Corticothalamic interactions in the transfer of visual information

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Thalamic function does not stand apart, as a discrete processing step, from the cortical circuitry. The thalamus receives extensive feedback from the cortex and this influences the firing pattern, synchronization and sensory response mode of relay cells. A crucial question concerns the extent to which the feedback simply controls the state and transmission mode of relay cells and the extent to which the feedback participates in the specific processing of sensory information. Using examples from experiments examining the influence of feedback from the visual cortex to the lateral geniculate nucleus (LGN), we argue that thalamic mechanisms are selectively focused by visually driven feedback to optimize the thalamic contribution to segmentation and global integration. This involves effects on both the temporal and spatial parameters characterizing the responses of LGN cells and includes, for example, motion-driven feedback effects from MT (middle temporal visual area) relayed via layer 6 of V1 (primary visual cortex).

Keywords: lateral geniculate nucleus; corticofugal feedback; primary visual cortex; middle temporal visual area

1. INTRODUCTION

The past decade has seen a growing recognition that the thalamus does more than simply relay sensory information to the cortex (McCormick & Bal 1997; Sillito & Jones 1997; Sherman & Koch 1998; Jones 2001; Sherman 2001). The emerging detail and complexity of the circuitry and neurotransmitter systems (Szentagothai 1970; Sherman & Guillery 2002) alone highlight the issue. Above all it is clear that its function does not stand apart, as a discrete processing step, from the cortical circuitry. The thalamus receives extensive feedback from the cortex and this influences the firing pattern, synchronization and sensory response mode of relay cells. A crucial question concerns the extent to which the feedback simply controls the state and transmission mode of relay cells (Steriade *et al.* 1993; Sherman 2001) and the extent to which the interaction between the cortex and thalamus participates in the specific processing of sensory information in the waking state. We consider this issue with reference to the visual system and the LGN. At the heart of the problem is the distinction between a generic role for the feedback systems as evinced by corticothalamic interactions in sleep, and a discrete role where fine stimulus-dependent interactions influence the way thalamic cells transfer sensory information.

In the visual system the feedback to the LGN is retinotopically organized, and the cells in layer 6 of the visual cortex that provide the feedback have functionally selective visual-response properties (see § 3) and low spon-

taneous activity. Thus the unique signature of any retinal image will in turn evoke a unique pattern of feedback from the visual cortex to the thalamus. This reflection of the influence of the cortical mechanism, therefore, has the capacity to produce a selective retinotopic and possibly feature-linked pattern of change in the thalamic mechanisms. An argument that could be placed against this is that the spread of the arborization of the feedback axons in the LGN is such that any fine distinctions of this type would be simply diffused and lost. Conversely, the presence of asymmetries in the axonal projections of feedback cells that link to the visual-response properties of the parent cells (see Murphy *et al.* 1999) supports the concept of a spatial focus to the influence of feedback. Likewise, it is not clear that one would expect any and every stimulus to reset the behaviour of the relay in the same way. These issues are not, however, simply resolved. A further question is the extent to which the feedback from V1 to the LGN in the primate, for example, is itself influenced by feedback from higher visual areas. Area MT provides feedback to layer 6 of primate V1 that accesses the feedback cells linked to all the processing streams. Do changes in MT-cell responses thus precipitate changes in the LGN? The magnocellular driven responses in MT occur at a very short latency and so could reflect an influence back to the LGN that, for example, influences parvocellular-driven responses as they are beginning to evolve. A particularly important problem is whether the feedback connections inject spikes into the response of relay cells. It is clear that this can occur under certain very restricted experimental paradigms but it is much less clear that it occurs during visual stimulation. There are strong arguments for a predominantly modulatory influence on relay cells and interneurons but again this needs to be clearly resolved.

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We consider in the following sections examples of experimental data that provide insight into some of these questions and discuss their implications. The balance of our evidence favours a pattern of influence from the corticogeniculate feedback that, by shifting the balance of mechanisms underlying the centre-surround organization of the receptive field, highlights processes that aid both local segmentation and contour integration. In addition, our data suggest that visual stimuli highlighting foci of activity in V1 have the potential to shift relay cells between burst and tonic modes in a fashion that matches the ideas contained in the arguments framed by Sherman & Guillery (2002).

