The Global Pattern of Cytochrome Oxidase Stripes in Visual Area V2 of the Macaque Monkey

Jaime F. Olavarria and David C. Van Essen

Department of Psychology, University of Washington, Box 351525, Seattle, WA 98195-1525 and Department of Anatomy and Neurobiology, Washington University School of Medicine, Box 8108, St Louis, MO 63110, USA

In primate visual area V2, histochemical staining for cytochrome oxidase (CO) reveals a tripartite pattern of densely labeled thick and thin stripes separated by pale interstripes. This modularity is believed to be related to functionally distinct processing streams that course through the hierarchy of visual areas. Here, we studied the overall pattern of CO stripes in V2 of the macaque monkey, using tissue that had been physically unfolded and flattened prior to histological sectioning. CO stripes were identified on the basis of their physical dimensions and on their differential immunoreactivity for the monoclonal antibody Cat-301. We observed several distinctive features of compartmental organization in V2. The most prominent was a dorso-ventral asymmetry in the stripe pattern, occurring in the majority of cases studied. In dorsal V2, most stripes measure ~10 mm in length and run roughly orthogonal to both the posterior and anterior borders of V2. In contrast, many stripes in ventral V2 have a curved or oblique trajectory, and some extend up to 20 mm in length. Stripes following a curved trajectory often become nearly parallel to the anterior border of V2. These differences imply an asymmetry in how the visual field maps onto dorsal versus ventral stripes. Occasionally, thin stripes fail to alternate with thick stripes but instead occur next to one other, separated only by interstripes. In the three most complete reconstructions, we found that unfolded V2 is ~110 mm in length, ~900 mm² in surface area, and that it contains ~28 complete sets of stripes (one thick, one thin and two interstripes), yielding an average of ~4 mm per set of stripes. The maximum width of ventral V2 (13–14 mm) exceeds that of dorsal V2 (10 mm), and there is a consistent narrowing of V2 in the region of foveal representation (3–5 mm).

Introduction

The discovery that many areas of visual cortex are subdivided into anatomically distinct compartments has focused much attention on both qualitative and quantitative aspects of cortical modularity. The best studied aspect of modularity is the system of ocular dominance stripes in area V1 of the macaque monkey (e.g. Hubel and Wiesel, 1972; Horton, 1984; LeVay et al., 1985; Blasdel 1992; Malach et al., 1993; Yoshioka et al., 1996). Ocular dominance stripes intersect the V1/V2 border at approximately right angles, and there are >100 pairs of ocular dominance stripes along this boundary (LeVay et al., 1985; Horton and Hocking, 1996a,b). In addition, staining for the oxidative enzyme cytochrome oxidase (CO) in V1 reveals a pattern of densely stained ‘blobs’ immersed in a paler ‘interblob’ matrix (Horton and Hubel, 1981; Horton, 1984; Livingstone and Hubel, 1984; reviewed by Hendrickson, 1985; Wong-Riley, 1989). The blobs tend to run along the center of each ocular dominance stripe, and there are altogether ~6000 CO blobs in V1 of the macaque (Horton, 1984).

In V2, CO histochemistry reveals a coarser system of stripe-like subregions involving densely labeled thick and thin stripes separated by pale interstripes (Livingstone and Hubel, 1983, 1984; Tootell et al., 1983; Horton, 1984; Hendrickson, 1985). The connectivity and function of these stripes have been intensely investigated and, in general, the results support the notion that V2 stripes are associated with separate functional pathways (e.g. see Van Essen and Gallant, 1994; Olavarria and Abel, 1996). Just as information about the numbers, dimensions and geometric relationships of CO blobs and ocular dominance stripes has been instructive in understanding the organization of V1 (LeVay et al., 1985; Blasdel 1992; Florence and Kaas, 1992; Rosa et al., 1992; Malach et al., 1993; Horton and Hocking, 1996b; Yoshioka et al., 1996), it is of interest to know the detailed arrangements of stripe compartments in V2.

