Spatial frequency tuning of orientation-discontinuity-sensitive corticofugal feedback to the cat lateral geniculate nucleus

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1. The influence of spatial frequency on the inhibitory component of the effects mediated by feedback from the visual cortex has been examined in X and Y cells in the A laminae of the feline dorsal lateral geniculate nucleus (dLGN). Experiments utilized a concentric, bipartite visual stimulus centred over the receptive fields of the cells studied. The responses of dLGN cells to selective stimulation of receptive field centre (with the inner window) were compared with those to stimulation of centre and surround mechanisms (both inner and outer window), with the stimuli either in or out of orientation alignment.

2. With these same stimuli, layer VI cells in the visual cortex showed a marked increase in response magnitude when the inner and outer components of the stimulus were in orientation alignment, and presented at the preferred orientation. In the case of dLGN X and Y cells we observed an enhancement of the surround antagonism of the centre response when the inner and outer sections of the stimulus were in orientation alignment.

3. The effects of varying spatial frequency on these responses were examined in dLGN cells in the presence of corticofugal feedback. With the stimulus sections in orientation alignment, surround stimulation produced a powerful and significant reduction in the response to stimulation of centre mechanism alone with the most marked effects for stimuli in the range 0·1–0·85 cycles per degree (c.p.d.). The reduction produced by surround stimulation in the range 0·1–0·5 c.p.d. was notably more potent in X cells than in Y cells.

4. The responses to the same stimuli were examined in dLGN cells with the corticofugal feedback inactivated. Comparison of data from cells studied with and without feedback revealed a significant decrease in surround-mediated attenuation of the centre response in Y cells for spatial frequencies in the range 0·1–0·85 c.p.d. For X cells the decrease in strength of the surround antagonism was also clear and significant but only seen in the range 0·1–0·5 c.p.d.

5. The influence of the orientation alignment of inner and outer stimulus sections revealed a marked difference between cells studied with and without feedback. In the presence of feedback fully aligned stimuli enhanced surround antagonism of centre responses for spatial frequencies in the range 0·1–0·5 c.p.d., in X and Y cells. In the absence of corticofugal feedback this alignment effect was essentially eliminated.

6. These data show that surround antagonism of the centre response is influenced by orientation alignment of the stimulus sections at low spatial frequencies and in the presence of corticofugal feedback. They support a cortically driven enhancement of the inhibitory mechanisms reinforcing surround mechanisms in the dLGN. We propose that feedback enhances a low spatial frequency cut-off in the dLGN, that this effect is maximal for a continuous iso-orientated contour, but diminished whenever there is an orientation discontinuity. The hyperpolarizing influence underlying this effect may contribute to the recently described synchronizing influence of the direct corticofugal contacts onto relay cells. We suggest feedback of the cortical level of analysis refines the transfer of the visual input at geniculate level in a stimulus-context-dependent fashion.

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Ever since the early papers of Hubel & Wiesel (1961, 1962) our view of the way in which the visual input is processed has drawn a strong contrast between mechanisms operating at the level of the dorsal lateral geniculate nucleus (dLGN) and visual cortex. Essentially the geniculate relay has been seen merely to fine-tune the concentric centre–surround fields exhibited by the retinal ganglion cells providing its afferent input, whilst in the visual cortex there is a substantive step change involving amongst other things the generation of orientation, direction and length-selective receptive fields. The sharpness of this distinction is in fact rather paradoxical, because at least in the anatomical sense the major input to the dLGN comes not from the retina, but from a retinotopically organized feedback projection originating in layer VI of the visual cortex (Hollander, 1970; Kawamura, Sprague & Nimi, 1974; Updyke, 1975; Wilson, Friedlander & Sherman, 1984; Weber & Kalil, 1987; Weber, Kalil & Behan, 1989). Thus one might speculate that there ought to be a strong component reflecting cortical properties in the mechanisms influencing the transfer of visual information at the level of the dLGN. One reason for the tendency to neglect this possibility may be that investigators working at the level of the dLGN have not routinely attempted to use stimuli that would be optimal for cortical cells. Nonetheless there are a series of reports in the literature that identify the presence of a corticofugal influence on visual processing in the dLGN and descriptions of response properties in the dLGN that certainly blur the distinction between cortical and subcortical processes (Cleland, Lee & Vidyasagar, 1983; Murphy & Sillito, 1987; Jones & Sillito, 1991). In the quest to understand the logic of the synaptic organization of the central visual mechanisms it is clear that we require a better understanding of the nature of the influence of the corticofugal feedback to the dLGN. The corticofugal projection is retinotopically organized; layer VI cells have orientation- and direction-selective receptive fields, with characteristic patterns of length tuning and an apparent bias to low spatial frequencies (Gilbert, 1977; Grieve & Sillito, 1991, 1992, 1995). Because the cells are driven by visual stimuli in a selective way, the pattern of feedback must reflect the nature of the visual stimulus and influence the transfer of retino-geniculate information in a fashion that follows from their response pattern.

In this paper we report an investigation that follows from previous work in our laboratory attempting to track the cortical influence on geniculate mechanisms. Here we focus on the influence of spatial frequency on the corticofugal modulation of the centre–surround antagonism in the field of dLGN cells. We have previously shown the presence of a cortically driven enhancement of the surround antagonism of centre responses in dLGN cell receptive fields (Murphy & Sillito, 1987; Sillito, Cudeiro & Murphy, 1993). The present experiments involved the use of a bipartite, concentric, sinusoidal grating stimulus subdivided into an inner component overlying the receptive field centre and an outer component. We have explored the effect of varying the spatial frequency of the grating on the degree of surround antagonism of the centre response elicited by the outer stimulus. In order to isolate the corticofugal element in these interactions we have varied the orientation alignment of the two components of the stimulus, since the concentric nature of the receptive field of dLGN cells would suggest that the inhibitory drive elicited from the surround mechanism by the outer stimulus would not be dependent on its orientation alignment with the inner. We have shown however, that there is a significant increase in the inhibitory drive when the two components of the stimulus are in orientation alignment and that this is strongly dependent on the presence of corticofugal feedback (Sillito *et al.* 1993). This effect appears to follow logically from the way the elongated orientation-tuned fields of layer VI cells respond to the stimulus protocol, giving an optimal response when the two components of the stimulus are in orientation alignment. These ideas are summarized in Fig. 1. Our present protocol has examined the spatial frequency tuning of the component of the surround antagonism that is dependent on orientation alignment. As a further control to this we have repeated the observations with the corticofugal feedback inactivated.

