Primer

The lateral geniculate nucleus

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The lateral geniculate nucleus (LGN) is a huge embarrassment to visual neuroscientists. Virtually all the visual information that leaves the retina to be analysed in the visual cortex is relayed through synapses in this nucleus. It is a dogma of neurophysiology that the cost imposed by putting a synapse in any pathway must be repaid by some benefit in terms of processing. Unfortunately it is not yet possible to say exactly what benefit accrues from the synapse in the LGN. However it is at last becoming clear what kind of benefit it is likely to be.

Early studies of the responses of neurons in the retina and visual cortex showed that visual processing consists of changing the way information is represented so that important properties of the stimulus are directly signalled by the responses of individual neurons (Figure 1). Naturally, early studies of the physiology of the LGN attempted to analyse the way the nucleus transforms visual information. They looked for differences between the relay cells that constitute its output and the retinal ganglion cells that form its input, in the way visual information is represented by the firing of the neurons. In principle this should have revealed the contribution of the nucleus to visual processing.

Unfortunately this approach did not deliver. Rather than showing distinctive differences between LGN and retina, these experiments showed a division of the early visual pathway into a number of parallel sub-pathways. In both the retina and LGN there are parallel groups of distinctive physiological subtypes of neuron. Although within each subtype there are subtle differences between the response properties of relay cells and those of retinal ganglion cells, the differences between the parallel subtypes are more striking than the differences between retina and LGN. However, by combining what we know about the organisation of the nucleus with the results of physiological experiments on the nature of neural responses a clearer picture of its function is at last beginning to emerge.

There are three distinctive aspects to the organisation of the LGN. First, its non-retinal inputs massively outweigh its retinal input. Second, retinal and non-retinal inputs drive the relay neurons through a distinctive set of microcircuits. Third, the various different physiological subtypes of relay neuron are segregated into different parts of the nucleus which project to different subcompartments of the visual cortex.

Inputs to the nucleus

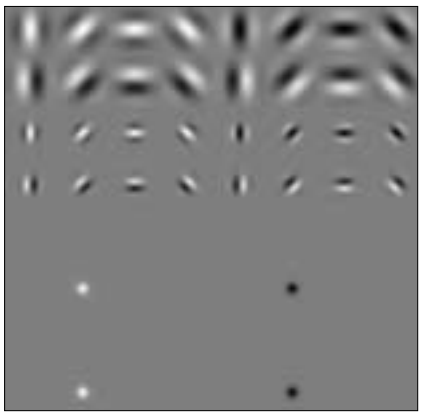
Although we think of the LGN as a relay for retinal signals on their way to the cortex, the retina probably provides fewer than 10% of the synapses on relay cells. Retinal ganglion cells form excitatory synapses both on relay cells and on interneurons both within the LGN and in the neighbouring thalamic reticular nucleus. The retinal inputs are topographically ordered so that each lamina of the nucleus contains a map of the contralateral visual field.

The visual cortex is probably the biggest contributor of excitatory synapses to the relay cells of the nucleus, contributing about 30% of the total. This projection, which like all cortical feedback projections, arises from pyramidal cells in the deepest layer, is topographically ordered in a way that matches the retinal input: cortical cells excite the LGN cells that drive them. There is also an indirect projection to relay cells from midbrain visual structures, particularly the pretectum.

The brainstem parabrachial region is the biggest subcortical input. It provides about the same number of synapses as the cortex. Several other brainstem regions provide smaller projections. It is not clear whether any of the brainstem projections are organised topographically. However, it is not safe to assume that such a large projection is diffuse, particularly since it is not clear *a priori* what principles might be used for imposing order on the projection.

All of these projections to the LGN also affect the inhibitory inputs to relay cells from the neighbouring perigeniculate nucleus and from interneurons within the nucleus itself. These local connections provide about 30% of the synapses on relay cells. The perigeniculate nucleus also receives an inhibitory projection from the basal forebrain.

