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Neurocomputing 38–40 (2001) 659–665

NEUROCOMPUTING

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A biophysically realistic simulation of the vertebrate retina

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Abstract

Retinal ganglion cells can be classified as ON, OFF, X- and Y-cells which exhibit different temporal and spatial properties. While X-cells respond with a small transient at stimulus onset and a strong sustained component, Y-cells show a strong transient response. In this work, simulation results from a biological highly realistic model of the retina are presented that could explain the origins of these findings. The general purpose of the model is (1) to study functional aspects of different connection patterns and (2) to generate a realistic spike output that could be used as afferent input for models of higher vision. © 2001 Published by Elsevier Science B.V.

Keywords: Computational model; Retina; Ganglion cell; Photoreceptor

1. Introduction

The retina is the first stage of visual information processing. Even though it is an extensively studied neural structure its functional aspects are not yet fully understood.

The vertebrate retina is organised in layers, each containing special cell types. The information flow starts at the photoreceptors where the light is translated into electrical signals. The photoreceptors are connected to bipolar cells, which themselves are connected to the ganglion cells. Ganglion cells, the output elements of the retina, transform the graded electrical potential into spike trains which are sent to central visual areas via the optic nerve.

Parallel to this feed-forward pathway two lateral cell layers exist. In the outer retina the horizontal cells build a layer of lateral interneurons, providing negative feedback to the photoreceptors and generating the antagonistic centre-surround receptive fields

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0925-2312/01/$ - see front matter © 2001 Published by Elsevier Science B.V.
PII: S0925-2312(01)00426-X

of the bipolar cells. In the inner retina a great diversity of amacrine cells are responsible for lateral interaction. There might exist up to 40 different types of amacrine cells and their functional roles still remain an unsettled question [9].

Apart from the anatomical findings, retinal cells can be subdivided into several functional classes. Bipolar and ganglion cells can be subdivided into on-centre (ON) and off-centre (OFF) cells. Ganglion cells can be further divided into X- and Y-cells. Both show some kind of non-linear luminance response characteristic expressed by a transient response overshoot at light on- and offsets. However, X-cells show a more sustained behaviour and posses a smaller receptive field than Y-cells with almost linear spatial contrast integration, while Y-cells show also spatial non-linearities [1].

An important question is how this non-linearity is generated in the retina. Starting from recent evidence that X- and Y-cells seem to have equivalent intrinsic properties [2], it is not likely that there is a special neural property in Y-cells that generates non-linear responses, more likely would be a different wiring pattern.

This work presents a computer simulation of the vertebrate retina with high biological realism that could be used to study the wiring and function of the retina. It gives a brief overview of the simulator and shows results that could explain the tonic and phasic behaviour of X- and Y-ganglion cells, respectively.

2. The model retina

The model of the retina consists of single cell units that are assembled in layers, as explained in the previous chapter. The activity of each cell type is calculated by solving differential equations. To match the model to physiological data, mainly experimental data from primates was taken into account, although there do not seem to be significant differences among other vertebrate studies. No colour vision was implemented, only luminance distributions were used as stimuli.

2.1. The photoreceptor

A close look at the properties of photoreceptors shows that their response already provides important aspects of the visual response of retinal ganglion cells like saturation and adaptation. For this reason the model of the photoreceptor was designed to realistically simulate the temporal characteristics of the voltage hyperpolarization to light stimuli. The temporal responses of vertebrate photoreceptors show an initial hyperpolarising transient at stimulus onset followed by a sustained component until the stimulus is turned off [7]. When the stimulation ends, a small depolarising transient is observed. The model is based on the biochemical processes in photoreceptors. The basic processes involved in phototransduction are summarised in [5,6]. Light transduction takes place via an enzymic cascade: photons activate rhodopsin which in turn activates the GTP binding protein transducin, then transducin activates the phosphodiesterase (PDE). This amplification cascade is calculated

by a low-pass filtering of the stimulus $S(t)$. The concentration of activated PDE is expressed by

$$\frac{\mathrm{d}[PDE](t)}{\mathrm{d}t} = \frac{1}{\tau_{PDE}}(A_S S(t) - [PDE](t)), \tag{1}$$

where τ_{PDE} is a time constant and A_S an amplification factor. PDE hydrolyses the enzyme cyclic guanosine monophosphate (cGMP), this step is described by

$$\frac{\mathrm{d}[\mathrm{cGMP}](t)}{\mathrm{d}t} = -\beta([\mathrm{Ca}](t) - 1) - a_G[PDE](t)[\mathrm{cGMP}](t), \tag{2}$$

where a_G is an amplification factor and β a constant. The drop of the cGMP concentration leads to a closure of membrane bound cation channels. These channels regulate the flow of Na^+ and Ca^{2+} into the cell. Here, only the change of the concentration of Ca^{2+} was simulated, because this ion acts as a second messenger and regulates the re-synthesis of cGMP via the enzyme guanylylcyclase (GC). The concentration of intracellular Ca^{2+} is calculated by

$$\frac{\mathrm{d}[\mathrm{Ca}](t)}{\mathrm{d}t} = \gamma(1 + c([\mathrm{cGMP}](t) - 1)) - \alpha[\mathrm{Ca}](t), \tag{3}$$

where α, γ and c are constants. The coupling of the two messengers in this cycle, cGMP and Ca^{2+} by the enzyme GC is expressed by the factor β in Eq. (2).