METHODS

Experiments were carried out on female cats in the weight range 2·2–3·0 kg, anaesthetized with a mixture of N_2O (70%), O_2 (30%) and halothane (0·1–5·0%). The level of halothane was varied as necessary over the course of the experiment, with 5% at the induction of anaesthesia, 2–4% during surgical procedures, and a subsequent long-term maintenance level of 0·1–0·5% after paralysis with gallamine triethiodide (40 mg initial dose, then 10 mg kg^{-1} h^{-1}). End-tidal CO_2 levels, ECG waveform, intersystolic interval, and the frequency of spindles in the EEG were monitored continuously through the experiment (2–3 days). The rate and depth of artificial ventilation was adjusted to maintain end-tidal CO_2 at 3·8–4·2%; the level of halothane was chosen to give a state of light anaesthesia. Once a stable state was reached, any variation in the monitored parameters (change in the frequency of spindles, fall or fluctuation in intersystolic interval, rise in end-tidal CO_2) commensurate with a change in the depth of anaesthesia was immediately compensated for by adjusting the level of halothane. Once a stable baseline had been established any variation in the parameters monitored triggered an alarm system. All wound margins were treated with subcutaneous injections of lidocaine (lignocaine) hydrochloride and adrenaline, and the ear bars of the stereotaxic apparatus were coated with antiseptic lidocaine hydrochloride gel. Local anaesthetic injections to wound margins were repeated at 6 h intervals during the experiment. The eyes were treated with atropine methonitrate and phenylephrine hydrochloride, and protected with plastic contact lenses. They were brought to focus on a semi-opaque tangent screen at a distance of 0·57 m, using supplementary lenses and 2 mm diameter artificial pupils.

Extracellular recordings of single-unit activity in the A laminae of the dLGN were made with glass micropipettes filled with 3 M NaCl and inserted in an angled rostrocaudal plane to avoid damage to the cortical areas overlying the dLGN. The data were collected and

the visual stimuli generated using the 'VS' system commissioned by our laboratory and developed in conjunction with Cambridge Electronic Design, UK and John Daughman, USA (Sillito *et al.* 1993). Spikes are stored with a 0·1 ms interval resolution and can subsequently be processed with respect to any aspect of the stimulus variables used during data collection. We first identified and handmapped receptive fields using an overhead projector and the tangent screen of a plotting table. Once the receptive field was characterized in this way we introduced a 45 deg front-surfaced mirror into the light path deflecting the animal's plane of vision to a vertically mounted 608 Tektronix tube at a distance of 0·57 m for computer-controlled presentation of visual stimuli. The 608 tube was mounted on a cradle which could be shifted over a set of floor-mounted tracks, and tracks mounted in a slave carrier, to roughly centre the display on the receptive field. We used the alignment of the receptive field location on the tangent screen and 45 deg beam splitter to achieve this. We could fine-tune the centring of the receptive field on the 608 tube using micrometer adjustments on the carrier mechanism and, if required, software adjustment of the display centre. These adjustments were checked with reference to the peristimulus time histograms (PSTHs), generated by drifting bars with the sweep centred on the display centre over the receptive field at different orientations, and the symmetry of the location of the discharge centres. Small flashing spots, stepped sequentially in a grid over the field, were also used to aid this process. Accurate centring of the display over the

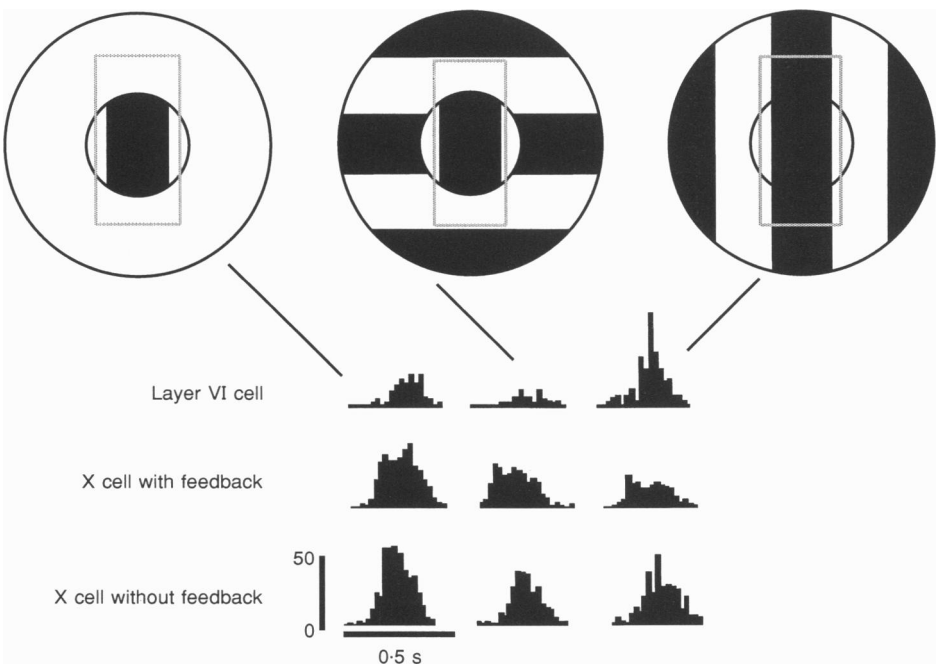


Figure 1. Summary of the effects of orientation alignment in the visual stimulus protocol on the responses of a layer VI visual cortical cell and dLGN X cells, with and without feedback, respectively

