How Inhibitory Circuits in the Thalamus Serve Vision

Judith A. Hirsch,[1] Xin Wang,[2] Friedrich T. Sommer,[3] and Luis M. Martinez[4]

[1]Department of Biological Sciences/Neurobiology, University of Southern California, Los Angeles, California 90089-2520; email: jhirsch@usc.edu

[2]Computational Neurobiology Laboratory, The Salk Institute for Biological Studies, La Jolla, California 92037; email: xinw@salk.edu

[3]Redwood Center for Theoretical Neuroscience, University of California, Berkeley, California 94720-3198; email: fsommer@berkeley.edu

[4]Instituto de Neurociencias de Alicante, Instituto de Neurociencias of the Spanish Research Council and Universidad Miguel Hernández, Sant Joan d'Alacant, Alicante 03550, Spain; email: luis.m.martinez.otero@gmail.com

Annu. Rev. Neurosci. 2015. 38:309–29

The *Annual Review of Neuroscience* is online at neuro.annualreviews.org

This article's doi: 10.1146/annurev-neuro-071013-014229

Keywords

interneuron, lateral geniculate, reticular nucleus, whole-cell

Abstract

Inhibitory neurons dominate the intrinsic circuits in the visual thalamus. Interneurons in the lateral geniculate nucleus innervate relay cells and each other densely to provide powerful inhibition. The visual sector of the overlying thalamic reticular nucleus receives input from relay cells and supplies feedback inhibition to them in return. Together, these two inhibitory circuits influence all information transmitted from the retina to the primary visual cortex. By contrast, relay cells make few local connections. This review explores the role of thalamic inhibition from the dual perspectives of feature detection and information theory. For example, we describe how inhibition sharpens tuning for spatial and temporal features of the stimulus and how it might enhance image perception. We also discuss how inhibitory circuits help to reduce redundancy in signals sent downstream and, at the same time, are adapted to maximize the amount of information conveyed to the cortex.

Contents

INTRODUCTION

Circuits in the visual thalamus and the cortex differ in many ways, but perhaps none as striking as the relative weight of inhibitory versus excitatory intrinsic circuits. The excitatory neurons of the cortex, spiny stellate and pyramidal cells are densely interconnected with each other (Binzegger et al. 2004, Stepanyants et al. 2008). By contrast, the excitatory neurons of the thalamus, relay cells, make few intranuclear connections (Bickford et al. 2008); rather, inhibitory neurons dominate intrinsic networks (Bickford et al. 1999, Cucchiaro et al. 1991). These inhibitory cells divide into two main classes. The first and most numerous type is composed of local interneurons within the lateral geniculate nucleus (LGN) of the thalamus (Fitzpatrick et al. 1984). These receive retinal input (Van Horn et al. 2000) and synapse onto relay cells (Montero 1987, Sherman 2004) and each other (Pasik et al. 1976) to form a feedforward inhibitory pathway. The second class of inhibitory neurons populates the visual sector of the thalamic reticular nucleus (TRN), a thin network of interconnected γ-aminobutyric acid (GABA)-ergic neurons that are innervated by relay cells and suppress them in return to form a feedback pathway (Cucchiaro et al. 1991, Uhlrich et al. 1991). Anatomical evidence reveals little cross-talk between these two inhibitory networks (Cucchiaro et al. 1991, Wang et al. 2001), and so they are viewed as independent; **Figure 1** provides an overview of thalamic connections. This review focuses on the functional roles for inhibition in the LGN from the dual perspectives of feature detection and information theory. We also provide a brief comparison with counterpart inhibitory circuits in the cortex. The principal experimental subject is the cat, with results from primate and murine species described in context.

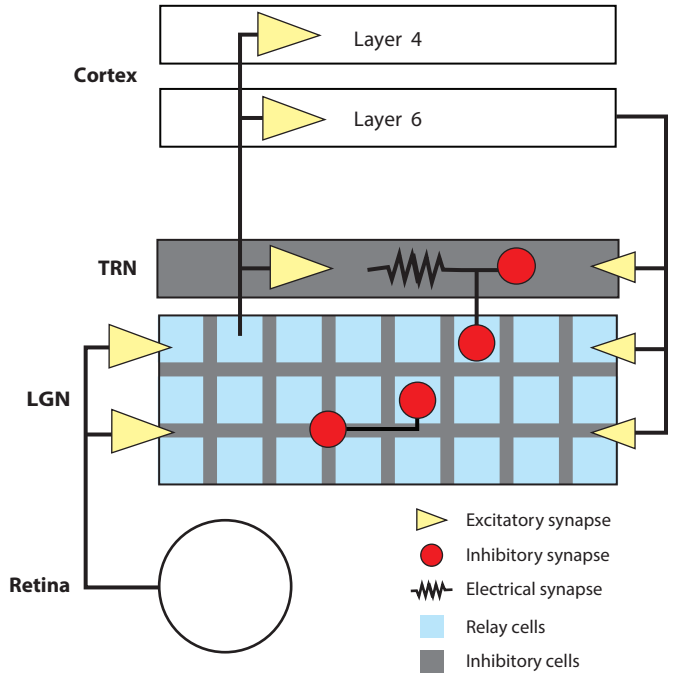

Figure 1

Block diagram of connections of the visual thalamus. The connections shown hold for all layers of the lateral geniculate nucleus (LGN). Populations of interneurons and relay cells are arranged as a grid in the figure for clarity, but they are mixed in situ. TRN, thalamic reticular nucleus.

OVERVIEW OF RECEPTIVE FIELDS IN THE LATERAL GENICULATE NUCLEUS

Relay cells have receptive fields built from two concentrically arranged subregions, a center and a surround, with the opposite preference for stimulus contrast (Hubel 1960), much as in retina (Kuffler 1953, Wiesel 1959). This pattern is shared by relay cells associated with the form (X cell) and motion (Y cell) pathways (Wang et al. 2007) as well as by interneurons (Wang et al. 2011b). Optimal stimuli, thus, are bright or dark spots shown against a background of the opposite luminance polarity. This center-surround organization provides a means to encode local contrast borders, which the cortex subsequently links to form contours.

The thalamus does not merely copy retinal input. Ganglion cells often diverge to target more than one relay cell, thus reorganizing the representation of visual space (Hamos et al. 1987, Usrey et al. 1999). Moreover, the pattern of excitation that the retina supplies to relay cells and interneurons is complemented by postsynaptic inhibition such that there is a push-pull pattern of response to stimuli of the opposite sign (Martinez et al. 2005; Wang et al. 2007, 2011a,b) (**Figure 2**). Specifically, in On subregions bright light excites whereas dark inhibits and vice versa. Thus, "push" is defined as excitation evoked by a stimulus of the preferred sign and "pull' as inhibition elicited by a stimulus of the reverse, or nonpreferred, sign. Push-pull was first found in the retina (Wiesel 1959), where it is often called cross-over inhibition (Werblin 2010) but is generated de novo in the thalamus (Martinez et al. 2014; Wang et al. 2007, 2011b).

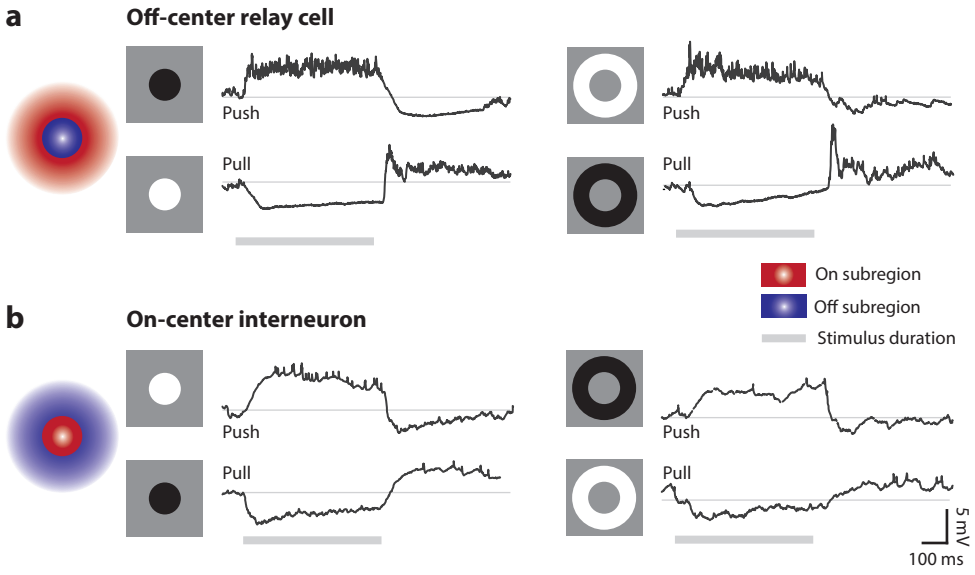

Figure 2

Push-pull responses of an Off-center relay cell and On-center interneuron. Averaged records (membrane voltage) for responses to dark and bright disks flashed in the center (*left*) and annuli flashed in the surround (*right*) of the receptive field of an Off-center relay cell (*a*) and an On-center interneuron (*b*). For the stylized versions of the receptive fields, On and Off subregions are shaded with colored gradients. Grayscale icons depict stimulus shape and polarity. The relay cell was an (anatomically identified) X cell, but similar profiles have been recorded from Y and W cells, and in all layers of the lateral geniculate nucleus (LGN). Interneurons can be distinguished from relay cells by the presence of bulbous appendages attached to distal dendrites. For a fuller explanation of anatomical criteria used to sort relay cells into X, Y, and W categories, see Wang et al. (2007), and to distinguish these from interneurons, see Wang et al. (2011b).