In New World monkeys, CO stripes run across the width of V2, approximately orthogonal to both the V1/V2 border and anterior V2 border (Tootell et al., 1983, 1985; Horton, 1984; Cusick and Kaas, 1988; Shipp and Zeki, 1989; Krubitzer and Kaas, 1990). In the macaque, CO stripes in area V2 also intersect the V1/V2 border at approximately right angles. While it is natural to suspect that they would maintain this trajectory across the width of V2, this has not been adequately tested for ventral V2 because of the irregular folding of the cortical surface in this region.

The present study analyzed the overall layout of stripes in macaque V2 using a method for physically unfolding and flattening the cortex of gyrencephalic brains (Olavarria and Van Sluyters, 1985). With this approach, we were able to reveal several intriguing aspects of the geometry and topology of different compartments in macaque V2 that differ from that seen in New World monkeys. Some of these findings have been briefly presented elsewhere (Olavarria et al., 1989; Van Essen et al., 1990).

Materials and Methods

Ten adult adult macaque monkeys (Macaca fascicularis) weighing 2.5–3.5 kg were used to examine the stripe pattern in area V2. Experimental procedures followed the principles of laboratory animal care (NIH publication 85-23, 1985), and protocols approved by animal care and use committees at Caltech and the University of Washington. The pattern of CO stripes in large regions of V2 was reconstructed from 10 hemispheres (left hemisphere in all but one case). In three hemispheres, the region analyzed included nearly all of area V2. In addition, we present data on the distribution of ocular dominance columns in striate cortex of one animal that underwent monocular enucleation as an adult as part of a different experiment, under an institutionally approved protocol at the University of Southern California.

In both V1 and V2, we visualized the pattern of CO staining over large regions of cortex using a physical unfolding technique (Olavarria and Van Sluyters, 1985) to flatten the cortex prior to sectioning and histochemical staining. Animals were killed by administering an overdose of Nembutal and perfused for 7–8 min with 2% formaldehyde or 2% glutaraldehyde in 0.1 M phosphate buffer. The posterior pole of the brain, including the calcarine, lunate and inferior occipital sulci, was separated from the rest of the hemisphere by a transverse cut. Due to the intrinsic curvature of the cortical mantle, it was necessary to make several additional cuts in the...
Figure 1. (A) Global pattern of cytochrome oxidase (CO) stripes in dorsal and ventral V2 (case 90AL). The data come from the left hemisphere, but are shown as from the right hemisphere to facilitate comparison with other data from our laboratory. This figure is a montage from two sections taken from separate blocks containing all of dorsal and ventral V2, along with large portions of surrounding cortex. Area V1 is the darkly staining region situated posteriorly (to the left). The representation of the periphery is in the uppermost and lowermost regions of unfolded V2, representing inferior and superior visual quadrants respectively. The foveal representation (in lateral V2) is in the middle of the montage, where the photographs of the two sections are adjoined; no actual tissue is missing in this region. Several pale streaks are visible in regions of folding where the cortex is relatively thin. This is most noticeable ventrally, along the fundus of the inferior occipital sulcus (diagonal streak near the middle). Note that there is a pronounced dorso-ventral asymmetry in the stripe pattern. Triangles indicate stripes labeled with the monoclonal antibody Cat-301 (see B,C). (B) Correlation between the pattern of CO stripes (outlines) reconstructed from three neighboring CO-stained sections with the pattern of Cat-301 labeling (dots) shown in C. Dashed line indicates anterior border of V2 estimated from CO-stained sections. (C) Cat-301 labeling pattern reconstructed from two nearby flat sections separated by 60 µm. Dots represent individual Cat-301 positive cells. Triangles indicate finger-like accumulations of Cat-301 positive cells determined in C and transposed to A and B. By comparing panels A and B it can be noted that all stripes that can be identified as thick based on their appearance contain high numbers of Cat-301 labeled cells, whereas all stripes that can be identified as thin by their appearance, as well as interstripes, contain few or no Cat-301 labeled cells. Scale bar = 1 cm.
margin of the cortex so that the areas studied would lie completely flat, while preserving as much as possible the continuity of V2. A cut across the roof of the calcarine sulcus and the middle of the operculum separated area V1 into dorsal and ventral components. This cut passed through the foveal representation of V1 and extended anteriorly to separate the dorsal and ventral components of V2 (see Figs 1 and 3), making it easier to handle the large tangential sections.