Schematics above the records summarize the stimulus situation in concept, they do not attempt to reflect the actual scale of the receptive fields, the size of the stimulus windows, the actual spatial frequency, or the real orientation of the inner stimulus. The cortical cell field is represented by the grey rectangular outline. The centres of the dLGN cell fields correspond to the inner circle of the stimulus. In the case of the cortical cell the inner grating is held at the optimal orientation of the cell, the orientation of the inner grating is arbitrarily chosen for the two dLGN cells. Stimulus and protocol details are as follows. Layer VI cell: simple family cell; spatial frequency of grating, 0·66 cycles per degree (c.p.d.); contrast, 0·36; drift rate, 2 Hz; inner window, 2 deg. Each peristimulus time histogram (PSTH) is the average of 50 trials. X cell with feedback: spatial frequency of grating, 0·5 c.p.d.; contrast, 0·36; drift rate, 1 Hz; inner window, 1·0 deg; number of trials, 100. X cell without feedback: same details but number of trials, 49. The bin sizes of the display are 25 ms, vertical calibration shows the counts per bin. The records document the responses of the cells to the inner stimulus alone, inner stimulus plus outer stimulus at orthogonal orientation and inner stimulus plus outer stimulus at the same orientation. The motion of the inner and outer stimulus is phase locked so when in orientation alignment they appear as a single stimulus. The layer VI cell in the visual cortex shows a strongly enhanced response when the stimuli are in orientation alignment and a somewhat reduced response when they are orthogonally oriented (cross-orientation inhibition, see for example Sillito, 1979, 1984, 1992; Morrone, Burr & Maffei, 1982). The dLGN X cell with corticofugal feedback shows a reduced response when the surround is stimulated by the cross-oriented grating and an even greater reduction when it is stimulated by the orientation-aligned grating. The X cell studied in the absence of feedback shows a response reduction when the surround is stimulated by the cross-oriented grating but no further reduction when the two stimuli are in orientation alignment.

receptive fields studied was critical to our experiments and so these adjustments were carried out with extreme care and checked again after each data run. The accurate centring in this procedure ensured that varying the orientation of the concentric display (see below) did not vary the spatial phase of the stimulus with respect to the centre of the field.

Visual stimulus

For the preliminary evaluation of the cell response properties we used simple visual stimuli comprising flashing spots, drifting bars, phase reversing or drifting sinusoidal gratings. Parameters such as spatial frequency or phase, bar length or spot size were varied in a randomized interleaved fashion. The contrasts ($L_{max} - L_{min}$/ $L_{max} + L_{min}$) routinely used were in the range 0·36–0·72 with a mean luminance of 14 cd m^{-2}. The concentric bipartite sinusoidal gratings were centred over the receptive field centre as described above. When in orientation alignment these appeared as a single grating; varying the orientation did not change the phase – the appropriate contrast of the outer stimulus, notionally extended through the inner window, would cross the centre of the field at the same time as that of the inner stimulus, whatever the orientation. All tests were done with monocular visual stimulation of the cell's dominant eye.

Experimental protocol

When a spike was isolated and its receptive field centre determined as described above, we checked the linearity of spatial summation using phase-reversing sinusoidal gratings. The results from this, together with information regarding centre size, strength of surround antagonism and the presence or absence of a shift effect, were used to categorize the cell as X- or Y-type (Enroth-Cugell & Robson, 1967; Cleland, Dubin & Levick, 1971; Derrington & Fuchs, 1979).

Length-tuning curves were constructed for each cell using a drifting bar (0·2–0·5 deg width) with length varied on a randomized interleaved sequence. We used the optimum length of the field obtained from this data to determine the diameter of the centre window of our stimulus. In essence we attempted to ensure that the diameter of the central window of our visual stimulus matched the bar length producing the optimal responses in the cell. The diameter of the outer window was 9 deg. Once the basic receptive field parameters had been established we explored the effect of varying the orientation alignment and spatial frequency of the inner and outer stimuli on a randomized interleaved sequence. A zero modulation blank was included in the sequence for both inner and outer components of the stimulus.

It was important to check that any effects we observed did indeed dissect out an influence of the corticofugal system. For this reason we carried out two sets of control experiments. In one we removed areas 17, 18 and 19 surgically by aspiration and in the other we used microinjection of a mixture of the powerful GABA agonist muscimol (25 mM in 160 mM NaCl) and the local anaesthetic

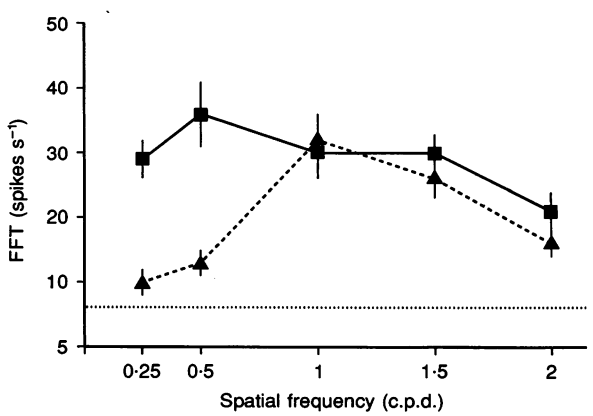


Figure 2. Spatial frequency tuning curve illustrating the response of an on-centre X cell recorded in lamina A of the dLGN with intact corticofugal feedback

The cell was stimulated with a sinusoidal drifting grating subdivided into an inner window located over the receptive field centre, and an outer window. The continuous curve shows the response to the inner grating alone, and the dashed curve represents the response to both gratings drifting with the same orientation, same temporal frequency (1 Hz) and phase locked, so they are perceived as a single full-field grating. Responses were calculated here and in the following figures as the fast Fourier transform of the first harmonic of the cell (FFT 1) and are shown ± 1 S.E.M. averaged from 90 trials. The lower dotted horizontal line shows mean background activity level. At low spatial frequencies stimulation of the surround produces a profound depression of the response to centre stimulation.

