Rabbit Lateral Geniculate Nucleus: Sharpener of Directional Information

Abstract. *Direction-selective neurons in the rabbit lateral geniculate nucleus signal movement-direction more precisely than their retinal counterparts. This increased selectivity arises from the interaction of retinal inputs to the geniculate cell. A direction-selective geniculate neuron is fed by at least two retinal direction-selective cells, whose preferred directions are 180 degrees apart. One retinal input is excitatory to the geniculate cell and the other is inhibitory.*

Fundamental to an analysis of visual pattern recognition is an understanding of the nature of information available to the pattern recognizer. In some species, particularly those which are not strongly binocular, the information stream is heavily edited peripherally at the retinal ganglion cell (*1–3*).

The rabbit's retinal ganglion cells have been divided into six classes, based on the stimuli for which the cells are most selective. We are particularly interested here in the class of ganglion cells which are direction-selective; these cells respond vigorously to an object moving in a particular preferred direction, but not to the same object moving in the opposite null direction. In a large sample of retinal direction-selective cells, the preferred directions are not distributed randomly, but fall into four well-defined groups, whose mean directions are approximately 90° apart (*4*).

What happens to the retinal direction-information? Since the optic tract is a major input to the rabbit lateral geniculate nucleus (LGN), it would not be surprising to find direction-selective neurons here. At the time of previous studies of the LGN (*5, 6*), there was little detailed information about the retinal input. Arden (*5*) described behavior which could represent selectivity for direction but various controls were omitted.

We now establish the existence of a class of direction-selective cells in the rabbit LGN with properties in general similar to their retinal counterparts. We will show that LGN neurons specify direction of movement with more precision and we suggest a neural mechanism, based on experimental evidence, to account for this increased selectivity.

The experimental techniques have been described (*2, 4, 7*). Briefly, the surgical anesthetic was thiamylal sodium, and the maintenance anesthetic consisted of 70 percent N_2O, 28.5 percent O_2, and 1.5 percent CO_2. Eye movements were reduced by a constant infusion of Flaxedil (gallamine triethiodide) and cervical sympathectomy. Contact lenses were always used, and

