A minimal mechanistic model for temporal signal processing in the lateral geniculate nucleus

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Abstract The receptive fields of cells in the lateral geniculate nucleus (LGN) are shaped by their diverse set of impinging inputs: feedforward synaptic inputs stemming from retina, and feedback inputs stemming from the visual cortex and the thalamic reticular nucleus. To probe the possible roles of these feedforward and feedback inputs in shaping the temporal receptive-field structure of LGN relay cells, we here present and investigate a minimal mechanistic firing-rate model tailored to elucidate their disparate features. The model for LGN relay ON cells includes feedforward excitation and inhibition (via interneurons) from retinal ON cells and excitatory and inhibitory (via thalamic reticular nucleus cells and interneurons) feedback from cortical ON and OFF cells. From a general firing-rate model formulated in terms of Volterra integral equations, we derive a single delay differential equation with absolute delay governing the dynamics of the system. A freely available and easy-to-use GUI-based MATLAB version of this minimal mechanistic LGN circuit model is provided. We particularly investigate the LGN relay-cell impulse response and find through thorough explorations of the model's parameter space that both purely feedforward models and feedback models with feedforward excitation only, can account quantitatively for previously reported experimental results. We find, however, that the purely feedforward model predicts two impulse response measures, the time to first peak and the biphasic index (measuring the relative weight of the rebound phase) to be anticorrelated. In contrast, the models with feedback

predict different correlations between these two measures. This suggests an experimental test assessing the relative importance of feedforward and feedback connections in shaping the impulse response of LGN relay cells.

Keywords LGN · Mechanistic · Rate model · Thalamocortical · Corticothalamic · Feedback · Feedforward · Impulse response

Introduction

Relay cells in the lateral geniculate nucleus (LGN) in the early visual system receive synaptic inputs from a variety of sources (Sherman and Guillery 2001): direct *feedforward excitation* from retinal ganglion cells, indirect *feedforward inhibition* via intrageniculate interneurons in turn excited by retinal ganglion cells, *feedback inhibition* from the thalamic reticular nucleus (TRN) and *feedback excitation* from primary visual cortex. Both intrageniculate interneurons and TRN cells also receive excitatory feedback from cortex opening up for *feedback inhibition* involving the entire thalamocortical loop, acting on the LGN relay cells.

LGN relay cells typically inherit their most salient receptive-field structure features from the retinal ganglion cells providing the dominant feedforward inputs (Mastrorade 1987a,b; Usrey et al. 1999; Rukzenas et al. 2000). The role of the prominent cortical feedback to LGN is more unclear, however (Briggs and Usrey 2008, 2011). This cortical feedback has been shown to be able to switch LGN relay cells from burst to tonic firing modes (McCormick and von Krosigk 1992; Godwin et al. 1996) and to modify the response properties of LGN cells to visual stimuli both in cat (Geisert et al. 1981; Vidyasagar and Urbas 1982; Murphy and Sillito 1987; Sillito et al. 1993, 1994; Cudeiro and Sillito 1996;

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Wörgötter et al. 1998; Andolina et al. 2007) and monkey (Marrocco et al. 1982; McClurkin and Marrocco 1984; McClurkin et al. 1994; Marrocco et al. 1996). For example, cortical feedback has been shown to affect the length tuning of relay-cell responses (Murphy and Sillito 1987), the response to patch-grating stimuli (Sillito et al. 1993; Cudeiro and Sillito 1996; Sillito and Jones 2002) and the temporal response precision to drifting gratings (Andolina et al. 2007). However, experiments with selective blocking of cortical feedback are notoriously difficult to do, and studies have reported both enhanced and reduced responses of LGN neurons from cortical feedback. The identification of a particular role of this feedback has thus been difficult.

Mathematical models in neuroscience can be categorized into three types: *descriptive*, *mechanistic*, and *interpretive* (Dayan and Abbott 2001). *Descriptive* models are used to summarize experimental data compactly (see, e.g., Jing et al. 2010), while *mechanistic* models aim to account for the observed neural properties on the basis of known neural physiology and anatomy (see, e.g., Wang and Zhang 2007; Saglam et al. 2009; and Liang et al. 2010). The third category, *interpretive* models, aims instead to model the functional roles of neural systems, for example, relating neuronal responses to the task of processing useful information for the animal (see, e.g., Satoh and Usui 2009).

Following the introduction of the difference-of-Gaussians (DOG) model for the spatial receptive-field of retinal ganglion cells by Rodieck (1965), most modeling of the response properties of cells in retina, LGN and visual cortex have been descriptive. Numerous spatiotemporal receptive-field functions have been suggested (see, e.g., Ch.2 in Dayan and Abbott 2001), essentially identifying filter functions accounting for the signal processing done by the underlying neural networks (Cruse 1997). In contrast, *mechanistic* models have aimed to find out how these filtering properties arise from the underlying neural circuitry in the visual system (Einevoll and Heggelund 2000; Einevoll and Plesser 2002, 2011).

A few mechanistic mathematical models have been investigated to elucidate effects of cortical feedback on LGN neurons. They have focused on cortical feedback effects on visual latency (Köhn and Wörgötter 1996), thalamocortical oscillations (Destexhe et al. 1998; Destexhe 2000; Mayer et al. 2007; Bhattacharya et al. 2011), temporal structure of spike trains (Wörgötter et al. 1998), synchronization of LGN cells (Kirkland and Gerstein 1998; Kirkland et al. 2000), object segmentation based on motion cues (Hillenbrand and van Hemmen 2000), LGN relay-cell responses to bipartite drifting grating stimuli (Hayot and Tranchina 2001), and cortical feedback effects on recorded relay-cell impulse responses (Yousif and Denham 2007). In these models, each of the different populations in the early visual pathway (retinal, LGN, TRN, and cortical cells) have typically been

represented by spatially structured grids of neurons, and comprehensive numerical simulations have been necessary for model analysis. Importantly, the large number of parameters in the models have generally precluded thorough analysis of the properties of the model across the parameter space.

In the present paper, we develop a minimal mechanistic mathematical model aimed at highlighting salient feedforward and feedback effects on LGN relay cells following visual stimulation. A particular focus is the investigation of how the detailed shape of the LGN impulse response is formed by the interplay between feedforward and feedback actions (Cai et al. 1997; Usrey et al. 1999; Yousif and Denham 2007).

Our mechanistic model is framed in terms of *firing rates* (Einevoll and Plesser 2002) and focuses solely on the temporal aspects of the signal processing; the lateral spatial dimension is thus omitted. For simplicity, we do not model the intrageniculate interneurons or TRN cells explicitly. Instead we incorporate their effects in a more general way by allowing for both feedforward inhibition via interneurons and inhibitory cortical feedback effects via TRN cells or interneurons. The LGN cells divide into two types, ON and OFF. The first responds preferably to light spots on a dark background, the latter preferably to dark spots on a light background. Here we assume the feedforward parts of the ON and OFF pathways to be separate, but we allow for ON/OFF cross-connections in the cortical feedback (Wang et al. 2006). The model is formulated in terms of coupled integral equations (Ermentrout 1998; Nordbø et al. 2007), but a crucial feature is that it can be mapped onto a much simpler differential form. The final model is represented by a single delay differential equation with absolute delay (MacDonald 1979) which is readily solved by standard mathematical software. To further facilitate its use we have made a freely available MATLAB version of the model, *LGNcircuit*, with a simple graphical user interface (GUI).

Mathematical model

The overall structure of our firing-rate model is illustrated in Fig. 1. The focus of attention is the firing rate of an LGN relay cell with ON symmetry. It receives both direct feedforward excitation and indirect feedforward inhibition (via intrageniculate interneurons not explicitly represented in the model) from an ON ganglion cell in retina. It further receives cortical feedback both from cortical ON cells and cortical OFF cells. The cortical feedback can be both excitatory (direct) and inhibitory (indirect via TRN cells or intrageniculate interneurons). The cortical ON and OFF cells are in turn assumed to be driven by the LGN ON and OFF relay cells, respectively.

General firing-rate model on integral form

Below we present the model for the firing rate of an ON LGN relay cell, but a completely analogous derivation can be done for OFF LGN relay cells. The time-dependent firing rate $\hat{R}_r^{\text{ON}}(t)$ for such an ON cell is assumed to be given by (Dayan and Abbott 2001)

$$\hat{R}_r^{\text{ON}}(t) = F_r^{\text{ON}}(\hat{I}_r^{\text{ON}}(t)), \quad (1)$$

where $\hat{I}_r^{\text{ON}}(t)$ denotes the time-dependent input to the ON LGN cell, and $F_r^{\text{ON}}(x)$ is a firing-rate function converting the input into an output firing rate. For convenience we choose the input $\hat{I}_r^{\text{ON}}(t)$ to have the same dimension as firing rates.

It is further convenient to separate the time-dependent from the background activities, and we thus use the notation

$$\begin{aligned} \hat{R}_r^{\text{ON}}(t) &\equiv R_{r0}^{\text{ON}} + R_r^{\text{ON}}(t), \\ \hat{I}_r^{\text{ON}}(t) &\equiv I_{r0}^{\text{ON}} + I_r(t). \end{aligned} \quad (2)$$

Here R_{r0}^{ON} and $R_r^{\text{ON}}(t)$ are set to denote the background firing rate (assumed to be stationary) and the stimulus-evoked change of the firing rate, respectively. Further, I_{r0}^{ON} denotes the background input to the ON LGN cell, while $I_r(t)$ denotes the stimulus-evoked change in this input. With this notation the firing rate of the LGN ON cell is given by

$$\hat{R}_r^{\text{ON}}(t) \equiv R_{r0}^{\text{ON}} + R_r^{\text{ON}}(t) = F_r^{\text{ON}}(I_{r0}^{\text{ON}} + I_r(t)). \quad (3)$$

A common choice of firing rate functions $F_r(x)$ for LGN neurons has been the half-wave rectification function

($F(x) = [x]_+$; $[x < 0]_+ = 0$, $[x \geq 0]_+ = x$) (Gazères et al. 1998; Troyer et al. 1998, 2002; Einevoll and Heggelund 2000), but sigmoidal functions have also been used (Hayot and Tranchina 2001; Yousif and Denham 2007). For now we leave $F_r^{\text{ON}}(x)$, as well as the other firing-rate functions introduced below, unspecified.

In our model the ON and OFF pathways are coupled via the cortical feedback (Wang et al. 2006; Yousif and Denham 2007), and we consequently also need a model for OFF LGN relay cells. Here we model OFF LGN relay cells as ‘shadow’ cells of the ON cells, i.e., they are assumed to receive the same time-dependent input with opposite phase, i.e., opposite sign (Troyer et al. 2002). The firing rate of an OFF cell is thus in analogy with (3) given by

$$\hat{R}_r^{\text{OFF}}(t) = F_r^{\text{OFF}}(I_{r0}^{\text{OFF}} - I_r(t)), \quad (4)$$

where I_{r0}^{OFF} is the background input to the OFF LGN cell.

The total input to the ON LGN relay cell is obtained by summing the excitatory and inhibitory feedforward contributions stemming from retina and the feedback contributions from cortex, i.e.,

$$\begin{aligned} \hat{I}_r^{\text{ON}}(t) &= w_{\text{rg}}^{\text{ON}}(h_{\text{rg}}^{\text{ON}} * \hat{R}_g^{\text{ON}})(t) - w_{\text{rig}}^{\text{ON}}(h_{\text{rig}}^{\text{ON}} * \hat{R}_g^{\text{ON}})(t) \\ &\quad + w_{\text{rc}}^{\text{ON}}(h_{\text{rc}}^{\text{ON}} * \hat{R}_c^{\text{ON}})(t) + w_{\text{rc}}^{\text{OFFx}}(h_{\text{rc}}^{\text{OFFx}} * \hat{R}_c^{\text{OFF}})(t). \end{aligned} \quad (5)$$

Here $w_{\text{rg}}^{\text{ON}}$ is the weight of the direct feedforward excitatory connection from retina onto the ON LGN cell, and $w_{\text{rig}}^{\text{ON}}$ the weight of the corresponding indirect feedforward inhibitory connection via intrageniculate interneurons. The parameter $w_{\text{rc}}^{\text{ON}}$ represents the weight of the feedback connection from the ON cortical cells, while the parameter $w_{\text{rc}}^{\text{OFFx}}$ represents the weight of the feedback cross-connection from the OFF cortical cell to the ON LGN cell. Further, $h_{\text{rg}}^{\text{ON}}(t)$, $h_{\text{rig}}^{\text{ON}}(t)$, $h_{\text{cr}}^{\text{ON}}(t)$, and $h_{\text{cr}}^{\text{OFFx}}(t)$ are *temporal coupling kernels*, and $(h * r)(t)$ is a *temporal convolution* between the kernel $h(t)$ and the firing rate $r(t)$ defined by

$$(h * r)(t) \equiv \int_{-\infty}^t h(t-s)r(s)ds. \quad (6)$$

The coupling kernel $h_{\text{rg}}^{\text{ON}}(t)$, for example, represents the contribution to the present input to the ON relay cell due to firing that has occurred in the ON retinal ganglion cell a time t in the past. The kernels must thus be causal, i.e., $h(t < 0) = 0$, and presently we assume that all coupling kernels are normalized, i.e., $\int_{-\infty}^{\infty} h(t)dt = 1$.

