

Turning a Blind Eye to Cortical Receptive Fields

Minireview

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In 1992, Pettet and Gilbert used a large-field visual stimulus with a hole over the receptive field (RF) of the tested neuron (artificial scotoma) to mimic the lack of direct stimulation that occurs after deafferentation (real scotoma). They found large increases in the RF size of striate cortical neurons within the scotoma after sustained exposure to this conditioning stimulus. However, DeAngelis et al. (1995) showed that this RF size increase is caused by an increase in responsiveness of the cortical cell in question, without any change in the underlying RF structure. Furthermore, De Weerd et al. (1995) found that, during the conditioning period, neurons within the patch of cortex covered by the artificial scotoma gradually increase their firing rate up to the level generated by the same stimulus pattern without the hole. In this minireview, we discuss these findings and show that all of these results are consistent with the artificial scotoma modifying the effectiveness of normal topographic inputs via habituation of long-range inhibitory pathways.

RF properties of cells in adult cerebral cortex exhibit remarkable plasticity in response to peripheral injury. Changes in cortical topography caused by deafferentation have been demonstrated in a wide variety of areas, including motor, somatosensory, auditory, and visual cortex (see Chino et al., 1992; Gilbert and Wiesel, 1992; and references therein). In the visual cortex, initial reports studied long-term changes in RF properties of cells within the boundaries of cortical scotomas (Gilbert et al., 1990; Kaas et al., 1990). More recent studies have shown significant changes in RF size occurring just minutes after the retinal lesions (Chino et al., 1992; Gilbert and Wiesel, 1992).

The immediate alterations in RF size seen in cells at the borders of a scotoma have been attributed to the lack of stimulation of a cell's RF, in conjunction with continued stimulation of neighboring regions outside the scotoma (Pettet and Gilbert, 1992). To test this hypothesis, Pettet and Gilbert used an artificial scotoma that was produced by occluding a cell's RF while presenting stimuli in the area surrounding the RF. This artificial scotoma stimulus consisted of a large array of moving, short light bars parallel to the preferred orientation of the cell's RF, with the RF itself covered by a blank area with the same luminance as the background behind the moving bars. The diameter of the artificial scotoma was approximately three times that of the cell's RF, so that the cell was never directly stimulated by the moving bars. RFs were quantitatively mapped before and after a several minute long presentation of the artificial scotoma (conditioning) stimulus. The mapping stimuli consisted of very short light bars (approximately one-tenth the length of the cell's RF) of the cell's preferred orientation swept across the RF perpendicular to the orientation axis at different consecutive positions along the

orientation axis. Spike counts of the cell's response were collected from sweeps at each location along the axis, generating a one-dimensional response profile parallel to the preferred orientation. The authors found the RF size increased for three-quarters of the cells studied. The size changes were large, averaging a 5-fold increase in area. Pettet and Gilbert concluded that the observed changes in RF size caused by the artificial scotoma are important not only because they demonstrate a marked degree of plasticity in adult visual cortical RFs caused by visual stimulation alone, but also because they provide a possible explanation of the psychophysical phenomenon of "filling-in." When a large-field pattern with a hole is viewed by a human observer during prolonged fixation, the hole gradually disappears (reviewed in Ramachandran and Gregory, 1991).

A recent report from another laboratory (DeAngelis et al., 1995) challenges the findings of RF expansion in response to artificial scotomas. In this study, RF measurements were made before and after presentation of artificial scotoma stimuli, using a conditioning stimulus similar to those used previously. Their mapping technique, however, was different from that used in the earlier study. Flashing light bars slightly longer than the RF were presented at 20 equally spaced intervals along the axis perpendicular to the preferred orientation; reverse correlation was used to generate response profiles. The mapping stimuli differ from those used by Pettet and Gilbert in two ways: first, the bars were an order of magnitude longer than those used in the previous study and flashed rather than moved, and second, one-dimensional response profiles were generated along the axis perpendicular to the preferred orientation. Although these methodological differences make exact comparisons difficult, examination of data presented by the two laboratories suggests that the major differences between the two studies are not in the data but rather in the interpretation. Pettet and Gilbert found a change in cells' minimum response fields and concluded that RF size had increased. DeAngelis et al., on the other hand, contend that if a response-level threshold is used to determine RF size, then changes in the amplitude of the response or changes in the baseline firing rate of the cell could be mistakenly interpreted as an increase in RF size.

