Surround suppression and temporal processing of visual signals

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Abstract

Extraclassical surround suppression strongly modulates responses of neurons in the retina, lateral geniculate nucleus (LGN), and primary visual cortex. Although a great deal is known about the spatial properties of extraclassical suppression and the role it serves in stimulus-size tuning, relatively little is known about how extraclassical suppression shapes visual processing in the temporal domain. We recorded the spiking activity of retinal ganglion cells and LGN neurons in the cat to test the hypothesis that extraclassical suppression influences temporal features of visual responses in the early visual system. Our results demonstrate that extraclassical suppression not only shifts the distribution of interspike intervals (ISIs) in a manner that decreases the efficacy of neuronal communication, it also decreases the reliability of neuronal responses to visual stimuli, and it decreases the duration of visual responses, an effect that underlies a rightward shift in the temporal frequency tuning of LGN neurons. Taken together, these results reveal a dynamic relationship between extraclassical suppression and the temporal features of neuronal responses.
Introduction

Gain control mechanisms, including extraclassical surround suppression, are a prominent feature of visual responses in the retina and lateral geniculate nucleus (LGN), providing non-linear modulation to otherwise linear receptive fields (Enroth-Cugell and Robson, 1966; Shapley and Victor, 1979b; Murphy and Sillito, 1987; Sclar, 1987; Baccus and Meister, 2002; Bonin et al., 2005; Scholl et al., 2012). Past work examining the spatial organization of these non-linear mechanisms demonstrates that the suppressive influence of gain control becomes increasingly prominent as the size of the visual stimulus increases, resulting in the phenomenon commonly referred to as extraclassical surround suppression (Hubel and Wiesel, 1961; Solomon et al., 2002; Alitto and Usrey, 2008; Camp et al., 2009). Importantly, extraclassical suppression cannot be explained by the classical, center-surround receptive field structure (Shapley and Victor, 1979b; Bonin et al., 2005; Alitto and Usrey, 2008). Although a great deal is known about the spatial properties of extraclassical suppression, relatively little is known about its influence on the temporal features of neuronal responses. Perceptually, nonlinear influences of stimulus intensity are correlated with changes in the duration of human visual impulse responses (Georgeson, 1987; Stromeyer and Martini, 2003; Tadin et al., 2006), and suppressive surround mechanisms influence the temporal dynamics of center processing (Tadin et al., 2003). Given these reported effects and the prominence of suppression in the visual system, we performed experiments to determine the influence of extraclassical suppression on the temporal features of visual responses in the cat retina and LGN.

Although multiple circuits are implicated in the generation of surround suppression, surround suppression has been successfully integrated into a unified framework with several other seemingly disparate features of nonlinear gain control commonly referred to as retinal contrast gain control (Shapley and Victor, 1979b; Felisberti and Derrington, 1999; Solomon et al, 2002; Bonin et al., 2005; Mante et al., 2008; Usrey and Reid, 2000). As originally described by
Shapley and colleagues, the gain of many retinal ganglion cells and LGN neurons is not constant, but instead decreases as stimulus contrast increases (illustrated in Figures 1A and B), causing contrast response functions to saturate at high contrasts. The temporal properties of retinal ganglion cells and LGN neurons are also dependent on stimulus contrast; response durations and latencies decrease and neurons become more responsive to higher temporal frequencies as stimulus contrast increases (illustrated in Figures 1C-F). As such, there is a key prediction that surround suppression, like retinal gain control, should decrease the duration of neuronal responses to visual stimuli and shift the temporal frequency tuning of neurons towards higher frequencies. Proposed mechanisms underlying these non-linear phenomena include divisive inhibition and conductance-based changes in temporal dynamics (Murphy and Miller, 2003; Ayaz and Chance, 2009; Carandini and Heeger, 2011).

Understanding the influence of surround suppression in the temporal domain is important, as the timing of visual activity is likely to have dramatic effects on both the strength of interneuronal communication and the ability of neurons to follow dynamic stimuli. Surround suppression is predicted to influence neuronal communication by shifting the distribution of interspike intervals (ISIs) towards greater values. Because retinal spikes are most effective in driving LGN action potentials when they are preceded by short ISIs compared to long ISIs (Mastronarde, 1987; Usrey et al., 1999; Levine and Cleland, 2001; Sincich et al., 2007; Weyand, 2007; Rathbun et al., 2010), extraclassical suppression is predicted to reduce the efficacy of individual spikes in evoking postsynaptic responses and restructure the temporal organization of spikes delivered to downstream targets (reviewed in Usrey, 2002).

In this study, we examine the influence of surround suppression on the temporal features of visual responses in the retina and LGN. Results reveal that surround suppression interacts with ISI-based mechanisms to adjust the strength of interneuronal communication in a manner that progressively amplifies the relative magnitude of suppression in the retina, LGN,
and V1. Surround suppression also has a significant influence on response reliability, the time
course of impulse response functions, and the temporal frequency tuning of LGN neurons.
These results collectively demonstrate that the nonlinear surround is much more than a spatial
receptive field property; it plays a major role in systematically transforming temporal features of
visual signals en route from the retina to the visual cortex.
Materials and Methods

Surgery and preparation

Single-unit recordings were made from LGN neurons in 13 adult cats (both sexes). All surgical and experimental procedures conformed to NIH guidelines and were carried out with the approval of the Animal Care and Use Committee at the University of California, Davis. Surgical anesthesia was induced with ketamine (10 mg/kg, IM) and maintained with thiopental sodium (20 mg/kg, IV, supplemented as needed). Animals received a tracheotomy and were placed in a stereotaxic apparatus where temperature, EKG, EEG, and expired CO₂ were monitored continuously throughout the experiment. The level of anesthesia was maintained by a continuous infusion of thiopental sodium (2-3 mg/kg/hr, IV). If physiological monitoring indicated a low level of anesthesia, additional thiopental was given and the rate of continuous infusion increased.

A midline scalp incision was made and wound margins were infused with lidocaine. A small craniotomy was made above the LGN and/or optic tract and the dura was removed. The eyes were secured to posts attached to the stereotaxic frame to minimize eye movements, fitted with appropriate contact lenses, and focused on a tangent screen located 172 cm in front of the animal. The positions of area centralis and the optic disk were plotted by back-projecting the retinal vasculature of each eye onto the tangent screen. Once all surgical procedures were complete, animals were paralyzed with vecuronium bromide (0.2 mg/Kg/hr, IV) and mechanically respired.

