References and Notes

1. R. J. Schultz, in *Polyploidy, Biological Relevance*, W. H. Lewis, Ed. (Plenum, New York, 1980), p. 313; J. P. Bogart, in *ibid*, p. 341.
2. C. Moritz, paper presented at the meeting of the Australian Genetics Society, Melbourne, May 1982.
3. T. P. Maslin, *Am. Zool.* **11**, 361 (1971).
4. The ratio of males to females in a museum sample from Norseman, Western Australia, and a study site near Alice Springs is 13:17 and 30:27, respectively. H. R. Bustard [*J. Zool.* **156**, 483 (1968)] reported a ratio of 98:97 in the Pilliga, New South Wales, Australia.
5. L. M. Hardy and C. J. Cole, *J. Morphol.* **170**, 215 (1981).
6. O. Cuellar, *Am. Nat.* **108**, 625 (1974).
7. C. J. Cole, in *Intersexuality in the Animal Kingdom*, R. Reinboth, Ed. (Springer-Verlag, Berlin, 1975), p. 340.
8. The most recent taxonomic treatment of this genus is by A. G. Kluge [*J. R. Soc. West. Aust.* **46**, 63 (1963)]. The available karyological data indicate that diploid *H. binoei* may represent a species complex and that the triploid clones are best regarded as an agamic complex [V. Grant, *Plant Speciation* (Columbia Univ. Press, New York, ed. 2, 1981) p. 434]. More detailed electrophoretic and morphometric studies are needed to clarify the taxonomy of this genus.
9. O. Cuellar and C. O. McKinney, *J. Exp. Zool.* **196**, 341 (1976); C. J. Cole, *J. Hered.* **70**, 95 (1979).
10. C. D. Darlington, *Evolution of Genetic Systems* (Oliver & Boyd, London, 1958), pp. 167–168.
11. E. D. Parker, Jr., *Am. Zool.* **19**, 753 (1979); R. G. Zweifel, *Am. Mus. Novit., No. 2235* (1965).
12. See various papers from a symposium in *Am. Zool.* **19** (1979).
13. M. J. D. White, in *Essays in Evolution and Genetics in Honour of Theodosius Dobzhansky*, M. K. Hecht and W. C. Steere Eds. (North-Holland, Amsterdam, 1970), p. 237.
14. J. Lokki and A. Saura, in *Polyploidy, Biological Relevance*, W. H. Lewis Ed. (Plenum, New York, 1980), p. 277.
15. E. D. Parker, Jr., and R. K. Selander, *Genetics* **84**, 791 (1976).
16. R. C. Vrijenhoek, R. A. Angus, R. J. Schultz, *Evolution* **31**, 767 (1977).

17. I thank S. Donnellan, R. Honeycutt, M. King, M. J. D. White, D. King, G. Mengden, D. Roberts, P. Baverstock, H. Cogger, and T. Schwaner for providing specimens; R. Martin for his able assistance in the field; and R. Honeycutt, B. John, M. J. D. White, D. Shaw, and M. King for discussion and comments on the manuscript. Supported by the ANU and an Australian postgraduate research award.

23 August 1982; revised 20 December 1982

Functional Organization of the Second Cortical Visual Area in Primates

Abstract. *The functional organization of the second cortical visual area was examined with three different anatomical markers: 2-[^{14}C]deoxy-D-glucose, cytochrome oxidase, and various myelin stains. All three markers revealed strips running throughout the area, parallel to the cortical surface. The boundaries of these strips provide an anatomical criterion for defining the borders of this extrastriate region. Further, the demonstration of these strips allows a functional and anatomical analysis of modules in the area, just as the recent demonstration of spots in the primary visual cortex has allowed an analysis of modules there. The strips differ structurally and functionally from interstrip regions and these differences are similar to those seen between the spots and the interspot regions in the primary visual cortex. In the macaque the strips and spots differ with regard to binocular organization.*

Primates have at least nine visual areas beyond the primary visual cortex (V1) (*1, 2*). Of these, the second visual cortical area (V2) is certainly one of the most important (*3*). Area V2 is almost as large as V1 (*2, 4*), and, like V1, it contains a well-ordered representation of the visual field within its boundaries (*4, 5*). Area V2 surrounds V1, and considerable information is reciprocally transmitted between these two areas (*1, 2, 4–7*). Most of the information in V1 destined for other cortical visual areas goes first to V2 (*4*). Despite its obvious importance in the chain of cortical visual information processing, V2 has received much less attention than V1. For example, the functional anatomy of the primate V1 has been much studied during the last decade (*8–13*), but little is known about the functional anatomy of the primate V2.

