Lateral interactions in the perception of flicker and in the physiology of the lateral geniculate nucleus

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The perception of flicker strength in a center stimulus can be affected by the presence of a surrounding stimulus. We correlated this effect with the interactions between centers and surrounds of the receptive fields (RFs) of neurons in the retino-geniculate pathways. The responses of cells in the lateral geniculate nucleus (LGN) of two New World monkey species, the common marmoset (Callithrix jacchus), and the owl monkey (Aotus azarae) were measured to two spatially non-overlapping sinusoidally modulating luminance stimuli of equal temporal frequency, one of which mainly stimulated the RF center, the other the RF surround. The relative temporal phase between the center and surround stimuli was varied. The response amplitude as a function of relative phase between the center and surround stimuli can be described by a simple model where the RF center and surround responses are vector-added. A minimal response was reached for stimuli in which the surround stimulus led the center stimulus, indicating that the RF surround response lagged the center response. The flicker strength in the center stimulus perceived by human observers was measured psychophysically. It was found that the perceived flicker strength could be described by the same function as was used for the cell data. There were qualitative similarities between the physiological and the psychophysical data, suggesting that the physiological basis of the psychophysically measured spatial interactions is present as early as the LGN. The data indicated the presence of a nonlinearity in center-surround interactions that is influenced by the stimulus contrast. The possible source of this nonlinearity was studied by comparing the center and the surround responses with those in which they were selectively stimulated.

Keywords: human psychophysics, receptive field, marmoset, owl monkey, retino-geniculate pathway.

Introduction

The perceived contrast of a central visual stimulus can be altered by the presence of neighboring stimuli. Previous psychophysical studies concentrated on the influence of center-surround interactions on the perception of a spatial grating in the center stimulus (e.g., Ejima & Takahashi, 1985; Takeuchi & DeValois, 2000; Xing & Heeger, 2000), on the perceived brightness in the center (e.g., DeValois, Webster, DeValois, & Lingelbach, 1986), on the perceived spatial contrast in the central disk filled with binary noise (e.g., Singer & D'Zmura, 1994, 1995), or on the influence of the state of adaptation in the surround on the flicker perception in the center (e.g., Eisner, 1994, 1995).

To date, no quantitative studies have been performed on how center-surround interactions may influence the perception of a temporal modulation at moderate or high temporal frequencies in a spatially homogeneous circular center stimulus. Here, we present the results of psychophysical experiments that concentrate on the changes in the perception of a temporal modulation (the “perceived flicker strength”) as a function of the relative temporal phase between the center and the surround stimuli. The receptive field (RF) of retinal ganglion cells and of neurons in the lateral geniculate nucleus (LGN) consists of a center and a surround (Kuffler, 1953; Rodieck & Stone, 1965). The centers and the surrounds are coextensive, have approximately Gaussian responsivity profiles (Rodieck, 1965; Enroth-Cugell & Robson, 1966), and are antagonistic at low temporal frequencies. This is the difference of Gaussians (DOG) model. Owing to the antagonism, the surround response to a stimulus will reinforce the center response when the surround stimulus is modulated in counter-phase with the center stimulus. An in-phase modulation of the two will lead to an overall response that is smaller than the center response alone. The antagonism is...
modified at higher temporal frequencies because of a small latency difference between center and surround responses (Gouras & Zrenner, 1979; Enroth-Cugell, Robson, Schweitzer-Tong, & Watson, 1983; Dawis, Shapley, Kaplan, & Tranchina, 1984; Frishman, Freeman, Troy, Schweitzer-Tong, & Enroth-Cugell, 1987; Smith, Lee, Pokorny, Martin, & Valberg, 1992; Yeh, Lee, & Kremers, 1995; Benardete & Kaplan, 1997a).

Because of the difference between the time courses of the center and of the surround regions and because of the spatially overlapping RF centers and surrounds, the two regions cannot be stimulated independently with either spatial or temporal stimuli. Nevertheless, we show that by using a combination of two modulating stimuli with an appropriate spatial arrangement, it is possible to obtain a reliable assessment of the RF center and surround response components.

Apart from the exclusively linear DOG model of the receptive field centers and surrounds, there are some interactions that are more complicated and involve nonlinearities. For instance, it was found that the responses of cat retinal ganglion cells to a stimulus that covers the RF center will be altered by the presence of a non-overlapping stimulus in the RF surround (Shapley & Victor, 1979). There are indications that similar interactions are present in the responses of primate retinal ganglion cells (Benardete & Kaplan, 1997b, 1999). But, these interactions have not yet been studied systematically in primate LGN cells.

It is the purpose of this work to correlate the above mentioned center-surround interactions in the responses of the LGN neurons of two New World monkey species, the common marmoset (Callithrix jacchus) and the owl monkey (Aotus azarae), with the psychophysical data from human observers. The stimuli that were used in the two measurements were very similar. The physiological data can be explained on the basis of a linear spatial summation, although some nonlinearities can be recognized. We also investigated the influence of temporal frequency and stimulus contrast on the cell responses and on flicker perception. The study further focuses on the influence of the presence of a RF surround response on the response of the RF center and vice versa by comparing the responses of each subfield with and without stimulation of the other subfield. We found that there are nonlinear interactions that are influenced by stimulus contrast. We found that the nonlinearities influence the response properties of the cells and visual perception. Finally, the implications of the lateral interactions for the signals passed on to the brain are discussed.

Parts of the results were presented in abstract form (Kremers, 2001; Kozyrev & Kremers, 2002; Kremers & Kozyrev, 2002).

Methods

Psychophysical experiments

Subjects

Three authors participated as observers in the present study. At the time the psychophysical measurements were performed, subjects VK and BDK were unaware of the purpose of the study. The subjects rested their head on a chin rest. Head movements were further restricted by viewing the stimulus monocularly through a 3-mm diameter artificial pupil.

Visual stimuli

The stimuli were presented on a BARCO monitor (CCID 7751 MKII) controlled by a VSG 2/2 graphics card (Cambridge Research System). Two different stimuli (a reference and a test stimulus) were displayed in an alternate manner. The reference stimulus consisted of a spatially homogenous circular center and a spatially homogenous annulus. Two different spatial configurations were used: the diameter of the center stimulus was either 1° or 0.4°. In combination with the 1° circle, the inner and the outer diameter of the annulus were 1.1° and 10.2°, respectively. With the 0.4° center stimulus, the inner and the outer diameter of the annulus were 0.5° and 10.2°, respectively. Thus, there was a small (3 arcmin) gap between the center and the surround stimuli, which enabled the subjects to identify the center stimulus at all conditions (without the gap, the border between the center and the surround stimulus would not be recognizable at a 0°-phase difference between the two stimuli).

The center and surround stimuli had equal mean luminances (66 cd/m²) and chromaticities (20, 40, and 6 cd/m² mean luminance of the red, green, and blue phosphors, respectively, resulting in a white; CIE, 1964, large field coordinates were [0.33,0.32]). The stimuli were viewed through a 3-mm artificial pupil resulting in a mean retinal illuminance of about 470 td.

The luminance of both the center and the surround sub-stimuli was sinusoidally modulated in time. The strength of the modulation around the mean luminance in the center and surround stimuli was expressed in terms of Michelson contrast, being either 25% or 50%. These two relatively high contrasts were chosen to compare the data with the physiological measurements and to get reliable psychophysical data at all stimulus conditions. As will be explained below (see the description of the physiological measurements), we believe that saturation has only a minor influence on the results. The measurements were performed with all combinations of contrasts in the center and surround stimuli and at three different temporal frequencies (4, 8, and 20 Hz).

The test stimulus consisted of only one stimulus with the same size, temporal frequency, time averaged luminance, and time averaged chromaticity as the central circle.
of the reference stimulus. The contrast was varied until the perceived flicker strengths in the test stimulus and in the center of the reference stimulus were identical.

