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Extrastriate feedback to primary visual cortex in primates: a quantitative analysis of connectivity

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Knowledge-based or top-down influences on primary visual cortex (area V1) are believed to originate from information conveyed by extrastriate feedback axon connections. Understanding how this information is communicated to area V1 neurons relies in part on elucidating the quantitative as well as the qualitative nature of extrastriate pathway connectivity. A quantitative analysis of the connectivity based on anatomical data regarding the feedback pathway from extrastriate area V2 to area V1 in macaque monkey suggests (i) a total of around ten million or more area V2 axons project to area V1; (ii) the mean number of synaptic inputs from area V2 per upper-layer pyramidal cell in area V1 is less than 6% of all excitatory inputs; and (iii) the mean degree of convergence of area V2 afferents may be high, perhaps more than 100 afferent axons per cell. These results are consistent with empirical observations of the density of radial myelinated axons present in the upper layers in macaque area V1 and the proportion of excitatory extrastriate feedback synaptic inputs onto upper-layer neurons in rat visual cortex. Thus, in primate area V1, extrastriate feedback synapses onto upper-layer cells may, like geniculocortical afferent synapses onto layer IVC neurons, form only a small percentage of the total excitatory synaptic input.

Keywords: extrastriate; cortical feedback; visual cortex; area V1; area V2; macaque

1. INTRODUCTION

Knowledge about the visual world can be used to bias perception. The purpose of such knowledge-based or 'top-down' influences is to actively integrate the different types of stimulus information present in an impoverished two-dimensional retinal image into an accurate three-dimensional representation of the visual scene. In mammalian visual cortex, 'top-down' information is believed to be communicated via the synaptic connections of descending or 'feedback' pathways originating from higher-order to lower-order visual areas (see Salin & Bullier 1995). For example, macaque primary visual cortex (area V1), the main target for parvocellular and magnocellular geniculocortical afferents relaying retinal signals (Blasdel & Lund 1983; Freund *et al.* 1989), receives feedback connections from a number of extrastriate areas including V2, V3, V4 and MT (Perkel *et al.* 1986). Individual neurons in each of these extrastriate areas possess larger receptive field (RF) size for any given retinal eccentricity and more specialized stimulus response properties than cells in V1 (Van Essen & Zeki 1978; Zeki 1978; Gattass *et al.* 1981; Levitt *et al.* 1994). The spatial and temporal behaviour of high-order contextual modulation of area V1 neurons for a variety of visual cues outside the classical RF of area V1 neurons in awake, behaving macaque monkeys suggests that these effects could be mediated by extrastriate feedback connections (Zipser *et al.* 1996). The contextual modulation, however, is very weak when only surround stimuli are presented (Zipser *et al.* 1996), implying that extrastriate feedback on its own may have relatively little influence on the response of area V1 neurons. Results from the global reversible inactivation of area V2 in squirrel monkeys support this suggestion, since only a minority of area V1 cells show reduced visual responsiveness, with no apparent change in RF selectivity (Sandell & Schiller 1982). Extrastriate feedback axons may also provide a mechanism for the attentional modulation of area V1 neurons (Motter 1993).

Through its many synaptic connections, therefore, each area V1 neuron receives and integrates a variety of different types of stimulus information about the visual field. Understanding the nature and source of each connection adds to knowledge about the information contributed by each different visual pathway to the functional properties of single neurons (see Ahmed *et al.* 1994). This paper is concerned with quantifying the contribution of extrastriate feedback axons to the synaptic organization of area V1. The vast majority of synaptic inputs to a cortical neuron are believed to originate from other cortical neurons in the same cortical area (Abeles 1991; Braitenberg & Schüz 1991). For instance, the main geniculocortical input to layer IVC in macaque area V1 is believed, according to both anatomical tracing and quantitative connectivity analysis, to form only a small proportion ($<10\%$) of all excitatory synaptic inputs onto spiny neurons (Garey & Powell 1971; Peters *et al.* 1994). This finding is supported by similar empirical and theoretical studies of geniculocortical innervation in cat primary visual cortex (Ahmed *et al.* 1994; Peters & Payne 1993). Based on these and other observations, including intracellular electrophysiological recordings, Douglas &

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Martin (1991) have proposed that a weak geniculocortical signal is selectively amplified and sustained by massive local intracortical excitation from intrinsic spiny neurons. This recurrent model is able to account for some of the key receptive field properties of 'simple' cells in cat primary visual cortex such as orientation and direction of motion selectivity (Douglas *et al.* 1995). However, quantitative data concerning the numerical size of extrastriate pathways in primates are very limited (see Felleman & Van Essen 1991). Recently, however, in the rat, Johnson & Burkhalter (1997) observed and quantified the anterograde degeneration of terminals onto labelled pyramidal area V1 neurons following lesions in secondary visual (latero-medial) cortex. They reported that only 7–8% of all excitatory terminals of upper-layer pyramidal cells degenerated, suggesting that extrastriate feedback weakly innervates primary visual cortical neurons (Johnson & Burkhalter 1997). Given the differences between the organization of rat and macaque visual systems, it is reasonable to examine whether extrastriate feedback connectivity may be quantitatively similar in the macaque primary visual cortex. A level of innervation similar to the rat may suggest that the microcircuitry for communicating top-down influences follows the same general principles across species. Here, a quantitative analysis of anatomical evidence concerning the connectivity of macaque monkey extrastriate feedback pathway from area V2 to V1 is presented.

