

THE EFFECT OF ORIENTATION ADAPTATION ON RESPONSES OF LATERAL GENICULATE NUCLEUS NEURONS WITH HIGH ORIENTATION BIAS IN CATS

X. YE,^a G. LI,^a Y. YANG^a AND Y. ZHOU^{a,b*}

^aHefei National Laboratory for Physical Sciences at Microscale, School of Life Science, University of Science and Technology of China, Hefei, Anhui 230027, P R China

^bState Key Laboratory of Brain and Cognitive Science, Institute of Biophysics, Chinese Academy of Science, Beijing 100101, P R China

Abstract—Adaptation to stimulus orientation is assumed to have a cortical basis, but few studies have addressed whether it affects the activity of subcortical neurons. Using single-unit recording, we studied the effects of orientation adaptation on the responses of lateral geniculate nucleus (LGN) neurons with high orientation bias (OB) in anesthetized and paralyzed cats. Following adaptation to one stimulus orientation, the response at the adapting orientation was decreased, and the preferred orientation was shifted away from the adapting orientation. This phenomenon was similar to the effects observed for orientation adaptation in the primary visual cortex (V1), and was obvious when the adapting orientation was at an appropriate location relative to the original preferred orientation. Moreover, when the V1 was inactivated, the response at the adapting orientation was also decreased but the preferred orientation did not show a systematic shift after orientation adaptation in LGN. This result indicates that cortical feedback contributes to the effect of orientation adaptation on LGN neurons, which have a high OB. These data provide an example of how the corticothalamic loop modulates the processing of visual information, and suggest that the LGN is not only a simply passive relay but also a modulator of visual information. © 2009 IBRO. Published by Elsevier Ltd. All rights reserved.

Key words: adaptation, orientation bias, the lateral geniculate nucleus, feedback.

Adaptation is a common phenomenon in the visual system. It has been found in the retina of salamanders (Baccus and Meister, 2002), the lateral geniculate nucleus (LGN) of cats and monkeys (Shou et al., 1996; Yang et al., 2003; Solomon et al., 2004), primary visual cortex (V1) of cats and monkeys (Movshon and Lennie, 1979; Saul and Cynader, 1989a,b; Sclar et al., 1989), and the middle temporal area (MT) of monkeys (Kohn and Movshon, 2003, 2004; Krekelberg et al., 2006). Neural correlation of adaptation to spa-

tial frequency (Movshon and Lennie, 1979; Saul and Cynader, 1989a,b), temporal frequency (Saul and Cynader, 1989b), orientation (Muller et al., 1999; Dragoi et al., 2000; Dragoi and Sur, 2000; Dragoi et al., 2001) and motion direction (Kohn and Movshon, 2004), have been reported in neurons of cat's V1 and monkey's MT.

Perceptually, adaptation usually results in various after-effects or illusions. Prolonged exposure to an oriented visual stimulus causes subsequent stimuli to appear shifted away from the adapting orientation; this is called the tilt after-effect (TAE). As one of the pattern adaptation aftereffects, the TAE has been studied extensively (Gibson and Radner, 1937; Magnussen and Johnsen, 1986; He and MacLeod, 2001). Adaptation to stimulus orientation is thought to be the physiological substrate of the TAE, and studies of this phenomenon (Muller et al., 1999; Dragoi et al., 2000, 2001; Felsen et al., 2002) have led to the view that the TAE originates from the V1 (Jin et al., 2005). However, recent neurophysiological findings (Shou et al., 1996; Chung et al., 2002; Yang et al., 2003; Solomon et al., 2004) suggest that adaptation effects may happen within the LGN.

The LGN is often thought of as a passive relay of visual information to the cortex. However, recent studies have demonstrated that the LGN could play an important role as an early "gatekeeper" for controlling the gain of attentional responses and visual awareness (O'Connor et al., 2002; Kastner et al., 2006). Previous studies demonstrated that some LGN neurons exhibited an orientation bias (OB) (Vidyasagar and Urbas, 1982; Shou et al., 1986; Soodak et al., 1987; Smith et al., 1990; Xu et al., 2002; Sun et al., 2004), and also showed adaptation phenomena (Shou et al., 1996; Yang et al., 2003; Solomon et al., 2004). In the light of these studies, it seems that orientation adaptation could have specific effects on the activities of LGN neurons with high OB.

In the central visual system, the properties of neurons at each stage are modulated by feedback from higher structures (Sillito et al., 2006). For cats and primates, retinal afferents comprise 10% of the inputs to LGN relay cells, whereas corticofugal feedback comprises 30% of their inputs (Wilson, 1993; Erisir et al., 1997; Van Horn et al., 2000; Sherman and Guillery, 2002). Previous studies have shown that cortical feedback influences the spatial structure and centre-surround interaction of LGN receptive fields (Marrocco et al., 1982; McClurkin and Marrocco, 1984; Murphy and Sillito, 1987; Sillito et al., 1993; Cudeiro and Sillito, 1996), controls temporal synchronization of LGN spiking activity (Sillito et al., 1994), and increases transmission of visual information (McClurkin et al., 1994).

*Corresponding author. Y. Zhou, Hefei National Laboratory for Physical Sciences at Microscale, School of Life Science, University of Science and Technology of China, Hefei, Anhui 230027, P R China. Tel: +86-551-3601436; fax: +86-551-3607014. E-mail address: zhouy@ustc.edu.cn (Y. Zhou).

Abbreviations: FFT1, fundamental Fourier component; LGN, lateral geniculate nucleus; OB, orientation bias; MT, middle temporal area; SEM, standard errors of the mean; TAE, tilt after-effect; V1, primary visual cortex.

Thus, it is possible that corticogeniculate feedback contributes to the orientation adaptation of LGN neurons.

Here we studied the effects of orientation adaptation on the response properties of a sub-population of LGN neurons which exhibited high OB. We also explored the possible role of cortical feedback in these effects. In this study, we attempted to reveal how orientation adaptation was processed in the LGN.

EXPERIMENTAL PROCEDURES

Animal preparation

This study utilized 15 healthy adult cats (10 male, five female). Before the experiment, we examined all cats with an ophthalmoscope to confirm that they had no optical or retinal problems, which would impair visual function. All experiments were done strictly in accordance with the National Institutes of Health Guide for the Care and Use of Laboratory Animals, and were approved by the USTC Animal Care Committee. All procedures were approved by the Institutional Animal Care and Use Committee of University of Science and Technology of China and conformed to the guidelines of the National Institutes of Health Guide for the Care and Use of Laboratory Animals. All efforts were made to minimize the number of animals used and their suffering.