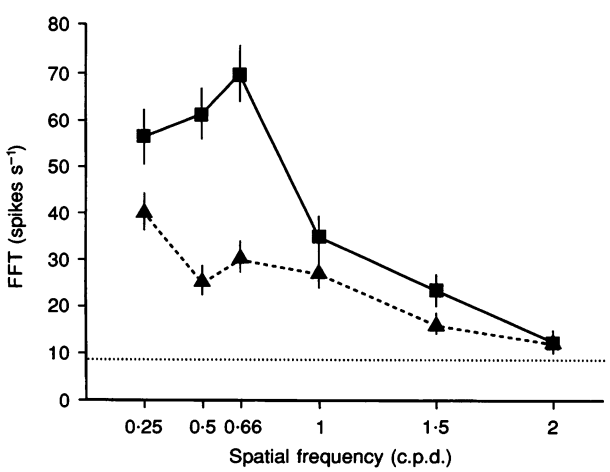


Figure 3. Response of an off-centre Y cell

Details as for Fig. 2 but the number of trials is 42.

lidocaine (1·5%). In the latter procedure we implanted twelve fine injection cannulae and associated fine tungsten electrodes into the layer V–VI border region at a series of locations through the extent of the representation of the central 15 deg of areas 17, 18 and 19. These were inserted through and held in place by a resin template matched to the surface of the cortex. The area of visual space covered by the placement was checked from the visual fields of the recording electrodes. Drugs were infused via Hamilton syringes and we monitored the effectiveness of our blockade by assessing the visual driving through the fine tungsten in glass electrodes. We routinely silenced all activity for 3–6 h by a single application. In each case the amount of the injection was determined by that required to silence cell activity and driving. We checked for visual driving at routine intervals and applied a further dose of the drugs if there was any sign of recovery. We adopted this latter procedure because it was less traumatic and also controlled for effects that could be elicited by a discharge in the damaged corticofugal axons left by the aspiration. For the aspiration procedure we photographed the lesioned area and reconstructed the lesion histologically. Similarly the locations of the microinjection/recording electrodes were reconstructed histologically.

RESULTS

The data described here were obtained from fifty-eight cells recorded in the A laminae of the dLGN of fourteen cats with corticofugal feedback and eight cats without. All these cells were recorded within 12 deg of the area centralis, with a mean eccentricity of 6·7 deg and exhibited good length tuning and centre–surround antagonism. Of these, thirty-six (21 X, 15 Y) were studied in the presence of corticofugal feedback and twenty-two (11 X, 11 Y) without feedback.

Iso-orientation centre–surround effects

The first test we carried out on all cells was to ascertain the influence of varying spatial frequency on the response to a patch of grating localized to the receptive centre and compare this with the situation when the surround mechanism was activated by a full-field stimulus (inner and outer grating together with the same relative orientation and phase). This information was obtained from tests run on a randomized interleaved sequence, as described in Methods. Examples of the records obtained from individual

Figure 4. The influence of spatial frequency on the surround antagonism of the centre response for the whole sample of X cells

The continuous curve shows the response to a patch of grating drifting over the receptive field centre. The dashed curve shows the change in response when the surround is also stimulated by a grating of the same spatial frequency, orientation and spatial phase so that the inner and outer stimuli appear as a single stimulus (see Fig. 1). The data for the sample of X cells has been grouped into a series of spatial frequency categories (c.p.d.: 0·1–0·25, 0·4–0·5, 0·7–0·85, 1–1·5, 2, 3) and for each point the error bars show ±1 S.E.M. of the response. * Points at which the results obtained from stimulation of centre alone, and centre plus surround, are significantly different (Wilcoxon test, $P < 0·01$). Although there is surround attenuation of the response at frequencies in the range 0·1–1·5 c.p.d. there is marked enhancement of the strength of the cut-off for the points in the range 0·1–0·5 c.p.d.

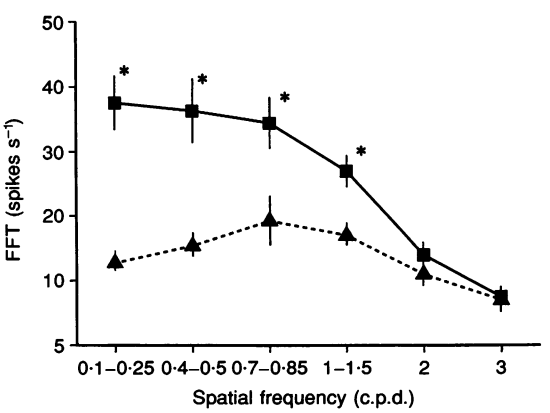
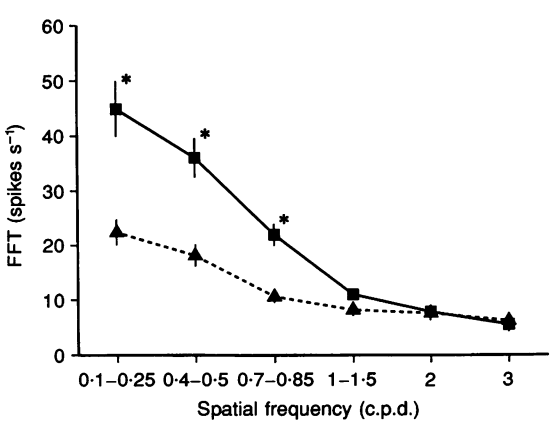


Figure 5. The influence of spatial frequency on the surround antagonism of the centre response for the whole sample of Y cells

The details are as for Fig. 4. The level of surround effect at low spatial frequencies is less than seen for X cells in Fig. 4.



X and Y cells are given in Figs 2 and 3. The continuous curves show the response to centre stimulation alone and the dashed curves the response to full-field stimulation. The mean background activity of the cells in the absence of visual stimulation is shown by the dotted horizontal line. In the case of the X cell (Fig. 2), stimulation of the surround produces a powerful suppression of the centre response at low spatial frequencies (< 1·0 c.p.d.), almost eliminating the response at 0·25 c.p.d. There is almost no surround effect on the response at spatial frequencies of 1 c.p.d. and above, despite a good excitatory response to the centre stimulus alone. The Y cell (Fig. 3) shows a particularly marked suppression in the range 0·5–0·66 c.p.d., but the attenuation at 0·25 c.p.d. is less marked than that in the X cell. In order to quantify these effects over the population of cells studied, we grouped all observations from the responses to the inner grating alone for each spatial frequency into a series of spatial frequency categories (see Fig. 4) and compared them with those from the full-field grating in the same range. The results for the populations of X and Y cells analysed in this way are shown in Figs 4 and 5. The curves are represented here in the same way as Figs 2 and 3 and show a very similar pattern of effect. Activation of the surround causes a clear and statistically significant attenuation of the response (Wilcoxon matched pairs test) to centre stimulation alone. In the case of the X cells (Fig. 4) the potency of this effect is clearly and significantly greater at low spatial frequencies, 0·1–0·85 c.p.d., than higher ($P < 0·01$), producing the low frequency cut-off that characterizes the strong surround