**Procedure**

The reference stimulus was viewed foveally as long as the subject desired. By pressing a button, the subject replaced the reference stimulus by the test stimulus. The subject had to indicate by pressing a button whether the perceived flicker in the test stimulus was stronger or weaker than in the center of the reference stimulus. A two-alternative forced-choice method with a PEST procedure (Taylor & Creelman, 1967) was used to match the perceived flicker strength in the test stimulus to the one in the center of the reference stimulus. Within a run, the reference stimulus was not altered, whereas the contrast in the test stimulus was varied, depending on the responses of the subject. The contrast in the test stimulus was decreased when the subject indicated that the perceived flicker in the test stimulus was stronger than in the center of the reference stimulus and was increased when the flicker of the test stimulus was subjectively weaker than in the center of the reference stimulus. Two randomly interleaved staircases of test stimuli, one starting at 0% and the other at 100% contrast, were used. This excluded the possibility of guessing.

Initially, the contrasts in the test stimulus were changed in steps of 60% (from 0% to 60% or from 100% to 40%). After a reversal in direction of contrast change, the contrast steps were halved. When the contrast change in the test stimulus was less than 0.14 times its actual contrast, it was assumed that the perceived flicker strengths in the test stimulus and in the center of the reference stimulus matched. Thus, in each run two independent estimates of the perceived flicker strength were obtained. This procedure was preferred rather than the measurement of a flicker detection threshold in the center stimulus because at low center contrasts the modulation of the surround could induce a flicker percept in the center, preventing reliable measurements of a threshold. Furthermore, the use of fixed contrasts in the center of the reference stimulus enabled a better direct comparison with the physiological data described below.

The measurements were repeated at several phase differences between the central and the surrounding subfields of the reference stimulus, varying between –180° and +180° in steps of 30°. In addition, the measurements were performed at –15° and +15° phase differences. By definition, negative phase differences indicate that the surround stimulus was lagging the center. Positive phase differences indicate a phase lead of the surround stimulus. Two refer-
ence stimuli can be viewed in Movie 1. In these examples, the center and surround stimuli are modulated at 4 Hz, with 50% contrast in the two subfields. The relative phase difference is 0° in the left movie and 180° in the right one. All other parameters are identical.

The different reference stimuli were presented in a quasi-random order. The quasi-random order was changed regularly, and subjects VK and BEK were not informed about these changes. Therefore, the results cannot be the result of "educated guesses."

In one session, at least one trial, comprising all phase differences for a certain combination of contrasts and at a certain frequency in the reference stimulus, was completed. Each trial was repeated three times. The means and standard deviations of the six estimates of the perceived flicker strengths were then calculated.

**Physiological experiments**

**Animal preparation**

All animal experiments were approved by a local ethical commission and conducted in accordance with the ethical guidelines and with the principles regarding the care and use of animals adopted by the Society for Neuroscience.

The animals were initially sedated by an intramuscular injection of 15-30 mg·kg⁻¹ ketamine hydrochloride (Ketanest®, Parke-Davies) and either 3.5 mg·kg⁻¹ xylazin hydrochloride with 1.5 mg·kg⁻¹ methyl-4-hydrobenzoate (0.15 ml·kg⁻¹ Rompun®, 2% solution, Bayer) or 1 mg·kg⁻¹ diazepam (Valium®, MM Roche), and they were respired with a mixture of 70% N2O and 30% O₂ or carbogen. Anesthesia was achieved by either adding 0.2-0.8% enflurane (Ethrane®, 0.40.8% during surgery and 0.20.4% during recordings) to the respired gas mixture or by a continuous intravenous application of 4-8 µg·kg⁻¹·hr⁻¹ sufentanil (Sufenta®, Janssen) with an initial dose of 5 µg·kg⁻¹. Our observations confirmed previous reports that marmoset LGN cells are more responsive when the animals were anesthetized with sufentanil in comparison with isoflurane anesthesia, which is an isomer of enflurane (Solomon, White, & Martin, 1999). To prevent eye movements, 5 mg·kg⁻¹·hr⁻¹ gallamine triethiodide (Flaxedil®) was administered intravenously. A warming blanket connected to a rectal probe was used to maintain the rectal temperature at 37.2°C. Depth of anesthesia was monitored by continuous recording of ECG and EEG.

The pupils were dilated with atropine sulfate (1%) and neosynephrine (5%). The eyes were refracted with contact lenses and focused on a tangent screen and the stimulus monitor at a distance of 114 cm. The contact lenses also protected the eyes against desiccation. Artificial pupils of 2-mm diameter were placed in front of the eyes.

A craniotomy was performed and a tungsten-in-glass electrode was lowered into the LGN. The layers from which we recorded were identified by the sequence of ocular input of the cells and from small lesions made at the end of the electrode track. After the experiments, the animals were sacrificed by an overdose of sodium pentobarbital (Nembutal®). Blood samples were obtained for genetic analysis. After perfusion, the brains were removed and prepared histologically to visualize the lesions.

The experiments were performed on 13 animals: 12 marmosets and one owl monkey. Among the marmosets, 8 animals (6 males, 2 females) were dichromats, 2 females were trichromats, and in 2 females the color vision phenotype could not be determined with certainty, but there was no indication of color opponent responses in PC-cells of these animals. In 9 marmosets (5 males and 4 females), the present alleles on the gene locus coding for the cone photopigments were determined by a genetic analysis of blood samples of each animal (Weiss, Kremers, & Maurer, 1998). In addition, the phenotype of the dichromats was determined electrophysiologically by searching for a silent substitution condition using the red and green phosphors of a computer controlled stimulus monitor (Weiss et al., 1998). One female owl monkey was used in the present experiments. The owl monkey is a monochromat without a polymorphism: S-cones are absent, and the single cone type is sensitive in the long- and middle-wavelength range.

The neuronal responses to achromatic stimuli described below do not demonstrate any dependency on the phenotype of the animals applied. It was shown that basic anatomical and physiological properties of PC- and MC-cell pathways (with the exception of those connected with color coding), at least on the retinal and LGN levels, in New World monkeys are very similar to those in the Old World monkeys (e.g., Kremers & Lee, 1998, Silveira, Yamada, Perry, & Picanço-Diniz, 1994, Wilder, Grunert, Lee, & Martin, 1996), suggesting that the features of early visual performance determined on marmosets may be reliably transferred to those present in humans. The cell properties of owl monkey retinal ganglion and LGN cells show basic differences (Usrey & Reid, 2000; Xu, Ichida, Allison, Boyd, Bonds, & Casagrande, 2001; Kilavik, Kremers, & Silveira, 2001). It is therefore interesting to compare the physiological properties of LGN cells in the marmoset and the owl monkey.

The experiments with each animal lasted between 2 and 4 days. A whole battery of stimuli was applied during these experiments. The present results are based on a subset of all obtained data.

**Visual stimuli**

The stimuli were displayed on the same computer controlled monitor as was used in the psychophysical measurements. The location of the receptive field (RF) center was determined with a bipartite field stimulus with identical but counter-phase 4 Hz modulation in the two hemifields. When the common border of the two hemifields is located in the middle of the RF, a sharp minimum in the response amplitudes or a frequency double response of the cells can be observed (Enroth-Cugell & Robson, 1966;
Kremers & Weiss, 1997; Lee, Kremers, & Yeh, 1998). Vertical and horizontal edges were used to determine the RF location in the horizontal and the vertical directions, respectively. The size of the center stimulus was determined by presenting a 4 Hz luminance modulation in a circular stimulus simultaneously with a counter-phase modulating annulus. At this temporal frequency, the RF center and surround respond approximately antagonistically. Owing to the counter-phase modulation in the surround stimulus, the response of the RF surround reinforces the RF center response. The size of the circular stimulus was changed to obtain a maximal response (as estimated from the audio output). The data points in Figure 1 depict the response amplitude of an on-center PC-cell as a function of the center stimulus size (Kilavik, Silveira, & Kremers, 2003): a maximum can be observed. It can be shown that with the spatial arrangement at maximal response, the center stimulus mainly stimulates the RF center and the surround stimulus mainly stimulates the RF surround (i.e., that an optimal separation of the RF subfield responses is achieved) (see “Appendix A”). Hence, the center and surround responses described in the rest of the work are the responses to the center and surround stimuli, respectively, and can be viewed as a good approximation of the responses of the RF center and surround.