The preparation for extracellular single-unit recording was carried out as previously described (Shou et al., 1996). Briefly, cats were initially anesthetized with ketamine HCl (20 mg/kg; Ben Venue Lab Inc., Bedford, OH, USA). Lidocaine (1%; Abbott Labs, Chicago, IL, USA) was applied to all points of surgical incision. After insertion of i.v. and tracheal cannulae, the cats were placed in a stereotaxic apparatus. Pupils were dilated with atropine (1%; Wuhu, China). Phenylephrine (5%; Shanghai, China) was administered to retract the nictitating membranes, and appropriate contact lenses were used to protect the corneas. A mixture of urethane (20 mg/h/kg body weight; SCR, Shanghai, China) and galamine triethiodide (10 mg/h/kg body weight; Sigma) was infused i.v. to maintain anesthesia and paralysis. Expired pCO₂ and body temperature were maintained at approximately 4% and at 38 °C, respectively. Heart rate (about 180–220 pulses/min) and electroencephalogram were monitored throughout the experiment to assess the level of anesthesia. For recording from the LGN, a small hole was drilled in the skull at Horsley–Clark A 6/L 9, and for V1 at P 4/L 2. A glass-coated tungsten microelectrode (3–5 MΩ) was inserted and advanced using a hydraulic micromanipulator (Narishige, Tokyo, Japan). The craniotomy was filled with a 4% solution of agar in saline and sealed with wax.

In five cats, effects of adaptation on LGN neurons were measured after we applied liquid nitrogen to irreversibly inactivate the visual cortex (Shou et al., 1996; Huang et al., 2004). Liquid nitrogen soaked in a Q-tip was touched to area 17 and 18 locally several times (four to five times within a minute). According to retinotopic maps (Tusa et al., 1978, 1979), these locations were chosen to inactivate an area of at least the central 15° of visual space. We subsequently recorded neurons in the LGN at eccentricities of up to 10°. After cooling for 1 h, recording was performed on layer six to confirm that the neurons were inactivated.

Visual stimulation

Visual stimulus patterns were drifting sinusoidal gratings shown on a 17 inch cathode ray tube monitor (Philips 107P20, Suzhou, China) (1024×768, 85 Hz), which had a mean luminance of 60 cd/m² and was placed 57 cm from the animal's eyes. The program to generate the stimulus was written in MATLAB (Mathworks, Natick, MA, USA), using the extensions provided by the high-level Psychophysics Toolbox (Brainard, 1997) and low-level Video Toolbox (Pelli, 1997). When a single unit was isolated, the neuron's

receptive field was carefully mapped by consecutively presenting a series of spots of light of variable size. Using this method, we obtained a tuning curve of receptive field size and used the peak value of the tuning curve as the optimal receptive field size. All stimuli were gamma-corrected and centered on the mapped receptive field. We first examined the spatial frequency tuning curve for each neuron. The peak value of the tuning curve was used as the spatial frequency of test, adaptation and top-up gratings in the latter experiment. The temporal frequency and contrast of gratings were fixed at 4 Hz and 0.8 ($contrast = \frac{L_{max} - L_{min}}{L_{max} + L_{min}}$, where L_{max} and L_{min} are the maximum and the minimum luminance of sine grating, respectively), respectively. Next, we measured the responses to drifting sine gratings, which were surrounded by a gray field of mean luminance. A trial consisted of a single randomized sequence of 1-s test stimuli (16 directions spanning 360° in 22.5° steps), each preceded by a 5-s mean luminance stimulus, followed by a 2 min adapting stimulus (moving randomly in one of the two opposite directions at the selected orientation, where each direction was presented in 30 s epochs) and finally a second sequence of test stimuli, each interleaved with an additional 5-s 'top-up' of the adapting stimulus (Fig. 1). Each 'test-adapt-test/top-up' trial was followed by a recovery period of at least 5 min. We recorded three to five such trials for each adapting orientation. Because the pre-adaptation response of next trial was actually the recovery response, we did not record a separate recovery response.

Data collection and analysis

After the signal was amplified with a microelectrode amplifier (Nihon KOHDEN, Tokyo, Japan) and a differential amplifier (FHC, ME, USA), action potentials were fed into a window discriminator and audio monitor (Winston electronics, St. Louis, USA). The original voltage traces were digitized using a data acquisition board (National Instruments, Austin, USA) controlled by Igor software (WaveMetrics, USA), and saved for later analysis.

Post-stimulus time histograms (PSTHs) of the grating responses (10 ms bin width) were Fourier transformed and used to obtain the amplitude of the fundamental Fourier component (FFT1) at the stimulus temporal frequency. The FFT1 value for

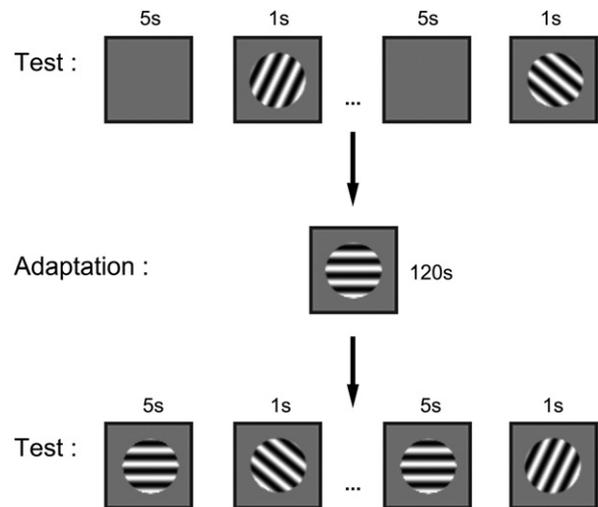


Fig. 1. Diagram for one trial of adaptation protocol. Responses to 16 stochastic orientations of drifting gratings (1 s for each presentation) were measured before and after adaptation to a grating drifting in the neuron's preferred, flank or null orientation for 120 s; the adaptation level was maintained by a 5 s 'top-up' stimuli preceding each test stimulus. Each trial was followed by a 5 min waiting period to ensure the recovery before the next trial was started.

each stimulus direction was used to draw the neuron's orientation tuning curve. The method for calculation of OB has been described previously (Levick and Thibos, 1982). Briefly, the responses to different stimulus orientations were stored as a series of vectors. These vectors were added, and divided by the sum of the absolute values of the vectors. The angle of the resultant vector gave the preferred direction of the neuron. The length of the resultant vector was defined as the OB, and provided a quantitative measure of the OB of the neuron. Because the periodicity of orientation is 180°, the angles of the orientation of the stimulus grating were multiplied by a factor of two. A neuron with bias ≥ 0.1 was considered significantly biased for orientation, and a neuron with bias ≥ 0.2 was considered strongly biased. Only neurons with OB ≥ 0.2 were used to study orientation adaptation, to enable better estimates of their orientation preferences. A null phase test and the 2nd/1st harmonic ratio of spatial phase response were used to identify units as X- or Y-type (Enroth-Cugell and Robson, 1966; Shapley and Hochstein, 1975; Hochstein and Shapley, 1976; So and Shapley, 1979).

To describe our results conveniently, we defined $\Delta\Psi$ as the shift of preferred orientation after adaptation, and $\Delta\theta$ as the difference between the neuron's preferred orientation and the adapting orientation. A positive $\Delta\Psi$ value indicates a shift away from the adapting stimulus orientation; a negative $\Delta\Psi$ value indicates a shift towards the adapting stimulus orientation.