2. SUMMARY OF NUMERICAL DATA ON AREA V2 TO V1 FEEDBACK PATHWAY

Area V2, which lies directly adjacent and anterior to area V1 within the posterior bank of the lunate sulcus (Van Essen & Zeki 1978; Gattass *et al.* 1981), is by far the largest extrastriate cortical area, around 1190 mm^2 compared with area V1 which has a surface area of approximately 1120 mm^2 (Felleman & Van Essen 1991). Anatomical tracing studies suggest that both central and peripheral regions of area V2 project heavily, more densely apparently than any other extrastriate area, and reciprocally to area V1 (Van Essen *et al.* 1986; Perkel *et al.* 1986; Barone *et al.* 1995). For these reasons it is expected that area V2 provides the strongest innervation of any single extrastriate area to V1.

Figure 1 illustrates the basic microcircuitry of the area V2- to V1-pathway. The feedback axons originate from V2 pyramidal cells with cell bodies mostly in layer VI and fewer in layer IIIA (Rockland & Pandya 1979; Kennedy & Bullier 1985; Rockland & Virga 1989). Recent counts of the peak frequency of retrogradely labelled neurons suggest approximately 8000–12 800 neurons under 1 mm^2 of cortical surface of area V2 project following focal injections into area V1 (Rockland 1997). The V2 efferent axons travel through the white matter, ascend vertically, and then arborize parallel to the cortical surface over a distance of 1–2 mm, typically in patches, mainly within the vicinity of layer I in area V1 (Rockland & Virga 1989). The total number of boutons counted from labelled and reconstructed arbors varies between 146 and 644 boutons ($n = 28$, Rockland & Virga 1989). The number of synapses made on average by a single bouton is unknown, but it has been assumed that, like intrinsic pyramidal cell boutons in

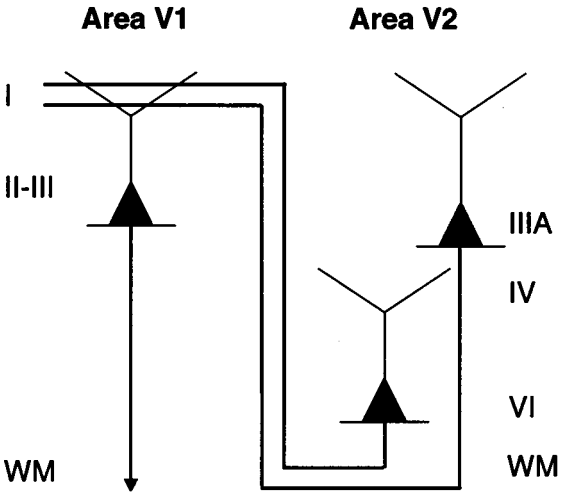

Figure 1. Simplified schematic diagram of the cortical feedback from area V2 to V1. Efferent axons from area V2 emerge from layer VI and IIIA pyramidal cells and arborize in long (1–2 mm), thin axons mostly in layer I of area V1. The main dendritic targets in layer I are the apical dendrites of layer II–III (shown) as well as some layer V (not shown) pyramidal cells.

macaque V1 (McGuire *et al.* 1991), an average of only one synapse is formed by each afferent bouton. The synapses formed by the arbors in area V1 are asymmetric or Gray's Type 1 (putative excitatory) and, like the intrinsic pattern of connectivity of area V1 pyramidal cells (McGuire *et al.* 1991), most appose dendritic spines (Rockland 1994), a distinctive morphological feature of pyramidal cells. Layer I is, however, cell-sparse (Beaulieu *et al.* 1992) and the vast majority of dendritic targets are thought to originate from apical dendritic tufts of layer II–III pyramidal cells (Peters & Sethares 1991), more than 40 000 tufts under 1 mm^2 of cortical surface (Beaulieu *et al.* 1992). Assuming each postsynaptic cell has an equal chance of afferent input, it is possible to estimate using simple algebra (see Peters & Payne 1993; Peters *et al.* 1994) the average number of area V2 axons (convergence) and synapses received by each upper-layer pyramidal neuron in area V1.

It is important to note that areas V1 and V2 are treated uniformly here not because the functional segregation indicated by cytochrome oxidase (CO) reactivity (e.g. Livingstone & Hubel 1984; Levitt *et al.* 1994) is thought to be unimportant, but owing to a lack of evidence regarding any differences in the nature, origin, or termination of individual area V2 feedback axons according to CO parcellation.

3. CALCULATIONS AND ESTIMATES

(a) *Main estimates*

Table 1 summarizes the calculations made to estimate the proportion of putative excitatory (asymmetric or Gray's Type I) synapses onto layer II–III pyramidal neurons from area V2, shown here as not more than 6%. These calculations also give a ratio of 3–5 neurons for every V2 afferent axon, as approximately 10–15 million axons project back from area V2 onto around 45 million potential target cells in area V1. The total number of area V2 axons is roughly more than ten times the total number