Voltage clamp experiments suggest that the initial transient is enhanced by a rectified depolarising current, namely the I_h current [3], that gets activated when the photoreceptor is hyperpolarised. This is a non-linear voltage dependent current that is modelled by

$$\frac{\mathrm{d}I_h(t)}{\mathrm{d}t} = \frac{1 - I_h(t)}{\mathrm{e}^{(V_P(t) + A_I)S_I} + 1} - \delta_I I_h(t), \tag{4}$$

where $V_P(t)$ is the potential of the cell and A_I and S_I are constants that characterise the sigmoidal function and δ_I is a decay rate. Finally, the potential V_P of the cell is calculated by

$$\frac{\mathrm{d}V_P(t)}{\mathrm{d}t} = \frac{q_P}{C_P}\frac{\mathrm{d}[\mathrm{Ca}](t)}{\mathrm{d}t} + \frac{q_I}{C_I}\frac{\mathrm{d}I_h(t)}{\mathrm{d}t}, \tag{5}$$

where q_P, C_P, q_I and C_I are constants. The responses of a single photoreceptor to different stimulus intensities are plotted in Fig. 1A. Fig. 1B shows that the saturation characteristics to high stimulus intensities are in good agreement with the Michaelis–Menten function, as shown by Schneeweis and Schnapf [8].

2.2. Models of horizontal, bipolar and ganglion cells and the spike encoder

The remaining cells were implemented as digital filter equations. The horizontal cell acts as a simple low pass filter of the incoming signals from the photoreceptors. The

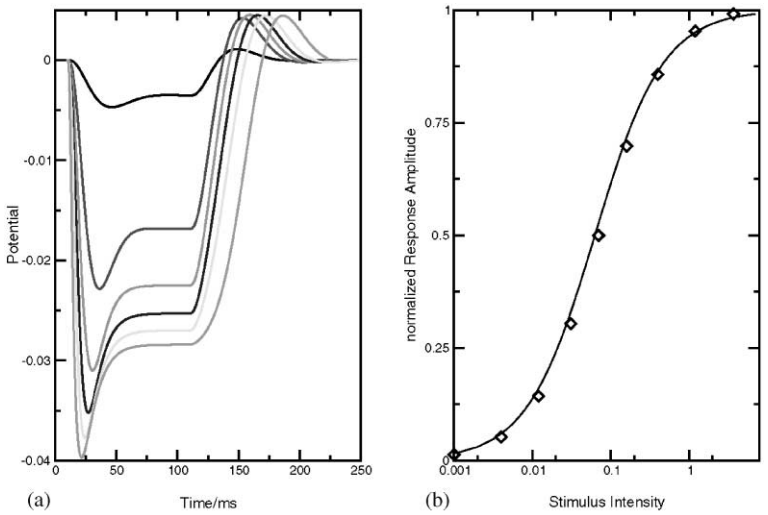

Fig. 1. (A) Responses of the simulated photoreceptor to different stimulus intensities. (B) Response amplitude of the simulated photoreceptor in dependence of the stimulus intensity. The straight line is a fit with the Michaelis Menten function.

ON- and OFF-bipolar cell acts as a PD filter combined with a low pass filter, ensuring that it responds in a transient fashion. Different types of amacrine cells were implemented, but here only results are shown that involve low pass filtering amacrine cells. The ganglion cells convert the analogue signals they receive into spikes. First the incoming signals from the bipolar cells are summed up according to their receptive field characteristics (see below) and then fed into the spike generator.

2.3. Layer and circuit structure of the model

The simulated cells are arranged in a regular hexagonal layer. Thus each cell has six nearest neighbours. Each photoreceptor has excitatory connections to the six nearest horizontal cells and to an ON-bipolar cell and an inhibitory connection to an OFF-bipolar cell. The horizontal cells are connected mutually as a syncytium with a wide receptive field and provide inhibitory feedback to the neighbouring photoreceptors and additionally connect to the nearest bipolar cells to create their centre-surround antagonism. Bipolar cells in turn provide the input for the ganglion cells.

Ganglion cells receive their input from the bipolar cells. According to the Difference of Gaussians model cells, the centre of their receptive field is mediated by bipolar cells of the same type (ON or OFF) and the surround by bipolar cells of the opposite type (OFF or ON) as the ganglion cell.