2. FUNCTIONAL CONNECTIVITY

For cats and primates the retinal afferents comprise *ca.* 10% of the input to LGN relay cells, whereas the corticofugal feedback connections to the relay cells represent 30% of the input (Wilson 1993; Erisir *et al.* 1997; Van Horn *et al.* 2000; Sherman & Guillery 2002). As well as the relay cells, the cortical feedback connections target intrinsic inhibitory interneurons in the LGN and inhibitory neurons in the thalamic reticular nucleus/PGN. In considering this, a further critical perspective comes from the fact that the projections from LGN relay cells provide a surprisingly small component of the excitatory synaptic input to the main geniculate recipient cells in layer 4 of the visual cortex. In the cat this is just 6%, with 45% linked to the collaterals of layer 6 cells that provide feedback to the LGN and 28% from neighbouring spiny stellate cells (Ahmed *et al.* 1994). In the primate the magnocellular input to layer 4C α comprises 8.7% of the asymmetric synapses and the parvocellular input to 4C β just 6.9% of the asymmetric synapses. The remaining asymmetric synaptic inputs to cells in 4C α and 4C β may be presumed to follow the same overall balance of the pattern reported in the cat with strong inputs from layer 6 and surrounding spiny stellates (Latawiec *et al.* 2000). The intriguing issue here is the unique role of the layer 6 cells in relation to the transfer of retinal information to the cortex. Numerically they contribute most of the connections to LGN relay cells and to the spiny stellate cells receiving the input from the relay cells. The role of the feedback to the LGN cannot be considered in isolation from the role of the collateral projection to layer 4.

The main details of the circuitry are summarized in figure 1. In the cat the projection to the LGN, which derives primarily from areas 17 and 18, is dense and individual corticofugal axon's arborizations have a central core projection of *ca.* 180–1080 μm with a sparse scattering of long-range axons which spread over 500–2000 μm (Robson 1984; Murphy & Sillito 1996; Murphy *et al.* 2000). Note that the average spread of the retinal X axonal arborizations is 150 μm and the Y axons 375 μm (Bowling & Michael 1984). Thus, even within their central core, individual corticofugal axons innervate an area of the LGN that extends significantly beyond their own location in retinotopic space. These points and the circuitry in the LGN are summarized in figure 1. This, and their longer range connections, means that they can influence inputs that may lie outside their own classical receptive field. There is also good evidence favouring the view

Figure 1. Schematic diagram summarizing the main components of the geniculo-cortico-geniculate circuitry. The retinotopic extent of the axonal arborizations of X and Y retinal ganglion cells (at 5° eccentricity) within the LGN are denoted by the red and yellow ovals, respectively. The extent of the feedback arborization from layer 6 is summarized by the two green ovals. The central oval depicts the dense central core of the projection while the larger oval depicts the overall distribution of the terminal arbor. The inset to the bottom right summarizes the relative proportions (in per cent) of synaptic contacts on LGN relay cells from retinal ganglion cells, layer 6 cells and inhibitory interneurons. The upper inset summarizes the relative proportions of excitatory contacts on layer 4 spiny stellate cells.

that the projection comprises axons of several diameters and conduction velocities. Individual axons, both coarse and fine, seem to innervate both PGN and LGN (Robson 1983; Boyapati & Henry 1984; Murphy & Sillito 1996; Murphy *et al.* 2000). Similarly, estimates of the conduction velocity from latency measurements provide support for two groups of corticofugal afferents (Tsumoto *et al.* 1978; Tsumoto & Suda 1980; Boyapati & Henry 1987; Grieve & Sillito 1995a) projecting to the LGN and PGN. The fastest pathway allows for a very rapid influence of the corticofugal system on the developing response and would enable the loop from LGN-cell response to cortex and back within a time window of *ca.* 3–5 ms. Even the slower group would enable a loop within 4–10 ms. The organization of layer 6, and its interactions in the LGN, in the primate is particularly interesting because there is a clear segregation of cells in relation to the incoming channels. Cells projecting to the parvocellular layers of the LGN lie in the upper part of layer 6 whereas the lower part contains cells projecting to both magnocellular and parvocellular laminae (Fitzpatrick *et al.* 1994). In addition, the intercalated cells in the LGN that send axons to layer 1 and the cytochrome oxidase-rich blobs (Hendry & Yoshioka 1994; Ding & Casagrande 1997) seem to receive feedback from a distinct group of layer 6