To quantify RFs independently of response amplitude, they fit their RF profiles with either Gaussian functions (for complex cells and simple cells with unimodal RFs) or Gabor functions (for multimodal simple cells). For the remainder of this discussion, we will consider only complex cells, although similar arguments could be made regarding simple cells. DeAngelis et al. fit their one-dimensional response profiles with a Gaussian function:

$$R(x) = R_0 + K \exp[-(x - x_0)^2/a^2],$$

where R_0 is the cell's baseline firing rate, K is the amplitude of the response, x_0 is the RF center, and a is the half-width of the function at e^{-1} of the maximum response

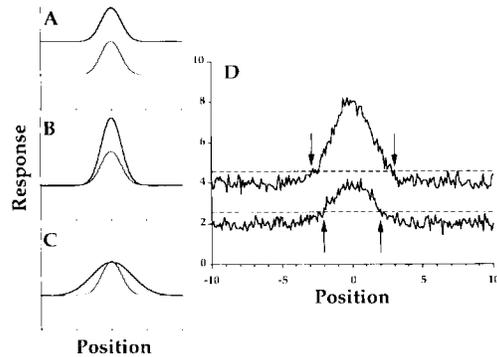


Figure 1. Gaussian Fits to Receptive Fields
(A–C) Effect of a 2-fold change in R_0 (baseline; A), K (amplitude; B), or a (width; C).
(D) Parallel 2-fold increases of R_0 and K (each from 2 to 4) can cause a change in RF size without a change in the value of a (fixed at 2). Dashed lines indicate a threshold of three SDs above baseline. Higher K allows the response to rise above noise ($SD = 0.2$) over a larger extent (downward arrows) than lower K (upward arrows).

amplitude. The effects of changing the values of R_0 , K , and a are illustrated in Figures 1A–1C. DeAngelis et al. found that stimulation with an artificial scotoma caused large increases in both the baseline firing rate, R_0 , and the amplitude of the response, K . However, they found only a small (although statistically significant) increase of the width of the response, a , which they equate with RF size. Furthermore, this small increase did not properly reverse. (This lack of reversibility, however, is difficult to interpret because the reversal mapping series was preceded by a 5–10 min full-field stimulus, while the mapping series was not.) DeAngelis et al. also note that the quantitative data presented in the earlier study (Figure 3 of Pettet and Gilbert, 1992) appear consistent with a change in baseline firing rate and response amplitude rather than width, and conclude that artificial scotomas cause an increase in response gain rather than a change in RF size. It should be noted that a more recent study from Gilbert's group (Das and Gilbert, 1995) reports that in some cells RFs expanded in response to an artificial scotoma without a clear increase in gain. Unfortunately, the stimuli used to measure gain changes were not optimal for exciting the cell, so this finding is inconclusive. The fact that the mean luminance over the RF in the conditioning period (0.7 cd/m^2) was different from that during the test period (0.35 cd/m^2) is an additional confounding issue.

The controversy over RF expansion appears semantic, the source being the definition of RF size. Pettet and Gilbert define RF size in the usual way, as the area of the visual field in which stimuli elicit an increase in the cell's firing rate over the spontaneous level. DeAngelis et al. point out that if this definition is used, changes in resting rate or response amplitude will cause changes in RF size. Figure 1D illustrates this point by showing that a change in R_0 and K will make the response resolvable from noise over a larger portion of the visual field, without any change in the value of a . However,

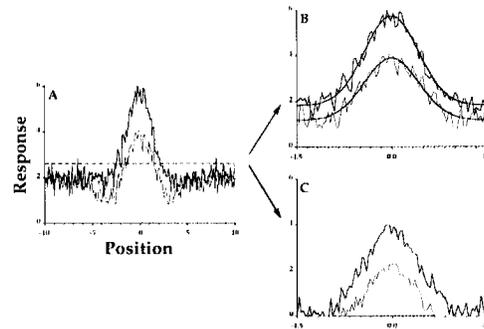


Figure 2. DOG Models of Receptive Fields
Red and blue traces indicate RF profiles before and after conditioning, respectively.
(A) Simulating the effect of an artificial scotoma by decreasing the amplitude of the inhibitory Gaussian (K , goes from 2 to 0.5), leaving all other DOG parameters constant ($R_0 = 2$; $K = 4$; $a = 2$; $a_i = 4$; $SD \text{ noise} = 0.3$). Dashed line indicates a threshold of two noise SDs.
(B) Expanded traces with Gaussian fits over restricted range (-4.5° to $+4.5^\circ$) to simulate the results of Figure 3A of DeAngelis et al. (1995). The apparent after: before ratio is 1.55 for R_0 , 1.44 for K , and 0.99 for a , showing that changing K of a DOG can mimic the parallel increases in R_0 and K and largely unchanged a seen by DeAngelis and colleagues. The root mean square errors of the two fits are within $\sim 10\%$ of each other.
(C) Expanded traces with a lower R_0 (0.2) to simulate the Figure 3 of Pettet and Gilbert (1992). The threshold shown by the dashed line (two SDs above baseline) would result in an increase in RF size of 78% along one dimension, but subjective mapping would likely yield an even greater increase.