The position of the RF and the optimal size of the center stimulus were checked regularly.

In the subsequent measurements, a stimulus similar to the reference stimulus in the psychophysical experiments was used. It consisted of a circular center stimulus that matched the RF center (as described above) and a surrounding field covering the rest of the RF. Unlike the reference stimulus in the psychophysical experiments, there was no gap between the central and surrounding subfields. The temporal frequencies in the two stimuli were identical (4, 8, or 24 Hz). The 24 Hz data were obtained as a part of a different series of recordings on a partially overlapping population of marmoset LGN neurons. No 24 Hz data were obtained in the owl monkey.

The mean luminance (66 cd/m2) and chromaticity of the stimuli were identical to those in the reference stimuli employed in the psychophysical measurements. We calculated that the total retinal illuminance in quanta per unit retinal area in the marmoset is about 4.9 times larger than in the human eye, and, therefore, is equivalent to about 1000 td. The total retinal illuminance in the owl monkey is about 2.3 times larger than in the human eye, and that is equivalent to approximately 480 td. The contrast in the center stimulus was 50%. The contrast in the surround stimulus was either 25% or 50%. The measurements at 24 Hz were performed only with 50% contrast surrounds. The contrasts were chosen to be high enough to result in a relatively large signal-to-noise ratio at all stimulus conditions.

Cell responses were measured to 12 different combinations of center and surround stimuli, in which the relative phase of the temporal modulation in the two stimuli was varied between -180° and +180° in steps of 30°. The different conditions were presented in a quasi-random order. In addition, responses were measured when only the center stimulus modulated and the surround was kept constant at the mean luminance, and when only the surround modulated while keeping the center stimulus steady at the mean luminance. At 24 Hz, no measurements to selective center and surround stimuli were performed. Assuming that response saturation is mainly contrast dependent, the influence of saturation on the results is probably relatively small because stimulus contrast is not altered within a series of experiments of stimuli with different relative phases. If series of experiments, in which different stimulus contrasts were used, are compared, then saturation might play a role. However, as described in “Results”, a change in contrast mainly influenced the measured response phases. This cannot be explained by saturation, which would only influence response amplitudes.

Figure 1. The response amplitude of an on-center PC-cell to a stimulus that consists of a sinusoidally modulating center and a counter-phase modulating surround stimulus. The response amplitude is given as a function of the size of the center stimulus. The temporal frequency was 4 Hz. There is an obvious maximum in the responses, at which the center stimulus mainly stimulates the RF center and the surround stimulus mainly stimulates the RF surround. Due to the counter-phase modulation in the center and surround stimuli and the antagonism between RF center and surround, the responses of the two RF subfields reinforce each other, leading to a response that is larger than the full-field response (0° center stimulus size or at very large center sizes). The center stimulus size at the maximal response (about 14 arcmin for the shown cell) was used in the subsequent measurements. The solid curve is a fit of a model, based on Gaussian responsivity profiles of the RF center and surround, to the data (Kilavik et al., 2003). The dashed curve is the difference between the response amplitude to the center stimulus and the response amplitude of the RF center (see “Appendix A”). Clearly, this difference is minimal near the maximal response of the cell, indicating that the stimulus indeed optimally separates RF center and RF surround contributions at this spatial stimulus arrangement.
Data acquisition

Spike occurrences were sampled at a rate of 2 kHz and stored on a CED 1401 data acquisition system (Cambridge Electronic Design Ltd.). Synchronization between the stimulus presentation and data acquisition was provided by TTL-pulses from the VSG-card, which were used to trigger the CED 1401. To avoid stimulus onset artifacts, the responses to the first period of stimulus presentation were disregarded. Spike occurrences were recorded during 6 s of stimulus presentation. During the measurements, the recording program constructed peristimulus time histograms (PSTHs) of the cells responses.

Results

Psychophysics

The subjects’ task in the psychophysical measurements was to set the contrast of the test stimulus so that the perceived flicker matched the perceived flicker strength in the center of the reference stimulus (see “Methods”). The equivalent contrast was defined as the physical contrast of the test stimulus when perceive flicker strengths matched. Figure 2 shows the equivalent contrast as a function of the phase difference between the center and surround modulation in the reference stimulus for a subset of the measurements performed with all three observers. The size of the center stimulus was 1°, and the contrasts in the center and in the surround stimuli were both 50%. The data are shown for the three different temporal frequencies. Generally, for the psychophysical data, it was found that the perceived flicker strength strongly depends on the relative phase between the center and surround stimuli. The perceived flicker strength was minimal at slightly positive relative phases (see Figure 2). This was found for nearly all conditions and all observers.

The curves displayed on the plots are fits of a model to the data points. Details of the model will be given below and discussed in relation with the physiological data.

The effects of the relative phase on the perceived flicker strength in the center stimulus are visualized in Movie 1. In

![Figure 2](https://jov.arvojournals.org/pdfaccess.ashx?url=/data/journals/jov/933506/)
the two demonstrations, the central and surrounding subfields are modulated sinusoidally at 4 Hz. The contrasts are 50% in both subfields. The observer should pay attention to the flicker in the center. The physical contrast in the central circle is identical in the two demonstrations (this can be appreciated when covering the surround stimulus). But in the left movie, the surrounding annulus is modulated in-phase relative to the modulation of the circle. The perceived flicker in the center is weak and less than the perceived flicker in a single circle modulated with the same physical contrast. Thus, the presence of the surround stimulus results in a lateral inhibition. In the right movie, counter-phase modulation is presented in the surrounding subfield. The perceived flicker in the center stimulus is stronger than that in a single modulating circle with the same contrast.

As it will be argued below, the physiological basis for the lateral interactions in the perception of flicker can be found in the receptive field properties of neurons in the retino-geniculate pathway.

**Electrophysiology**

The visual responses of 21 magnocellular (MC), 37 parvocellular (PC) and 9 koniocellular (KC) LGN cells in the marmosets and of 6 (2 PC and 4 MC) LGN cells in the owl monkey were recorded. Some of these cells were measured only with a subset of the stimuli. Original PSTHs of the responses of an on-center MC-cell in the marmoset LGN to the different conditions are displayed in Figure 3. The stimulus frequency was 4 Hz and the contrast in the surround stimulus was 50%. The cell response depends on the phase difference between the center and surround stimuli and is minimal when the two have similar phases. The responses are large when the absolute phase differences are large. These results qualitatively confirm the antagonism between the RF center and surround.

We have used two different approaches to express the response amplitudes. In the first approach, the PSTHs were Fourier analyzed. The amplitude and phase of the component at the stimulus frequency were used as estimates of the response amplitude (in spikes per second) and phase (in
degrees). Response phase delays relative to the center stimulus were given by negative values. Hence, the response of the cell can be linearized by extraction the linear component from a generally nonlinear PSTH and described as a vector with its length (denoting the response amplitude) and the angle with the positive x-axis (denoting the response phase).

The shapes of the responses displayed in Figure 3 are not completely sinusoidal. As a result, the first harmonic component might not always be a reliable approximation of the total response. Therefore, we performed a second analysis, in which a peak-to-trough detector was applied to the same PSTHs. In this algorithm, a 25-ms window slides over the actual PSTH with 1 bin steps. At each location of the window, the spike rate is calculated. The output of the peak-to-trough detector is the difference between the maximal and the minimal firing rate. Such an approach does not need the assumption of a sinusoidal response and might be a realistic model for a central detection mechanism that has a time constant comparable to the selected window size (Swanson, Ueno, Smith, & Pokorny, 1987; Kremers, Lee, Pokorny, & Smith, 1993). On the other hand, the response amplitudes are determined on the basis of 25-ms time windows within each PSTH and not on the basis of the complete PSTH. Hence, the output of the peak-to-trough detector is more variable than the first harmonic component.

