Numerical Relationships between Geniculocortical Afferents and Pyramidal Cell Modules in Cat Primary Visual Cortex

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An analysis has been made of the quantitative data available on the number of pyramidal cell modules of layer IV neurons, and of geniculocortical axons and their synapses in cat striate cortex. It is found that the convergence of geniculocortical afferents upon any one pyramidal cell module is enormous, since in any one location there is overlap between 360–540 X-axons and 300–540 Y-axons. In total, the X- and Y-axonal arbors provide some 1640 × 10^6 synapses to area 17, which is equivalent to a ratio of 160–200 synapses per layer IV neuron. These values assume that geniculocortical terminals synapse only with the spiny stellate cells of layer IV. The values are reduced to 100–125 per spiny stellate cell when account is taken of the synapses that involve the dendrites that enter layer IV from neurons with cell bodies in other layers. Since each layer IV neuron receives some 2500 asymmetric synapses, this means that only 5% of the total excitatory input to a layer IV neuron seems to be provided by the geniculocortical afferents. Further, if the boutons in the geniculocortical axonal arbors are distributed homogeneously across layer IV, each axon could only provide one synapse to about one in four of the layer IV neurons encompassed by its plexus. It may be, however, that instead of being spread evenly, boutons in individual arbors converge upon individual neurons to supply a number of synapses to them. But even so, it seems unlikely that any individual geniculate axon could dominate the activity of a particular cortical neuron.

The geniculate input to the primary visual cortex is one of the most extensively studied neuronal systems in the cat, because fundamentally it is this input that determines the response properties of the visual cortical neurons. Consequently, in recent years a variety of quantitative analyses have been carried out to ascertain the numbers of neurons and synapses in this system, but so far little effort seems to have been made to synthesize these data beyond a brief discussion in an article by Freund et al. (1985b). The present article will attempt to provide such a synthesis, with the focus being the modules of pyramidal cell that we have recently shown to be present in area 17 of the cat visual cortex (Peters and Yilmaz, 1993), as they are in the primary visual cortex of the monkey (Peters and Sethares, 1991) and rat (Peters and Kara, 1987).

When an antibody to microtubule-associated protein 2 is used to visualize the microtubules in the cell bodies and dendrites of neurons (Bernhardt and Matus, 1984; De Camilli et al., 1984; Kosik et al., 1984); it is evident that the apical dendrites of the layer V and layer II/III pyramidal cells in area 17 of cat visual cortex are organized into vertically oriented groups, or clusters (Peters and Yilmaz, 1993). On average, the pyramidal cell clusters have center-to-center spacings of 56 μm, and their axes are defined by discrete clusters of apical dendrites (left side of Fig. 1). The clusters are initiated by the apical dendrites of the large- and medium-sized pyramidal cells in layer V, and as the clusters pass through layer II/III, the apical dendrites of the pyramidal cells in that layer are added to them, such that the dendritic clusters gradually become thicker as they ascend toward layer I. Layer VIa also contains pyramidal cells, but their apical dendrites do not contribute to the clusters. Instead, they group together to form independent aggregates that are referred to as bundles, and these bundles seem to be organized such that their apical dendrites pass between the groups of neuronal cell bodies in layer V to reach layer IV, where most of the layer VIa apical dendrites form their terminal tufts. And neither do the neurons in layer IV contribute to the dendritic clusters, because in cat visual cortex layer IV largely contains spiny stellate cells, which lack apical dendrites but resemble pyramidal cells in all other respects.

As has been shown in a number of studies (e.g., Garey and Powell, 1971; LeVay and Gilbert, 1976;

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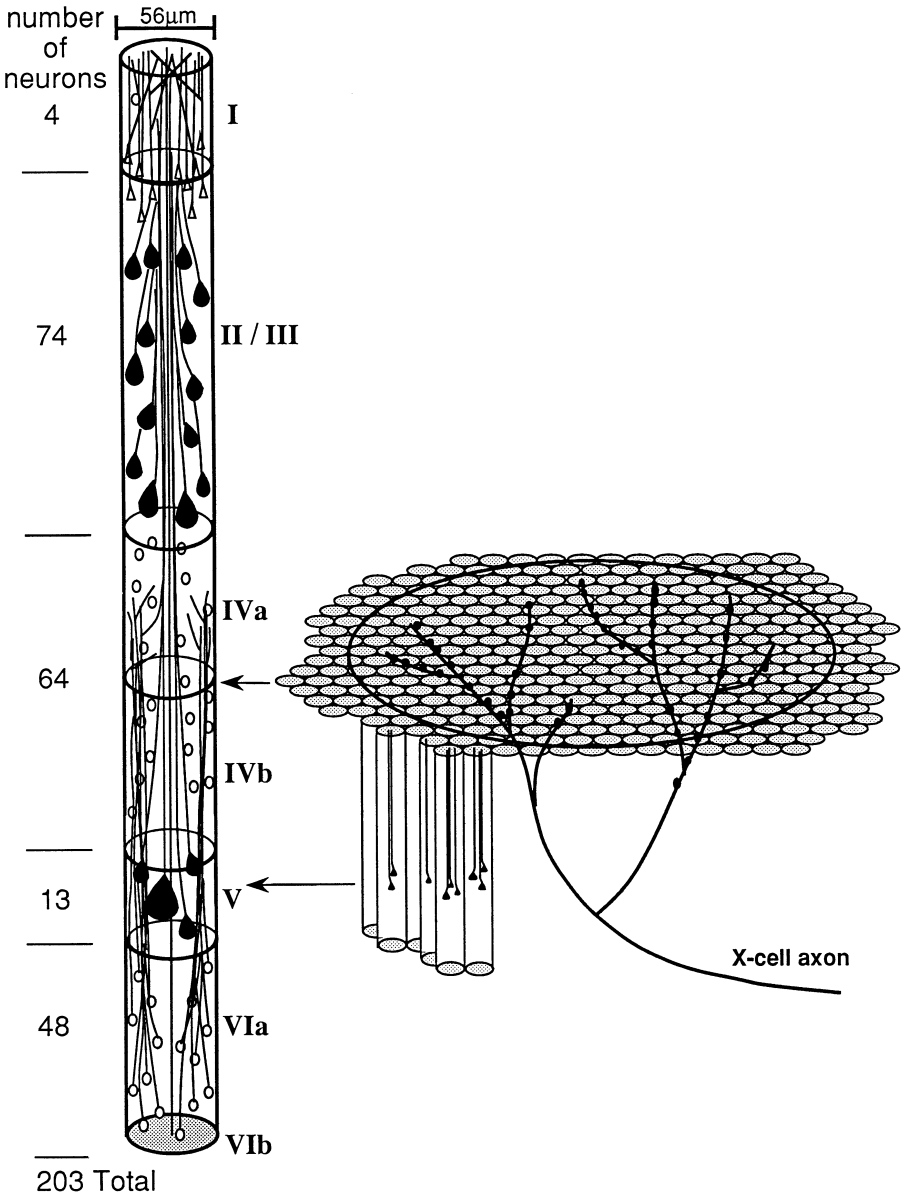

