Binocularly Deprived Cats: Binocular Tests of Cortical Cells Show Regular Patterns of Interaction

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If an animal is prevented from receiving visual experience during an early developmental phase, pronounced dysfunctions are observed. Physiological tests reveal gross abnormalities in the striate cortex. Cells in visual cortex are either unresponsive or their response characteristics are erratic. Although fewer than normal numbers of binocular cells are found in cats reared with binocular lid suture, a population remains that can be activated by stimulation through either eye.

We have studied cortical cells in binocularly deprived cats in order to specify monocular and binocular response characteristics. The primary hypothesis we have examined is that the abnormal response properties of these cells are a result of an irregular structure or substructure of the receptive fields. Kittens were binocularly lid-sutured soon after birth, and were studied physiologically at ages between 7 and 11 months. Standard techniques were used to record from single cells in striate cortex. Drifting gratings were presented to either eye or to both eyes together. In the latter case, the relative interocular phase was varied between the gratings so that the retinal disparity of the stimuli was changed.

We confirmed the expected finding that most cells were either unresponsive or erratic in their response. Of the cells that responded, monocular tuning functions for orientation and spatial frequency of the stimulus were often irregular. However, even in these cases, binocular interaction patterns of cortical responses were nearly always highly regular and displayed phase-specific profiles. A model is presented that explains this finding and suggests how binocular deprivation may result in disorganized receptive-field structure.

Binocular deprivation of visual experience has profound effects on the response properties of cells in the visual cortex. Most neurons become either unresponsive to visual stimuli or erratic in their response characteristics (see recent reviews by Frégnac and Imbert, 1984; Mitchell and Timney, 1984). Although the extent and types of effects on cortical response properties may vary according to the mode of deprivation, i.e., dark-rearing or binocular lid-suture (Mower et al., 1981), a population of cortical cells remains excitable by stimulation of either eye. There is evidence, in fact, that with appropriate stimulation using

excitatory or inhibitory amino acids, all cells in striate cortex can be activated (Ramoia et al., 1987; Tsumoto and Freeman, 1987). These cells provide a rather unique opportunity for studying the effects and possible mechanisms of gross sensory deprivation. By examining the monocular and binocular response properties of these neurons in a quantitative manner, we wish to gain useful information about the effects of visual deprivation.

Using sinusoidal gratings presented dichoptically, we have established the manner by which signals from the two eyes converge onto different types of cortical neurons in normal cats (Ohzawa and Freeman, 1986a, b). Although highly schematic, the results provide a functional neural wiring diagram for these cells. This is made possible because the highly regular and periodic nature of grating stimuli can provide measurements in forms that are amenable to quantitative analyses, thus allowing us to infer the functional neural connections required to achieve particular response properties. Using a similar technique for binocularly deprived animals, we hope to determine an aspect of the wiring of these cells that is disrupted and produces anomalous response properties. Specifically, we wish to know if the linearity of binocular summation that predominates in the normal visual cortex is affected by binocular deprivation. This is of particular interest because it may allow us to infer possible causes of anomalies resulting from the deprivation procedure. A loss of linearity implies disruptions of synaptic mechanisms that underlie the spatial antagonism of receptive fields.

Our results show that the linearity of spatial summation, which is the basis of most binocular interactions in the normal visual cortex (Ohzawa and Freeman, 1986a, b), appears to be intact in binocularly deprived animals. On the basis of this and monocular response properties, we propose that the cause of abnormal response characteristics is a spatially disorganized arrangement of excitatory and inhibitory inputs from each eye.

Materials and Methods

Animal rearing and preparation. Four binocularly deprived cats were studied. Two of these were from the same litter, and the other 2 were from different mothers. Kittens were deprived of normal vision by binocular lid suture at postnatal days 24–26. Deprivation was continued until the day of recording, at 7–11 months. Eyes were inspected daily for possible openings in the closed lids or fluid accumulation, and no problems were observed.

