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Feedback Connections to the Lateral Geniculate Nucleus and Cortical Response Properties

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The cerebral cortex receives sensory input from the periphery by means of thalamic relay nuclei, but the flow of information goes both ways. Each cortical area sends a reciprocal projection back to the thalamus. In the visual system, the synaptic relations that govern the influence of thalamic afferents on orientation selectivity in the cortex have been studied extensively. It now appears that the connectivity of the corticofugal feedback pathway is also fundamentally linked to the orientation preference of the cortical cells involved.

An abiding challenge for vision research is to determine the role of the massive feedback pathway from the visual cortex to the dorsal lateral geniculate nucleus (dLGN), the specific visual relay nucleus in the thalamus. Axons feeding back from cortical areas 17 and 18 contribute substantially more synapses to the geniculate neuropil than any other source of input, including the retina (*1–3*). It has been suggested that they might simply provide a nonspecific facilitation of the thalamic circuit, but growing evidence (*4, 5*) favors a more active role in visual processing. Cells in this pathway are selective for both the orientation and the direction of movement of a visual stimulus (*6, 7*), and their influence has been shown to reflect both properties (*8–10*). Geniculate cells respond to stimuli at any orientation (*11*), but feedback makes them sensitive to orientation context (*8*). Feedback also influences the level of synchronization of cells responding to the presence of a single elongate stimulus, as distinct from those responding to individual, more localized stimuli (*12*). It has been proposed that this might enhance the salience of such contours within a visual image, which in turn might influence both the generation and expression of orientation selectivity at the cortical level.

Corticofugal axons have large arborizations, which can encompass substantial regions of the geniculate retinotopic map (*4*). Given entirely random connections, a cortical cell responding to one contour might be expected to synchronize geniculate cells responding to widespread and entirely unrelated aspects of a complex natural scene. Any selectivity would have to arise from precise temporal links between the ascending and descending inputs. Alternatively, the effectiveness of the system could be enhanced by a more specific pattern of connections that link the oriented cortical cells with the array of geniculate afferents from which they receive input. Corticofugal axons are for the most part extremely sparse, which suggests that they exert only a weak influence over the majority of their postsynaptic targets. However, they show restricted regions of greatly increased bouton density (*4*), within which they ought to exert a more effective influence. An obvious question is whether there is any relation between these anatomical "hot spots" and the representation of visual space in the dLGN.

We stained 25 single corticofugal axons, 13 from area 17 and 12 from area 18 of the cat visual cortex (*4, 13, 14*). The orientation preferences of the cells of origin were determined before staining, either by direct recording of intracellularly stained cells or by mapping representative cells from the same orientation columns (*15, 16*). Stained axons were identified and reconstructed from serial sections, and the distribution of their synaptic boutons within the A layers of the dLGN was quantified with respect to the geniculate retinotopic map (*17*) (Fig. 1, A, D, and E).

The boutons from individual axons are sparsely distributed over a wide region of the dLGN; the average range spread from 755 ± 85μm to 940 ± 130μm rostrocaudal, and from 1020 ± 75 μm to 1240 ± 100μm mediolateral, for areas 17 and 18, respectively. This delineates an area many times the size of the geniculate representation of the corticofugal cell receptive fields (Fig. 2, B to D). Within this area, however, are regions of much higher bouton density, which more closely match the receptive field dimensions. In some cases, a single discrete peak is formed (Fig. 3, C and E) and in others, multiple peaks (Fig. 3, B, D, and F). In either case, these zones are almost invariably elongate. To quantify the degree of elongation, only regions with a greater than half-maximal bouton count were selected. Under these cir-