In addition to carrying out CO histochemistry (Wong-Riley, 1979), we also examined immunoreactivity for the monoclonal antibody Cat-301, which preferentially labels the thick stripes in V2 (Hendry et al., 1988; DeYoe et al., 1990; Abel et al., 1997). Some of the tissue analyzed in this study comes from monkeys also used in other experiments, and in these cases intervening tangential sections were sometimes processed according to other protocols.

Anatomical data were recorded and analyzed using a computerized neuroanatomy system. Histological sections (60 μm thick) were examined under a Leitz microscope that had a motorized stage coupled to an IBM PC-XT via an electronic interface (Stahl Instruments). The locations and identifying characteristics of CO stripes, Cat-301 labeled cells, section outlines and various fiducial marks were entered using customized software. An immediate hardcopy of the data was obtained with a pen plotter that printed the locations of cells onto an enlarged drawing of the section outlines and other tissue landmarks. The data contained in the PC-XT could also be transported to a graphics workstation (Silicon Graphics) for subsequent analysis of two-dimensional and three-dimensional relationships using customized software. Sections containing Cat-301 labeled cells were aligned with adjacent sections stained for CO histochemistry by using fiducial marks such as tissue edges and blood vessels. Data on the length and area of V2, and on the perimeter and area of V1 were corrected for a modest increase in size (~3.5% linear expansion), which was estimated by comparing photographs of the flattened tissue block before sectioning with subsequent CO-stained sections.

The patterns of CO stripes in V2 are illustrated using photographs of single CO-stained tangential sections through dorsal or ventral V2. Montages of a single dorsal and ventral section from the same hemisphere are used to illustrate the global pattern of CO stripes in some cases (Figs 1 and 3). The pattern of ocular dominance columns in V1 was reconstructed using Photoshop 3.0 (Adobe Systems) software to photomontage several neighboring sections that had been carefully aligned using tissue edges, blood vessels and the contours of corresponding ocular dominance patches. All image-processing steps (contrast enhancement, intensity level adjustments and high-pass filtering) used to reconstruct the ocular dominance columns were applied to the entire digitized image of each section or of the reconstructed pattern and never locally.

**Results**

Figure 1A shows the pattern of CO stripes over a large portion of V2, as seen in a montage containing one section of dorsal occipital cortex (upper half) and another section of ventral occipital cortex (lower half) in case 1L (90AL). The V1/V2 border runs vertically along the middle of the dorsal section but has a more curved trajectory in the ventral section. The pattern of

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**Figure 2.** (A) Pattern of CO stripes in ventral V2. The photograph shows a second, more superficial section through ventral V2 from the case shown in Figure 1A (case 90AL). Note that the pale streak corresponding to the fundus of the inferior occipital sulcus is smaller than in Figure 1A. (B) Photomontage from a single section processed for Cat-301 histochemistry showing a 3 mm long, stripe-like, distribution of Cat-301 labeled cells. This labeling corresponds to a segment of the thick CO stripe marked with an arrow in A. Scale bar = 1 cm in A; 1 mm in B.
stripes is evident in regions where the section passes through the middle layers of area V2 (layers 3–5), where the density of CO reactivity and the contrast between adjacent stripes are greatest (Tootell et al., 1983; Horton, 1984). For both dorsal and ventral V2, the CO stripes start approximately orthogonal to the V1/V2 border, but take different trajectories in the region away from this border (to the right in the figure). In dorsal V2 the CO stripes run fairly directly from the border with V1 on the left to the border with V3 on the right. In contrast, the CO stripes in ventral V2 do not simply run directly across to the anterior border of V2 with area VP. Rather, the stripes that start in the foveal region bend around those from more peripheral regions, outflanking them and eventually running roughly parallel with the adjoining area VP before they terminate. More peripherally in ventral V2, the stripes again adopt a more direct trajectory between V1 and VP.