Figure 1

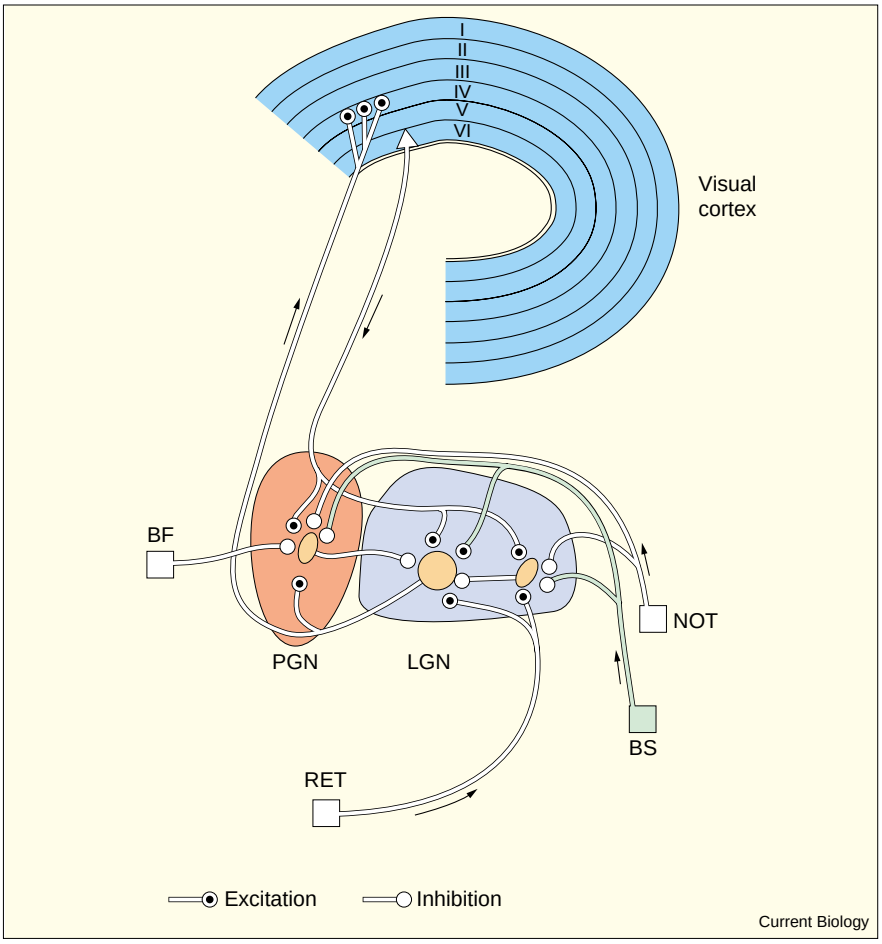


Optimal stimuli of neurons in the visual cortex (top 4 rows) and retina and LGN (bottom 2 rows). In the retina and LGN, cells are selective for only the sign of the stimulus, whether it is a dark or a light spot. In the cortex cells are selective for lines or edges. Individual cells are also selective for the width and orientation of their preferred stimulus type.

Circuitry

The pattern of inputs to LGN relay cells is shown in Figure 2. As a circuit it seems fairly complicated with two prominent inhibitory loops. The retinal input excites the relay cells directly and inhibits them indirectly

Figure 2



Organisation of inputs to lateral geniculate nucleus neurons. NOT, nucleus of the optic tract; BF, basal forebrain; BS, brainstem; RET, retina; PGN, perigeniculate nucleus; LGN, lateral geniculate nucleus.Redrawn from Figure 4 of Sherman and Guillery (1996).

through interneurons. The relay cell output is fed back in a second inhibitory loop through the perigeniculate nucleus and the cortex feeds back with direct excitation and indirect inhibition through both the inhibitory loops. The brainstem also excites the relay cells directly. All the other non-retinal inputs to the nucleus also act through one or other of the inhibitory loops.

At face value, with the retinal synapses vastly outnumbered by other excitatory synapses, it seems hard to imagine that this complicated circuit could be driven by the retina. However this simple view neglects two factors. First, the retinal synapses are located close to the relay cell soma. This enables the retinal inputs to drive the cell directly. Indeed when LGN cells are in 'relay' mode (see section on response modes below) a large fraction of the spikes in a geniculate relay cell are driven directly, spike for spike, by the spikes in a single retinal ganglion cell. Second, all the non-retinal inputs to the nucleus have a metabotropic component. Their neurotransmitters cause slow, long-lasting post-synaptic effects through second messenger systems rather than the rapid post-synaptic potentials that result from opening ion channels directly as in the ionotropic synapses of the retinal input. Thus by their location and their mode of operation, non-retinal synapses appear to be designed to modulate the responsiveness of LGN relay cells. We should expect them to alter the fidelity with which retinal signals are relayed to the cortex but not to generate signals themselves. Unfortunately, specific information about the function of these modulatory influences is scanty. However it may be important that the layout of the nucleus makes it possible for feedback to be exerted independently on neurons of different subtypes as well as on signals that originate in different parts of the visual field.

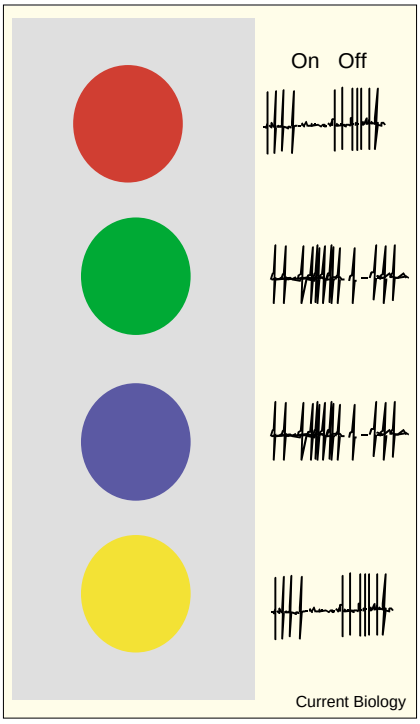
Sub-divisions of the nucleus

Even to the naked eye it is obvious that the LGN is divided into layers. In humans and old-world primates there are six clearly visible layers, each of which receives a complete map of half of the visual field as seen through one eye. The eye of input alternates from layer to layer. The four dorsal layers contain small cells and are hence called parvocellular. The two ventral layers contain larger cells, are known as magnocellular layers and constitute a functionally distinct component of the nucleus. A less well-defined third functional component is based on relay cells in the interlaminar, and superficial zones of the nucleus. In prosimian primates the homologous division of the nucleus also occupies a separate K lamina of nucleus. The relay cells in these three different components of the nucleus project to different parts of visual cortex.