Prior to surgery for electrophysiological recording, the animals were given subcutaneous injections of atropine sulfate ($0.2 \text{ mg} \cdot \text{kg}^{-1}$) and Acepromazine ($1 \text{ mg} \cdot \text{kg}^{-1}$). A venous cannula was placed under halothane (Fluothane; Ayerst) anesthesia (3% in oxygen), after which the anesthesia was continued with sodium thiamylal for the rest of the surgery. A tracheal cannula was implanted for later artificial ventilation, and the animal was placed in a stereotaxic apparatus. The closed lids were then opened and Ophthalmine was applied to the corneas and lid margins. Neosynephrine (Winthrop) and atropine were topically applied

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Figure 1. Spatial frequency tuning characteristics of 4 cells that had substantial differences in optimal frequency between the 2 eyes. For all 4 panels, left and right eye tuning curves are marked by open circles and asterisks, respectively.

to retract the nictitating membranes and to dilate the pupils. Contact lenses with 3 mm artificial pupils were fitted immediately to protect the corneas from drying. The rest of the surgical procedures, physiological preparation, and monitoring were identical to those described in the preceding paper (Freeman and Ohzawa, 1988).

Protocol. Our standard procedures for single-unit recording, described in the preceding paper (Freeman and Ohzawa, 1988), were used with the following modifications: Since we have found, in the early phase of this study, that orientation tuning was often abnormal and broad, we tested the cell at 12–15 orientations spanning the entire 360°, instead of the limited range used for normal animals. Similarly, an extended test range of spatial frequencies was used for possible responses at unexpected frequencies. Then, a standard binocular phase-shift experiment was carried out with matched parameters for the 2 eyes. When the results of this run showed an irregular curve, we tried to repeat the measurement. If the curve was not repeatable, we abandoned the cell, since further tests would be meaningless. This point is considered further in the Discussion. For cells that had reliable responses, additional binocular tests were performed with mismatched orientations for the 2 eyes. Typically, the orientation of the grating for the nondominant eye was set orthogonal to the optimal orientation for the dominant eye.

At the end of each electrode penetration, 2–4 electrolytic lesions (10 μ A, 5 sec) were made along the track, while the electrode was slowly withdrawn. At the end of each experiment, the animal was deeply anesthetized with Nembutal, and perfused through the heart with formalin in saline. Blocks of tissue containing the electrode tracks were sectioned and stained with thionin to allow reconstruction of electrode tracks and identification of recording sites.

Results

We have recorded from 136 cells in 4 binocularly deprived cats. Of these, 66 cells responded reliably to visual stimuli, and a complete set of quantitative tests was performed. Of the re-

maining 70 cells, 10 were lost before the completion of the binocular experiment, and 60 cells were either unresponsive to visual stimuli or had highly variable responses. The data from these cells were eliminated from subsequent analyses. Therefore, the cells presented in this paper belong to a special group in that they exhibited response properties sufficiently regular and repeatable to make quantitative measurements possible. The implications of this selection of cells are considered in the Discussion.

Monocular properties

Monocular tests were performed on each cell by varying either spatial frequency or orientation. Although these tests formed a part of the routine procedure to determine optimal parameters for use in a binocular test, abnormalities of cells were quite apparent from these measurements. Figure 1 shows spatial frequency tuning characteristics of 4 cells that responded to stimulation of either eye. In each case, the optimal spatial frequency for the left (open circles) and right (asterisks) eyes is markedly different, by a factor of 3, in 3 cases. In addition, the example shown in Figure 1C had a large difference in the bandwidth of tuning. This degree of difference in the optimal frequency and bandwidth is not observed in normal animals (Skottun and Freeman, 1984).