Figure 2. Retinotopic asymmetries in the distribution of feedback terminals links to physiological response properties of the parent cells. (a) Summary of method. The response properties of layer 6 cells were quantified before the injection of biocytin and their receptive fields were overlaid on the geniculate retinotopic map. The bouton distribution of single axons was reconstructed in three dimensions and analysed for the geniculate representation of visual space. (b) In general, feedback axons contacted LGN cells lying in a line either parallel to, or perpendicular to, the axis of the orientation preference of the parent layer 6 cell. Modified from Murphy *et al.* (1999).

cells in the deepest part of layer 6 (Fitzpatrick *et al.* 1994). The intracortical connections of these layer 6 cells are equally discrete, showing dendritic and axonal configurations that are extremely laminar specific, so that some parvocellular projecting layer 6 cells may have dendritic axonal arborizations that are, for example, almost exclusively focused on layer 4C α or layers 4C β and 4A. Magnocellular projecting cells, however, may have axonal and dendritic arborizations that distribute through layer 4C α whereas others may distribute through 4C and enter 4A (or above). Cells in the middle of layer 6 do not project to the LGN although some project to the claustrum but they have very specific patterns of axonal distribution within 4C and include some that seem to sample both parvocellular and magnocellular sections of 4C (Wiser & Callaway 1996; Callaway 1998). In the cat there is less apparent specificity among corticogeniculate cells in V1.

In considering the issue of specific versus generic roles for the feedback to the LGN the presence of retinotopic asymmetries in the distribution of the feedback terminals that link to the physiological response selectivity of the parent cell is a highly important factor. In the cat the experiments that have reconstructed the axonal arborization of single feedback axons originating from cortical cells that have been functionally studied with visual stimuli show just such an asymmetry. The most dense component of the terminal arborizations are extended either parallel or perpendicular to the axis of the orientation preference of the parent cell in layer 6 of the visual cortex (Murphy *et al.* 1999) as shown in figure 2. This anatomical asymmetry indicates that the feedback might be organized to influence the processing of information relevant to the extraction of the orientation of contours in the visual cortex.

Figure 3. Effect of corticofugal feedback on LGN-cell area summation properties. (a–d) Area summation curves recorded to flashing spots (a,b) and drifting gratings (c,d) of varying diameter. The records in (a) and (c) are from cells with intact corticofugal feedback, those in (b) and (d) show the responses of cells recorded in the absence of feedback. (e,f) Median box plots compare the percentage suppression observed in the control and decorticate conditions across the population of cells tested for flashing spots (e) and drifting gratings (f).

3. FUNCTIONAL PROPERTIES OF LAYER 6 FEEDBACK CELLS

A proper characterization of the visual-response properties of identified corticofugally projecting cells is very important because it identifies the type of stimuli that will influence the transfer of visual information in the LGN and layer 4 of V1. For the feline visual system feedback projections originate from both simple and complex cells (Grieve & Sillito 1995a) with simple cells predominating

(Gilbert 1977; Tsumoto *et al.* 1978; Harvey 1980; Tsumoto & Suda 1980; Grieve & Sillito 1995a). The complex cells are spontaneously active and are strongly binocular, directional, broadly orientation tuned and capable of responding at high stimulus velocities. The simple cells, on the other hand, have little or no spontaneous activity, are sharply orientation tuned and include cells strongly or exclusively dominated by one eye. Despite the widespread belief that the corticofugal projection originates from cells

Figure 4 (*Caption opposite.*)

with very long fields (generally 8° or more, Gilbert (1977)) the cells that project back to the LGN actually have much shorter receptive fields whereas cells with longer fields project to the claustrum (Grieve & Sillito 1995a). Indeed, in layer 6 as a whole short field cells predominate (Grieve & Sillito 1991a, 1995a). One factor stands out from all the available evidence: both the simple and complex cells projecting to the LGN tend to be strongly directionally sensitive. Although there is no direct evidence about the properties of corticogeniculate cells in the primate, there is a wide consensus (Dow 1974; Schiller *et al.* 1976; Livingstone & Hubel 1984; Orban *et al.* 1986; Hawken *et al.* 1988) for a preponderance of directionally selective

cells in layer 6 along with layer 4 (A, B and $C\alpha$). Moreover, directionally selective simple cells have been reported to be the dominant cell type in layer 6 (Hawken *et al.* 1988), although there is substantive variance among investigators regarding this issue. It is also pertinent to note a report by Anderson *et al.* (1993) of a labelled cell in layer 6 with an intrinsic axonal arborization that is largely restricted to $4C\beta$ and 4A. The details of this are consistent with the type of cell from upper layer 6 thought to project to the parvocellular laminae of the LGN. It had a non-oriented receptive field and was excited by long wavelengths. Other investigators have reported colour-coded and/or non-oriented cells in layer 6 (Livingstone & Hubel