This report describes several basic features of the organization of V2. We have found an array of parallel columnar strips running throughout V2; these strips seem to be the basic modular elements in this cortical area. By using three different markers, we have been able to describe different anatomical and physiological aspects of the strips. The V2 strips resemble the recently discovered spots in V1 (*10–14*) and provide a conspicuous anatomical landmark that should prove useful in defining the borders of V2 in an otherwise vaguely defined cortex. Preliminary results have been presented (*15–17*).

In order to label short-term variations in metabolic activity occurring during visual stimulation, we injected 2-[^{14}C]-deoxy-D-glucose (2DG) while monkeys viewed a particular stimulus. As in V1, different visual stimuli produced different 2DG patterns. During the course of this study, many different visual stimuli were used. In a typical experiment, one stimulus characteristic (for example, orientation, color, spatial frequency, temporal frequency) was held constant while others were varied. More than half of the monkeys viewed binocular patterns, and in these cases the binocular disparity was often varied. The monkeys were then killed, and the brains processed for histology. Early experiments (*15, 16, 18, 19*) indicated a columnar organization of function in V2; in order to see the topography of these columnar systems clearly, we mounted both V2 and V1 flat and cut our sections parallel to the flat-mounted cortical surface (*20*).

In order to label long-term differences in metabolic activity, many of the same tissue sections were treated to reveal cytochrome oxidase, a metabolic enzyme found in all neurons. Concentrations of this enzyme reflect variations in neural activity over periods of weeks or months (*10, 21, 22*).

We also stained some sections for myelin with hematoxylin and Luxol fast blue. In this report, we only include data from macaque and squirrel monkeys, but we have seen many of the same anatomical features in several other primate species.

Since we wish to emphasize the parallels between V1 and V2, we will first briefly describe what is known about the V1 spots and then what we have found about the V2 strips. Area V1 contains spotlike regions of high long-term metabolic activity (as measured by concentrations of cytochrome oxidase), surrounded by regions of lower activity (Fig. 1A) (*10–14*). A less prominent (but otherwise identical) array of spots appears in underlying cortical layers (Fig. 1B). Spotlike differences in cytochrome oxidase activity coincide with certain differences in 2DG activity (*10–12, 17, 18*), in the distribution of putative neurotransmitter (*14, 22*), in single-unit functional properties (*23*), and in afferent terminal distribution (*23, 24*).

Striplike regions of high cytochrome oxidase activity are seen in V2, in the area surrounding V1 (Fig. 1A). The cytochrome oxidase strips are most obvious in layers 4, 5, and the lower part of layer 3 (Fig. 1B), but they often extend through all cortical laminae. Thus, the strips are basically a columnar anatomical organization. The strips run approximately perpendicular to the V1-V2 border in all the primate species we have examined. In the squirrel monkey, the strips are about 0.4 to 0.7 mm wide with an interstrip spacing (center to center) of about 1 to 1.5 mm. In the macaque, the strips are slightly wider, with center-to-center spacings of about 1.5 to 2.5 mm. In the lower layers, the strips are alternately thick and thin (Fig. 1B). In the squirrel monkey, the thin strips merge with the V1-V2 border, but the thick strips fall short of this border by about 0.7 mm.