Abnormality of monocular properties is not restricted to spatial frequency tuning. Orientation selectivity is also severely disrupted by binocular deprivation. The unit shown in Figure 2 is such an example. For this cell, however, spatial frequency

Figure 2. Tuning characteristics for a cell from a binocularly deprived cat. *A*, Spatial frequency tuning for the left (open circles) and right (asterisks) eyes. Orientation tuning was measured for the dominant right eye at spatial frequencies indicated in *A* by open and filled triangles (0.6 and 0.4 cycles/deg, respectively). *B*, PST histograms for different orientations in 12° steps. The spatial frequency was fixed at 0.6 cycle/deg. Orientation angle is depicted to the left of selected histograms. In this and all subsequent figures, orientation angles in the range 0–360° are used to indicate 2 possible directions of motion for drifting grating stimuli. *C*, Response amplitudes calculated from the histograms shown in *B* (open circles). The second curve shows the results of a repeated run. *D*, The orientation tuning measured at another spatial frequency (0.4 cycle/deg, as shown by the filled triangle in *A*). *E*, Action potentials resulting from stimulation at 4 orientations corresponding to the 4 maxima of the curves in *C*. Approximately 30 spike waveforms are shown superimposed. A horizontal line slicing the peak of the waveforms is the trigger level of the window discriminator.

selectivity was not particularly abnormal, as shown in Figure 2*A*. Since the right eye (asterisks) is dominant, orientation tuning is measured in detail only for this eye. Figure 2*B* contains peristimulus time (PST) histograms obtained by presenting gratings of different orientations around the clock. These histograms were harmonically analyzed, and the resulting response amplitudes (first harmonic) are plotted in Figure 2*C* as a function of stimulus orientation (open circles). Unlike most cells in normal cats, for which the number of peaks in this type of graph is at most 2 (for opposite directions at one orientation), 4 peaks are clearly present at nearly 90° intervals. An identical run carried out 20 min later produced a curve (asterisk) that is nearly superimposed on the first curve, indicating the reliability and stability of the measurements.

In normal animals, orientation tuning properties, such as optimal orientation and bandwidth, do not vary greatly when spatial frequency of the stimulus is changed. Although a small change in these values can be observed, the effects appear to be secondary, and usually only the response amplitude is scaled proportionally in accordance with the effectiveness of a particular spatial frequency (De Valois et al., 1982; Webster and De Valois, 1985). It is of interest to examine whether this constancy holds for a cell in a binocularly deprived animal despite an abnormality of orientation tuning. Therefore, the orientation tuning was measured at another spatial frequency, slightly lower than that of the run shown in Figure 2, *B*, *C*. The result is illustrated in Figure 2*D*. Apparently, the constancy does not hold, in that the relative strength of the 4 peaks has changed.

Figure 3. Results of monocular and binocular tests from a cell with abnormal receptive-field characteristics. *A*, Orientation selectivity of the cell for the left (open circles) and the right (asterisks) eyes. *B*, Spatial frequency tuning characteristics of each eye in a similar manner. *C*, The peristimulus time (PST) histograms resulting from a standard binocular phase-shift experiment. Relative phase between gratings shown to the left and right eyes was varied over 360° , as indicated to the left of each histogram. The stimulus set contained conditions to test monocular responses (RE and LE), and to estimate the spontaneous activity (NULL). *D*, The response amplitude calculated from histograms in *C* as a function of relative phase (open circles). The second curve (filled circles) is the result of a repeated measurement. In column *M* at the right, monocular responses are represented from left (asterisk, open square) and right (plus, filled square) eyes. Binocular tests, shown in *C* and *D*, were carried out using gratings of 240° orientation and a spatial frequency of 0.4 cycle/deg.

In particular, the fourth peak at 320° has nearly vanished. These results suggest that the underlying receptive-field structure is not organized into elongated ON and OFF flanks placed side by side. Instead, there is probably a much more complex and irregular organization. This point will be considered further in the Discussion.

However, before drawing conclusions regarding orientation tuning properties of this type of cell, we must consider an alternative possibility. The result described above could be the result of responses of 2 cells tuned to nearly orthogonal orientations. Although the occurrence of such a pair of nearby units tuned to orientations that differ by 90° is probably rare in normal animals, the organization of orientation columns may be disrupted in binocularly deprived cats. To examine this possibility, spike waveforms of cells were observed continuously for the presence of multiple units. Figure 2*E* shows a photographic superposition of approximately 30 spike waveforms displayed on a monitoring oscilloscope connected to the window discriminator. Spikes on this record were generated by presentations of 4 optimal orientations determined from the data of Figure 2*C*. In this case, we were able to confirm that at least 2 spikes were generated at each orientation during exposure of the film. No evidence of a second unit is apparent from the photograph. In addition, the spike waveform remained single while the unit was subsequently injured and destroyed by advancing the electrode.