Data acquisition and visual stimuli

Recordings were made from neurons in layers A and A1 of the LGN or from the axons of retinal ganglion cells in the optic tract using parylene-coated tungsten electrodes (AM Systems,
Everett, WA) or borosilicate glass-coated tungsten electrodes (Theodore Weyand, LSU Medical Center), respectively. Neuronal responses were amplified, filtered and recorded to a PC equipped with a Power 1401 data acquisition interface and the Spike 2 software package (Cambridge Electronic Design, Cambridge, England). Spike isolation was based on waveform analysis and the presence of a refractory period, as indicated by the autocorrelogram (Alitto et al., 2005).

Visual stimuli were created with a VSG2/5 visual stimulus generator (Cambridge Research Systems, Rochester, England) and presented on a gamma-calibrated Sony monitor running at 140Hz. The mean luminance of the monitor was 38 candelas/m². Visual responses of LGN neurons and optic tract fibers were characterized quantitatively using drifting and contrast-reversing sinusoidal gratings (described below). Drifting gratings were shown for 4 seconds, followed by 4 seconds of mean grey. Contrast-reversing gratings were shown for 3 seconds, followed by 2 seconds of mean grey. For drifting gratings, firing rate is reported as the first harmonic of the temporal frequency, while mean firing rate is reported for all other, non-periodic stimuli. Because surround suppression is maximal with high-contrast stimuli (Bonin et al., 2005; Sceniak et al., 2006) and contrast gain control mechanisms occur across the range of stimulus contrast, including high contrasts (Shapley and Victor, 1979b; Felisberti and Derrington, 1999; Bonin et al., 2005; Mante et al., 2008; Solomon et al, 2002), all recordings were made while neurons were excited with high-contrast stimuli (100%; Michelson contrast).

Classical receptive field response properties

For each cell, the center of the receptive field was localized with a custom mapping program, utilizing a mouse-controlled drifting sine wave grating. The center of the receptive field was determined by reducing the size of the grating to the smallest diameter (typically 0.1°-0.3°) to
evoke an audible change in firing rate. Using this diameter, the center was set as the location that evoked the maximal firing rate. This process was repeated 2-3 times to ensure accuracy. Next the preferred spatial frequency was determined by presenting full-field drifting sine wave gratings (4-Hz) of various spatial frequencies (typically 12 frequencies from 0.1 cycles/° – 3.0 cycles/°) repeated 3 times each (4 second presentations followed by 4 seconds of mean grey).

**Area summation response functions**

To determine the relationship between stimulus diameter and neuronal firing rate, drifting sine-wave gratings (4 Hz, preferred spatial frequency) of various diameters (typically 20 sizes, logarithmically spaced between 0.1° and 10°) were presented centered over the receptive field of the neuron under investigation. The responses evoked by these stimuli were then fit to a difference of Gaussians (DOG) equation,

\[ R(x) = K_c \sum_{s2} \exp\left(-\left(2x/r_c\right)^2\right) - K_s \sum_{s1} \exp\left(-\left(2x/r_s\right)^2\right) \]

where \( R(x) \) is the response evoked by diameter \( x \), \( K_c \) is amplitude of the center subunit, \( r_c \) is the radius of the center subunit, \( K_s \) is the amplitude of the surround subunit, and \( r_s \) is the radius of the surround subunit. The surround subunit radius was taken to be the spatial extent of the extraclassical receptive field. A suppression index was used to quantify the amount of suppression using the equation,
Linear versus nonlinear contributions to surround suppression

In order to accomplish the goal of characterizing the influence of nonlinear suppression on the temporal response properties of LGN neurons, it was essential to first estimate the contribution of linear mechanisms from the classical receptive field to what would otherwise be mistaken as nonlinear suppression. We began by assuming a difference of Gaussians (DOG) spatial profile for each LGN neuron in our data set (Figure 2A-2C; Rodieck, 1965). With this assumption, the spatial parameters of the classical center and surround were estimated by fitting a spatial frequency response function to a frequency domain difference of Gaussians equation (DOG, Figure 2C; So and Shapley, 1981; Alitto and Usrey, 2008):

$$\text{SF}(x) = K_c \cdot \exp(-1 \pi r_c^2 x^2) - K_s \cdot \exp(-1 \pi r_s^2 x^2)$$

where, $K_c$ and $K_s$ are the amplitudes of the classical center and surround, respectively, and $r_c$ and $r_s$ are the radii of the classical center and surround, respectively.

The contribution of linear mechanisms to the measured surround suppression depends on the visual stimulus used to measure the area summation response function. Linear suppression will occur when there is a mismatch between the visual stimulus and the polarity of the classical receptive field. For example, a hypothetical, purely linear, on-center/off-surround neuron will display linear suppression when a white spot extends beyond the balance point of the classical center and the classical surround (Figure 2B and D, point a). By contrast, little or no linear suppression is evoked when the same linear neuron is stimulated with a sine wave grating of the preferred spatial frequency (Figure 2E, black line). This is because the visual stimulus and the polarity of the classical receptive field closely match, regardless of the size of the visual stimulus (Figure 2F). In the majority of neurons recorded from in this study, the linear model
predicts little or no surround suppression when using sine wave stimuli with the preferred spatial frequency (Alitto and Usrey, 2008), despite the finding that the same neurons show pronounced surround suppression when presented with sinusoidal stimulus at the preferred spatial frequency (Figure 2E, grey dashed line). It is this phenomenon—suppression exceeding the linear estimate—that is known as extraclassical, nonlinear, surround suppression.

Although visual responses of an LGN neuron in the absence of nonlinear influences cannot be directly measured, they can be estimated from the linear DOG model obtained from the spatial frequency response function by convolving the linear estimate of the classical receptive field with the visual stimuli used to generate the area summation response function (Figure 3). From this, the predicted influence of linear suppression on measured area summation response functions was quantified using the same suppression index shown above. For this analysis, only the spatial properties were considered, temporal properties were not included.