Figure 1. Diagrammatic representation of an X-cell axon arbor terminating in layer IV, where it spreads over about 250 pyramidal cell modules. On the *left* is a pyramidal cell module, which has a diameter of about 56 μm and contains 203 neurons; 64 of these neurons are contained within layer IV.

Freund et al., 1985a), the geniculocortical afferents to layers IV of cat visual cortex form asymmetric synapses, and their prime targets are the dendritic spines. In layer IV, the majority of these spines belong to the spiny stellate cells that reside in that layer, but other spines belong to those portions of the apical dendrites of the layer V and layer VIa pyramidal cells within layer IV, and to the basal dendrites of those layer III pyramidal cells that dip down into layer IV (e.g., Freund et al., 1985b). Still other geniculocortical afferents synapse with the cell bodies and dendritic shafts of non-pyramidal cells in cat visual cortex, but information about which kinds of non-pyramidal cells receive these afferents is still sketchy.

We have previously proposed that the clusters of pyramidal cell apical dendrites are a morphological manifestation of the existence of modules, which represent the basic neuronal aggregates in area 17 of cat visual cortex (Peters and Yilmaz, 1993). Since the dendritic clusters have an average center-to-center spacing of 56 μm (Table 1, line 1), this spacing also reflects the widths of the pyramidal cell modules, which are envisioned as cylinders of neurons, which consequently have cross-sectional areas of 2500 μm^2 (Table 1, line 2) and extend through the entire depth of the cortex (see Fig. 1). On the basis of analyses of the numbers of neurons in cat visual cortex (Beaulieu and Colonnier, 1983; Peters and Yilmaz, 1993); such a module would contain some 203 neurons (Table 1, line 3), and if the average surface area of area 17 in one hemisphere is taken to be 399 mm^2 (Table 1, line 4; Anderson et al., 1988), then each striate cortex would contain about 160,000 of the pyramidal cell modules (Table 1, line 5). It was further suggested that if the pyramidal cell modules are the basic neuronal aggregates in cat visual cortex (Peters and Yil-

maz, 1993), then groups of modules would be excited by different sets of thalamic and other afferents, to produce the columnar systems or slabs subserving eye preference (e.g., Hubel and Wiesel, 1963; Shatz and Stryker, 1978; Löwel and Singer, 1987; Anderson et al., 1988; Löwel et al., 1988; Jones et al., 1991) and stimulus orientation preference (Hubel and Wiesel, 1963; Albus, 1975; Löwel et al., 1988). These two functional systems of columns occupy the same space, and as demonstrated by Löwel et al. (1988), they both tend to form regularly spaced bands, whose organizations appear to be independent of each other. The systems also differ in a number of features. Iso-orientation columns tend to form well-defined branching bands that have a center-to-center spacing of 900–1000 μm, while the eye preference or ocular dominance columns have the form of beads or patches. Anderson et al. (1988) have shown such beads to have an average diameter of 667 μm, and their counts suggest that there are 650–675 beads in each hemisphere. Since these columnar systems occupy the same cortical space, it follows that any one pyramidal cell module can be part of each of them. It is further suggested that each module receives a unique set of information, not only about the orientation of an image and the eye receiving the image, but also about the position of the image on the retina.

This proposition led us to consider what is known about the geniculocortical afferent system in the cat striate cortex, and to examine such factors as how many of the proposed pyramidal cell modules are contained within the axonal arbors of geniculate axons, how many axonal arbors converge upon an individual module, and how many synapses the neurons within a module might receive from the geniculate afferents (see Table 1).

Thalamic Axon Arbors and Pyramidal Cell Modules

It is now generally accepted that in the cat visual system there are X-, Y-, and W-pathways that form parallel, but largely separate, routes through which information from the retina is passed via the dorsal lateral geniculate nucleus (dLGN) to the visual cortex (see reviews by Stone et al., 1979; Lennie, 1980; Orban, 1984; Sherman, 1985). In the retina and dLGN, X-cells give brisk discharges. The pattern of their responses is linearly related to stimulus form and size, and the cells are characterized by sensitivity to high spatial frequency patterns. Y-cells also give brisk, nonlinear discharges and show a sensitivity to high temporal frequencies. By analogy with the primate (Schiller and Logothetis, 1990), the X- and Y-pathways can be considered as two separate but overlapping systems that extend visual capacities in the spatial and temporal domains. W-cells are rather heterogeneous in their stimulus sensitivities, and the primary criterion on which they are grouped into a single pool is one of exclusion, since they are neither X-cells nor Y-cells. Numerically, each of the different types of cells that compose the W-cell group has relatively minor importance, and many give rather sluggish discharges even to optimal stimuli.