In Figure 4, the response amplitudes of an on-center PC-cell and an on-center MC-cell are displayed as a function of the relative phase between the center and surround stimuli. The temporal frequency was 4 Hz and the contrast in the surround was either 25% or 50% (the PSTHs of the MC-cell responses to the latter condition are shown in Figure 3). Results for the two analyses are given. Both algo-

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**Figure 4.** Response amplitudes of an on-center PC- and an on-center MC-cell estimated using the 1st harmonics from the Fourier analysis of the PSTHs (upper row) and using a peak-to-trough detector algorithm (lower row) displayed as a function of the phase difference between center and surround stimuli. By definition, a positive phase difference indicates a phase lead of the surround stimulus. The data are given for two conditions (25% or 50% surround contrast). Center contrast is 50% and the temporal frequency is 4 Hz. Note that the responses of the MC-cell are larger than those of the PC-cell. Further, an increase of the surround contrast results in an increased phase at the minimal response (i.e., the curve is shifted rightward) without a clear change in shape of the curves, both in the PC- and MC-cells. If a change in surround contrast would alter cell response saturation, then a change in curve form would be expected. This is not the case, indicating that saturation does not influence the responses greatly.
rithms resulted in almost proportional amplitudes with the scaling factor of about 3; the results are well correlated (in the shown example: for the PC-cell, $r = 0.88$ and $p < .01$; for the MC-cell, $r = 0.81$ and $p < .02$). This was the case for the responses of all cells. Moreover, the subsequent calculations based on the two types of analysis yielded similar results. However, the results of the peak-to-trough detector were more variable. Therefore, in the subsequent sections, we present the data obtained with the Fourier analysis.

**Linear analysis**

To correlate the results of the LGN neurons recording with the psychophysical data, we first analyzed the response amplitudes. The response amplitudes of individual cells were averaged at each relative stimulus phase. The averages were obtained separately for the different cell types as well as for all neurons in the marmosets and the owl monkey. The mean response amplitudes for one condition (4 Hz, 50% surround contrast) are shown in Figure 5, plots A-D.

![Figure 5](https://jov.arvojournals.org/pdfaccess.ashx?url=/data/journals/jov/933506/)
Large differences in response amplitude between individual cells make the use of error bars in these plots not useful. To compensate for differences between individual cells, we normalized the response amplitudes in each cell to the maximal response encountered in the same cell. The averaged normalized response amplitudes of all marmoset cells are shown in Figure 5E. The correlation between the normalized and non-normalized average amplitudes in all sets of data is very high ($r \geq 0.99$ and $p < .001$). By directly averaging the responses, the cells with larger responses implicitly have a larger weight in the averages. It seems to be plausible that cells with larger responses may also have a larger weight in the generation of a percept. Because it was the purpose of the present study to compare the physiological responses with the psychophysical data, we preferred to use the averages of the non-normalized responses.

At all conditions, the mean response amplitude strongly depends on the relative phase difference in the stimulus. We assumed that the response to the combined stimulus represents a combination of the responses to the center and the surround stimuli. As stated above, each response can be described by a vector $\mathbf{r}$. Assuming a linear summation of the responses to the center $\mathbf{R}_c$ and surround $\mathbf{R}_s$ stimuli, the measured response may be expressed as a vector sum:

$$\mathbf{R} = \mathbf{R}_c + \mathbf{R}_s.$$  \hspace{1cm} (1)

The response amplitudes $|\mathbf{R}| = R$ can be expressed using the law of cosines (see Figure 6):

$$R = \sqrt{R_c^2 + R_s^2 - 2 \cdot R_c \cdot R_s \cdot \cos(S - P)},$$  \hspace{1cm} (2)

in which $R_c$ and $R_s$ are the center and surround response amplitudes, respectively; $S$ is phase difference between the center and the surround stimuli; $P$ is the phase difference between the center and surround stimuli at which the response amplitude is minimal. Figure 5 shows that $P$ is positive for all conditions. Thus, the surround stimuli had to be presented phase advanced relative to the center stimuli to obtain minimal response amplitudes.

Equation 2 was fitted to the data using the Solver routine of the Excel 98 program. The curves displayed in Figure 5 are the best fits. The estimated parameters result-

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Table 1. Average receptive field properties of the monkey LGN cells. The estimates of the center response amplitude, $R_c$, surround response amplitude, $R_s$, and the relative stimulus phase at the minimal response, $P$, obtained from the fits of Equation 2 to the mean response amplitudes of the marmosets’ PC- and MC-cells, as well as of all cells recorded in the marmosets and in the owl monkey to the combined stimuli. The data are given separately for the five stimulus conditions.

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<th>All cells, owl monkey</th>
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<tr>
<td>24 Hz 50%</td>
<td>29</td>
<td>14.2</td>
</tr>
</tbody>
</table>

Figure 6. The response $\mathbf{R}$ of a cell to a combined stimulus with relative phase $S$ between center and surround modulation is assumed to be the vector sum (Equation 1) of the center and the surround response ($\mathbf{R}_c$ and $\mathbf{R}_s$, respectively), which have an intrinsic phase difference $P$. The surround response depends on $S$; endpoints of the vectors $\mathbf{R}_s(S)$ lie on the dashed circle. The lengths $R$, $R_c$, and $R_s$ of the corresponding vectors can be banded together by the law of cosines (Equation 2).
ing from the fits of Equation 2 to the average cell data are given in Table 1 for all stimulus conditions, separately for PC- and MC-cells in the marmoset and lumped for all cells in the marmoset and the owl monkey.

At all temporal frequencies and for all cell types, the amplitudes of the surround response $R_s$ are larger when the contrast in the surround is larger. Further, all estimates for $R_c$ and three estimates for $R_s$ are larger for MC-cells than for PC-cells. Furthermore, on average the LGN neurons in the owl monkey respond more vigorously (and have larger values of $R_c$ and $R_s$) than those in the marmoset.

As noted above, the values of $P$ are generally positive, resulting in a rightward shift of the fitted curve and indicating that the responses are minimal when the surround stimulus leads the center stimulus. This indicates that the response of the RF surround lags the response of the RF center. In the owl monkey, the phases at the minimal response are generally smaller than in the marmoset.

A similar simple linear model can be used to describe the psychophysical data. Most probably, the central and the surrounding subfields of the stimulus contribute to the perception of flicker in the center of the combined stimulus. Assuming that the linear addition is also applicable to the psychophysical data. Most probably, the central and the surround perception of flicker in the center of the combined stimulus.

The curves displayed in Figure 2 are the best fits of Equation 2 to the psychophysical data. In some conditions there were ranges of relative phases in the reference stimulus, in which no flicker was perceived in the center. At these phases, the equivalent contrast was identical with the flicker detection threshold. However, we ignored the threshold effects in the fits because the influence on the fits was relatively small. Similar to the data shown in Figure 2, all other psychophysical data could be described satisfactorily by Equation 2. In some cases (particularly at 4 Hz), the fits could be improved by introducing a saturating nonlinearity. However, the improvement was only marginal and the fit parameters would not be directly comparable anymore with those obtained from the physiological data. We therefore did not include saturation in the fits.

The fits were well constrained by the psychophysical data if the modulation of the equivalent contrast as a function of the relative phase was large enough in comparison with the variability within each data point. We therefore ignored the estimates from those fits in which the difference between the estimated maximal and the estimated minimal equivalent contrast was less than 3 times the average of the standard deviations at all data points. As a result, all estimates could be used for subjects VK and JK. For subject BEK, the results obtained with all 20 Hz stimuli and one 8 Hz stimulus (1° diameter 50% center and 25% surround) were disregarded. Parameters resulting from the fits of Equation 2 to the psychophysical data of each subject were averaged. Table 2 displays these data separately for all stimulus conditions.