As seen from (5) the cortical feedback to the LGN relay cells is assumed to be provided by cortical cells of both symmetries, i.e., ON and OFF (cf. Fig. 1). For simplicity we neglect that cortical cells exhibit different orientation tuning, and we thus include only one ON and one OFF cell type. We further make the assumption that the cortical cells

Fig. 1 Schematic overview of the present minimal mechanistic thalamocortical circuit model. Cell types are: retinal ganglion cells (g), LGN relay cells (r), and cortical cells (c). OFF pathway is included in an indirect way with the OFF LGN relay cell modeled as a ‘shadow cell’ of the corresponding ON LGN relay cell. Synaptic connections explicitly included in the model are represented by *solid lines*; connections included implicitly are shown with *dotted lines*. Feedforward connections in the ON pathway are shown with *thick lines*

are driven by relay cells of the same symmetry only (Hubel and Wiesel 1962; Jin et al. 2008). The firing rates of these cortical ON and OFF cells are mathematically represented by (Ermentrout 1998; Nordbø et al. 2007)

$$\hat{R}_c^{\text{ON}}(t) = F_c^{\text{ON}}(w_{\text{cr}}^{\text{ON}}(h_{\text{cr}}^{\text{ON}} * \hat{R}_r^{\text{rmON}})(t)), \quad (7)$$

$$\hat{R}_c^{\text{OFF}}(t) = F_c^{\text{OFF}}(w_{\text{cr}}^{\text{OFF}}(h_{\text{cr}}^{\text{OFF}} * \hat{R}_r^{\text{rmOFF}})(t)), \quad (8)$$

where $w_{\text{cr}}^{\text{ON}}$ and $w_{\text{cr}}^{\text{OFF}}$ are feedforward connection weights from LGN to cortex, and $h_{\text{cr}}^{\text{ON}}(t)$ and $h_{\text{cr}}^{\text{OFF}}(t)$ the corresponding temporal coupling kernels.

If we now, in analogy to (2), separate the firing rates of the ON retinal ganglion cells and the cortical cells into background and stimulus-evoked contributions, i.e.,

$$\begin{aligned} \hat{R}_g^{\text{ON}}(t) &\equiv R_{g0}^{\text{rmON}} + R_g^{\text{ON}}(t), \\ \hat{R}_c^{\text{ON}}(t) &\equiv R_{c0}^{\text{ON}} + R_c^{\text{ON}}(t), \\ \hat{R}_c^{\text{OFF}}(t) &\equiv R_{c0}^{\text{OFF}} + R_c^{\text{OFF}}(t), \end{aligned} \quad (9)$$

Eq. (5) can be split up into two separate equations determining the net background and stimulus-evoked inputs:

$$I_{r0}^{\text{ON}} = (w_{\text{rg}}^{\text{ON}} - w_{\text{rg}}^{\text{ON}})R_{g0}^{\text{ON}} + w_{\text{rc}}^{\text{ON}}R_{c0}^{\text{ON}} + w_{\text{rc}}^{\text{OFFx}}R_{c0}^{\text{OFF}}, \quad (10)$$

$$\begin{aligned} I_r(t) &= w_{\text{rg}}^{\text{ON}}(h_{\text{rg}}^{\text{ON}} * R_g^{\text{ON}})(t) - w_{\text{rg}}^{\text{ON}}(h_{\text{rg}}^{\text{ON}} * R_g^{\text{ON}})(t) \\ &\quad + w_{\text{rc}}^{\text{ON}}(h_{\text{rc}}^{\text{ON}} * R_c^{\text{ON}})(t) + w_{\text{rc}}^{\text{OFFx}}(h_{\text{rc}}^{\text{OFFx}} * R_c^{\text{OFF}})(t), \end{aligned} \quad (11)$$

where we have used that the coupling kernels $h(t)$ are normalized. Provided we now specify (1) the firing-rate functions (F_r^{ON} , F_r^{OFF} , F_c^{ON} , F_c^{OFF}), (2) the coupling kernels $h(t)$, (3) the firing rate of the retinal ganglion cell $\hat{R}_g^{\text{ON}}(t)$ providing the feedforward input to LGN ON cells, and (4) the background firing rate of the LGN OFF cell I_{r0}^{OFF} , the Eqs. (3)–(11) constitute a complete mathematical model in terms of integral equations. This integral equation set can in principle be solved numerically for any choice of coupling kernels and firing-rate functions, but this approach will not be pursued here.

Model on differential form

To obtain a simpler model which also can be mapped to a differential form more amenable to numerical evaluation, we now choose the following normalized temporal kernels for the thalamocortical feedback loop:

$$h_{\text{cr}}^{\text{ON}}(t) = h_{\text{cr}}^{\text{OFF}}(t) = \delta(t - \Delta_{\text{cr}}), \quad (12)$$

$$h_{\text{rc}}^{\text{ON}}(t) = h_{\text{rc}}^{\text{OFFx}}(t) = e^{-(t-\Delta_{\text{rc}})/\tau_{\text{rc}}} \Theta(t - \Delta_{\text{rc}})/\tau_{\text{rc}}, \quad (13)$$

where $\delta(t)$ is the Dirac δ -function, and $\Theta(t)$ is the Heaviside unit step function. The feedforward kernels $h_{\text{cr}}^{\text{ON}}(t)$ and $h_{\text{cr}}^{\text{OFF}}(t)$ represent simple delays in the feedforward connections between LGN and cortex. The kernel $h_{\text{rc}}^{\text{ON}}(t)$,

which represents the feedback coupling between the cortical ON cell and the LGN ON cell, is modeled as a delayed decaying exponential, i.e., a delayed (RC) low-pass filter (Einevoll and Plesser 2002). The same kernel is assumed for the feedback cross-connection $h_{\text{rc}}^{\text{OFFx}}(t)$ from the cortical OFF cell to the LGN ON cell. The choice of imposing a low-pass filter in the feedback connections, and not in the feedforward connections, was made to allow for a straightforward mapping of the model from integral to a differential form (see below). We nevertheless expect the combined use of a simple delay and a low-pass filter kernel to represent salient features of how relay cell responses are affected by the thalamocortical loop.

For the retinal ganglion cell driving the ON LGN relay cell we define the normalized firing rate $r_g^{\text{ON}}(t)$ as

$$r_g^{\text{ON}}(t) \equiv R_g^{\text{ON}}(t)/A_g, \quad (14)$$

where A_g is the maximum deviation of the ganglion-cell firing rate from the background firing rate R_{g0}^{ON} . $|r_g^{\text{ON}}(t)|$ will thus always be between 0 and 1.

Finally we require that model parameters and firing-rate functions are such that the model predicts the *background* firing rates of the cortical neurons providing the feedback to be zero (Heeger 1991), i.e., that there is no cortical feedback effects onto the relay cells in the background state. This means that

$$R_{c0}^{\text{ON}} = R_{c0}^{\text{OFF}} = 0, \quad (15)$$

so that $\hat{R}_c^{\text{ON}}(t) = R_c^{\text{ON}}(t)$ and $\hat{R}_c^{\text{OFF}}(t) = R_c^{\text{OFF}}(t)$.

We then introduce the auxiliary dynamical variable $z(t)$ as

$$z(t) \equiv \frac{w_{\text{rc}}^{\text{ON}}}{A_g w_{\text{rg}}^{\text{ON}}} (h_{\text{rc}}^{\text{ON}} * R_c^{\text{ON}})(t) + \frac{w_{\text{rc}}^{\text{OFFx}}}{A_g w_{\text{rg}}^{\text{ON}}} (h_{\text{rc}}^{\text{OFFx}} * R_c^{\text{OFF}})(t). \quad (16)$$

This new dynamical variable essentially corresponds to the filtered feedback onto the ON LGN relay cell. Note that $z = 0$ when no visual stimulus is present.

As described in detail in Appendix 1 the system described by (3)–(11) can be transformed into the following differential delay equation with absolute delay (MacDonald 1979) in terms of the auxiliary variable $z(t)$:

$$\begin{aligned} \frac{d}{dt}z(t) &= -\frac{z(t)}{\tau_{\text{rc}}} + \frac{w_{\text{rc}}^{\text{ON}}}{A_g w_{\text{rg}}^{\text{ON}} \tau_{\text{rc}}} R_c^{\text{ON}}(t - \Delta_{\text{rc}}) \\ &\quad + \frac{w_{\text{rc}}^{\text{OFFx}}}{A_g w_{\text{rg}}^{\text{ON}} \tau_{\text{rc}}} R_c^{\text{OFF}}(t - \Delta_{\text{rc}}) = -\frac{z(t)}{\tau_{\text{rc}}} + \frac{w_{\text{rc}}^{\text{ON}}}{A_g w_{\text{rg}}^{\text{ON}} \tau_{\text{rc}}} F_c^{\text{ON}} \\ &\quad \times \left[w_{\text{cr}}^{\text{ON}} F_r^{\text{ON}} \left(A_g w_{\text{rg}}^{\text{ON}} (\bar{r}_{r0}^{\text{ON}} + \bar{r}_g(t - \Delta_{\text{fb}}) + z(t - \Delta_{\text{fb}})) \right) \right] \\ &\quad + \frac{w_{\text{rc}}^{\text{OFFx}}}{A_g w_{\text{rg}}^{\text{ON}} \tau_{\text{rc}}} F_c^{\text{OFF}} \left[w_{\text{cr}}^{\text{OFF}} F_r^{\text{OFF}} \left(A_g w_{\text{rg}}^{\text{ON}} (\bar{r}_{r0}^{\text{OFF}} - \bar{r}_g(t - \Delta_{\text{fb}}) \right. \right. \\ &\quad \left. \left. - z(t - \Delta_{\text{fb}})) \right) \right] \end{aligned} \quad (17)$$

where we have introduced the auxiliary variable $\bar{r}_g(t)$, corresponding to the stimulus-evoked retinal firing rate filtered through the feedforward kernel, i.e.,

$$\bar{r}_g(t) \equiv (h_{rg}^{ON} * r_g^{ON})(t) - \eta_{ffi}(h_{rg}^{ON} * r_g^{ON})(t). \quad (18)$$

Here we have defined η_{ffi} as the ratio of the feedforward inhibitory and excitatory weights, i.e.,

$$\eta_{ffi} \equiv w_{rg}^{ON} / w_{rg}^{ON}. \quad (19)$$

In addition the *total feedback delay* Δ_{fb} has been introduced as

$$\Delta_{fb} \equiv \Delta_{cr} + \Delta_{rc}, \quad (20)$$

and we also have introduced the dimensionless quantities

$$\bar{i}_{r0}^{ON} \equiv I_{r0}^{ON} / A_g w_{rg}^{ON}, \quad \bar{i}_{r0}^{OFF} \equiv I_{r0}^{OFF} / A_g w_{rg}^{ON}. \quad (21)$$

With the introduction of $\bar{r}_g(t)$ in (18) and $z(t)$ in (16), $I_r(t)$ in (11) can be compactly written as

$$I_r(t) = A_g w_{rg}^{ON} (\bar{r}_g(t) + z(t)), \quad (22)$$

and we now have the following relationships between the firing rates and our new variables,

$$\hat{R}_r^{ON}(t) = F_r^{ON} \left(A_g w_{rg}^{ON} (\bar{i}_{r0}^{ON} + \bar{r}_g(t) + z(t)) \right), \quad (23)$$

$$\hat{R}_r^{OFF}(t) = F_r^{OFF} \left(A_g w_{rg}^{ON} (\bar{i}_{r0}^{OFF} - \bar{r}_g(t) - z(t)) \right), \quad (24)$$

$$R_c^{ON}(t) = F_c^{ON} \left[w_{cr}^{ON} F_r^{ON} \left(A_g w_{rg}^{ON} (\bar{i}_{r0}^{ON} + \bar{r}_g(t - \Delta_{cr}) + z(t - \Delta_{cr})) \right) \right], \quad (25)$$

$$R_c^{OFF}(t) = F_c^{OFF} \left[w_{cr}^{OFF} F_r^{OFF} \left(A_g w_{rg}^{ON} (\bar{i}_{r0}^{OFF} - \bar{r}_g(t - \Delta_{cr}) - z(t - \Delta_{cr})) \right) \right]. \quad (26)$$

Given (1) the firing-rate functions (F_r^{ON} , F_r^{OFF} , F_c^{ON} , F_c^{OFF}), (2) the retinogeniculate coupling kernels h_{rg}^{ON} and h_{rg}^{ON} , and (3) the retinal ganglion-cell firing rate $r_g^{ON}(t)$ providing the feedforward input, the above equations provide a straightforward numerical recipe for calculating the response of the LGN and cortical neurons. The central equation is the differential delay equation with absolute delay (17) describing the dynamics of the auxiliary variable $z(t)$, while (23)–(26) simply translate the result for $z(t)$ into the desired firing rates.