Each ganglion cell type has a differential pattern of projection to the sublaminae within the dLGN, and cells in each layer of the dLGN have differential patterns of projection to area 17 and the numerous areas that comprise the remainder of the visual cortex. In the dLGN, X-cells are primarily present in the A laminae, although a very small fraction of these neurons may also occur in the C laminae and in the medial interlaminar nucleus (MIN). Virtually all of the X-cells project to area 17. The Y-cells are also present in the A laminae, and they are the dominant kind of neuron in the C laminae, as well as in MIN. The Y-cells in the A laminae project to areas 17 and 18, most Y-cells in the C laminae project to area 18, and the Y-cells in MIN project to areas 18 and 19 and the visual areas on the medial bank of the lateral suprasylvian sulcus. The W-cells are a heterogeneous group of neurons that is largely confined to the C laminae, with a small number of them in MIN. They project to all or most of the contiguous visual cortical areas. In area 17, W-cells project to layers I, III, and V (Leventhal, 1979). Thus, with the exception of a small number of W-cells in the C laminae, all geniculocortical projections to area 17 arise from the X- and Y-cells in layers A and A_1 of the dLGN. These cells have overwhelming numbers of terminations in layer IV and much smaller numbers of terminations in layer VI (LeVay and Gilbert, 1976).

Humphrey et al. (1985a) and Freund et al. (1985a) have injected single, physiologically identified X- and Y-cell geniculocortical axons passing in the optic radiations with HRP to reveal the axonal arborizations in area 17 of cat visual cortex. They find that the X-cell axons terminate in layer IV, either across its full thickness or only in one sublayer. The arbors of termination form single clumps of boutons that have projected areas of 0.6–0.9 mm^2 beneath the cortical surface (Table 1, line 6). Given that each pyramidal cell module has a cross-sectional area of about 2500 μm^2 (Table 1, line 2) or 0.0025 mm^2, the arbors of single X-cell axons would encompass between 240 and 360 such modules (Table 1, line 7). This is shown diagrammatically in Figure 1. The Y-cells projecting to area 17 all terminate in layer IVa, and they have more complex arborizations than the X-cell axons because they terminate in two or three clumps of boutons separated by terminal-free gaps. If the gaps are ignored, Humphrey et al. (1985a) find that the areas delimited by the terminals of Y-cell afferents are between 1.0 and 1.8 mm^2 (Table 1, line 8), which is about twice the areas of the X-cell terminal fields. Consequently, the Y-cell axons each spread over between 400 and 720 pyramidal cell modules (Table 1, line 9).

While these calculations give an answer as to how many pyramidal cell modules each X- and Y-cell axonal arborization encompasses, it does not answer the question of how many axonal arborizations converge upon the neurons contained in a single pyramidal cell module. The studies by Madarasz et al. (1978)

Table 1
Summary of numerical data and estimates on pyramidal cell modules and geniculocortical axonal arbors

Parameter	Value	Source
1. Diameter of pyramidal cell modules	56 μm	Peters and Yilmaz, 1993
2. Cross-sectional areas of modules	2500 μm^2	—
3. Number of neurons per module	203	Peters and Yilmaz, 1993
4. Surface area of area 17	399 mm^2	Anderson et al., 1988
5. Number of modules in area 17	160,000	line 4 ÷ line 2
6. X-cell axon termination area	0.6–0.9 mm^2	Humphrey et al., 1985a
7. Number of modules per x-cell axon	240–360	line 6 ÷ line 2
8. Y-cell axon termination area	1.0–1.8 mm^2	Humphrey et al., 1985a
9. Number of modules per Y-cell axon	400–720	line 8 ÷ line 2
10. Number of projection neurons in A laminae of dLGN	360,000	Madarasz et al., 1978; Williams et al., 1989; LeVay and Ferster, 1979
11. Ratio of X- to Y-cells	2:1	Friedlander et al., 1981; LeVay and Ferster, 1977
12. Number of X-cells in A laminae of dLGN	240,000	2/3 × line 10
13. Number of Y-cells in A laminae dLGN	120,000	1/3 × line 10
14. Convergence of X-axons onto each module	360–540	line 6 × line 12 ÷ line 5
15. Convergence of Y-axons onto each module	300–540	line 7 × line 13 ÷ line 5

and by Williams et al. (1989) suggest that there are about 480,000 neurons within laminae A and A_1 of the dLGN, and since some 25% of them are interneurons (LeVay and Ferster, 1979), then there must be about 360,000 neurons in the A laminae that project from the dLGN to the cortex (Table 1, line 10). These are all X- or Y-cells. As pointed out by Sherman (1985), there are many factors that confound estimates of the relative proportion of W-, X-, and Y-cells in the dLGN, but the evidence presented by LeVay and Ferster (1977) and by Friedlander et al. (1981) suggest that in laminae A and A_1 the ratio of X- to Y-cells is about 2:1 (Table 1, line 11). On this basis, there should be 240,000 X-cells and 120,000 Y-cells in the A laminae (Table 1, lines 12, 13). It should be pointed out, however, that other studies suggest ratios of 1:1 and of 3:1 (see Orban, 1984).

Since the 240,000 X-cells in laminae A and A_1 project to area 17, their axonal arborizations must be confined within the 399 mm^2 that this piece of cortex occupies. If all of the X-cell arborizations were spread out evenly in a single nonoverlapping and contiguous sheet, they would occupy between 0.6 and 0.9 × 240,000 mm^2, that is, 144,000–216,000 mm^2. But since they are confined within 399 mm^2, they must overlap, and we calculate that the number of X-cell axon arbors that would overlap at any one point, or converge on the neurons in any one pyramidal cell module, is 360–540 (Table 1, line 14). Looked at another way, since there are 160,000 pyramidal cell modules (Table 1, line 5) and 240,000 X-cell axons (Table 1, line 12), if they are evenly spaced each module would be in register with the center of one or two X-cell axon arbors. For efficient visual information processing, it may be proposed that the correct relationship is one module per two X-cell axon arbors. Such a relationship would accommodate one *on* X-cell and one *off* X-cell axon per cortical module.

For the Y-cells in laminae A and A_1 of the dLGN, evidence suggests that virtually all of them project to area 17 and that some have collateral branches to area 18 (Humphrey et al., 1985a,b). This means that the number of Y-cell afferents that would converge upon a single pyramidal cell module in area 17 is 1.0–1.8 mm^2 × 120,000/399 mm^2, or 300–540 (Table 1, line 15). These values are similar to those for the X-cell arbors, because although there are only half as many Y-cells in laminae A and A_1 of the dLGN as there are X-cells, their axonal spreads in area 17 encompass areas that are twice those covered by X-cell axon arbors. When viewed from a different perspective, since there are 160,000 pyramidal cell modules in area 17 and 120,000 Y-cell axons, one module lies approximately in register with the center of each Y-cell axon arbor.