To further explore the effect of adapting at a range of $\Delta\theta$, we divided our orientation adaptation data into three categories, according to the value of $\Delta\theta$, following the method of Kohn (Kohn and Movshon, 2003). These categories were termed as "preferred adaptation" ($0^\circ \leq \Delta\theta < 20^\circ$), "flank adaptation" ($20^\circ \leq \Delta\theta < 70^\circ$) and "end of flank adaptation" ($70^\circ \leq \Delta\theta \leq 90^\circ$).

As the orientation tuning curves following adaptation could be significantly asymmetric, we characterized orientation tuning, both before and after adaptation, by fitting the mean response with the difference of Gaussians function:

$$a_1 \cdot \exp\left[-\left(\frac{x-\mu_1}{\sigma_1}\right)^2\right] - a_2 \cdot \exp\left[-\left(\frac{x-\mu_2}{\sigma_2}\right)^2\right] + m \quad (1)$$

The centers of the two Gaussians were not constrained to be equal, and usually the center of the second Gaussian was constrained to the adapting orientation. This procedure allowed the model to fit asymmetric orientation tuning curves, and also fit symmetric curves where the second Gaussian would have zero effect. We found that our data fitted this model well; the mean goodness of the fit was 0.9534 for normal LGN neurons and 0.9458 for LGN neurons without feedback.

From each such curve fit, we concentrated our analysis on the preferred orientation and the peak response. The preferred orientation was estimated by calculating the value of orientation which corresponds to the highest point of the best-fit curve. The peak response was the highest point of the best-fit curve. We then calculated the peak response ratio (post-adaptation/pre-adaptation) and the $\Delta\Psi$ that represented how the orientation tuning changed after adaptation.

Using a method similar to that of Sowden's (Sowden et al., 2002), we could quantitatively study how adaptation affected a neuron's orientation tuning curve. We compared the adaptation effects on neurons of normal LGN, V1 and LGN without feedback. We calculated the decrease in normalized response between the pre-adaptation test and the post-adaptation test for each orientation used in the experiments for these three sorts of data. Then we plotted these values against orientation relative to the adapted orientation, and fitted it using a Gaussian function:

$$A \cdot \exp\{-[(x-x_0)/W]^2\} + m \quad (2)$$

where A is the height of the tuning curve, x is the orientation of the adapting stimulus, x_0 is the location of the midpoint of the tuning

curve, W is its half-width at half-height, and m is its baseline. We primarily evaluated the height and half-width at the half-height of each tuning curve. These data represented the strength of adaptation and the range of adaptation, respectively.

Using a bootstrap method, we evaluated the significance of change of orientation preference in individual neuron. For each neuron, after combining all trials of pre- and post-adaptation data, we created 1000 'pre-adaptation' and 'post-adaptation' datasets by choosing random subsets of the data with replacement. Then we fitted each of the 1000 datasets by the same method used in fitting the measured responses. Thus, the rank of the measured values in the set of bootstrap fits provided an estimation of the statistical significance.

All indications of variation in the graphs and text are standard errors of the mean (SEM.). The statistical significance of all results was evaluated with the nonparametric Wilcoxon test unless specified otherwise.

RESULTS

We studied 328 LGN neurons from 10 anesthetized and paralyzed normal cats and 174 LGN neurons from five anesthetized and paralyzed cats whose V1 was inactivated by cooling. In the LGN, some neurons have little or modest OB and others have high OB (Fig. 2). Because it is hard to estimate the exact preferred orientation of the neurons with little or modest OB, we only focused on neurons which showed a high OB (≥ 0.2 , normal neurons $n=59$, 18%; neurons without feedback $n=28$, 16%), to enable better estimates of preferred orientation and the shift of preferred orientation. The adapting stimulus orientation was chosen randomly on alternative tuning flanks.

We explored the effect of orientation adaptation ($\Delta\theta \sim 0-90^\circ$) on the $\Delta\Psi$ of LGN neurons. In normal cats, adaptation significantly shifted the preferred orientation: the mean $\Delta\Psi$ value was $3.26 \pm 0.81^\circ$ ($P=0.000045$ for difference from a shift of zero, Wilcoxon signed rank test, Fig. 3). Additionally, there was no significant difference between X neurons ($n=41$) and Y neurons ($n=18$) in shifts of preferred orientation ($P=0.26$).

Preferred adaptation

An example of the effect of preferred adaptation is shown in Fig. 4A; the peak response falls from 70 to 50 ips (impulses per second), while the preferred orientation is not shifted.

Across the sample population, we found that the preferred adaptation had little effect on the responses of LGN neurons other than decreasing the peak response. Preferred adaptation did not shift the preferred orientation of LGN neurons (Fig. 4B); the mean value of $\Delta\Psi$ was $0.96 \pm 1.08^\circ$ ($P=0.55$, $n=17$). However, the preferred adaptation decreased the peak response (Fig. 4C); the mean of peak response ratio was 0.84 ± 0.05 ($P=0.0027$ for difference from one).

Flank adaptation

An example is shown in Fig. 4D; flank adaptation shifts the preferred orientation repulsively, and decreases the peak response.

Across the population, flank adaptation evokes the strongest orientation adaptation effects on LGN neurons,

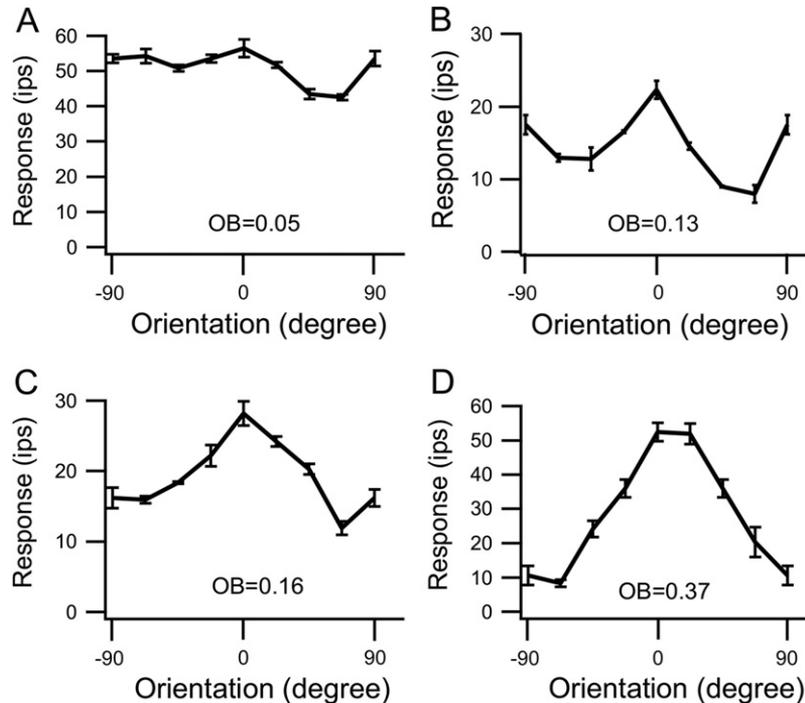


Fig. 2. Examples of orientation selectivities of LGN neurons. (A) Orientation tuning curve of an LGN neuron with little orientation sensitivity (stimuli parameter: stimuli diameter 4.6°, spatial frequency 0.2 Hz, temporal frequency 4 Hz, contrast 0.8); (B, C) Orientation tuning curves of two LGN neurons with modest OB (stimuli parameter for (B): stimuli diameter 4.6°, spatial frequency 0.2 Hz, temporal frequency 4 Hz, contrast 0.8; stimuli parameter for (C): stimuli diameter 5.2°, spatial frequency 0.1 Hz, temporal frequency 4 Hz, contrast 0.8); (D) Orientation tuning curve of an LGN neuron with strong OB (stimuli parameter: stimuli diameter 4.6°, spatial frequency 0.2 Hz, temporal frequency 4 Hz, contrast 0.8). Error bar: \pm SEM.