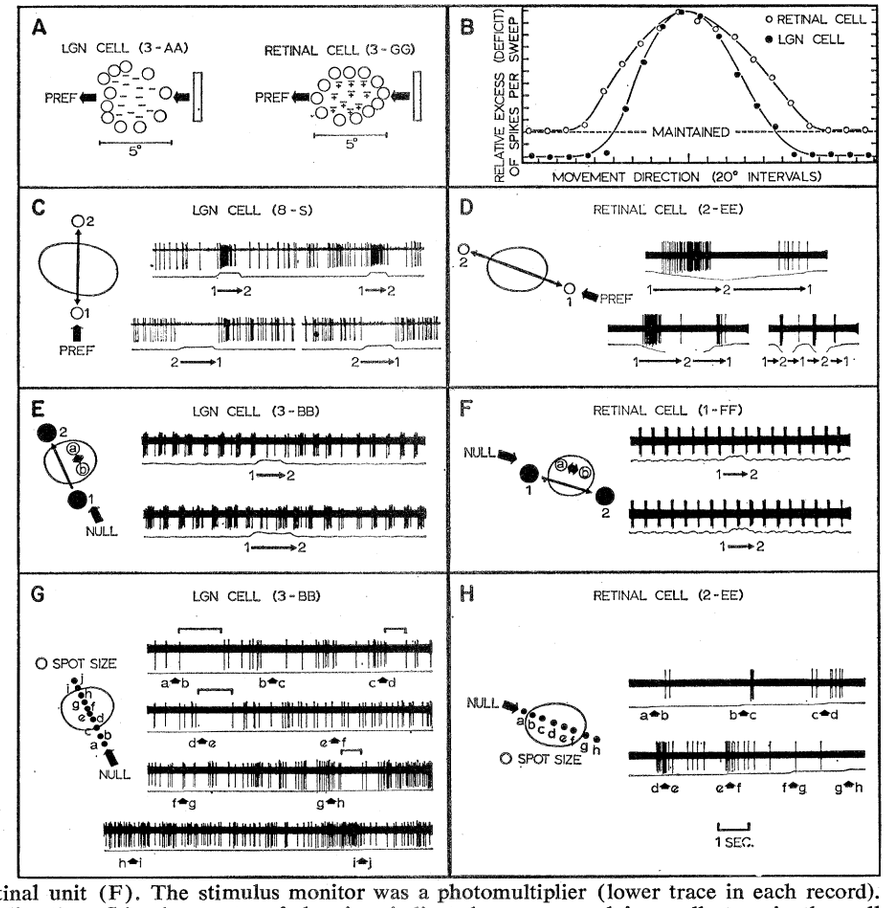

Fig. 1. Comparison of LGN and retinal direction-selective cells. (A and B) Receptive field maps and direction-sensitivity functions. The receptive field maps were plotted with stationary flashed spots, the sizes of which are given by the size of the open circles (indicating no response). The + sign means response at light on, − sign means response at light off. The ordinates of the direction-sensitivity functions are spikes per second scaled so that the maximums and maintained firing levels coincide. Each data point is the mean of ten responses; the maintained firing rate is the mean of ten 10-second counting periods. The stimulus used for the direction-sensitivity functions (B) is shown with the receptive field maps (A). (C and D) Responses to preferred and null motions. All records consist of a pair of traces; the upper is the record of cell activity, and the lower is the stimulus monitor. The lower traces (C) are from a photomultiplier aimed at the receptive field, and in (D) a voltage proportional to the rotation of a mirror which deflected the stimulus spot. The receptive field outlines and stimulus spot sizes are given at the same scale as in (A). The most striking result is the complete inhibition produced by null movement across the LGN cell's receptive field (C). (E and F) Cancellation experiment. A small target was oscillated between positions a and b, producing a modulated discharge; another spot was then moved in the null direction (from position 1 to 2). This second spot produced a reduction of the discharge from the LGN cell (E), but not for the retinal unit (F). The stimulus monitor was a photomultiplier (lower trace in each record). (G and H) Interrupted movement in null direction. Stimulus spots, of the sizes indicated, were moved in small steps in the null direction, pausing at the positions shown. The steps do not show well on the lower traces so they are indicated by arrows. For the LGN cell (G), the movements produced inhibition (brackets), whereas bursts of spikes were elicited from the retinal cell (H). Target details. Background luminances were about 15 cd/m² except for the direction-sensitivity functions (65 cd/m²). Spot luminances in parts A, C, D, G, and H ranged from 137 to 275 cd/m², while in E and F the luminances were 5 cd/m² (black) and 50 cd/m² (white). For the direction-sensitivity functions (B), the target sizes were 3.4° by 0.5°, luminances were 135 cd/m², and target velocities were 4.9°/sec.

any residual spherical refractive error was corrected by determination of the added lens power which permitted the optimum resolution of striped patterns by an LGN cell.

A small craniotomy was made over the left LGN, the dura was dissected away, and a glass-insulated tungsten microelectrode was advanced down into the LGN. Cell recordings were identified primarily on the basis of waveform (inflected positive-going phase) and marked amplitude decrease during high frequency bursts of activity. At the end of an electrode track a lesion was made by passing 5 μa of current through the electrode for 5 seconds. The lesions and electrode tracks permitted histological verification of the recording site.

During our first few experiments we discovered that some LGN neurons were direction-selective, superficially resembling the on-off type of retinal direction-selective cells (*1*). They had receptive fields in the same range of sizes. Also, null and preferred directions were easily defined and similarly distributed; this selectivity for direction was unaffected by altering the size, shape, velocity or contrast of moving test targets, just as with retinal ganglion cells. Having established general similarity, we turned to (i) the specific ways in which LGN cells differ from retinal units and (ii) the mechanism by which the differences arise. Our sample of LGN cells is now 200, of which 27 were definitely direction-selective; most of these were studied in some detail. Five other units were probably direction-selective retinal fibers, but we have not included them here; instead, data from ganglion cells recorded in the retina have been included for purposes of comparison.

The receptive fields of LGN neurons, when mapped with small, stationary flashed spots, do not differ markedly in size from retinal units mapped by the same technique. In general, however, LGN cells do not respond well to flashed spots, and some cannot be mapped by this technique. When flashed spots proved to be ineffective, we used moving targets to delimit a minimum response field (*8*), thus locating the border of an area which was sensitive to movement of the particular stimulus target. Receptive field maps of LGN and retinal direction-selective neurons are shown in Fig. 1A.