Figure 4. Corticofugal feedback enhances local segmentation effects in LGN cells. (a,b) LGN-cell responses to orientation contrast in the presence (a) and absence (b) of feedback. The bar histogram shows the cells' responses (spikes $s^{-1} + 1$ s.e.m.) to three stimulus conditions (shown diagrammatically by the stimulus icons above). These comprised a circular patch of grating overlying the receptive-field centre, the introduction of a surrounding field of identical grating drifting in the same direction of motion and the presence of an orthogonally oriented surrounding grating. The drift direction is denoted by white arrowheads. (c,d) LGN-cell response to temporal/phase contrast in the presence (c) and absence (d) of feedback. Stimulus details as for (a), but the last record shows the effect of changing the drift rate of the surrounding grating. (e,f) Detailed dissection of the influence of feedback on temporal frequency/phase contrast. The tuning curve in (e) plots the effect of varying the temporal frequency of the surround annulus on the percentage suppression observed (with respect to the response to the central stimulus alone) in the presence of feedback. The inner temporal frequency was fixed at 2 Hz. An example recorded in the absence of feedback is shown in (f). (g,h) Detailed dissection of the influence of feedback on orientation contrast. The surface plot in (g) shows the response of an LGN cell (in the presence of feedback) to varying the orientation of an inner patch of grating in the presence of an outer patch of grating also of varying orientation. The diagonal running from the bottom left to the top right represents all those points where the orientation of the centre and surround stimuli were the same, over a complete sequence of absolute orientations. The response magnitude is shown by the height and colour of the contour. An example recorded in the absence of feedback is shown in (h). Note the absence of the pronounced diagonal trough. (i,j) Population summary of the influence of feedback on orientation contrast. These histograms plot the percentage change in the response observed between the iso-oriented and orthogonally oriented surround configurations (normalized with respect to the centre-only response) in the presence (i) and absence (j) of corticofugal feedback. The mean increase in response magnitude for the switch from iso- to cross-oriented surround was 24.3% and this reduced to 5.6% without feedback. These observations are summarized from Cudeiro & Sillito (1996) and Sillito *et al.* (1993).

1984). This introduces the possibility of a feedback influence that might be segregated for wavelength processing.

4. EFFECTS OF FEEDBACK ON LATERAL GENICULATE NUCLEUS-RESPONSE PROPERTIES

(a) *Influence on response properties linked to centre-surround interactions*

A major characteristic of the influence of feedback on LGN-cell visual responses seems to be an enhancement of the strength of the inhibitory surround in the presence of moving stimuli, so that cells are more strongly patch suppressed (and end-stopped) and the excitatory discharge zone for a moving stimulus is more focused (see Murphy & Sillito 1987; Sillito *et al.* 1993; Cudeiro & Sillito 1996; Jones *et al.* 2000a; Andolina *et al.* 2000). Thus the records in figure 3a–d give examples of the effect of feedback on the area summation curves of LGN cells generated by varying the diameter of either a flashing spot of light centred over the receptive field (figure 3a,b) or a

patch of drifting grating centred over the receptive field (figure 3c,d). Interestingly, the surround suppression seen in the area summation curve for the flashing spot is unaffected by the loss of feedback whereas that for the drifting grating is greatly reduced. This point is summarized for the population of cells studied in figure 3e (flashing spots with and without feedback) and 3f (drifting grating with and without feedback). The enhancement of the inhibitory surround for moving stimuli also seems to lead to an increased sensitivity to orientation contrast, direction contrast and temporal/phase contrast between the centre and surround mechanisms (Sillito *et al.* 1993; Cudeiro & Sillito 1996; Sillito & Jones 1997). Some examples of this are illustrated in figure 4a–j. The block histograms in figure 4a–d illustrate the sensitivity of LGN cells to an orientation difference (figure 4a,b) or a temporal frequency difference (figure 4c,d) between a stimulus over the receptive-field centre and a surrounding stimulus in the presence and absence of feedback. It is clear that this sensitivity is lost when there is no feedback. These issues are explored in more detail in figure 4e–j. The curves in figure 4e,f show the effect of varying the temporal frequency of the surround stimulus through a range of values while holding that of the central stimulus constant (temporal frequency of the inner stimulus indicated by grey bars) for example, Y cells studied in the presence and absence of feedback.