Table 1. *Summary of calculations to estimate the number and proportion of area V2 synapses onto layer II–III pyramidal cells in area V1*

line	parameter	value	source
1	number of area V2 cells projecting to V1 under 1 mm^2	8000–12 800 neurons	Rockland (1997)
2	surface area of area V2	1190 mm^2	Felleman & Van Essen (1991)
3	total number of area V2 cells projecting to area V1	$9.52–15.2 \times 10^6$ neurons	line 1 × line 2
4	number of boutons in area V1 per area V2 afferent[a]	146–644 boutons	Rockland & Virga (1989)
5	total number of area V2 synapses in area V1	$1.39–9.81 \times 10^9$ synapses	line 3 × line 4
6	number of layer II–III pyramidal cells (target cells) in area V1 under 1 mm^2	41.3×10^3 neurons	Beaulieu *et al.* (1992)
7	surface area of area V1	1120 mm^2	Felleman & Van Essen (1991)
8	total number of area V1 target cells	46.3×10^6 neurons	line 6 × line 7
9	mean number of area V2 synapses per target cell	30–212 synapses $cell^{-1}$	line 5/line 8
10	total mean number of excitatory synapses per V1 neuron	3500 synapses $cell^{-1}$	Beaulieu *et al.* (1992)
11	proportion of area V2 synapses per V1 neuron	0.9–6.1%	(line 9/line 10) × 100

[a]Assumption: each bouton makes only one synapse similar to intrinsic connections of pyramidal cells in area V1 (McGuire *et al.* 1991).

of parvocellular and magnocellular geniculocortical axons projecting to layer IVC, about 1.1 million (see Peters *et al.* 1994), which means that to achieve roughly the same proportion of synaptic input a single geniculocortical axon must make on average ten times more synapses than a single V2 axon.

In choosing parameter values for the analysis there was an intentional bias towards selecting data that would maximize the estimated number of area V2 synapses per target cell. First, contrary to most other comparative studies (Gattass *et al.* 1981; Weller & Kaas 1983; Van Essen *et al.* 1986), area V2 was taken to be larger than area V1, so increasing the total number of projecting neurons. Second, although the visualization of clusters of apical dendrites of area V1 pyramidal neurons by antibodies to microtubule-associated protein 2 (MAP2) clearly demonstrates that most dendritic tufts in layer I originate from upper-layer pyramidal cells (Peters & Sethares 1991), there are other area V1 pyramidal and non-pyramidal neurons whose dendrites impinge either partly or wholly on layer I and could, therefore, potentially receive synaptic input from area V2 afferents (Lund & Boothe 1975; Peters & Sethares 1991; Anderson *et al.* 1993). Pyramidal apical dendritic clusters are formed by a mean of eight layer V apical dendrites that arborize in layer I, and with around 1200 apical dendritic clusters under 1 mm^2 of cortical surface (Peters & Sethares 1991), this gives 9600 layer V apicals under 1 mm^2, or for the whole of area V1, around ten million layer V apicals. With approximately 6300 layer II smooth cells and 1500 layer I cells under 1 mm^2 of cortical surface (Beaulieu *et al.* 1992), then an extra nine million or so neurons in area V1 could potentially receive synaptic input from area V2 afferents. Taken together, these other cell types offer a further 19 million target cells that were not considered in the calculations shown in table 1, so reducing (possibly by as much as 40%) the total number of potential target neurons in area V1. Third, although area V2 afferents terminate mainly in layer I of area V1 (Rockland & Virga 1989), the afferent boutons from axon collaterals that terminate in other layers (such as layer V) have been included in the calculations, thereby increasing the total number of area V2 boutons available to synapse with upper-layer area V1 neurons.

The estimates given in table 1 are consistent with recent data on the number of radially orientated myelinated axons entering and leaving the upper layers of V1, nearly all of which will be afferent or efferent axons (see Braitenberg & Schüz 1991). At the level of layer IVA there are around 50 500 radially orientated myelinated axons under 1 mm^2 of cortical surface in macaque primary visual cortex (Peters & Sethares 1996). The radial trajectory of area V2 axons terminating in area V1 (Rockland & Virga 1989) suggests that a proportion of these myelinated axons will be area V2 afferents. Because many radially orientated myelinated axons will originate from layer II–III area V1 efferent neurons—more than 40 000 under 1 mm^2 of cortical surface (see table 1, line 8)—this implies that the remainder, a maximum of approximately 10 500 axons under 1 mm^2 of cortical surface, originate from extrinsic sources (subcortical and extrastriate). The results from table 1 predict an average of 8500–13 570 area V2 afferent axons under 1 mm^2 of cortical surface of area V1. The upper end of this predicted range exceeds the likely total number of afferent axons, but the lower end of the range is consistent with area V2 afferents forming a high proportion of radially orientated myelinated axons entering the upper layers of area V1.

(b) *Effects of parameter variation*

The reliability of the estimates derived in the analysis depend upon the accuracy of the experimentally measured parameter values and the assumptions made in the absence of empirical evidence. Two main parameter values were varied over a realistic range to investigate the robustness of the results (see figure 2). The particular parameters, the number of efferent neurons and the number of synapses per arbor, were chosen because of the technical difficulties associated with establishing their value accurately (Rockland 1997). There is also, however, a degree of uncertainty regarding the total mean number of excitatory synapses per pyramidal cell. The synapse-to-neuron ratio of 3500 is estimated from the density of excitatory synapses in layer II–III neuropil per pyramidal cell body (Beaulieu *et al.* 1992), rather than from the serial reconstruction of synaptic inputs onto a single pyramidal neuron, which has yet to be performed in macaque.