Numbers of Geniculate Synapses per Pyramidal Cell Module

In addition to giving the dimensions of the arbors of geniculate afferents to area 17 of the cat visual cortex, Humphrey et al. (1985a) give the numbers of boutons contained within individual axonal plexuses within layer IV. For the X-cell axons Humphrey et al. (1985a) find the number of boutons per arbor in layer IV to be 1000–4800, with an average of 2620 boutons. This and other data cited in this section are to be found in Table 2. For comparison, Ferster and LeVay (1978) counted 1543 boutons within one X-cell arbor. Freund et al. (1985a) have also filled individual X-cell axons in area 17, and while they do not give values for the total number of boutons per axon, they do show that on average each X-cell bouton forms 1.27 synapses (Table 2, line 2). Taking the average number of boutons to be 2620, the average X-cell arbor would therefore form 3327 synapses (Table 2, line 3). Extrapolating from this value, the number of synapses that the total population of X-cells in laminae A and A_1 of

Table 2
Summary of numerical data and estimates on pyramidal cell modules and geniculocortical synapses

Parameter	Value	Source
Total numbers of synapses		
1. Mean number of boutons per X-cell arbor	2620	Humphrey et al., 1985a
2. Mean number of synapses per X-bouton	1.27	Freund et al., 1985a
3. Mean number of synapses per X-cell arbor	3327	line 1 × line 2
4. Total number of X-cell synapses in area 17	800 × 10^6	Table 1, line 3 × line 12
5. Total number of X-cell synapses per module	5000	Table 1, line 4 ÷ line 5
6. Mean number of boutons per Y-cell arbor	4280	Humphrey et al., 1985a
7. Mean number of synapses per Y-bouton	1.64	Freund et al., 1985a
8. Mean number of synapses per Y-cell arbor	7020	line 6 × line 7
9. Total number of Y-cell synapses in area 17	840 × 10^6	Table 1, line 8 × line 13
10. Total number of Y-cell synapses per module	5250	Table 1, line 4 ÷ line 5
Synapses per layer IV neuron		
From data by Peters and Yilmaz		
11. Total number of X- and Y-synapses per module	10,250	line 5 + line 10
12. Layer IV neurons per module	64	Peters and Yilmaz, 1993
13. Synapses per neuron	160	line 11 ÷ line 12
From data by Beaulieu and Colonnier		
14. Total number of X- and Y-synapses in area 17	1640 × 10^6	Table 1, line 14 ÷ line 4
15. Number of X- and Y-synapses under 1 mm^2 of surface area	4.1 × 10^6	Table 1, line 14 ÷ line 4
16. Total number of asymmetric synapses in layer IV per 1 mm^2	83 × 10^6	Beaulieu and Colonnier, 1985
17. Proportion of asymmetric synapses from dLGN	5%	line 15 ÷ line 16
18. Number of asymmetric synapses per layer IV neuron	4000	Beaulieu and Colonnier, 1987
19. Number of dLGN synapses per layer IV neuron	200	line 18 ÷ line 17
Synapses per layer IV spiny stellate cell		
20. Number of spines per stellate cell	2000	Anderson et al., 1988
21. Percentage of all asymmetric synapses on dendritic spines	80%	Beaulieu and Colonnier, 1987
22. Number of asymmetric synapses on each spiny stellate cell	2500	line 20 ÷ line 21
23. Percentage of all layer IV asymmetric synapses on spiny stellate cells	62.5%	line 22 ÷ line 18
24. Number of geniculocortical synapses per spiny stellate cell	100 125	line 13 × line 23 line 19 × line 23

the dLGN establish in area 17 is 240,000 × 3327, or about 800 × 10^6 synapses (Table 2, line 4). Assuming that there are 160,000 pyramidal cell modules, this is 5000 synapses per module (Table 2, line 5). However, because 360–540 X-cell axon arbors converge on any one pyramidal cell module (Table 1, line 15), any one such axonal arbor would provide a mere 9–14 of these boutons. And since there are some 64 layer IV neurons per module (Peters and Yilmaz, 1993), this would not even provide one synapse per layer IV neuron.

For the Y-cell afferents to area 17, Humphrey et al. (1985a) counted between 2100 and 6700 boutons per axonal arbor, with an average of 4280 boutons (Table 2, line 6), while Freund et al (1985a) find that the average Y-cell bouton forms 1.64 synapses (Table 2, line 7). Combining these two values, the average Y-cell arbor in area 17 would form some 7020 synapses (Table 2, line 8). Assuming that there are 120,000 Y-cells in laminae A and A_1 of the dLGN that project to area 17, then the total number of Y-cell synapses in layer IV would be about 840 × 10^6 (Table 2, line 9). Each pyramidal cell module would therefore receive some 5250 Y-cell synapses (Table 2, line 10), which is similar to the number of X-cell synapses in layer IV.

If the values for the number of X-cell and Y-cell synapses are added together, the neurons in each pyramidal cell module would receive an average of about 10,250 synapses from the dLGN afferents terminating in layer IV (Table 2, line 11).

The Number of Synapses per Layer IV Neuron

From the data just presented, if it is assumed that each pyramidal cell module contains 64 layer IV neurons (Table 2, line 12; Peters and Yilmaz, 1993) and that the geniculocortical axons synapse only with these neurons, then each layer IV neuron would receive 160 geniculocortical synapses (Table 2, line 13).

