

Role of inhibition in the specification of orientation selectivity of cells in the cat striate cortex

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Abstract

Mechanisms supporting orientation selectivity of cat striate cortical cells were studied by stimulation with two superimposed sine-wave gratings of different orientations. One grating (base) generated a discharge of known amplitude which could be modified by the second grating (mask). Masks presented at nonoptimal orientations usually reduced the base-generated response, but the degree of reduction varied widely between cells. Cells with narrow orientation tuning tended to be more susceptible to mask presence than broadly tuned cells; similarly, simple cells generally showed more response reduction than did complex cells.

The base and mask stimuli were drifted at different temporal frequencies which, in simple cells, permitted the identification of individual response components from each stimulus. This revealed that the reduction of the base response by the mask usually did not vary regularly with mask orientation, although response facilitation from the mask was orientation selective. In some sharply tuned simple cells, response reduction had clear local maxima near the limits of the cell's orientation-tuning function.

Response reduction resulted from a nearly pure rightward shift of the response *versus* log contrast function. The lowest mask contrast yielding reduction was within 0.1-0.3 log unit of the lowest contrast effective for excitation.

The temporal-frequency bandpass of the response-reduction mechanism resembled that of most cortical cells. The spatial-frequency bandpass was much broader than is typical for single cortical cells, spanning essentially the entire visual range of the cat.

These findings are compatible with a model in which weak intrinsic orientation-selective excitation is enhanced in two stages: (1) control of threshold by nonorientation-selective inhibition that is continuously dependent on stimulus contrast; and (2) in the more narrowly tuned cells, orientation-selective inhibition that has local maxima serving to increase the slope of the orientation-tuning function.

Keywords: Visual cortex, Visual receptive fields, Inhibition, Orientation selectivity

Introduction

The response amplitude of cells in the striate cortex typically depends on the orientation of moving, one-dimensional stimuli (see Orban, 1984 for review). Two general models have been proposed to account for cortical orientation selectivity, one relying principally on excitation, the other on a combination of excitation and inhibition. Hubel and Wiesel (1962) hypothesized that the receptive field of a simple cell is constructed from the convergence of excitatory afferent fibers from lateral geniculate nucleus (LGN) cells whose receptive fields formed a roughly linear array. Bars oriented in parallel with these arrays would provide maximum excitation, while orthogonally oriented bars would excite minimally as well as invoke inhibition from LGN receptive-field surrounds. This hypothesis is attrac-

tive in its simplicity, but is insufficient by itself. A linear array is unlikely to be adequate to support tuning as narrow as 5 deg, which is seen in some cells (Orban, 1984). Even though LGN cells have been reported to show some innate orientation preference (Vidyasagar & Urbas, 1982; Soodak et al., 1987), they nonetheless respond vigorously to stimuli presented at all orientations. Suppression of some kind is required to account for the failure of most cortical cells to respond when stimulated by bars with orientations orthogonal to the optimal axis (Hubel & Wiesel, 1962).

The alternate model proposes that excitation of cortical cells is influenced minimally by stimulus orientation, and that selectivity is shaped instead by intracortical inhibition. The inhibition is itself considered to be orientation selective and is tuned in opposition to a cell's excitatory tuning function so that the inhibition would be greatest for orthogonal stimuli (e.g. Bishop et al., 1973; Creutzfeldt et al., 1974b; Sillito, 1975; Nelson & Frost, 1978). This hypothesis was first suggested by the observation that an artificially elevated maintained discharge could be

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suppressed by presentation of a stimulus at the orthogonal orientation (Bishop et al., 1973; Sillito, 1979; Heggelund, 1981a,b; Morrone et al., 1982). Support for this hypothesis also comes from work with agents that block gamma-aminobutyric acid (GABA), a neurotransmitter that mediates intracortical inhibition. Iontophoretic application of the GABA-blocker bicuculline has been reported to reduce or eliminate orientation selectivity in both simple and complex cells, although not all cells were affected in this way (Sillito, 1977, 1979; Tsumoto et al., 1979; Sillito et al., 1980).

The work presented here is intended to define more completely the nature of intracortical inhibition and its role in controlling the spatial organization of the cortical receptive field. The experimental approach is an extension of the double-stimulus paradigm introduced by Bishop et al. (1973) in which one stimulus is used to elevate the discharge of a cell, providing a background against which the suppressive or facilitatory impact of a second stimulus can be seen. This has the advantage of avoiding complex pharmacological interactions that may arise from iontophoresis of neurotransmitter blocking agents. Here, one sine-wave grating pattern (the base) is configured at the orientation and spatial frequency that is optimal for driving the cell. A second grating (the mask) is electronically superimposed on the first. Variation of the spatial characteristics of the mask reveals facilitatory or suppressive influences on the cell under study as reflected by modification of the base-induced response.