PUSH-PULL EXCITATION AND INHIBITION IN VISION

Detecting Spatial Features

Common roles for push-pull in neural circuits include extending the dynamic range of operation and restoring linearity of response lost by rectification across the synapse (Werblin 2010). In vision, push-pull confers additional advantages. First, it improves feature selectivity by producing a mutually antagonist relationship between neighboring subregions, as originally described in the retina (Kuffler 1953, Wiesel 1959). A spot of the preferred luminance contrast (bright or dark) that is confined to the center evokes vigorous excitation (push). However, if that same stimulus expands to fill the surround, the pull mechanism is recruited to suppress the excitatory response. Thus, the geometry of the receptive field, coupled with interactions between push and pull across subregions, fine-tunes sensitivity to stimulus size and location.

Note that the strength of the surround varies according to cell type, station in the visual pathway, and stimulus regime. For example, the suppressive effect of the surround is greater for X cells than for Y cells and more pronounced in the thalamus than in the retina (Bullier & Norton 1979). In addition, the surround vanishes in darkness, reappearing as the environment grows lighter (Barlow et al. 1957). Furthermore, the receptive field center shrinks at high contrasts (Martinez et al. 2014). These results are consistent with the view that small centers, complemented by strong surrounds, help resolve spatial detail.

Improving Efficiency

Considered from another vantage point, push-pull mediated antagonism between subregions reduces responses to diffuse or homogeneous patterns. This view is interesting in the context of information theory in general, and Barlow's scheme of efficient coding (Barlow 1961), in particular. The framework of efficient coding holds that early stages of sensory processing reduce redundancy in signals sent downstream and is important because it is relevant to the statistical structure of the visual environment. In nature, neighboring regions within a given field of view often have similar luminance values, leading to extensive spatial correlations and substantial redundancy. That is, natural scenes have 1/f statistics; the power spectrum of a given image is skewed toward low spatial frequencies (Field 1987, Simoncelli & Olshausen 2001). Furthermore, it has long been recognized that the structure of retinal and thalamic receptive fields can be represented as a difference of two Gaussians, one matched to the center and the other to the surround (Enroth-Cugell & Robson 1966, Marr & Hildreth 1980). This filter operates on the image to form the second spatial derivative of the stimulus and enhances edges (Chandler & Field 2007, Marr & Hildreth 1980); the emphasis on the higher frequency components reduces redundancy.

Improving Image Perception

So far, we have discussed push and pull as if they might be mirror images of one another, but this is not the case (Martinez et al. 2005, 2014). The area of the pull exceeds the area of the push for relay cells whose receptive fields lie within the central 10–15° of visual space [which corresponds to roughly half of the cat's LGN (Sanderson 1971)]. To understand how this spatial asymmetry might aid visual processing, one can think about the larger circuit—specifically, the convergence of ganglion cell axons onto relay cells (Hamos et al. 1987, Usrey et al. 1999, Yeh et al. 2009).

The consequences of convergence for vision have been explored with a circuit model of the LGN (for the X cell population) (Martinez et al. 2014). The model is based on the statistics of retinal mosaics (Eglen et al. 2005, Wässle et al. 1983), physiological measurements of excitation and inhibition in the receptive field (Martinez et al. 2014), and the stereological observations that relay cells outnumber ganglion cells by a factor of ∼2 (Madarasz et al. 1978, Peters & Payne 1993) and interneurons by a factor of ∼3 (Fitzpatrick et al. 1984). Simulations performed with the model suggest that relay cells receive, on average, input from ∼3 different ganglion cells and that the pattern of convergence is such that each relay cell samples a slightly different mixture of inputs than that its neighbor receives (Martinez et al. 2014). In this way, the visual system not only upsamples (there are more relay than ganglion cells) but also interpolates (diverging retinal afferents converge on different relay cells) retinal input.

This rewiring of space confers significant advantages. Assuming that the visual information each ganglion cell transmits is contaminated by that cell's own internal noise, convergence could improve the signal to noise ratio by averaging across input channels. An analysis with a Bayesian decoder (Ruderman & Bialek 1992) supports this view by showing that retinothalamic convergence allows the LGN to estimate the position of a point stimulus in noise with far greater precision than the retina can achieve (Martinez et al. 2014).

Furthermore, upsampling and interpolation across the retinogeniculate synapse increase the resolution of image representation. This benefit has the potentially harmful disadvantage of introducing image blur. Recall, however, that the pull is larger than the push in the receptive field center. Thus, a suppressive moat surrounds the region of peak excitation, helping to sharpen neural sensitivity to local differences in luminance. Indeed, simulations with the circuit model show that this nested arrangement of push within pull can boost the response to contrast borders and

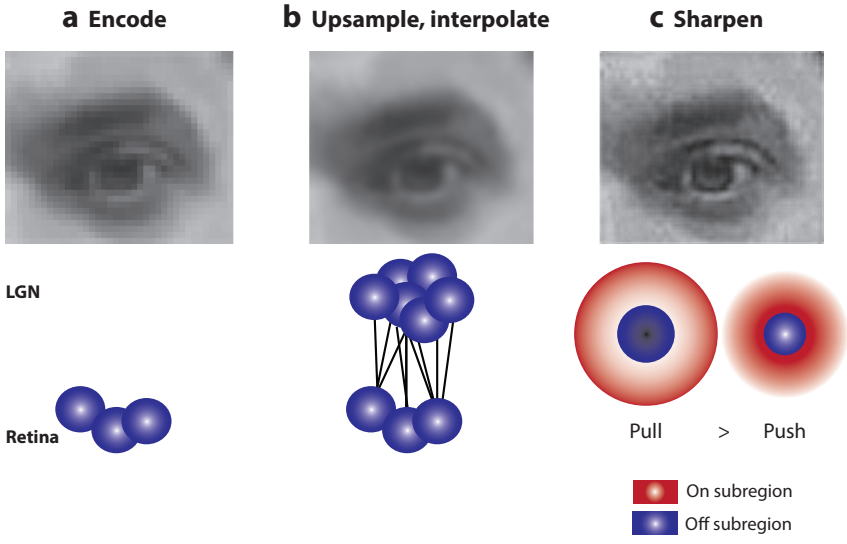

Figure 3

Image encoding and subsequent thalamic processing. (*a*) Encoding: Retinal ganglion cells encode visual information. The small discs illustrate the receptive field centers of three Off relay cells that encode part of the photo of the eye above. The retinal representation of the image is noticeably pixelated. (*b*) Upsampling and interpolation: Relay cells outnumber ganglion cells by a ratio of ~2:1. Retinal axons diverge to innervate multiple thalamic relay cells. Each relay cell receives convergent input from neighboring ganglion cells organized such that no two thalamic receptive fields are the same. Image of the eye shows that upsampling improves resolution but that interpolation introduces blur. (*c*) Sharpening: The spatial extent of the pull (*indicated by reverse shading*) in the relay cell's receptive field is larger than that of the push. This arrangement boosts contrast borders, improving image quality (to generate the snapshot in panel *c*, an unsharp mask was applied to the image in panel *b*. LGN, lateral geniculate nucleus.

thereby help to mitigate blur (Martinez et al. 2014). Thus, the thalamus seems to operate much like techniques used in digital image processing such as unsharp masking or local contrast enhancement. All told, local circuits in the thalamus have the potential to improve image perception without increasing the number of cells at the initial encoding stage. A summary of this process is provided in **Figure 3**.

The work just discussed is based on studies of cat. In primate, there are about as many relay cells as ganglion cells. However, there are more thalamorecipient cells in the monkey cortex than in the LGN (Chow et al. 1950), and most of these have center-surround receptive fields (Blasdel & Fitzpatrick 1984, Hubel & Wiesel 1968). Thus, the situation we have described in cat may apply to the thalamocortical stage in primate. All told, the combination of upsampling and interpolation coupled with border enhancement by inhibition may contribute to resolving a long-standing question in cat and human vision: why perceptual acuity is greater than the number of retinal photoreceptors predicts (Barlow 1981, Hall & Mitchell 1991, Westheimer 1975).