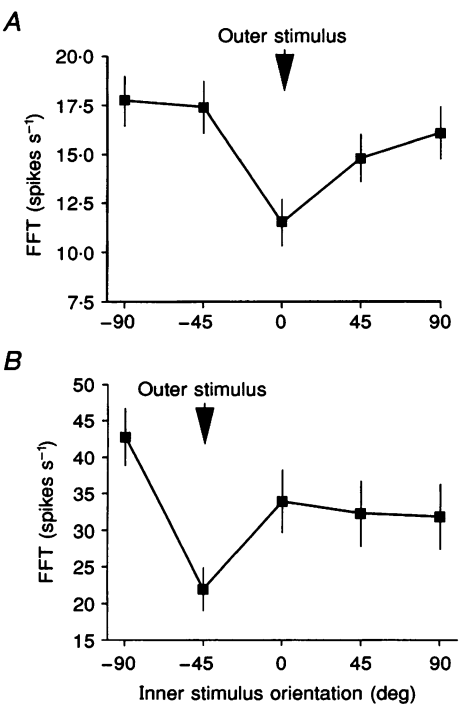


Figure 6. Effect of varying orientation alignment on the surround antagonism of the centre response of one X and one Y cell

Influence of varying the orientation alignment of the inner and outer stimuli (see Fig. 1) on the degree of surround antagonism of the centre response for the X cell shown in Fig. 2 (*A*) and the Y cell shown in Fig. 3 (*B*). In these examples the orientation of the inner stimulus was varied whilst that of the outer stimulus was held constant at the value shown by the arrow. Thus the surround stimulus is always present and the curves show the variation of the strength of the surround effect with orientation disparity between the inner and outer stimuli. There is a clear enhancement of the surround effect when the inner and outer stimuli are in orientation alignment. Test spatial frequency, 0·5 c.p.d.

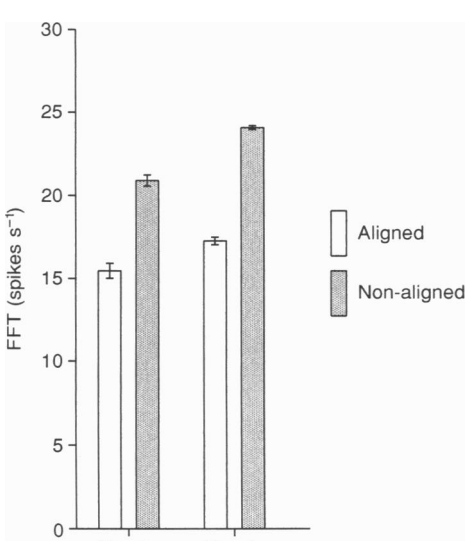


Figure 7. Effect of orientation alignment on whole sample of X and Y cells

Influence of orientation alignment of inner and outer stimuli on responses of the whole sample of X and Y cells. Columns compare mean response with stimuli in alignment (open columns) and 90 deg out of alignment (shaded columns) for X cells and Y cells as labelled. Other details as for Fig. 6. In both cases there is a highly significant difference in response levels (Wilcoxon test, $P < 0·007$) between aligned and non-aligned conditions.

influence in X cells and almost eliminating the response at the 0·1–0·25 c.p.d. point. In Y cells (Fig. 5) the influence of the surround is also marked and produces a substantial and significant response (Wilcoxon test, $P < 0·01$) reduction at low spatial frequencies (0·1–0·85 c.p.d.) but the degree of response reduction is less than that seen in the X cells for frequencies in the range 0·1–0·5 c.p.d.

Effect of orientation alignment and the contribution of corticofugal feedback

The results described so far do not give any indication of whether there is a corticofugal contribution to the response profile and could well be considered simply to reflect the concatenation of the known retinal and geniculate mechanisms establishing the surround antagonism of centre responses. However, these observations were all made with inner and outer stimulus components in orientation alignment. Varying the orientation alignment showed that the surround attenuation was significantly influenced by the relative orientation of the two components. This is shown by the curves in Fig. 6 which illustrate the effect of orientation alignment on the X and Y cells illustrated in Figs 2 and 3. In each case these curves refer to data obtained at 0·5 c.p.d. and show the variation in the level of surround attenuation as the orientation alignment was changed. The data points illustrated show the effect of holding the outer stimulus orientation constant at the value indicated by the arrow and varying the orientation of the inner stimulus. It is apparent that the response is decreased at the alignment condition; that is, the degree of surround suppression of the response appears to increase when the stimuli are in alignment. This point is summarized for all the X (21) and Y (15) cells with feedback in our sample in Fig. 7. The columns show the mean change in response between the aligned and non-aligned conditions. The difference in response is highly significant for both groups (Wilcoxon test, $P < 0·007$). It seems likely that there may be a corticofugal contribution to the observations obtained with the outer and inner stimuli in alignment (see Fig. 1).

Comparison of the data obtained from the samples of cells with and without corticofugal feedback underline the latter point. Figures 8 (X cells) and 9 (Y cells) compare the surround attenuation of the centre response in the two groups. The filled columns show the percentage attenuation of the centre response seen in the presence of feedback and the hatched columns the attenuation in the absence of feedback. For the Y cell group the loss of feedback results in a significant reduction in the surround-mediated attenuation of the centre response for points in the range 0·1–0·85 c.p.d. (Mann–Whitney U test, $P < 0·005$ at 0·1–0·25 c.p.d. point). Referring back to Fig. 5 it is clear

Figure 8. Effect of corticofugal feedback on centre *versus* full-field response in X cells

Influence of corticofugal feedback on the surround antagonism of centre responses in X cells. The data are grouped into the same spatial frequency groups as in Figs 4 and 5. The filled bars show the percentage reduction in centre response when the surround is stimulated for X cells under control conditions. The hatched bars show the same information for the sample of X cells studied without feedback. There is a marked and significant (Mann–Whitney U test: $^{**}P < 0·005$) decrease in the level of reduction for spatial frequencies in the range 0·1–0·5 c.p.d. These figures concatenate the data from all the cells studied in the group with feedback and the group without feedback. The conclusions also hold at the same level of significance if the observations for each experiment are first averaged and then pooled. n.s., not significant.