which show a repulsive shift of preferred orientation and a reduction in peak response. Flank adaptation repulsively shifted the preferred orientation of most LGN neurons (Fig. 4E), with a mean $\Delta\Psi$ value of $5.2 \pm 1.2^\circ$ ($P=0.000021$, $n=33$). Similarly, flank adaptation significantly decreased

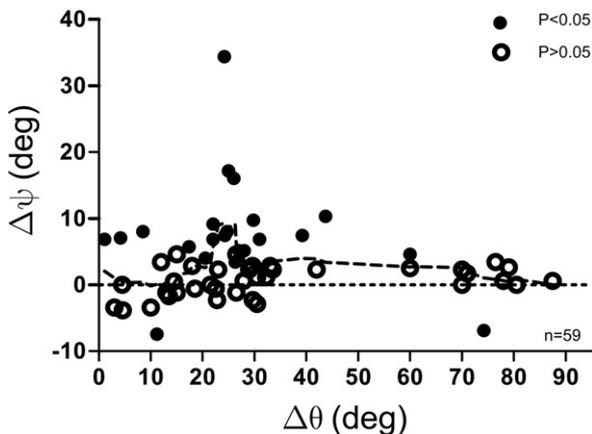


Fig. 3. The relationship between $\Delta\theta$ (difference between the neuron's preferred orientation and the adapting orientation) and $\Delta\Psi$ (shift of preferred orientation after adaptation). Each point represents the result from one adapting orientation. The dashed line shows a running average of the shift, which was calculated by averaging the neighboring \pm five data points. Positive and negative values indicate a repulsive shift from and an attractive shift to the adapting stimulus orientation, respectively. \bullet indicates the shift of preferred orientation is statistically significant, and \circ indicates it is not.

the peak response (Fig. 4F), with a mean peak response ratio of 0.896 ± 0.03 ($P < 0.001$).

End of flank adaptation

The end of flank adaptation barely changed preferred orientation or peak response of LGN neurons at statistically significant level. The mean values of $\Delta\Psi$ and peak response ratio were $0.48 \pm 1^\circ$ ($P=0.17$, $n=9$) and 1.10 ± 0.12 ($P=0.65$), respectively. These data showed that the end of flank adaptation had little effect on the orientation tuning curves of LGN neurons.

Cortical feedback contributes to effects of orientation adaptation

In five other cats, we studied whether the cortical feedback affected orientation adaptation of LGN neurons, by using the method of cooling to inactivate area 17 and 18. We recorded the orientation tuning curves of 174 LGN neurons in these cats. About 16% of these neurons had $OB > 0.2$ ($n=28$), which was similar to previous studies (Vidyasagar and Urbas, 1982; Thompson et al., 1994). We studied the effects of orientation adaptation on these 28 neurons. On average, we found there was little or no consistent repulsive shift of preferred orientation after adaptation in these neurons (Fig. 5A). The mean $\Delta\Psi$ was 0.5 ± 1.1 ($P=0.795$).

Since the flank adaptation had the strongest after-effects on LGN neurons as shown in Fig. 4, we concentrated our analysis on the effects of flank adaptation on 22

Fig. 4. Effects of 'preferred adaptation' ($\Delta\theta$ within 20°) and 'flank adaptation' ($\Delta\theta$ from 20 to 70°) on the orientation tuning of LGN neurons. (A) Orientation tuning of an LGN neuron before (\circ) and after (\bullet) preferred adaptation (adapting orientation is indicated by an arrow). For the neuron, before adaptation, the peak response was 70 ips (impulses per second), the preferred orientation was -2.3° , and the goodness of fit was 0.988; after adaptation the peak response was 50 ips, the preferred orientation was -1.8° , and the goodness of fit was 0.987. Error bar: \pm SEM. Across the population, preferred adaptation shifted the preferred orientation little, reduced peak responsiveness. (B) Histogram of shifts in preferred orientation after preferred adaptation for a population of LGN neurons ($n=17$), positive values indicate repulsive shifts from the adapting orientation, \blacktriangledown indicates the mean shift of preferred orientation (0.96 ± 1.08 , $P=0.55$ for difference from a shift of zero). (C) Distribution of peak response ratios (post-adaptation/pre-adaptation), \blacktriangledown indicates the mean peak response ratio (0.84 ± 0.05 , $P=0.0027$ for difference from 1). Preferred adaptation significantly reduced peak response. (D) Orientation tuning of an LGN neuron before (\circ) and after (\bullet) flank adaptation (adapting orientation indicated by an arrow). For the neuron, before adaptation, the peak response was 88 ips, the preferred orientation was -2.3° , and the goodness of fit was 0.99; after adaptation the peak response was 80 ips, the preferred orientation was -9.7° , and the goodness of fit was 0.97. Error bar: \pm SEM. Across the population, after flank adaptation, preferred orientation was repulsively shifted and the responsiveness was reduced. (E) Histogram of shifts in preferred orientation after flank adaptation for a population of LGN neurons ($n=33$), \blacktriangledown indicates the mean shift of preferred orientation ($5.2 \pm 1.2^\circ$, $P=0.000021$), positive values indicate repulsive shifts from the adapting orientation. (F) Distribution of peak response ratios. Flank adaptation typically decreased peak response (\blacktriangledown indicates the mean value, 0.896 ± 0.03 , $P < 0.001$).