Temporal Processing

Neurons respond to changes in luminance contrast and thus signal both stimulus onset and withdrawal. For example, a dark disc flashed in an Off subregion elicits push when the stimulus appears and induces pull when it exits; **Figure 4*a*** illustrates patterns of push-pull in space (top panel) and time (bottom panel). Conversely, introducing and then removing a bright disc to and from the

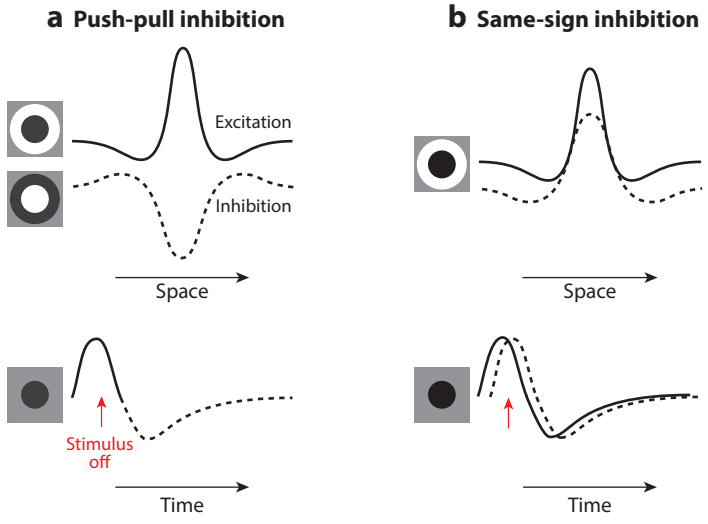

Figure 4

Spatial and temporal profiles of push-pull versus same-sign inhibition for an Off-center relay cell. (*a*) Diagram of push-pull excitation (*solid line*) and inhibition (*dashed line*) for an Off-center cell in (*top*) space and (*bottom*) time, as denoted in the figure. Icons at left of the traces depict stimulus shape and polarity; the vertical arrow under each temporal envelope indicates the time of stimulus withdrawal. (*b*) Diagram for same-sign excitation and inhibition; conventions as in panel *a*.

same Off subregion evoke a sequence of pull then push (not shown). In this fashion, relay cells select for biphasic (dark to bright or bright to dark) stimuli, thereby forming the temporal derivative of the image and reducing redundancy of signals dominated by low spatial frequencies, such as natural stimuli (Dan et al. 1996, Olshausen & Field 1996, Simoncelli & Olshausen 2001). Hence, the pull promotes efficient coding in time as well as in space.

Moreover, visual sequences that change from the nonpreferred to the preferred luminance contrast are particularly effective in driving relay cells (Alitto et al. 2005, Wang et al. 2007). Presumably, the pull enhances neural excitability via mechanisms akin to those that lead to anode break excitation (membrane depolarization following the cessation of a strong hyperpolarizing pulse) first described for the squid axon (Hodgkin & Huxley 1952).

In the thalamus, sequential push-pull has a special role. Relay cells fire in two modes: tonic and burst (Sherman 2001). Neurons typically fire tonic trains of action potentials that track (an edited version of) retinal input patterns (Carandini et al. 2007, Wang et al. 2010); in this mode it is thought that virtually every spike is preceded by a retinogeniculate excitatory postsynaptic potential (EPSP) (Carandini et al. 2007, Koepsell et al. 2009, Sincich et al. 2007, Wang et al. 2010). Bursts are rapid trains of action potentials that provide a means of amplifying retinal input (Sherman 2001). Bursts ride the crests of currents mediated by T-type calcium channels (Jahnsen & Llinas 1984). These channels are activated at voltages below the threshold for sodium spikes but also inactivate quickly and must be strongly hyperpolarized in order to reopen (Huguenard & Prince 1992, Jahnsen & Llinas 1984). Thus, burst mode predominates during sleep (Steriade et al. 1993), when neuromodulators that hyperpolarize relay cells are released.

Still, there is no absolute dichotomy between behavioral state and firing pattern; rather, convincing evidence indicates that bursts play a role in vision (Alitto & Usrey 2005, Niell & Stryker 2010, Sherman 2001). Natural stimulation engages with push-pull inhibition to drive the membrane from tonic to burst mode (Wang et al. 2007), as follows. When the animal moves through

its environment or scans the terrain, luminance values sometimes remain similar for long periods and then abruptly change (Simoncelli & Olshausen 2001) (these temporal correlations are a simple consequence of spatial correlations in natural scenes). Thus, in the course of natural viewing, there will be times when the receptive field is covered by a stimulus of the nonpreferred sign (Denning & Reinagel 2005, Lesica & Stanley 2004, Wang et al. 2007). In these cases, the pull can deinactivate T-type channels such that when stimulus contrast reverses and retinal input resumes, a burst is fired (Wang et al. 2007).

What can bursts contribute to vision beyond simple amplification of the incoming spike train? Physiological studies show that bursts, versus tonic trains of spikes, evoke postsynaptic action potentials with maximum efficacy (Swadlow & Gusev 2001, Usrey et al. 1998) and help ensure that sensory information propagates downstream. Also, from an information theoretic point of view, bursts encode information different from that conveyed by tonic activity (Denning & Reinagel 2005, Lesica et al. 2006) to signal special spatiotemporal features of the stimulus.

SAME-SIGN AND TONIC INHIBITION

One can think of the pull component of push-pull as opposite-sign inhibition. Accordingly, same-sign inhibition is evoked by a stimulus of the preferred luminance contrast (the same stimulus polarity that produces excitation). Same-sign inhibition is difficult to study because, unlike pull, it cannot be evoked in isolation. Computational models made using recordings of spike trains show how same-sign inhibition that lags behind or that outlasts excitation may improve temporal precision (Butts et al. 2011, Babadi et al. 2010, Casti et al. 2008), presumably by narrowing the window for successful launch of the action potential (sequential push-pull inhibition could serve a similar purpose). The spatial and temporal arrangements of same-sign inhibition within the receptive field are illustrated in **Figure 4*b***.

Some investigators report a population of relay cells, categorized as lagged, that seem to combine push-pull and same-sign inhibition; these are more frequently X than Y cells (Humphrey & Murthy 1999, Mastronarde 1987, Mastronarde et al. 1991, Vigeland et al. 2013). For these cells, the same-sign component is strong near the beginning of the response and then attenuates slowly. Thus, firing is initially suppressed and does not reach peak rates for tens or even hundreds of milliseconds. There is also a range of response timings between classical lagged and nonlagged response envelopes (Wolfe & Palmer 1998). One potential role for temporal diversity in response timing is to generate direction selectivity in the cortex, as per the Reichardt detector scheme (Saul & Humphrey 1990).

Same-sign inhibition may also be involved in contrast gain control (Sherman 2004). This mechanism, which extends the range of neural sensitivity to stimulus contrast, first appears in the retina (Shapley & Victor 1980, 1981) and is enhanced in the LGN (Kaplan et al. 1987). The idea is that as stimulus strength intensifies, inhibition increases more quickly than does excitation. Hence the number of spikes evoked by each increment in contrast is reduced at mid to high stimulus strengths.

Tonic (Stimulus-Independent) Inhibition

So far, we have discussed only stimulus-evoked inhibition. There is also evidence for inhibition that is generated constitutively. This tonic form of inhibition has been studied most intensively in the context of neurological and psychiatric disease, sleep and consciousness, and learning and memory (Brickley & Mody 2012). Current evidence suggests that tonic inhibition is mediated by extrasynaptic GABA receptors (Brickley & Mody 2012), unlike inhibition driven by sensory input,

which acts mainly at the synaptic locus. These extrasynaptic receptors have been identified as the targets of various drugs (Brickley & Mody 2012) and anesthetics (Jia et al. 2008) and thus are of therapeutic interest. The role of tonic inhibition in sensory processing per se has received little attention, however. Tonic inhibition may set the tone of neural excitability, either by subtly altering transmission or by promoting the transition from tonic to burst modes (Bright et al. 2007, Cope et al. 2005). Thus, tonic inhibition may influence the pattern of activity that a given stimulus evokes.

CIRCUITS FOR PUSH-PULL OR FOR SAME-SIGN INHIBITION

Push

The shape of the excitatory component of the thalamic receptive field is almost certainly inherited from retinal inputs (Koepsell et al. 2009, Levick et al. 1972, Sincich et al. 2009, Usrey et al. 1999, Wang et al. 2010). First, it has the same center-surround profile seen in retinal receptive fields. Second, the EPSPs that form the push in vivo resemble those recorded from thalamic brain slices following selective stimulation of the optic tract (Chen & Regehr 2000). Third, these EPSPs occur at the high rates characteristic of retinal spike trains (Frishman & Levine 1983). Fourth, even though relay cells receive substantial cortical feedback, their receptive field structure is not appreciably changed when V1 is removed or silenced (Jones & Sillito 1994, Sanderson et al. 1971). Last, unitary corticothalamic EPSPs are vanishingly small (Granseth & Lindstrom 2003), and the cortical cells that project to the thalamus have very low maintained firing rates (Gilbert 1977).