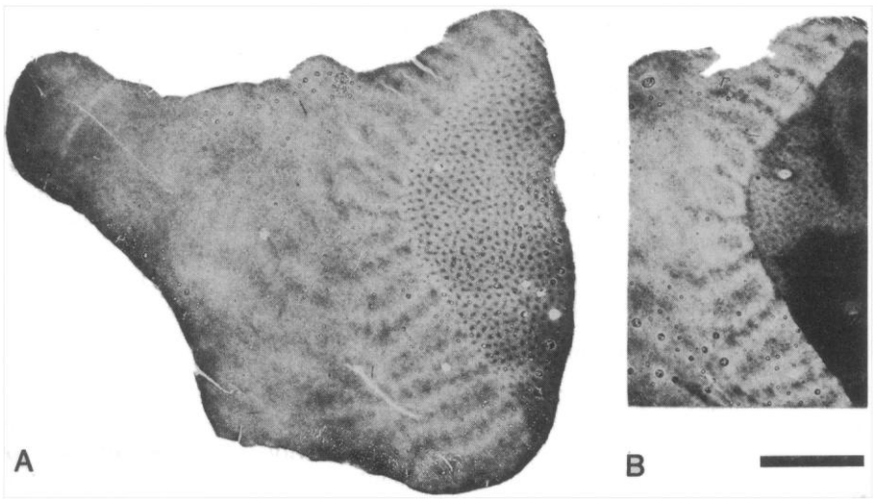

Fig. 1. Flat-mounted sections from the lateral surface of squirrel monkey cortex treated to reveal cytochrome oxidase. Anterior in the brain is toward the left, and dorsal is toward the top. The semicircular region on the right (marked by an array of spots) is central V1; the adjoining region (marked by parallel strips) is central V2. (A) From layer 3. (B) From layers 4 and 5 of the same hemisphere. Calibration bar, 5 mm.

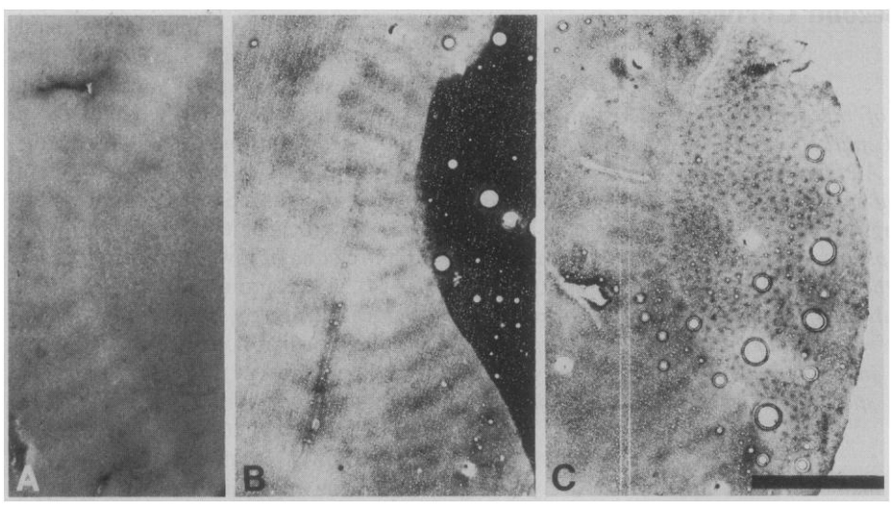

Fig. 2. Views parallel to the lateral surface of squirrel monkey cortex showing myelin differences. (A) Horizontal differences in myelination in a frozen unstained tissue block; the V2 strips are faintly visible on the left. (B and C) Sections stained for myelin with Luxol fast blue. Despite histological artifacts, the V2 strips show clearly in layer 4 (B) and more faintly in layer 3 (C); the V1 spots show clearly in layer 3 (C). Calibration bar, 5 mm.