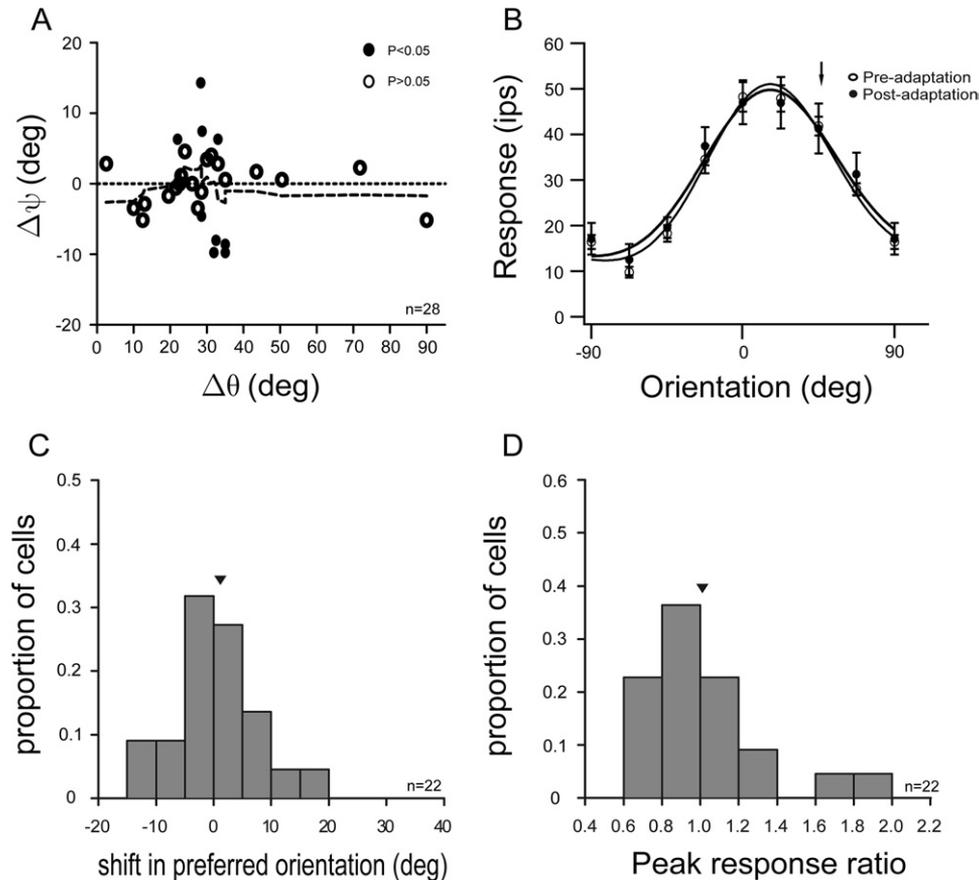


Fig. 5. Effect of adaptation on the LGN neurons without feedback. (A) The relationship between $\Delta\theta$ (difference between the neuron's preferred orientation and the adapting orientation) and $\Delta\Psi$ (shift of preferred orientation after adaptation) in LGN neurons without feedback. $\Delta\Psi$ was estimation by fitting with the Von Mises function. On average, there was no systematic shift of preferred orientation after adaptation, when the V1 was inactivated. The dashed line shows a running average of the shift, which was calculated by averaging the neighboring \pm five data points. Positive and negative values indicate repulsive shifts from and attractive shifts to the adapting stimulus orientation, respectively, \bullet indicates the shift of preferred orientation is statistically significant, and \circ indicates it is not. (B–D) Effect of flank adaptation on LGN neurons without feedback. (B) Orientation tuning of an LGN neuron without feedback before (\circ) and after (\bullet) flank adaptation (adapting orientation indicated by an arrow). For the neuron, before adaptation, the peak response was 51 ips, the preferred orientation was 16.6° , and the goodness of fit was 0.98; after adaptation the peak response was 50 ips, the preferred orientation was 16.6° , and the goodness of fit was 0.97. Error bar: \pm SEM. (C) Histogram of shifts in preferred orientation, after flank adaptation for a population of LGN neurons ($n=22$), \blacktriangledown indicates the mean shift of preferred orientation ($0.53 \pm 1.44^\circ$, $P=0.91$, $n=22$), positive values indicate repulsive shifts from the adapting orientation. (D) Distribution of peak response ratios. On average, flank adaptation did not decrease peak response of LGN neurons without feedback (\blacktriangledown indicates the mean value, 1.02 ± 0.06 , $P=0.79$).

out of the 28 neurons. An example is shown in Fig. 5B; flank adaptation decreases the neuron's response but causes little shift in its preferred orientation. Across the population, we found that flank adaptation had little effect on LGN neurons without feedback. First, we did not observe a systematic shift of preferred orientation (Fig. 5C). The mean $\Delta\Psi$ for the flank adaptation was $0.53 \pm 1.44^\circ$ ($P=0.91$, $n=22$). Second, we found that flank adaptation did not decrease the peak response of LGN neurons without feedback (Fig. 5D). After flank adaptation, the mean of peak response ratios was 1.02 ± 0.06 ($P=0.79$). Comparing these results with the flank adaptation data of normal cats, the aftereffects of orientation adaptation on LGN neurons were significantly reduced. After cooling V1, the magnitude of preferred orientation shift was decreased ($P=0.015$), and adaptation's effect on peak response was diminished ($P<0.05$).

Strength and bandwidth of adaptation

We further studied what induced the systematic shift of preferred orientation observed in LGN neurons. This was accomplished by means of comparing the strength and bandwidth of adaptation of normal LGN neurons with those of LGN neurons without feedback. We found that, in contrast to normal LGN neurons, the strength and bandwidth of adaptation of LGN neurons without feedback were decreased. The strength of adaptation was 0.06 for LGN neurons without feedback, and 0.093 for normal LGN neurons (Fig. 6A, B). The bandwidth of adaptation was 15.8° for LGN neurons without feedback, and 34.2° for normal LGN neurons (Fig. 6A, B). We further questioned whether there was a difference between the strength and bandwidth of adaptation of V1 neurons and those of normal LGN neurons. Therefore, we ran the above adaptation

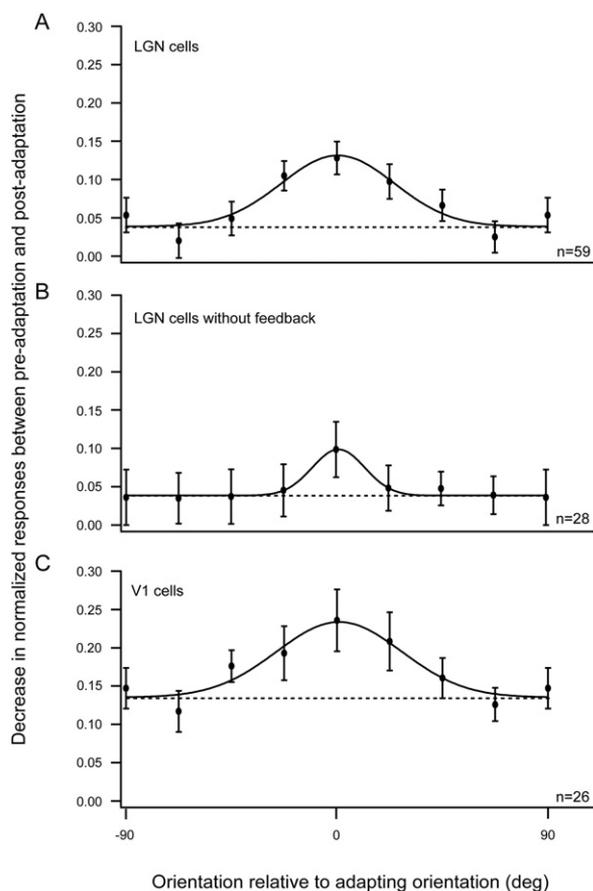


Fig. 6. Decrease in normalized responses at all test orientations between pre- and post-adaptation, after orientation adaptation. All tuning curves were fit using a Gaussian function. We focused on the height (termed strength of adaptation) and the bandwidth at half height of this tuning curve (termed bandwidth of adaptation). (A) Responses decrease in LGN neurons of normal cats. The strength and bandwidth of adaptation were 0.093 and 34.2° respectively. (B) Responses decrease in LGN neurons without feedback. Effects of adaptation on LGN neurons without feedback were diminished. The strength and bandwidth of adaptation were 0.06 and 15.8°, respectively. (C) Responses decrease in V1 neurons of normal cats. The strength and bandwidth of adaptation were 0.098 and 37.8°, respectively. The dotted line is the baseline of Gaussian function. Error bar: \pm SEM.