Pull

The prime candidate to supply the pull is local interneurons, which themselves have receptive fields with a center-surround structure (they even have push-pull) (**Figure 2*b***). There is also compelling physiological evidence that interneurons preferentially select relay cells with the reverse center sign (Martinez et al. 2014). For example, it has been possible to record intracellularly from one neuron and extracellularly from another with a single patch pipette; the patched cell can be classified with certainty and the identity of the extracellular neuron inferred by the presence or absence of bursts in the spike train. Interneuron/relay cell pairs were much more likely to have the opposite preference for stimulus contrast than predicted by chance (Martinez et al. 2014). Moreover, the receptive field centers of the interneurons were larger than those of the partner relay cells (Martinez et al. 2014), consistent with the finding that the circumference of the pull is larger than that of the push.

A priori, the receptive fields of interneurons should be relatively large if they are to tile visual space because these cells are fewer in number than ganglion cells. The origin of the large receptive field probably results from pooling input from multiple retinal afferents. Ultrastructural studies suggest that interneurons are supplied by 2–7 times more retinal boutons than relay cells receive (Datskovskaia et al. 2001, Van Horn et al. 2000). Furthermore, recordings from brain slices show that all cells in the LGN are contacted by many retinal afferents early in development (Chen & Regehr 2000, Seabrook et al. 2013). As the circuit matures, most inputs to relay cells are pruned (Chen & Regehr 2000, Seabrook et al. 2013). By contrast, afferent innervation of interneurons does not decline over time (Seabrook et al. 2013). Complementary work in vitro indicates that relay cells receive input from multiple interneurons (Crunelli et al. 1988, Ziburkus et al. 2003). Thus convergence of several interneurons, each with a large receptive field, could account for the large extent of the pull in relay cells.

Axodendritic Versus Dendrodendritic Connections for Push-Pull Versus Same-Sign Inhibition

Interneurons contact their targets using two very different types of synapse (Guillery 1969b, Hamos et al. 1985, Montero 1987, Sherman 2004). One means of communication is through axonal (or axon-like) processes that provide boutons called F1 terminals to the somas and dendrites of relay cells and other interneurons (Guillery 1969b, Hamos et al. 1985, Montero 1987). F1 boutons could contact cells with the opposite center sign to provide push-pull or, just as easily, link cells with the same preference for luminance contrast to provide same-sign inhibition. Thus, F1 terminals provide a flexible means of distributing feedforward inhibition.

The second type of synapse that interneurons form with their targets is specialized; in this case, the presynaptic compartment is dendritic instead of axonal. Whereas some of these dendrodendritic synapses are made *en passant*, many are made via dendritic appendages known as F2 terminals. F2 terminals (Guillery 1969b, Hamos et al. 1985, Montero 1986) are key components of triads, structures in which a single retinal bouton synapses with a dendrite of a relay cell as well as with a dendrite of an interneuron that, in turn, forms a dendrodendritic synapse with the relay cell (Guillery 1969b, Hamos et al. 1985, Szentágothai et al. 1966). Triads most commonly involve grape-like appendages that cluster near proximal dendrites of X-cells (Hamos et al. 1985, Sherman 2004), although some triads involve Y cells instead (Dankowski & Bickford 2003, Datskovskaia et al. 2001). Hence, the triads are hardwired to provide same-sign inhibition because they are engaged by a single, shared retinal input. By contrast, dendrodendritc (or dendrosomatic) synapses that are excluded from triads, as is often the case for Y cells (Dankowski & Bickford 2003, Datskovskaia et al. 2001) and for interneurons (Ohara & Lieberman 1993, Pasik et al. 1976), could contribute either to same-sign or to push-pull inhibition.

At present, unfortunately, there remains no clear-cut empirical evidence about the physiological role of the triads in vision. For example, one might predict that the EPSPs recorded from X relay cells would decay more rapidly (e.g., Blitz & Regehr 2005) than those recorded from Y and W cells, but this does not seem to be the case (J. Hirsch, personal observations; see Wang et al. 2007). Still, dendrodendritic synapses, whether part of triads or not, have unique properties that may alter visual function. They provide a means for subthreshold excitation to evoke release of GABA (Cox et al. 1998, Pressler & Regehr 2013). Hence dendrites can, in theory, act as individual compartments (Bernander et al. 1991, Sherman 2004), supplying inhibition even in the absence of firing. On the contrary, activation of F1 terminals requires spikes.

The pharmacology of F2 terminals is complex, as work with murine brain slices has shown. The connection between retinal boutons and F2 terminals includes both ionotropic and metabotropic receptors (Crandall & Cox 2012, Govindaiah & Cox 2006, Pressler & Regehr 2013). Metabotropic receptors mediate long-lasting EPSPs whose impact may be further extended in space and time by means of L-type calcium channels present along the length of the dendrite (Acuna-Goycolea et al. 2008, Casale & McCormick 2011, Govindaiah & Cox 2006, Pressler & Regehr 2013). The consequences of this lasting source of inhibition for postsynaptic cells have yet to be successfully explored in vivo but may contribute to mechanisms of contrast gain control or luminance adaptation (Pressler & Regehr 2013, Sherman 2004). Hypothetical circuits for push-pull and same-sign inhibition are illustrated in **Figure 5**.

SYNAPTIC PHYSIOLOGY OF RELAY CELLS VERSUS INTERNEURONS

Although relay cells and interneurons have receptive fields with similar structure, their synaptic physiology is very different. The intracellular waveforms recorded from these two types of cells

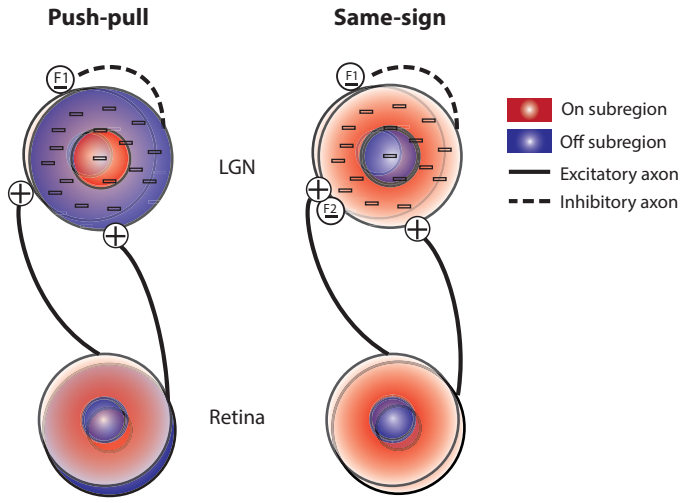

Figure 5

Hypothetical circuit for push-pull and for same-sign inhibition for an Off-center relay cell. Retinal ganglion cells (*bottom row*) connect with thalamic cells (*top row*). Neurons are drawn as their receptive fields. Off and On subregions are color-coded, as in the legend; overlaid dashes indicate interneurons. Excitatory axons are solid and inhibitory axons are dashed; plus and minus signs in the boutons match the sign of input and F1 versus F2 terminals are labeled as such. Receptive fields are partially transparent to help depict spatial overlap. Note that unlike push-pull inhibition, same-sign inhibition can be initiated by the same ganglion cell that provides excitation to the relay cell and/or by a nearby ganglion cell with the shared preference for stimulus polarity. LGN, lateral geniculate nucleus.

are quantitatively distinct and have almost inverted profiles (Wang et al. 2011b). For relay cells, excitatory stimuli drive trains of single, peaked excitatory postsynaptic currents (EPSCs), but evoke graded and smooth depolarizations in interneurons. Conversely, suppressive stimuli evoke smooth hyperpolarizations in relay cells and jagged trains of unitary inhibitory postsynaptic currents (IPSCs) in interneurons (**Figure 6**).

To understand the functional consequences of these differences in intracellular waveform, one must consider specializations of the retinogeniculate synapse. Not only do retinal axons form unusually large boutons, but these preferentially select the proximal dendrites of relay cells (Cucchiaro et al. 1991, Guillery 1969a, Hamos et al. 1985, Van Horn et al. 2000, Wilson 1989); these synaptic properties explain why retinogeniculate EPSCs are large and rise rapidly. Furthermore, relay cells receive only one to a few retinal inputs (Chen & Regehr 2000, Hamos et al. 1987, Tavazoie & Reid 2000, Usrey et al. 1999), so the shapes of most individual EPSPs remain prominent in the intracellular record, even during strong sensory drive. On the contrary, recordings from cortical neurons in vivo indicate that many small inputs blend to form compound graded EPSPs (Borg-Graham et al. 1998; Hirsch et al. 1998, 2002; Ferster et al. 1996).