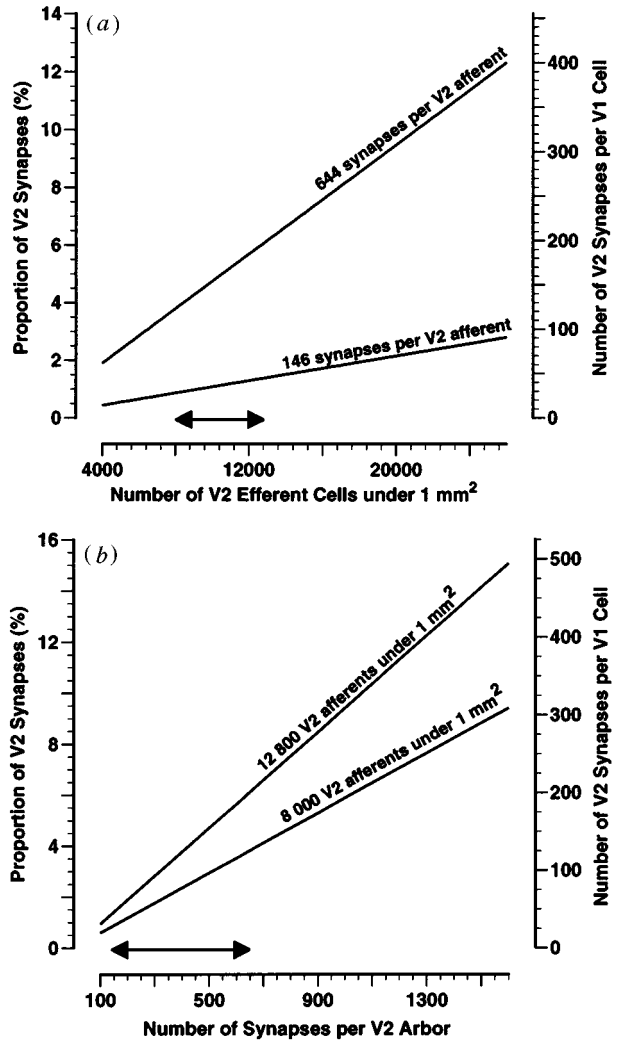

Figure 2. Effect of parameter variation on estimates of area V2 synaptic input to upper-layer pyramidal cells in area V1. (*a*) Variation in the number of efferent cells under 1 mm^2 of area V2 projecting to area V1 (table 1, line 1). (*b*) Variation in the mean number of synapses per V2 arbor formed in area V1 (table 1, line 4). All other parameters were kept constant (as given in table 1) for these calculations. Arrow indicates empirical range of parameter values.

Owing to the intermixing of axonal and dendritic processes across laminar boundaries, the actual mean number of synapses per pyramidal cell may be higher or lower than that used here.

Figure 2*a* shows how variation in the number of area V2 efferent neurons under 1 mm^2 of cortical surface projecting to area V1, for both a low and high number of synapses per arbor, produces a linear change in the degree of innervation. For example, doubling the density of efferent neurons (equivalent to halving the assumed number of potential target neurons in V1) doubles the degree of innervation, around 90–400 synapses per cell or 2–12% of the total number. Even with such an extreme variation, which preliminary numerical estimates suggest would be more than half of all layer III and VI neurons in area V2 (Rockland 1997), this proportion is, at most, still close to the estimated range of less than 10% for the main geniculate input (Garey & Powell 1971; Peters *et al.* 1994).

Figure 2*b* shows the linear effect of variation in the average number of synapses per area V2 arbor, for both a low and a high density of efferent neurons, on the innervation of area V1 recipient neurons. Again, doubling the number of synapses per arbor (equivalent to doubling the assumed synapse-to-bouton ratio of one) doubles the degree of innervation to about 260–400 synapses per cell or 8–12% of the total innervation. From single axon analysis, the estimated bouton density of area V2 arbors in area V1 is typically half or less than the number of geniculate arbors in layer IVC (Blasdel & Lund 1983; Freund *et al.* 1989; cf. Rockland 1994), which suggests that the total length of area V2 bouton-studded arbors would need to double for the same number of afferent axons.

In summary, only substantial variation in these two main parameters would lead to a significantly higher proportion of synaptic input from area V2, and even then the numerical estimates are still close to the estimated degree of parvocellular and magnocellular geniculate synaptic input to layer IVC neurons (Garey & Powell 1971; Peters *et al.* 1994). The results of these manipulations, which often extend parameter values to extremes and counter to current evidence, suggest that the main estimate given in table 1 is reasonably robust.

(c) *Total extrastriate innervation of area V1*

If the numerical estimates of area V2 innervation above are broadly correct, what could be the approximate maximum size of the total extrastriate projection to area V1? Although there is an increasing body of quantitative data relating to the pathways from other extrastriate areas projecting to area V1 (see Rockland 1997), it is not yet possible to estimate to the same degree of accuracy what their synaptic contribution is to area V1. Suppose, however, the other extrastriate areas project equally as strongly as area V2 (i.e. they have the same density of efferent neurons and same number of synapses per arbor). Area V1 receives projections from the following extrastriate visual areas: V2, V3, V3A, V4, V4t, MT (V5), PO and PIP (Perkel *et al.* 1986; Felleman & Van Essen 1991). The total cortical surface area (including V2) of these extrastriate areas is 2210 mm^2 (Felleman & Van Essen 1991). Assuming a uniform projection from each area and performing the same calculation shown in table 1 (substituting 2210 mm^2 in line 2) leads to an estimate of the maximum total number of afferents projecting as 28.3×10^6 axons and 1.82×10^{10} synapses in area V1 from other visual cortical areas. Each upper-layer pyramidal cell would therefore receive a maximum of 394 synapses from other visual cortical areas, around 11% of the total putative excitatory input and almost double the estimated level of innervation from area V2 only. Available evidence regarding these pathways from extrastriate areas suggests that this value is likely to be a considerable overestimate because (i) the density of efferent neurons and the number of boutons per arbor is generally much lower than the values reported for area V2 (see Rockland 1997), and (ii) many areas project to only a restricted region of area V1, e.g. MT afferents terminating in layer I are restricted to the peripheral visual field representation (Shipp & Zeki 1989). Further, this estimated maximum level of innervation is equivalent to around 25 260 axons under 1 mm^2 of cortical surface in area V1, around half of all radial myelinated axons