Note that there is a qualitative similarity between the psychophysical and physiological data, not only because Equation 2 gives a satisfactory fit to both sets of data, but also because the response amplitudes and the perceived flicker strengths are both minimal at positive relative phases. However, the estimated values of $P$ are on average larger in physiology than in psychophysics (cf., Tables 1 and 2). This issue will be addressed in the “Discussion.”

### Table 2

<table>
<thead>
<tr>
<th>Center size</th>
<th>Temporal frequency</th>
<th>Surround contrast</th>
<th>Center contrast 25%</th>
<th>Center contrast 50%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>$R_c$ (%)</td>
<td>$R_s$ (%)</td>
</tr>
<tr>
<td>1°</td>
<td>4 Hz</td>
<td>25%</td>
<td>42.2</td>
<td>24.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50%</td>
<td>48.1</td>
<td>34.2</td>
</tr>
<tr>
<td></td>
<td>8 Hz</td>
<td>25%</td>
<td>34.4</td>
<td>22.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50%</td>
<td>30.3</td>
<td>27.0</td>
</tr>
<tr>
<td></td>
<td>20 Hz</td>
<td>25%</td>
<td>37.8</td>
<td>16.7</td>
</tr>
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<td></td>
<td></td>
<td>50%</td>
<td>31.7</td>
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</tr>
<tr>
<td>0.4°</td>
<td>4 Hz</td>
<td>25%</td>
<td>47.9</td>
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</tr>
<tr>
<td></td>
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<td>53.5</td>
<td>34.6</td>
</tr>
<tr>
<td></td>
<td>8 Hz</td>
<td>25%</td>
<td>36.0</td>
<td>23.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50%</td>
<td>37.2</td>
<td>27.0</td>
</tr>
</tbody>
</table>

Table 2. Psychophysically measured characteristics of flicker perception in the central stimulus. The averaged estimates of the contributions of the center ($R_c$) and surround ($R_s$) stimuli to the perceived flicker strength in the center and the relative stimulus phase at the minimally perceived flicker strength ($R$) obtained from the fits of Equation 2 to the individual psychophysical thresholds. The data are given separately for 20 different stimulus conditions.
Influence of contrast

In Figure 7, the estimates of $R_c$, $R_s$, and $P$ obtained from the electrophysiological recordings and their psychophysical equivalents are displayed as a function of surround contrast. The center contrast was 50% and the temporal frequencies were 4 Hz and 8 Hz. The physiological data points represent the fitting parameters of the Equation 2 to the average responses of all LGN cells, plotted separately for the marmoset and the owl monkey. The results of the fits to the measurements with the different sizes of the stimulus center (1° and 0.4° diameter) are plotted separately. The results of the psychophysical measurements with 25% center contrast are not shown, but they are qualitatively similar to those with 50% center contrast.

Figure 7A and 7D show that the contribution of the center stimulus to the cell response amplitude, and the psychophysically measured perceived flicker strength is larger when the contrast in the surround is smaller. Furthermore, $R_c$ of psychophysical and physiological data decrease slightly as the temporal frequency increases. Figure 7B and 7E show the estimates of the surround stimulus contribution, $R_s$, as a function of the surround contrast. For both physiological and psychophysical data, this value increases with increasing surround contrast.

Finally, the estimates of the relative surround phase at the minimal cell response or the minimally perceived flicker strength are displayed Figure 7C and 7F. Again, there are important qualitative similarities between the physiological and the psychophysical data. First, almost all phase shifts are positive, indicating that the surround response lags the center response. Second, an increase of the surround contrast results in an increased phase shift (especially in the physiological data; see also Figure 4). The influence of surround contrast on $P$ cannot be explained on the basis of a linear model as described by Equation 1. Apparently, nonlinearities influence the physiological and the psychophysical data when surround stimulus contrast is changed. In the next section, we explore a possible source of these nonlinearities.

Figure 7. The estimated amplitudes of the center (A and D) and surround (B and E) responses expressed in spike per second for the cell data (closed squares for the marmoset cells and open squares for the owl monkey data) and equivalent contrasts for the psychophysical data (closed circles for 1° center stimulus size; open circles for 0.4° center stimulus size) as a function of contrast in the surround stimulus. C and F display the phase difference between center and surround responses at minimal response or minimal perceived flicker strength as a function of the surround stimulus contrast. The center stimulus contrast is 50% and temporal frequency is 4 Hz (top panels) and 8 Hz (lower panels).
Nonlinearities in the physiological data

The analysis described below was performed on the responses recorded at 4 and 8 Hz temporal frequencies from 11 MC, 18 PC, and 2 KC-cells of 6 marmosets (a subset of LGN neurons used in the above described linear analysis). Basically, the contributions of the RF center and the RF surround to responses to the combined stimuli were extracted and compared with the responses to selective center and surround stimulation.

In Figure 8A, the characteristics of the same responses as shown in Figure 3 are displayed as vectors in a polar plot, in which the response amplitude is encoded by the distance to the origin and the response phase by the angle with the positive x-axis. By definition, positive phases and phase advances are indicated by angles in the counter-clockwise direction. The closed symbols represent the actual measurements at corresponding surround stimulus phases. Obviously, the latter has a systematic influence on the measured responses. Obvi-
sously, the latter has a systematic influence on the measured responses of the cell. The vectors labeled \( \vec{R}_C \) and \( \vec{R}_S \) are the responses to exclusive center and surround stimuli, respectively.

It is possible to extract the center response to the combined stimuli by adding the responses to two combined centersurround stimuli with surround phases 180° apart (Shapley & Victor, 1979). An example of the predictions is given in Figure 8A. The center response can be estimated as follows:

\[
\vec{R}_C^* = \frac{1}{2} \left[ \vec{R}(S) + \vec{R}(S + 180°) \right]
\]  

(3)

Note that \( \vec{R}_C^* \) is the predicted center response in the presence of a simultaneous response in the surround, whereas \( \vec{R}_C \) is the measured center response without a surround response. There were six pairs of combined center-surr
ound stimuli for which the surround phases were 180° apart, enabling six estimates of \( \vec{R}_C \) (given by the open circles in Figure 8A). Similarly, six estimates of the surround response in the presence of a center stimulus can be predicted from:

\[
\vec{R}_S^*(S) = \frac{1}{2} \left[ \vec{R}(S) - \vec{R}(S + 180°) \right]
\]  

(4)

The surround response for each pair of combined responses is phase shifted by 90° degrees. In the final prediction, we corrected for this phase shift. These surround responses are displayed by the open triangles in Figure 8A. Observe that \( \vec{R}_S^* \) is the predicted surround response in the presence of a center response. \( \vec{R}_S^* \) is the measured surround response with no stimulation in the center. The estimates of \( \vec{R}_C \) and surround \( \vec{R}_S \) from one pair of responses to combined stimuli (with center and surround stimuli phase differences of 90° and -90°, respectively) are marked with an asterisk. To visualize the differences between \( \vec{R}_C^* \) and \( \vec{R}_C \), we added the PSTHs to the two conditions and halved them to obtain a PSTH correspond-
ing to \( \vec{R}_C^* \). The two PSTHs were subtracted, halved, and shifted by 90° to obtain a PSTH corresponding to \( \vec{R}_S^* \). The corresponding PSTHs are shown in Figure 8B. Although this procedure is not identical with the vector addition and subtraction procedures (because the PSTHs are not only determined by the first harmonics but also by higher harmonics introduced, e.g., by rectifying nonlinearities), it is a good approximation. Obviously, there are only minor differences between the center responses in the presence and absence of a response in the surround. However, the sur-
round response in the presence of a center response is sub-
stantially smaller and phase advanced in comparison with the surround response without a response in the center, indicating that linear superposition fails especially for the RF surround.