The sensitivity to an orientation difference between the centre and surround mechanism reflects sensitivity to orientation contrast and is not influenced by the absolute orientation of the stimulus. This is demonstrated by the surface plot in figure 4g, which shows the response of an LGN cell when the orientation of a central and surrounding stimulus are varied independently in a random and interleaved fashion. Those instances where the orientation of the inner and outer are the same lie along a diagonal line from the top right to the bottom left. This diagonal is marked by a trough of low response levels that is absent for the example shown without feedback (figure 4h). Thus, with feedback, cells are able to signal orientation contrast. The difference in the sensitivity to orientation contrast is summarized by the population histograms in figure 4i,j that show the percentage change in response seen for a shift from an iso-oriented to a cross-oriented surround for cells studied with (figure 4i) and without (figure 4j) feedback. The arrowhead highlights the point for zero change. For all these records the influence of the feedback might broadly be described as enhancing fine-scale segmentation and the spatial focus of the receptive fields.

(b) *Influence on synchronized firing of LGN cells coactivated by drifting contours*

A key to the detection of the common elements of a contour is integration. The inputs driven by the components of a moving contour at a particular orientation would need to be integrated by a mechanism detecting the orientation. At the most basic level simple cells in the visual cortex integrate the inputs from LGN cells to detect the presence of contours of a particular orientation (see figure 5). An appropriately oriented bar would co-activate the converging inputs illustrated in figure 5 and synchronize their firing. The degree of synchronization of the inputs has a strong bearing on their ability to influence the simple

Figure 5. Stimulus-linked synchronization in the LGN. (a) Experimental method. The responses of pairs of LGN cells to drifting gratings of varying orientation were recorded and raw cross correlograms constructed for each stimulus orientation. (b) Raw cross correlograms recorded from a pair of LGN cells for three stimulus orientations. The shaded bar centred at time 0 indicates a 5 ms time epoch and highlights the correlated events occurring within the supra-linear integration window of a cortical layer 4 cell. (c) Surface representation showing the cross correlation data (y-axis) versus orientation (x-axis) for an LGN-cell pair recorded in the presence of feedback. The colour scale represents the number of correlated events from low (dark blue) to high (dark red). The tuning curve above the plot depicts how an orientation tuning curve could be derived from the numbers of correlated events occurring in a 5 ms integration window. (d) Orientation tuning curves for two LGN cells plotting the number of events in a 5 ms integration window recorded in the presence (black line) and absence (red line) of feedback. (e) Median box plots compare the derived orientation tuning curve half widths at half height recorded across the population of cells studied in the presence and absence of feedback. The observations are summarized from Andolina *et al.* (2002).

Figure 6. The concept diagram summarizes the view that feedback-linked enhanced surround antagonism leads to greater synchronization of LGN-cell firing to coherent contours and thus increases the probability of firing in cortical layer 4 cells.

cell. Indeed, evidence shows supralinear enhancement of transmission from hetero-synaptic geniculate inputs to layer 4 simple cells in the visual cortex for spikes occurring within *ca.* 5 ms of each other (Usrey *et al.* 2000). It is thus very interesting that the feedback-enhanced centre-surround antagonism influences the stimulus-driven synchronization (Andolina *et al.* 2002) of the discharges of LGN cells when they are precisely coactivated by a moving contour. We suggest in figure 6 that the enhanced surround antagonism 'focuses' the effective spatial extent of the receptive-field centre of the LGN cells, leading to greater precision in the firing when the two inputs are pre-

cisely coactivated. The evidence for this is summarized in figure 5*a–d*. The experiments involved recordings in the feline LGN A laminae, using electrode assemblies configured to sample three cells of varying separation (figure 5*a*) in the presence and absence of feedback (Jones *et al.* (2000*b*); Andolina *et al.* (2002); see also Gerstein *et al.* (2002) for a theoretical consideration). A grating patch was centred over one of the fields, and used to drive the responses of the three cells at a range of orientations that included the angles linking each cell pair. Raw cross correlograms (raw cross correlograms show the stimulus linked information that the second-order neuron sees)