To distinguish between thick and thin stripes, we scored the distribution of Cat-301 immunoreactive cells in two nearby sections (Fig. 1C). In V2, the immunoreactive cells are concentrated in elongated clusters, most of which have an orientation similar to that of the CO stripes in panel A. Figure 2B shows a segment of the finger-like cluster of Cat-301 labeling associated with one of the thick stripes in this case (marked with an arrow in Fig. 2A).

To allow a more precise and extensive comparison of CO and Cat-301 patterns, we mapped the CO stripes in two additional pairs of dorsal and ventral sections from this case. The pattern for ventral V2 in one of these additional sections is shown in Figure 2 to illustrate that corresponding regions of the stripe pattern are consistent across different sections from the same tissue block. The reconstructed pattern of CO stripes from all three pairs of sections was transferred to the section containing the Cat-301 label, and the combined pattern is shown in Figure 1B. Arrowheads indicate thick stripes, based primarily on the Cat-301 data shown in Figure 1C. To assist in making comparisons, these arrowheads have been transposed back to the corresponding positions in Figure 1A,B. In agreement with previous studies (Hendry et al., 1988; DeYoe et al., 1990; Abel et al., 1997), Cat-301 labeling in V2 is heaviest in alternating CO-dense stripes. These are always thick stripes when a distinction based on dimensions can be made. However, in confirmation of other reports (e.g. Shipp and Zeki, 1989), we observed that alternate stripes are sometimes quite similar in width, particularly in ventral V2 (see Figs 1 and 2). When referring to the identity of stripes, we will continue to use the terms ‘thick stripe’ and ‘thin stripe’ as convenient descriptive labels even for stripes that are not distinguishable on dimensions alone.

Nearly all thin stripes and most thick stripes intersect directly with the V1/V2 border in case 1L. However, some thick stripes become relatively narrow near the V1/V2 border, and others appear to terminate altogether before they intersect the border, as also occurs in squirrel monkeys (Tootell et al., 1985). This occurs in both dorsal and ventral V2, but perhaps to a greater extent dorsally.

As noted previously (DeYoe et al., 1990), the distribution of Cat-301 labeling in thick stripes was often irregular and patchy in individual sections. We found a similar pattern of patchiness in nearby sections, suggesting that the distribution of Cat-301 in thick stripes is intrinsically patchy. However, given that individual cortical layers may undulate in and out of the tangential plane of sectioning, it is possible that the pattern would be more homogeneous along each thick stripe if the reconstruction had included sections that were unavailable because they had been stained for other purposes.

The overall extent of V2 was estimated by drawing a boundary (indicated by the dashed line) just outside the domain of clearly visible CO stripes in the reconstruction of Figure 1B. The estimated length (104 mm) and surface area (904 mm²) are similar to previously published values (Gattass et al., 1981; Weller and Kaas, 1983; Van Essen et al., 1986). The width of dorsal V2 is fairly constant at ∼10 mm in the hemisphere shown. In ventral V2, the maximal width is 13–14 mm, which is somewhat wider than dorsal V2, but the range of stripe lengths is even greater. Several of the ventral stripes are slightly more than 20 mm in length, whereas others are only 5–6 mm long. In the region of foveal representation, the width of V2 is ∼4 mm, in agreement with data shown by Tootell and Taylor (1995). In this and the other cases studied, we were unable to determine the exact relationship of V2 with the monocular crescent of V1 since this crescent cannot be easily recognized in CO-stained sections from normal monkeys (Horton, 1984).

We counted 28 CO-dense stripes in dorsal V2 of case 1 (Fig. 1A,B). The number of thick stripes in dorsal V2 was similar in both hemispheres. As in case 1L, several long stripes were observed in the right side, and these also originated perpendicular to the V1/V2 border and ended roughly parallel to the border with area VP. Except for this right hemisphere, all our data come from left hemispheres. The fact that ventral stripes in both the right and left hemispheres of case 1 showed the same characteristics suggests that our results from the other cases are not hemisphere-specific.