The vector averages of the six estimates of \( \vec{R}_C^* \) and \( \vec{R}_S^* \) were calculated and displayed in Figure 8A as vectors labeled \( \vec{R}_C \) and \( \vec{R}_S \), respectively. A difference between \( \vec{R}_C \) and \( \vec{R}_C^* \) and between \( \vec{R}_S \) and \( \vec{R}_S^* \) is caused by the presence or absence of the response in the complementary part of the RF. For this cell, the amplitudes of \( \vec{R}_C \) and \( \vec{R}_S \) are smaller than those of \( \vec{R}_C^* \) and \( \vec{R}_S^* \), respectively. The influence of the presence of a surround response on the phase of the center response is negligible because \( \vec{R}_C \) and \( \vec{R}_C^* \) have similar phases. But, the response of the receptive field surround has become phase advanced in the presence of a center response (\( \vec{R}_S \) is phase advanced relative to \( \vec{R}_S^* \)). In spite of this phase advance, the surround response to the combined stimuli (\( \vec{R}_S \)) is not completely 180° out of phase with the center response (\( \vec{R}_C \)), indicating that the surround response still lags the center response.

We calculated logarithms of the ratios between the measured and mean predicted response amplitudes for the RF centers and surrounds, \( \log \left[ \left| \vec{R}_C^* \right| / \left| \vec{R}_C \right| \right] \) and \( \log \left[ \left| \vec{R}_S^* \right| / \left| \vec{R}_S \right| \right] \), respectively. The logarithms were used to obtain a normal distribution of the individual cell data. Positive values indicate that the response amplitude in the center or the surround has decreased in the presence of a response in the complementary part of the RF. Furthermore, the phase differences between \( \vec{R}_C \) and \( \vec{R}_C^* \) and between \( \vec{R}_S \) and \( \vec{R}_S^* \) were calculated. Positive values of that difference indicate that the response of the center or the surround has become phase advanced in the presence of a response in the complementary part of the RF.

The results for each cell type and lumped for all cells are given in Figure 9 for one stimulus condition (4 Hz, 25% surround contrast). The arrows in the plots denote the means of the changes, which are also given in Table 3 for all four stimulus conditions. We did not observe an obvious difference in the amplitude and phase changes between MC- and PC-cells. The lumped data for all cells show that the presence of a stimulus in the surround leads to a signi-
ficant (t test: \( \alpha(2) < 0.01 \), except one condition) decrease in center response amplitude, resulting in positive values of

\[
\frac{\vec{R}(S)}{\vec{R}(S + 180°)} = \frac{\vec{R}(S)}{\vec{R}_S(S)}
\]
Figure 8. A. Polar plot of the same responses as those shown in Figure 3. The responses to combined stimuli are displayed as vector end points (closed circles; with indication of the phase difference between the center and surround stimuli). Length of the vector depicts the response amplitude, and an angle between the vector and the positive x-axis encodes the response phase. Vectors labeled \( \mathbf{R}_C \) and \( \mathbf{R}_S \) indicate the responses to selective stimulation of the receptive field center and surround respectively. The open circles and triangles represent vector end points of \( \mathbf{R}_C' \) and \( \mathbf{R}_S' \). These responses are obtained by adding (for the center responses) or subtracting (for the surround responses; see text) pairs of response vectors in which the stimulus phases in the surround are 180° apart. In total, six estimates of \( \mathbf{R}_C \) and \( \mathbf{R}_S \) are obtained. Observe that these estimated responses do not differ strongly from each other (with small but systematic variations between the different estimates of \( \mathbf{R}_S' \)). Vectors labeled \( \mathbf{R}_C' \) and \( \mathbf{R}_S' \) depict the averages of the six estimates of \( \mathbf{R}_C \) and \( \mathbf{R}_S' \), respectively, and indicate the responses of the center and surround in the presence of a response in the other subfield. Thus, the difference between the vectors \( \mathbf{R}_C \) and \( \mathbf{R}_C' \) gives the influence of the presence of a surround response on the center response. The presence of a surround stimulus decreases the center response amplitude moderately and has no significant effect on the center response phase. On the other hand, the difference between the vectors \( \mathbf{R}_S \) and \( \mathbf{R}_S' \) gives the influence of the presence of a center response on the surround response. In the shown cell, the presence of a center response results in a decrease and a phase advance (counter-clockwise rotation) of the surround response. B. Measured PSTHs to selective center (left panel) and the surround (right panel) stimulation (same as the two top panels in Figure 3). An illustration of the center and surround response predictions from a pair of responses to the combined stimuli (with the +90° and −90° surround stimulus phases) using the above described procedure is displayed by thick lines. The predictions correspond to \( \mathbf{R}_C \) and \( \mathbf{R}_S \) marked by asterisks in Figure 8A.
Figure 9. Summary of the effects of the presence of a response in the complementary subfield on the response properties of the center and surround at one stimulus condition: 4-Hz temporal frequency, 50% contrast in the center, and 25% contrast in the surround. For this condition, data of 16 PC-, 9 MC-, and 2 KC-cells were considered. The data have approximately Gaussian distributions and averages can be calculated (given by the arrows below the plots). A. Influence of the presence of a surround response on the amplitude of the center response, estimated by \( \log \left( \frac{|R_C|}{|R_S|} \right) \). Positive values indicate a decrease in the response amplitude owing to the presence of the response in the surround. Generally, the center response decreases slightly in the presence of a surround response (see also Table 3). There are no significant differences between PC-, MC-, and KC-cells. B. Effects of presence of a surround response on the phase of the center response. A positive phase difference between \( \Delta \gamma \) indicates a phase advance in the center responses owing to the presence of surround response. The phases of the center responses are not altered by the presence of a surround response (see also Table 3). Lower panels. Influence of the presence of a center response on the amplitude (C) and phase (D) of the surround response. The data are presented in the same formats as in the corresponding plots A and B. C. Although the mean surround response amplitudes do not change largely in the presence of a center response (see also Table 3), the distribution of differences is broad, indicating that the presence of a center response can result in large response decreases in some cells and large response increases in others. D. The presence of a center response results in a significant phase advance of the surround response (see also Table 3).

<table>
<thead>
<tr>
<th>Conditions</th>
<th>PC-cells</th>
<th>MC-cells</th>
<th>All cells</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Center</td>
<td>Surround</td>
<td>Center</td>
</tr>
<tr>
<td>4 Hz</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25%</td>
<td>0.13</td>
<td>-2.67</td>
<td>0.11</td>
</tr>
<tr>
<td>50%</td>
<td>0.10</td>
<td>-0.85</td>
<td>0.13</td>
</tr>
<tr>
<td>8 Hz</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25%</td>
<td>-0.02</td>
<td>0.76</td>
<td>0.02</td>
</tr>
<tr>
<td>50%</td>
<td>0.05</td>
<td>-0.44</td>
<td>0.05</td>
</tr>
</tbody>
</table>

Table 3. Mean changes in the receptive field properties of the marmoset LGN cells due to the presence of a response in the complementary subfield.
log \left( \frac{|\overline{R}_c|}{|\overline{R}_s|} \right) \), of about a factor of 1.3, and has no effect on the center response phase (see Table 3). The effects of the presence of a center response on the surround response are more pronounced. Although the average change in response amplitude is relatively small, there are large differences between individual cells resulting in large standard deviations of \( \log \left( \frac{|\overline{R}_c|}{|\overline{R}_s|} \right) \) (Figure 9C). For some cells the surround response amplitude changes substantially in the presence of a center stimulus, but this change can be either an increase or a decrease. An example of the latter case is shown in Figure 8. Moreover, the surround response on average becomes phase advanced between 10 and 30 deg owing to the presence of a center response (Table 3); these phase changes are significantly different from zero (t test; \( \alpha(2) < 0.001 \)).

The cell used for Figures 3 and 8 is a relatively typical example for the magnitude of the changes in responses, because the estimated changes in the response properties of this cell are close to the averages, with the exception of the decrease in surround amplitude, which was not present in all cells. However, such amplitude decreases were not uncommon.