A value of 200 geniculocortical synapses per layer IV neuron is calculated if the data generated by Beaulieu and Colonnier (1985, 1987) are used. This value is determined as follows. The total number of geniculate synapses in layer IV of area 17 that are derived from the X- and Y-cells is 800 × 10^6 plus 840 × 10^6, which equals 1640 × 10^6 (Table 2, line 14). Assuming that the surface area of area 17 is 399 mm^2, then the

number of geniculate synapses beneath 1 mm^2 of cortical surface would be 4.1×10^6 (Table 2, line 15). This number can be compared with the total number of synapses in layer IV calculated by Beaulieu and Colonnier (1985). They have ascertained the total number of synapses beneath 1 mm^2 of cortical surface, and they calculate that for layer IV in the monocular portion of area 17 the number is 103×10^6. However, the geniculate axons form only asymmetric, or excitatory, synapses, which comprise only 84% of the total synaptic population, in the entire cortex, so Beaulieu and Colonnier (1985) estimate that there are 83×10^6 asymmetric synapses in layer IV beneath 1 mm^2 of cortical surface (Table 2, line 16). This being so, then on the basis of the calculation in the previous section for the number of synapses that are estimated to be formed by the axon arbors of the X- and Y-cells projecting to area 17, the proportion of asymmetric synapses in layer IV that would be derived from the dLGN would be $4.1 \times 10^6/83 \times 10^6$, or about 5% (Table 2, line 17). Since the ratio of asymmetric synapses to neuronal cell bodies in layer IV is about 4000:1 (Table 2, line 18; Beaulieu and Colonnier, 1987), 200 of these excitatory synapses should be from geniculate afferents (Table 2, line 19).

These values of 160 and 200 geniculocortical synapses per layer IV neuron represent the upper limits, since they assume that only spiny stellate cells occupy layer IV. But as shown in a number of different cortices, thalamic afferents also synapse with the apical dendrites of layer V and layer VIa pyramidal cells that pass through layer IV, as well as the basal dendrites of some layer III pyramids and the surfaces of nonpyramidal cells contained in the layer (e.g., Peters et al., 1979; Freund et al., 1985a; White, 1989). Consequently, the values cited above need to be modified as follows. Anderson et al. (quoted in Dehay et al., 1991) state that each layer IV spiny stellate cell in area 17 of the cat has about 2000 dendritic spines (Table 2, line 20), the vast majority of which receive only a single asymmetric synapse (Dehay et al., 1991), while Beaulieu and Colonnier (1987) estimate that 80% of asymmetric synapses involve spines and 20% involve dendritic shafts (Table 2, line 21). Thus, in addition to the synapses on its spines, each layer IV spiny stellate cell should receive 500 more asymmetric synapses on its dendritic shafts, making a total of 2500 asymmetric synapses from all sources (Table 2, line 22). Since Beaulieu and Colonnier (1987) estimate that the ratio of asymmetric synapses to layer IV neuronal cell bodies is 4000 (Table 2, line 18), the 1500 asymmetric synapses not on spiny stellate cells are presumably on the other neuronal elements included within layer IV. This being so, the fraction of asymmetric synapses in layer IV that are associated with spiny stellate cells would be 2500/4000, or 62.5% (Table 2, line 23). If this percentage is applied to modify the derived values of 160 (Table 2, line 13), and 200 (Table 2, line 19) geniculocortical synapses per layer IV neuron, then the number of geniculocortical synapses per spiny stellate cell would be 100 or 125 (Table 2, line 24). These values assume that there is no selectivity by the geniculocortical axons for spiny stellate cells compared with the dendrites of other neuronal elements also contained within layer IV.

Discussion

Relationship of Geniculate Axon Arbors to Columnar Systems

Although it is generally accepted that the forms of the eye preference and orientation systems are determined by the thalamic afferents, how the systems are produced and how the X- and Y-afferents contribute to them is not known. In the case of the eye preference columns or bands, it is usually assumed that the thalamic afferent arbors carrying information from each eye are lined up in alternating rows. When viewed from the cortical surface, the dimensions of the bands demonstrated using the deoxyglucose labeling technique and of the axonal arbors fit with this notion, since the eye preference bands are between 0.7 and 1.0 mm wide (e.g., Löwel and Singer, 1987; Löwel et al., 1988) and the diameters of the X- and Y-cell arbors are similar or even less (e.g., Humphrey et al., 1985a). However, Anderson et al. (1988) have shown, using transneuronal transport of label injected into the eye, that the eye preference columns are composed of beads or patches that have average diameters of 667 μm. Beads of this diameter would have areas of about 0.35 mm^2, which is much less than the areas covered by the spreads of individual arbors of either X- or Y-cell axons, namely, 0.6–0.9 mm^2 and 1.0–1.8 mm^2, respectively. Thus, the arbors of both sets of axons are significantly larger than the eye preference beads, and the correlation is difficult to understand when it is considered that Anderson et al. (1988) estimate that there are 650–675 beads or eye preference patches in each hemisphere, which is 550 times less than the combined number of X- and Y-axon arbors contained within one hemisphere. However, this value is reassuring because it is in the realm calculated for the convergence of 360–540 X-axon arbors (Table 1, line 14) and 300–540 Y-axon arbors (Table 1, line 15) onto an individual pyramidal cell module.

Even so, the discrepancy between the size of the geniculate axon arbors and eye preference beads needs some consideration. Since both X- and Y-axon arbors of one eye are larger than the beads, we must conclude that the arbors extend a substantial distance beyond each demonstrated bead into zones innervated by axons driven by the other eye. Thus, there is likely to be a substantial overlap between populations of axons driven by the two eyes and not the strict demarcation suggested by tracers transported from the eye to the cortex along geniculate axons (Anderson et al., 1988; Jones et al., 1991). This overlap can be envisaged, in a given transverse plane across the cortical layers, as a reciprocal waxing and waning of the densities of innervation by the two populations of axons, akin to two more-or-less truncated, out-of-phase sine waves.

In the cat, the iso-orientation columns or bands in area 17 have a center-to-center spacing of 1.0–1.1 mm and they are more regular in shape than the eye preference columns, although they also show periodic variations in width. In this case, variations occur every 0.9–1.0 mm along their length (Löwel et al., 1987, 1988). As with the eye preference columns, the iso-orientation bands are similar in width to the geniculate axon arbors, and it might be suggested that the periodic thickening of the bands is produced by concentrations of geniculate axon arbors. But whether the orientation system in layer IV is generated from information carried by either the X- or Y-cell systems, or both, is not known. Outside layer IV, orientation may be linked to the periodic, long-range intrinsic projections of pyramidal cells (Gilbert and Wiesel, 1983; Martin and Whitteridge, 1984; T'so et al., 1986; Kisvarday and Eysel, 1991); and to afferents from extrastriate regions converging on area 17 (Malpeli, 1983; Malpeli et al., 1986).