Model with threshold firing-rate functions

We now assume the firing-rate functions of both the LGN and cortical cells to be half-wave rectifying functions (Gazères et al. 1998; Troyer et al. 1998, 2002; Einevoll and Heggelund 2000; Dayan and Abbott 2001), i.e.,

$$F_r^{ON}(x) = [x - \Lambda_r^{ON}]_+, \quad (27)$$

$$F_r^{OFF}(x) = [x - \Lambda_r^{OFF}]_+, \quad (28)$$

$$F_c^{ON}(x) = [x - \Lambda_c^{ON}]_+, \quad (29)$$

$$F_c^{OFF}(x) = [x - \Lambda_c^{OFF}]_+, \quad (30)$$

where Λ_r^{ON} , Λ_r^{OFF} , Λ_c^{ON} and Λ_c^{OFF} are threshold values. With the additional prior assumption (15) that the background firing rates of the cortical neurons providing the feedback are zero, the delay differential Eq. (17) for $z(t)$ simplifies substantially. As described in Appendix 2 we find

$$\begin{aligned} \frac{d}{dt} z(t) = & -\frac{z(t)}{\tau_{rc}} + \frac{w_{fb}^{ON}}{\tau_{rc}} [\bar{r}_g(t - \Delta_{fb}) + z(t - \Delta_{fb}) - \lambda_c^{ON}]_+ \\ & + \frac{w_{fb}^{OFFx}}{\tau_{rc}} [-\bar{r}_g(t - \Delta_{fb}) + z(t - \Delta_{fb}) - \lambda_c^{OFF}]_+, \end{aligned} \quad (31)$$

where the total weights of the thalamocortical feedback loop are given by

$$w_{fb}^{ON} \equiv w_{cr}^{ON} w_{rc}^{ON}, \quad w_{fb}^{OFFx} \equiv w_{cr}^{OFF} w_{rc}^{OFFx}, \quad (32)$$

and we have introduced new *effective firing thresholds* for the cortical cells as

$$\lambda_c^{ON} \equiv -\left(\bar{i}_{r0}^{ON} - \Lambda_r^{ON} / (A_g w_{rg}^{ON}) - \Lambda_c^{ON} / (A_g w_{rg}^{ON} w_{cr}^{ON})\right), \quad (33)$$

$$\lambda_c^{OFF} \equiv \bar{i}_{r0}^{OFF} - \Lambda_r^{OFF} / (A_g w_{rg}^{ON}) - \Lambda_c^{OFF} / (A_g w_{rg}^{ON} w_{cr}^{OFF}). \quad (34)$$

The formulas relating the dynamical variable $z(t)$ to the firing rates (23)–(26) are also substantially simplified,

$$\hat{R}_r^{ON}(t) = A_g w_{rg}^{ON} [\bar{r}_g(t) + z(t) - \lambda_r^{ON}]_+, \quad (35)$$

$$\hat{R}_r^{OFF}(t) = A_g w_{rg}^{ON} [-\bar{r}_g(t) + z(t) - \lambda_r^{OFF}]_+, \quad (36)$$

$$R_c^{ON}(t) = A_g w_{rg}^{ON} w_{cr}^{ON} [\bar{r}_g(t - \Delta_{cr}) + z(t - \Delta_{cr}) - \lambda_c^{ON}]_+, \quad (37)$$

$$R_c^{OFF}(t) = A_g w_{rg}^{ON} w_{cr}^{OFF} [-\bar{r}_g(t - \Delta_{cr}) + z(t - \Delta_{cr}) - \lambda_c^{OFF}]_+, \quad (38)$$

where we further have introduced new effective firing thresholds for the relay cells as

$$\lambda_r^{ON} \equiv -\left(\bar{i}_{r0}^{ON} - \Lambda_r^{ON} / (A_g w_{rg}^{ON})\right), \quad (39)$$

$$\lambda_r^{OFF} \equiv \bar{i}_{r0}^{OFF} - \Lambda_r^{OFF} / (A_g w_{rg}^{ON}). \quad (40)$$

In the absence of visual stimuli both $\bar{r}_g(t)$ and $z(t)$ are zero. From (37) and (38) we thus see that in order to fulfill the requirement (15) of zero background firing rates of the

cortical cells feeding back to the LGN, λ_c^{ON} must be non-negative and λ_c^{OFF} must be non-positive.

A notable feature of the differential delay equation for $z(t)$ in (31), is that the relay-cell threshold values Λ_r^{ON} and Λ_r^{OFF} only enter indirectly via λ_c^{ON} and λ_c^{OFF} , cf. (33) and (34). These threshold values thus mainly affect the translation of the dynamical variables $\bar{r}(t)$ and $z(t)$ into predictions for the relay-cell firing rates as described by (35) and (36). From the expressions (31)–(38) we further see that the product $A_g w_{\text{rg}}^{\text{ON}}$ essentially is a trivial scaling factor that only affects the overall magnitude of resulting firing rates.

Throughout the rest of the paper we will focus on the model with threshold firing-rate functions specified by (31)–(40) as well as previous definitions. To facilitate an easier communication of our model, we present, in accordance with ‘good model description practice’ (Nordlie et al. 2009a), an overview of our model in Tables 1 and 2. We also illustrate some salient elements of the model in Fig. 2.

Linear model for balanced ON/OFF feedback

The differential Eq. (31) for the filtered feedback effect $z(t)$ is non-linear due to the presence of the half-wave rectification functions. However, for the special case when (1) the ON and OFF feedback weights are opposite with the same magnitude, i.e., $w_{\text{fb}}^{\text{ON}} = -w_{\text{fb}}^{\text{OFF}} \equiv w_{\text{fb}}$, and (2) the thresholds of the ON and OFF cortical cells both are zero, i.e., $\lambda_c^{\text{ON}} = \lambda_c^{\text{OFF}} = 0$, the combined effect of the feedback from the cortical ON and OFF cells turns out to be linear. In this case the two half-wave rectifying functions on the right hand side of (31) add up to a linear function, i.e., $[x]_+ - [-x]_+ = x$, and the differential delay equation for $z(t)$ simplifies to

$$\frac{d}{dt}z(t) = -\frac{z(t)}{\tau_{\text{rc}}} + \frac{w}{\tau_{\text{rc}}}(\bar{r}_{\text{g}}(t - \Delta_{\text{fb}}) + z(t - \Delta_{\text{fb}})). \quad (41)$$

If in addition the relay-cell threshold λ_r^{ON} is sufficiently low so that $\bar{r}_{\text{g}}(t) + z(t) - \lambda_r^{\text{ON}} > 0$, the half-wave rectification function $[x]_+$ can be replaced with x in (35), and we then have a completely linear model for the stimulus-evoked relay-cell response (Einevoll and Plesser 2002, 2011).

Feedforward temporal coupling kernels

While the particular choice of thalamocortical and corticothalamic temporal coupling kernels in (12) and (13), respectively, is required to map the system on integral form onto a single first-order differential system, no particular requirements are imposed on the feedforward excitatory and inhibitory temporal kernels $h_{\text{rg}}^{\text{ON}}(t)$ and $h_{\text{rg}}^{\text{OFF}}(t)$. For simplicity, we here assume that they both are decaying

exponentials (Einevoll and Plesser 2002) where the onset of the inhibitory effect, which is disynaptic since it is mediated by the intrageniculate interneuron, is delayed by a time Δ_{rig} compared to the onset of the excitatory effect, i.e.,

$$h_{\text{rg}}^{\text{ON}}(t) = \frac{1}{\tau_{\text{rg}}} e^{-t/\tau_{\text{rg}}} \Theta(t), \quad (42)$$

$$h_{\text{rg}}^{\text{OFF}}(t) = \frac{1}{\tau_{\text{rig}}} e^{-(t-\Delta_{\text{rig}})/\tau_{\text{rig}}} \Theta(t - \Delta_{\text{rig}}). \quad (43)$$

Here τ_{rg} and τ_{rig} are the time constants of the two feed-forward pathways.

Linear systems analysis

Linear systems such as (41) with a linear relay-cell firing rate function are most transparently described in frequency space. For linear systems the response to a sinusoidal input is a (phase-shifted) sinusoidal output, and the *transfer function*, i.e., the ratio between the output and input sinusoidal signals, completely specifies the system (Oppenheim and Willsky 1996; Einevoll and Plesser 2002). But also for non-linear neural systems, this measure has been used to characterize input/output relationships (e.g., Blomquist et al. 2009).

For our geniculate model circuit the transfer function $\tilde{T}_{\text{rg}}^{\text{ON}}(\omega)$ is defined via (Einevoll and Plesser 2002)

$$\tilde{T}_{\text{rg}}^{\text{ON}}(\omega) = \tilde{R}_{\text{r}}^{\text{ON}}(\omega)/A_{\text{g}}^{\text{osc}}. \quad (44)$$

Here ω is the so called *angular* temporal frequency related to the more traditional temporal frequency f via $\omega = 2\pi f$. Further, $A_{\text{g}}^{\text{osc}}$ is the amplitude of the sinusoidally oscillating input firing rate $R_{\text{g}}^{\text{ON}}(t)$, while $\tilde{R}_{\text{r}}^{\text{ON}}(\omega)$ is a complex representation of the first harmonic Fourier amplitude, as well as phase-shift, of the evoked relay-cell firing-rate $R_{\text{r}}^{\text{ON}}(t)$ (Einevoll and Plesser 2002).

This firing-rate transfer function $\tilde{T}_{\text{rg}}^{\text{ON}}(\omega)$ from retina to LGN can in the general case be evaluated numerically by solving our model (31) with sinusoidal retinal input imposed, and then perform a numerical Fourier transform of the resulting relay-cell firing rate (see ‘‘Appendix 3’’ for details). However, for our linear system (41), with feed-forward coupling kernels described by (42)–(43), we can find a closed-form solution. Following the approach in Einevoll and Plesser (2002) we find

$$\tilde{T}_{\text{rg}}^{\text{ON}}(\omega) = w_{\text{rg}}^{\text{ON}} \frac{\tilde{h}_{\text{rg}}^{\text{ON}}(\omega) - \eta_{\text{ff}} \tilde{h}_{\text{rig}}^{\text{ON}}(\omega)}{1 - w_{\text{fb}} \tilde{h}_{\text{fb}}(\omega)}. \quad (45)$$

Here $\tilde{h}_{\text{fb}}(\omega)$ is the Fourier transform of the total kernel for the thalamocortical loop, i.e.,

Table 1 Tabular description of the model, part 1

Model summary			
Neural elements			
Retina (ON), lateral geniculate nucleus (ON/OFF), cortex (ON/OFF)			
Neurons modeled as firing rate units			
Drifting sinusoidal gratings, light impulses			
Neural elements			
Name	Elements	Size	
g	Retina (retinal ganglion cell)	1	
r	Lateral geniculate nucleus (geniculate relay cell)	2	
c	Cortex (cortical cell)	2	
Connectivity			
Syn. weight	Source	Target	Temporal kernel
w_{rg}^{ON}	g	r	$h_{rg}^{ON}(t) = e^{-t/\tau_{rg}}\Theta(t)/\tau_{rg}$
w_{rg}^{ON}	g	r	$h_{rg}^{ON}(t) = e^{-(t-\Delta_{ig})/\tau_{ig}}\Theta(t-\Delta_{ig})/\tau_{ig}$
$w_{cr}^{\{ON,OFF\}}$	r	c	$h_{cr}(t) = \delta(t-\Delta_{cr})$
$w_{rc}^{\{ON,OFF\}}$	c	r	$h_{rc}(t) = e^{-(t-\Delta_{rc})/\tau_{rc}}\Theta(t-\Delta_{rc})/\tau_{rc}$
General firing-rate model			
Firing rate ganglion cell (ON)			
Firing rate relay cells			
Firing rate cortical cells			
<div>$\hat{R}_g^{ON}(t) \equiv R_{g0}^{ON} + R_g^{ON}(t)$ $\hat{R}_r^{ON}(t) \equiv R_{r0}^{ON} + R_r^{ON}(t) = F_r^{ON}(I_{r0}^{ON} + I_r(t))$ $\hat{R}_r^{OFF}(t) \equiv R_{r0}^{OFF} + R_r^{OFF}(t) = F_r^{OFF}(I_{r0}^{OFF} - I_r(t))$ $\hat{R}_c^j(t) \equiv R_{c0}^j + R_c^j(t) = F_c^j(w_{cr}^j(h_{cr}^j * \hat{R}_r^j)(t))$, where $\hat{R}_{k0}^j$ ($k = g, r, c$; $j = ON, OFF$) is background firing rate, $\hat{R}_k^j(t)$ is stimulus-evoked change in firing rate. Background input: $I_{r0}^{ON} = (w_{rg}^{ON} - w_{rg}^{OFF}) R_{g0}^{ON} + w_{rc}^{ON} R_{c0}^{ON} + w_{rc}^{OFF} R_{c0}^{OFF}$ Stimulus-evoked input: $I_r(t) = w_{rg}^{ON}(h_{rg}^{ON} * R_g^{ON})(t) - w_{rg}^{OFF}(h_{rg}^{OFF} * R_g^{OFF})(t) + w_{rc}^{ON}(h_{rc}^{ON} * R_c^{ON})(t) + w_{rc}^{OFF}(h_{rc}^{OFF} * R_c^{OFF})(t)$ F is the firing rate function, $F_i^j(x) = [x - \Lambda_i^j]_+$ and $F_c^j(x) = [x - \Lambda_c^j]_+$ Drifting sinusoidal gratings: $\hat{R}_g^{ON}(t) = R_{g0}^{ON} + A_g^{osc} \sin(2\pi f t)$ Light impulses: $\hat{R}_g^{ON}(t) = R_{g0}^{ON} + A_g r_g^{ON}(t)$, with $r_g^{ON}(t) = \begin{cases} \sin(\pi t/a), & 0 \leq t \leq a \\ B \sin(\pi t/a), & a < t \leq 2a \\ 0, & \text{otherwise} \end{cases}$</div>			
Stimulus			