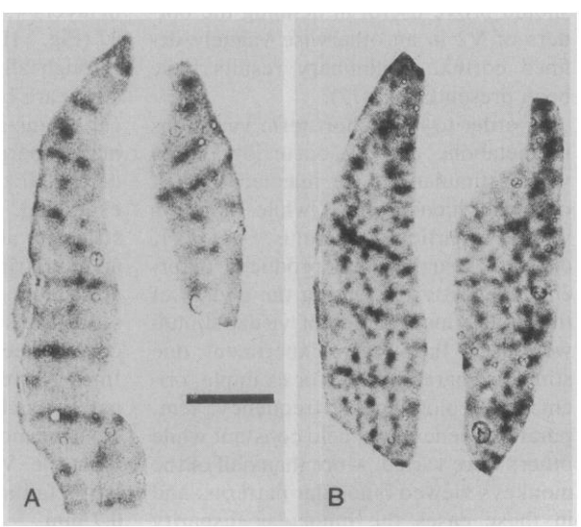

Fig. 3. Deoxyglucose autoradiographs from tangential sections of central V2 in the macaque. (A) The animal viewed a grating of low spatial frequency (1 cycle/degree) at all orientations, and the binocular disparity was varied continuously over 1° of visual angle. The 2DG is confined to the cytochrome oxidase strips (which look somewhat spotty because the section plane includes several layers). (B) The animal viewed an identical visual stimulus, except that the grating was of a high spatial frequency (7 cycle/degree). The 2DG labeled every other strip and isolated columns scattered throughout V2. Calibration bar, 5 mm.

Anteriorly the strips all end abruptly at an invisible border (Fig. 1). Here again the thin strips may extend slightly farther than the thick strips. Comparing the position of the anterior border of the strips to previously published electrophysiological maps of various extrastriate areas (*1, 2, 4, 5, 25*), we conclude that this anatomical border is the anterior border of electrophysiologically defined V2, along the representation of the horizontal meridian. This seems to be true in both macaque and squirrel monkeys. Thus, one may be able to use the strips to define the anatomical extent of V2, just as the stripe of Gennari has been used to define the anatomical extent of V1.

While cutting these sections, we could sometimes see the V2 strips in the unprocessed tissue (Fig. 2A). It may be that the strips are visible because they are more heavily myelinated than surrounding tissue: in unprocessed brain tissue, white and gray matter can easily be discriminated for the same reason. A simple myelin stain clearly reveals the V2 strips (Fig. 2B). The same myelin stain also indicates a spotlike array in V1 (Fig. 2C). Here again, the strips in V2 and the spots in V1 are similar.

The myelin patterns in both V1 and V2 are often more restricted than corresponding cytochrome oxidase patterns, but otherwise the two look similar. By in adjacent sections, we were able to establish that the regions of high myelination overlie the regions of high cytochrome oxidase activity. Since myelin is found on axons, and since cytochrome oxidase (and 2DG) may be concentrated in the neuropil, we may be looking at an afferent input (labeled by the myelin stain) and the axonal arborizations of those afferents (labeled by the cytochrome oxidase and 2DG). The afferent input to the V1 spots may be from the lateral geniculate nucleus (LGN) (*23, 24, 26*), and a striplike input to V2 has been reported from the pulvinar (*27*), but additional possibilities remain. The input to the V2 strips is complicated by the fact that the pulvinar feeds only into layers 3 and 5 of the strips, although the myelin, cytochrome oxidase, and 2DG patterns are often most obvious in layer 4 (which receives input almost exclusively from the upper layers of V1). This suggests that V1 input (perhaps from the spots) may be sandwiched between pulvinar input in the V2 strips.

This latter idea receives some support from 2DG studies. The V1 spots take up slightly more 2DG than interspot regions if the animal views a blank field during

2DG infusion (*11, 13*). This result might be expected if cells in the spots receive inputs from neurons with high spontaneous activity (for example, from the LGN) or if these regions had a higher endogenous metabolic activity than surrounding regions. The V2 strips seem to behave similarly in this kind of 2DG experiment. Both macaque and squirrel monkeys that viewed a blank screen or total darkness during 2DG infusion showed a slightly higher uptake of 2DG in the strips of high cytochrome oxidase activity. The idea that regions of high cytochrome oxidase activity in V1 and V2 also have higher metabolic activity is supported by electron microscopic evidence (*28*).