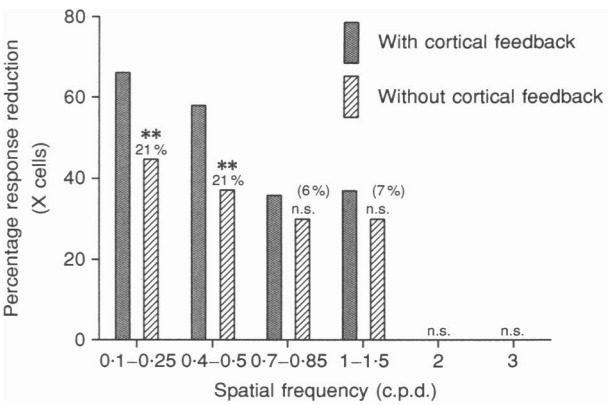
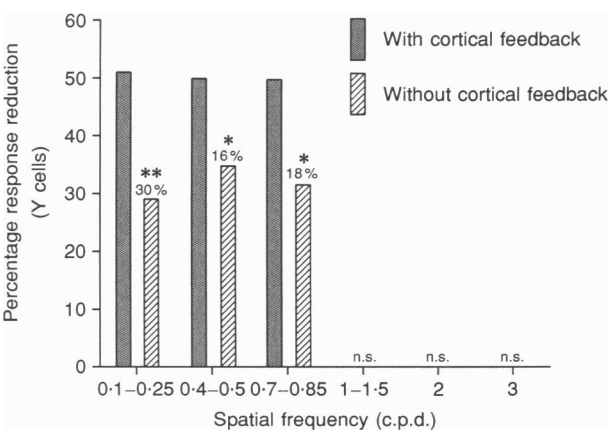


Figure 9. Effect of corticofugal feedback on centre *versus* full-field response in Y cells

Influence of corticofugal feedback on the surround antagonism of centre responses in Y cells. Details are the same as for Fig. 8. The decrease in level of surround attenuation of centre responses linked to the loss of feedback extends from 0·1 to 0·85 c.p.d. in our Y cell sample and is significant throughout the range (Mann–Whitney U test: $^{**}P < 0·005$, 0·1–0·25 c.p.d.; $^{*}P < 0·05$, 0·4–0·85 c.p.d.). n.s., not significant.



that this encompasses all the points where the Y cells exhibited a strong centre response and evidence of strong surround effects. The same is not true for the X cells, since although the sample without feedback shows smaller surround effects at all points in the range 0·1–1·5 c.p.d., these are only significantly different from the group with feedback for points in the range 0·1–0·5 c.p.d. (Mann–Whitney U test, $P < 0{\cdot}005$). This suggests that the corticofugal feedback is primarily enhancing surround effects at low spatial frequencies in the X cells.

The bias of the corticofugal influence to low spatial frequencies is brought into a sharp focus when the alignment effect is examined. Figures 10 (X cells) and 11 (Y cells) show the increase in response reduction seen when the inner and outer stimuli move from the non-aligned to aligned condition. The filled columns again show observations made in the sample of cells with feedback and the hatched columns observations made in those without. Two things are noticeable from these figures. Firstly, for both X and Y cells the alignment effect is only significant at low spatial frequencies, in the range 0·1–0·5 c.p.d. Secondly, in the absence of corticofugal feedback, it is virtually eliminated in both the X and Y cells, although the 0·4–0·5 c.p.d. point in X cells is slightly less affected. It seems the alignment effect is very dependent on the corticofugal feedback and is strongly biased to low spatial frequencies. The persistence of a small element of the alignment effect in the absence of corticofugal feedback could reflect a contribution from a subcortical mechanism or it could reflect an incomplete loss of the corticofugal feedback. Both our procedures for disenabling the feedback were subject to limitations. In the experiments using aspiration of areas 17 and 18 we were aware that we frequently left islands of cortex that could have remained functional. Equally in those using drug blockade, despite our monitoring procedures, it was impossible to be sure that all layer VI cells had been silenced. The cardinal point is that removing the feedback produces a massive reduction in the alignment effect suggesting a very strong dependence on the feedback.

Intriguingly, our data also suggest the presence of an element of influence from the cortex that is independent of the alignment effect and is exemplified by the data for the 0·7–0·85 c.p.d. point for Y cells (compare Figs 9 and 11). Here there is a significant reduction in the surround attenuation in the sample without feedback for the iso-orientation condition (i.e. centre alone *versus* centre + surround), but no variation of this with the switch between aligned and non-aligned conditions (i.e. centre + surround, non-aligned *versus* centre + surround, in alignment).

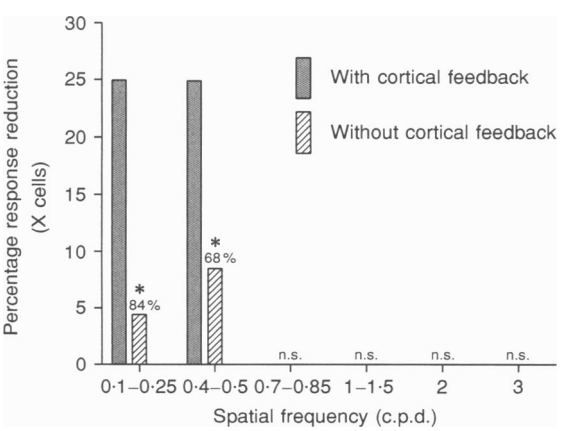


Figure 10. Corticofugal effects on alignment *versus* non-alignment response in X cells

The effect of corticofugal feedback on the enhancement of the surround effect seen in X cells when the inner and outer stimuli move to the orientation-aligned condition (see Fig. 6). The filled columns show the percentage enhancement of the surround effect for the alignment condition with feedback present ($n = 21$ cells). The hatched columns show enhancement seen in the absence of feedback ($n = 11$ cells). The two sets of results are highly statistically different (Mann–Whitney U test: $*P \leqslant 0{\cdot}001$). n.s., not significant. See text for further details.