From the combined results of spatial frequency and orientation-selectivity measurements, we confirm that monocular receptive-field properties of cortical cells in binocularly deprived

cats are often markedly abnormal. Additional cases of monocular abnormality in cells that were also tested binocularly are illustrated below.

Binocular properties

To examine binocular properties of cortical cells in the deprived cats, drifting gratings were presented simultaneously to each eye, with one phase-shifted with respect to the other. Figure 3 presents the results of monocular and binocular measurements from a representative cell that exhibited abnormal orientation and spatial frequency tuning properties. Orientation tuning curves are shown for each eye in Figure 3*A*. Tuning for the right eye (asterisks) is broad for a striate neuron (full-width at half-height is 90° ; for comparison with normal cats, see Skottun and Freeman, 1984). Moreover, orientation selectivity was essentially absent in the left eye response (open circles). Spatial frequency tuning also differed greatly between the eyes, as shown in Figure 3*B*. This cell was then subjected to the binocular tests with varying relative phases between the gratings shown to the 2 eyes. The results are presented as PST histograms in Figure 3*C*. Response amplitudes computed from these histograms (first harmonic components) are plotted in Figure 3*D* as a function of relative phase (open circles). The result of a repeated measurement (filled circles) is similar to the first curve, establishing the reliability of the response. These binocular responses appear quite normal as to shape of the curves, and are indistinguishable from those observed from cells of normal animals (Ohzawa and Freeman, 1986a), despite the monocular abnormalities of response properties.

Figure 4. Results are shown for another cell with abnormal monocular characteristics. Data are presented in the same format used in Figure 3. Orientation and spatial frequency values used in experiments shown in C and D were 180° and 0.8 cycle/deg, respectively.

Again, as with the previous cell whose responses are shown in Figure 2, a question may be raised as to whether the responses for the left and right eyes originate in 2 different cells—possibly a lateral geniculate fiber for the left eye and a cortical cell for the right eye. This seems unlikely for the following reasons. First and foremost, a phase-specific binocular interaction is clearly present. Similar binocular experiments performed directly on cells in the LGN do not show relative phase sensitivity (Xue et al., 1987). Second, nearly total suppression of the response at a relative phase angle of 200° would not occur if the response were from an LGN fiber. This is because, for LGN cells, the silent eye could not exert inhibition strong enough to suppress responses from the dominant eye below 50% of the uninhibited response level (Xue et al., 1987). Third, the spike waveforms were continuously monitored, and they remained single throughout the measurements. Therefore, responses depicted in Figure 3 represent true abnormalities of a single cortical neuron.

An additional point should be noted concerning the results shown in Figure 3C. The response for a relative phase of 210° is nearly zero, and it is certainly smaller than those for monocular stimulation of the left or right eye alone (Fig. 3C, LE and RE). This demonstrates the presence of an *antagonistic* interaction of inputs from the 2 eyes, such that excitation from one eye is canceled by the inhibitory input from the other eye at this relative phase. This is evidence against the possibility that the apparent tuning for relative phase is due to *nonantagonistic* convergence of modulated inputs to a single neuron at various relative phases. This possibility is considered further in the Discussion.

Results from another cell are presented in Figure 4. Orientation tuning curves for this cell are shown in A. Again, tuning properties of the left eye (open circles) appear disrupted. Although small peaks are present at orientations corresponding to the peaks for the other eye, responses are evoked at all orientations. Despite this abnormality of orientation tuning of the left eye, spatial frequency tuning appears normal in this eye, as shown in Figure 4B. The spatial frequency tuning for the right eye appears irregular, but reliability of this curve is uncertain because the run was not repeated. Binocular responses, illustrated in Figure 4, C, D, are again quite normal. Note also, in Figure 4C, that, as with the cell shown in Figure 3, the response for a relative phase of 120° is nearly zero, and is smaller than either of the monocular responses, indicating the presence of antagonistic interaction.