**Modeling the influence of nonlinear surround suppression on retinogeniculate and thalamocortical interactions**

To estimate the influence of nonlinear surround suppression on retinogeniculate spike-efficacy, we modeled LGN spikes trains by weighting retinal spikes, recorded from the optic nerve during the presentation of stimuli that varied in size (details described above), according to their predicted efficacy based on previously published interspike-interval (ISI) spike-efficacy functions (Usrey et al., 1998), where efficacy equals the percentage of presynaptic spikes that evoke postsynaptic spikes. Because the efficacy of retinal spikes in evoking postsynaptic spikes is inversely related to the preceding ISI, retinal spikes following short ISIs were assigned higher weights than those following longer ISIs. For example, if 10% of retinal spikes with a preceding ISI of 20-22 msec and 20% of retinal spikes with a preceding ISI of 15-17 msec were reported to evoke LGN spikes, then these retinal spikes were assigned weights of 0.1 and 0.2, respectively.
Firing rates for each stimulus diameter were then calculated by averaging across multiple repeats (3-5 repeats per stimulus diameter). Modeled LGN spike trains were transformed into area summation curves and analyzed in the same manner as the experimentally measured retinal and thalamic area summation curves. A similar model was created to estimate the influence of LGN surround suppression on the strength of geniculocortical communication using previously published ISI-spike efficacy functions for LGN neurons (Usrey et al, 2000).

Temporal frequency response functions

Temporal frequency response functions were calculated from neuronal responses to drifting sine-wave gratings (0.5-64 Hz, occasionally lower than 0.5 Hz, preferred spatial frequency, 100% contrast). Response curves were interpolated with a cubic spline to determine each neuron's preferred temporal frequency and the lowest and highest temporal frequencies to evoke a response 50% of maximum (TF50 low and TF50 high, respectively). To determine the influence of surround suppression on the temporal frequency tuning properties of LGN neurons, temporal frequency response functions were generated using optimal size drifting gratings (determined from area summation response functions, typically 1°-2°diameter) and large gratings (~10°diameter) that extended into and beyond the extent of the suppressive surround. To examine the influence of surround suppression on the attenuation of responses to low temporal frequencies, we assessed low-frequency attenuation for both optimal size and large stimuli using the equation,

\[
\text{Low frequency attenuation} = 1 - \frac{\text{Response (lowest temporal frequency examined)}}{\text{Response (preferred temporal frequency)}}
\]

Time course and reliability of visual responses

To quantify the influence of surround suppression on the time-course of visual responses, LGN neurons were excited with a non-drifting, sine-wave grating stimulus (100% contrast, optimal spatial frequency) that was modulated (180° phase shift) in time by an m-sequence of length 2^{15}-1.
Specifically, the phase of the stationary grating changed by 180° each time the term of the m-sequence changed (from 1 to -1 or -1 to 1). The phases alternated between the cell’s preferred phase and the null phase (180° shifted from preferred). The term of the m-sequence was updated every fourth refresh of the monitor (refresh rate = 140 Hz, 28.6 msec per term). This experiment was conducted twice: once with the optimal size stimulus (typically 1°-2° diameter) and once with a large stimulus (~10° diameter) that extended into and beyond the extent of the suppressive surround. Standard reverse-correlation analysis was performed on the spike trains evoked by both stimulus sets.

To quantify the influence of surround suppression on the reliability of LGN spikes, we presented many repeats (generally 50 or more) of a 3-sec clip of the m-sequence modulated, contrast-reversing stimulus (described above). Each presentation of the 3-sec clip was followed by a 2-second interval of mean grey before the clip was repeated. Two sets of data were collected for each neuron, one using the optimal size stimulus (typically 1°-2° diameter) and one using a large stimulus that extended into and beyond the suppressive surround (~10° diameter). The Fano factor (spike count variance/mean spike count) was then calculated using the spike trains evoked by each stimulus set. The mean spike count and spike count variance were calculated with a sliding 30 ms window. The Fano factor was calculated for each time point and the average value across the 3-second stimulus presentation was used for further analysis. To determine whether or not a relationship between stimulus size and response reliability could be explained by changes in firing rate, we fit the spike count mean-to-variance relationship to a power function (variance = c*mean^n). This was done using the variance and mean values for each time bin (240, 30 ms bins for 3 seconds of stimulation). Fitting was done independently for each cell and both stimulus conditions (optimal size stimulus and large stimulus).

**Statistical analysis**
When statistical analysis was performed to compare two distributions, we first used Lilliefors modification of the Kolmogorov-Smirnov test (Chakravarti et al, 1967) to determine if the distributions in question were significantly different from normal distributions of unspecified mean and variance ($\alpha=0.05$). If the distributions were not statistically different from normal, then a t-test was used to compare the means of the two samples; if the samples were statistically different from normal distributions, then a Wilcoxon rank sum test or a sign test was used. Although Y cells typically display greater nonlinear surround suppression than X cells (Shapley and Victor, 1979b), classification of LGN neurons and retinal ganglion cells as X or Y type on the basis of response transience and latency (Usrey et al., 1999) did not influence the results (X Cells = 61, Y Cells = 15, unclassified = 5). Thus, X and Y cells have been combined for all statistical analyses.
Results

Strength of surround suppression in the Retina and LGN

To assess the strength of nonlinear surround suppression in the early visual system, we measured the spiking activity of 81 LGN neurons (layers A and A1) and 28 retinal ganglion cells (optic tract recordings) to drifting sinusoidal gratings as a function of stimulus size (4 Hz, 100% contrast, preferred spatial frequency). Because surround suppression increases with stimulus contrast (Bonin et al., 2005; Sceniak et al., 2006), all recordings were made while neurons were excited with high-contrast stimuli. Consistent with previous reports (Murphy and Sillito, 1987; Solomon et al., 2002; Webb et al., 2003; Sceniak et al., 2006; Alitto and Usrey, 2008), the firing rates of recorded neurons initially increased with stimulus size until a peak response was reached (Figure 3A-D, black traces). This increase in firing rate reflects a progressive increase in excitatory drive from the stimulus as the stimulus increased in size to fill both the classical center and the classical surround of the receptive field. Visual responses then decreased as the stimulus increased in size beyond the classical receptive field. This falling phase reflects the suppressive influence of the extraclassical or nonlinear surround—a region that extends beyond the cells' preferred size, where nonlinear suppressive mechanisms exceed linear excitatory mechanisms.

We quantified the strength of surround suppression using an index based on difference of Gaussians (DOG) fits to the area-summation response functions (see Materials and Methods; DeAngelis et al., 1994; Sceniak et al., 1999; Jones et al., 2000, 2001). Across our sample of LGN neurons, there was a broad distribution of suppression index values, with nearly all neurons showing some degree of suppression (Figure 3E). Suppression was also evident in our sample of retinal ganglion cells, albeit with a more restricted distribution of suppression index values (Figure 3F). On average, the strength of surround suppression in the retina was
approximately 70% of that in the LGN (mean suppression index: retina = 0.30 +/- 0.02, LGN = 0.43 +/- 0.02), a difference that was statistically significant (p<0.001).