The shape of the intracellular waveform has consequences for the propagation of information. Thalamic spikes lock to the crests of retinogeniculate EPSPs with millisecond precision (Koepsell et al. 2009, Usrey et al. 1999); thus they can transmit information encoded in the fine timing of retinal spikes (Koepsell et al. 2009, Wang et al. 2010). A smooth pull signal, such as that recorded from relay cells, is, in principle, able to hyperpolarize without interfering with the peaky structure of the retinogeniculate EPSPs. Indeed, conductance-based models of relay cells show that artificially smoothing the tips of the EPSPs reduces the amount of information encoded at

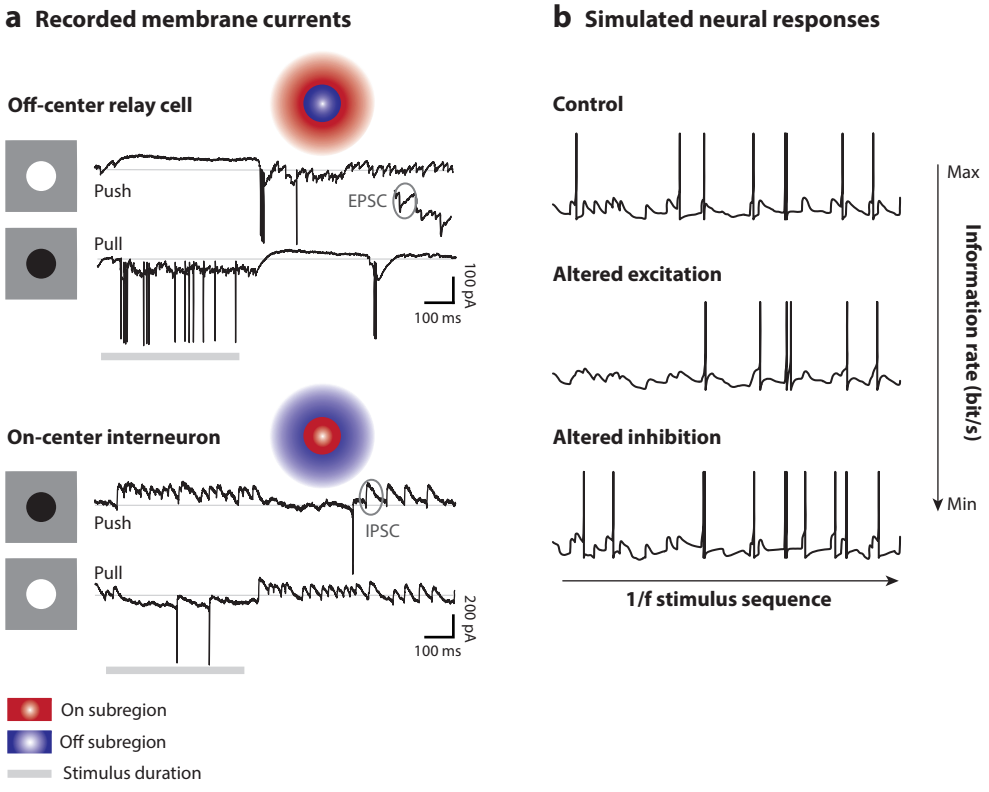

Figure 6

Shapes of synaptic inputs and the transmission of retinal information to the cortex. (*a*) Examples of membrane currents recorded from an Off-center relay cell (*top pair of traces*) and an On-center interneuron (*bottom pair of traces*) in response to stimuli of the opposite sign, as indicated by the icons at left. Unitary events recorded from relay cells are excitatory postsynaptic currents (EPSCs) (*inset* shows EPSCs at expanded gain) and from interneurons are inhibitory postsynaptic currents (IPSCs). An example of each type of event is circled in gray and labeled; the EPSCs are downward deflections that dip rapidly and decay slowly, whereas IPSCs rise rapidly and then decay slowly. (*b*) Simulations of neural responses (membrane voltage) to a stimulus sequence with 1/f statistics. For the top trace, excitatory and inhibitory inputs are modeled as in nature [peaked excitatory postsynaptic potentials (EPSPs) and smooth pull] for the middle trace EPSPs are smoothed, and for the bottom trace inhibitory postsynaptic potentials (IPSPs) are made unitary. Smoothing EPSPs reduces the amount of information transmitted to the cortex but not as severely as modifying the pull.

fine time scales, presumably because smoothing disrupts the mechanism by which thalamic spikes lock precisely to retinal inputs. By contrast, modeling the IPSCs to have jagged shapes significantly reduces the amount of information conveyed across timescales, likely because the sharpened IPSCs bite into the crests of the EPSCs, thus preventing the tight temporal coupling between retina and thalamus (**Figure 6*b***). Reduced temporal precision translates to reduced information in the spike train. Hence, the combination of peaked (versus rounded) EPSPs and smooth (versus jagged) inhibition optimizes the amount of information that is transmitted from the eye to the cortex (Wang et al. 2011b).

How is the graded pull signal recorded from relay cells made? The smooth shape of the push signal recorded from interneurons might provide a clue. Recall that excitatory synaptic drive onto interneurons activates L-type calcium currents. These regenerative depolarizations help to propagate retinal input, which often arrives at electrotonically remote dendritic sites (Sherman

2004), to the soma. Thus, L-type currents are likely responsible for the low-passed profile of the push in interneurons. Moreover, work in vitro shows that these currents, rather than the EPSP itself, drive firing and thereby decouple the timing of input from output spike trains (Acuna-Goycolea et al. 2008). Other mechanisms such as filtering of distal retinal inputs by the dendritic cable and transduction via metabotropic receptors may also contribute to smoothing the push. Last, correlograms constructed from spike trains of retinal afferents and putative interneurons are broad and those for relay cells are narrow (Dubin & Cleland 1977), supporting the idea of jitter in the feedforward inhibitory pathway.

All told, even if interneurons share common input from neighboring ganglion cells, the spike trains of the coactivated interneurons may be desynchronized. Furthermore, asynchronously arriving inputs from convergent interneurons to the relay cell may blend to provide smooth pull. Extratriadic, dendrodendritic connections between cells of the opposite sign may provide a complementary source of graded inhibition. Last, what advantage might the interneurons' jagged pull (which is formed by serial unitary events) provide? Perhaps it can disinhibit relay cells at timescales as rapid as the duration of a single inhibitory postsynaptic potential (IPSP).

THE THALAMIC RETICULAR NUCLEUS

The perigeniculate sector of the TRN represents the first stage of feedback in the geniculostriate pathway. It receives input from thalamic axons en route to the cortex and projects back to relay cells in all layers of the LGN (Cucchiaro et al. 1991, Sillito & Jones 2008, Wang et al. 2001). Connections between the TRN and interneurons are rare (Cucchiaro et al. 1991, Wang et al. 2001), if they occur at all, although reticular cells contact each other via electrical (Landisman et al. 2002, Long et al. 2004) and chemical synapses (Cucchiaro et al. 1991, Sanchez-Vives et al. 1997, Wang et al. 2001).

Previously, the TRN had been described as playing two different, somewhat contradictory, roles. One hypothetical role was to regulate overall levels of excitability (Bonin et al. 2005, Levick et al. 1972, So & Shapley 1981). Early recordings from relay cells had revealed a region beyond the boundaries of the center and surround in which bright or dark stimuli reduced excitation. This remote domain was called the suppressive field (Bonin et al. 2005, Levick et al. 1972, Sanderson et al. 1971) and was found to survive cortical ablation (Jones & Sillito 1994, Sanderson et al. 1971, Xue et al. 1988). Complementary studies suggested that receptive fields in the TRN were larger than those of relay cells and that many reticular neurons were binocular and responded to both bright and dark stimuli (Dubin & Cleland 1977, Levick et al. 1972). Taken together, these observations suggested that the TRN supplied the suppressive field (Bonin et al. 2005, Levick et al. 1972, Sanderson et al. 1971). However, recent work shows that the suppressive surround is generated by the retina, not by the thalamus (Alitto & Usrey 2008), thereby challenging the early idea that the TRN merely exerts a global gain control.

The second school of thought was that the TRN is involved in spatial attention because the nucleus lies between the sensory thalamus and the cortex and is reciprocally connected with both of these structures (Bickford et al. 2008, Cucchiaro et al. 1991, Ide 1982). The original idea was that attentionally regulated cortical input would excite reticular neurons and that these, in turn, would transiently inhibit relay cells and promote bursts, thus amplifying input to the cortex (Crick 1984). Later experiments modified the scheme by showing how attention can reduce activity in the TRN and thus disinhibit relay cells (McAlonan et al. 2006, 2008). In any event, a role in spatial attention is more consistent with selective rather than large and amorphous receptive fields. Anatomical studies support this view, in that there seems to be a topographic mapping from the TRN to the LGN (Lam & Sherman 2011, Sillito & Jones 2008, Uhlrich et al. 1991).

Although a truly quantitative assessment of the size of reticular receptive fields is yet to come, qualitative descriptions in primate suggest these are spatially discrete (McAlonan et al. 2006, 2008). Furthermore, spike-triggered receptive field analysis shows that reticular neurons are selective for highly complex and localized visual features (Vaingankar et al. 2012).

Recent observations indicate a new role for the TRN (Vaingankar et al. 2012). Even if reticular cells are excited by both dark and bright stimuli, there is often a strong preference for one or the other stimulus polarity. Thus, feedback inhibition may sum with feedforward inhibition to prime bursts in relay cells, a scenario in which the roles of both inhibitory circuits would interact to serve a common purpose.