One interesting fact that does emerge from the data on the orientation columns in cat area 17 is that Albus (1975) has shown that in the tangential plane, adjacent recorded neurons have preferred stimulus orientations that differ by 5–10°. Albus (1975) finds that on average the separation between recorded neurons is about 50 μm. Thus, there is a change in preferred orientation of 5–10° every 50 μm. This figure of 50 μm is very similar to the 56 μm diameters of the pyramidal cell modules (see Fig. 1), and it might be suggested that the orientation preference of neurons in one module is different from that of neurons in the adjacent modules, such that a change in orientation occurs as the recording electrode passes from one pyramidal module into another.

Convergence of Geniculate Axons onto Cortical Modules and Layer IV Neurons

The analysis of the relationships between the 56 μm pyramidal cell modules and the axonal arbors of the geniculate axons shows that there is considerable overlap between them, such that each axonal arbor can synapse with neurons in several hundred molecules. Indeed, each module can receive synaptic input from as many as 300–500 separate axons, but only receive a few synapsing boutons from each one of them. On the face of it, this arrangement is such that no individual axon would appear capable of exerting a significant influence over the excitatory input to any one module. However, it does appear that geniculate axon arborizations bear a greater concentration of boutons toward their centers than in their peripheries (Humphrey et al., 1985a), such that there may be a somewhat greater input to modules that are located in the centers of axonal arbors. The overlap between the thalamic axonal arbors and the pyramidal cell modules might be such that the combined input to each module from several hundred converging axonal arbors, each providing a few synapses, might be sufficiently different from that of its neighbors to make each module unique; these differences might be exaggerated by the patchiness of the Y-cell arborizations. For example, neurons in neighboring modules might respond more strongly to stimuli with slightly different orientations or positions in the visual field and viewed slightly differently by each eye. Clearly, though, with the extent of convergence of inputs that seems to exist among thalamic axonal arbors, one particular synapse is unlikely to play a critical role in how the neurons in a module respond to a given stimulus.

The overlap and convergence of geniculate afferents representing a broad region of the visual field are reflected in microelectrode recordings from layer IV in the ferret, which is a carnivore like the cat. Zahs and Stryker (1988) and Chapman et al. (1991) have shown in the ferret that the small-amplitude extracellular action potentials generated by geniculate axon arbors in layer IV can be unmasked in electrophysiological recordings by applying kainate or muscimol to silence the activity of nearby nerve cell bodies. When the activity of numerous geniculate afferent axons in layer IV is recorded along vertical electrode penetrations in such a preparation, and the axons' receptive fields plotted, the receptive fields are scattered across a small region of the visual field; most of the receptive fields do not overlap, and many are separated by distances equivalent to several receptive field diameters. Despite this scattering of receptive fields, it seems that the long axis of the aggregate visual field region represented by the geniculate axons is aligned with the preferred stimulus orientation of nerve cell bodies in the vicinity that had been recorded immediately prior to the silencing of cell body activity (Chapman et al., 1991). This alignment is consistent with the wiring diagram proposed by Hubel and Wiesel (1962) to explain the orientation selectivity of simple cells, which are the dominant cell type in layer IV.

Number of Asymmetric Synapses in Layer IV of Area 17 Derived from Geniculate Input

Estimates of the number of asymmetric synapses in area 17 that are derived from the dLGN are disparate. Even if we assume that all of the X- and Y-cells in the A laminae of the dLGN project to area 17, our calculations suggest that they only account for about 5% of the total synaptic population in layer IV. This is about the same as the percentage of axon terminals that are seen to degenerate after large lesions have been made in the dLGN (e.g., Garey and Powell, 1971; Hornung and Garey, 1981). However, it is far short of the 28% of axonal boutons that LeVay and Gilbert (1976) found to be labeled in layer IV after injections of tritiated proline into the dLGN, and the similar value of 22% recorded by Einstein et al. (1987). At present there seems to be no way to reconcile these sets of data. Perhaps the number of boutons observed after injections of label into single axons is far less than the total that is actually present, or it may be that the higher percentages derived from the studies using transported amino acids are too high due to diffusion of the label. A number of other suggestions could also be made, but eventually one has to conclude that we

do not know what proportion of the excitatory input to neurons in layer IV of cat visual cortex is derived from the dLGN. And a survey of the literature suggests that the same is true for the thalamic input to most other cortical areas. An exception to this generalization is to be found in the studies that White and his colleagues have done on the mouse. White (e.g., 1989) has shown that lesions in the ventrobasal thalamus in the mouse cause about 20% of the axonal boutons in layer IV of the primary sensorimotor cortex to degenerate, a value confirmed by use of the anterograde transport of lectins (Keller et al., 1985). White and his colleagues (see White, 1989) have gone on to show that although many different types of neurons with dendrites in layer IV form asymmetric synapses with the thalamocortical afferents, different types of neurons receive varying proportions of their synaptic input from this source. As already pointed out, it is also known that the geniculocortical afferents to layer IV of cat striate cortex synapse with a variety of postsynaptic targets. But it is not known whether various types of neurons in this cortex similarly receive different proportions of their total synaptic input from the dLGN. Interestingly, while the observations made by Freund et al. (1985b) show that the X- and Y-axons may synapse with different kinds, or sets, of inhibitory neurons, they only found one axonal arbor to form as many as eight synapses with the same postsynaptic element, in this case a basal dendrite of a layer III pyramidal cell: most postsynaptic elements seemed to receive only a single bouton from a particular axonal arbor, but as pointed out in the next paragraph, it may be worthwhile to reexamine this point.