We also find that both the V1 spots and the V2 strips respond similarly (in terms of 2DG uptake) to various visual stimuli. In the macaque, certain visual stimuli produce robust, stimulus-specific 2DG uptake confined to the cytochrome oxidase spots in V1; the same visual stimuli also produce 2DG uptake in V2, confined to the cytochrome oxidase strips (*16*). The visual patterns producing such 2DG results include stimuli that are unoriented, diffuse, and of low spatial frequency (Fig. 3A). The converse is also true: those visual stimuli which produce patterns of high 2DG uptake in regions between the V1 spots also produce patterns of high 2DG uptake extending between the V2 strips. This latter pattern of 2DG uptake is produced by oriented stimuli of high spatial frequency (*16, 17*). Thus, strong circumstantial evidence suggests that the V1 spots and the V2 strips (as well as adjacent areas between the spots and strips) are functionally related to each other.

Oriented visual stimuli of high spatial frequency invariably produce isolated columns of high 2DG uptake in the regions between the V2 strips. Since these isolated V2 columns are not produced by nonoriented or multioriented stimuli of low spatial frequency, they may be analogous to the orientation and spatial frequency columns in V1 (*9, 17*).

Studies of single units have shown that cells in the input layers of V1 are largely monocular, but that the cells in other layers (including those projecting to V2) are largely binocular and disparity-specific (*19, 29*). The binocular cells in V2 may also be grouped into disparity columns (*19*). Our anatomical evidence is consistent with this model. (i) Although 2DG and cytochrome oxidase evidence exists for a segregation of the monocular inputs into ocular dominance columns in macaque V1 (*8, 10*), we find no such anatomical evidence for ocular dominance columns in V2. (ii) The V2 strips (like the V1 ocular dominance columns) are seen only in the binocular representation of the visual field. These results suggest that the transformation of visual information in V1 and V2 includes a systematic conversion of monocular inputs into a binocular disparity code, presumably as a prerequisite for the neural computation of stereoscopic depth. A columnar arrangement of orientation and spatial frequency sensitivity may facilitate this computation (*30*).

Note added in proof: Livingston and Hubel (*31*) have recently confirmed that the thalamus projects onto the V2 strips.

ROGER B. H. TOOTELL
Department of Psychology, University of California, Berkeley 94720
MARTIN S. SILVERMAN
Department of Physiology, University of California, San Francisco 94143
RUSSELL L. DE VALOIS
Department of Psychology, University of California, Berkeley
GERALD H. JACOBS
Department of Psychology, University of California, Santa Barbara 93106