BRIEF COMPARISON OF INHIBITORY CIRCUITS IN THE LGN AND V1

Circuits in the cortex are far more diverse than in the thalamus. This discussion focuses on similarities between the LGN and its main target, cortical layer 4, where (in cat) most cells have simple receptive fields (Hirsch & Martinez 2006a,b; Hubel & Wiesel 1962; Martinez et al. 2005). As in the LGN, these receptive fields are built of segregated, neighboring On and Off subregions with push-pull (Ferster 1986, Hubel & Wiesel 1962, Jin et al. 2011, Martinez et al. 2005, Reid & Alonso 1995). However, within the simple receptive fields of the cortex, subregions are elongated and lie side by side; they are not circular and concentrically arranged, as for the LGN (Hubel & Wiesel 1962). This change in geometry forms the basis for orientation selectivity (Ferster et al. 1996; Hubel & Wiesel 1962; Martinez et al. 2002, 2005; Reid & Alonso 1995), the best known emergent cortical property. Most remaining cells in layer 4 have complex receptive fields in which On and Off responses overlap (Hirsch et al. 2002, Hirsch & Martinez 2006a, Hubel & Wiesel 1962, Martinez et al. 2005, Usrey et al. 2003).

There are both excitatory and inhibitory simple and complex cells (Azouz et al. 1997, Gilbert & Wiesel 1979, Hirsch et al. 2003, Martinez et al. 2005). The inhibitory simple cells could provide the pull, analogous to push-pull circuitry in the LGN, and contribute orientation-tuned inhibition to their postsynaptic targets (Hirsch et al. 2003, Martinez et al. 2005). Evidence also indicates that the inhibitory component of the cortical receptive field is larger than the excitatory component (Haider et al. 2010), as in the LGN (Martinez et al. 2014). Thus, the same inhibitory mechanisms proposed to emphasize contrast borders at the level of the thalamus (Martinez et al. 2014) may also operate in the cortex.

The inhibitory complex cells could provide a source of inhibition insensitive to stimulus polarity or orientation and thus be suited to provide gain control (Troyer et al. 1998), somewhat analogous to same-sign inhibition in the LGN. Inhibitory neurons in layers that lack direct thalamic input have various types of complex receptive fields and seem tuned for stimulus orientation (Azouz et al. 1997, Cardin et al. 2007, Hirsch 2003, Martinez et al. 2005). Some of these project to layer 4 (Binzegger et al. 2004, Stepanyants et al. 2008) and thus could provide a second source of orientation-selective inhibition. The population of anatomically classified interneurons whose spatial receptive fields have been mapped quantitatively remains small, however. Hence it is unclear whether some morphological types are exclusively simple, complex, or otherwise functionally specific.

Optogenetic approaches in the mouse suggest that different anatomical families of cortical inhibitory interneurons (DeFelipe et al. 2013, Taniguchi et al. 2011) have very different impacts on sensory processing (Hangya et al. 2014, Lee et al. 2012, Lovett-Barron & Losonczy 2014, Nienborg et al. 2013, Pfeffer et al. 2013). In part, this functional specificity might correlate with the different subcellular targets (i.e., distal versus proximal dendrites, soma, axon hillock) that

a given type of interneuron innervates (DeFelipe et al. 2013). These interneuron-type specific differences in connectivity may be preserved across species (DeFelipe et al. 2013).

Before comparing studies in mouse to those in cat, however, note that there are not only similarities but also substantial differences across species. One striking species difference is the murine approximation of the simple receptive field, in which the On and Off subregions largely overlap (Liu et al. 2009), unlike the segregated arrangement that is a hallmark of the classical simple receptive field (Martinez et al. 2005, Hubel & Wiesel 1962). In addition, the concept of push-pull does not apply to mouse because the inhibitory component of the simple-like field is On-Off (Lien & Scanziani 2013, Liu et al. 2009). Accordingly, excitatory cells in the mouse primary visual cortex are selective for stimulus orientation, but interneurons, with rare exception, are not (Kerlin et al. 2010, Kuhlman et al. 2011, Niell & Stryker 2008, Runyan et al. 2010). Also, murine simple-like cells are abundant in all cortical layers rather than restricted to thalamorecipient zones (Bonin et al. 2011, Niell & Stryker 2008, Smith & Hausser 2010), an observation that suggests substantial differences in cortical wiring among animal models. The extent to which these cross-species variations in the cortex reflect commensurate differences in the thalamus remains an open question. A current and future challenge is to develop a framework for meaningful comparisons across species.

DISCLOSURE STATEMENT

The authors are not aware of any affiliations, memberships, funding, or financial holdings that might be perceived as affecting the objectivity of this review.

ACKNOWLEDGMENTS

We thank Manuel Molano-Mazón, Cristina Soto Sanchez, and Vishal Vaingankar for their irreplaceable contributions to some of the projects described here. J.A.H. was supported by NIH EY09593; F.T.S. was supported by NSF 0855272 and 1219212; and L.M.M. was supported by the Spanish Ministry of Economy and Competitiveness BFU2010-22220 and his home institution, Instituto de Neurociencias, a "Center of Excellence Severo Ochoa."

LITERATURE CITED

Acuna-Goycolea C, Brenowitz SD, Regehr WG. 2008. Active dendritic conductances dynamically regulate GABA release from thalamic interneurons. *Neuron* 57:420–31

Alitto HJ, Usrey WM. 2005. Dynamic properties of thalamic neurons for vision. *Prog. Brain Res.* 149:83–90

Alitto HJ, Usrey WM. 2008. Origin and dynamics of extraclassical suppression in the lateral geniculate nucleus of the macaque monkey. *Neuron* 57:135–46

Alitto HJ, Weyand TG, Usrey WM. 2005. Distinct properties of stimulus-evoked bursts in the lateral geniculate nucleus. *J. Neurosci.* 25:514–23

Azouz R, Gray CM, Nowak LG, McCormick DA. 1997. Physiological properties of inhibitory interneurons in cat striate cortex. *Cereb. Cortex* 7:534–45

Babadi B, Casti A, Xiao Y, Kaplan E, Paninski L. 2010. A generalized linear model of the impact of direct and indirect inputs to the lateral geniculate nucleus. *J. Vis.* 10:22

Barlow HB. 1961. The coding of sensory messages. In *Current Problems in Animal Behaviour*, ed. WH Thorpe, OL Zangwill, pp. 330–60. Cambridge, UK: Cambridge Univ. Press

Barlow HB. 1981. Critical limiting factors in the design of the eye and visual cortex. *Proc. R. Soc. B* 212:1–34

Barlow HB, Fitzhugh R, Kuffler SW. 1957. Dark adaptation, absolute threshold and Purkinje shift in single units of the cat's retina. *J. Physiol.* 137:327–37

Bernander O, Douglas RJ, Martin KA, Koch C. 1991. Synaptic background activity influences spatiotemporal integration in single pyramidal cells. *PNAS* 88:11569–73

Bickford ME, Carden WB, Patel NC. 1999. Two types of interneurons in the cat visual thalamus are distinguished by morphology, synaptic connections, and nitric oxide synthase content. *J. Comp. Neurol.* 413:83–100

Bickford ME, Wei H, Eisenback MA, Chomsung RD, Slusarczyk AS, Dankowsi AB. 2008. Synaptic organization of thalamocortical axon collaterals in the perigeniculate nucleus and dorsal lateral geniculate nucleus. *J. Comp. Neurol.* 508:264–85

Binzegger T, Douglas RJ, Martin KA. 2004. A quantitative map of the circuit of cat primary visual cortex. *J. Neurosci.* 24:8441–53

Blasdel GG, Fitzpatrick D. 1984. Physiological organization of layer 4 in macaque striate cortex. *J. Neurosci.* 4:880–95

Blitz DM, Regehr WG. 2005. Timing and specificity of feed-forward inhibition within the LGN. *Neuron* 45:917–28

Bonin V, Histed MH, Yurgenson S, Reid RC. 2011. Local diversity and fine-scale organization of receptive fields in mouse visual cortex. *J. Neurosci.* 31:18506–21

Bonin V, Mante V, Carandini M. 2005. The suppressive field of neurons in lateral geniculate nucleus. *J. Neurosci.* 25:10844–56

Borg-Graham LJ, Monier C, Fregnac Y. 1998. Visual input evokes transient and strong shunting inhibition in visual cortical neurons. *Nature* 393:369–73

Brickley SG, Mody I. 2012. Extrasynaptic $GABA_A$ receptors: their function in the CNS and implications for disease. *Neuron* 73:23–34

Bright DP, Aller MI, Brickley SG. 2007. Synaptic release generates a tonic $GABA_A$ receptor-mediated conductance that modulates burst precision in thalamic relay neurons. *J. Neurosci.* 27:2560–69

Bullier J, Norton TT. 1979. Comparison of receptive-field properties of X and Y ganglion cells with X and Y lateral geniculate cells in the cat. *J. Neurophysiol.* 42:274–91

Butts DA, Weng C, Jin J, Alonso JM, Paninski L. 2011. Temporal precision in the visual pathway through the interplay of excitation and stimulus-driven suppression. *J. Neurosci.* 31:11313–27

