. A minor role, that of sharpening the receptive fields of RE cells, has been attributed to this feed-forward mechanism. However, recent studies have significantly increased our knowledge on local interneurons which exhibit a wide range of behavioral responses depending on their state [4,23]. The aim of the present study is to propose a specific pattern of connectivity and a possible role for the thalamic feed-forward inhibition in resolving the problem of loss of spatial resolution in the retinal output signal.

2. Simulation methods

2.1. Retinal ganglion cells stratification

To study multiple overlapping receptive fields sharing a common stimulus we have introduced a normalized parameter, the overlap factor (OF), to determine the extent of their overlap. For two equal and circular receptive fields, OF is defined as follows:

\[ OF = 1 - \frac{d_c}{D_r}, \]

where \( d_c \) is the distance between the central points of the receptive fields and \( D_r \) their diameter.

Receptive fields with

\[ d_c < D_r \]

overlap. An OF value of zero indicates no overlap, while a value of one denotes fully overlapping receptive fields. A schematic representation is given in Fig. 1.

![Fig. 1. Two equal, circular, overlapping receptive field groups, c and a. The diameter of c \( D_c \) and the distance between their centers \( d_c \) are represented by dashed lines. Light stimulus (small white circle) acts on the center of group c and simultaneously on the surround of group a.](image-url)
2.2. Retinal output

The simulation of retinal output was achieved through the following procedure: Two groups of receptive fields were positioned in the plane at some distance determined by their OF. The response of each receptive field group was calculated by the integral over space and time for a flashing spot of diameter $D_d$ at the center of one of the receptive field groups.

The spatial response of retinal receptive fields was described as the sum of two Gaussians. The ratio between the diameter of the receptive field center and the diameter of its surround was 1:3. The temporal response was estimated as the sum of a transient exponential-like decay plus a sustained component. The sustained component, representing the maintained activity of RG cells, had a higher value for ON than for OFF cells. The discharge rate function of each RG cell has been estimated as the integral of its response over the stimulus duration and size [18].

The transformation of the discharge rate function into a point process was achieved through a gamma renewal process with different statistics for the transient and the sustained components. An order of 5 was used during transient activity whereas an order of 1 (Poisson process) during maintained activity [7].

2.3. Thalamic model

A network composed of RE and LI cells was constructed to test our hypothesis. Each neuron was simulated as a single uniform compartment, incorporating various ionic currents described by a Hodgkin-Huxley-type formalism.

The RE model is derived from that developed by Huguenard and McCormick [10], and McCormick and Huguenard [11]. The LI model is a modified version of the model developed by Zhu et al. [25]. The principal equations describing the change in membrane potential ($V$) of the RE and LI cells, were

$$C_m \frac{dV}{dt} = -I_{\text{K Leak}} - I_{\text{Na Leak}} - I_T - I_L - I_{K2} - I_C - I_A - I_h - I_{Na} - I_{Nap} - I_{\text{GABA}(A)} - I_{\text{GABA}(B)} - I_{\text{AMPA}}$$

and

$$C_m \frac{dV}{dt} = -I_{\text{Leak}} - I_{Tli} - I_L - I_{K} - I_h - I_{A} - I_{\text{CAN}} - I_{\text{AHP}} - I_{Na} - I_{Nap} - I_{\text{GABA}(A)} - I_{\text{GABA}(B)} - I_{\text{AMPA}},$$

respectively.

The specific membrane capacitance ($C_m$) was set to 1 $\mu$F/cm$^2$ for both cell types. $I_{\text{Leak}}$, $I_{K\text{Leak}}$ and $I_{Na\text{leak}}$ are leak currents, $I_T$ ($I_{Tli}$ for LI cells) and $I_L$ are the low- and high-threshold calcium (Ca$^{2+}$) currents, $I_K$, $I_{K2}$ an $I_A$ slow potassium (K$^+$) currents, $I_C$ and $I_{AHP}$ are Ca$^{2+}$-activated K$^+$ currents, $I_{\text{CAN}}$ is a Ca$^{2+}$-activated cation current, $I_h$ is the hyperpolarization activated cation current, and $I_{Na}$ and $I_{Nap}$ are the transient and persistent sodium (Na$^+$) currents. The total membrane area was 29,000 $\mu$m$^2$ for RE cells and 10,000 $\mu$m$^2$ for LI cells.
Retinal input activated (α)-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (AMPA) receptors on RE and LI cells. Each RE and LI cell received inhibition via γ-aminobutyric acid receptors (GABA_A and GABA_B) from each adjacent interneuron. Synaptic currents, for AMPA and GABA receptors, were modelled by the same kinetic scheme used for active currents. Transmitter was released in pulses of fixed duration and concentration for simplicity [5]. Larger neurotransmitter concentration in the synaptic cleft was needed to activate GABA_B than GABA_A receptors.