In normal animals, binocular interactions of the type shown in Figures 3 and 4 are orientation-dependent. If one of the gratings is rotated 90° from the optimal orientation, so that gratings move in orthogonal directions in the 2 eyes, the binocular interaction disappears and the response becomes essentially identical to that generated by stimulation of one eye alone (Ohzawa and Freeman, 1986a, b). We have attempted to determine for a few cells if this property is affected by binocular deprivation. Figure 5 shows data from a cell that is nearly completely dominated by one eye. Orientation and spatial frequency tuning curves are shown in Figure 5, A and B, respectively. These monocular properties appear rather normal, unlike those presented in Figures 3 and 4. As before, binocular interaction was then tested using optimal parameters determined from the

Figure 5. Data are shown for tests of binocular interaction in which matched and mismatched orientations were used in the 2 eyes. *A, B*, Orientation and spatial frequency tuning characteristics, respectively, for a cell nearly completely dominated by the right eye (asterisks). *C*, Binocular interaction when orientation of the gratings in both eyes was optimal for the dominant eye (-30°). The second curve shows the results of a repeated run. In *D*, the orientation for the nondominant (left) eye was made orthogonal to that of the dominant eye, producing an orientation mismatch of 90° . Again, results of 2 repeated runs are shown.

results shown in Figure 5, *A, B*. This measurement was repeated twice, and the results are presented in Figure 5*C*. Robust and repeatable phase-specific binocular interaction indicates a clear but subthreshold input from the nearly silent left eye. Next, an orientation mismatch of 90° was presented by rotating the pattern to the left eye. This orientation is indicated by a triangle in Figure 5*A*. The test was repeated twice more, and the results are shown in Figure 5*D*. Surprisingly, the same degree of interaction is maintained for this normally ineffective condition. It appears, therefore, that subthreshold input from the left eye was present at 2 orientations separated by 90° . This type of behavior is not observed in normal animals. Despite this abnormality, however, it should be noted that the shape of the curves in Figure 5, *C, D*, appears completely normal.

Another example of a response set from this group of cats is presented in Figures 6 and 7. In Figure 6, all tuning curves for orientation (*A*), spatial frequency (*B*), and relative phase (*C, D*) appear quite normal, except that the tuning for orientation is somewhat broad. This cell exhibits responses that approach those from normal cats. As with the cells shown in Figures 3 and 4, the presence of antagonistic interaction is demonstrated by the null response at a relative phase of 330° .

The results of tests with mismatched grating orientations are shown in Figure 7. Again, the orientation for the right eye was set 90° off-optimal, as indicated by open and filled triangles in Figure 7*A*. The results are shown as 2 curves in Figure 7*B*. Although the response is smaller than that for when both eyes are stimulated at optimal orientation (Fig. 6*D*), the phase-specific interaction is clearly present. This demonstrates again that stimuli at nonoptimal orientations, which are ineffective mon-

ocularly, can nonetheless exert an influence in a manner different from that observed in normal animals.

Additional examples of binocular interaction from 6 cells are illustrated in Figure 8. In all cases, the nature of binocular interaction is indistinguishable from that found in cells of normal animals. In 4 of these, a repeat run of the experiment produced nearly identical tuning curves. Monocularly, however, these cells show irregular tuning curves for either spatial frequency, orientation, or both, and in some cases a reliable response cannot be elicited from either eye. This apparent normality of binocular interaction, as revealed by dichoptic grating stimuli, is striking, considering the substantial abnormality of monocular properties.

From histological reconstruction of electrode tracks, recording sites and lamina of each cell were identified. We looked for possible clustering, in a specific layer, of cells that exhibited reliable responses, or, on the other hand, produced variable or weak responses. We did not find any evidence of such clustering. The large number of visually unresponsive units makes this analysis difficult, since included in this group are cells that are intrinsically unresponsive and those that have been made unresponsive by injury.