The data suggest that individual geniculocortical axons provide only few synapses to any particular postsynaptic element in layer IV of cat primary visual cortex, such that the total geniculocortical input to a particular neuron is the consequence of an enormous convergence and overlap of individual axonal arbors. In the extreme situation in which a layer IV spiny stellate cell, for example, receives only one synapse from any individual axonal arbor, its total geniculocortical input of 5%, or 100–125 synapses (Table 2, line 24), may all originate from different axonal arbors; this is only 12–20% of the total number of 660–1080 X- and Y-cell axonal arbors that may converge onto one neuronal module (Table 1, lines 14, 15). But rather than a neuron receiving one synapse from each of 100–125 geniculate axons, it is more likely that each postsynaptic neuron receives several synapses from a smaller number of geniculate axons. On the basis of electrophysiological results, Tanaka (1983) has estimated that at least 10 and possibly as many as 30 geniculate axons converge onto each area 17 neuron, and so it follows that each axon would supply between 4 and 12 synapses to a neuron. This would account for practically all of the 9–14 synapses we have calculated that an individual geniculate axon arbor supplies to a pyramidal cell module. It suggests that the terminals of individual geniculocortical axons are not spread out evenly, but tend to converge in groups onto one to four neurons.

Douglas and Martin (1991) have calculated that at least 100 active synapses or inputs are necessary to generate an output discharge from spiny neurons. This is almost identical to the 100–125 geniculocortical synapses that we have calculated each spiny stellate cell receives. The similarity of these numbers indicates that only 5% of the afferent input to a layer IV stellate cell is sufficient to evoke a discharge.

There are important implications about cortical circuits that can be derived from this value of 5%. Under normal circumstances, objects in the visual field cast images in both eyes and the signals from the two eyes converge on neurons in layer IV via geniculocortical synapses, which we have calculated to compose 5% of the total asymmetric synapse population on layer IV neurons. Under certain circumstances, such as monocular viewing conditions, neurons can be driven by stimuli presented to one eye or the other. Activation under these circumstances must be mediated either by less than the 5% of geniculocortical synapses alone, or in conjunction with other intrinsic or transcortical excitatory circuits. Presumably, a similar argument can be made to account for the activation of layer IV neurons by nonoptimal stimuli. Nevertheless, it is quite remarkable that the exquisite selectivity of a layer IV neuron for particular visual parameters may be based upon only 5% or less of its synaptic input. That begs the question of what roles the remaining 95% of asymmetric synapses that are derived from other sources, probably intrinsic ones, play in the operations and responses of layer IV neurons.

Conclusion

From these analyses, we can conclude that there is a massive convergence of thalamic input on to the neurons within a cortical pyramidal cell module. Consequently, an individual geniculate axon is unlikely to be the dominant driving force underlying the activity of a given neuron in layer IV, even if the number of synapses that the geniculate axon makes with that neuron is as high as 10. Surprisingly, we do not know whether the terminals of individual geniculocortical axons converge onto one or a small number of neurons or whether they are distributed more uniformly across the population of layer IV dendrites. In addition, we do not know whether the geniculocortical input to layer IV accounts for as little as 5% or as much as 25% of the total number of synapses in that layer. This fundamental information needs to be obtained before simple and realistic models can be conceived to explain the response properties of neurons in the layer that receives the majority of ascending visual signals in cat primary visual cortex.

Notes

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References

Albus K (1975) A quantitative study of the projection area of the central and the paracentral visual field in the area 17 of the cat. II. The spatial organization of the orientation domain. Exp Brain Res 24:181–202.

Anderson PA, Olavarria J, Van Sluyters RC (1988) The overall pattern of ocular dominance bands in cat visual cortex. J Neurosci 8:2183–2200.

Beaulieu C, Colonnier M (1983) The number of neurons in the different laminae of the binocular and monocular regions of area 17 in the cat. J Comp Neurol 217:337–344.

Beaulieu C, Colonnier M (1985) A laminar analysis of the number of round-asymmetric and flat-symmetric synapses on spines, dendritic trunks, and cell bodies in area 17 of the cat. J Comp Neurol 231:180–189.

Beaulieu C, Colonnier M (1987) Effect of the richness of the environment on the cat visual cortex. J Comp Neurol 266:478–494.

Bernhardt R, Matus A (1984) Light and electron microscopic studies of the distribution of microtubule-associated protein 2 in rat brain: a difference between dendritic and axonal cytoskeletons. J Comp Neurol 226:207–222.

Chapman B, Zahs KR, Stryker MP (1991) Relation of cortical cell orientation selectivity to alignment of receptive fields of geniculocortical afferents that arborize within a single orientation column in ferret visual cortex. J Neurosci 11:1347–1358.

De Camilli P, Miller PE, Navone F, Theurkauf WE, Vallee RB (1984) Distribution of microtubule-associated protein 2 in the nervous system of the rat studied by immunofluorescence. Neuroscience 11:819–846.

Dehay C, Douglas RJ, Martin KAC, Nelson C (1991) Excitation by geniculocortical synapses is not "vetoed" at the level of dendritic spines in cat visual cortex. J Physiol (Lond) 440:723–734.

Douglas RJ, Martin KAC (1991) Opening the grey box. Trends Neurosci 14:286–293.

Einstein G, Davis TL, Sterling P (1987) Pattern of lateral geniculate synapses on neuron somata in layer IV of the cat striate cortex. J Comp Neurol 260:76–86.

Ferster D, LeVay S (1978) The axonal arborizations of lateral geniculate neurons in the striate cortex of the cat. J Comp Neurol 182:923–944.

Freund TF, Martin KAC, Whitteridge D (1985a) Innervation of cat visual areas 17 and 18 by physiologically identified X- and Y-type thalamic afferents. I. Arborization patterns and quantitative distribution of postsynaptic elements. J Comp Neurol 242:263–274.

Freund TF, Martin KAC, Somogyi P, Whitteridge D (1985b) Innervation of cat visual areas 17 and 18 by physiologically identified X- and Y-type thalamic afferents. II. Identification of postsynaptic targets by GABA immunocytochemistry and Golgi impregnation. J Comp Neurol 242:275–291.

Friedlander MJ, Lin CS, Stanford LR, Sherman SM (1981) Morphology of functionally identified neurons in lateral geniculate nucleus of the cat. J Neurophysiol 46:80–129.