Figure 3 shows data from a different brain (case 2, 88BL) in which an extensive region of V2 was reconstructed. The main features of the CO pattern illustrated in Figures 1 and 2 are also present in this case. In particular, there is a pronounced dorso-ventral asymmetry in the configuration of stripes (Fig. 3A). Some stripes in ventral V2 are significantly longer than the stripes in dorsal V2 and follow a markedly curved trajectory from the V1/V2 border to the border with VP (Fig. 3A). Cat-301 labeling in V2 showed a stripe-like pattern (Fig. 3C) that coincides with alternating CO-dense stripes (Fig. 3B). The distinction between thick and thin stripes based on dimensions is again more pronounced in dorsal V2 than in ventral V2, as is the tendency of thick stripes in dorsal V2 to become narrower or to terminate some distance away from the V1/V2 border.

The estimated anterior boundary of V2 in case 2 is shown in Figure 3B, but there is greater uncertainty than for case 1.
Figure 3. (A) Global pattern of CO stripes in dorsal and ventral V2 in a second monkey (case 88BL). Montage constructed as that of Figure 1. A pronounced dorso-ventral asymmetry is also apparent in this case. (B) Correlation between the patterns of CO stripes (outlines) with the pattern of Cat-301 labeling (dots) shown in C. Dashed line indicates anterior border of V2 estimated from CO-stained sections. (C) Cat-301 labeling pattern reconstructed from three neighboring flat sections separated by 180 µm from each other. Dots represent individual Cat-301 positive cells. Arrows indicate finger-like accumulations of Cat-301 positive cells. Note in B that all stripes that can be identified as thick based on their appearance contain high numbers of Cat-301 labeled cells, whereas all stripes that can be identified as thin by their appearance, as well as interstripes, contain few or no Cat-301 labeled cells. Other conventions as in Figure 1.
because of the difficulty in determining the full extent of V2 stripes medially (top and bottom of figure). We estimated that V2 in case 2 measures 103 mm in length and 860 mm$^2$ in surface area. The width of V2 in the region of foveal representation is ∼3–4 mm in this case. In a third animal (case 3, 88FL), the length of unfolded V2 was 111 mm and the surface area 893 mm$^2$.

As in case 1L, there is a dorso-ventral asymmetry in the pattern of Cat-301 labelling anterior to V2 in case 2. In particular, there is a strip of dense Cat-301 labeling in dorsal V2, in the expected location of area V3, whereas no such strip is evident ventrally, along the expected location of VP.

A dorso-ventral asymmetry in the pattern of V2 stripes was evident to some degree in 8/10 cases examined. The stripes in dorsal V2 ran fairly directly from the border with V1 to the presumed border with V3 in all cases studied. In ventral V2 the wrapping of the central (lateral) CO stripes around the more peripheral (medial) ones was pronounced in five hemispheres (including cases 1 and 2) and present to a lesser degree in three of the remaining five hemispheres. In the cases that had less stripe bending, the stripes in ventral V2 ran oblique to the V1/V2 border and were therefore still longer than those in dorsal V2.

Irregularities in the alternation of thin and thick stripes were evident in a few cases, particularly in ventral V2 of case 4 (89DL) and dorsal V2 from case 5 (88DL). Figure 4 shows the pattern in case 4, as seen in two nearby CO-stained sections (Fig. 4A,B), a section scored for Cat-301 immunoreactivity (Fig. 4C), and in a drawing of the Cat-301 pattern overlaid on the CO stripe outlines (Fig. 4D). The pattern away from the V1/V2 border (right half of