It is important to note that linear mechanisms from the classical surround can contribute to the falling phase of the area summation response function if there is poor spatial correspondence between the classical receptive field and the spatial frequency of the sine-wave grating used to measure neuronal responses (see Materials and Methods for detailed explanation). To determine the extent to which linear mechanisms influenced our measures of suppression, we first determined the spatial parameters of the classical receptive field (center and surround subunits) by fitting a frequency domain difference-of-Gaussians (DOG) equation to each neuron’s spatial frequency tuning curve. We then convolved the stimulus used for the area summation experiments with the estimated spatial profiles of the classical receptive field (see Materials and Methods) to estimate the extent to which linear mechanisms contribute to surround suppression. The temporal kernel was not considered in this analysis. For the four neurons shown in Figure 3 (A-D; grey traces), predicted area summation tuning curves based solely on spatial estimates of the classical receptive field displayed little or no suppression as stimulus size increased beyond the preferred. In contrast, the actual tuning curves (black traces) for each neuron showed significant suppression as stimulus size increased beyond the preferred. Using this method, linear suppression was found to make a minimal contribution to the total suppression observed experimentally in both the retina and LGN (Figure 3G and H; mean linear suppression index: retina = 0.02 +/- 0.01, LGN = 0.03 +/- 0.02). To minimize the contribution of linear suppression to our analyses, we excluded all neurons (n=6) with linear suppression index values greater than 0.1 from further examination (Figure 3G and H, grey data points; likely the result of poor online estimation of preferred spatial frequency).

The finding that retinal surround suppression is ~70% of that measured in the LGN is consistent with the view that retinal mechanisms make a major contribution to LGN surround
suppression (Bonin et al., 2005; Solomon et al., 2006; Alitto and Usrey, 2008). With this in mind, we wished to know whether the feed forward influence from the retina may actually exceed 70% via synaptic and/or spike threshold mechanisms. We therefore performed an analysis to assess the strength of retinal suppression taking into account the role of spike timing in retinogeniculate communication. Past work from several laboratories demonstrates that retinal spikes following short interspike intervals (ISIs; <20 ms) are significantly more likely to evoke postsynaptic responses in the LGN compared to retinal spikes following longer ISIs (Mastronarde, 1987; Usrey et al., 1999; Levine and Cleland, 2001; Sincich et al., 2007; Weyand, 2007; Rathbun et al., 2010). Because surround suppression lowers the average firing rate of retinal ganglion cells, it is reasonable to expect that it should shift their interspike interval distribution toward longer ISIs (i.e. less effective spikes). As a result, modeled area summation response functions that take into account retinal ISI should show a larger difference between responses to optimal size stimuli and large stimuli.

To test the hypothesis that an ISI-based filter of retinogeniculate communication can increase the strength of surround suppression in the LGN, we passed each of the spike trains from our sample of ganglion cells through an ISI-based spike-efficacy filter derived from physiological recordings previously published (Figure 4A, inset; Usrey et al., 1998; see Materials and Methods). As expected, lowering the firing rate of retinal ganglion cells through surround suppression shifted the ISI distribution toward longer, less effective ISIs (Figure 4A and B). Importantly, the average spike evoked by an optimal size stimulus had a greater likelihood of driving a postsynaptic spike (i.e. higher efficacy value; Cleland et al., 1971; Usrey et al., 1998, 1999) compared to the average spike triggered by a large stimulus (Figure 4C; retinal spike efficacy: optimal size stimulus = 14.6% +/- 0.5, large stimulus = 12.0% +/- 0.6, p<0.005).

For each retinal ganglion cell in our sample, we next applied the efficacy filter to spikes comprising the full area summation response function and recalculated the suppression index.
As predicted, the magnitude of surround suppression increased (Figure 4E, mean suppression index: full spike train = 0.30±0.02, ISI-filtered spike train = 0.36±0.02; p<0.01). Thus, when taking into account the influence of ISI on retinogeniculate interactions, feedforward mechanisms can account for an average of 84% of LGN extraclassical suppression.

These results indicate that one consequence of ISI on spike efficacy is to increase the contribution of feedforward mechanisms to LGN surround suppression. It is worth noting that this analysis was conducted on the spike trains of individual retinal ganglion cells, and LGN neurons in the cat are known to receive retinal input from 1-4 retinal ganglion cells (reviewed in Cleland, 1986). Although each of the inputs to an LGN neuron have highly overlapping receptive fields and likely share similar size preferences (Usrey et al., 1999), a full account of the feedforward influence of ISI on surround suppression will require simultaneous recordings of all participating members of the circuit.

Given the significant influence that retinal ISI has on increasing the estimated strength of surround suppression in the LGN, we applied the same rationale to estimate the strength of surround suppression supplied from the LGN to primary visual cortex (V1) using an ISI-based spike-efficacy filter previously reported for LGN cells with monosynaptic connections to simple cells in layer 4 of V1 (Figure 4F, inset; Usrey et al., 2000). As with the retinal ganglion cells described above, surround suppression shifted the distribution of LGN spikes towards spikes with longer ISIs (Figure 4F and G). An analysis of the average efficacy of LGN spikes generated from optimal size and large-size stimuli revealed that spikes occurring in response to a large stimulus were, on average, less effective than spikes occurring in response to an optimal size stimulus (Figure 4H; optimal size stimulus = 3.8±0.1; large stimulus = 2.9±0.001; p <0.001). Moreover, as with the retinogeniculate pathway, the influence of stimulus size on the distribution of LGN ISIs augmented the estimated magnitude of surround suppression propagated to V1.
(Figure 4I and J; suppression index: full spike train = 0.41 +/- 0.02, filtered spike train = 0.50 +/- 0.03; p<0.01).

**Surround suppression and the reliability of LGN responses**

The ability of LGN neurons to transmit information from the retina to the cortex is also dependent on the variance of the responses to visual stimulation. Although visual neurons are often modeled as Poisson spike generators, response reliability, as measured by the Fano factor (variance/mean), is reported to increase as the mean firing rate increases (Kara et al., 2000). Consequently, the influence of surround suppression on firing rate could affect the reliability of LGN responses to visual stimulation. To test this prediction, we compared the Fano factor of LGN neurons (n=28) excited with a repeating 3-5 second clip of an m-sequence modulated, contrast-reversing, sine-wave grating stimulus presented at the optimal size and at a size that evoked maximal surround suppression (Figure 5A).