Table 2 Tabular description of the model, part 2

Final numerical model	
Dynamical system	Auxiliary variable
	$z(t) \equiv \frac{w_{rc}^{ON}}{A_g w_{rg}^{ON}} (h_{rc}^{ON} * R_c^{ON})(t) + \frac{w_{rc}^{OFFx}}{A_g w_{rg}^{ON}} (h_{rc}^{OFFx} * R_c^{OFF})(t)$
	Delay differential equation
	$\frac{d}{dt} z(t) = -\frac{z(t)}{\tau_{rc}} + \frac{w_{fb}^{ON}}{\tau_{rc}} [\bar{r}_g(t - \Delta_{fb}) + z(t - \Delta_{fb}) - \lambda_c^{ON}]_+ \\ + \frac{w_{fb}^{OFFx}}{\tau_{rc}} [-\bar{r}_g(t - \Delta_{fb}) + z(t - \Delta_{fb}) - \lambda_c^{OFF}]_+$
	where
	$\bar{r}_g(t) \equiv (h_{rg}^{ON} * r_g^{ON})(t) - \eta_{ff} (h_{rg}^{ON} * r_g^{ON})(t)$
Firing rate relay cells	$\hat{R}_r^{ON}(t) = A_g w_{rg}^{ON} [\bar{r}_g(t) + z(t) - \lambda_r^{ON}]_+$
	$\hat{R}_r^{OFF}(t) = A_g w_{rg}^{ON} [-\bar{r}_g(t) + z(t) - \lambda_r^{OFF}]_+$
Firing rate cortical cells	$R_c^{ON}(t) = A_g w_{rg}^{ON} w_{cr}^{ON} [\bar{r}_g(t - \Delta_{cr}) + z(t - \Delta_{cr}) - \lambda_c^{ON}]_+$
	$R_c^{OFF}(t) = A_g w_{rg}^{ON} w_{cr}^{OFF} [-\bar{r}_g(t - \Delta_{cr}) + z(t - \Delta_{cr}) - \lambda_c^{OFF}]_+$

Fig. 2 Illustration of salient features of the LGN circuit model described by (31)–(40). **a** shows an example trace of the ON LGN relay-cell firing rate $\hat{R}_r^{ON}(t)$ (in units of $A_g w_{rg}^{ON}$) where λ_r^{ON} is so small that the relay-cell firing-rate function in (35) always is in the linear regime. In **b** the stimulus-evoked (i.e., time-dependent) part $\hat{R}_r^{ON}(t)$ of this relay-cell firing rate is shown. **c** Shows the corresponding firing rate in the cortical ON cell for two cases: without thalamocortical feedforward delay ($\Delta_{cr} = 0$, solid line) and with a feedforward delay $\Delta_{cr} = 20$ ms (dashed line). The half-wave rectification function implies that there is only non-zero cortical firing at times when $R_r^{ON}(t - \Delta_{cr})/A_g w_{rg}^{ON}$ is larger than λ_c^{ON} , cf. **b**. The corresponding firing rate of the cortical OFF cell is shown in **d**. Here a response is only elicited when $R_r^{ON}(t - \Delta_{cr})/A_g w_{rg}^{ON}$ is less than λ_c^{OFF} , cf. **b**. In the example we have set $w_{cr}^{ON} = w_{cr}^{OFF} = 1$, and cortical feedback to LGN is absent, i.e., $w_{rc}^{ON} = w_{rc}^{OFFx} = 0$

$$\tilde{h}_{fb}(\omega) \equiv \tilde{h}_{rc}^{ON}(\omega) \tilde{h}_{cr}^{ON}(\omega) = \tilde{h}_{rc}^{OFFx}(\omega) \tilde{h}_{cr}^{OFF}(\omega). \quad (46)$$

With the convention

$$\tilde{f}(\omega) = \int_{-\infty}^{\infty} f(t) e^{-i\omega t} dt, \quad (47)$$

we find with the use of (12) and (13) that

$$\tilde{h}_{fb}(\omega) = \tilde{h}_{rc}^{ON}(\omega) \tilde{h}_{cr}^{ON}(\omega) = \frac{e^{-i\omega \Delta_{fb}}}{1 + i\omega \tau_{rc}}. \quad (48)$$

The Fourier transform of the feedforward kernels in (42) and (43) are

$$\tilde{h}_{rg}^{ON}(\omega) = 1/(1 + i\omega \tau_{rg}), \quad (49)$$

$$\tilde{h}_{rg}^{ON}(\omega) = e^{-i\omega \Delta_{rig}}/(1 + i\omega \tau_{rig}), \quad (50)$$

and the resulting transfer function becomes (Einevoll and Plesser 2002)

$$\tilde{T}_{rg}^{ON}(\omega) = w_{rg}^{ON} \frac{1/(1 + i\omega \tau_{rg}) - \eta_{ff} e^{-i\omega \Delta_{rig}}/(1 + i\omega \tau_{rig})}{1 - w_{fb} e^{-i\omega \Delta_{fb}}/(1 + i\omega \tau_{rc})}. \quad (51)$$

A core feature of such a linear-system transfer function is that it is independent of retinal processing. This implies that the analysis of results from experiments with drifting-grating stimuli, where the input firing-rate from retinal ganglion cells will be sinusoidally modulated, in principle is more straightforward than for other choices of visual stimuli (e.g., flashing spots and white-noise).

Results

Our model can in principle predict responses of LGN relay cells to any kind of visual stimuli, i.e., any kind of

incoming firing-rate patterns from retinal ganglion cells. Many types of visual stimuli have been used, e.g., flashing spots, drifting gratings or white-noise stimuli to extract impulse responses. The main emphasis in this paper is on how the feedforward and feedback elements of the thalamocortical circuit modify the impulse responses of LGN relay cells compared to the impulse response of the retinal ganglion cells driving the circuit (Cai et al. 1997; Usrey et al. 1999; Yousif and Denham 2007). First, however, we will briefly investigate the model response to sinusoidal gratings.

Drifting sinusoidal gratings

The use of sinusoidal drifting gratings as visual stimuli has a long history in visual neuroscience (Enroth-Cugell and Robson 1966; Shapley and Lennie 1985). A main advantage of such stimuli is that for linear systems each frequency component can be probed individually. Drifting sinusoidal stimuli have also been used to probe the temporal signal processing properties of LGN relay neurons (Derrington and Fuchs 1979; Kaplan et al. 1987, 1993; Mukherjee and Kaplan 1995; Marrocco et al. 1996). Typically the temporal frequency tuning curves have exhibited maxima between 6 and 10 Hz, but the measured tuning curves have been quite variable (Derrington and Fuchs 1979; Kaplan et al. 1979, 1987), and have further been found to depend on the level of arousal (Kaplan et al. 1993; Mukherjee and Kaplan 1995). Further, the retinogeniculate *transfer ratio*, i.e., the amplitude of the transfer function (44), has correspondingly been found to exhibit a band-pass property where the peak also occurs for temporal frequencies f around 6–10 Hz (Kaplan et al. 1987, 1993; Mukherjee and Kaplan 1995). Attempts have also been made to unravel cortical feedback effects by investigating changes in the tuning curves when feedback effects are altered by cortical inactivation. However, such experiments have proved very difficult to do, and the reported results have been inconclusive (Marrocco et al. 1996; Casti et al. 2004).

In the modeling of drifting-grating response the retinal firing rate providing the feedforward input is assumed to be linear, i.e.,

$$\hat{R}_g^{\text{ON}}(t) = R_{g0}^{\text{ON}} + A_g^{\text{osc}} \sin(2\pi ft). \quad (52)$$

In the general case the relay-cell firing rate must first be evaluated numerically for each input frequency separately by solving the differential Eq. (31) to get the auxiliary variable $z(t)$, followed by use of (35) to obtain the relay-cell firing rate $\hat{R}_r^{\text{ON}}(t)$. Then in the second step, the amplitude of the first Fourier component $|\hat{R}_r^{\text{ON}}(\omega)|$ of this relay-cell firing rate must be calculated to get the

(complex-valued) transfer function; see “Appendix 3” for details. This extracted amplitude divided by the amplitude A_g^{osc} of the oscillating retinal input gives the transfer ratio.

For the cases where the cortical feedback is absent, i.e., $w_{\text{fb}}^{\text{ON}} = w_{\text{fb}}^{\text{OFFx}} = 0$, or the ON/OFF feedback is ‘balanced’ so that (41) applies, and the amplitude of the resulting sinusoidal variation of the relay-cell firing rate is so small that the argument of the half-wave rectification in (35) is always positive, the system will be linear. In these situations we already have the transfer function: it is given by the closed-form expression in (51).

In Fig. 3 we show the transfer ratio, i.e., the magnitude $|\tilde{T}_{\text{rg}}^{\text{ON}}(f)|$ of the transfer function, for four example cases: (1) only feedforward excitation and inhibition, i.e., no cortical feedback, (2) feedforward excitation and *inphase* inhibition, i.e., inhibitory feedback driven by cortical ON cells ($\eta_{\text{ffi}} = 0$, $w_{\text{fb}}^{\text{ON}} < 0$, $w_{\text{fb}}^{\text{OFFx}} = 0$), (3) feedforward excitation plus a balanced combination of inphase

Fig. 3 Example retinogeniculate transfer ratios $|\tilde{T}_{\text{rg}}^{\text{ON}}(f)|$ for various combinations of feedforward and feedback LGN circuit connections. *Solid line* Linear model with feedforward excitation and inhibition only, so that (51) is applicable. Parameters: $\eta_{\text{ffi}} = 0.5$, $\tau_{\text{rg}} = 10$ ms, $\tau_{\text{rig}} = 30$ ms, $\Delta_{\text{rig}} = 0$ ($w_{\text{fb}}^{\text{ON}} = w_{\text{fb}}^{\text{OFFx}} = 0$). *Dashed line* Non-linear model with feedforward excitation and inphase inhibition. Parameters: $\tau_{\text{rg}} = 26$ ms, $w_{\text{fb}}^{\text{ON}} = -1$, $w_{\text{fb}}^{\text{OFFx}} = 0$, $\tau_{\text{rc}} = 39$ ms, $\Delta_{\text{fb}} = 15$ ms and $\lambda_c^{\text{ON}} = 0.2$ ($\eta_{\text{ffi}} = 0$). *Dash-dotted line* Balanced non-linear model with feedforward excitation and a combination of inphase inhibitory and antiphase excitatory feedback. Parameters: $\tau_{\text{rg}} = 26$ ms, $w_{\text{fb}}^{\text{ON}} = -w_{\text{fb}}^{\text{OFFx}} = -1$, $\tau_{\text{rc}} = 39$ ms, $\Delta_{\text{fb}} = 14$ ms, $\lambda_c^{\text{ON}} = 0.2$, $\lambda_c^{\text{OFF}} = -0.2$ ($\eta_{\text{ffi}} = 0$). *Dotted line* Linear model with feedforward excitation and balanced linear feedback so that (51) is applicable. Parameters: $\tau_{\text{rg}} = 21$ ms, $w_{\text{fb}} = -1$, $\tau_{\text{rc}} = 42$ ms, $\Delta_{\text{fb}} = 10$ ms. The relay-cell threshold λ_r^{ON} is in all cases set to be negative ($\lambda_r^{\text{ON}} = -1$), and the amplitude A_g^{osc} of the sinusoidal driving input from retina set to be so small ($A_g^{\text{osc}} = 0.7$) in the numerical simulations so that the firing-rate function for the relay ON cell always is in the linear regime

inhibition (driven by cortical ON cells) and *antiphase* excitation (driven by cortical OFF cell), i.e., $\eta_{\text{ff}} = 0$, $w_{\text{fb}}^{\text{ON}} < 0$, $w_{\text{fb}}^{\text{OFFx}} > 0$, and (4) feedforward excitation and balanced, effectively linear, feedback from cortical ON and OFF cells. For cases (2)–(3) the results are found using the numerical scheme briefly outlined above. For cases (1) and (4) the transfer ratio is found directly from the analytical formula (51). The different transfer-ratio tuning curves for our four example models are seen to be quite similar and also in qualitative accordance with previous experimental observations (Kaplan et al. 1987; Mukherjee and Kaplan 1995).

Our results for drifting-grating stimuli indicate that it might be difficult to disambiguate feedforward and feedback effects from transfer function frequency tuning curves. We thus turn to another type of visual stimulus.

Impulse response

For neurons in the visual system the *impulse response* corresponds to the change in firing rate following a very brief light stimulation by a point-like light source. White-noise analysis of LGN neurons, as well as their retinal input, has revealed characteristic biphasic temporal structures of this impulse response (DeAngelis et al. 1995; Cai et al. 1997; Usrey et al. 1999). For ON neurons, for example, a brief point-like increased illumination in the receptive field center typically gives a positive impulse-response phase lasting for about 50 ms or so, followed by a negative rebound phase lasting for about the same time or longer (Cai et al. 1997; Usrey et al. 1999). Usrey et al. (1999) did a comprehensive study of impulse responses of LGN neurons and their dominant retinal input, and their investigations revealed characteristic differences between the input and output impulse responses: (1) the peak of the maximum impulse response of the LGN neuron was delayed compared to its retinal input, (2) the amplitude of the negative rebound phase for the LGN neurons was typically larger in relative terms than for their retinal input.

Here we explore within the context of our model how the detailed form of the impulse response of LGN neurons is affected by feedforward and feedback circuit effects. The relatively simple model structure, and thus modest number of crucial model parameters, allow for a comprehensive investigation of the model parameter space.

Following Yousif and Denham (2007) we model the (normalized) biphasic impulse response of the retinal input as follows:

$$r_{\text{g}}^{\text{ON}}(t) = \begin{cases} \sin(\pi t/a), & 0 \leq t \leq a \\ B \sin(\pi t/a), & a < t \leq 2a \\ 0, & \text{otherwise.} \end{cases} \quad (53)$$

Here B is a positive number smaller than one, and a is the duration of each phase of the signal. The form of this retinal impulse response function with $B = 0.38$ and $a = 42.5$ ms is shown in Fig. 4. These parameter values give the time 21.2 ms for the maximum of the impulse response and a relative amplitude value of 0.38 for the negative rebound phase compared to the amplitude of the first positive phase. These numbers correspond to the mean of the range of values reported by Usrey et al. (1999).