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**Figure 4.** (A,B) Superficial (A) and deeper (B) CO-stained sections through ventral V2 (case 89DL) showing breakdown of sequence of thick and thin stripes. (C) Cat-301 labeling pattern reconstructed from one flat section. Dots represent individual Cat-301 positive cells. (D) Correlation between the pattern of CO stripes shown in A and B (outlines) with the pattern of Cat-301 labeling (dots) shown in D. In all panels, thin arrows indicate thin stripes and thick arrows indicate thick stripes. Scale bar = 5 mm.
In the left-hand portion of the figure, there is a conventional alternation between thick stripes, heavily labeled with Cat-301, and thin stripes lacking in Cat-301 label (leftward-pointing thick and thin arrows respectively). In contrast, the pattern closer to the V1/V2 border (left half of figure) includes a region in which neighboring thick stripes (identifiable by their width and their Cat-301 immunoreactivity) are separated by two thin stripes, rather than a single thin stripe (rightward-pointing thick and thin arrows in Fig. 4A,B,D). The junction between these two patterns occurs midway across V2 and involves a bifurcation of single thin stripes on the right into a pair of thin stripes on the left, thereby disrupting the continuity of thick stripes between the left and right halves of the figure.

Figure 5 illustrates a different type of breakdown in the thick-thin alternation that occurred in dorsal V2 of case 5. Two CO-stained sections separated by 120 µm are shown in Figure 5B,C, while the outline of CO stripes along with the pattern of Cat-301 labeling from two nearby sections is shown in Figure 5A. The lowest part of these sections (lateral in the hemisphere) contains two or perhaps three stripes that appear to be thin stripes, based on their width and their lack of Cat-301 label. Adjoining them is a short stretch involving a conventional alternation between two clearly identifiable thick stripes, heavily labeled with Cat-301 (arrows) and thin stripes lacking in Cat-301. Next in the sequence (medially, upward in the figure), there is a stretch of 16 mm in length containing six CO stripes that all appear to be thin stripes based on their width and their lack of Cat-301 label. In the most medial region (top of figure) there are three thick stripes, with a thin stripe interposed between one pair of thick stripes but an apparent absence of a thin stripe between the most medial pair of thick stripes. The similarities of the CO pattern in the two sections shown in Figure 5B,C indicate that the main features of this pattern were not dependent on the cortical depth at which the sections were taken.

The absence of clearly identifiable thick stripes over a large expanse of V2 raises the prospect that a portion of the V2 topographic map in case 5 lacks any representation associated with thick stripes. However, in the region lacking thick stripes, the thin stripes are only 6–7 mm in overall length, whereas this part of dorsal V2 is generally 9–10 mm in width in other hemispheres (Van Essen et al., 1986; see Figs 1 and 3 above). Moreover, anterior to the clearly identifiable thin stripes is a set of coarse CO-dark patches that are heavily labeled with Cat-301. Thus, an alternative interpretation is that the V2 thick stripes missing along the V1/V2 boundary are present but located along the V2/V3 boundary. Since it is difficult to distinguish area V3 from thick stripes in V2 on the basis of CO density and Cat-301 labeling (but see Tootell and Taylor, 1995), determination of the V2/V3 boundary in cases like this would require an independent marker, such as receptive field size.
Comparison with Ocular Dominance Stripes in V1

The complete pattern of ocular dominance columns in V1 of macaques has previously been reconstructed using conventional sections (LeVay et al., 1985), or flat-mounted material (Florence and Kaas, 1992; Horton and Hocking, 1996a,b). In order to directly compare some features of the CO pattern in V2 with that in V1, we revealed the complete pattern of ocular dominance columns in striate cortex. Figure 6A shows a photograph of one, 60 µm thick, CO-stained section through the unfolded and flattened striate cortex of a monkey that had undergone monocular enucleation. This section was cut through layer 4 of the striate cortex ipsilateral to the remaining eye. Dark regions indicate territory dominated by the remaining eye (Horton and Hubel, 1981). The global pattern shown in Figure 6B was reconstructed by photomontaging portions of the pattern from neighboring section onto the section in Figure 6A. The number of ocular dominance column pairs intersecting the V1/V2 border in this case is 132, slightly greater than the counts of 118 by LeVay et al. (1985). Horton and Hocking (1996a,b) examined a larger group of macaque monkeys and found that the number of ODC pairs along the V1/V2 border ranged from 101 to 154 sets. The perimeter of area V1 in the case shown in Figure 6 is 120 mm, and the surface area is 1070 mm², which compares well with values reported in other studies (Gattass et al., 1981; Van Essen et al., 1984; Purves and LaMantia, 1993; Horton and Hocking, 1996b).