were then computed. These reflect the synchronicity of the inputs as 'seen' by a theoretical simple cell, for each pair at each orientation. Figure 5*b* shows representative results for a pair of X cells. A 5 ms window centred at zero lag (red) indicates those spikes that might generate supralinear enhancement of transmission. Note that shifts in orientation as small as 2° to either side of the angle linking the fields changed the count in this integration window. Converting the data to a surface representation of cross correlogram time against grating orientation (figure 5*c*) reveals that the peak of the cross correlogram shifted systematically through the time domain as the orientation was varied. The 'tuning curve' standing above this shows the way the count in the central 5 ms window varied with orientation. The mean half width at half height of such tuning curves was 4.4°. Interestingly, orientation tuning curves constructed from the synchronized spikes within the 5 ms window were much broader in the absence of feedback (see figure 5*d,e*, mean half width at half height without feedback 13.17°). Essentially this means that feedback greatly enhances the sensitivity to orientation in the stimulus-driven synchronization of the firing of LGN cells and thus the input to simple cells. In this sense the organization is linked to contour and possibly motion 'integration'.

(c) The question of stimulus-linked influences on the transition from burst to tonic firing modes

The suggestion that burst-mode firing in relay cells, originally associated with synchronized firing of relay cells and slow wave sleep, also occurs in the waking state (Guido & Weyand 1995; Ramcharan *et al.* 2000) adds another dimension to the potential role of feedback in visual processing (Rowe & Fischer 2001). Burst-mode firing occurs when relay cells have been hyperpolarized for periods of 100 ms or more and follows the de-inactivation of a voltage and time-dependent calcium current (I_T). Under these conditions, when the cell receives a suprathreshold depolarizing input there is a calcium influx generating a low threshold depolarizing spike that then activates a burst of conventional spikes. The size of the low threshold depolarizing spike and the number of conventional spikes in the burst depends on the degree of hyperpolarization of the membrane not the magnitude of the suprathreshold activating input. A sustained depolarization of relay cells for 100 ms or more inactivates I_T and the cell switches to tonic-mode firing associated with a linear transmission of sensory information and in this sense more conventionally with the waking state. We suggest that the key to the reported presence of burst-mode firing in the waking state is the strength of the hyperpolarization that can follow from visual inputs that drive the surround mechanism strongly. Following from this visually driven hyperpolarization, an appropriate visual stimulus over the receptive field would provoke a depolarizing input and a low threshold calcium spike driving a burst of action potentials.

It has been suggested that burst-mode firing in thalamic cells in the waking state serves as a 'wake up' call to the cortical cells receiving the input (Sherman 2001). The burst of action potentials in the input to the cortex would provide a high-security signal to focus the circuitry on the new feature driving attention in the cortical mechanism. One suggested role for the corticotectal feedback system is

that it may contribute to selective attention by its influence on geniculate firing patterns. As the feedback axons influence LGN relay cells both directly, via synapses involving ionotropic and metabotropic receptors (Von Krosigk *et al.* 1999; Sherman 2001), and indirectly via an input to inhibitory interneurons, they have the capacity to exert a complex pattern of control over relay cells that could switch the behaviour of LGN cells between tonic and burst modes. In recent work we questioned whether the patterned activity that occurs normally in the visual cortex during visual stimulation might switch the behaviour of LGN cells via the feedback system (Wang *et al.* 2001). While recording simultaneously in the cortex and LGN, focal iontophoretic application of a GABA_B receptor antagonist, CGP 55845, was used to produce a local relief of the GABA_B inhibition of layer 6 cells (figure 7). This reversibly enhanced the gain of their visually driven responses without affecting their spontaneous firing rate, making it possible to isolate the effects of this change in a controlled fashion. This change in cortical visual responses led to a statistically significant shift in the ratio of burst to tonic firing for 68% of LGN cells tested. Of these, 43% showed a shift from tonic to bursting (e.g. bottom panels in figure 8*a-f*) and 25% from bursting to tonic firing (upper panels in figure 8*a-f*). These effects did not follow from the drug application causing a state-dependent shift in the state of the cortex because simultaneously recorded LGN cells showed opposite direction shifts in firing pattern. Thus the data indicate that a focal change in the visual-response magnitude of layer 6 cells can produce a clear switch in the firing pattern of LGN cells. In some cases it moves them towards the tonic-mode firing pattern, and the faithful relay of their visual input, in others it moves them to burst-mode firing and a response mode that is thought to underlie early signal detection (Sherman 2001). With the complex input derived from stimuli in the natural visual world, the selective adjustment of the transfer properties of the LGN provides a means of alerting the system to salient change, while at the same time optimizing its capacity to relay accurate information about what has already engaged the system.