In the present model application we assume for simplicity that the relay-cell threshold value and the magnitude of the retinal input pulse are such that the half-wave rectification non-linearity $[x]_+$ in the firing-rate function for the relay ON cell in (35) never comes into play, and can be replaced by x , i.e., that the firing-rate function always operates in the linear regime, cf., top panel in Fig. 2. Beyond the requirement of assuring a linear impulse response, the choice of relay-cell threshold value $\lambda_{\text{r}}^{\text{ON}}$ will thus not affect the calculated impulse response.

In Fig. 4 we also show an illustration of an LGN impulse response driven by the retinal-input impulse response depicted in the same figure (see caption for model parameters). Compared to the input impulse response, the example LGN impulse response exhibits both of the characteristic features observed by Usrey et al. (1999): delayed maximum response in the first phase and a larger negative rebound, both in absolute and relative terms, in the second phase. The example LGN response in the figure is *triphasic*, i.e., it has a

Fig. 4 Impulse response. Biphasic normalized impulse response for a retinal ganglion cell (*dashed line*) and the corresponding impulse response of an LGN relay cell driven by the ganglion cell (*solid line*). The depicted normalized retinal-input impulse response is used throughout this paper and is described by the formula in (53) with parameter values $B = 0.38$ and $a = 42.5$ ms. $R_{r,\text{max}}$ the maximal value of the relay-cell response in the first phase (occurring at t_{max}), and $R_{r,\text{min}}$ the magnitude at the minimum of for the second phase (occurring at t_{min}). The *biphasic index* I_{BP} is defined as the ratio of these two quantities, i.e., $I_{\text{BP}} \equiv R_{r,\text{min}}/R_{r,\text{max}}$

second positive rebound phase after the negative rebound phase. While Cai et al. (1997) reported most of the measured LGN impulse responses to be biphasic, some cells were also found to have mono- or triphasic responses.

In Fig. 5 we illustrate the formation of the ON LGN impulse response $R_r^{ON}(t)$ by feedforward and feedback contributions in a variety of situations. In all cases the normalized retinal impulse response $r_g^{ON}(t)$ is the same as in Fig. 4.

In the top row we focus on *feedforward* contributions only, i.e., cortical feedback effects are assumed to be absent, $w_{fb}^{ON} = w_{fb}^{OFFx} = 0$, and the relative weight of the feedforward inhibition compared to the feedforward excitation is fixed at $\eta_{ff} = 0.7$. In panel a we show results for a feedforward model with time constants $\tau_{rg} = 20$ ms and $\tau_{rig} = 65$ ms. The total impulse response, given by a sum of a biphasic excitatory (positive) response and a monophasic

Fig. 5 Example LGN impulse responses illustrating various effects of feedforward and feedback connections in the LGN circuit. *Solid lines* Example impulse responses for relay ON cells $R_r^{ON}(t)$ calculated from Eqs. (18), (31), and (35) for the situation when λ_r^{ON} is such that there are no rectification effects on the response, $R_r^{ON}(t) = A_g w_{rg}^{ON}(\bar{r}_g(t) + z(t))$. *Dashed lines* Contribution from feedforward excitation alone, i.e., $A_g w_{rg}^{ON}(h_{rg}^{ON} * R_g^{ON})(t)$. *Dotted lines* Contribution from feedforward inhibition, i.e., $-A_g w_{rg}^{ON} \eta_{ff} (h_{rig}^{ON} * R_g^{ON})(t)$, or feedback, i.e., $A_g w_{rg}^{ON} z(t)$, alone, see specification for each panel. All quantities are shown in units of $A_g w_{rg}^{ON}$. **a–c** Feedforward excitation and inhibition only with $\eta_{ff} = 0.7$. **A**: $\tau_{rg} = 20$ ms, $\tau_{rig} = 65$ ms. **b**

$\tau_{rg} = 5$ ms, $\tau_{rig} = 65$ ms. **c** $\tau_{rg} = 5$ ms, $\tau_{rig} = 20$ ms. **d** Feedforward excitation and inphase inhibitory feedback: $\tau_{rg} = 10$ ms, $w_{fb}^{ON} = -0.75$, $w_{fb}^{OFFx} = 0$, $\tau_{rc} = 20$ ms, $\Delta_b = 10$ ms, $\lambda_c^{ON} = 0$. **e**: Feedforward excitation and antiphase excitatory feedback. Parameters as in **d** except $w_{fb}^{ON} = 0$, $w_{fb}^{OFFx} = 0.75$, $\lambda_c^{OFF} = 0$. **f** Feedforward excitation and balanced non-linear feedback. Parameters as in **d** except $w_{fb}^{ON} = -0.75$, $w_{fb}^{OFFx} = 0.75$, $\lambda_c^{ON} = 0.15$, $\lambda_c^{OFF} = -0.15$. **g** Feedforward excitation and balanced linear feedback: $\tau_{rg} = 10$ ms, $w_{fb} = w_{fb}^{ON} = -w_{fb}^{OFFx} = -1.8$, $\tau_{rc} = 20$ ms, $\Delta_b = 20$ ms, $\lambda_c^{ON} = \lambda_c^{OFF} = 0$. **h** Same as **g** with $w_{fb} = w_{fb}^{ON} = -w_{fb}^{OFFx} = -1.0$. **i** Same as **g** with $\lambda_c^{ON} = 0.15$, $\lambda_c^{OFF} = -0.15$. Note different time axes in **g–i**

inhibitory (negative) response, is biphasic and long-lasting. With a reduction of the excitatory time constant to $\tau_{\text{rg}} = 5$ ms as for panel b, the excitatory part of the LGN impulse response is shifted to shorter times and increases in amplitude both for the initial positive phase and for the negative rebound phase. As a consequence the total impulse response becomes stronger than in a. Panel c shows an example of a situation where a triphasic impulse response arises. Here the same small value $\tau_{\text{rg}} = 5$ ms for the excitatory time constant is combined with the choice $\tau_{\text{rig}} = 20$ ms for the inhibitory time constant giving a biphasic inhibitory contribution as well. Since τ_{rig} is larger than τ_{rg} , the duration of the inhibitory contribution will be longer than the excitatory contribution. As seen in panel c the second phase of the inhibitory component will thus give rise to a third phase of the total impulse response $R_r^{\text{ON}}(t)$.

In the second row of Fig. 5 we correspondingly illustrate the formation of the LGN impulse response $R_r^{\text{ON}}(t)$ by *feedback* contributions. Here the feedforward inhibition is set to zero, i.e., $\eta_{\text{ffi}} = 0$, and the feedforward excitatory time constant is fixed to $\tau_{\text{rg}} = 10$ ms. In panel d we show results for $R_r^{\text{ON}}(t)$ for a model with inphase cortical inhibitory feedback, i.e., inhibitory feedback from ON cortical cells only. For the choice of feedback model parameters used in panel d with (1) substantial feedback ($w_{\text{fb}}^{\text{ON}} = -0.75$), (2) low firing threshold for the cortical ON cell ($\lambda_c^{\text{ON}} = 0$), and (3) significant time delays in the thalamo-cortical loop ($\tau_{\text{fb}} = 20$ ms, $\Delta_{\text{fb}} = 10$ ms) a sizable monophasic inhibitory feedback contribution to the impulse response is observed. The total impulse response, i.e., the sum of the feedforward excitatory and feedback inhibitory contribution, thus adds up to a biphasic response qualitatively similar to the purely feedforward impulse responses seen in panels a–c.

Panel e shows the corresponding results for a model with antiphase cortical excitatory feedback only, i.e., excitatory feedback from OFF cortical cells. Even with a similarly strong feedback as in the previous inphase case ($w_{\text{fb}}^{\text{OFFx}} = 0.75$), as well as the same temporal parameters for the cortical loop, a much weaker feedback effect on the relay ON cells is observed. This is because the cortical OFF cells providing this feedback will only be activated during the second phase of the excitatory feedforward contribution to the ON LGN-cell impulse response. Only during this negative phase for the ON relay cells will the OFF relay cells be activated and thus drive the cortical OFF cells responsible for the antiphase feedback. As seen in panel e this weak feedback effect nevertheless gives rise to a small third phase, i.e., a triphasic impulse response.

In panel f in Fig. 5 we show an example where the inphase inhibitory and antiphase excitatory feedback illustrated in panels d and e, respectively, are combined. The same temporal parameters are used, but we have raised

the threshold for firing for the cortical cells by imposing non-zero threshold values, i.e., $\lambda_c^{\text{ON}} = 0.15$, $\lambda_c^{\text{OFF}} = -0.15$. For this particular non-linear balanced-feedback case we find a total impulse response very similar to what is obtained by assuming inphase inhibitory feedback alone, cf. panel d.

For the special case when (1) the ON and OFF feedback weights are opposite with the same magnitude, i.e., $w_{\text{fb}}^{\text{ON}} = -w_{\text{fb}}^{\text{OFFx}} \equiv w_{\text{fb}}$, and (2) the threshold values of the ON and OFF cortical cells both are zero, i.e., $\lambda_c^{\text{ON}} = \lambda_c^{\text{OFF}} = 0$, the model becomes fully linear, cf. (41). For this situation the simulated LGN impulse response often shows characteristic oscillations. An example is given in panel g in the lower row of Fig. 5 where we used $w_{\text{fb}} = -1.8$, i.e., a strong feedback weight, and altogether nine phases can be seen. In panel h w_{fb} has been reduced to -1.0 , and the oscillatory behavior is less prominent.

The oscillatory characteristics of the impulse response function seen in panels g and h can be understood on the basis of the expression for the linear transfer function in (51). For the model parameters employed in these two panels, this transfer function formula predicts resonance peaks in the transfer ratio for frequencies corresponding to periods of about 65–70 ms, in accordance with the characteristic oscillation times observed in panels g and h. The transfer function formula (51) further predicts lower resonance peaks in panel h than in panel g due to the reduced weight of the cortical feedback, $w_{\text{fb}} = -1$ versus $w_{\text{fb}} = -1.8$. This is again in accordance with the less prominent oscillations seen in panel h compared to panel g.

In panel i we see that the introduction of thresholding non-linearities, i.e., $\lambda_c^{\text{ON}} = 0.15$ and $\lambda_c^{\text{OFF}} = -0.15$, in the neurons providing the cortical feedback also has the effect of reducing the oscillations in the impulse response.

Feedforward versus feedback effects on impulse response

The various examples in Fig. 5 illustrate the large variety of LGN impulse responses that can be produced by our model. In this section we do a more systematic exploration of the model with the aim of identifying regions of the model parameter space for which the predicted impulse responses are compatible with what has been observed in previous experiments (Cai et al. 1997; Usrey et al. 1999). We thus need specific measures characterizing salient features of the LGN impulse response. In accordance with these previous experimental studies we focus on three measures: (1) the time of the first maximum of the response t_{max} , (2) the *biphasic index* (I_{BP}) (Cai et al. 1997), and (3) the *normalized rebound magnitude* (*NRM*) (Usrey et al. 1999). I_{BP} corresponds to the ratio between the peak

magnitude of the (negative) rebound phase and the peak magnitude of the first (positive) phase, cf. Fig. 4. *NRM* is defined as the magnitude of the integral over the impulse response from the start of the second phase to the end of the impulse response, divided by the integral over the first phase of the impulse response. We only calculate *NRM* for the cases where the impulse response has three or fewer dominant phases, see “Appendix 3”.

In Figs. 6, 7, 8 we show the three measures ($t_{\max}$, I_{BP} , *NRM*) for different combinations of model parameters.