Geniculate cells do not respond to as wide a range of directions as do the retinal units; in other words, LGN cells are more selective about direction. Retinal cells, for example, respond well to movements in either direction along a line perpendicular to the preferred-null axis, whereas the LGN cells do not respond to movement in these directions. By recording responses to movement in different directions through the center of the receptive field, one can determine how the cell's response varies as a function of movement direction. (*9*). The curves in Fig. 1B have been scaled so that the response maximums and the maintained firing rates coincide. The maintained firing, for both units, was recorded with a uniform background of 15 cd/m^2. The retinal unit has a fairly broad response curve; at $\pm$ 90° from the preferred direction, the response is still about 25 percent of the maximum. The LGN cell's response, however, has fallen below the maintained rate at $\pm$ 80° from the maximum, indicating the presence of an inhibitory input; this does not happen with the retinal cell, whose response, though low, is always above the maintained firing rate.

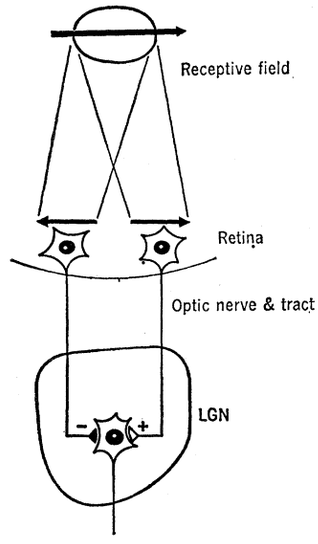

Fig. 2. Representation of inputs to an LGN direction-selective cell. The LGN cell receives inputs from two retinal ganglion cells, both of which are direction-selective, and whose preferred directions are 180° apart. One retinal input is excitatory, and the other is inhibitory. The receptive fields of the two retinal cells are coincident, and the LGN cell has the same preferred direction as the excitatory input cell.

A simple demonstration of strong inhibition of the LGN cell is given in Fig. 1C. The upper record shows the response to preferred direction movement, and the lower shows null direction movement. Clearly, the null movement very effectively cuts off the ongoing discharge. A similar situation is shown for the retinal unit in Fig. 1D (here, the preferred and null movements occur in sequence on the same photorecord). There are a few spikes fired during null movement, indicating perhaps that the movement was not exactly in the null direction. Even so, null movement is definitely not producing the profound inhibition seen with the LGN cell.

Another example of inhibition is provided by a cancellation experiment. A small target was oscillated back and forth along the preferred-null axis, producing a rhythmic discharge from the cell. A second target was then moved through the receptive field in the null direction. This null movement resulted in a reduction of the modulated discharge from the LGN cell (Fig. 1E) but had little effect on the retinal cell's discharge (Fig. 1F).

A final observation concerns the response to interrupted movement; the stimuli were small movements in the null direction, interrupted by brief pauses. As explained by Barlow and Levick (*7*), retinal units give a short burst of spikes as each new null movement commences (Fig. 1H). On the other hand, LGN cells do not exhibit these short bursts of activity at the onset of the null movements (Fig. 1G). In fact one often observes inhibition of the ongoing discharge, as indicated by the brackets above the records in Fig. 1G.

The foregoing observations are readily explained by a simple convergence of retinal direction-selective cells onto an LGN neuron; the arrangement of inputs, in its most elementary form, is shown in Fig. 2. There are two retinal fibers feeding the LGN cell; one is excitatory, the other inhibitory. The latter connection may not be direct as shown in the figure, but by way of another principal cell and interneuron, as postulated for other reasons in the case of the rat LGN by Burke and Sefton (*10*). None of our evidence bears directly on this detail.

The preferred directions of the two retinal inputs are 180° apart, or opposing, and the preferred direction of the LGN cell coincides with that of the excitatory retinal cell. If both retinal inputs are from the common on-off direction-selective ganglion cells, the poor response of LGN neurons to flashed spots is explained; both retinal inputs are activated at the on and off of the flash, but their effects are opposing and cancel, though not always completely. The lack of any escape

discharge to interrupted null motion is also expected from this scheme. The null movements produce brief bursts of firing in the excitatory cell, but these movements are in the preferred direction of the inhibitory cell, which is strongly driven, thereby inhibiting the LGN cell and preventing any escape discharge. The narrowness of the direction-sensitivity function is also a natural consequence of the inhibitory input. For example, movement at 90° to the preferred-null axis will activate both retinal inputs, resulting in balanced excitation and inhibition, and again no response from the LGN cell occurs. The cancellation experiment (Fig. 1, E and F) gives a negative result at the retinal level because inhibition by movement in the null direction is strictly localized to the region immediately ahead of the test target. However, the LGN neuron receives powerful inhibition from the retinal neuron which is active throughout the test-target's motion. Thus excitation and inhibition are opposed at the geniculate, and the evoked response is canceled.