The phase advance of the surround response due to the presence of the center response is larger when the contrast in the surround stimulus is smaller (see Table 3). This difference was significant for MC-cells (two-factor ANOVA, F-test: \( \alpha(2) < 0.05 \)), but only marginal for PC-cells because of larger variation between individual cells. Nevertheless, generally the surround phase lag relative to the center response will be smaller when contrast in the surround stimulus is smaller. This is in agreement with the results of the above described linear analysis based on the response amplitudes (see Figure 7C and 7F; Figure 4).

The results of the vector analysis and the linear amplitude analysis can be directly compared because the parameters in Equation 2 correspond to \( |\overline{R}_c|, |\overline{R}_s| \) and the phase difference between \( \overline{R}_c \) and \( \overline{R}_s \). We performed the vector analysis and the linear analysis on the data of individual cell types (MC-, PC- and KC-cells) and found a strong correlation between the parameters estimated with the two methods: for phase lags \( 0.81 < r < 0.97, \alpha(2) < 0.002 \); for center amplitudes \( 0.96 < r < 0.995, \alpha(2) < 0.001 \); and for surround amplitudes \( 0.93 < r < 0.98, \alpha(2) < 0.001 \) (r was calculated for the four stimulus conditions). From this, we conclude that the response amplitudes are sufficient to obtain reliable estimates of center and surround response amplitudes and of the phase difference between them. But, the vector analysis additionally enables the estimation of the absolute center and surround response phases and can identify more clearly the nonlinear interactions within the RF.

### Discussion

The present study shows that the responses of LGN cells depend on the relative phase between the center and surround stimuli. Similar to the cell responses, the perceived flicker strength in the center of a combined stimulus depends on the relative phase. The modulation of the response amplitude and the perceived flicker strength is not caused by an influence of stray light from the surround, because stray light would decrease the contrast in the central circle when the center and surround stimuli are modulated in counter-phase, resulting in a reduced response or a decrease in the perceived flicker strength. The actual responses show the opposite effect, indicating that if stray light has an influence, it is overruled by neuronal interactions. Moreover, stray light effects cannot explain the presence of the described nonlinearities.

### Comparison with other types of lateral interactions

To our knowledge, this is the first study showing that the relative phase between the center and surround stimuli influences the perceived strength of flicker in the center, although the phenomenon has been mentioned briefly (DeValois et al., 1986). In the literature, many types of lateral interactions are described. These mainly involve brightness induction, influences of surround adaptation, and changes in the perceived spatial contrast of stimuli (usually gratings). There are several indications that suggest that the interactions between the responses to the center and the surround stimuli described in the present study involve a separate mechanism.

Brightness induction (DeValois et al., 1986; Rossi & Paradiso, 1996; Rossi, Rittenhouse, & Paradiso, 1996; Rossi & Paradiso, 1999) involves a change in the perceived brightness in a static field caused by a modulation in the surrounding area. Instead of changes in the static mean brightness, the effects described in the present work involve a modulation of the perceived dynamic flicker strength. Brightness induction is also perceptually dissociated from flicker perception (DeValois et al., 1986). The physiological basis of brightness induction probably resides in the visual cortex. The responses of LGN cells do not show the effects necessary for brightness induction (Rossi et al., 1996).

It has been found that the threshold for flicker perception may be influenced by the state of adaptation in a surround (e.g., Eisner 1994, 1995). In the experiments presented here, the time averaged luminance and chromaticity of the two subfields were constant in all measurements. Therefore, the changes in perceived flicker strength, described in the present work, are caused by the temporal modulation in the stimuli, rather than a change in the state of adaptation.
Detection thresholds of spatial gratings can be influenced by the presence of a spatially inhomogeneous surrounding (Ejima & Takahashi, 1985; Cannon & Fullenkamp, 1991; Cannon & Fullenkamp, 1993; Polat & Sagi, 1993; Takeuchi & DeValois, 2000; Xing & Heeger, 2000). Thus, the perception of spatial properties of a stimulus can be influenced by lateral interactions. In contrast, we present data on the influence of lateral interactions on the perception of temporal features of a stimulus.

Our data are to some extent comparable with those of Singer and D'Zmura (1994, 1995). They found that a temporal modulation of spatial noise in an annulus induces a modulation of perceived spatial contrast in a center stimulus. The perceived modulation is nulled by adding a modulation to the center stimulus that is given in phase with the inducing stimulus. In agreement with our data, they also observed that a modulation in the surround induces a perceived modulation in a stationary center stimulus. However, they found stronger effects of temporal frequency of luminance modulation in the surround on the induced flicker strength in the center than we do (see Table 2). Moreover, unlike our data, they found that the temporal frequency of achromatic inducing stimuli does not strongly influence the phase difference between center and surround stimuli for an optimal null. Therefore, we think that their results might involve a different mechanism.

**Physiological processes**

The response amplitudes to the combined stimuli, in which the physical properties of the center and surround are not altered, can be described well by a linear summation of the responses to the center and surround stimuli (Equation 2; see Figure 5). Identical models have been used previously for describing responses in retinal ganglion cells and LGN neurons (Enroth-Cugell et al., 1983; Dawis et al., 1984; Frishman et al., 1987; Smith et al., 1992; Lee et al., 1998; Kremers & Weiss, 1997). However, our data show that a linear model is not adequate to describe the changes in lateral interactions in the RFs of LGN cells when the responses to the combined stimuli were compared with the responses to selective center or surround stimulation or with the responses to combined stimuli using a different surround contrast. Thus, it seems that the response properties can be considered to be quasi-linear if contrast in the stimulus is kept constant. But, nonlinear mechanisms may become apparent when the stimulus strength and/or the response amplitude in one of the RF subfields is altered. We believe that the contrast dependent nonlinearity is not related to saturation or to a contrast gain control mechanism (Shapley & Victor, 1978; Benardete, Kaplan, & Knight, 1992; Yeh et al., 1995; Kremers, Weiss, & Zrenner, 1997) because an increased contrast results in a decreased response phase, whereas a saturating nonlinearity would not involve phase changes and the contrast gain control would be expected to result in a positive correlation between contrast and response phase.

Clearly, the surround responses generally lag the center responses at all conditions. The average phase lag increases when the temporal frequency increases from 4Hz to 24Hz (Table 1). The data suggest that a fixed time delay of between 6 and 8 ms may generally account for the surround phase lag. This value is similar to those obtained by others (Smith et al., 1992; Benardete & Kaplan, 1997a; Kilavik et al., 2003). However, the responses to selective stimuli displayed much longer surround delays of about 20-30 ms. These values were more similar to those found by Enroth-Cugell and Lennie (1975) and Winters and Hamasaki (1976) in cat retinal ganglion cells. Winters and Hamasaki presented a temporal step stimulus in the RF surround followed by a temporal step assessed in the RF center. They found that the surround response maximally inhibited the center response when it was presented between 7 and 38 ms prior to the center stimulus. With this configuration, the surround is selectively stimulated. Their data therefore suggest that indeed the response phase difference may be larger with selective stimulation. However, Enroth-Cugell and Lennie (1975) found a 10-30 ms relative delay with combined center and surround stimulation.

The center response is not strongly influenced by the presence of a surround response except for a slight decrease in its amplitude. This result is in contrast with previous data on cat and macaque retinal ganglion cells (Shapley & Victor, 1979; Benardete & Kaplan, 1997b, 1999) where it was found that mainly the center response was attenuated and phase advanced due to the presence of surround modulation. Furthermore, they found that mainly the center responses in cat Y-cells and macaque M-cells were effected, whereas the nonlinearity described in the present study can be observed in all marmoset LGN cells. The observed small decrease in mean response amplitude of the center when simultaneously stimulated by a surrounding annulus may originate in the stimulation of an inhibitory extra-classical RF (Solomon, White, & Martin, 2002; Webb, Tinsley, Barraclough, Easton, Parker, & Derrington, 2002).