The retinal impulse response depicted in Fig. 4, which has a time to first maximum and biphasic index corresponding to the average of the experimental results reported by Usrey et al. (1999), provides in all cases the input. These three measures have been recorded experimentally by Cai et al. (1997) and Usrey et al. (1999) for LGN neurons, and as an aid in the interpretation of the ‘phase diagrams’ of our model, we have marked the parameter regions where the model results are within previously obtained experimental bounds. From Cai et al. (1997) we extracted

Fig. 6 Dependence of LGN impulse-response measures on relative weight (η_{ff}) and time constant (τ_{ri}/τ_{rg}) of feedforward inhibition. Parameter dependence of the three impulse-response measures $t_{\max}$ (left column), biphasic index (I_{BP} ; middle column), and normalized rebound magnitude (*NRM*; right column) for models with feedforward excitation and inhibition, only. The retinal impulse response providing the input is depicted in Fig. 4. In all cases $\Delta_{ri} = 0$. Top row $\tau_{rg} = 5$ ms; middle row $\tau_{rg} = 10$ ms; bottom row $\tau_{rg} = 20$ ms. The regions confined by thick black lines and marked

‘exp.’ correspond to parameter values which give impulse-response model predictions in agreement with the experimental bounds described in the text. The experimental bounds are $t_{\max} \in [25, 40]$ ms, $I_{BP} \in [0.2, 0.6]$, $NRM \in [0.5, 0.95]$. The dashed lines represent separatrices between regions with biphasic ($N = 2$) and triphasic ($N = 3$) impulse responses. The circles in the top row panels and the diamonds in the bottom row correspond to the examples in c and a in Fig. 5, respectively

Fig. 7 Dependence of LGN impulse-response measures on weight (w_{fb}) and time delay (Δ_{fb}) of cortical feedback via thalamocortical loop. Parameter dependence of the three impulse-response measures t_{max} (left column), biphasic index (I_{BP} ; middle column), and normalized rebound magnitude (NRM ; right column) for models with feedforward excitation and various types of cortical feedback. The retinal impulse response providing the input is depicted in Fig. 4. In all cases $\tau_{ig} = 10$ ms, $\tau_{ic} = 20$ ms. *Top row* inphase inhibitory feedback only: $\lambda_c^{ON} = 0$, $w_{fb}^{OFFx} = 0$. *Middle row* balanced linear feedback: $w_{fb}^{ON} = -w_{fb}^{OFFx} \equiv w_{fb}$, $\lambda_c^{ON} = \lambda_c^{OFF} = 0$. *Bottom row* balanced non-linear feedback: $w_{fb}^{ON} = -w_{fb}^{OFFx} \equiv w_{fb}$, $\lambda_c^{ON} = 0.15$, $\lambda_c^{OFF} = -0.15$. The regions confined by thick black lines and marked 'exp.' in top and bottom row panels, correspond to parameter values which give impulse-response model predictions in agreement with the experimental bounds, see text. The experimental bounds are

$t_{max} \in [25, 40]$ ms, $I_{BP} \in [0.2, 0.6]$, $NRM \in [0.5, 0.95]$. In the middle row only two tiny regions compatible with these bounds were found. The dashed lines in the panels in the bottom row represent separatrices between regions with biphasic ($N = 2$), triphasic ($N = 3$), and multiphasic ($N > 3$) impulse responses. For the models in the top row, only biphasic ($N = 2$) responses are found, and all models in the middle row have three or more phases (for $w_{fb} < 0$). The circles in the top row panels correspond to the example in Fig. 5d. The diamonds and triangles in the middle row correspondingly point out the examples in Fig. 5g and h, respectively. Likewise, the square and triangle in the bottom row show the examples in Fig. 5f and i. In the middle and last rows NRM cannot be evaluated for all parameter combinations according to our criteria (cf. Appendix 3), and this region of phase space is shown in white

(for adult cats) rough lower and upper bounds for t_{max} to be 25 and 40 ms, respectively. Further, their data suggested that corresponding bounds for I_{BP} could be set to 0.2 and 0.6. Rough lower and upper bounds for NRM

were found in Usrey et al. (1999) to be 0.5 and 0.95, respectively.

In Fig. 6 we show the three measures t_{max} , I_{BP} , and NRM for the case with only feedforward connections as a

Fig. 8 Dependence of LGN impulse-response measures on relative weight of feedforward inhibition (η_{ff}) and weight of cortical feedback via thalamocortical loop (w_{fb}) for models with feedforward excitation and inhibition and balanced linear cortical feedback. Parameter dependence of the three impulse-response measures t_{max} (left column), biphasic index (I_{BP} ; middle column), and normalized rebound magnitude (NRM ; right column) for linear models with feedforward excitation, feedforward inhibition and balanced linear feedback ($w_{\text{fb}}^{\text{ON}} = -w_{\text{fb}}^{\text{OFF}} \equiv w_{\text{fb}}$, $\lambda_{\text{c}}^{\text{ON}} = \lambda_{\text{c}}^{\text{OFF}} = 0$). The retinal impulse response providing the input is depicted in Fig. 4. In all cases $\tau_{\text{rg}} = 10$ ms, $\tau_{\text{rc}} = 20$ ms. *Top row* $\tau_{\text{rig}} = 20$ ms, $\Delta_{\text{fb}} = 10$ ms.

Middle row $\tau_{\text{rig}} = 20$ ms, $\Delta_{\text{fb}} = 20$ ms. *Bottom row*: $\tau_{\text{rig}} = 40$ ms, $\Delta_{\text{fb}} = 10$ ms. The regions confined by thick black lines and marked ‘exp.’ correspond to parameter values which give impulse-response model predictions in agreement with the experimental bounds described in the text, i.e., $t_{\text{max}} \in [25, 40]$ ms, $I_{\text{BP}} \in [0.2, 0.6]$, and $NRM \in [0.5, 0.95]$. The dashed lines represent separatrices between regions with biphasic ($N = 2$), triphasic or multiphasic ($N \geq 3$) impulse responses. In the middle row NRM cannot be evaluated for all parameter combinations according to our criteria (cf. Appendix 3), and this region of phase space is shown in white

function of two quantities: the relative strength of the feedforward inhibition η_{ff} (19) and the ratio of the feedforward time constants $\tau_{\text{rig}}/\tau_{\text{rg}}$. The three rows show the same plots for three choices of the feedforward excitatory time constants: $\tau_{\text{rg}} = 5$ ms, $\tau_{\text{rg}} = 10$ ms, and $\tau_{\text{rg}} = 20$ ms. A sizable fraction of the model parameters considered in Fig. 6 is seen to give impulse-response predictions in accordance with the rough experimental bounds found from Cai et al. (1997) and Usrey et al. (1999).

The peak time t_{max} (first column) generally decreases with increasing weight η_{ff} of the feedforward inhibition. This can be qualitatively understood by inspection of panels a–c in Fig. 5. With a longer inhibitory than excitatory time constant, i.e., $\tau_{\text{rig}} > \tau_{\text{rg}}$, the first peak of the excitatory contribution will occur earlier than the corresponding negative peak for the inhibitory contribution. This implies that the peak of the total impulse response will occur earlier than for the excitatory contribution alone.

With larger inhibitory weights this effect will be even more prominent, resulting in the observed 'anti-correlation' of $t_{\max}$ and η_{ff} . For the two other measures I_{BP} and NRM we observe the opposite trend in Fig. 6. Both I_{BP} and NRM increase with increasing inhibition η_{ff} . This correlation is as expected as both quantities essentially measure the depth of the rebound phase which naturally is expected to increase with increased feedforward inhibition.

The different dependency of the experimental measures on η_{ff} suggests an anti-correlation between $t_{\max}$ and the two rebound depth measures I_{BP} and NRM . This is indeed confirmed by direct evaluation of the correlation coefficient ρ , i.e.,

$$\rho(x, y) = \frac{1}{N-1} \sum_{i=1}^N \frac{(x_i - \langle x \rangle)(y_i - \langle y \rangle)}{\text{std}(x)\text{std}(y)}. \quad (54)$$

when $x = t_{\max}$ and $y = I_{\text{BP}}$. In (54) N is the number of data points considered, and $\langle x \rangle$ and $\text{std}(x)$ represent the mean and standard deviation, respectively, of the quantity x evaluated over the same data points. The marked regions in Fig. 6 found to have model predictions within the experimental bounds for $t_{\max}$, I_{BP} and NRM , might serve as a tentative indicator for the spread in biologically appropriate model parameters that can be expected in impulse-response experiments. The correlation coefficient $\rho(t_{\max}, I_{\text{BP}})$ evaluated over these marked regions may thus be a model prediction that can be compared with experimental data. When evaluated over these marked parameter regions, the models in Fig. 6 give $\rho(t_{\max}, I_{\text{BP}}) = -0.93$, $\rho(t_{\max}, I_{\text{BP}}) = -0.76$ and $\rho(t_{\max}, I_{\text{BP}}) = -0.95$ for $\tau_{\text{rg}} = 5, 10$, and 20 , respectively.

While these results assume undelayed onset of feedforward inhibition compared to excitation, i.e., $\Delta_{\text{rig}} = 0$, they do not change much when non-zero onset delays are assumed. The observed anticorrelation remained for $\Delta_{\text{rig}} < 20$ ms, i.e., $\rho(t_{\max}, I_{\text{BP}})$ was found to always be more negative than -0.7 for the models considered in Fig. 6 (results not shown).

In Fig. 6 we also show the number of phases the impulse response has for the various parameter choices. For these purely feedforward models the response is either biphasic ($N = 2$) or triphasic ($N = 3$), and the results indicate that an increase in excitatory time constant τ_{rg} tends to increase the likelihood for observing biphasic impulse responses.

In Fig. 7 we turn to models with cortical feedback and no feedforward inhibition and show the three same measures $t_{\max}$, I_{BP} , and NRM as functions of the strength of the cortical feedback ($w_{\text{fb}}^{\text{ON}}$ and/or $w_{\text{fb}}^{\text{OFFx}}$) and the total feed-back delay Δ_{fb} (20). We mainly focus on the models for which the net effect of the cortical feedback is to increase the size of the negative rebound compared to the retinal input, and in the top row of Fig. 7 we show results for the case where the only cortical feedback effect is inphase and

inhibitory, i.e., $w_{\text{fb}}^{\text{ON}} < 0$, $w_{\text{fb}}^{\text{OFFx}} = 0$ (and $\lambda_{\text{c}}^{\text{ON}} = 0$). As for the feedforward models considered in Fig. 6, the peak time $t_{\max}$ decreases with increasing magnitude of the inhibitory weight. This effect will necessarily always be present due to the unavoidable delay imposed on the inhibitory action by the round trip in the thalamocortical loop. As for the feedforward-inhibition case, the rebound measures I_{BP} and NRM also increase with increased inhibition, i.e., increased $|w_{\text{fb}}^{\text{ON}}|$, for the inphase feedback case, cf. panels b and c in Fig. 7. However, unlike for the feedforward-inhibition case, Fig. 7 shows a less clear pattern of covariation between $t_{\max}$ and I_{BP} or NRM when the model parameters $w_{\text{fb}}^{\text{ON}}$ and Δ_{fb} are varied. This is confirmed by evaluation of the correlation coefficient $\rho(t_{\max}, I_{\text{BP}})$ in (54). For the inphase inhibitory-feedback model in the top row only a modest negative correlation coefficient, $\rho(t_{\max}, I_{\text{BP}}) = -0.30$, was obtained when evaluating (54) over the region found to be compatible with the experimental bounds.

Another difference from the feedforward-inhibition models is that there can only be two phases in the impulse response. This is a consequence of our assumption of absence of cortical feedback effects when only the background inputs are present, i.e., the effective threshold $\lambda_{\text{c}}^{\text{ON}}$ in (31) must be non-negative. The requirement $\lambda_{\text{c}}^{\text{ON}} \geq 0$ implies for the case with inphase feedback alone, that only the positive phase of the feedforward excitatory contribution to the impulse response can drive the cortical ON population. Consequently, the cortical response will be monophasic, and the resulting relay-cell response biphasic. Thus all models in the top row of Fig. 7 corresponds to $N = 2$.

In the middle row of Fig. 7 we show results for $t_{\max}$, I_{BP} , and NRM when the inphase inhibitory feedback is supplemented by an antiphase excitatory feedback of the same magnitude, i.e., $w_{\text{fb}} \equiv w_{\text{fb}}^{\text{ON}} = -w_{\text{fb}}^{\text{OFFx}}$. It is further assumed that $\lambda_{\text{c}}^{\text{OFF}} = \lambda_{\text{c}}^{\text{ON}} = 0$, making the model fully linear (41). The addition of the antiphase excitation makes the impulse response prone to oscillations. In fact, for all combinations of w_{fb} and Δ_{fb} considered in the middle row panels the number of phases N is three or more (for $w_{\text{fb}} < 0$), and for the white-colored part of the plot of NRM in panel f the oscillations persisted so long that the NRM measure could not be calculated. An example of this situation is given by the impulse-response plot depicted in panel g of Fig. 5. For this linear feedback model only a small set of combinations of w_{fb} and Δ_{fb} give impulse-response functions in accordance with all three aforementioned experimental bounds.

The example impulse response function in panel i of Fig. 5 suggests that the introduction of thresholding nonlinearities in the cortical cells providing the cortical feedback will counteract the tendency for models with balanced inphase and antiphase feedback to have oscillatory impulse

responses. This is confirmed by the plots in the bottom row of Fig. 7. Here the cortical thresholds are set to $\lambda_c^{\text{ON}} = 0.15$ and $\lambda_c^{\text{OFF}} = -0.15$, respectively. While t_{max} is little affected by the introduction of the thresholds compared to the linear case in the middle row, the tendency to oscillate for large feedback weights is strongly reduced, as manifested by lower values of I_{BP} , and NRM . In fact, a sizable region of the $(w_{\text{fb}}, \Delta_{\text{fb}})$ phase space now gives impulse-response functions in accordance with the experimental bounds.

For the purely feedforward models in Fig. 6, t_{max} and I_{BP} were strongly anticorrelated, and $\rho(t_{\text{max}}, I_{\text{BP}})$ was between -0.76 and -0.95 . A much weaker correlation between t_{max} and I_{BP} is found for the feedback models in Fig. 7. As mentioned above the value found for the inphase inhibitory-feedback model in the top row was $\rho(t_{\text{max}}, I_{\text{BP}}) = -0.30$. For the balanced linear feedback models in the middle row, a small positive correlation coefficient $\rho(t_{\text{max}}, I_{\text{BP}}) = 0.29$ was found for the small regions of parameter space satisfying all criteria. For the balanced non-linear feedback model in the bottom row of Fig. 7, a larger positive correlation coefficient $\rho(t_{\text{max}}, I_{\text{BP}}) = 0.64$ was found.