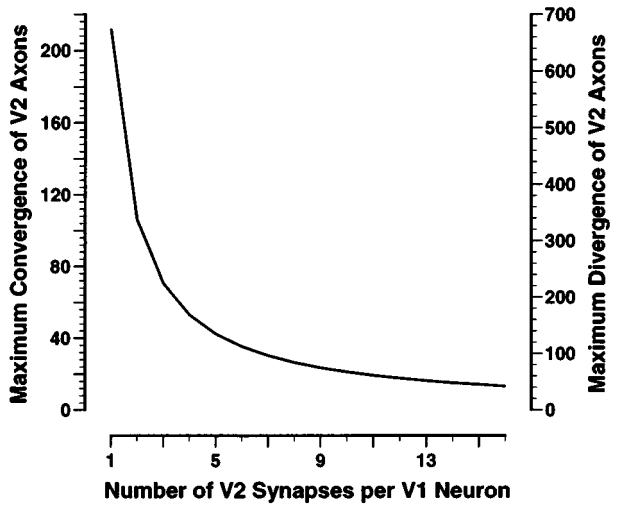

Figure 3. Predicted maximum convergence and divergence of area V2 afferents based on the result of calculations derived in table 1 (see text for details).

associated with the upper layers of area V1 (Peters & Sethares 1996). Because most radial myelinated axons are expected to leave rather than enter the upper layers, about 40 000 axons under 1 mm^2, this strength of projection suggests a substantial overestimation of the synaptic input from extrastriate areas to area V1. In any case, the maximum synaptic input from extrastriate areas still represents a similar level of synaptic input to that from geniculocortical sources (Garey & Powell 1971; Peters *et al.* 1994), although with up to 20 times more afferent axons originating from extrastriate cortex as a whole.

(d) *Convergence and divergence of area V2 afferents*

The mean convergence of V2 afferents onto upper-layer pyramidal neurons in area V1 can be estimated, using data given in table 1, from the mean divergence and ratio of afferent axons to postsynaptic target cells. Let each afferent axon make a total of p synapses within area V1, where each connection to a single postsynaptic cell has a mean of q synapses. The mean divergence, $D=p/q$, is independent of the number of postsynaptic neurons. Let N afferents from area V2 project onto M postsynaptic neurons in area V1, and let the ratio of presynaptic to postsynaptic target cells $R=N/M$. Thus, the mean convergence can be given as

$$C = (N/M) \times (p/q) = RD.$$

From table 1, $N=9.52$–15.2×10^6 cells, $M=43.6\times10^6$ cells (so $R=0.21$–0.33), and assuming one synapse per bouton (McGuire *et al.* 1991), $p=146$–644 synapses. The absence of dual-labelled, connected pairs of presynaptic area V2 axons and postsynaptic area V1 neurons means, however, that the mean number of synapses each area V2 afferent makes with an individual area V1 cell (q) is unspecified. Based on intrinsic connections by area V1 spiny neurons in macaque, q will be in the range of one to less than ten synapses per connection (McGuire *et al.* 1991; Sawatari & Callaway 1996), the higher end of this range reflecting interlaminar connections that are generally regarded to be stronger than horizontal or oblique lateral connections (see Salin & Buller 1995).

Figure 3 shows that both mean V2 afferent convergence (C) and divergence (D) are inversely proportional to the mean number of synapses per connection (q). For a single afferent synapse per postsynaptic neuron, which is the most likely case based on geniculocortical afferent connectivity (Freund *et al.* 1989), a minimum of 30 and a maximum of around 200 area V2 afferents converge onto a single area V1 upper-layer pyramidal cell, with each area V2 afferent expected to contact, respectively, 150 and 650 separate area V1 cells. If connectivity is stronger, say five afferent synapses per cell, then a maximum of around 40 afferents converge onto a single upper-layer area V1 cell, with each afferent contacting an average of less than 150 area V1 cells. This last example is similar to the estimated degree of convergence of magnocellular and parvocellular geniculate afferents terminating in layer IVC (24–32; Peters *et al.* 1994), as is the minimum estimate for a single synapse per connection. So provided that the mean number of synapses per target neuron is less than five, then, for the maximum estimate predicted in this analysis, area V2 afferents will have a higher degree of convergence than parvocellular and magnocellular geniculocortical afferents.