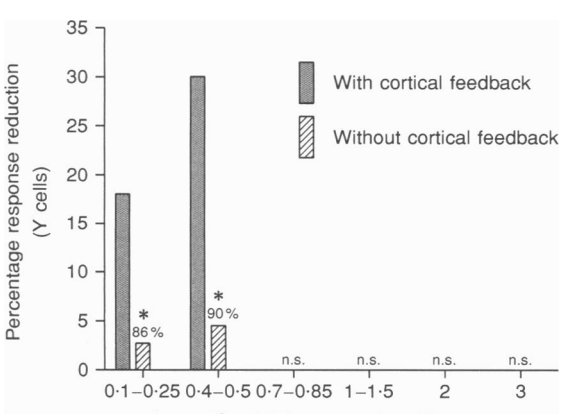


Figure 11. Corticofugal effects on alignment *versus* non-alignment response in Y cells

The effect of corticofugal feedback on the enhancement of the surround effect seen in Y cells when the inner and outer stimuli move to the orientation-aligned condition (see Fig. 6). Details as for Fig. 10 ($n = 15$ cells with feedback, 11 without). $*P \leqslant 0{\cdot}001$ (Mann–Whitney U test). n.s., not significant. See text for further comment.

DISCUSSION

The data reported here encompass observations at several levels. The comparison of the responses to stimulation confined to the receptive field centre alone, or centre and surround together in the aligned orientation condition, illustrate the influence of surround mechanisms on the spatial frequency tuning of dLGN cells. The term 'surround' needs to be used with caution, because our observations obviously concatenate influences deriving from retinal, geniculate and cortical mechanisms. Nonetheless it is very clear from our data that in the most simple sense there is a powerful surround-mediated antagonism of responses elicited from the receptive field centre. In X cells this is strongest at low spatial frequencies whilst in Y cells the influence is more uniform across the range of spatial frequencies driving the cell, but still marked. This is compatible with evidence showing that spatial selectivity is enhanced in dLGN cells by an enhanced surround inhibition of centre-elicited responses (Hubel & Wiesel, 1961; Sillito & Kemp, 1983). It is known that the surround mechanism at the level of the dLGN is strongly reinforced by GABAergic inhibitory mechanisms relating to the intrinsic and perigeniculate inhibitory interneurones (Sillito & Kemp, 1983; Sillito, 1992) and that these mechanisms provide a major component of the enhanced low frequency cut-off seen in dLGN X cell fields (Berardi & Morrone, 1984). There is not complete accord on this view, however, because Kaplan, Purpura & Shapley (1987), for example, have reported that the dLGN cell response was only slightly more tuned than its retinal input. They observed a 'mild attenuation' at low spatial frequencies of the retinal response profile judged from simultaneous recordings of S potentials (presumed to derive from retinal afferents; see Kaplan *et al.* (1987). The effects seen here certainly reveal a much stronger effect than Kaplan *et al.* (1987) and match the predictions that would follow from Hubel & Wiesel's original work and the subsequent observations utilizing GABA blockade (Sillito & Kemp, 1983; Berardi & Morrone, 1984). One reason for this distinction may lie in the anaesthetic regime employed by Kaplan *et al.* (1987), who used ketamine followed by urethane, in contradistinction to the halothane and nitrous oxide employed in our laboratory.

It might seem that our observations could be entirely explained in terms of the subcortical and retinal mechanisms known to contribute to centre–surround antagonism. However, the study of the effects of both stimulus alignment and cortical inactivation show the presence of a strong cortical contribution to the observations. The corticofugal system enhances the surround antagonism of the centre response and does this most strongly when the stimuli overlying the surround and centre mechanisms are in orientation alignment. The logic of this follows from the observed responses of layer VI cells and is summarized in Fig. 1. The assumption is that the dLGN cell receives its feedback from layer VI cells with their receptive fields centred on that of the projection column containing the dLGN relay cell under study. Two factors may contribute to the layer VI cell response; firstly, the elongate nature of the orientation-tuned receptive field, and secondly, the known excitatory connections between columns of like orientation (Gilbert, 1977; Grieve & Sillito, 1991; Ts'o, Gilbert & Wiesel, 1986; Martin, 1988; Gilbert & Wiesel, 1989; Engel, König, Gray & Singer, 1990). The orientation-aligned condition produces the maximal level of facilitation in the layer VI cell. This assumes non-end-stopped layer VI cells provide the feedback (e.g. Gilbert, 1977); it could hardly be otherwise because an end-stopped layer VI cell would not respond to the longer stimulus seen in the orientation-aligned condition. Previous work (Sillito *et al.* 1993) has provided evidence to indicate that feedback from the cortex to any given dLGN cell derives from a complete set of orientation columns. This follows from the observation that the orientation-alignment effect is seen for any given overall orientation of the inner and outer stimuli. Thus, for any given 'centre' orientation, only the responses of the particular layer VI cells responding to that orientation in the subset providing the feedback will be modulated by the alignment protocol. In our data, the move from non-aligned orientation to orientation-aligned stimuli results in a marked enhancement of the surround antagonism of the centre response of dLGN cells, at all orientations tested.