Methods

Surgical preparation

Studies were conducted on 18 adult (2.5–4.0 kg) cats. Anesthesia was induced with 5% Fluothane (halothane) in O₂ and a forelimb vein was cannulated for subsequent infusion of anesthetic and paralyzing agents. During the remainder of surgery, the gas was discontinued and 2.5% sodium thiamylal was infused as required. A tracheal cannula was inserted and the cat was mounted in a stereotaxic apparatus. The scalp was reflected on the midline and electrodes were inserted over the lateral suprasylvian gyri for the monitoring of generalized-brain activity. A 1 mm × 3 mm hole was drilled at Horsley–Clarke coordinates P4-L2, directly over the *area centralis* representation in area 17. The dura was incised and after positioning of the electrode over an area free of surface vessels the hole was covered with agar mixed in mammalian Ringer's solution. Melted Tackiwax (Cenco, Chicago, IL) was then poured over the agar to provide an effective hydraulic seal.

Recording conditions

In order to suppress eye movements, the cats were paralyzed with gallamine triethiodide (Flaxedil) at 10 mg/kg-h and ventilated with a mixture of N₂O:O₂:CO₂ (75:23.5:1.5) at 30 min⁻¹ with a stroke volume sufficient to hold expired pCO₂ at 3.9%. The infusate also included 1 mg/kg-h Surital to maintain effective anesthesia (Hammond, 1978) as well as lactated Ringer's solution. Monitoring of the EEG and EKG provided general indications of the animal's state of anesthesia and health. Rectal temperature was maintained at 37.5°C with a servo-controlled heat pad. Eyelids were retracted and the natural pupils were dilated by instillation of 10% phenylephrine

HCl and 1% atropine sulfate in the conjunctival sacs. Contact lenses with 4-mm-diam artificial pupils were fitted to the nearest 0.5-m base curve radius and auxiliary lenses were added as dictated by direct ophthalmoscopy to render the retinae conjugate with the viewing screen 57 cm distant. Retinal landmarks (optic disk and *area centralis*) were projected onto the plotting screen with a reversible ophthalmoscope. All recorded cells had receptive fields located within 5 deg of the *area centralis*. Action potentials were recorded with tungsten-in-glass microelectrodes (Levick, 1972) with uninsulated tips 18–20 μm long and 2 μm wide at the shoulder.

Stimulation

The primary stimulator was a CRT display (Tektronix 608; mean luminance 110 cd/m², P31 phosphor) with a 10-deg circular field. The display was compensated for linear modulation up to 75% contrast. Sine-wave gratings were generated with a microprocessor-based pattern generator similar in concept to that described by Milkman et al. (1978). The pattern generator supported independent control of the spatial frequency and phase, contrast, orientation, and drift rate of up to four patterns. Multiple patterns were superimposed by alternating frames of each pattern at a rate of 256/s; with two patterns, each was presented at 128/s. All stimulation was monocular.

Data acquisition and processing

The primary data analysis tool was construction of 2-s, 128 bin/s poststimulus time histograms. To reduce artifact from the inherent nonstationarity of visual cortex, the interleaved histogram technique of Henry et al. (1973) with randomization was used exclusively. Each experiment was constructed with measurements parametric on one or two variables. A stimulus set was specified comprising each measuring condition as well as a null condition (uniform field at the mean luminance of the gratings) to assess the maintained discharge. Each element in the stimulus set was presented once, in random order with 1 s of mean luminance between each presentation, until the set was exhausted. Presentation of the set was then repeated in a different random order until each stimulus condition had been tested ten times. With 4-s presentation periods, results are based on 40 s of averaging for each condition. The number of impulses per presentation was tracked to permit calculation of response variability.

Cell classification and response measurement

Receptive-field properties were first plotted by hand and cells were initially categorized as simple or complex according to the criteria of Hubel and Wiesel (1962). Cells with noticeable end-stopping were discarded, as that property would cause complications in these experiments. Final cell classification was based on responses to drifting sine-wave gratings. All simple cells, even the most spatially nonlinear, respond to moving gratings with a modulation of discharge rate in synchrony with the temporal frequency of drift, at least when the spatial frequency of the stimulus is near the cell's optimum. At all but the lowest spatial frequencies, complex cells respond with an increase in the mean firing rate without temporal modulation (e.g. Movshon et al., 1978a,b; DeValois & Tootell, 1983). Calculation of the modulation index (ratio of the fundamental response com-

ponent to the mean response) (Movshon et al., 1978a) for simple cells with a modulation index less than 1.0. Responses to simple cells are composed of stimulation of several pairs of gratings expressed by the components of the response to drifting gratings which the screen luminance of the response component d.c. for complex cells made at several orientations of experiment and to assume

Interpretation of

In these experiments to drive the cell so that any increase in the presence of the stimulus. In order to maintain response modification value that produces firing rate found measurement. The modulation and spatial by independent stimulus was in selective inhibition was probably not