The simulation program was written in C.

3. Results

3.1. Thalamic model cells

The single compartmental model used for RE cells proved to be sufficient in replicating their basic electrophysiological properties, namely rebound low-threshold calcium spike underlying burst discharges, a delayed onset to firing during depolarization and a general lack of pronounced spike frequency accommodation [12]. Local interneurons are much less studied than the RE cells mainly due to experimental difficulties. The classical view is that they fire action potentials which are on the average shorter in duration than those of RE cells, lack a delayed onset to firing and have higher input resistance [12]. Their most significant feature is that a regenerative calcium response, caused by the low-threshold calcium current $I_T$, is prevented by its interplay with the A-type potassium current, $I_A$ [15]. Therefore, burst discharges are not observed following hyperpolarization. The interneuron’s intrinsic current orchestra has been described and modelled [25], but the $I_A$ current was absent from that study. We have added an A-type conductance to prevent rebound bursting. Depending on the conductance values of the various ionic currents incorporated, the cell could also exhibit bursting and oscillating behavior.

3.2. dLGN model

The direct excitatory pathway from RG cells to geniculate relay cells has been described in earlier studies [2]. Each RE cell receives all of its retinal input from one to five RG cell of the same type (ON or OFF center). Thus, the receptive field of RE cells is nearly (but not entirely) identical to that of their retinal input cells and we can speak of X ON and OFF center RE cells. RE cells are also subjected to a large number of modulatory inputs from cortical feedback, brainstem structures, and perigeniculate cells. The rest of the synapses derive from feed-forward inhibition exerted by local geniculate interneurons [22]. The anatomical details of this intrageniculate circuit are much less elucidated than those of the direct excitatory pathway [9]. Both antagonistic (from RG ON cells to RE OFF cells and from RG OFF to RE ON) and synergetic (from RG ON cells to RE ON cells and from RG OFF to RE OFF) inhibitions have been experimentally demonstrated [20]. Furthermore, local interneurons form mutual inhibitory connections [8,22].
Fig. 2. Network architecture. Circles represent cells at the retinal (row RG) and thalamic level (rows LI for local interneurons and RE for relay cells). Columns represent X-ON and X-OFF pathways alternatively. In the two middle columns, cells ascribed as ONc and OFFc, belong to the retinal receptive field c. OFFa represents the X OFF cell of group a and ONa its X ON cell. Arrow head lines represent anatomical connections. RG cells are excitatory whereas LI cells are inhibitory.

Based on the above anatomical and physiological data we propose the following connectivity: each geniculate X cell and a local interneuron close by, receive their retinal input from a group of RG cells of the same type (ON or OFF) via AMPA receptors. The LI cell makes synaptic contacts with all adjacent LI and RE cells via GABA_A receptors forming the mutual inhibition among interneurons and the antagonistic and synergetic inhibition exerted on X RE cells. This model is depicted in Fig. 2 for the receptive field groups of Fig. 1, c and a. Each receptive field group might contain several largely overlapping RG ON and RG OFF receptive fields which are clustered into its ON and OFF pathways (ONc, OFFc for group c; ONa, OFFa for group a).

3.3. Model performance

In order to demonstrate the effects of such a configuration in the retinal visual signal processing we consider two receptive field groups (Fig. 1) with OF = 0.61. Receptive field group c is stimulated by a light disk (white spot), equal in size with the group’s center. The disk flashed on and off 100 times and the average response rate (spikes/bin) of each cell type was measured.