Consistent with previous reports, the Fano factor of most cells was less than 1.0 indicating sub-Poisson statistics (optimal size stimulus = 0.76, large stimulus = 0.82; Kara et al., 2000; Alitto et al., 2011). More importantly, there was a significant correlation between the change in Fano factor calculated from responses to optimal size stimuli and large stimuli and the change in mean spike count (Figure 5B; r = -0.54, p<0.005). This correlation was significant regardless of the bin size of the window (5 ms to 1,000 ms) used to perform the analysis (Figure 5B shows results using a 30 ms window). To quantify the relationship between surround suppression and response reliability further, we fit the spike-count variance and spike-count mean to a power function (Figure 5C and D). Results of this analysis show that the majority of LGN neurons have a power exponent less than 1.0 (Figure 5D). These findings indicate that as an LGN neuron is excited more robustly by the visual stimulus, the Fano factor decreases, resulting in a statistically more reliable response. The change in Fano factor associated with the
activation of surround suppression, however, can be accounted for by the corresponding change in firing rate. The best-fitting exponent of the power function was unchanged when the extraclassical surround was stimulated (Figure 5D, optimal size stimulus = 0.85 +/-0.01, large stimulus = 0.85 +/-0.02; p = 0.56). Thus, similar to other forms of response modulation, including contrast, orientation and spatial attention (Tolhurst et al., 1981; Tolhurst et al., 1983; McAdams and Maunsell, 1999), surround suppression influences the reliability of visual responses without altering the fundamental relationship between spike-count variance and mean.

Surround suppression, impulse response functions, and temporal frequency tuning

Mounting evidence, including the results described above, indicates that surround suppression in the LGN relies heavily on retinal mechanisms, including retinal contrast gain control (Bonin et al., 2005)—a phenomenon where neurons become less responsive to changes in stimulus intensity as stimulus contrast increases (Figure 1; Shapley and Victor, 1978). If so, then stimulation of the extraclassical receptive field should affect the temporal properties of neuronal responses in the LGN in a manner similar to increasing stimulus contrast. Specifically, visual responses in the LGN should become shorter in duration with surround suppression, and temporal frequency response functions should shift toward higher frequencies (as in Figure 1). To test these predictions, we generated impulse response functions using noise-modulated, contrast-reversing, sine-wave grating stimuli of optimal and large size (see Materials and Methods), and we calculated temporal frequency response functions using drifting gratings of optimal and large size.

We first examined the hypothesis that surround suppression modulates the temporal properties of LGN impulse responses. Consistent with the general view that the extraclassical surround serves to suppress visual responses, the magnitudes of the peak and rebound phases...
of impulse responses were significantly reduced when LGN neurons were stimulated with large
stimuli compared to optimal size stimuli (Figures 6 and 7A; mean peak magnitude: large
stimulus = 0.52 +/- 0.06 spikes, optimal size stimulus = 0.83 +/- 0.08 spikes, p<0.001; mean
rebound magnitude: large stimulus = 0.52 +/- 0.06 spikes, optimal size stimulus = 0.82 +/- 0.09
spikes, p<0.001). More interestingly, there was a significant influence of surround suppression
on the temporal properties of LGN impulse responses in a manner consistent with retinal
contrast gain control. Namely, the duration of both the peak and rebound phases was
significantly shorter when neurons were excited with the large stimulus compared to the optimal
size stimulus (Figure 7B, peak phase duration: large stimulus = 46.9 +/- 3.1 ms, optimal size
stimulus = 51.7 +/- 3.2 ms, p<0.05; rebound phase duration: large stimulus = 229.3 +/- 30.8 ms,
optimal size stimulus = 355.5 +/- 47.0 ms, p<0.05).

Given that the impulse response is the inverse Fourier transformation of the response
power spectrum, a decrease in the duration of the impulse response predicts a shift in the
temporal frequency response function towards higher frequencies, a phenomenon also
observed as a consequence of contrast gain control. To test this prediction, we used Fourier
analysis to convert the impulse responses in our data set into temporal frequency response
functions (Figure 8A-C). We also performed experiments to compare temporal frequency
response functions generated from responses to large and optimal size drifting gratings (Figure
8D-F). Both methods revealed a significant influence of surround suppression on the temporal
frequency tuning properties of LGN neurons.

Extraclassical suppression modulated the temporal frequency tuning of LGN neurons in
a manner similar to contrast gain control. Specifically, there was an increased attenuation of
responses to low-frequency stimuli relative to high-frequency stimuli (Figure 9A). Likewise, there
was an inverse relationship between stimulus temporal frequency and the strength of
extraclassical suppression (Figure 9B). Extraclassical suppression also induced a significant
rightward shift in the temporal frequency response functions of LGN neurons towards higher frequencies. This shift was evident in the lowest temporal frequency to evoke a half-maximum response (TF$_{50_{\text{low}}}$; Figure 9C; for contrast-reversing gratings: optimal size = 1.1 ±0.1 Hz, large size = 1.7 ±0.2 Hz, p<0.001; for drifting gratings: optimal size = 0.7 ±0.1 Hz, large size = 1.8 ±0.3 Hz, p<0.001) and the highest temporal frequency to evoke a half-maximum response (TF$_{50_{\text{high}}}$; Figure 9D; for contrast-reversing gratings: optimal size = 19.4 ±2.0 Hz, large size = 19.9 ±1.8 Hz, p>0.01; for drifting gratings: optimal size = 20.1 ±2.8 Hz, large size = 24.3±2.9 Hz, p<0.01).
Discussion

The goal of this study was to determine the influence of nonlinear extraclassical surround suppression on temporal features of visual responses in the early visual system. Our results demonstrate that surround suppression is first established in the retina and then undergoes amplification in the LGN and layer 4 of V1 by mechanisms that include changes in the distribution of presynaptic interspike intervals and temporal summation of feedforward signals. Extraclassical suppression also influences LGN temporal integration in a manner qualitatively similar to retinal contrast gain control, decreasing the duration of LGN visual responses and causing a subsequent rightward shift in the temporal frequency response function. Collectively, these results indicate that feedforward inputs from the retina make a major contribution to the nonlinear receptive field properties of neurons in the LGN.