Considered together, cells in binocularly deprived cats, even when they respond reliably, usually show abnormalities in their response characteristics. These abnormalities generally are expressed as (1) markedly different optimal spatial frequencies in the 2 eyes (and hence, by inference, different ON and OFF flank sizes), and (2) loss of selectivity to a specific orientation. The loss of orientation selectivity may be moderate, in that monocular measurements yield near-normal tuning curves. How-

Figure 6. Results for a cell that had nearly normal monocular and binocular properties. The data are shown in a format similar to that of Figures 3 and 4. Optimal orientation and spatial frequency, determined from *A* and *B*, were 90° and 0.8 cycle/deg, respectively. These optimal values were used in the binocular experiment shown in *C* and *D*.

ever, even in these moderate cases, we find that stimuli at non-optimal orientations can still provide a phase-specific input to the cell. This is not observed in normal animals. Surprisingly, however, characteristics of tuning curves for relative interocular phase are apparently normal, despite these monocular abnormalities.

Discussion

We have studied quantitatively the monocular and binocular properties of cells in the visual cortex of binocularly deprived cats. In agreement with previous qualitative investigations (Pet-

tigrew, 1974; Spear et al., 1978; Watkins et al., 1978; Frégnac and Imbert, 1984; Mitchell and Timney, 1984), we have found that many cells are unresponsive to visual stimuli, and often show abnormal characteristics even when they are visually responsive. In what follows, we discuss possible problems in this study, and implications of the abnormalities of responses.

One of the problems of recording from an abnormal cortex is that it is difficult to determine whether the unresponsiveness and variability observed for many cells result from disturbances to the brain by the physiological recording procedure itself, or if they represent true abnormalities caused by the rearing con-

Figure 7. Results of binocular phase-shift experiments, with orthogonally oriented gratings, are shown for the same cell as that of Figure 6. *A*, The same orientation tuning curves as in Figure 6*A*. Triangles at 0° and 180° indicate the nonoptimal orientations that do not evoke responses from either eye. *B*, The relative phase dependence of the binocular response when gratings were orthogonal in the 2 eyes. The curve indicated by open circles resulted when the orientation was optimal (90°) for the left eye, but 90° off-optimal (180°) for the right eye. The second curve (filled circles) is for orientations of 90° and 0° for the left and right eyes, respectively.

Figure 8. Results of binocular phase-shift experiments are shown for 6 additional cells from the binocularly deprived cats. The orientation and spatial frequency used for each cell were, respectively, for *A*, 25°, 0.8 cycle/deg; *B*, 209°, 1.2 cycles/deg; *C*, 170°, 0.6 cycle/deg; *D*, 0°, 0.8 cycle/deg; *E*, 167°, 0.6 cycle/deg; *F*, 215°, 1.2 cycles/deg.

dition. For this reason, cells that exhibited a high level of spontaneous discharge without any influence by visual stimuli, or irregular tuning characteristics that were not repeatable, were not studied further and were excluded from the analysis. Therefore, the cells described in this paper have exhibited responses with sufficient reliability that they can be assessed by quantitative measurements. Because of these complications, we did not attempt to classify cells and compile statistics. In spite of this problem, however, examination of the abnormalities of these cells is useful because they can provide clues about what is disrupted during abnormal development.

Cells in binocularly deprived cats show abnormalities of varying degree when tested monocularly. In striking contrast to this, however, binocular interactions appear quite normal, and always have a single peak over 360° of relative phase. In no case, for both binocularly and monocularly deprived cats, have we observed a binocular phase-tuning curve that had 2 or more peaks. This is partly because of the use of sinusoidal grating stimuli, which are periodic. But is this a trivial consequence of the stimuli? For example, is it possible that abnormal binocular convergence may cause a 2-peaked curve for phase tuning? Indeed, it is possible, and Figure 9 shows schematic illustrations of such a model.