(e) *Sparse connectivity of area V2 afferents*

A single extrastriate feedback neuron is most unlikely to project to all neurons in area V1 within its large receptive field (Perkel *et al.* 1986), suggesting sparse connectivity. Area V2 afferents have a heterogeneous morphology although most arbors produce one or more terminal clusters within layers I–II (Rockland & Virga 1989). These clusters tend to have an elliptical shape, but the size of individual clusters varies; they are typically around 100–300 μm in diameter (Rockland & Virga 1989), which suggests an elliptical surface area of 0.0943 mm^2 (based on the formula: area$=\pi ab$, where major axis (a) is 0.3 mm and minor axis (b) is 0.1 mm). Under this amount of surface area there are approximately 3900 layer II–III pyramidal cells in area V1, using data given in table 1. Assuming the same number of boutons per afferent given in table 1 (146–644 boutons), and only a single synapse per connection, each of these upper-layer pyramidal cell has a maximum probability of connection (see Abeles 1991) of 0.037–0.165 from a single area V2 afferent. The range of connection probability is similar to the range of 0.014–0.100 obtained from dual intracellular recordings in *in vitro* rat visual cortical slice preparations between pyramidal cells in the same cortical area (Nicoll & Blakemore 1990; Markram *et al.* 1997). This estimated degree of sparse connectivity may suggest that the connectivity statistics of pyramidal cells are maintained between cortical areas, although this statistic clearly does not take account of neuronal specificity (see Markram *et al.* 1997).

4. FUNCTIONAL CONSIDERATIONS

Although the proportion of synaptic inputs offers an anatomical measure of the strength of visual pathway connectivity, it does not give any direct metric of the efficacy of postsynaptic potentials (PSPs) generated as a whole or for each connection. The type of electrophysiological recordings needed to establish the parameters of extrastriate feedback quantal synaptic communication in

macaque have yet to be performed, so there is no evidence with which to infer how the estimated number of release sites (synapses) per area V1 cell relates to peak quantal conductance and connection reliability (see Markram *et al.* 1997). However, intracellular recordings *in vitro* from neurons in rat primary visual cortex slices following stimulation in secondary (lateromedial) visual area, suggest that feedback corticocortical connections generate a lower mean-amplitude excitatory PSP than either thalamocortical or feedforward corticocortical connections (Shao & Burkhalter 1996). In this study, all recorded upper-layer primary visual cortical neurons received monosynaptic excitatory input from secondary (lateromedial) visual cortex (Shao & Burkhalter 1996), giving indirect support to the assumption made in the analysis that most, if not all, area 17 neurons may be targets for extrastriate feedback afferents. If the efficacy and pattern of connection is similar in macaque, then these estimates suggest that area V2 may exert only a relatively weak modulatory influence on quiescent upper-layer V1 neurons, consistent with physiological studies in primates (Sandell & Schiller 1982; Zipser *et al.* 1996). Synapses from extrastriate afferents onto the distal dendrites of area V1 pyramidal cells, however, may be facilitated by the activation of voltage-gated (active) dendritic conductances (Amitai *et al.* 1993). However, the purpose of this nonlinear mechanism may be to prevent the decoupling of distal synaptic inputs (linearization) from the parent cell body while under massive synaptic activation in more proximal regions of the dendritic tree, such as during visual stimulation (Bernander *et al.* 1991).

A main function of cortical feedback may be to reduce conflict between sensory input and stored knowledge or expectation (Mumford 1992; Ullman 1995). This idea has recently received support from observations that corticothalamic and intrahemispheric feedback may improve the spatio-temporal coherence between different brain regions by the synchronization of neural activity (Nowak *et al.* 1995; Contreras *et al.* 1996). In the context of the model proposed by Douglas & Martin (1991), a cortical module in area V1 receives geniculocortical connections (sensory input) and extrastriate feedback connections (top-down input). The initial response of area V1 neurons to the onset of a stimulus pattern will probably be determined by the activation pattern of geniculocortical (sensory input) connections (Celebrini *et al.* 1993), followed by selective intracortical amplification to enhance and sustain the response above background levels of activity, depending on the nature of the stimulus pattern (Douglas & Martin 1991). The response may then be enhanced by delayed excitation from extrastriate cortical cell assemblies, or the extrastriate feedback may be blocked by relatively small levels of intracortical inhibition, similar to geniculocortical signals (see Douglas & Martin 1991). If an area V1 neuron is already receiving amplification via recurrent excitation, then extrastriate feedback excitation will further sustain the response, although area V1 neurons not receiving amplification (i.e. the initial transient response is not sustained) may respond little to relatively weak extrastriate feedback excitation. According to this interpretation, the effectiveness of extrastriate feedback may function nonlinearly or competitively depending on whether the current pattern of activation in area V1 matches or is synchronized with the spatio-temporal pattern of feedback activity provided by extrastriate feedback connections.

5. CONCLUSIONS

A quantitative analysis of extrastriate feedback connectivity between area V2 and primary visual cortex in macaque monkey suggests that ten million or so feedback axons, roughly ten times the number of geniculocortical afferents (Peters *et al.* 1994), project to area V1, and that extrastriate synapses form a small proportion of all excitatory synaptic inputs to upper-layer pyramidal cells (not more than 6%), which is very similar to the synaptic proportion observed in an anatomical tracing study of extrastriate feedback to primary visual cortex in the rat (7–8%; Johnson & Burkhalter 1997). This numerical correspondence may suggest a common synaptic organization for extrastriate feedback across species, a hypothesis that is supported to some extent by other anatomical evidence such as the pattern of postsynaptic target innervation, laminar origin of efferents, and laminar arbor termination (Rockland 1994; Johnson & Burkhalter 1996). In both cases, the proportion of afferent synaptic input is similar to that estimated empirically and theoretically for the main geniculocortical synaptic input to layer IV in both macaque and cat primary visual cortex (macaque, Garey & Powell 1971; Peters *et al.* 1994; cat, Ahmed *et al.* 1994; Peters & Payne 1993). This lends support to the idea embodied in the canonical cortical model of Douglas & Martin (1991) that most connections in the neocortical microcircuitry derive from intrinsic rather than extrinsic sources of synaptic input. However, relative differences between geniculocortical feedforward and area V2 feedback pathways, in terms of afferent geometry and spatial correlation (cf. Blasdel & Lund 1983; Freund *et al.* 1989; Rockland & Virga 1989), sparse connectivity (this report), RF size of presynaptic afferents (e.g. Gattass *et al.* 1981), and estimated degree of convergence of the afferent arbors (this report), suggest that whereas geniculocortical axons will provide a driving influence to area V1 neurons, area V2 axons may provide only a modulatory influence to area V1 neurons. If this interpretation is correct, then it may explain why high-order contextual modulation of non-classical RFs of area V1 neurons (Zipser *et al.* 1996) is relatively ineffective on its own.