paradigm on V1 neurons with $OB > 0.2$ in two cats. For these V1 neurons, the mean shift of preferred orientation was 3.29 ± 1.11 ($P < 0.05$, $n = 26$) after adaptation. The strength and bandwidth of adaptation of V1 neurons were 0.098 and 37.8°, respectively (Fig. 6C). We then compared the differences of strength and bandwidth of adaptation between normal LGN neurons, V1 neurons, and LGN neurons without feedback by using the same bootstrap estimation, which was used in evaluating the significance of change of orientation preference after adaptation. We found that the strength and bandwidth of adaptation of normal LGN neurons were greater than those of LGN neurons without feedback (both $P < 0.000001$) and were similar to those of V1 neurons (both $P > 0.05$). The difference between normal LGN neurons, LGN neurons without feedback and V1 neurons in strength and bandwidth of

adaptation indicates that sufficient strength and bandwidth of adaptation are necessary for a systematic shift of the preferred orientation.

DISCUSSION

Previous studies have documented OB in LGN neurons (Soodak et al., 1987; Shou and Leventhal, 1989; Smith et al., 1990; Xu et al., 2002; Sun et al., 2004). Several studies have further shown that LGN neurons without feedback also present OB (Vidyasagar and Urbas, 1982; Thompson et al., 1994). Our results confirmed these previous findings and further showed that LGN neurons with high OB exhibited a repulsive shift of preferred orientation after exposure to an oriented stimulus of prolonged duration. Furthermore, while after irreversibly inactivating the V1, we found that LGN neurons also showed orientation adaptation but did not exhibit a systematic shift of preferred orientation.

The shift of preferred orientation

For a normal neuron, using the Von Mises function is a good method to estimate the preferred orientation (Swindale, 1998). However, it is likely that this model is not suitable for estimating the preferred orientation of a neuron after adaptation, because the orientation tuning curve after adaptation is asymmetric. Therefore, we employed the fitting of the difference of Gaussians to estimate the preferred orientation. In the difference of Gaussians model, the dominant Gaussian should have a peak around the preferred orientation of the LGN cell, and the second Gaussian should have a peak near the adapting orientation. Before adaptation, the orientation tuning curve is symmetric or may be asymmetric but the degree of asymmetry is probably to be low. Thus, the amplitude of the second Gaussian should be small in this case. After adaptation, the effect of the second Gaussian should increase with the degree of asymmetry increasing.

Our results demonstrate that orientation adaptation systematically shifts the preferred orientation, and that this shift requires two conditions. The first condition is that the adapting orientation is at an appropriate location relative to the original preferred orientation. A previous study (Kohn and Movshon, 2004) showed that flank adaptation effectively shifted the preferred direction of MT neurons. Similar to the results for MT neurons, our data have also shown that only flank adaptation has obvious effects on LGN neurons. The second condition is that sufficient strength and bandwidth of adaptation are necessary (Fig. 6). The adapting protocol we adopted produced changes in responses of sufficient strength and bandwidth, which were enough to produce a significant shift in preferred orientation when the adapting stimulus was appropriately selected with respect to the test stimulus (Movshon and Lennie, 1979; Saul and Cynader, 1989a,b; Carandini et al., 1997). In the absence of cortical input, the extent of adaptation was insufficient to induce this shift.

The shift of preferred orientation is the main effect of orientation adaptation on LGN neurons, which is similar to previous studies on the V1 in two ways. One is that the

shifts of preferred orientation are repulsive to the adapting orientation (Muller et al., 1999; Dragoi et al., 2000; Felsen et al., 2002). The other is that the shift magnitude of LGN neurons is similar to that of most V1 neurons, which are outside the pinwheel centers (Dragoi et al., 2001).

The influence of cortical feedback

We suggest that cortical feedback plays a modulating role in orientation adaptation of LGN neurons, because these cells exhibit a systematic shift of preferred orientation after adaptation only when cortical feedback is intact. Anatomically, the connections of layer six neurons and LGN relay cells are direct or through inhibitory interneurons in the LGN and the peri geniculate nucleus (Robson, 1983; Boyapati and Henry, 1984; Murphy and Sillito, 1996; Murphy et al., 2000). Functionally, the effect of cortical feedback can be evoked by the visual stimuli used in our study, because the layer six feedback neurons are sensitive to orientation (Grieve and Sillito, 1995). In addition, it is worth noting that feedback from layer six neurons to LGN neurons is retinotopically organized and functionally correlated (Murphy and Sillito, 1996; Murphy et al., 1999, 2000; Wang et al., 2006). Therefore, in principle, cortical feedback could contribute to the repulsive shift of preferred orientation of LGN neurons.

In fact, previous studies have shown that cortical feedback influences the properties of LGN neurons, such as the center-surround interaction (Murphy and Sillito, 1987; Sillito et al., 1993; Cudeiro and Sillito, 1996), facilitation of visual information (Waleszczyk et al., 2005), improvement of the timing of retino-geniculate signal transmission (Funke et al., 1996) and synchronized firing (Sillito et al., 1994). In this report, the results suggest that cortical feedback might play an important role in the effects of orientation adaptation on LGN neurons. A previous study showed that cortical feedback increased the response of LGN neurons (Przybylski et al., 2000). It is likely that a normal direct excitation, which comes from the cortex, is decreased after adaptation, and that this decrease acts as a disfacilitation to enhance the strength of adaptation and widen the bandwidth of adaptation. This then causes the preferred orientation to repulsively shift. However, the cortico-thalamic-cortico loop is very complicated (Cudeiro and Sillito, 2006; Sillito et al., 2006), and further research is needed to explore the potential mechanism of how cortical feedback contributes to the effects of orientation adaptation on LGN neurons.

We noticed that there was a large fluctuation of the preferred orientation after flank adaptation, when cortical activity was inactivated. One possible explanation is that, when cortical activity is inactivated, the responses at the adapting flank are facilitated in some neurons after adaptation. Thus, responses of this flank increase, when responses of the other flank do not change or decrease. This would induce an attractive shift of the preferred orientation and widen the bandwidth of orientation tuning. As a result, there would be a large fluctuation of preferred orientation due to some neurons showing an attractive shift and others showing a repulsive shift after flank adaptation. In contrast

to normal LGN neurons, the proportion of this facilitation in LGN neurons without feedback is indeed increased ($P=0.013$, chi square-test). This facilitation increase is likely due to a decrease of adaptation effects, which is caused by inactivity of cortical feedback.