Visual response properties

The visual response properties of neurons in the different anatomical sub-divisions of the LGN are distinctive. Neurons in the magnocellular layers have very high sensitivity, especially to coarse patterns, particularly when they flicker or move rapidly. Sensitivity in the parvocellular layers is lower

Figure 3



Colour coding responses in the LGN. There are two classes of cells, based on the colour directions to which they respond best. (a,b) Cells in the P layers are excited by green and inhibited by red or vice versa. (c,d) Cells in the I layers are excited by blue and inhibited by yellow or vice versa.

generally, and the neurons respond better to fine patterns. Neurons in the parvocellular layers also respond well to colours because their retinal inputs have differential connections from different types of cone. There are two categories of colour-responsive neuron in the LGN (Figure 3) that are distinguished by whether they respond better to changes between blue and yellow or between red and green. Recently it has become clear that the red–green cells are in the parvocellular layers proper, and the blue–yellow cells are in the I layers.

The fact that signals about different aspects of a stimulus and signals originating in different eyes are segregated into different layers of the LGN is very striking. It means that whatever job the LGN performs, it can be done independently on all these different categories of visual signal. The obvious experiment to address this question is to test how non-retinal inputs to the LGN modulate the responses of relay cells. It is very difficult to make subtle manipulations of the influence of the non-retinal inputs to the LGN. The main experimental approach is to block the input from a given structure by cooling it, inactivating it pharmacologically, or removing it surgically. In general the effects are surprisingly subtle, possibly because the manipulations have only been attempted in anaesthetised animals. However it has recently been demonstrated that even in an anaesthetised preparation LGN cells are consistently less responsive when the cortex is inactivated by cooling.

Response modes

Like relay cells in other thalamic nuclei, those in the LGN can switch between two modes of firing behaviour. In relay mode the cell responds by firing spikes at a rate proportional to the stimulus, relaying retinal spikes more-or-less faithfully. In burst mode the cell fires bursts of high frequency spikes separated by longer periods of silence. In deep sleep, all the cells in the nucleus fire in burst mode and until recently it was believed that cells in burst mode were effectively disconnected from stimulus input.

It has become clear however not only that individual cells can switch in and out of burst mode independently, even in awake animals, but also that burst mode may be a more effective way of signalling the presence of weak stimuli to the cortex. Switching a cell between burst mode and relay mode is accomplished by holding the cell in a depolarised state for a few hundred milliseconds. Switching back to burst mode is achieved by a similar period of hyperpolarisation. Metabotropic synapses, like those involved in all the non-retinal inputs to relay cells, have long-lasting effects of the sort that would be ideal for switching between modes. Thus it is extremely likely that this is an important aspect of the function of the non-retinal inputs to the LGN.

Conclusions

The detailed circuitry of the LGN, its connections, and the fact that the stimulus preferences of geniculate neurons seem identical to those of their retinal inputs make it clear that this nucleus is concerned with regulating the way in which visual information gains access to the cortex rather than with performing visual processing. The elaborate layout of the nucleus, particularly the precise segregation of different types of information and of information from different parts of the visual field suggests that the LGN is designed to perform its regulatory function extremely selectively. One possibility is that switching between burst mode and relay mode enables it to switch between detecting stimuli and analysing them. However, a clearer understanding of the regulatory function performed by this enigmatic nucleus is most likely to emerge from experiments in which awake animals perform realistic visual tasks.

Key references

Derrington AM, Lennie P: Spatial and temporal contrast sensitivities of neurones in lateral geniculate nucleus of macaque. *J Physiol* 1984, 357:219-240.

Derrington AM, Krauskopf J, Lennie P: Chromatic mechanisms in lateral geniculate nucleus of macaque. *J Physiol* 1984, 357:241-265.

Hendry SHC, Reid RC: The koniocellular pathway in primate vision. *Annu Rev Neurosci* 2000, 23:127-153.

Przybyszewski AW, Gaska JP, Foote W, Pollen DA: Striate cortex increases contrast gain of macaque LGN neurons. *Vis Neurosci* 2000, 17:485-494.

Sherman SM, Guillery RW: Functional organization of thalamocortical relays. *J Neurophysiol* 1996, 76:1367-1395.

Sherman SM, Guillery RW: On the actions that one nerve cell can have on another: Distinguishing "drivers" from "modulators". *Proc Natl Acad Sci USA* 1998, 95:7121-7126.

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