Suppose that the input from each eye to a cortical cell comes from a pair of ON- and OFF-center lateral geniculate neurons via a nonlinearity indicated by triangles in Figure 9A. Also, suppose that the receptive-field centers of the input cells are at

the same position. Responses of each ON- and OFF-center LGN cell to a drifting grating consist of bursts of spikes at the temporal frequency of the drift, much like responses from a simple cell. In addition, the timing of the bursts is complementary, or 180° out of phase, between the ON- and OFF-center types. Thus, for each eye, the combined input from the 2 LGN cells to the cortical cell will have a time course depicted in the lower trace of Figure 9B. The cortical cell receives 2 excitatory bursts for each cycle of temporal modulation of the stimulus (upper trace in *B*). When both eyes contribute such inputs to the cell, a change in the relative phase between the gratings for the 2 eyes has the effect illustrated in Figure 9C. At 2 relative phases θ of 0, and 180° as shown in the top and bottom traces, the input bursts from the 2 eyes become coincident, and give rise to a large response. A threshold in the spike-generation mechanism (Dean et al., 1982; Ohzawa and Freeman, 1986a) will have relatively little effect in these conditions because a large part of the excitation level exceeds the threshold (filled area of the simulated histogram of Fig. 9C). On the other hand, at $\theta = 90^\circ$, the excitation level remains largely subthreshold because the inputs from the 2 eyes are not coincident. Consequently, the response amplitude of discharge for such a cell will have 2 peaks, as the relative phase θ is varied from 0° to 360°, as plotted in Figure 9D. While this is a special case, where the resulting curve is quite regular, the point should be made that the neural circuitry required for these responses is not particularly unique. All neural components, such as a nonlinearity and a threshold for the spike-

Figure 9. A hypothetical scheme of binocular convergence that gives rise to an unusual relative phase-tuning curve, to demonstrate the nontriviality of a normal, single-cycle tuning curve. *A*, Schematic representation of such binocular convergence, where signals converge onto a cortical cell via a non-linearity from a pair of ON- and OFF-center LGN cells with receptive fields in each eye. The presence of threshold in the spike-generating mechanism is indicated by the inset. *B*, The temporal modulation resulting from stimulation by a drifting grating as a function of time (S), and the concomitant input from each eye to the cortical cell (R_L, R_R). Summing these inputs from the 2 eyes at relative phases $\theta = 0^\circ, 90^\circ$, and 180° , and applying a threshold, results in the responses shown in *C*. Th , level of threshold. In *D*, response amplitudes of this hypothetical model to a standard binocular stimulus are plotted as a function of relative phase. Note that there are 2 cycles of response change over 360° .

generation mechanism, are rather common (Movshon et al., 1978; Victor, 1981; Dean et al., 1982; Ohzawa and Freeman, 1986a).

Apparently, however, binocular convergence of the type shown above (Fig. 9) does not occur even when other properties are anomalous because of binocular deprivation. What, then, is the property that allows the cell to maintain normal binocular phase tuning? What kind of binocular receptive-field organization produces abnormal properties monocularly, and normal tuning binocularly? We propose the following model as the most likely explanation of what happens to these neurons. First, the spatial arrangement of excitatory and inhibitory inputs is disrupted, as illustrated in Figure 10*B*, in binocularly deprived animals. In normal animals, spatial organization of these inputs is highly regular, giving rise to clearly defined discrete ON and OFF flanks (Fig. 10*A*). Second, despite this spatial disorganization, the overall balance of excitatory and inhibitory inputs remains intact, thereby maintaining linearity of spatial summation (i.e., spatial antagonism).

If the above 2 conditions are met, the result is the type of abnormality we have observed. The first condition, spatial disorganization, is responsible for monocular abnormalities observed in orientation and spatial frequency tuning. However, because the second factor, linearity, is normal, tuning for the interocular relative phase remains normal. This follows from the fact that the output of a linear system driven by a single sinusoid is a sinusoid of the same single frequency. Any arbitrary receptive-field profile produces a phase-tuning function of a particular form (Ohzawa and Freeman, 1986a). For example, the receptive field may be a spatially limited, noise-like profile, a 2-dimensional version of which is probably a reasonable approximation to the receptive field shown in Figure 10*B*.