Carandini M, Horton JC, Sincich LC. 2007. Thalamic filtering of retinal spike trains by postsynaptic summation. *J. Vis.* 7(20):1–11

Cardin JA, Palmer LA, Contreras D. 2007. Stimulus feature selectivity in excitatory and inhibitory neurons in primary visual cortex. *J. Neurosci.* 27:10333–44

Casale AE, McCormick DA. 2011. Active action potential propagation but not initiation in thalamic interneuron dendrites. *J. Neurosci.* 31:18289–302

Casti A, Hayot F, Xiao Y, Kaplan E. 2008. A simple model of retina-LGN transmission. *J. Comput. Neurosci.* 24:235–52

Chandler DM, Field DJ. 2007. Estimates of the information content and dimensionality of natural scenes from proximity distributions. *J. Opt. Soc. Am. A* 24:922–41

Chen C, Regehr WG. 2000. Developmental remodeling of the retinogeniculate synapse. *Neuron* 28:955–66

Chow K, Blum JS, Blum RA. 1950. Cell ratios in the thalamo-cortical visual system of *Macaca mulatta*. *J. Comp. Neurol.* 92:227–39

Cope DW, Hughes SW, Crunelli V. 2005. $GABA_A$ receptor-mediated tonic inhibition in thalamic neurons. *J. Neurosci.* 25:11553–63

Cox CL, Zhou Q, Sherman SM. 1998. Glutamate locally activates dendritic outputs of thalamic interneurons. *Nature* 394:478–82

Crandall SR, Cox CL. 2012. Local dendrodendritic inhibition regulates fast synaptic transmission in visual thalamus. *J. Neurosci.* 32:2513–22

Crick F. 1984. Function of the thalamic reticular complex: the searchlight hypothesis. *PNAS* 81:4586–90

Crunelli V, Haby M, Jassik-Gerschenfeld D, Leresche N, Pirchio M. 1988. Cl^-- and K^+-dependent inhibitory postsynaptic potentials evoked by interneurones of the rat lateral geniculate nucleus. *J. Physiol.* 399:153–76

Cucchiaro JB, Uhlrich DJ, Sherman SM. 1991. Electron-microscopic analysis of synaptic input from the perigeniculate nucleus to the A-laminae of the lateral geniculate nucleus in cats. *J. Comp. Neurol.* 310:316–36

Dan Y, Atick JJ, Reid RC. 1996. Efficient coding of natural scenes in the lateral geniculate nucleus: experimental test of a computational theory. *J. Neurosci.* 16:3351–62
Dankowski A, Bickford ME. 2003. Inhibitory circuitry involving Y cells and Y retinal terminals in the C laminae of the cat dorsal lateral geniculate nucleus. *J. Comp. Neurol.* 460:368–79
Datskovskaia A, Carden WB, Bickford ME. 2001. Y retinal terminals contact interneurons in the cat dorsal lateral geniculate nucleus. *J. Comp. Neurol.* 430:85–100
DeFelipe J, López-Cruz PL, Benavides-Piccione R, Bielza C, Larrañaga P, et al. 2013. New insights into the classification and nomenclature of cortical GABAergic interneurons. *Nat. Rev. Neurosci.* 14:202–16
Denning KS, Reinagel P. 2005. Visual control of burst priming in the anesthetized lateral geniculate nucleus. *J. Neurosci.* 25:3531–38
Dubin MW, Cleland BG. 1977. Organization of visual inputs to interneurons of lateral geniculate nucleus of the cat. *J. Neurophysiol.* 40:410–27
Eglen SJ, Diggle PJ, Troy JB. 2005. Homotypic constraints dominate positioning of on- and off-center beta retinal ganglion cells. *Vis. Neurosci.* 22:859–71
Enroth-Cugell C, Robson JG. 1966. The contrast sensitivity of retinal ganglion cells of the cat. *J. Physiol.* 187:517–52
Ferster D. 1986. Orientation selectivity of synaptic potentials in neurons of cat primary visual cortex. *J. Neurosci.* 6:1284–301
Ferster D, Chung S, Wheat H. 1996. Orientation selectivity of thalamic input to simple cells of cat visual cortex. *Nature* 380:249–52
Field DJ. 1987. Relations between the statistics of natural images and the response properties of cortical cells. *J. Opt. Soc. Am. A* 4:2379–94
Fitzpatrick D, Penny GR, Schmechel DE. 1984. Glutamic acid decarboxylase-immunoreactive neurons and terminals in the lateral geniculate nucleus of the cat. *J. Neurosci.* 4:1809–29
Frishman LJ, Levine MW. 1983. Statistics of the maintained discharge of cat retinal ganglion cells. *J. Physiol.* 339:475–94
Gilbert CD. 1977. Laminar differences in receptive field properties of cells in cat primary visual cortex. *J. Physiol.* 268:391–421
Gilbert CD, Wiesel TN. 1979. Morphology and intracortical projections of functionally characterised neurones in the cat visual cortex. *Nature* 280:120–25
Govindaiah G, Cox CL. 2006. Metabotropic glutamate receptors differentially regulate GABAergic inhibition in thalamus. *J. Neurosci.* 26:13443–53
Granseth B, Lindstrom S. 2003. Unitary EPSCs of corticogeniculate fibers in the rat dorsal lateral geniculate nucleus in vitro. *J. Neurophysiol.* 89:2952–60
Guillery RW. 1969a. The organization of synaptic interconnections in the laminae of the dorsal lateral geniculate nucleus of the cat. *Z. Zellforsch. Mikrosk. Anat.* 96:1–38
Guillery RW. 1969b. A quantitative study of synaptic interconnections in the dorsal lateral geniculate nucleus of the cat. *Z. Zellforsch. Mikrosk. Anat.* 96:39–48
Haider B, Krause MR, Duque A, Yu Y, Touryan J, et al. 2010. Synaptic and network mechanisms of sparse and reliable visual cortical activity during nonclassical receptive field stimulation. *Neuron* 65:107–21
Hall SE, Mitchell DE. 1991. Grating acuity of cats measured with detection and discrimination tasks. *Behav. Brain Res.* 44:1–9
Hamos JE, Van Horn SC, Raczkowski D, Sherman SM. 1987. Synaptic circuits involving an individual retinogeniculate axon in the cat. *J. Comp. Neurol.* 259:165–92
Hamos JE, Van Horn SC, Raczkowski D, Uhlrich DJ, Sherman SM. 1985. Synaptic connectivity of a local circuit neurone in lateral geniculate nucleus of the cat. *Nature* 317:618–21
Hangya B, Pi HJ, Kvitsiani D, Ranade SP, Kepecs A. 2014. From circuit motifs to computations: mapping the behavioral repertoire of cortical interneurons. *Curr. Opin. Neurobiol.* 26:117–24
Hirsch JA. 2003. Synaptic physiology and receptive field structure in the early visual pathway of the cat. *Cereb. Cortex* 13:63–69
Hirsch JA, Alonso JM, Reid RC, Martinez LM. 1998. Synaptic integration in striate cortical simple cells. *J. Neurosci.* 18:9517–28