DeAngelis et al. argue that such size changes are not real and chose to define the parameter a as the RF size because this measure is independent of responsiveness and of noise. This approach has the advantage of allowing DeAngelis et al. to show that the spatial structure of the underlying excitatory input to the cell is not likely altered. Nonetheless, it seems counterintuitive to deny that a neuron has undergone an increase in RF size when the region of the visual field over which it responds has grown 5-fold. Thus, the DeAngelis definition of RF size has the disadvantage of deemphasizing the functional consequences of the observed RF changes on the output signal. The neuron now “sees” things where it did not “see” them before, which has considerable potential perceptual implications.

A weakness of the Gaussian fit approach is that it relies on a specific RF model. Any RF features that are not described by a Gaussian but that can be altered without changing the width of the best-fitting Gaussian could contribute to the observed RF changes without being properly identified. Figure 2 illustrates this point by assuming that the RF is better described by a difference of Gaussians (DOG), one narrower excitatory and one wider inhibitory Gaussian:

$$R(x) = R_0 + K \exp[-(x - x_0)^2/a^2] - K_i \exp[-(x - x_0)^2/a_i^2].$$

Changing the amplitude of the inhibitory Gaussian, K_i (rather than changing both R_0 and K of a simple Gaussian), can cause large changes in RF size (Figures 2A and 2C) while minimally affecting the width of the best-fitting Gaussian (Figure 2B).

Another report on the physiological effects of artificial scotomas measured cells' firing rates directly during the period when the conditioning stimulus was present (De Weerd et al., 1995). This study found that the firing rates of cells whose RFs are within the artificial scotoma gradually increased during the stimulus presentation. The firing rate eventually reached a plateau at a rate similar to that seen when the cell was directly stimulated by the texture pattern used in the surround of the artificial scotoma. This result was seen in a subset of cells recorded both in primary visual cortex and in extrastriate visual areas. The time between stimulus onset and the firing rate plateau was found to be very similar to the latency with which human subjects reported perceptual filling-in using the same artificial scotoma stimuli. Both the time for a cell's firing rate to plateau and the time for reported perceptual filling-in to occur covaried with the size of the scotoma. These results provide correlative evidence that the firing rate increases seen in response to artificial scotomas may be involved in perceptual filling-in.

There is considerable disagreement over the mechanism of the physiological changes induced by artificial scotomas. While the interocular transfer of the effect (Volchan and Gilbert, 1994) rules out subcortical locations, several kinds of cortical connections have been proposed to mediate the effect. Feedback from extrastriate cortex could be involved; this idea is weakly supported by psychophysical data showing different time courses for filling-in of color and texture (Ramachandran and Gregory, 1991) and by the finding that increases in firing rate in response to artificial scotomas may be more common in V2 and V3 than in V1 (De Weerd et al., 1995).

Das and Gilbert (1995), however, argue for a mechanism occurring within striate cortex. In their cross-correlation study, they found that RF expansion is usually associated with an increase in the proportion of common inputs, but the cross-correlogram peaks appear too thin for extrastriate feedback. Das and Gilbert believe that this increase in shared input is mediated by selective enhancement of intrinsic inputs from the long-range patchy connections between columns of like orientation, because it was found in cells separated by as much as 3 mm and was not associated with any change in the cells' orientation selectivity. Although their conclusion is consistent with the view that filling-in is orientation specific (Ramachandran and Gregory, 1991), the above arguments are not conclusive. Afferent arbors from the lateral geniculate nucleus of the thalamus can in fact extend as far as 3 mm (Humphrey et al., 1985), and their influence is further spread by the arborizations of layer IV cells, which can exceed 1 mm in extent (Gilbert and Wiesel, 1981). In addition, a decrease in inhibition, mediated either by iso-orientation or by non-orientation-specific connections, would not be expected to change orientation selectivity. More importantly, the fact that the width of the response, a , does not change rules out a selective modification of inputs driven from outside the original RF, and therefore argues convincingly against Das and Gilbert's contention that selective enhancement of patchy connections can explain the effects of artificial scotoma. Rather, the conditioning stimulus appears to modulate the overall gain of a fixed set