(d) Feedback from MT influences LGN-cell visual responses via V1 layer 6 cells

The very early visual responses seen in MT (Raiguel *et al.* 1989; Orban 1994, 1997) and its pattern of termination in layers 4B and 6 in V1 (Shipp & Zeki 1989; Rockland & Knutson 2000) suggest that it is in a position to exert a substantial influence on the early processing of the input in V1 and from this via the contacts in layer 6, the LGN. The termination pattern of feedback connections from MT in layer 6 of V1 provides access to the layer 6 cells associated with feedback for all three processing streams relaying through the LGN. Thus feedback containing information that is relevant to the high-level processing of motion in the visual world could influence visual processing in the LGN for moving stimuli at a very early stage in the development of visual responses.

To test this hypothesis we assumed that MT feedback would provoke the primary change in V1 processing when the stimulus contained motion features that activated MT. Next, we considered that these stimuli, by their spatial focus and specific trigger features, would provoke differen-

Figure 7. The influence of feedback axons on LGN relay cells. Layer 6 cortical cells can influence the responses of LGN relay cells directly through excitatory synaptic connections and indirectly, via excitatory synapses on GABAergic inhibitory interneurons located in the overlying PGN. The feedback connections therefore have the capacity to depolarize or hyperpolarize relay cells, and may thus have a profound influence on the response mode of relay cells. A micropipette array inserted in layer 6 can be used to focally change the gain of layer 6 cell responses and its influence assessed on the responses of several simultaneously recorded LGN cells.

tial activation of MT and the 'high spots' of enhanced activity in MT would in turn provide highlights in the pattern of feedback. Although it is clearly possible to generate stimuli that should cause a differential pattern of activation of MT, it is very difficult to disassociate any consequent reflected influence to the LGN via feedback from potential direct effects of the stimulus on circuitry in the LGN and V1 itself. To isolate the effects of MT we used stimuli that activated MT cells but, in addition, by a drug and recording electrode assembly inserted in area MT, we produced focal and reversible changes in the gain of the response of the recorded MT cells to these stimuli. In many ways this could be argued to simply increase or decrease the salience of the stimuli to the cell recorded by the MT electrode. Thus the effect of the manipulation was

to produce a very local change in the size of the visual response in MT, and because we could reverse this and repeat it we could check for effects in the LGN (Jones *et al.* 2000c, 2001, 2002).

We implanted arrays of three to seven recording electrodes in the LGN and examined the effect of the focal gain changes in MT on the responses of the cells recorded from these electrodes. The stimulus used was a drifting texture patch displaced through a sequence of XY coordinates that encompassed the MT field and the LGN-cell receptive fields. The experimental paradigm is summarized in figure 9a. The texture-patch drift direction was selected to match the directional preference of the recorded MT cell. Although the stimulus was not in any sense optimal or tuned to the classical receptive field characteristics of the various LGN cells it none the less provoked responses that enabled us to see effects from the MT feedback. Focal enhancement of the response of the MT cell produced marked changes in the responsiveness of LGN cells in parvo, magno and koniocellular layers. Overall, we observed a significant change in responsiveness in 75% of our sample ($n = 55$) and an example is shown in figure 9b. These included increases and decreases in the response magnitude of groups of simultaneously recorded LGN cells.

These data show that the feedback loop from MT influences the transfer of the retinal input for moving stimuli at the level of the LGN and introduces the dynamic of the high-level motion processing to the earliest stage in the central visual pathway.

5. SUMMARY AND SPECULATION

It seems clear that the feedback to the LGN changes the way LGN cells respond to visual stimulation and the nature of the signal that they transfer to the visual cortex. The primary action seems to be a fine tuning of the processes that build the receptive field via the underlying centre and surround mechanisms. The outcome, primarily directed to responses to moving stimuli, is that the surround mechanism influence is enhanced and the centre mechanism is more sharply focused. Viewed from the perspective of the difference of Gaussian's Model (Sceniak *et al.* 1999, 2001), these effects could follow from a change in the gain or space constant of the inhibitory mechanism or a change in the gain or space constant of the excitatory mechanism. Realistically, given the direct feedback connections to relay cells, perigeniculate inhibitory interneurons and intrageniculate inhibitory interneurons, it is probable that there are shifts in both sets of mechanisms. The net effect of this is to enhance the sensitivity and focus of the LGN receptive fields to a discontinuity in moving stimuli engaging their centre and surround mechanisms. This could be regarded as highlighting a very fine-scale segmentation process and in so doing enhancing the resolution of the input to the cortex identifying foci of change. Almost paradoxically, we suggest that the very same mechanism serves to aid the more global integration of events driven by a moving contour in terms of the fine-scale resolution of the synchronization of the firing of LGN cells coactivated by the contour. We believe that all these effects could follow from modulatory influences of the feedback on the elements of the thalamic circuitry,