Cortical feedback plays a functional role in visual information processing. In terms of visual information coding theory, adaptation provides a reduction of visual information redundancy (Wainwright, 1999; Clifford et al., 2000). Work by Hillenbrand and van Hemmen has suggested that the corticothalamic loop may reduce information redundancy (Hillenbrand and van Hemmen, 2002). In this report, the results show that cortical feedback could increase effects of orientation adaptation of LGN neurons by increasing the strength and bandwidth of adaptation, inducing a systematic shift of preferred orientation and decreasing the proportion of facilitation. Thus, cortical feedback is likely to enhance the efficiency of visual information processing in the cortex by redundancy reduction.

CONCLUSION

In summary, orientation adaptation occurs in LGN neurons with high OB, and a main effect of this adaptation is a systematic shift of preferred orientation. When the V1 is inactivated, the preferred orientation of LGN neurons is not systematically shifted. We suggest that cortical feedback contributes to orientation adaptation in LGN neurons. Our results provide an example of how the corticothalamic loop modulates the processing of visual information. Consistent with previous studies (O'Connor et al., 2002; Kastner et al., 2006), our results also suggest that the LGN is not only a simply passive relay but also a modulator of visual information.

Acknowledgments—We thank Dr. Curtis L. Baker for his helpful comments on the manuscript and polishing the English. This investigation was supported by grants from the National Basic Research Program of China (2006CB500804).

REFERENCES

- Baccus SA, Meister M (2002) Fast and slow contrast adaptation in retinal circuitry. *Neuron* 36:909–919.
- Boyapati J, Henry G (1984) Corticofugal axons in the lateral geniculate nucleus of the cat. *Exp Brain Res* 53:335–340.
- Brainard DH (1997) The psychophysics toolbox. *Spat Vis* 10:433–436.
- Carandini M, Barlow HB, O'Keefe LP, Poirson AB, Movshon JA (1997) Adaptation to contingencies in macaque primary visual cortex. *Philos Trans R Soc Lond B Biol Sci* 352:1149–1154.
- Chung S, Li X, Nelson SB (2002) Short-term depression at thalamo-cortical synapses contributes to rapid adaptation of cortical sensory responses in vivo. *Neuron* 34:437–446.
- Clifford CW, Wenderoth P, Spehar B (2000) A functional angle on some after-effects in cortical vision. *Proc Biol Sci* 267:1705–1710.
- Cudeiro J, Sillito AM (1996) Spatial frequency tuning of orientation-discontinuity-sensitive corticofugal feedback to the cat lateral geniculate nucleus. *J Physiol* 490(2):481–492.
- Cudeiro J, Sillito AM (2006) Looking back: corticothalamic feedback and early visual processing. *Trends Neurosci* 29:298–306.
- Dragoi V, Rivadulla C, Sur M (2001) Foci of orientation plasticity in visual cortex. *Nature* 411:80–86.