How this type of disorganization occurs at a synaptic level is still an open question. It appears, however, that visual experi-

ence plays an important role in "guiding" synaptic connections such that excitatory and inhibitory inputs are arranged spatially in a highly regular manner in normal visual cortex. In the absence of such visual inputs, the synaptic connections may be made randomly thereby producing irregular receptive fields.

We have observed for nearly all cells that had a clear binocular interaction that the response at the null phase was smaller than that of either monocular response (with the obvious exception of apparently monocular cells, for which the response from one eye was zero). This is additional evidence for linear binocular convergence in these neurons, since such behavior demonstrates the presence of antagonistic cancellation of inputs from the 2 eyes. This observation is important because an apparent tuning for relative phase may be produced with a nonlinear convergence similar to the one depicted in Figure 9, especially if the first harmonic is plotted. A model of such a convergence may be constructed by simply removing the OFF-center LGN cell

Figure 10. Hypothetical receptive fields of cortical cells. *A*, An example of a normal, simple-cell receptive field, where elongated discrete ON and OFF regions are positioned regularly side by side. *B*, A spatially disorganized positioning of ON and OFF areas, which causes abnormalities in orientation and spatial frequency tuning properties.

for each eye in Figure 9A. In that case, inputs from the LGN cell for one eye would be similar to what is shown in Figure 9B, except that every other burst in the response would be removed. The result would be only one burst in each temporal cycle of the stimulus. When the inputs from the 2 eyes converge with various relative phases, the resulting response is similar to those shown in Figure 9C, but again with half as many bursts. Therefore, such convergence will result in an apparent tuning for relative phase that is not much different from the normal tuning curve. Fortunately, we can rule out this possibility as a basis for the binocular interactions we have observed in these animals. This is because, given such a mechanism, the response at the null phase cannot be smaller than the lower of 2 monocular responses, owing to a lack of antagonistic cancellation. Obviously, this was not the case in cells we recorded (see Figs. 3C, 4C, 6C).

As an aside, however, we note that this type of nonantagonistic convergence does seem to exist. One cell recorded in a monocularly deprived cat, discussed in the previous paper, seems to be such an example (see fig. 14, Freeman and Ohzawa, 1988). We did not find, however, any other cell of this type in monocularly or binocularly deprived or in normal cats from which we recorded. For such a cell, if the threshold for firing is zero, the DC component will show no apparent tuning for relative phase, but it will clearly show tuning if the first harmonic is used. This may be predicted from the manner by which the bursts are added at various relative phases, as shown in Figure 9C. The first harmonic amplitude is at a maximum when the bursts coincide, but reaches a minimum when the bursts from each eye are interleaved. On the other hand, the DC component is unaffected (in the absence of a threshold) because it is the total number of spikes per unit time, which is independent of the manner by which the bursts add up. Interestingly, in a recent study by Xue et al. (1988), such behavior of cells of the perigeniculate nucleus of the cat was commonly observed. This finding suggests a rather unique form of binocular convergence in that area.

Our use of sinusoidal gratings as stimuli is an important factor in allowing us to distinguish between what is disrupted and what is not. The independence of relative phase (disparity)-tuning curves from the functional form of the monocular receptive-field profile holds only with sinusoidal grating stimuli (Ohzawa and Freeman, 1986a). If a bar of light were presented to each eye, as in other physiological investigations of binocular vision (Poggio and Fischer, 1977; von der Heydt et al., 1978; Ferster, 1981), binocular disparity-tuning curves would be no more regular than tuning for orientation and spatial frequency in binocularly deprived cats.

The results of the histological analysis did not show any clustering of those cells that had reliable responses, nor a grouping of cells that were unresponsive or had variable responses. However, this lack of laminar difference may be a consequence of the difficulty discussed above, of differentiating problems due to cell injury from unresponsiveness and variability inherent to the cell itself. Unfortunately, there seems to be no easy way to solve this difficulty with current single-unit recording techniques.

In conclusion, our results provide a quantitative description of the nature of abnormalities found in response properties of cells in binocularly deprived cats. The data are consistent with

the idea that linearity of spatial summation is intact in these cells despite a spatially disorganized arrangement of excitatory and inhibitory inputs.

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