Only a limited number of the models in Fig. 7d–f with balanced linear feedback alone give predictions in accordance with the experimental bounds for t_{max} , I_{BP} , and NRM simultaneously. However, this can be remedied by inclusion of feedforward inhibition. In such combined linear models with both feedforward and feedback interaction, large values of I_{BP} and NRM (in accordance with experimental observation) can be obtained without the generation of oscillations typically accompanying strong cortical feedback. In Fig. 8 we show results for such combined models with feedforward inhibition added to the balanced linear cortical feedback. In the top row we show results for $\tau_{\text{rg}} = 10$ ms, $\tau_{\text{rig}} = 20$ ms, $\tau_{\text{fb}} = 20$ ms, and $\Delta_{\text{fb}} = 10$ ms. For these parameters a sizable number of combinations of w_{fb} and η_{ffi} give predictions within the experimental bounds. The required amount of feedforward inhibition η_{ffi} needed in order to obtain the large values of I_{BP} and NRM seen in experiments, is reduced with the present addition of cortical feedback with inhibitory inphase action, i.e., $w_{\text{fb}} < 0$. For the part of parameter space compatible with the experimental bounds, t_{max} and I_{BP} are only weakly anticorrelated, $\rho(t_{\text{max}}, I_{\text{BP}}) = -0.30$.

When the delay parameter Δ_{fb} is increased from 10 to 20 ms as shown in the middle row of Fig. 8, the cortical feedback inhibition arrives closer to the minimum provided by the feedforward contributions to the impulse-response function. Consequently, the total impulse response gets more prone to oscillations, and this leads to a shrinking of the size of the region in the $(w_{\text{fb}}, \eta_{\text{ffi}})$ parameter space where the impulse-response predictions are within the experimental bounds. In this region t_{max} and I_{BP} is found to have a weak positive correlation, $\rho(t_{\text{max}}, I_{\text{BP}}) = 0.32$.

In the bottom row of Fig. 8 we have instead modified the situation in the top row by increasing the inhibitory time constant τ_{rig} to 40 ms. This gives an even larger region of the parameter space where model predictions are in accordance with the experimental observations. Here t_{max} and I_{BP} are moderately anticorrelated, $\rho(t_{\text{max}}, I_{\text{BP}}) = -0.46$.

Scheme for comparison with experiments

In Fig. 6, 7, 8 we calculated the experimental measures (t_{max} , I_{BP} , NRM) for different combinations of LGN circuit model parameters, but only the single retinal impulse response depicted in Fig. 4 was considered as input. This retinal impulse response was chosen to have time to first maximum $t_{\text{max}}^{\text{ret}}$ and biphasic index $I_{\text{BP}}^{\text{ret}}$ corresponding to average values of the experimental results reported in Usrey et al. (1999). We found the correlation coefficient $\rho(t_{\text{max}}, I_{\text{BP}})$ to vary significantly between different variations of the LGN circuit. This suggests an experimental test for assessing the relative importance of feedforward and feedback effects in shaping the LGN relay cells according to predictions from our model.

The response latency of relay cells and their retinal input may vary over tens of milliseconds (Guido and Sherman 1998; Wolfe and Palmer 1998). However, this large variability appears to be mainly due to the variability of the latency of the retinal input: Usrey et al. (1999), for example, found the latency difference between the relay-cell firing and the retinal input for cat X cells to vary with less than 1 ms around the mean value of about 4 ms. One approach for comparison with experiments would thus be to (1) consider subsets of experimental data of the type reported in Usrey et al. (1999) comprising, say, (nonlagged) X cell pairs with similar shapes of retinal impulse responses, (2) temporally align the different experimental traces according to the values of $t_{\text{max}}^{\text{ret}}$ of the retinal input, (3) calculate correlation coefficients of the type in Eq. (54), and (4) compare with model predictions.

This approach limits the number of cell pairs that can be used in the evaluation of the correlation coefficients. A better approach may be to search for other experimental measures with characteristic correlations also in data including variations in the retinal impulse response. For example, one may consider the correlations between relative differences in time to first maximum and biphasic index, i.e., between

$$\tilde{t}_{\text{max}} \equiv (t_{\text{max}} - t_{\text{max}}^{\text{ret}})/t_{\text{max}}^{\text{ret}}, \quad \text{and} \quad \tilde{I}_{\text{BP}} \equiv (I_{\text{BP}} - I_{\text{BP}}^{\text{ret}})/I_{\text{BP}}^{\text{ret}} \quad (55)$$

The study of Usrey et al. (1999) provides an estimate for the typical spread in the shape of the retinal impulse response, and we extracted the following intervals of the

Fig. 9 Correlation coefficients between $\tilde{t}_{\max}$ and $\tilde{I}_{BP}$ for various ensembles of retinal impulse responses providing input. The correlation coefficient (54) for the quantities $\tilde{t}_{\max}$ and $\tilde{I}_{BP}$ defined in (55) is calculated for various ensembles of retinal inputs, i.e., various fractions of the interval of time to first max and biphasic index of retinal impulse responses observed in Usrey et al. (1999): $t_{\max}^{\text{ret}} \in [13.4, 29.1]$ ms, $I_{BP}^{\text{ret}} \in [0.26, 0.5]$. The fraction zero corresponds to a single retinal impulse response modeled by (53) corresponding to the median value, i.e., $t_{\max}^{\text{ret}} = 21.2$ ms and $I_{BP}^{\text{ret}} = 0.38$, the fraction one corresponds to the entire interval, the fraction 1/2 to the intervals $t_{\max}^{\text{ret}} \in [17.3, 25.2]$ ms, $I_{BP}^{\text{ret}} \in [0.32, 0.44]$, etc.. For each value of the fraction a total about 2,000 simulations are done with (1) retinal input parameters $t_{\max}^{\text{ret}}$ (a/2 in (53)) and I_{BP}^{ret} (B in (53)) randomly drawn from

measures involved: $t_{\max}^{\text{ret}} \in [13.4, 29.1]$ ms, $I_{BP}^{\text{ret}} \in [0.26, 0.5]$. The retinal impulse response used in Figs. 4, 5, 6, 8 corresponds to the median value, i.e., $t_{\max}^{\text{ret}} = 21.2$ ms and $I_{BP}^{\text{ret}} = 0.38$. When only a single retinal impulse response is used, the correlation coefficient $\rho(\tilde{t}_{\max}, \tilde{I}_{BP})$ will be identical to the previously calculated correlation coefficient $\rho(t_{\max}, I_{BP})$. When the ensemble of models included in the calculation of $\rho(\tilde{t}_{\max}, \tilde{I}_{BP})$ incorporates spread in the form of the retinal impulse response function, however, this will no longer be so. In Fig. 9 we show the variation of $\rho(\tilde{t}_{\max}, \tilde{I}_{BP})$ as a function of the size of the ensemble of retinal impulse responses, i.e., from including only a single retinal impulse response (corresponding to the average value) to including the full intervals measured by Usrey et al. (1999). Panel a in the figure shows the results for $\rho(\tilde{t}_{\max}, \tilde{I}_{BP})$ for the pure feedforward model in the middle row of Fig. 6 ($\tau_{rg} = 10$ ms) as well as the three feedback models considered in Fig. 7. While the correlation coefficients are seen to vary somewhat when including more variation in the retinal impulse responses, clear separations between the various model types are largely maintained. The corresponding results for $\tau_{rg} = 20$ ms are shown in panel b, where the pure feedforward model corresponds to the model in the bottom row of Fig. 6 while the feedback models have no direct counterparts in the presented phase plots. Here the various model types exhibit even clearer

uniform distributions on the relevant intervals, and (2) LGN circuit model parameters drawn from uniform distributions over the two depicted parameters in the relevant 'phase plots' in Figs. 6 and 7. Only the parameter choices that give models producing LGN impulse responses within the experimental bounds $t_{\max} \in [25, 40]$ ms, $I_{BP} \in [0.2, 0.6]$, and $NRM \in [0.5, 0.95]$ are included in the evaluation of the correlation coefficients. Result for the pure feedforward model in Fig. 6(d–f) ('FF only') and all three feedback models in Fig. 7 (top row 'Inph FB', middle row 'Linear FB', bottom row 'Bal. FB') are shown. **a** $\tau_{rg} = 10$ ms. **b** $\tau_{rg} = 20$ ms. In **B**, no LGN impulse responses within the experimental bounds were obtained for the linear feedback model for small fractions of the parameter intervals, hence the absent line for fractions < 0.6

differences in their correlation coefficients. This suggests that evaluation of $\rho(\tilde{t}_{\max}, \tilde{I}_{BP})$ over an ensemble of measurements including different retinal impulse responses may be used to distinguish between different candidate LGN circuit models.

MATLAB GUI-version of model

To further facilitate the use of our new LGN circuit model we have made a freely available MATLAB version of it *LGNcircuit*, with a simple graphical user interface (GUI). In this program the retinal input is read in as a simple data file. In addition to investigating the response of LGN cells to a retinal impulse response, the program also readily handles retinal inputs characteristic for stimulation with flashing spots or drifting sinusoidal gratings. This freely available program can be downloaded from the model repository *ModelDB*.

Discussion

We have presented and investigated a conceptually simple 'minimal mechanistic' model describing temporal processing of visual stimuli in the lateral geniculate nucleus (LGN). The model has been tailored to highlight salient

feedforward and feedback effects on LGN relay cells while keeping a modest model complexity and thus a modest number of model parameters. The final model (31) is mathematically represented by a delay differential equation with absolute delay, readily amenable for numerical analysis. To further facilitate use of the model we have made a MATLAB version of it, *LGNcircuit*, with a simple graphical user interface (GUI).

In terms of model applications the main focus in the present paper has been on impulse responses, i.e., the firing-rate response to a very brief stimulation of a small test spot placed in the receptive-field center of the LGN neuron in question. Unlike previous modeling efforts aimed to investigate cortical feedback effects on LGN cells, the modest model complexity has allowed us to do comprehensive investigations of the model parameter space. In particular we have investigated in Figs. 6, 7, 8 how characteristic experimental measures of this impulse response, such as the time to first peak, the biphasic index, and the normalized rebound magnitude (Cai et al. 1997; Usrey et al. 1999), vary with model parameters. We find here that both purely feedforward models (Fig. 6) as well as models with feedforward excitation combined with cortical feedback (Fig. 7) can account for the experimental results reported so far for the LGN impulse responses (Cai et al. 1997; Usrey et al. 1999). Thus it appears that we cannot based on such observations alone make any statement of whether feedforward or feedback effects dominate in determining the detailed shape of the impulse responses.

However, our study suggests that the measures of time to first peak and the biphasic index over a population of LGN neurons receiving similar retinal input will be differently correlated depending on whether feedforward or feedback effects dominate. For the feedforward models considered in Fig. 6 we found (for the collection of models compatible with present experiments) that the time to first peak and the biphasic index were strongly anticorrelated. In contrast, weak or positive correlations between these measures were found for the experimentally relevant feedback models in Fig. 7. As illustrated by Fig. 9 this qualitative difference remains also when a variety of retinal impulse responses are considered and a generalized correlation measure is used. This points to a specific suggestion for how to probe the relative importance of the feedforward and feedback contributions in shaping the temporal part of LGN impulse responses.

It should be noted, however, that our model, like all previous models we are aware of that address the role of corticothalamic feedback on relay-cell firing (Köhn and Wörgötter 1996; Lumer et al. 1997; Wörgötter et al. 1998; Kirkland and Gerstein 1998; Kirkland et al. 2000; Hillenbrand and van Hemmen 2000; Yousif and Denham 2007), assume the cortical cells providing the feedback to be driven

by the relay cells in the model. It could instead be that some of the corticothalamic feedback to a relay cell is driven by cortical cells that are activated by *other* relay cells with a shorter latency. If so, all models including ours is inaccurate on this point. Since the corticothalamic feedback loops can be quite fast (Sillito and Jones 2004; Briggs and Usrey 2005, 2007, 2011), the first feedback onto a particular relay cell may arrive simultaneously with or even before the retinal input. If so, the above model prediction cannot be trusted, as a main factor affecting the differences in the correlation coefficients for the different circuit models likely is the differences in timing between the feedforward and feedback inputs. Such early cortical feedback will in our model be similar to adding a term to the expression for the feedforward input in Eq. (18). While this is not pursued here, one would expect that such 'early-feedback' models generally would give correlation coefficients more similar to values for the present feedforward models, so that the presently described test will not be applicable.

A recent study by Wang et al. (2006) found a characteristic pattern in the feedback connections to LGN cells: the functional effect of the feedback cross-connections (i.e., from cortical ON to LGN OFF cells, or from cortical OFF to LGN ON cells) is phase-reversed from the effect of the in-phase connections (i.e., from cortical ON to LGN ON cells, or from cortical OFF to LGN OFF cells). Partially motivated by this observation, we have in the present paper focused on two situations in terms of the cortical-feedback organization: (1) inphase inhibitory feedback alone, and (2) inphase inhibition combined with antiphase excitation (from the cross connection). Under the latter point, we have specifically investigated the situation where the magnitude of the inphase and antiphase feedback weights are the same. With such balanced feedback, and perfect half-wave rectifying cortical firing-rate functions with zero firing thresholds, the net effect of the feedback becomes effectively linear (41). Provided the background relay-cell firing rate is so large that no rectification effects occur at the relay-cell level, the whole relay-cell model then becomes linear, allowing for straightforward analysis of its properties (Einevoll and Plesser 2002), and even an analytical formula for the transfer function (45). In this linear-feedback regime the impulse response typically becomes more prone to oscillations due to thalamocortical loop effects, but whether this regime has its experimental counterpart is not known.

Most parameters in our firing-rate model are *a priori* unknown as they are difficult to measure directly in experiments, particularly in an *in vivo* setting. Also, the appropriate numbers for time constants to use in the coupling kernels in a firing-rate model is not necessarily directly given by corresponding time constants of the EPSPs and IPSPs connecting individual neurons (Gerstner 2000). Recently, our group has undertaken a systematic

and comprehensive numerical investigation of the response of leaky integrate-and-firing spiking neurons to strong synaptic inputs, characteristic for the retinogeniculate connection (Nordlie et al. 2010). The results of the study is that the time constant of a rate model might in many situations be well approximated by the time constant of the synaptic connection. However, this finding should be tested further using a similar numerical approach one available spike-based models made particular for the retinogeniculate transmission (Carandini et al. 2007; Casti et al. 2008). Rate-model time constants extracted from such a study would reduce the number of unknown parameters in our model and thus make the predictions better constrained.