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REFERENCES

Abeles, M. 1991 *Corticonics: neural circuits of the cerebral cortex*. Cambridge University Press.

Ahmed, B., Anderson, J. C., Douglas, R. J., Martin, K. A. C. & Nelson, J. C. 1994 Polyneuronal innervation of spiny stellate neurons in cat visual cortex. *J. Comp. Neurol.* **341**, 39–49.

Amitai, Y., Friedman, A., Connors, B. W. & Gutnick, M. J. 1993 Regenerative activity in apical dendrites of pyramidal cells in neocortex. *Cerebr. Cort.* **3**, 26–38.

Anderson, J. C., Martin, K. A. C. & Whitteridge, D. 1993 Form, function, and intracortical projections of neurons in the striate cortex of the monkey *Macacus nemestrinus*. *Cerebr. Cort.* **3**, 412–420.

Barone, P., Dehay, C., Berland, M., Bullier, J. & Kennedy, H. 1995 Developmental remodeling of primate visual cortical pathways. *Cerebr. Cort.* **5**, 22–38.

Beaulieu, C., Kisvárday, Z. F., Somogyi, P., Cynader, M. & Cowey, A. 1992 Quantitative distribution of GABA-immunopositive and -immunonegative neurons and synapses in the monkey striate cortex. *Cerebr. Cort.* **2**, 295–309.

Bernander, Ö., Douglas, R. J., Martin, K. A. C. & Koch, C. 1991 Synaptic background activity influences spatiotemporal integration in single pyramidal cells. *Proc. Natn. Acad. Sci. USA* **88**, 11 569–11 573.

Blasdel, G. G. & Lund, J. S. 1983 Termination of afferent axons in macaque striate cortex. *J. Neurosci.* **3**, 1389–1413.

Braitenberg, V. & Schüz, A. 1991 *Anatomy of the cortex: statistics and geometry.* Berlin: Springer Verlag.

Celebrini, S., Thorpe, S., Trotter, Y. & Imbert, M. 1993 Dynamics of orientation coding in area V1 of the awake primate. *Vis. Neurosci.* **10**, 811–825.

Contreras, D., Destexhe, A., Sejnowski, T. J. & Steriade, M. 1996 Control of spatiotemporal coherence of a thalamic oscillation by corticothalamic feedback. *Science* **274**, 771–774.

Douglas, R. J. & Martin, K. A. C. 1991 A functional microcircuit for cat visual cortex. *J. Physiol., Lond.* **440**, 735–769.

Douglas, R. J., Koch, C., Mahowald, M., Martin, K. A. C. & Suarez, H. H. 1995 Recurrent excitation in neocortical circuits. *Science* **269**, 981–988.

Felleman, D. J. & Van Essen, D. C. 1991 Distributed hierarchical processing in the primate cerebral cortex. *Cererb. Cort.* **1**, 1–47.

Freund, T. F., Martin, K. A. C., Soltesz, I., Somogyi, P. & Whitteridge, D. 1989 Arborisation pattern and postsynaptic targets of physiologically identified thalamocortical afferents in striate cortex of the macaque monkey. *J. Comp. Neurol.* **289**, 315–386.

Garey, L. J. & Powell, T. P. S. 1971 An experimental study of the termination of the lateral geniculo-cortical pathway in cat and monkey. *Proc. R. Soc. Lond.* B **179**, 41–63.

Gattass, R., Gross, C. G. & Sandell, J. H. 1981 Visual topography of V2 in the macaque. *J. Comp. Neurol.* **201**, 519–539.

Johnson, R. R. & Burkhalter, A. 1996 Microcircuitry of forward and feedback connections within rat visual cortex. *J. Comp. Neurol.* **368**, 383–398.

Johnson, R. R. & Burkhalter, A. 1997 A polysynaptic feedback circuit in rat visual cortex. *J. Neurosci.* **17**, 7129–7140.

Kennedy, H. & Bullier, J. 1985 A double-labeling investigation of the afferent connectivity to cortical area V1 and V2 of the macaque monkey. *J. Neurosci.* **5**, 2815–2830.

Levitt, J. B., Kiper, D. C. & Movshon, J. A. 1994 Receptive fields and functional architecture of macaque area V2. *J. Neurophysiol.* **71**, 2517–2542.

Livingstone, M. S. & Hubel, D. H. 1984 Anatomy and physiology of a colour system in the primate visual cortex. *J. Neurosci.* **4**, 309–356.

Lund, J. S. & Boothe, R. G. 1975 Interlaminar connections and pyramidal neuron organisation in the visual cortex, area 17 of the macaque monkey. *J. Comp. Neurol.* **159**, 305–334.