While this scheme is sufficient to explain our experimental facts, more complex arrangements are not excluded. Each retinal input in Fig. 2, for example, may actually be a group of units with similar preferred directions. The number of similar units could be a factor in the relative weighting of excitation and inhibition, and the weighting does seem to vary somewhat from cell to cell. Another possible arrangement is to include inputs from the two retinal direction-selective groups with preferred directions at right angles to those shown in the figure, making a total of four inputs. These two extra inputs could be either excitatory or inhibitory, but, if present, their contribution is probably small.

We note as a final point, one other difference between the retinal and LGN direction-selective cells; namely, the LGN cells are more variable than retinal units in their responses to repetitions of a given stimulus. This observation has implications for the reliability of the LGN neuron as an information channel or may be related to the role of nonvisual inputs to the LGN (*11*).

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9. The stimulus for the direction-sensitivity functions was a rectangular raster on a CRT face. The raster could be driven across the screen in a direction perpendicular to the long axis of the rectangle. The whole CRT could be rotated around its center, thus changing the direction of movement. Action potentials were converted to standard pulses and counted during the traverse of the raster sweep.
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12. We thank L. M. Davies, Miss B. Ferguson, and R. M. Tupper for technical assistance. C.W.O. is a postdoctoral research fellow of Fight for Sight, Inc., New York, and E.T. is a postdoctoral fellow of the National Institute of Neurological Diseases and Stroke, U.S. Public Health Service.

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Viral Infection Across Species Barriers: Reversible Alteration of Murine Sarcoma Virus for Growth in Cat Cells

Abstract. *Infection of cat embryo cells by a centrifugally induced aggregate of murine sarcoma virus and feline leukemia virus gave rise to a defective, focus-forming virus which propagated in cat cells, but not in mouse cells. This virus, apparently enveloped with a feline leukemia virus coat, was later subjected to aggregation with murine leukemia virus, whereupon it regained the capacity for growth in mouse cells.*

The infection of mouse cell cultures with the Moloney isolate of murine sarcoma virus (MSV) is defective since superinfection with murine leukemia virus (MLV) is required for production of focal lesions and release of progeny virus (*1*). Titration patterns of various stocks of MSV revealed that such stocks contained, in addition to defective MSV and excess endogenous MLV, variable amounts of competent MSV, which could form foci on mouse embryo cultures without superinfection by the free endogenous MLV. The competent MSV appeared to consist of a temporary association of the sarcoma and leukemia viral genomes in a single effective particle having an exterior antigenicity similar to that of defective MSV or MLV (*2*).

Further investigations showed that competent sarcoma virus consists of an interviral aggregate of defective MSV and MLV which has an enhanced infectious capacity (*3*). Of particular interest was the observation that sedimentation of defective MSV and MLV in the preparative ultracentrifuge could lead to the formation of competent MSV. These findings raised the question whether MSV would form aggregates with other viruses, with alterations of the biological specificities of the combinations.

We now report the successful aggregation of defective MSV with feline leukemia virus (FelLV) which resulted in a focus-forming, defective virus capable of indefinite propagation in cat cells but not in mouse cells. This modified virus, tentatively designated MSV-FelLV, could after several passages in cat cells be restored for successful propagation in mouse cells by a similar aggregation with MLV.

Feline embryo fibroblast cultures, derived from approximately 30-day-old embryos, were established, and all virus infections were done between the third and the tenth tissue culture passages (*4*). The feline leukemia virus and MSV were used as tumor extracts in 0.05*M* sodium citrate (*5*). The MSV had a titer on Swiss mouse embryo cells of about 1×10^6 focus-forming units (FFU)/ml, of which 15 percent were competent (*2*). Briefly, the aggregation technique (*3*) consists of a tenfold dilution of MSV in Dulbecco's phosphate-buffered saline without calcium or magnesium and an initial cycle of centrifugation for 15 minutes at 5,000 rev/min. The supernatant contained defective MSV devoid of competent MSV. This defective MSV in the supernatants was sedimented at 25,000 rev/min (Spinco-39L rotor, 45 minutes); the resulting viral pellet was resuspended and contained 17 percent of competent MSV. The defective su-