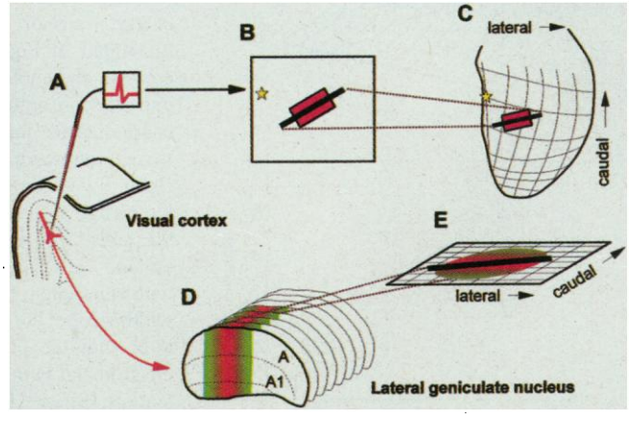

Fig. 1 Experimental protocol. (**A**) Cells in visual cortical areas 17 and 18 were recorded, mapped, and then labeled with biocytin (*4, 13*). (**B** and **C**) Their receptive fields (B) were superimposed on the geniculate retinotopic map of visual space (C). This map (*18*) is highly nonlinear. Therefore, key points from each field were accurately located with respect to the grid of iso-azimuth and iso-elevation lines, and the field's axis of orientation was redrawn with correction for local scale. The angle of this line was measured with respect to the mediolateral axis of the map. Stars represent the area centralis; rectangle, minimum discharge zone of cortical receptive field; thick bar, preferred orientation. (**D** and **E**) Single axons were reconstructed from the histochemically treated sections, and the distributions of their boutons were quantified in three dimensions (*17*) and then analyzed with respect to their relation to the geniculate representation of visual space.

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cumstances, 11 out of 13 (11/13) area 17 axons and 11/12 area 18 axons have ratios of elongation (longest:orthogonal axis) greater than 1.5:1 (average 2.1 for area 17; 2.4 for area 18). This strict definition can exclude much of the high-density region, and we were concerned that the elongate profiles might be an artifact of too small a sample. However, in most cases, dropping the threshold for inclusion increased the degree of elongation, provided that the surrounding area of low-density boutons was not included in the sample. Thus, the influence of these axons is highly unlikely to follow a simple circular symmetry.

Given the orientation selectivity of the feedback pathway, the next question is whether there is any relation between the angle of elongation and the orientation preference of the cells of origin. We used the map of visual space within the dLGN (*18*) to translate the receptive fields recorded at the injection sites into anatomical coordinates (Fig. 1, A to C) and thus to derive the anatomical correlate of each cell's orientation axis. This axis was then directly compared with the axis of elongation of the corticofugal bouton field. We performed a series of control experiments to confirm that it is possible to match anatomical and visual data in this way (Fig. 2).

The analysis revealed a clear relation between the physiological and anatomical results, in that the axis of elongation of the majority of axons lies within 22.5° of being either parallel (Fig. 3, B to D) or perpendicular (Fig. 3, E and F) to the angle derived from the visual orientation preference of their parent cells. This applies only to the region of maximum bouton density; the more widely distributed surrounding area of sparser label shows no consistent relation to the axis of elongation. Figure 3G shows that for the population as a whole, 9/13 (70%) area 17 axons and 9/12 (75%) area 18 axons lay within either the parallel or perpendicular categories. In contrast, only 4/13 and 3/12 axons fell within the corresponding oblique categories. This is a significantly ($P < 0.05$, χ^2 test) nonrandom distribution. There is no correlation between the magnitude of the difference and any other quality that we could measure. A mild bias toward horizontal orientations, in both the anatomical and physiological results, may itself be an important observation.

The elongate regions spread further than the dendritic arborizations of the majority of geniculate relay cells. Thus, unless there is a precise and unlikely matching of feedback terminals to individual target cells, their potential role must be considered in the context of linking rows of cells. Axons with aligned anatomical and physiological orientations would signal the presence of an oriented stimulus to the very dLGN cells that were concurrently responding to that stimulus. They are ideally suited to highlighting coherent contours within a visual image. They could increase the responsiveness and orientation selectivity of the cortical network by synchronizing the arrival (*12*) and potential effectiveness (*19*) of inputs from appropriate-