The neural origin of extraclassical suppression in the LGN has been a subject of considerable investigation with studies providing evidence for involvement from corticogeniculate feedback (Murphy and Sillito, 1987; Nolt et al., 2007; Jones et al., 2012; Olsen et al., 2012; Andolina et al., 2013) and recurrent thalamic inhibition (Sclar, 1987; Chenbg et al., 1995; Webb et al., 2005; Vaingankar et al., 2012). Here we show that retinal ganglion cells in the cat exhibit ~70% of the suppression measured in the LGN (Figure 3). This agrees with previous reports demonstrating nonlinear surround suppression in retinal ganglion cells across a variety of species (Caldwell and Daw, 1978; Shapley and Victor, 1979b; Enroth-Cugell and Jakiela, 1980; Ahmed and Hammond, 1984; Passaglia et al., 2001; Solomon et al., 2006; Nolt et al., 2007; Alitto and Usrey, 2008). Results from the present study also indicate that the contribution of feedforward mechanisms to nonlinear suppression in the LGN may be even greater than that described above, as the expression of retinal suppression is predicted to be amplified in the LGN via temporal summation and retinal spike efficacy mechanisms (Figure 4). Feedforward contributions to extraclassical suppression are also indicated by previous results.
demonstrating that the onset of extraclassical suppression in the LGN is substantially faster than the response latency of corticothalamic feedback neurons in layer 6 of V1 (Briggs and Usrey, 2007; Alitto and Usrey, 2008). In addition, the tuning properties of LGN surround suppression more closely resemble the response properties of retinal ganglion cells than the response properties of V1 neurons (Solomon et al., 2002; Bonin et al., 2005; Durand et al., 2007; Camp et al., 2009). Based on these results, it appears that multiple mechanisms contribute to LGN surround suppression. Importantly, it is worth emphasizing that evidence demonstrating a role for one pathway does not negate involvement from other pathways. Rather, the existence of multiple mechanisms only further supports the assertion that surround suppression is an important strategy used by the brain to process visual information.

Previous work has suggested that extraclassical suppression in the retina and LGN can be explained as a manifestation of contrast gain control (Shapley and Victor, 1979b; Bonin et al., 2005; Mante et al., 2008). One of the distinguishing features of contrast gain control is an inverse relationship between stimulus contrast and the gain of retinal ganglion cell and LGN cell responses, which leads to a saturating contrast response function (Shapley and Victor, 1978; Kaplan and Shapley, 1986; Sclar, 1987; Alitto and Usrey, 2004). In addition, contrast gain control decreases the gain at low temporal frequencies to a greater degree than the gain at high temporal frequencies and decreases the duration of impulse response functions (Shapley and Victor, 1978; Shapley and Victor, 1979a; Lee et al., 1994; Benardete and Kaplan, 1999; Usrey and Reid, 2000). With this in mind, it is noteworthy that results from the present study reveal that extraclassical suppression in the LGN decreases the duration of impulse response functions (Figure 7) and has a greater suppressive influence with low temporal frequency stimuli compared to high temporal frequency stimuli (Figures 9). These findings agree with previous work demonstrating that surround suppression decreases the duration of impulse response functions in the LGN (Mante et al., 2008; Benardete and Kaplan, 1999; Solomon et al., 2010).
Viewed from a broader perspective, the seemingly distinct phenomena of extraclassical suppression and contrast gain control can be unified by considering the balance of excitatory and inhibitory mechanisms involved in each. Typically, the organization of retinal and geniculate classical and extraclassical receptive fields is viewed as two overlapping fields, centered on the same spatial location. Whether the extraclassical receptive field is spatially more extensive than the classical receptive field is disputed (see Bonin et al., 2005), but this does not change the fundamental nature of the model. In the periphery of a receptive field, an increase in stimulus size causes net suppression, while a more centrally located increase in contrast causes net excitation. As stimulus intensity increases, either as a function of contrast or diameter, the pool of recruited excitatory and inhibitory neurons increases, decreasing the integration time of neurons in the early visual system, resulting in the observed changes in temporal response properties.

LGN surround suppression certainly influences cortical activity; however, it is unlikely to contribute directly to the full spatial extent of cortical extraclassical suppression (Angelucci and Bressloff, 2006; Priebe and Ferster, 2008; Ozeki et al., 2009). Although the magnitude of LGN suppression is comparable to values reported for V1 neurons (DeAngelis et al., 1994; Sceniak et al., 2001; Cavanaugh et al., 2002; Naito et al., 2007), and its influence is likely amplified via mechanisms that include the temporal filtering of feed forward signals (Figure 4, see also Anderson et al., 2001), many features of extraclassical suppression in the LGN and V1 do not match (Ozeki et al., 2009). For instance, extraclassical suppressive fields in V1 are spatially much more expansive than in the LGN (Jones et al., 2000; Sceniak et al., 2001; Solomon et al., 2002; Bonin et al., 2005; Webb et al., 2005; Alitto and Usrey, 2008). In particular, cortical extraclassical fields are 2-5x the spatial extent of their corresponding classical receptive fields, whereas the same ratio in the LGN is between 1-2x (Jones et al., 2000; Sceniak et al., 2001; Solomon et al., 2002; Bonin et al., 2005; Webb et al., 2005; Alitto and Usrey, 2008). Moreover,
results indicate that visual stimuli presented at the preferred size of a V1 neuron are sufficiently large to evoke maximal surround suppression from retinotopically aligned neurons in the LGN (Ozeki et al., 2004). In addition, unlike V1 extraclassical receptive fields, LGN extraclassical fields are not selective for stimulus orientation or direction, follow higher temporal frequencies, and display significantly less adaptation (Girardin et al., 2002; Solomon et al., 2002; Webb et al., 2002; Bonin et al., 2005; Durand et al., 2007; but see Naito et al., 2007). With these results in mind, there is evidence that LGN surround suppression may contribute to the near surround (Kida and Sato, 2010) and/or the high-contrast summation fields of V1 neurons (Ozeki et al., 2004; Angelucci and Sainsbury, 2006). The more extensive surrounds of cortical neurons, however, likely rely on (1) feedback from extrastriate areas, which can account for the correct spatial parameters and onset latencies of V1 suppression (Bair et al., 2003; Angelucci and Bressloff, 2006; Nassi et al., 2013), and/or (2) somatostatin expressing local inhibitory neurons, the optogenetic inactivation of which blocks extraclassical suppression in mouse primary visual cortex (Adesnik et al., 2012; Nienborg et al., 2013).