Comparison of Figures 1 and 3 with Figure 6 shows that, as with CO stripes in V2, the ocular dominance stripes in V1 also have a systematic, but not entirely simple relationship with visual topography. In peripheral portions of the visual field, the ocular dominance stripes run approximately (but not perfectly) parallel to isoeccentricity contours, but in the representation of the central 5–10°, the relationship is much less orderly (Hubel and Freeman, 1977; LeVay et al., 1985; Florence and Kaas, 1992). Thus, the main asymmetry in V1 is between central and peripheral representations, whereas that in V2 is between upper and lower field representations.

Discussion

By examining the pattern of V2 stripes in unfolded and flattened tissue from both dorsal and ventral portions of many hemispheres, using a combination of CO histochemistry and Cat-301 immunoreactivity, we have been able to address issues of the geometry, topology and consistency of the stripe pattern in greater detail than in previous studies. The major findings — a dorso-ventral asymmetry in the stripe pattern and a moderate incidence of topological irregularities in thin-stripe/thick-stripe alternation — are of interest from both functional and developmental perspectives.

It is unlikely that the differences between the dorsal and ventral patterns of CO stripes we observed are due to distortions introduced by the unfolding and flattening method employed in
this study. Olavarria and Van Sluyters (1984) have presented evidence that this method does not significantly alter the laminar organization and cytoarchitecture of the cortex. In the present study, we cut across striate cortex and separated area V2 into dorsal and ventral components in order to minimize distortions caused by the intrinsic curvature of the cortical mantle and to allow the unfolded tissue to lie completely flat before processing it. Additional support for our conclusion comes from the observation that although all hemispheres were unfolded and flattened using the same procedure, not all showed the same dorso-ventral asymmetry in CO stripes.

Dorso-ventral Asymmetries
Marked dorso-ventral asymmetries in the configuration of V2 stripes have not been reported in other primates examined, namely squirrel monkeys and owl monkeys (Tootell et al., 1983, 1985; Horton, 1984; Cusick and Kaas, 1988; Shipp and Zeki, 1989; Krubitzer and Kaas, 1990). It will be interesting to determine if similar asymmetries are present in other Old World primates including humans (see Tootell and Taylor, 1995), and in the cebus, a New World monkey whose convolutions are similar to those of the macaque. This would help in assessing whether dorso-ventral asymmetries in V2 stripes are related primarily to overall brain size and degree of gyriﬁcation or to an evolutionary divergence between Old World and New World primates.

A basic feature of topographic organization in macaque V2 is that lines of constant eccentricity (isoeccentricity contours) run approximately orthogonal to its two boundaries, i.e. from the vertical meridian representation along the V1/V2 boundary to the horizontal meridian representation along the boundary with V3 and VP (Gattass et al., 1981; Van Essen et al., 1986). A similar topographic organization has been described in area V2 of the cebus monkey (Rosa et al., 1988). Thus, in dorsal V2, the isoeccentricity contours run approximately parallel to the CO stripes illustrated in the upper half of Figures 1A and 3A (cf. Roe and Ts’o, 1995). In ventral V2, however, the CO stripes would not simply run parallel to isoeccentricity lines in all animals, Assuming that the topographic map in ventral V2 is similar across animals, in cases with marked dorso-ventral asymmetry in stripe configuration, any given stripe would represent one particular eccentricity near the V1/V2 boundary and spiral out to represent a considerably higher eccentricity as it approaches the boundary with VP. This putative difference between dorsal and ventral stripes is illustrated in Figure 7, which presents a schematic back-projection of the orientation of V2 stripes onto the visual ﬁeld. Figure 7 is based on the stripe pattern shown in Figure 3 and on published summaries of the topography of V2 in macaque monkeys (Gattass et al., 1981; Van Essen et al., 1986) and cebus monkeys (Rosa et al., 1988). This hypothesis needs to be tested directly by mapping visual topography and the CO pattern in the same animal.