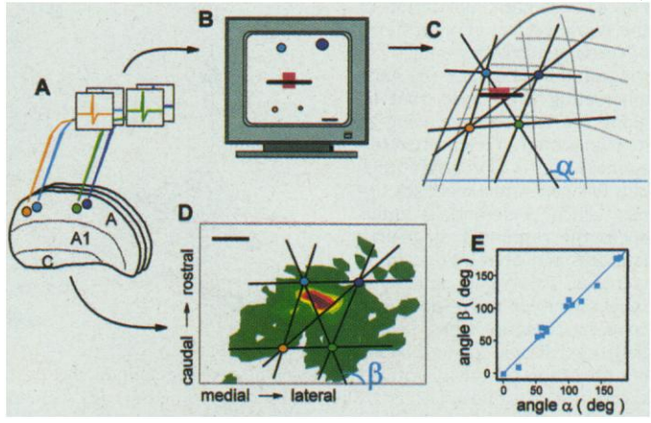

Fig. 2. Control experiments. (**A**) Multiple electrode penetrations were made into the dLGN. Cells were recorded near the upper border of layer A, and their locations were marked by electrolytic lesions. (**B**) The receptive fields of these cells were mapped (circles), and their locations were carefully measured with respect to the area centralis. Also shown (center) is the classical receptive field of a cortical cell, which was recorded at the site of a biocytin injection made in the same animal. Rectangle, minimum discharge zone; thick horizontal bar, preferred orientation. Scale bar, 2°. (**C**) The receptive fields were superimposed on the map (*18*) of visual space in the dLGN, as described in Fig. 1, B and C. (**D**) The lesion sites were identified in the histological sections, which were stacked and rotated to show the view from above, as described in Fig. 1, D and E. Also shown is the distribution of boutons stained by the cortical injection. A spline-smoothing algorithm was used to convert the two-dimensional matrix of bouton counts into a density map. Dark green, lowest density; dark red, highest density. Scale bar, 500 μm. (**E**) The orientation of lines linking the anatomically derived locations shown in (D) were compared with the orientation of lines linking the visually derived locations shown in (C). The two sets of data are highly correlated ($R^2 = 0.98$).

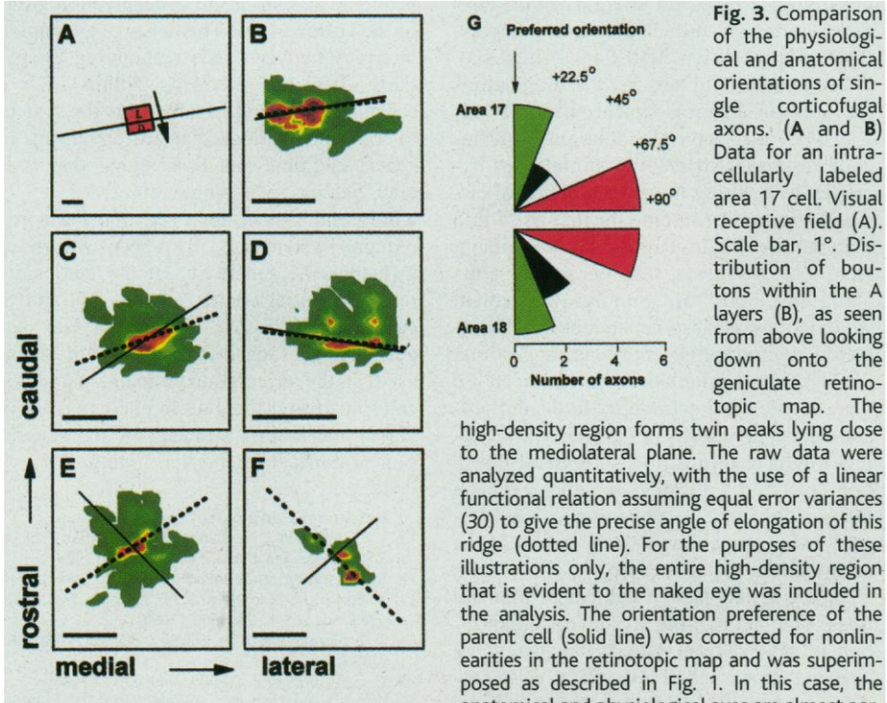

Fig. 3. Comparison of the physiological and anatomical orientations of single corticofugal axons. (**A** and **B**) Data for an intracellularly labeled area 17 cell. Visual receptive field (A). Scale bar, 1°. Distribution of boutons within the A layers (B), as seen from above looking down onto the geniculate retinotopic map. The high-density region forms twin peaks lying close to the mediolateral plane. The raw data were analyzed quantitatively, with the use of a linear functional relation assuming equal error variances (*30*) to give the precise angle of elongation of this ridge (dotted line). For the purposes of these illustrations only, the entire high-density region that is evident to the naked eye was included in the analysis. The orientation preference of the parent cell (solid line) was corrected for nonlinearities in the retinotopic map and was superimposed as described in Fig. 1. In this case, the anatomical and physiological axes are almost parallel. Conventions used were the same as for Fig. 2, B and D. (**C** to **F**) Examples of axons for which the anatomical axes lie approximately parallel (C and D) or perpendicular (E and F) to the physiologically determined orientation. Conventions used were the same as for B. (**G**) Difference between the orientation preference of the area 17 and area 18 corticofugal cells and the anatomically determined axis of elongation of their dLGN axons. The results are divided among four equal categories: axons for which the axis lies within 22.5° of being parallel (green) or perpendicular (red) to the preferred orientation and axons for which the axis lies at one of the corresponding obliques (black, white).

