Visual processing: **The Devil is in the details**

Guilherme Neves and Leon Lagnado

Ganglion cells convey information from the retina back to the brain. Recent experiments have examined how ganglion cell receptive fields are assembled from many incoming signals.

Address: MRC Laboratory of Molecular Biology, Hills Road, Cambridge CB2 2QH, UK.
E-mail: ll1@mrc-lmb.cam.ac.uk

Current Biology 2000, 10:R896–R898

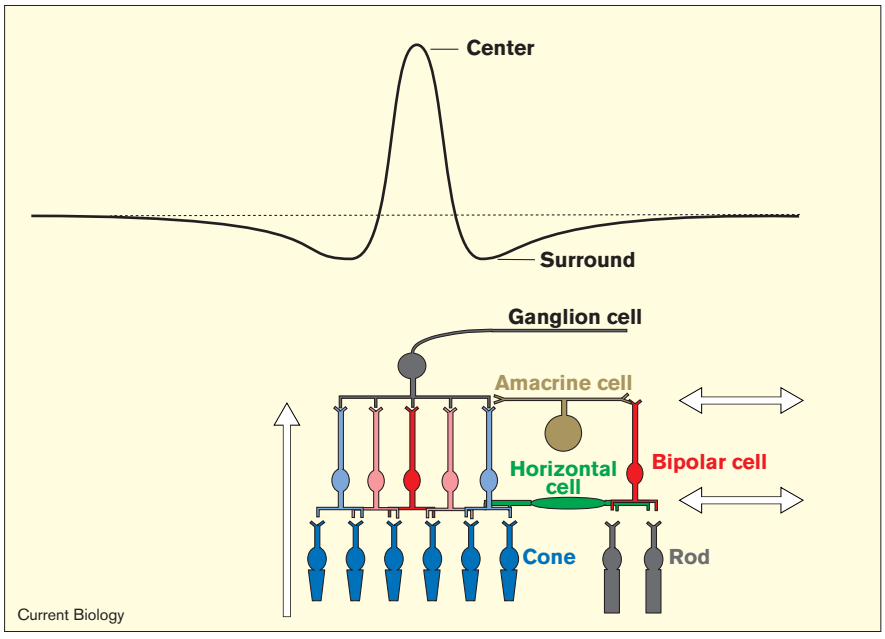
0960-9822/00/$ – see front matter

In any neural circuit, some neurons will receive signals from many others. To understand how this converging information is processed, we must measure how the electrical activity of such a neuron is affected by its various inputs. The vertebrate retina provides an excellent example in which to address this type of question [1,2]. In our retina, light is converted into an electrical signal by 125 million photoreceptors — rods and cones — but only 1 million ganglion cells carry the visual signal back to the brain. Most ganglion cells therefore receive signals from a large number of photoreceptors, although for each ganglion cell these receptors will be localized to a small patch of the retina. As a result, the ganglion cell will only respond to light falling on that area — its receptive field. Two recent studies [3,4] have provided fascinating insights into how the receptive fields of a ganglion cell is assembled from the many incoming signals.

The most direct pathway by which a visual signal is transmitted through the retina is from the rod and cone photoreceptors to bipolar cells to ganglion cells (Figure 1). Horizontal cells send inhibitory signals that modulate signal transfer from photoreceptors to bipolar cells, and amacrine cells modulate transmission from bipolar cells to ganglion cells (for further background on the function of the retina, see [1,2]). The job of the retina is to extract information about basic features of the visual world, such as light intensity, contrast, colour and motion. Different classes of ganglion cell are specialized to represent these different aspects of the visual stimulus, and the information is contained in the series of action potentials that they transmit along the optic nerve.

Steven Kuffler [5] and Horace Barlow [6] were among the first to investigate the receptive fields of ganglion cells. They demonstrated that the frequency of action potentials fired by a ganglion cell only changes when light is shone onto a restricted region of the retina. They mapped out these receptive fields using small spots of light, and found that they varied in size from a few tens to hundreds of microns. From these early studies it was clear that the sensitivity to light was not uniform across the whole receptive

Figure 1



Wiring a ganglion cell receptive field. The upper part of the diagram shows an idealized 'Mexican hat' profile for an ON ganglion cell. The lower part shows a simplified model of the connections generating the receptive field center. The ganglion cell collects signals from many cone photoreceptors. These signals do not arrive directly, but through bipolar cells which synapse at various sites on the dendritic tree. Signals from rods reach ganglion cells by a more complicated pathway that involves amacrine cells. The sensitivity profile falls off because synaptic currents injected further out in the dendritic arbour have less influence on the membrane potential at the cell body (the part of the cell that generates the action potentials which travel along the optic nerve back to the brain). Bipolar cells that have less influence on the response of this ganglion cell are coloured dimly. Note that inhibitory signals also travel laterally in the retina, through horizontal cells and amacrine cells.