Figure 8. Corticofugal feedback can switch relay-cell responses between burst and tonic modes. (a–c) These records show the responses of two LGN cells before (a), during (b) and after (c) focal enhancement of layer 6 (using iontophoretic application of the GABA_B antagonist CGP 55845). The peristimulus time histograms show the LGN cells' responses to an optimal diameter flashing spot located over the receptive field. The burst spikes are shown in red and the tonic spikes are shown in black. There was a clear change in the firing pattern during CGP application in layer 6. (Conventional criteria were used to divide the LGN-cell spike trains into periods of burst and tonic activity. The first action potential in a burst showed a preceding silent period of at least 100 ms followed by a second spike with an ISI of ≤ 4 ms. Any subsequent action potentials with preceding ISIs of ≤ 4 ms were also considered to be part of a burst. All other spikes were regarded as tonic.) (d–f) Records for a further two LGN cells before (d), during (e) and after (f) focal enhancement of layer 6. The joint ISI plots show the time interval before each spike (x-axis) plotted against the corresponding interval after each spike (y-axis). The red points to the lower right correspond to those spikes with pre-spike intervals of ≥ 100 ms, and post-spike intervals of ≤ 4 ms (initial spikes in a burst). The green points on the left indicate spikes with a pre- and post-spike interval of ≤ 4 ms. Most of these points are likely to reflect the intermediate spikes in a burst. Data summarized from Wang *et al.* (2001).

although some processes might be more directly driven by the feedback. The effects of a very focal and small manipulation of MT on LGN-cell responses in the primate is a

salutary reminder of how closely linked the elements of the central visual system are. Given the divergence of the feedback influence from MT to V1 and the spread of the

Figure 9. Effect of MT feedback on LGN-cell responses to drifting stimuli. (a) Experimental protocol. Simultaneous recordings were obtained from one or more LGN cells and an MT cell. The responses to visual stimuli were assessed before, during and after focal iontophoretic application of the GABA_B antagonist CGP in MT. The stimulus was a patch of drifting texture displaced (in randomized interleaved sequence) to cover a range of XY locations. The grid was centred over the receptive fields of the LGN cells as shown by the example diagrammatic icon of the relative locations of an MT field (orange) and several LGN-cell receptive fields. The dotted rectangle depicts the total area of visual space covered by the grid. The contour maps show the response of an MT cell before (top), during (middle) and after (bottom) CGP iontophoresis. The response magnitude (spikes s⁻¹) is represented by colour, from low (dark blue) to high (dark red). (b) Effects in the LGN. The contour maps plot the responses of four LGN cells tested in the presence of the type of change in MT shown in (a). Top row, control; middle row, MT response modification; bottom row, recovery.

layer 6 cell connections in the LGN, the visual world in motion would exert a constant but changing pattern of influence on the relay of information through the LGN. The asymmetries identified in the feedback connections to the LGN indicate that these influences might be spatially structured to aid the extraction of key features, such as orientation, in the early visual system. A crucial thing could be the predictive adjustment of the circuitry to aid the rapid locking of the system onto key features of a moving image.

The collaterals of layer 6 cells in layer 4 of the visual cortex should not be forgotten. We know that these exert clear and strong facilitatory effects on layer 4 simple cells (Grieve & Sillito 1991*b*, 1995*b*) and so the subcortical influence in the LGN will be paired with one on the cells receiving the input from the LGN. At the same time these layer 6 cells are also translating feedback influences from MT. For moving stimuli, the divergent influence of the feedback connections means that cells about to receive input from a stimulus moving towards their receptive field can be influenced by 'predictive' feedback at zero latency. This seems to bring the thalamus into the dynamic of the cortical mechanism and totally blur the segregation of the levels with a constant iteration of changes between the levels, each shifting the basis on which the previous state was defined. For the world in motion the thalamus is thus part of the cortical circuitry and *vice versa*. The main and final

point is that the feedback influences visual processing in a way that is not generic, but may involve generic mechanisms.

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GLOSSARY

- GABA: γ -aminobutyric acid
 LGN: lateral geniculate nucleus
 ISI: interspike interval
 PGN: perigeniculate nucleus