McGuire, B. A., Gilbert, C. D., Rivlin, P. K. & Wiesel, T. N. 1991 Targets of horizontal connections in macaque primary visual cortex. *J. Comp. Neurol.* **305**, 370–392.

Markram, H., Lübke, J., Frotscher, M., Roth, A. & Sakmann, B. 1997 Physiology and anatomy of synaptic connections between thick tufted pyramidal neurones in the developing rat neocortex. *J. Physiol., Lond.* **500**, 409–440.

Motter, B. C. 1993 Focal attention produces spatially selective processing in visual cortical areas V1, V2, and V4 in the presence of competing stimuli. *J. Neurophysiol.* **70**, 909–919.

Mumford, D. 1992 On the computational architecture of the neocortex. II. The role of cortico-cortical loops. *Biol. Cybern.* **66**, 241–251.

Nicoll, R. A. & Blakemore, C. 1990 Dual intracellular impalement *in vitro* reveals excitatory synaptic connections between pyramidal neurones in rat visual cortex. *J. Physiol., Lond.* **430**, 15. (Abstract of a presentation.)

Nowak, L. G., Munk, M. H. J., Nelson, J. I., James, A. C. & Bullier, J. 1995 Structural basis of cortical synchronization. I. Three types of interhemispheric coupling. *J. Neurophysiol.* **74**, 2379–2400.

Perkel, D. J., Bullier, J. & Kennedy, H. 1986 Topography of the afferent connectivity of area 17 of the macaque monkey: a double labeling study. *J. Comp. Neurol.* **253**, 374–402.

Peters, A. & Payne, B. R. 1993 Numerical relationships between geniculocortical afferents and pyramidal cell modules in cat primary visual cortex. *Cerebr. Cort.* **3**, 69–78.

Peters, A. & Sethares, C. 1991 Organization of pyramidal neurons in area 17 of monkey visual cortex. *J. Comp. Neurol.* **306**, 1–23.

Peters, A. & Sethares, C. 1996 Myelinated axons and the pyramidal cell modules in monkey primary visual cortex. *J. Comp. Neurol.* **365**, 232–255.

Peters, A., Payne, B. R. & Budd, J. 1994 A numerical analysis of the geniculocortical input to striate cortex in the monkey. *Cerebr. Cort.* **4**, 215–229.

Rockland, K. S. 1994 The organization of feedback connections from area V2 (18) to V1 (17). In *Cerebral cortex*, vol. 10 (*Primary visual cortex in primates*) (ed. A. Peters & K. S. Rockland), pp. 261–299. New York: Plenum.

Rockland, K. S. 1997 Elements of cortical architecture: hierarchy revisited. In *Cerebral cortex*, vol. 12 (*Extrastriate cortex in primates*) (ed. K. S. Rockland, J. H. Kaas & A. Peters), pp. 243–293. New York: Plenum.

Rockland, K. S. & Pandya, D. N. 1979 Laminar origins and terminations of cortical connections of the occipital lobe in the rhesus monkey. *Brain Res.* **179**, 3–20.

Rockland, K. S. & Virga, A. 1989 Terminal arbors of individual 'feedback' axons projecting from area V2 to V1 in the macaque monkey: a study using immunohistochemistry of anterogradely transported *Phaseolus vulgaris* leucoagglutinin. *J. Comp. Neurol.* **285**, 54–72.

Salin, P.-A. & Bullier, J. 1995 Corticocortical connections in the visual system: structure and function. *Physiol. Rev.* **75**, 107–154.

Sandell, J. H. & Schiller, P. H. 1982 Effect of cooling area 18 on striate cortex cells in the squirrel monkey. *J. Neurophysiol.* **48**, 38–48.

Sawatari, A. & Callaway, E. M. 1996 Convergence of magno- and parvocellular pathways in layer 4B of macaque primary visual cortex. *Nature* **380**, 442–446.

Shao, Z. & Burkhalter, A. 1996 Different balance of excitation and inhibition in forward and feedback circuits of rat visual cortex. *J. Neurosci.* **16**, 7353–7365.

Shipp, S. & Zeki, S. M. 1989 The organization of connections between areas V5 and V1 in macaque monkey visual cortex. *Eur. J. Neurosci.* **1**, 309–332.

Ullman, S. 1995 Sequence seeking and counter streams: a computational model for bidirectional information flow in the visual cortex. *Cerebr. Cort.* **5**, 1–11.

Van Essen, D. C. & Zeki, S. M. 1978 The topographic organization of the rhesus monkey prestriate cortex. *J. Physiol., Lond.* **277**, 193–226.

Van Essen, D. C., Newsome, W. T., Maunsell, J. H. R. & Bixby, J. L. 1986 The projections from striate cortex (V1) to areas V2

and V3 in the macaque monkey: asymmetries, areal boundaries, and patchy connections. *J. Comp. Neurol.* **244**, 451–480.

Weller, R. E. & Kaas, J. H. 1983 Retinotopic patterns of connections of area 17 with visual areas V–II and MT in macaque monkeys. *J. Comp. Neurol.* **220**, 253–279.

Zeki, S. M. 1978 Uniformity and diversity of structure and function in rhesus monkey prestriate cortex. *J. Physiol., Lond.* **277**, 273–290.

Zipser, K., Lamme, V. A. F. & Schiller, P. H. 1996 Contextual modulation in primary visual cortex. *J. Neurosci.* **16**, 7376–7389.