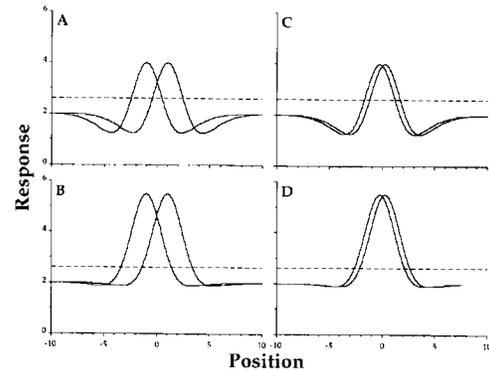


Figure 3. Effect of Artificial Scotoma on Common Input
(A) Two DOG RFs ($R_0 = 2$; $K = 4$; $a = 2$; $K_i = 2$; $a_i = 4$) separated by 2° .
(B) Same as (A), except that K_i was decreased to 0.5 to mimic the artificial scotoma effect. Overlap increased ~ 2 -fold, so one might expect a similar apparent increase in common excitatory input as seen by Das and Gilbert (1995).
(C and D) Same as (A) and (B), except that the separation was only 0.5° . In this case, overlap increased by only $\sim 20\%$. Greater initial overlap decreases the apparent increase in common excitatory inputs, as shown in Figure 7 of Das and Gilbert (1995).

of excitatory inputs (with a spatial distribution described by the parameter a). As DeAngelis et al. argue, the effects of artificial scotoma can be explained by a nonselective decrease in inhibition from cells with RFs outside the artificial scotoma, caused by the habituation of these cells by the conditioning stimulus.

Simulating RFs with DOGs rather than Gaussians emphasizes the possible role of nonselective disinhibition in mediating the effects of artificial scotomas and is consistent with the existence of inhibitory sidebands and end-stopping in complex cells (reviewed in DeAngelis et al., 1992). Using a DOG model (Figure 2), many of the effects of an artificial scotoma can be mimicked by reducing the amplitude, K_i , of the inhibitory Gaussian. Changing the single parameter, K_i , can explain the changes in best-fitting Gaussians seen by DeAngelis et al. (Figure 2B) and can also produce RF size increases similar to those seen by Pettet and Gilbert (Figure 2C). The model is also consistent with results of Das and Gilbert's cross-correlation study showing that RF expansion is accompanied by an increase in common inputs to cells within the scotoma and that the magnitude of this increase depends on the initial overlap (Figure 3). The simplest explanation of all these results is that the increase in common input is not due to an increase in the strength of synaptic inputs from long-range connections, but rather is due to decreased inhibition unmasking excitatory topographic inputs driven by geniculocortical connections. Whether this modulatory effect is mediated by orientation-specific, long-range patchy connections or by non-orientation-specific basket cell interneurons remains unresolved. However, this question could be addressed by determining whether a surround stimulus consisting of a single orientation perpendicular to the preferred orientation of the tested

cell can produce the effect. If this disinhibition were mediated by an iso-orientation pathway, then it might cause a rise in activity (as seen by De Weerd et al.) of cells within the scotoma that have the same orientation preference as the orientation present in the conditioning stimulus, which in turn would support the perception of an orientation-specific filling-in of the scotoma. It is likely, though, that inhibitory influences from outside a cell's classical RF are carried both by long-range patchy connections and by basket cell interneurons, and that both of these pathways would be habituated by the conditioning stimulus.

Selected Reading

- Chino, Y.M., Kaas, J.H., Smith, E.L., III, Langston, A.L., and Cheng, H. (1992). *Vision Res.* 32, 789–796.
- Das, A., and Gilbert, C.D. (1995). *J. Neurophysiol.* 74, 779–792.
- DeAngelis, G.C., Robson, J.G., Ohzawa, I., and Freeman, R.D. (1992). *J. Neurophysiol.* 68, 144–163.
- DeAngelis, G.C., Anzai, A., Ohzawa, I., and Freeman, R.D. (1995). *Proc. Natl. Acad. Sci. USA* 92, 9682–9686.
- De Weerd, P., Gattass, R., Desimone, R., and Ungerleider, L.G. (1995). *Nature* 377, 731–734.
- Gilbert, C.D., and Wiesel, T.N. (1981) In *The Organization of the Cerebral Cortex*, F. O. Schmidt, F. G. Worden, G. Adelman, and S. G. Dennis, eds. (Cambridge, Massachusetts: MIT Press), pp. 163–191.
- Gilbert, C.D., and Wiesel, T.N. (1992). *Nature* 356, 150–152.
- Gilbert, C.D., Hirsch, J., and Wiesel, T.N. (1990). *Cold Spring Harbor Symp. Quant. Biol.* 55, 663–677.
- Humphrey, A.L., Sur, M., Ulrich, D.J., and Sherman, S.M. (1985). *J. Comp. Neurol.* 233, 159–89.
- Kaas, J.H., Krubitzer, L.A., Chino, Y.M., Langston, A.L., Polley, E.H., and Blair, N. (1990). *Science* 248, 229–231.
- Pellet, M.W., and Gilbert, C.D. (1992). *Proc. Natl. Acad. Sci. USA* 89, 8366–8370.
- Ramachandran, V.S., and Gregory, R.L. (1991). *Nature* 350, 699–702.
- Volchan, E., and Gilbert, C.D. (1994). *Vision Res.* 35, 1–6.