References and Notes

1. J. M. Allman, J. F. Baker, W. T. Newsome, S. T. Petersen, in *Cortical Sensory Organization*, C. N. Woolsey, Ed. (Humana, Clifton, N.J., 1981), vol. 2, p. 502.
2. D. C. Van Essen, W. T. Newsome, J. L. Bixby, *J. Neurosci.* **2**, 265 (1982).
3. In some primates, area V2 (as mapped electrophysiologically) is not coextensive with area 18 (as described by Broadman). In the macaque, the anatomical patterns we describe appear coextensive with V2 rather than with area 18.
4. R. Gattas, C. G. Gross, J. H. Sandell, *J. Comp. Neurol.* **201**, 519 (1981).
5. J. M. Allman and J. H. Kaas, *Brain Res.* **76**, 247 (1974).
6. D. C. Van Essen, J. H. R. Maunsell, J. L. Bixby, *Soc. Neurosci. Abstr.* **5**, 812 (1979).
7. P. H. Schiller and J. G. Malpeli, *Brain Res.* **126**, 366 (1977).
8. C. Kennedy, M. H. D. Rosiers, O. Sakurda, M. Shinohara, M. Reivich, J. W. Jehle, L. Sokoloff, *Proc. Natl. Acad. Sci. U.S.A.* **73**, 4230 (1976).
9. D. H. Hubel, T. N. Wiesel, M. P. Stryker, *J. Comp. Neurol.* **177**, 361 (1978).
10. J. C. Horton and D. H. Hubel, *Nature (London)* **292**, 762 (1981).
11. A. Humphrey and A. Hendrickson, *Soc. Neurosci. Abstr.* **6**, 315 (1980).
12. J. C. Horton and D. H. Hubel, *ibid.*, p. 315.
13. A. L. Humphrey and A. E. Hendrickson, *J. Neurosci.* **3**, 345 (1983).
14. A. E. Hendrickson, S. P. Hunt, J.-Y. Wu, *Nature (London)* **292**, 605 (1981).
15. R. B. H. Tootell, M. S. Silverman, R. L. De Valois, *Invest. Ophthalmol. Visual Sci.* **19** (Suppl.), 226A (1980).
16. R. Tootell and M. Silverman, *Soc. Neurosci. Abstr.* **7**, 356 (1981).
17. R. B. H. Tootell, M. S. Silverman, G. Switkes, R. L. De Valois, *ibid.* **8**, 707 (1982).
18. D. H. Hubel and T. N. Wiesel, *J. Comp. Neurol.* **158**, 267 (1974).
19. ———, *Nature (London)* **225**, 41 (1970); P. G. H. Clarke, I. M. L. Donaldson, D. Whitteridge, *J. Physiol. (London)* **256**, 509 (1976).
20. R. L. De Valois and P. L. Pease, in *Methods in Physiological Psychology*, R. F. Thompson, Ed. (Academic Press, New York, 1973), p. 95; R. B. Tootell, M. S. Silverman, R. L. De Valois, *Science* **214**, 813 (1981).
21. M. Wong-Riley, *Brain Res.* **171**, 11 (1979).
22. J. Horton, thesis, Harvard University, in preparation.
23. D. H. Hubel and M. S. Livingston, *Soc. Neurosci. Abstr.* **7**, 357 (1981).
24. D. Fitzpatrick, K. Itoh, I. T. Diamond, *J. Neurosci.*, in press.
25. A. Cowey, *J. Neurophysiol.* **27**, 366 (1964); J. Tigges, W. B. Spatz, M. Tigges, *J. Comp. Neurol.* **158**, 219 (1974).
26. D. H. Hubel and T. N. Wiesel, *Soc. Neurosci. Abstr.* **4**, 632 (1978).
27. C. A. Curcio and J. K. Harting, *Brain Res.* **143**, 155 (1978).
28. E. Carroll and M. Wong-Riley, *Soc. Neurosci. Abstr.* **8**, 811 (1982); M. Wong-Riley and E. Carroll, *ibid.*, p. 706.
29. J. D. Pettigrew, T. Nikara, P. O. Bishop, *Exp. Brain. Res.* **6**, 391 (1968); H. B. Barlow, C. Blakemore, J. D. Pettigrew, *J. Physiol. (London)* **193**, 327 (1967); D. Ferster, *ibid.* **311**, 623 (1981); G. F. Poggio and B. Fischer, *J. Neurophysiol.* **40**, 1392 (1977).
30. D. Marr and T. Poggio, *Proc. R. Soc. London Ser. B* **204**, 301 (1979); J. P. Frisby and J. E. W. Mayhew, *Philos. Trans. R. Soc. London Ser. B* **290**, 95 (1980).
31. M. S. Livingston and D. H. Hubel, *Proc. Natl. Acad. Sci. U.S.A.* **79**, 6098 (1982).
32. Supported by PHS grants EY-00014 and EY-02052 and by NSF grant BNS 78-86171. We thank L. Thorell, J. Horton, and G. Switkes for incisive comments on the manuscript and G. Switkes for technical assistance.

2 August 1982; revised 2 December 1982

Lymphoid Cell–Glioma Cell Interaction Enhances Cell Coat Production by Human Gliomas: Novel Suppressor Mechanism

Abstract. *Certain human glioma lines produce mucopolysaccharide coats that impair the generation of cytolytic lymphocytes in response to these lines in vitro. Coat production is substantially enhanced by the interaction of glioma cells with a macromolecular factor released by human peripheral blood mononuclear cells in culture. This interaction thus constitutes an unusual mechanism by which inflammatory cells may nonspecifically suppress the cellular immune response to at least one class of solid tumors in humans.*

Although it is well documented that most glioma patients make humoral immune responses to their tumors (*1, 2*), there is little evidence of significant cellular immune responses (*3–6*). We studied the generation of allogenic cytolytic lymphocytes in response to cultured human glioma cells in vitro in order to identify those properties of glioma cells that enable them to escape cellular immune attack. We found that certain glioma lines produce thick coats of mucopolysaccharide that impair the generation of cytolytic lymphocytes specific for