It is very difficult to give a complete quantitative explanation of the nonlinearities that makes use of known physiological properties of the retina and the LGN. Nevertheless, a mechanism that possibly mediates some of the described nonlinearities can be identified. The LGN cells can operate in two modes, depending on the resting potential (for reviews, see Sherman, 1996; Sherman & Guillery, 1996). The change in response mode is a typical property of thalamic cells and might explain why the data are different with those obtained from retinal ganglion cells. The burst component appears in the responses at low and medium temporal frequencies (usually lower than 10Hz) and is phase advanced relative to the tonic response (Guido, Lu, & Sherman, 1992; Smith, Cox, Sherman, & Rinzel, 2000). Assuming that with simultaneous stimulation of the center and the surround the cell is hyperpolarized and consequently in a burst mode and that the cell is in a tonic mode when the center is not stimulated, the phase changes in the
The present data analysis is based on the first harmonic components in the responses. Although these components are indeed the largest components in the responses, the above described and other nonlinearities might also introduce higher harmonics in the response. A more detailed description of the physiological processes possibly should also consider the higher harmonics.

Although the RF center and surround responses summate similarly in marmoset MC- and PC-cells, the averaged response amplitudes show that MC-cells respond more vigorously than PC-cells to the luminance stimuli. This is in accordance with the previously described larger responses and contrast gains of marmoset LGN cells (Kremers et al., 1997; Solomon, White, & Martin, 1999), of macaque retinal ganglion cells (e.g., Kaplan & Shapley, 1986; Lee, Pokorny, Smith, Martin, & Valberg, 1990), and of macaque LGN cells (e.g., Kaplan & Shapley, 1982; Croner & Kaplan, 1995) to luminance stimuli. But, as was observed before (Kremers et al., 1997), the response amplitude differences are generally smaller than in the macaque retina.

In comparison with the marmoset, the response amplitudes of the owl monkey LGN cells were larger. Furthermore, they were more strongly modulated by the relative phase between the center and surround stimuli. This is possibly related to the larger RFs and the stronger rod driven signals in the owl monkey (Usrey & Reid, 2000; Xu et al., 2001; Kilavik et al., 2001). However, our data indicate that the center-surround interactions are similar in marmoset and owl monkey LGN cells suggesting that it involves a mechanism that is generally present in anthropoid primates.

**Correlation between physiology and psychophysics**

The physiological and psychophysical data clearly show many qualitative similarities. First, the response amplitudes and the perceived flicker strength in the center stimulus are both modulated by the phase difference between center and surround stimuli. Second, the modulation of the two can be described on the basis of a linear vector addition model described by Equation 2 (see Figure 2 and Figure 5). Third, the center amplitudes estimated from the psychophysical and the physiological data both decrease with increasing temporal frequency (cf., plots A and D in Figure 7). Fourth, the center amplitude decreases when the contrast in the surround increases (Figure 7A and 7D). Fifth, the psychophysical and physiological surround response amplitudes do not change strongly when the temporal frequency is changed between 4 and 8 Hz and the surround amplitude is larger when the contrast in the surround stimulus is larger (see Figure 7B and 7E). Sixth, both in the physiological and the psychophysical data, the surround stimulus has to be presented phase advanced to give a minimal response or a minimally perceived flicker strength, indicating that the RF surround response lags the center response (see Figure 2, and Figure 5 and Figure 7C and 7F). Finally, the relative phase between the center and surround responses increases with increasing contrast in the surrounding annulus (Figure 7C and 7F).

From these similarities between the psychophysical and the physiological data, we conclude that the physiological basis for the perception of flicker in the center stimulus probably resides in the retino-geniculate pathway. Hence, the center-surround organization of the receptive fields as well as possible interactions between their responses can be retraced in flicker perception.

But the physiological and psychophysical data display also some quantitative differences. For instance, the relative phases for a minimal response are generally larger (particularly in the marmoset) than those for a minimally perceived flicker strength. Furthermore, these phases depend more strongly on the surround contrast in the physiological data. For an explanation of these differences, it is probably important to consider that a visual percept is not based on the responses of a single cell. A stimulus is projected on an array of retinal ganglion cells. It is necessary to study all responding cells, including those for which the sizes of the stimulus and the RF do not match, and an effect of displacement between the stimulus and the RF should be taken into consideration. Preliminary data show (Kremers & Kozyrev, 2003) that the differences in response amplitudes of individual cells in an array of stimulated cells increases with increasing phase differences between center and surround stimuli. If the phase difference is zero, then the stimulus is a full field stimulus and all cells completely covered by the stimulus respond in a similar manner. When the phase difference in the stimulus is large, then there will be cells that respond vigorously and others that will hardly respond. A cortical mechanism, the output of which is proportional to the maximal response difference in the array of responding LGN cells, may link the LGN data to the psychophysical data. The influence of other factors, such as retinal eccentricity, size of the surround stimulus, and the differences between the parvocellular, magnocellular, and koniocellular pathways may play additional roles. Finally, it is important to know how the brain processes the responses of such cell arrays.

**Conclusions**

The percept of flicker strength in a center stimulus is influenced by the relative phase of modulation in a surround stimulus. The response amplitudes of LGN neurons depend in a comparable manner on the relative phase between the modulation in the center and surround stimuli. The contrast in the surround stimulus also has a similar effect on the psychophysical and the physiological data. These similarities suggest that the physiological basis of the perceived flicker strength in the center stimulus is already present in the retino-geniculate pathway. Furthermore, we were able to describe a new type of contrast dependent nonlinear interaction between RF center and surround.
Appendix A

Although the combined stimuli used in the physiological experiments, described in the present work, were carefully chosen to match the position and size of the cell's RF, it should be noted that such stimuli do not isolate completely the responses of the RF center and surround. Nevertheless, using a linear model of the RF (described in Kilavik et al., 2003), it can be shown that at a point where the radius of the circular stimulus is optimally selected (see “Methods” and Figure 1), the responses to the central and surround stimuli are closely approaching, respectively, the responses of the center and the surround of the cell's RF.

The model assumes Gaussian responsivity profiles of the cell's RF center and surround and a phase delay between the RF center and surround responses. Generally, each subfield of the combined stimuli contributes to the responses of both the RF center and surround:

\[ \bar{R}^C = \bar{R}^C_G + \bar{R}^C_S; \quad \bar{R}^S = \bar{R}^S_G + \bar{R}^S_S. \]

The total response, \( \bar{R} \), of the cell is a vector addition of the RF center (\( \bar{R}^C \)) and surround (\( \bar{R}^S \)) responses and, on the other hand, also of the responses to the center (\( \bar{R}^C \) and surround (\( \bar{R}^S \)) stimuli, as in the Equation 1

\[ \bar{R} = \bar{R}^C + \bar{R}^S = \bar{R}^C_G + \bar{R}^C_S + \bar{R}^S_G + \bar{R}^S_S = \bar{R}^C + \bar{R}^S. \]

Each vector component of this equation as well as the total response depends on the center stimulus size. To adjust the center size, we modulate the center and surround stimuli in counter-phase and look for maximum of the total response. The solid curve in Figure 1 is a fit of the model to the response amplitudes of a PC-cell (Kilavik et al., 2003; although only the response amplitudes are displayed here, the response phases were also used). The dotted curve on the same plot represents the modeled differences between \( \bar{R}^C \) and \( \bar{R}^C \) or \( \bar{R}^S \) and \( \bar{R}^S \) in the vector plane. Owing to the linearity,

\[ | \bar{R}^C - \bar{R}^C | = | \bar{R}^S - \bar{R}^S |. \]

One may see that the difference calculated at the optimal center radius ropt is very close to the minimum and for the given cell is about 4.6% of the response amplitude at this center size. Within the actual range of conditions, this discrepancy does not exceed 10%. Thus, indeed \( \bar{R}^C \) and \( \bar{R}^S \) are good approximations of the responses of the RF center and surround, respectively.

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References