Nonlinear suppression also modulates the response reliability of LGN neurons (Figure 5), as measured by the Fano factor (variance / mean), causing a larger decrease in response mean than response variance. Importantly, though, the relationship between spike count variance and mean is not dependent on stimulus size; the best fitting power equation was not influenced by the activation of surround suppression. Thus, a neuron’s response at a particular firing rate will have the same reliability regardless of whether it was generated by a suboptimal stimulus smaller than or larger than the preferred size. This general view agrees with past reports that the correlation between spike count mean and variance is unaltered by changes in stimulus parameters, such as contrast and orientation, or behavioral state, such as spatial attention (Tolhurst et al., 1981; Tolhurst et al., 1983; McAdams and Maunsell, 1999). The influence of surround suppression on response reliability can be explained by the relationship
between mean spike count and response reliability. Traditionally, spiking activity has been modeled as a Poisson process (e.g., Shadlen and Newsome, 1998); however, it has been established that a neuron’s response reliability is directly related to the mean spike count (Kara et al., 2000; Churchland et al., 2010). As mean spike count increases, the variance tends to increase at an exponential rate less than 1.0, often resulting in responses at high firing rates that are more reliable than a Poisson process. Thus, response reliability is fundamentally related to the amount of suprathreshold activity regardless of how that activity level was achieved.

Given the similarity between retinal and LGN receptive fields, it is interesting that the majority of synaptic input to LGN neurons comes from non-retinal sources (reviewed in Sherman and Koch, 1986). In addition to corticogeniculate feedback and recurrent inhibition, surround suppression and retinal spike efficacy may also be modulated by cholinergic inputs, directly from the brainstem or indirectly from the basal forebrain via the thalamic reticular nucleus (De Lima and Singer, 1987), which are reported to regulate LGN activity as a function of arousal (Steriade, 2004) and spatial attention (McAlonan et al., 2008). With future experiments conducted in animals engaged in controlled behavioral tasks, it should be possible to determine the contribution of these modulatory inputs to the dynamic interactions between extraclassical surround suppression and visual processing in the temporal domain.

In summary, results from this study reveal a dynamic relationship between extraclassical surround suppression and temporal processing of visual signals. In particular, extraclassical suppression interacts with ISI-based mechanisms to adjust the strength of neuronal communication, an effect that serves to progressively amplify the magnitude of suppression in the retinogeniculocortical pathway. Extraclassical suppression also influences response reliability, the time course of impulse response functions, and the temporal frequency tuning of LGN neurons. Taken together, these results demonstrate that the extraclassical surround plays a major role in transforming temporal features of visual signals delivered to cortex.
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References


Passaglia CL, Enroth-Cugell C, Troy JB. Effects of remote stimulation on the mean firing rate of

Priebe NJ, Ferster D. Inhibition, spike threshold, and stimulus selectivity in primary visual cortex.

Rathbun DL, Warland DK, Usrey WM. Spike timing and information transmission at

Rodieck RW. Quantitative analysis of cat retinal ganglion cell response to visual stimuli. Vision

Sincich LC, Adams DL, Economides JR, Horton JC. Transmission of Spike Trains at the


Sceniak MP, Chatterjee S, Callaway EM. Visual spatial summation in macaque geniculocortical

Scholl B, Latimer KW, Priebe NJ. A retinal source of spatial contrast gain control. J Neurosci

Sclar G. Expression of "retinal" contrast gain control by neurons of the cat's lateral geniculate

Shadlen MN, Newsome WT. The variable discharge of cortical neurons: implications for

Shapley R, Victor JD. The contrast gain control of the cat retina. Vision Research 19:431-434,
1979a.

Shapley RM, Victor JD. The effect of contrast on the transfer properties of cat retinal ganglion

Shapley RM, Victor JD. Nonlinear spatial summation and the contrast gain control of cat retinal


Figure Legends

Figure 1. Contrast Gain Control in the retina and LGN. A. The response of a hypothetical, linear retinal ganglion cell or LGN neuron as a function of stimulus contrast. Gain is constant regardless of the strength of the visual stimulus. C and E. Likewise, the temporal frequency response function (C) and impulse response (E) of a linear LGN neuron simply scale with stimulus contrast. Thus, measures like the TF50 and response duration remain constant as contrast changes (black line = high contrast; grey line = low contrast). B. The response gain of many real LGN neurons, however, decreases as stimulus contrast increases, a phenomenon known as contrast gain control. D and F. Further, the temporal frequency response function (D) and impulse response (F) of many LGN neurons are significantly transformed as stimulus contrast increases, becoming less sensitive to low frequencies and more sensitive to high frequencies.

Figure 2. Linear versus nonlinear surround suppression. A. The classical center/surround receptive field has a circularly symmetric, spatially antagonistic organization composed of two linear subunits: a classical center and a classical surround. B. The difference of Gaussians model based on the linear combination of the classical center and surround subunits. C. When the difference of Gaussians model is assumed, the spatial parameters can be estimated by fitting a spatial frequency response function to a frequency domain DOG equation (see Methods). D. The response function of a hypothetical, purely linear LGN neuron when presented with a spot of the preferred luminance polarity that varies in stimulus diameter. E. The response of the same hypothetical neuron to a sinusoidal grating of the preferred spatial frequency (solid black line; note: the decreased slope of the response at point “a” marks the transition point between the classical center and the classical surround: the point where the
strength of the surround subunit equals the strength of the center subunit). In contrast to the hypothetical response, most LGN neurons display a substantial amount of nonlinear, extraclassical suppression that cannot be accounted for by the linear model (dashed grey line). F. The amount of predicted linear suppression to a sinusoidal stimulus depends on how well the spatial properties of the classical receptive field match the stimulus.

Figure 3. Size tuning and extraclassical suppression in retinal ganglion cells and LGN neurons. Representative area summation response functions for two LGN neurons (A and C) and two retinal ganglion cells (B and D). Recordings of retinal ganglion cell activity made from the axons of retinal ganglion cells within the optic track. For each cell, the solid black lines shows the difference of Gaussians (DOG) fit to measured values (black dots). E and F. Histograms showing the distribution of suppression index values (see Materials and Methods) for the sample of LGN neurons (n = 81) and retinal ganglion cells (n=28). Dashed lines show the mean suppression index for the sample of LGN neurons and retinal ganglion cells (0.43 +/-0.02 and 0.30 +/-0.02, respectively; p<0.001). G and H. Scatterplots showing the relationship between measured suppression index values and suppression index values estimated for the linear contribution made by the classical surround of receptive fields (see Materials and Methods).