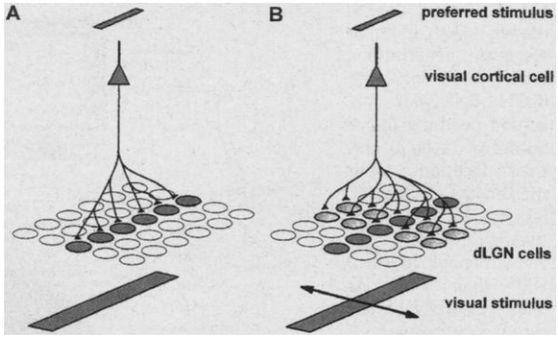

Fig. 4. Schematic illustration of the two most common patterns of corticogeniculate connectivity suggested by the data. **(A)** Axon innervating dLGN cells that lie along the line corresponding to its own preferred orientation (diagonal bar). An appropriate stimulus will generate a feedback signal, which preferentially influences the responses of geniculate cells activated by that same stimulus. This signal influences synchronicity in the responses to coherent contours, which potentially contributes to the buildup of orientation selectivity within the geniculo-cortical circuit, or the mechanisms underlying feature segmentation, or both (*12, 27*). Solid ovals, responding cells. **(B)** Axon innervating dLGN relay cells lying along the axis of stimulus movement. An appropriate stimulus will generate a feedback signal, which selectively influences geniculate cells in regions neighboring those that relay the presence of the stimulus. This could enhance responsiveness in anticipation of stimulus movement or entrain the activity of cells responding to associated contours within a complex visual environment. Solid ovals, responding cells; shaded ovals, cells with modified responsiveness; double-headed arrow, direction of stimulus movement.

ly aligned geniculate afferents (Fig. 4A). This mechanism would not impose orientation tuning upon individual geniculate cells, but it might increase the apparent specificity of the pool of afferents converging upon a first-order cortical cell, especially if that cell also received a direct input from recurrent collaterals of the corticofugal axons (*20, 21*).

Axons for which the anatomical and physiological axes lie at right angles contact regions of the dLGN that innervate their own receptive field flanks (Fig. 4B). These axons could help lay the foundations for cross-orientation synchronization (*22, 23*). They also have the potential to influence responses to moving stimuli, for example, by priming the geniculocortical circuit to respond to contours that drift into neighboring fields. One prediction arising from our results is that geniculate cells along the axis of stimulus movement should show a phase-dependent synchronization, and recent observations suggest that this synchronization occurs (*24*). Given the high degree of directionality in the corticogeniculate pathway (*6, 7*), this type of effect might in turn influence cortical direction selectivity. In all cases, the feedback effects observed in physiological experiments are compatible with the extent of the arborizations reported here.

These results have a number of implications. The fact that the anatomical organization of the pathway reflects the functional response properties of the parent cells provides another indication that feedback is an integral part of the neuronal circuitry responsible for analyzing the visual image. It also raises the possibility that this pathway is able to influence the mechanisms underlying the generation of orientation-tuned responses. However, feedback is unlikely to be concerned only with creating "classical" receptive field properties. For the network as a whole, the consequence of having independent systems directed along both orientation and direction axes could be to provide a continuous wave of spatiotemporal influence that moves with and remains linked to individual features within a scene. The large corticofugal arborizations provide substantial overlap between the connections arising from widespread regions of the cortex (*4, 5*). This ensures a complex interplay between cells responding to spatially displaced elements within such a scene, which could in turn allow the system to lock on to those that are covarying in space and time and thus signal that they may belong to a single object (*25*). We would emphasize, however, that the corticofugal system has also been shown to influence the sensitivity of the geniculate relay to spatial context (*8, 10, 26*) and to gain control (*27, 28*). The present data suggest that all such influences would be biased in the orientation domain, paradoxically mirroring the pattern encompassed in Hubel and Wiesel's model for the generation of cortical orientation tuning (*29*).

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