Experiments with cortical inactivation have proven very difficult to do, and the reports from such have been inconclusive in the sense that both excitatory and inhibitory effects have been reported, see [Introduction](#) for references. If future experiments are able to constrain the parameters describing the thalamocortical feedback loop, our MATLAB GUI-based model is so numerically undemanding and easy to use that the calculations reported here can easily be redone to make new and more precise predictions.

In our model only a single time constant is used to account for the excitatory and inhibitory synaptic connections. In reality these synaptic actions will be mediated by several receptor types with different characteristic time constants (e.g., AMPA and NMDA for the excitatory connection, and GABA_A and GABA_B for the inhibitory connections). The best choice of time constants in the synaptic coupling kernels in our model will likely reflect the underlying mixture of these different receptors. The model formalism can, however, be straightforwardly extended to include several time constants in the coupling kernels: for the feedforward connections term it would amount to add more terms to the expression describing the filtered retinal input (18), for the feedback connections it would increase the number of differential equations to be solved in the final numerical model (cf. 'linear chain trick' as described in [Appendix 1](#)). As the strategy behind the present paper is to limit the number of (unknown) model parameters and instead do a comprehensive evaluation of the parameter space of a more restricted number of salient model parameters, we have not pursued such an extension here. Further, we do not expect that the qualitative conclusions regarding the differences in correlation coefficients between $t_{\max}$ and I_{BP} for the different model types would change even with such a model extension. These differences rely mainly on the reduced firing of LGN relay cells being driven from the retina in the feedforward case and from the LGN relay cells themselves in the case of feedback through the thalamocortical loop, and will likely be relatively little affected by changes in the detailed form of the temporal coupling kernels.

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Appendix 1: Derivation of model on differential form

In the present appendix we derive the differential Eq. (17) for the dynamical variable $z(t)$ defined in (16) when the coupling kernels $h_{cr}^{ON/OFF}$ and $h_{rc}^{ON/OFF}$ in (12) and (13) are assumed.

Insertion of (12) into (7) gives, by means of (6),

$$\begin{aligned} R_c^{ON}(t) &= F_c^{ON} \left(w_{cr}^{ON} \int_{-\infty}^t h_{cr}^{ON}(t-s) \hat{R}_r^{ON}(s) ds \right) \\ &= F_c^{ON} \left(w_{cr}^{ON} \int_{-\infty}^t \delta((t-\Delta_{cr})-s) \hat{R}_r^{ON}(s) ds \right) \\ &= F_c^{ON} (w_{cr}^{ON} \hat{R}_r^{ON}(t-\Delta_{cr})) \\ &= F_c^{ON} \left(w_{cr}^{ON} F_r^{ON} \left(A_g w_{rg}^{ON} (\bar{r}_{r0}^{ON} + \bar{r}_g(t-\Delta_{cr}) + z(t-\Delta_{cr})) \right) \right) \end{aligned} \quad (56)$$

where we also have used the definition for $\bar{r}_g(t)$ in (18) and $\bar{r}_{r0}^{ON}$ in (21). (Note that the notation $\hat{R}_c^{ON}(t)$ in (7) has been replaced by $R_c^{ON}(t)$ in (56) since the background firing rates of the cortical cells have been assumed zero.) Correspondingly, we find that

$$\begin{aligned} R_c^{OFF}(t) &= F_c^{OFF} \left(w_{cr}^{OFF} F_r^{OFF} \right. \\ &\quad \times \left. \left(A_g w_{rg}^{ON} (\bar{r}_{r0}^{OFF} - \bar{r}_g(t-\Delta_{cr}) - z(t-\Delta_{cr})) \right) \right), \end{aligned} \quad (57)$$

and we have arrived at (25) and (26), respectively.

Differentiation of the expression for the differential delay equation with absolute delay z in (16) with respect to t gives

$$\begin{aligned} \frac{d}{dt} z(t) &= \frac{w_{rc}^{ON}}{A_g w_{rg}^{ON}} \frac{d}{dt} ((h_{rc}^{ON} * R_c^{ON})(t)) \\ &\quad + \frac{w_{rc}^{OFFx}}{A_g w_{rg}^{ON}} \frac{d}{dt} ((h_{rc}^{OFFx} * R_c^{OFF})(t)) \\ &= \frac{w_{rc}^{ON}}{A_g w_{rg}^{ON}} \frac{d}{dt} \left(\int_{-\infty}^t \frac{e^{-(t-\Delta_{rc}-s)/\tau_{rc}}}{\tau_{rc}} \Theta(t-\Delta_{rc}-s) R_c^{ON}(s) ds \right) \\ &\quad + \frac{w_{rc}^{OFFx}}{A_g w_{rg}^{ON}} \frac{d}{dt} \left(\int_{-\infty}^t \frac{e^{-(t-\Delta_{rc}-s)/\tau_{rc}}}{\tau_{rc}} \Theta(t-\Delta_{rc}-s) R_c^{OFF}(s) ds \right) \end{aligned} \quad (58)$$

where we have used (13). Since $\Theta(t-\Delta_{rc}-s) = 1$ only for $s < t - \Delta_{rc}$, the integrals in (58) can be rewritten as

$$\begin{aligned} & \int_{-\infty}^t \frac{e^{-(t-\Delta_{rc}-s)/\tau_{rc}}}{\tau_{rc}} \Theta(t - \Delta_{rc} - s) R_c^{ON/OFF}(s) ds \\ &= \int_{-\infty}^u \frac{e^{-(u-s)/\tau_{rc}}}{\tau_{rc}} R_c^{ON/OFF}(s) ds, \end{aligned} \quad (59)$$

where we have introduced $u = t - \Delta_{rc}$. By means of the general differentiation rule

$$\frac{d}{dt} \left(\int_a^t F(t, s) ds \right) = F(t, t) + \int_a^t \frac{\partial}{\partial t} F(t, s) ds \quad (60)$$

we now find for the first integral in (58),

$$\begin{aligned} & \frac{w_{rc}^{ON}}{A_g w_{rg}^{ON}} \frac{d}{du} \left[\int_{-\infty}^u \frac{e^{-(u-s)/\tau_{rc}}}{\tau_{rc}} R_c^{ON}(s) ds \right] \\ &= \frac{w_{rc}^{ON}}{A_g w_{rg}^{ON}} \frac{1}{\tau_{rc}} \left(R_c^{ON}(u) - \int_{-\infty}^u \frac{e^{-(u-s)/\tau_{rc}}}{\tau_{rc}} R_c^{ON}(s) ds \right) \\ &= \frac{w_{rc}^{ON}}{A_g w_{rg}^{ON}} \frac{1}{\tau_{rc}} \left(R_c^{ON}(t - \Delta_{rc}) - \int_{-\infty}^{t-\Delta_{rc}} \frac{e^{-(t-\Delta_{rc}-s)/\tau_{rc}}}{\tau_{rc}} R_c^{ON}(s) ds \right) \\ &= \frac{w_{rc}^{ON}}{A_g w_{rg}^{ON}} \frac{1}{\tau_{rc}} \left(R_c^{ON}(t - \Delta_{rc}) - \int_{-\infty}^t \frac{e^{-(t-\Delta_{rc}-s)/\tau_{rc}}}{\tau_{rc}} \right. \\ & \quad \left. \Theta(t - \Delta_{rc} - s) R_c^{ON}(s) ds \right) \\ &= \frac{w_{rc}^{ON}}{A_g w_{rg}^{ON}} \frac{1}{\tau_{rc}} (R_c^{ON}(t - \Delta_{rc}) - (h_{rc}^{ON} * R_c^{ON})(t)) \end{aligned} \quad (61)$$

For the OFF integral in (58) we correspondingly find

$$\begin{aligned} & \frac{w_{rc}^{OFFx}}{A_g w_{rg}^{ON}} \frac{d}{du} \left[\int_{-\infty}^u \frac{e^{-(u-s)/\tau_{rc}}}{\tau_{rc}} R_c^{OFF}(s) ds \right] \\ &= \frac{w_{rc}^{OFFx}}{A_g w_{rg}^{ON}} \frac{1}{\tau_{rc}} (R_c^{OFF}(t - \Delta_{rc}) - (h_{rc}^{OFFx} * R_c^{OFF})(t)) \end{aligned} \quad (62)$$

With the use of the definition for $z(t)$ in (16) we thus find that the differential equation for $z(t)$ in (58) simplifies to

$$\begin{aligned} \frac{d}{dt} z(t) &= -\frac{z(t)}{\tau_{rc}} + \frac{w_{rc}^{ON}}{A_g w_{rg}^{ON} \tau_{rc}} R_c^{ON}(t - \Delta_{rc}) \\ & \quad + \frac{w_{rc}^{OFFx}}{A_g w_{rg}^{ON} \tau_{rc}} R_c^{OFF}(t - \Delta_{rc}) \end{aligned} \quad (63)$$

Use of the expressions for $R_c^{ON}(t)$ and $R_c^{OFF}(t)$ in (56) and (57), respectively, and the definition $\Delta_{rb} \equiv \Delta_{rc} + \Delta_{cr}$ in (20), then gives the delay differential equation with absolute delay (17) for $z(t)$ in the main text.

Appendix 2 : Threshold firing-rate functions

Use of threshold firing-rate functions as described in (27)–(30) in the expression for $R_c^{ON}(t)$ in (25) gives

$$R_c^{ON}(t) = A_g w_{rg}^{ON} w_{rg}^{ON} \left[[\bar{r}_0^{ON} + \bar{r}(t - \Delta_{cr}) + z(t - \Delta_{cr}) - \bar{\lambda}_c^{ON}]_+ - \bar{\lambda}_c^{ON} \right]_+ \quad (64)$$

where we have introduced $\bar{\lambda}_r^{ON} \equiv \Lambda_r^{ON}/(A_g w_{rg}^{ON})$ and $\bar{\lambda}_c^{ON} \equiv \Lambda_c^{ON}/(A_g w_{rg}^{ON} w_{cr}^{ON})$. The requirement of zero background firing rate for the cortical ON cells translates to the constraint

$$\bar{\lambda}_c^{ON} \geq [\bar{r}_0^{ON} - \bar{\lambda}_r^{ON}]_+ = [-\bar{\lambda}_r^{ON}]_+ \geq 0, \quad (65)$$

where we have used the definition of λ_r^{ON} in (39).

Since we enforce that $\bar{\lambda}_c^{ON} \geq 0$, the innermost half-wave rectification in (64) can be removed. (For the cases where $(\bar{r}_g(t - \Delta_{cr}) + z(t - \Delta_{cr}) - \bar{\lambda}_r^{ON}) < 0$, the function (64) will be zero also with the innermost half-wave rectification function replaced by the linear function). The expression (64) thus simplifies to

$$R_c^{ON}(t) = A_g w_{rg}^{ON} w_{cr}^{ON} [\bar{r}_g(t - \Delta_{cr}) + z(t - \Delta_{cr}) - \bar{\lambda}_c^{ON}]_+ \quad (66)$$

corresponding to (37) in the main text. Here the definition of λ_{c0}^{ON} in (33) has been used. A corresponding argument for $R_c^{OFF}(t)$ gives

$$R_c^{OFF}(t) = A_g w_{rg}^{ON} w_{cr}^{OFF} [-(\bar{r}_g(t - \Delta_{cr}) + z(t - \Delta_{cr}) - \bar{\lambda}_c^{OFF})]_+ \quad (67)$$

corresponding to (38) in the main text. Insertion of these new expression for $R_c^{ON}(t)$ and $R_c^{OFF}(t)$ into

$$\begin{aligned} \frac{d}{dt} z(t) &= -\frac{z(t)}{\tau_{rc}} + \frac{w_{rc}^{ON}}{A_g w_{rg}^{ON} \tau_{rc}} R_c^{ON}(t - \Delta_{rc}) \\ & \quad + \frac{w_{rc}^{OFFx}}{A_g w_{rg}^{ON} \tau_{rc}} R_c^{OFF}(t - \Delta_{rc}) \end{aligned} \quad (68)$$

then gives (31) in the main text.

Appendix 3: Numerical methods

General: In the numerical investigations we needed to solve the delay differential equation in (31). This was done in MATLAB using the routine `dde23` (and in the case of zero delay the routine `ode45`). The auxiliary variable $z(t)$ was set to be zero for all times prior to stimulus onset.

Simulation of drifting-grating responses: In numerical evaluations of the responses to drifting gratings, the transient

part of the response following stimulus onset was omitted. The MATLAB routine `fft` implementing the fast Fourier transform was then used to extract the first harmonic component from the steady-state part of the response.

Simulations of impulse response: We first simulated the first 250 ms of impulse response after onset of the retinal input, cf. Fig. 4 to obtain $t_{\max}$ and I_{BP} . If four or more phases were present in these first 250 ms, we evaluated the impulse-response for 250 ms more. The normalized rebound magnitude (NRM) was then found by evaluating the integrals over the first and all subsequent phases, respectively, using the MATLAB routine `quadl`. However, if the area of the fourth phase was found to be larger than one hundredth of the area of the first phase, NRM was not calculated, cf. white regions in the phase plots in Figs. 7 and 8.

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