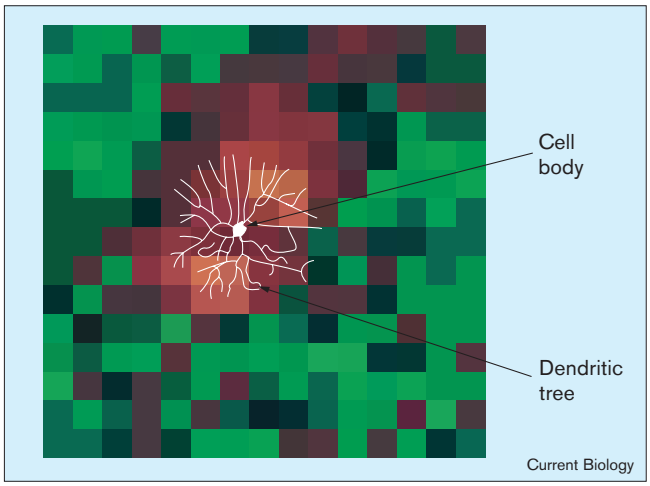
field. Most obviously, the central region and surround generate antagonistic responses [1,2]. For instance, 'ON' ganglion cells are excited by light in the center and inhibited by light in the surround, whereas 'OFF' ganglion cells are inhibited by light in the center and excited by light in the surround. More subtlely, the sensitivity of the receptive field center gradually falls as the spot is moved towards the edge.

Since the 1960s, the sensitivity profile of individual ganglion cells has often been described as a 'Mexican hat' (Figure 1), and this model has been very successful in accounting for many aspects of ganglion cell responses [7]. The gradual fall in sensitivity moving away from the peak does not reflect differences in the properties of the receptors. All rods have the same intrinsic sensitivity to light, as do each of the three classes of cone (red, green and blue). Rather, the central peak in the receptive field reflects the stronger weighting of the input originating from photoreceptors in that area. In other words, bipolar cells that collect the signals from central photoreceptors have a stronger influence on the activity of the ganglion cell than those that collect signals from the edge (Figure 1). It has generally been thought that the weighting of the synaptic input from a bipolar cell depends where the connection is made with the dendritic tree of the ganglion cell. The action potential generated by a ganglion cell originates in the cell body, so synaptic inputs close to the cell body are expected to have a strong influence on the firing rate. Synaptic connections from bipolar cells distant from the cell body are expected to have less influence because the voltage signal that they generate will be attenuated as it spreads along the dendritic tree to the cell body.

More recent methods of measuring receptive fields are based on the use of computers [8]. A checkerboard pattern on a monitor is projected onto the retina, and each square of the checkerboard is randomly altered at frequencies up to 70 Hz. The experimenter looking at the monitor is likely to get a headache, but ganglion cells see patterns. These patterns are calculated after the experiment by comparing the train of action potentials with the 'movie' that the ganglion cell had been viewing, and calculating what, on average, it saw before it fired a spike. This averaged movie is called the 'spike-triggered average'. For ON ganglion cells, the spike-triggered average will show an area that is dark and becomes bright just before the spike. For OFF ganglion cells, the spike-triggered average will show an area that starts bright and turns dark. A snapshot from the spike-triggered average of an OFF cell is shown in Figure 2.

Brown *et al.* [3] used the spike-triggered average to map the receptive fields of ganglion cells in the retina of rabbits. After recording spikes evoked by the stimulus, they injected the cell with a fluorescent dye, Lucifer Yellow,

Figure 2



Comparison of the receptive field and dendritic tree of an OFF ganglion cell in the rabbit retina. The checkerboard shows the average stimulus on the computer monitor 58 ms before the ganglion cell fired a spike. The dendritic tree is shown in white. Red regions stimulate rod photoreceptors less effectively, so this is an OFF cell. Note that the receptive field has two peaks of sensitivity, both displaced from the cell body. (Adapted from [3].)

and photographed the dendritic tree. Two basic findings demonstrated that the simple scheme shown in Figure 1 is not the whole story. First, only 40% of cells had a receptive field that could be described with the standard dome-shaped center. All these cells had small receptive fields, 100–400 μm in diameter. In contrast, the large receptive fields were irregular in shape, often elongated with more than one peak of sensitivity. An example of an irregular receptive field is shown in Figure 2. Second, in only three out of twenty one cells did the position of peak sensitivity coincide with the cell body. Again, all these cells had small receptive fields. For ganglion cells with large receptive fields, the sensitivity over the cell body could be up to 30% less than the peak.