A general feature of Y-cells, compared to X-cells, is their larger receptive field [4]. Thus, in these simulations, the centre of a X-cell gets input from one bipolar cell and

the surround from seven bipolar cells. A Y-cell in turn has a centre of seven and a surround of 19 bipolar cells. These ratios result from the hexagonal spatial arrangement of the cells.

2.4. Responses of the ganglion cells

Fig. 2 shows the responses of simulated X- and Y-ganglion cells while stimulated by a spot of light. Three different spot sizes were used.

The upper two rows show responses assuming the classic Difference of Gaussians model as described above. As expected, X-cells respond maximally to the stimulus that only covers the centre of their receptive field. Y-cells, in turn, respond stronger to a wider stimulus. The source of the temporal shape of the responses, which consists of an initial transient, followed by a sustained part, already lies in the shape of the photoreceptor response. In general, Y-cells show a weaker response, this is due to the stronger lateral inhibition they receive from the horizontal cells because of their larger receptive field. These findings already suggest that a simple description of the

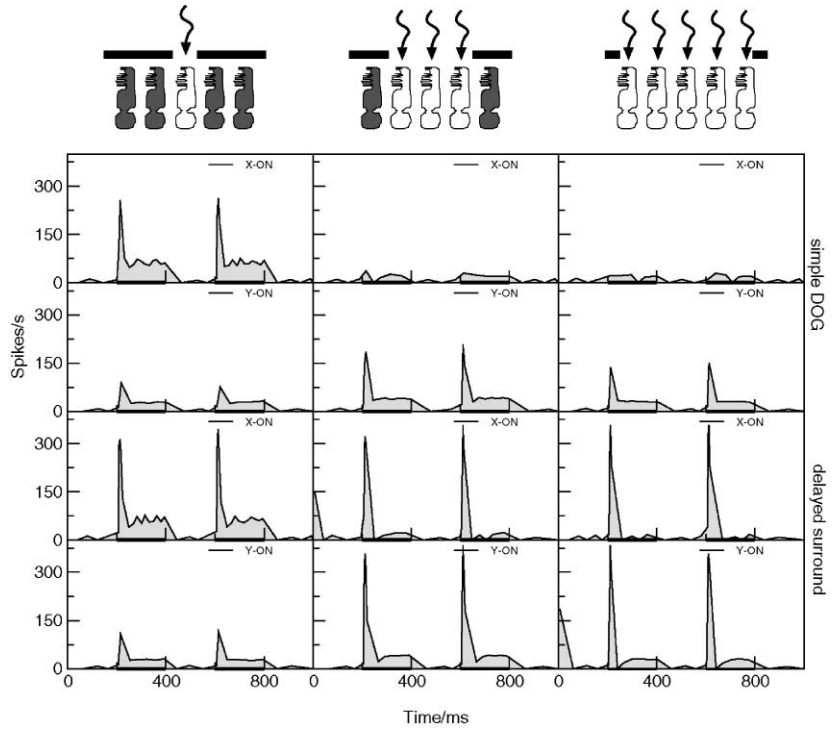

Fig. 2. Firing rates of simulated X- (first and third row) and Y-ganglion cells (second and fourth row) responding to different spot sizes (sketched above). In the upper two rows no temporal difference between the centre and the surround of the receptive field exists while in the lower two rows the surround is delayed relative to the centre.

receptive field of ganglion cells by a Difference of Gaussians model is probably not sufficient in all cases, rather the receptive field of the bipolar cells must be taken into account.

In the lower two rows of Fig. 2 responses of simulated ganglion cells are shown with the surround of their receptive fields delayed relative to the centre. This leads to a strong initial transient at light onset even in the cases where the receptive field is fully stimulated, because the inhibitory effect of the surround sets in later. This mechanism could explain the more phasic behaviour of Y-cells, compared to the tonic X-cells. In the simulation, the delay was achieved by transmitting the signals to the surround of the receptive field via amacrine cells, that were implemented as low pass filters. In this case, the surround of the receptive field could be generated by bipolar cells of the same type as the bipolar cells feeding into the centre of the receptive field as an inhibitory interneuron exists that could invert the signals from the bipolar cells. In this case, when the ON- and OFF-channels are fully seperated, these interneurons are required because bipolar cells only release the excitatory neurotransmitter glutamate. Thus, a bipolar cell cannot establish sign-inverting connections to other cells.

3. Conclusions

Summarising, the proposed model is capable to produce realistic spike output patterns for X- and Y-type ganglion cells. An important feature of the model is its simplicity as the single cells were simulated by simple low pass filtering of the signals. More simulations have been carried out proving that this simple approach is sufficient to reproduce a lot of experimental data.

The model provides a framework to study different connection patterns in order to explain the functional properties of the retina. Future work will be carried out to analyse the temporal and spatial non-linearities observed in the responses of Y-ganglion cells. It might also be used to provide more realistic spike patterns as afferent input for models of higher visual areas like the LGN.

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