In row RG of Fig. 3, the response of RG cells is depicted for such a case. The RG ONc cell responds with a high-frequency discharge during light stimulation (bar) and transmits information to the visual cortex through the thalamus and its corresponding RE cell. The RG OFFc cell responds in the same way soon after light stimulation is switched off. However, during light stimulation, the RG OFFa cell also responds, with a lower discharge rate, since it is stimulated on its receptive field surround. The same holds for the RG ONa cell in respect to the RG OFFc cell at the stimulus offset.

At the thalamic level, and thanks to the lateral inhibition exerted from LI cells, the only RE cell to be active during light stimulation is the RE ONc cell. Furthermore, spontaneous firing normally occurring at RG cells and constituting the background noise
The effect of feed-forward inhibition. The same notation as in previous figures is used. The first row represents the activity of RG cells. The firing rate of ONc and OFFa cells increased during the stimulus (horizontal bar) while the firing rate of OFFc and ONa increased at the stimulus offset. Note at the third row, which represents the RE cells activity that the only cell firing during the stimulus is the ONc cell, although at lower rates than its corresponding RG cell while the only cell transmitting information at the offset of the stimulus is the OFFc cell. OF = 0.61. Ordinate: mean number of spikes over 100 trials; abscissa: time, horizontal bar: 600 ms, bin size: 100 ms.

has been attenuated at the thalamic level. This comes in agreement with experimental results demonstrating lower levels of spontaneous and evoked activity in RE cells than their corresponding RG cells [3].

An evaluation of our model in respect to other possible configurations is presented in Fig. 4. Different network architectures are represented at the right side of each row. The performance comparison was made in terms of the shape of the response and of the spike number difference between competitive pathways (ONc–OFFa and OFFc–ONa). In row 1 the possibility that retinal input is able to activate both GABA_A and GABA_B receptors is examined. It has been argued that only GABA_A receptors are active during wakefulness [23], but no direct experimental evidence exists to support this view. Here, we show that when GABA_B receptors are participating in the inhibitory mechanism the performance of the model is poorer (compare row RE of Fig. 3 with row 1 of Fig. 4). Activation of GABA_B receptors caused a long-lasting inhibition at the end of which rebound bursting of RE cells could not be prevented. This activation is responsible for the lower performance of this configuration. In the case of absence of mutual inhibition (row 2 of Fig. 4), competitive interneurons were active as long as their associate RG cells, exerting inhibition on adjacent RE cells. This inhibition had the dramatic effects shown in row 2, where almost no cell is distinguishable from the others. At the absence of functional interneurons (row 3 of Fig. 4) we simply did not get any amelioration of spatial resolution with respect to the RG cells layer.

The proposed architecture is able to discriminate signals arriving from adjacent receptive field groups with overlapping factors up to 0.77 (results not shown). It is important to note that in all OF levels examined, the best performance was achieved by the network architecture of Fig. 2.

We propose that the following sequence of events occurs. RG cells, once stimulated, transmit their signal to RE and LI cells in the thalamus. As soon as the signal arrives
at LI cells, a “competition” starts among them by means of mutual inhibition. The interneuron receiving the signal with the higher frequency will first cease the activity of all adjacent RE and LI cells during the stimulus period and its associate RE cell will be the only cell to transmit information to the cortex without any inhibition from neighbor LI cells. A switch in the firing frequency of RG cells, thanks to a similar cascade of phenomena as the ones described above, will help another RE cell to differentiate from all others.

4. Discussion

The present study considers a flashing light spot stimulating overlapping receptive field groups. We chose to consider this case because a plethora of experimental demonstrations exist on the effect of such stimuli on receptive fields. Although it might seem a very simple case, it captures an essential task attributed to the non-lagged X-cell pathway: that of spatial resolution. A thalamic model with a specific pattern of connectivity between LI and RE cells was treated, able to discriminate receptive fields from adjacent overlapping ones. An important aspect of this model proved to be the mutual inhibition among interneurons. Finally, we wish to stress that the mechanism described above occurs before any feed-back inhibition from perigeniculate cells or excitatory feed-back from the cortex takes place. Therefore it provides a fast, forward mechanism for spatial resolution enhancement and noise attenuation which can act as a substrate for further modifications exerted by feed-back mechanisms.
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References