Figure 4. Extraclassical suppression is amplified from presynaptic to postsynaptic neurons via stimulus-size dependent effects on the distribution of presynaptic interspike intervals (ISIs) and the relationship between ISI and synaptic efficacy. Compared to optimal size stimuli, large stimuli shift the distribution of ISIs towards longer values. A and B. The distribution of ISIs for a representative retinal ganglion cell; (F and G) the distribution of ISIs
for a representative LGN neuron. Black lines show un-normalized (A and F) and normalized (B and G) responses to optimal size stimuli; grey lines show responses to large stimuli. A and F (insets). The influence of ISI on the efficacy (% presynaptic spikes to evoke postsynaptic spikes) of retinogeniculate and geniculocortical communication (based on Usrey et al., 1998 and 2000). At both locations in the visual pathway, efficacy is greatest for spikes following short ISIs. C and H. Estimated average efficacy of retinal (C) and LGN (H) spikes evoked with large and optimal size stimuli. Estimates based on the shift in ISIs with stimulus size and the relationship between ISI and efficacy (see Materials and Methods). Red “X” indicates mean values. D and I. Comparison of area summation response functions across cells calculated from experimentally observed values (“Obs”, solid black lines) and values adjusted to take into account the influence of ISI and spike efficacy (“SE”, dashed black lines) on synaptic communication. After accounting for suppression-dependent changes in spike efficacy, retinal area summation response functions are shifted towards the observed values for the LGN (D; grey line). E and J. Using a suppression index to quantify the strength of surround suppression (see Materials and Methods), the ISI-dependent enhancement of surround suppression from pre- to postsynaptic cells is significant (p<0.05) for the pathway from retina to LGN (E) and from LGN to V1 (J). Red “X” indicates mean values.

Figure 5. Extraclassical suppression modulates LGN response reliability via changes in firing rate. A. Raster plot showing the responses of a representative LGN neuron to repeated presentations of an optimal size, 5-second clip of an m-sequence modulated, contrast-reversing grating. The same sequence was also used for a large size stimulus (data not shown). B. Scatter plot showing the relationship between change in Fano factor (variance/mean) as a function of stimulus size and change in spike count. Across the sample of LGN neurons, there was a significant negative correlation (dashed line = linear regression). C. Scatter plot showing
the relationship between spike count variance and spike count mean for a representative cell stimulated with an optimal size stimulus (block dots) and a large stimulus (grey dots). Each dot represents the mean and variance for a specific time bin of the 5-second stimulus using 30 msec bins. The values for the two stimulus conditions (large stimuli, optimal size stimuli) were independently fit to power functions (dashed lines). D. Across the sample of LGN neurons, surround suppression did not significantly influence the best fitting power equation ($X = \text{mean value}$).

Figure 6. Extraclassical suppression modulates the impulse response of LGN neurons. Impulse responses were calculated from neuronal responses to an m-sequence modulated, contrast-reversing, sine-wave grating (see Materials and Methods). A. Schematic illustration of a typical impulse response. The biphasic response consists of an initial peak phase followed by a rebound phase. B-E. Impulse responses from four representative LGN neurons: two on-center cells (B and C) and two off-center cells (D and E). For each cell, two impulse responses are shown, one using an optimal size stimulus (black line) and one using a large stimulus that evoked extraclassical suppression (grey line).

Figure 7. Extraclassical surround suppression decreases the magnitude and duration of LGN impulse responses. Extraclassical surround suppression in the LGN decreases (A) the magnitude and (B) the duration of both the peak (left column) and rebound phases (right column) of LGN impulse responses. Cross hairs indicate mean values.
Figure 8. Extraclassical surround suppression modulates temporal frequency tuning in the LGN. The influence of stimulus size on temporal frequency tuning is evident from measurements using contrast-reversing grating stimuli (A-C) and drifting grating stimuli (D-F).

A. Impulse response functions of a representative LGN neuron excited with an optimal size stimulus (black line) and a large stimulus (grey line). B and C. Temporal frequency response functions derived from the impulse responses of two representative LGN neurons (black lines: optimal size stimuli; grey lines: large stimuli). Temporal frequency response functions were calculated by performing an inverse Fourier transformation on the impulse responses. D-F. Temporal frequency response functions of three representative LGN neurons calculated directly from their responses to drifting sine-wave grating stimuli (optimal size stimuli: black lines; large stimuli: grey lines) that varied in temporal frequency.

Figure 9. Extraclassical surround suppression shifts LGN temporal frequency response functions toward higher frequencies. A. Scatterplots showing the influence of stimulus size on low-frequency attenuation (see Materials and Methods). Non-linear suppression was greatest at low temporal frequencies, causing an increase in low-frequency attenuation in the LGN. B. Line graphs showing the relationship between stimulus temporal frequency and the strength of suppression (quantified with a suppression index, larger values correspond to greater suppression; see Materials and Methods) across the sample of LGN neurons. Suppression index values are inversely proportional to stimulus temporal frequency. Vertical lines indicate standard error. C and D. The influence of extraclassical surround suppression on shifting temporal frequency response functions towards higher temporal frequencies is also evident in scatterplots showing a significant influence of stimulus size on the lowest (C) and highest (D) temporal frequencies to evoke half-maximum responses (Low TF$_{50}$ and High TF$_{50}$, respectively).
Figure 1
Figure 2
Figure 3
Figure 4
Figure 5
Figure 6

(A) Graph showing response duration (peak phase) and rebound phase. Diagram includes labeled sections "A" and "B".

(A) Annotations:
- A = response duration (peak phase)
- B = response duration (rebound phase)
- Peak phase magnitude = \int \text{peak phase}
- Rebound phase magnitude = \int \text{rebound phase}

(B) Graph comparing responses to different stimulus sizes:
- Black line: optimal size stimulus
- Gray line: large stimulus (10°)

(C) Graph showing response to stimulus over time (msec).

(D) Graph showing response to another stimulus over time (msec).

(E) Graph showing response to yet another stimulus over time (msec).
Figure 7
Figure 8
Figure 9