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Michelson contrast representation of two dissimilar grating maximum luminance of the maximum gratings, which simple summation constructive interference contrast energy standard deviation of

ponent to the mean firing rate, or d.c. component; Movshon et al., 1978a) for each cell yielded a bimodal distribution. All cells with a modulation index greater than 1 corresponded to the simple class of Hubel and Wiesel, and those with a modulation index less than 1 corresponded to the complex class. Responses to single gratings were specified by the stronger response component, i.e. power at the fundamental frequency of stimulation for simple cells and d.c. power for complex cells. Because of temporal interactions between asynchronously drifting pairs of gratings, responses to these stimuli were usually expressed by the d.c. power component for all cells. Harmonic components were sometimes considered in defining the responses to double gratings, as indicated in the results. The maintained discharge rate, measured during an interval in which the screen was illuminated uniformly at the mean luminance of the gratings, was expressed by the appropriate response component (harmonic fundamental for simple cells, d.c. for complex cells) and is indicated by a star near the ordinate of each figure. Whenever practical, measurements were made at several contrasts both to observe the effect of alterations of experimental parameters on the contrast-response function and to assure the consistency of the result.

Interpretation of dual-grating results

In these experiments, the first grating, the base, was used simply to drive the cell under study to a moderate level of activity so that any influence on the firing level resulting from the presence of the second grating, the mask, could be clearly seen. In order to maximize the dynamic range of mask-induced response modification, the contrast of the base was set to a value that produced a response that was about half of highest firing rate found by a separate response *versus* log contrast measurement. The base was always presented at the best orientation and spatial frequency for the cell, which was determined by independent quantitative measures. Use of an optimal base stimulus was intended to minimize involvement of spatially selective inhibitory mechanisms. As will be seen, this strategy was probably not important.

The impact of the mask on the base-generated activity can most easily be understood by considering that each stimulus is presented in alternate frames by the stimulator. If the mask were not present, then the base would alternate with a frame of uniform luminance, which would yield an *effective* base contrast of half of its nominal contrast. For this reason, every experiment that used two gratings also included an interleaved control measurement of the response to the base at half its nominal contrast; this response level is indicated by a horizontal dotted line in all figures. Facilitation by the mask elevated the discharge above this level; mask-induced suppression reduced the discharge below this level.

Michelson contrast, which defines contrast on the basis of maximum and minimum luminances, will not yield a consistent representation of the amount of luminance modulation when two dissimilar gratings are superimposed. Maximum and minimum luminances will correspond to the signed algebraic sum of the maximum and minimum luminances of each of the two gratings, which would predict that combined contrast was the simple summation of the Michelson contrasts. However, destructive interference between dissimilar gratings will reduce the contrast energy in the field. If contrast is defined as the standard deviation of luminance from the mean integrated over the

field, by Parseval's theorem the contrast of any two superimposed gratings that differ spatially will be 0.707 times the sum of their individual contrasts. For this reason, the response, e.g. to two asynchronously drifted (but otherwise identical) gratings, is less than that to a single grating of a contrast that is the sum of the two. When double gratings are used here contrast will be described by stating the *effective contrast* (e.c.) of each constituent grating, which would be the Michelson contrast of that grating presented in alternation with a field of uniform mean luminance. The highest possible effective contrast of each grating is 50%, since each is presented only half of the time.

Results

Verification of the approach

Impact of interference

When the activity generated by the base grating is reduced in the presence of a superimposed mask grating, the claim that this suppression results from synaptic inhibition of the recorded cell by the mask is only valid if the reduction of response does not result from the reduction of excitation from the base, which could occur as a result of contrast cancellation between the gratings. Since the gratings are coextensive, destructive interference cannot be avoided. Two superimposed gratings of different orientation produce a Moire pattern with local bands of zero contrast that are oriented normal to a bisection of the angle between the two gratings. If the drift rate of the gratings is identical, these bands are stationary, with their location depending on both the angle and relative phase between the two gratings. Response reduction found for a particular mask orientation could therefore result not from synaptic inhibition generated by the mask but from reduction of contrast covering the receptive field.

Control experiments were designed to test both the impact of these bands on responsiveness as well as the effectiveness of a strategy intended to minimize this impact. In the first experiment, a mask grating was superimposed on a base grating and oriented so as to reduce excitation. Both base and mask were presented at the spatial frequency that was best for the cell under study. The mask was drifted at the same rate as the base grating (2 Hz) so that the zero-contrast bars were stationary. The initial spatial phase of the mask was varied over a full cycle (12 phases at 30 deg intervals). Every location in the stimulus field was therefore covered by a zero-contrast bar for at least one of these conditions. Results are shown in Fig. 1; all conditions showed some degree of response suppression, since all response levels fell below the control level generated by the base grating alone (horizontal dotted line). Most simple cells (26 of 32) showed organized sensitivity to phase manipulation in varying degrees (Fig. 1B, solid line), indicating some influence of the zero-contrast bands and posing a clear problem in deciding whether response reduction is due to synaptic inhibition or interference. Responses of the remaining six simple cells were independent of relative phase (Fig. 1A), as were responses from all (18) complex cells tested this way (Fig. 1C, solid line).

In order to apply the double-grating test unambiguously to all cells, an alternate approach was developed. When the base and mask gratings drift at different rates, the zero-contrast interference bands themselves drift at the beat frequency between the base and mask drift rates. Contrast is periodically