In general, the photoreceptors are distributed uniformly over the large ganglion cell receptive fields, so what causes the irregular sensitivity profile? Brown *et al.* [3] considered two main possibilities: irregularities in the density of ganglion cell dendrites that receive synaptic inputs, or variations in the probability that a bipolar cell makes contact with the dendrites of an underlying ganglion cell. The first possibility might predict that areas of peak sensitivity correlate with areas where the dendritic tree was densest, but several examples were found where ganglion cells with radially symmetric dendritic arbours had asymmetric receptive fields. One of these examples is shown in Figure 2. The authors favour the possibility that there are irregularities in the distribution of synaptic contacts between the terminals of bipolar cells and the dendrites of these large

ganglion cells. For instance, anatomical measurements indicate that the cell body and nearby dendrites receive very small numbers of synaptic inputs from bipolar cells.

The study by Chichilnisky and Baylor [4] goes one step back in the retinal circuit to analyse the impact of single cone photoreceptors on the receptive field of colour-sensitive ganglion cells. Instead of recording from ganglion cells one at a time, they placed isolated pieces of monkey retina on a multielectrode array to record from a large number of ganglion cells simultaneously [8]. The authors concentrated on 'BY' cells, which are excited by blue light and inhibited by yellow. BY cells collect excitatory signals from ON bipolar cells that connect exclusively to blue cones, and inhibitory signals from OFF bipolar cells that connect to both red and green cones. When receptive fields were mapped with stimuli designed to excite the blue cones selectively, several highly localized peaks of sensitivity were revealed. These peaks reflected the positions of single blue cones, because their spacing was very similar to the spacing of blue cones measured anatomically. Between two and eleven cone inputs contributed to the receptive fields of a BY cell.

Chichilnisky and Baylor [4] found that a single blue cone could contribute to the receptive field of more than one BY cell, causing receptive fields to overlap. The influence of a given blue cone, however, was not the same for all the BY cells it sent signals to, demonstrating that the strength of the synaptic connections from that cone were not constant. The strength of the various blue-cone inputs to a single BY cell were also different. These functional measurements therefore provide strong support for the idea that weaker signals from cones further from the center of the receptive field are due to weaker synaptic connections. But predicting ganglion cell responses simply from their anatomical connections is a tricky business because it is not always easy to guess how multiple signals interact. Chichilnisky and Baylor [4] found that, when more than one blue cone was stimulated, their effects on the response of the BY cell simply summed up. With this in mind, the structure of the BY receptive fields could be directly related to microscopic measurements of synaptic connections from blue cones to bipolar cells to BY ganglion cells [9].

For several years now our knowledge of the electrical properties of retinal neurons and their patterns of connections has allowed the quantitative modelling of the first stages of visual processing [9,10]. The studies of Brown *et al.* [3] and Chichilnisky and Baylor [4] provide beautiful examples of the way in which such models can be tested quantitatively. One of the goals of neuroscience is to understand how neural circuits extract and process information: the retina clearly provides a wonderful context in which to study this type of question.

References

1. Rodieck R: *The First Steps in Seeing*. Sunderland: Sinauer; 1998.
2. Neves G, Lagnado L: **The retina.** *Curr Biol* 1999, **9:**R674-R677.
3. Brown SP, He S, Masland RH: **Receptive field microstructure and dendritic geometry of retinal ganglion cells.** *Neuron* 2000, **27:**371-373.
4. Chichinisky EJ, Baylor DA: **Receptive-field microstructure of blue-yellow ganglion cells in the primate retina.** *Nat Neurosci* 1999, **2:**889-893.
5. Kuffler SW: **Discharge patterns and functional organization of mammalian retina.** *J Neurohysiol* 1953, **16:**37-68.
6. Barlow, HB: **Summation and inhibition in the frog's retina.** *J Physiol* 1953, **119:**69-88.
7. Enroth-Cugell C, Robson JG: **The contrast sensitivity of retinal ganglion cells of the cat.** *J Physiol* 1966, **187:**517-552.
8. Meister M, Lagnado L, Baylor DA: **Concerted signaling by retinal ganglion cells.** *Science* 1995, **270:**1207-1210.
9. Calkins DJ, Tsukamoto Y, Sterling P: **Microcicuitry and mosaic of a blue-yellow ganglion cell in the primate retina.** *J Neurosci* 1992, **12:**1233-1252.
10. Freed MA, Smith RG, Sterling P: **Computational model of the on-alpha ganglion cell receptive field based on bipolar cell circuitry.** *Proc Nat Acad Sci USA* 1992, **89:**236-240.