The crucial issue in this work concerns the way these effects elicited from the cortex are influenced by spatial frequency. Firstly, as indicated in Figs 10 and 11, the enhancement of surround antagonism as the stimulus components are shifted to alignment is strongly dependent on the presence of the cortical feedback. Secondly, the shift only produces a significant effect at spatial frequencies in the range 0·1–0·5 c.p.d., suggesting that the influence of the cortical feedback is strongly biased to low spatial frequencies. This raises the possibility that the layer VI cells providing the feedback might be biased towards low spatial frequencies. An earlier study supports this view, indicating that deep-layer cells of the visual cortex respond better to lower spatial frequencies than do the cells in layers II–III and IV (Maffei & Fiorentini, 1977) whilst other evidence (Tolhurst & Thompson, 1981) suggests there is no laminar variation. More recently Grieve & Sillito (1992) reported the mean optimum spatial frequency for layer VI cells in their sample to be 0·47 ± 0·04 c.p.d., with 61% having optimal spatial frequencies below 0·5 c.p.d. This is consistent with the spatial frequency range of the cortically dependent alignment effect. Nevertheless, it is important to note that in our sample of Y cells there is also evidence for a feedback-dependent enhancement of the surround antagonism of centre responses in the range 0·7–0·85 c.p.d. (Fig. 9), but this effect is not influenced by the move to stimulus alignment in a significant way (Fig. 11). This does not seem to apply to X cells. There are thus two components to our observations regarding the nature of the cortical influence on dLGN cells. One, affecting both X and Y cells, is sensitive to the orientation discontinuity and biased to low

spatial frequencies; the other, notable only in Y cells, is not sensitive to the discontinuity and extends up to higher spatial frequencies. Several lines of evidence support the view of two or more channels of feedback from the visual cortex and segregation of some effects between X and Y cells (Tsumoto, Creutzfeldt & Legendy, 1978; Boyapati & Henry, 1987; Vidnyansky & Hamori, 1994; Sillito, Jones, Gerstein & West, 1994; Grieve & Sillito, 1995). It is thus likely that the present observations reflect the interacting influence of the different components of the corticofugal feedback in the LGN and pick out a component that is discrete to the Y system.

The corticofugal projection makes synaptic contact on intrinsic inhibitory interneurones in the dLGN, inhibitory interneurones in the perigeniculate nucleus and relay cells (Weber *et al.* 1989; Montero, 1991). The relative bias in the distribution of connections to relay cells and GABAergic inhibitory interneurones is not clearly resolved at present, having been claimed to favour inhibitory interneurones (Weber *et al.* 1989) and relay cells (Montero, 1991). Our data reported here demonstrate a corticofugal enhancement of surround-mediated inhibitory mechanisms in the dLGN which seems to favour a bias to inhibitory interneurones. However, given the direct projection to relay cells, one might expect evidence of excitatory corticofugal effects. The absence of clear facilitatory effects seems to question the efficacy of the direct contacts to relay cells. These are known to contact distal, as opposed to proximal, dendritic processes on relay cells in contrast to the retinal afferents which synapse on proximal dendrites (Wilson *et al.* 1984) and thus their impact on the activity of the relay cells may be relatively subtle. Indeed, we have recently shown that the corticofugal feedback can synchronize the activity of dLGN cells with spatially separate receptive fields, when their receptive fields are simultaneously stimulated by a moving contour, because the layer VI cells, themselves activated by the contour, act as a common mode input (Sillito *et al.* 1994). This will increase the gain of their convergent input to cells in layer IV of the cortex, because it will cause temporal overlap of their EPSPs in the target cells. This may be the primary influence of the direct corticofugal contact on relay cells. The essential point from the present work is that when the spatial characteristics of the visual stimulus are appropriate, the gain of the inhibitory contribution of the surround to the response of dLGN cells is modulated, up or down, in a way that reflects the observed response properties of layer VI cells. Thus there are two facets to the corticofugal influence in the LGN and these seem to follow from the logic of the connections to relay cells and inhibitory interneurones.

How might the inhibitory and synchronizing influences of the corticofugal feedback relate to visual processing? Firstly, the net effect of the inhibitory component of the feedback would seem to be to diminish the output from cells in the dLGN with receptive fields underlying a continuous straight contour. The hyperpolarizing influence underlying this effect may serve to render the cells more susceptible to the synchronizing effect of the direct corticofugal synaptic contacts. The synchronization of the LGN cell firing results in overlapping EPSPs in their cortical target cells and hence an increase in the gain of the synaptic input. The net effect of the two processes may be to bring the access and temporal co-ordination of the geniculate input to the cortex strongly under cortical control.

One consequence of the length tuning of dLGN cells (Schiller, Finlay & Volman, 1976; Cleland *et al.* 1983; Jones & Sillito, 1991) and its enhancement from the cortex (Murphy & Sillito, 1987; Sillito *et al.* 1993) is that when a row of receptive fields is driven by the motion of an elongate contour it is those cells located at the ends of the contour that will provide the strongest input to the cortex, whilst those in the middle the least. Thus, considering the classical model for the input to a simple cell (Hubel & Wiesel, 1962), the potentially strongest drive will come from LGN inputs at either end of the field and these may be made even more potent by the synchronizing influence of the feedback (see Fig. 2*a–d* in Sillito *et al.* 1994). Where there is a variation in the orientation of the profile of a contour, the orientation discontinuity, as shown in these experiments and previously (Sillito *et al.* 1993), will result in a higher output from those cells with receptive field centres underlying the discontinuity. Thus, the orientation-domain discontinuity generates a reduction in the magnitude of the feedback to those cells underlying the discontinuity, with a resultant increase in their uncorrelated discharge. This effect is maximal at low spatial frequencies and the situation might be summarized by saying that the feedback seems to underpin a high-pass filter, but open it out at locations where there is a discontinuity in the orientation domain. Hypothetically, for a concentrically arranged dLGN receptive field, a patch of grating restricted to the receptive field centre of one dLGN cell and moving in phase with, but cross-oriented (90 deg) to a patch of surrounding grating, could evoke essentially the same pattern of output from the dLGN as would occur if it were iso-oriented. Thus there is a potential ambiguity in the output with respect to the concern of the cortex with contour orientation. The reduction in cortical feedback 'picks this out', however, and causes the geniculate output to distinguish between the situations. The upswing in the input to the cortex at the location of the discontinuity in turn may enable cortical circuitry to pick up and lock onto further correlations which might establish the presence of another contour centred around this location. Although these effects are complex they suggest a range of mechanisms by which the feedback can influence the gain and organization of the geniculate input to the cortex in

ways which reflect those facets of the input that are significant to the cortical mechanism, as reflected in the activity of layer VI cells.

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