Garey LJ, Powell TPS (1971) An experimental study of the termination of the lateral geniculo-cortical pathway in the cat and monkey. Proc R Soc Lond [Biol] 179:41–63.

Gilbert CD, Wiesel TN (1983) Clustered intrinsic connections in cat visual cortex. J Neurosci 3:1116–1133.

Hornung JP, Garey LJ (1981) The thalamic projection to cat visual cortex: ultrastructure of neurons identified by Golgi impregnation or retrograde horseradish peroxidase transport. Neuroscience 6:1053–1068.

Hubel DH, Wiesel TN (1962) Receptive fields, binocular interaction and functional architecture in the cat's visual cortex. J Physiol (Lond) 160:106–154.

Hubel DH, Wiesel TN (1963) Shape and arrangement of columns in cat's striate cortex. J Physiol (Lond) 165:559–568.

Humphrey AL, Sur M, Uhlrich DJ, Sherman SM (1985a) Projection patterns of individual X- and Y-cell axons from the lateral geniculate nucleus to cortical area 17 in the cat. J Comp Neurol 233:159–189.

Humphrey AL, Sur M, Uhlrich DJ, Sherman SM (1985b) Termination patterns of individual X- and Y-cell axons in the visual cortex of the cat: projections to area 18, to the 17/18 border region, and to both areas 17 and 18. J Comp Neurol 233:190–211.

Jones DG, Van Sluyters RC, Murphy KM (1991) A computational model for the overall pattern of ocular dominance. J Neurosci 11:3794–3808.

Keller A, White EL, Cipolloni PB (1985) The identification of thalamocortical axon terminals in barrels of mouse SMI cortex using immunohistochemistry of anterogradely transported lectin (*Phaseolus vulgaris*-leucoagglutinin). Brain Res 343:159–165.

Kisvarday ZF, Eysel UT (1991) Cellular organization of reciprocal patchy networks in layer III of cat visual cortex (area 17). Neuroscience 46:275–286.

Kosik KC, Duffy LK, Dowling MM, Abraham C, McClusky A, Selkoe DJ (1984) Monoclonal antibody to microtubule-associated protein 2 (MAP2) labels Alzheimer neurofibrillary tangles. Proc Natl Acad Sci USA 81:7941–7945.

Lennie P (1980) Parallel visual pathways: a review. Vision Res 20:561–594.

LeVay S, Ferster D (1977) Relay cell classes in the lateral geniculate nucleus of the cat and the effects of visual deprivation. J Comp Neurol 172:563–584.

LeVay S, Ferster D (1979) Proportions of interneurons in the cat's lateral geniculate nucleus. Brain Res 164:304–308.

LeVay S, Gilbert CD (1976) Laminar patterns of geniculocortical projection in the cat. Brain Res 113:1–19.

Leventhal AG (1979) Evidence that different classes of relay cells in the cat's lateral geniculate nucleus terminate in different layers of striate cortex. Exp Brain Res 37:349–372.

Löwel S, Singer W (1987) The pattern of ocular dominance columns in flat-mounts of the cat visual cortex. Exp Brain Res 68:661–666.

Löwel S, Bischof HJ, Leutenecker B, Singer W (1988) Topographic relations between ocular dominance and orientation columns in the cat striate cortex. Exp Brain Res 7:33–46.

Madarasz M, Gerle J, Hajdu F, Somogyi G, Tömböl T (1978) Quantitative histological studies on the lateral geniculate nucleus in the cat. II. Cell numbers and densities in the several layers. J Hirnforsch 19:159–164.

Malpeli JG (1983) Activity of cells in area 17 of the cat in absence of input from layer A of lateral geniculate nucleus. J Neurophysiol 49:595–610.

Malpeli JG, Lee C, Schwark HD, Weyand TG (1986) Cat area 17. I. Pattern of thalamic control of cortical layers. J Neurophysiol 56:1062–1073.

Martin KAC, Whitteridge D (1984) Form, function and intracortical projections of spiny neurones in the striate visual cortex of the cat. J Physiol (Lond) 353:463–504.

Orban GA (1984) Studies in brain function, Vol 11, Neuronal operations in the visual cortex. Berlin: Springer.

Peters A, Kara DA (1987) The neuronal composition of area 17 of rat visual cortex. IV. The organization of pyramidal cells. J Comp Neurol 260:573–590.

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

Peters A, Yilmaz E (1993) Neuronal organization in area 17 of cat visual cortex. Cereb Cortex 3:49–68.

Peters A, Proskauer CC, Feldman ML, Kimerer L (1979) The projection of the lateral geniculate nucleus to area 17 of the rat cerebral cortex. V. Degenerating axon terminals

synapsing with Golgi impregnated neurons. J Neurocytol 8:331–367.
Schiller PH, Logothetis NK (1990) The color-opponent and broad-band channels of the primate visual system. Trends Neurosci 13:392–398.
Shatz EJ, Stryker MP (1978) Ocular dominance in layer IV of the cat's visual cortex and the effects of monocular deprivation. J Physiol (Lond) 281:267–283.
Sherman SM (1985) Functional organization of the W-, X-, Y-cell pathways in the cat: a review and hypothesis. Prog Psychobiol Physiol Psychol 11:233–314.
Stone J, Dreher B, Leventhal A (1979) Hierarchical and parallel mechanisms in the organization of visual cortex. Brain Res Rev 1:345–394.
Tanaka K (1983) Cross-correlation analysis of interneural activity in cat visual cortex. J Neurophysiol 49:1301–1318.
T'so DY, Gilbert CD, Wiesel TN (1986) Relationships between horizontal interactions and functional architecture in cat striate cortex as revealed by cross-correlation analysis. J Neurosci 6:1160–1170.
White EL (1989) Cortical circuits: synaptic organization of the cerebral cortex: structure, function and theory. Boston: Birkhäuser.
Williams RW, Cavada C, Reinoso-Suárez F (1989) Evolutionary plasticity in the feline retino-geniculate system. Soc Neurosci Abstr 15:457.
Zahs KR, Stryker MP (1988) Segregation of on and off afferents to ferret visual cortex. J Neurophysiol 59:1410–1429.