- Dragoi V, Sharma J, Sur M (2000) Adaptation-induced plasticity of orientation tuning in adult visual cortex. *Neuron* 28:287–298.
- Dragoi V, Sur M (2000) Dynamic properties of recurrent inhibition in primary visual cortex: contrast and orientation dependence of contextual effects. *J Neurophysiol* 83:1019–1030.
- Enroth-Cugell C, Robson JG (1966) The contrast sensitivity of retinal ganglion cells of the cat. *J Physiol* 187:517–552.
- Erisir A, Van Horn SC, Sherman SM (1997) Relative numbers of cortical and brainstem inputs to the lateral geniculate nucleus. *Proc Natl Acad Sci U S A* 94:1517–1520.
- Felsen G, Shen YS, Yao H, Spor G, Li C, Dan Y (2002) Dynamic modification of cortical orientation tuning mediated by recurrent connections. *Neuron* 36:945–954.
- Funke K, Nelle E, Li B, Worgotter F (1996) Corticofugal feedback improves the timing of retino-geniculate signal transmission. *Neuroreport* 7:2130–2134.
- Gibson J, Radner M (1937) Adaptation, aftereffect and contrast in the perception of tilted lines: I. Quantitative studies. *J Exp Psychol* 20:453–467.
- Grieve KL, Sillito AM (1995) Differential properties of cells in the feline primary visual cortex providing the corticofugal feedback to the lateral geniculate nucleus and visual claustrum. *J Neurosci* 15:4868–4874.
- He S, MacLeod DI (2001) Orientation-selective adaptation and tilt after-effect from invisible patterns. *Nature* 411:473–476.
- Hillenbrand U, van Hemmen JL (2002) Adaptation in the corticothalamic loop: computational prospects of tuning the senses. *Philos Trans R Soc Lond B Biol Sci* 357:1859–1867.
- Hochstein S, Shapley RM (1976) Linear and nonlinear spatial subunits in Y cat retinal ganglion cells. *J Physiol* 262:265–284.
- Huang L, Chen X, Shou T (2004) Spatial frequency-dependent feedback of visual cortical area 21a modulating functional orientation column maps in areas 17 and 18 of the cat. *Brain Res* 998:194–201.
- Jin DZ, Dragoi V, Sur M, Seung HS (2005) Tilt aftereffect and adaptation-induced changes in orientation tuning in visual cortex. *J Neurophysiol* 94:4038–4050.
- Kastner S, Schneider KA, Wunderlich K (2006) Beyond a relay nucleus: neuroimaging views on the human LGN. *Prog Brain Res* 155:125–143.
- Kohn A, Movshon JA (2003) Neuronal adaptation to visual motion in area MT of the macaque. *Neuron* 39:681–691.
- Kohn A, Movshon JA (2004) Adaptation changes the direction tuning of macaque MT neurons. *Nat Neurosci* 7:764–772.
- Krekelberg B, van Wezel RJ, Albright TD (2006) Adaptation in macaque MT reduces perceived speed and improves speed discrimination. *J Neurophysiol* 95:255–270.
- Levick WR, Thibos LN (1982) Analysis of orientation bias in cat retina. *J Physiol* 329:243–261.
- Magnussen S, Johnsen T (1986) Temporal aspects of spatial adaptation. A study of the tilt aftereffect. *Vis Res* 26:661–672.
- Marrocco RT, McClurkin JW, Young RA (1982) Modulation of lateral geniculate nucleus cell responsiveness by visual activation of the corticogeniculate pathway. *J Neurosci* 2:256–263.
- McClurkin JW, Marrocco RT (1984) Visual cortical input alters spatial tuning in monkey lateral geniculate nucleus cells. *J Physiol* 384:135–152.
- McClurkin JW, Optican LM, Richmond BJ (1994) Cortical feedback increases visual information transmitted by monkey parvocellular lateral geniculate nucleus neurons. *Vis Neurosci* 11:601–617.
- Movshon JA, Lennie P (1979) Pattern-selective adaptation in visual cortical neurones. *Nature* 278:850–852.
- Muller JR, Metha AB, Krauskopf J, Lennie P (1999) Rapid adaptation in visual cortex to the structure of images. *Science* 285:1405–1408.
- Murphy PC, Duckett SG, Sillito AM (1999) Feedback connections to the lateral geniculate nucleus and cortical response properties. *Science* 286:1552–1554.
- Murphy PC, Duckett SG, Sillito AM (2000) Comparison of the laminar distribution of input from areas 17 and 18 of the visual cortex to the lateral geniculate nucleus of the cat. *J Neurosci* 20:845–853.
- Murphy PC, Sillito AM (1987) Corticofugal feedback influences the generation of length tuning in the visual pathway. *Nature* 329:727–729.
- Murphy PC, Sillito AM (1996) Functional morphology of the feedback pathway from area 17 of the cat visual cortex to the lateral geniculate nucleus. *J Neurosci* 16:1180–1192.
- O'Connor DH, Fukui MM, Pinsk MA, Kastner S (2002) Attention modulates responses in the human lateral geniculate nucleus. *Nat Neurosci* 5:1203–1209.
- Pelli DG (1997) The VideoToolbox software for visual psychophysics: transforming numbers into movies. *Spat Vis* 10:437–442.
- Przybyszewski AW, Gaska JP, Foote W, Pollen DA (2000) Striate cortex increases contrast gain of macaque LGN neurons. *Vis Neurosci* 17:485–494.
- Robson JA (1983) The morphology of corticofugal axons to the dorsal lateral geniculate nucleus in the cat. *J Comp Neurol* 216:89–103.
- Saul AB, Cynader MS (1989a) Adaptation in single units in visual cortex: the tuning of aftereffects in the spatial domain. *Vis Neurosci* 2:593–607.
- Saul AB, Cynader MS (1989b) Adaptation in single units in visual cortex: the tuning of aftereffects in the temporal domain. *Vis Neurosci* 2:609–620.
- Sclar G, Lennie P, DePriest DD (1989) Contrast adaptation in striate cortex of macaque. *Vis Res* 29:747–755.
- Shapley R, Hochstein S (1975) Visual spatial summation in two classes of geniculate cells. *Nature* 256:411–413.
- Sherman SM, Guillery RW (2002) The role of the thalamus in the flow of information to the cortex. *Philos Trans R Soc Lond B Biol Sci* 357:1695–1708.
- Shou T, Li X, Zhou Y, Hu B (1996) Adaptation of visually evoked responses of relay cells in the dorsal lateral geniculate nucleus of the cat following prolonged exposure to drifting gratings. *Vis Neurosci* 13:605–613.
- Shou T, Ruan D, Zhou Y (1986) The orientation bias of LGN neurons shows topographic relation to area centralis in the cat retina. *Exp Brain Res* 64:233–236.
- Shou TD, Leventhal AG (1989) Organized arrangement of orientation-sensitive relay cells in the cat's dorsal lateral geniculate nucleus. *J Neurosci* 9:4287–4302.
- Sillito AM, Cudeiro J, Jones HE (2006) Always returning: feedback and sensory processing in visual cortex and thalamus. *Trends Neurosci* 29:307–316.
- Sillito AM, Cudeiro J, Murphy PC (1993) Orientation sensitive elements in the corticofugal influence on centre-surround interactions in the dorsal lateral geniculate nucleus. *Exp Brain Res* 93:6–16.
- Sillito AM, Jones HE, Gerstein GL, West DC (1994) Feature-linked synchronization of thalamic relay cell firing induced by feedback from the visual cortex. *Nature* 369:479–482.
- Smith EL 3rd, Chino YM, Ridder WH 3rd, Kitagawa K, Langston A (1990) Orientation bias of neurons in the lateral geniculate nucleus of macaque monkeys. *Vis Neurosci* 5:525–545.
- So YT, Shapley R (1979) Spatial properties of X and Y cells in the lateral geniculate nucleus of the cat and conduction velocities of their inputs. *Exp Brain Res* 36:533–550.
- Solomon SG, Peirce JW, Dhruv NT, Lennie P (2004) Profound contrast adaptation early in the visual pathway. *Neuron* 42:155–162.
- Soodak RE, Shapley RM, Kaplan E (1987) Linear mechanism of orientation tuning in the retina and lateral geniculate nucleus of the cat. *J Neurophysiol* 58:267–275.
- Sowden PT, Rose D, Davies IR (2002) Perceptual learning of luminance contrast detection: specific for spatial frequency and retinal location but not orientation. *Vis Res* 42:1249–1258.
- Sun C, Chen X, Huang L, Shou T (2004) Orientation bias of the extraclassical receptive field of the relay cells in the cat's dorsal lateral geniculate nucleus. *Neuroscience* 125:495–505.

- Swindale NV (1998) Orientation tuning curves: empirical description and estimation of parameters. *Biol Cybern* 78:45–56.
- Thompson KG, Leventhal AG, Zhou Y, Liu D (1994) Stimulus dependence of orientation and direction sensitivity of cat LGNd relay cells without cortical inputs: a comparison with area 17 cells. *Vis Neurosci* 11:939–951.
- Tusa RJ, Palmer LA, Rosenquist AC (1978) The retinotopic organization of area 17 (striate cortex) in the cat. *J Comp Neurol* 177: 213–235.
- Tusa RJ, Rosenquist AC, Palmer LA (1979) Retinotopic organization of areas 18 and 19 in the cat. *J Comp Neurol* 185:657–678.
- Van Horn SC, Erisir A, Sherman SM (2000) Relative distribution of synapses in the A-laminae of the lateral geniculate nucleus of the cat. *J Comp Neurol* 416:509–520.
- Vidyasagar TR, Urbas JV (1982) Orientation sensitivity of cat LGN neurones with and without inputs from visual cortical areas 17 and 18. *Exp Brain Res* 46:157–169.
- Wainwright MJ (1999) Visual adaptation as optimal information transmission. *Vis Res* 39:3960–3974.
- Waleszczyk WJ, Bekisz M, Wrobel A (2005) Cortical modulation of neuronal activity in the cat's lateral geniculate and perigeniculate nuclei. *Exp Neurol* 196:54–72.
- Wang W, Jones HE, Andolina IM, Salt TE, Sillito AM (2006) Functional alignment of feedback effects from visual cortex to thalamus. *Nat Neurosci* 9:1330–1336.
- Wilson JR (1993) Circuitry of the dorsal lateral geniculate nucleus in the cat and monkey. *Acta Anat (Basel)* 147:1–13.
- Xu X, Ichida J, Shostak Y, Bonds AB, Casagrande VA (2002) Are primate lateral geniculate nucleus (LGN) cells really sensitive to orientation or direction? *Vis Neurosci* 19:97–108.
- Yang Y, Jin J, Zhou Y, Shou T (2003) GABA(A) and GABA(B) receptors mediated inhibition affect the pattern adaptation of relay cells in the dorsal lateral geniculate nucleus (LGNd) of cats. *Brain Res* 959:295–303.

(Accepted 6 August 2009)
(Available online 12 August 2009)