The marked dorso-ventral asymmetry in V2 stripe geometry observed in some monkeys adds to the list of differences between regions of cortex associated with lower versus upper visual ﬁelds (Burkhalter et al., 1986; Van Essen et al., 1986; Previc, 1990). We also found an asymmetry in the density of Cat-301 labeling immediately anterior to V2. Area V3, adjacent to dorsal V2, is associated with strong Cat-301 labeling, as reported previously by DeYoe et al. (1990). In contrast, we found consistently weaker Cat-301 labeling in area VP, adjoining ventral V2. This constitutes an additional difference between V3 and VP besides those reported previously. However, it does not resolve the issue of whether V3 and VP are genuinely distinct areas, each containing an incomplete representation of the visual field, or whether they are part of a single area (V3d and V3v) that is asymmetric in its architecture, connectivity and physiological characteristics. To some extent this matter depends upon what is meant by a ‘cortical area’ (see Van Essen et al., 1986; Krubitzer and Kaas, 1993; Felleman et al., 1997).

Irregularities in Stripe Topology
That V2 stripes in the macaque sometimes have an irregular pattern rather than a purely alternating thick–thin sequence has previously been reported by Shipp and Zeki (1989), who observed bifurcation of thin stripes identiﬁed by CO histochemistry and also occasional arrays of densely stained patches lacking clear alignment into stripes. Here, we have established that irregularities evident in the CO pattern can be conﬁrmed by Cat-301 labeling as an independent measure of stripe identity. In addition, we have provided evidence that in rare cases the irregularities may extend over a remarkably large expanse of V2. This is of particular interest in relation to questions of how the visual ﬁeld is represented in different stripe compartments. Roe and Ts’o (1995) recorded physiologically from two color (thin) stripes with no intervening disparity (thick) stripe between them. Consistent with this interpretation, they observed that the cortical magniﬁcation for the following disparity stripe was about half the magniﬁcation of most V2 stripes, suggesting that this thick stripe had to cover twice as much visual ﬁeld to compensate for the missing thick stripe. It will of interest to determine whether there are clear physiological or functional consequences in regions where the normal sequence of stripe classes in V2 breaks down.

Developmental Implications
The geometry and topology of V2 stripes is also of interest from a developmental standpoint. It has previously been suggested that the tendency of ocular dominance stripes in V1 to run in a consistent direction involves an anisotropic ordering inﬂuence, possibly associated with gradients in chemospeciﬁcity markers for the visuotopic map, which modulate the growth and retraction of geniculo-cortical arbors (von der Malsburg, 1979; Swindale, 1980; Fraser, 1985; LeVay et al., 1985). Likewise, the fact that CO stripes tend to run directly across the short axis of V2 in squirrel monkeys (Tootell et al., 1983; Livingstone and Hubel, 1984), owl monkeys (Tootell et al., 1985) and in the dorsal portion of V2 in the macaque (present results) suggests an analogous explanation based on an anisotropy in the steepness of the chemospeciﬁcity gradients involved in establishing an orderly topographic map in V2. However, our finding that CO stripes are oblique to (and sometimes approximately parallel to) the border of ventral V2 with VP in the macaque clearly indicates that a different explanation is needed for the anisotropy in this region.

Another possibility is that the development of stripe asymmetry between dorsal and ventral V2 is related to the overall differences in shape and width between these two portions of V2. The greater width of ventral V2 may impose different constraints on the mapping of the upper visual hemifield onto ventral V2, which could inﬂuence the development of long stripes that tend to bend ventrally. For example, there are consistent differences in the pattern of ocular dominance columns in striate cortex of cats and macaque monkeys. These differences may relate in part to the fact that in macaques the long axis of V1 maps the horizontal meridian, while in cats the long axis of V1 maps the vertical meridian.