Hirsch JA, Martinez LM. 2006a. Circuits that build visual cortical receptive fields. *Trends Neurosci.* 29:30–39
Hirsch JA, Martinez LM. 2006b. Laminar processing in the visual cortical column. *Curr. Opin. Neurobiol.* 16:377–84
Hirsch JA, Martinez LM, Alonso JM, Desai K, Pillai C, Pierre C. 2002. Synaptic physiology of the flow of information in the cat's visual cortex in vivo. *J. Physiol.* 540:335–50
Hirsch JA, Martinez LM, Pillai C, Alonso JM, Wang Q, Sommer FT. 2003. Functionally distinct inhibitory neurons at the first stage of visual cortical processing. *Nat. Neurosci.* 6:1300–8
Hodgkin AL, Huxley AF. 1952. A quantitative description of membrane current and its application to conduction and excitation in nerve. *J. Physiol.* 117:500–44
Hubel DH. 1960. Single unit activity in lateral geniculate body and optic tract of unrestrained cats. *J. Physiol.* 150:91–104
Hubel DH, Wiesel TN. 1962. Receptive fields, binocular interaction and functional architecture in the cat's visual cortex. *J. Physiol.* 160:106–54
Hubel DH, Wiesel TN. 1968. Receptive fields and functional architecture of monkey striate cortex. *J. Physiol.* 195:215–43
Huguenard J, Prince D. 1992. A novel T-type current underlies prolonged Ca^{2+}-dependent burst firing in GABAergic neurons of rat thalamic reticular nucleus. *J. Neurosci.* 12:3804–17
Humphrey AL, Murthy A. 1999. Cell types and response timings in the medial interlaminar nucleus and C-layers of the cat lateral geniculate nucleus. *Vis. Neurosci.* 16:513–25
Ide LS. 1982. The fine structure of the perigeniculate nucleus in the cat. *J. Comp. Neurol.* 210:317–34
Jahnsen H, Llinas R. 1984. Electrophysiological properties of guinea-pig thalamic neurones: an in vitro study. *J. Physiol.* 349:205–26
Jia F, Yue M, Chandra D, Homanics GE, Goldstein PA, Harrison NL. 2008. Isoflurane is a potent modulator of extrasynaptic $GABA_A$ receptors in the thalamus. *J. Pharmacol. Exp. Ther.* 324:1127–35
Jin J, Wang Y, Swadlow HA, Alonso JM. 2011. Population receptive fields of ON and OFF thalamic inputs to an orientation column in visual cortex. *Nat. Neurosci.* 14:232–38
Jones HE, Sillito AM. 1994. The length-response properties of cells in the feline perigeniculate nucleus. *Eur. J. Neurosci.* 6:1199–204
Kaplan E, Purpura K, Shapley RM. 1987. Contrast affects the transmission of visual information through the mammalian lateral geniculate nucleus. *J. Physiol.* 391:267–88
Kerlin AM, Andermann ML, Berezovskii VK, Reid RC. 2010. Broadly tuned response properties of diverse inhibitory neuron subtypes in mouse visual cortex. *Neuron* 67:858–71
Koepsell K, Wang X, Vaingankar V, Wei Y, Wang Q, et al. 2009. Retinal oscillations carry visual information to cortex. *Front. Syst. Neurosci.* 3:4
Kuffler SW. 1953. Discharge patterns and functional organization of the mammalian retina. *J. Neurophysiol.* 16:37–68
Kuhlman SJ, Tring E, Trachtenberg JT. 2011. Fast-spiking interneurons have an initial orientation bias that is lost with vision. *Nat. Neurosci.* 14:1121–23
Lam YW, Sherman SM. 2011. Functional organization of the thalamic input to the thalamic reticular nucleus. *J. Neurosci.* 31:6791–99
Landisman CE, Long MA, Beierlein M, Deans MR, Paul DL, Connors BW. 2002. Electrical synapses in the thalamic reticular nucleus. *J. Neurosci.* 22:1002–9
Lee S-H, Kwan AC, Zhang S, Phoumthipphavong V, Flannery JG, et al. 2012. Activation of specific interneurons improves V1 feature selectivity and visual perception. *Nature* 488:379–83
Lesica NA, Stanley GB. 2004. Encoding of natural scene movies by tonic and burst spikes in the lateral geniculate nucleus. *J. Neurosci.* 24:10731–40
Lesica NA, Weng C, Jin J, Yeh CI, Alonso JM, Stanley GB. 2006. Dynamic encoding of natural luminance sequences by LGN bursts. *PLOS Biol.* 4:e209
Levick WR, Cleland BG, Dubin MW. 1972. Lateral geniculate neurons of cat: retinal inputs and physiology. *Invest. Ophthalmol.* 11:302–11
Lien AD, Scanziani M. 2013. Tuned thalamic excitation is amplified by visual cortical circuits. *Nat. Neurosci.* 16:1315–23

Liu BH, Li P, Sun YJ, Li YT, Zhang LI, Tao HW. 2009. Intervening inhibition underlies simple-cell receptive field structure in visual cortex. *Nat. Neurosci.* 13:89–96
Long MA, Landisman CE, Connors BW. 2004. Small clusters of electrically coupled neurons generate synchronous rhythms in the thalamic reticular nucleus. *J. Neurosci.* 24:341–49
Lovett-Barron M, Losonczy A. 2014. Behavioral consequences of GABAergic neuronal diversity. *Curr. Opin. Neurobiol.* 26:27–33
Madarasz M, Gerle J, Hajdu F, Somogyi G, Tombol T. 1978. Quantitative histological studies on the lateral geniculate nucleus in the cat. II. Cell numbers and densities in the several layers. *J. Hirnforsch.* 19:159–64
Marr D, Hildreth E. 1980. Theory of edge detection. *Proc. R. Soc. B* 207:187–217
Martinez LM, Alonso JM, Reid RC, Hirsch JA. 2002. Laminar processing of stimulus orientation in cat visual cortex. *J. Physiol.* 540:321–33
Martinez LM, Molano-Mazon M, Wang X, Sommer FT, Hirsch JA. 2014. Statistical wiring of thalamic receptive fields optimizes spatial sampling of the retinal image. *Neuron* 81:943–56
Martinez LM, Wang Q, Reid RC, Pillai C, Alonso JM, et al. 2005. Receptive field structure varies with layer in the primary visual cortex. *Nat. Neurosci.* 8:372–79
Mastronarde DN. 1987. Two classes of single-input X-cells in cat lateral geniculate nucleus. I. Receptive-field properties and classification of cells. *J. Neurophysiol.* 57:357–80
Mastronarde DN, Humphrey AL, Saul AB. 1991. Lagged Y cells in the cat lateral geniculate nucleus. *Vis. Neurosci.* 7:191–200
McAlonan K, Cavanaugh J, Wurtz RH. 2006. Attentional modulation of thalamic reticular neurons. *J. Neurosci.* 26:4444–50
McAlonan K, Cavanaugh J, Wurtz RH. 2008. Guarding the gateway to cortex with attention in visual thalamus. *Nature* 456:391–94
Montero VM. 1986. Localization of gamma-aminobutyric acid (GABA) in type 3 cells and demonstration of their source to F2 terminals in the cat lateral geniculate nucleus: a Golgi-electron-microscopic GABA-immunocytochemical study. *J. Comp. Neurol.* 254:228–45
Montero VM. 1987. Ultrastructural identification of synaptic terminals from the axon of type 3 interneurons in the cat lateral geniculate nucleus. *J. Comp. Neurol.* 264:268–83
Niell CM, Stryker MP. 2008. Highly selective receptive fields in mouse visual cortex. *J. Neurosci.* 28:7520–36
Niell CM, Stryker MP. 2010. Modulation of visual responses by behavioral state in mouse visual cortex. *Neuron* 65:472–79
Nienborg H, Hasenstaub A, Nauhaus I, Taniguchi H, Huang ZJ, Callaway EM. 2013. Contrast dependence and differential contributions from somatostatin- and parvalbumin-expressing neurons to spatial integration in mouse V1. *J. Neurosci.* 33:11145–54
Ohara PT, Lieberman AR. 1993. Some aspects of the synaptic circuitry underlying inhibition in the ventrobasal thalamus. *J. Neurocytol.* 22:815–25
Olshausen BA, Field DJ. 1996. Natural image statistics and efficient coding. *Network* 7:333–39
Pasik P, Pasik T, Hámori J. 1976. Synapses between interneurons in the lateral geniculate nucleus of monkeys. *Exp. Brain Res.* 25:1–13
Peters A, Payne BR. 1993. Numerical relationships between geniculocortical afferents and pyramidal cell modules in cat primary visual cortex. *Cereb. Cortex* 3:69–78
Pfeffer CK, Xue M, He M, Huang ZJ, Scanziani M. 2013. Inhibition of inhibition in visual cortex: the logic of connections between molecularly distinct interneurons. *Nat. Neurosci.* 16:1068–76
Pressler RT, Regehr WG. 2013. Metabotropic glutamate receptors drive global persistent inhibition in the visual thalamus. *J. Neurosci.* 33:2494–506
Reid RC, Alonso JM. 1995. Specificity of monosynaptic connections from thalamus to visual cortex. *Nature* 378:281–84
Ruderman DL, Bialek W. 1992. Seeing beyond the Nyquist limit. *Neural Comput.* 4:682–90
Runyan CA, Schummers J, Van Wart A, Kuhlman SJ, Wilson NR, et al. 2010. Response features of parvalbumin-expressing interneurons suggest precise roles for subtypes of inhibition in visual cortex. *Neuron* 67:847–57
Sanchez-Vives MV, Bal T, McCormick DA. 1997. Inhibitory interactions between perigeniculate GABAergic neurons. *J. Neurosci.* 17:8894–908

Sanderson KJ. 1971. Visual field projection columns and magnification factors in the lateral geniculate nucleus of the cat. *Exp. Brain Res.* 13:159–77

Sanderson KJ, Bishop PO, Darian-Smith I. 1971. The properties of the binocular receptive fields of lateral geniculate neurons. *Exp. Brain Res.* 13:178–207

Saul AB, Humphrey AL. 1990. Spatial and temporal response properties of lagged and nonlagged cells in cat lateral geniculate nucleus. *J. Neurophysiol.* 64:206–24

Seabrook TA, Krahe TE, Govindaiah G, Guido W. 2013. Interneurons in the mouse visual thalamus maintain a high degree of retinal convergence throughout postnatal development. *Neural Dev.* 8:24

Shapley RM, Victor JD. 1980. The effect of contrast on the non-linear response of the Y cell. *J. Physiol.* 302:535–47

Shapley RM, Victor JD. 1981. How the contrast gain control modifies the frequency responses of cat retinal ganglion cells. *J. Physiol.* 318:161–79

Sherman SM. 2001. Tonic and burst firing: dual modes of thalamocortical relay. *Trends Neurosci.* 24:122–26

Sherman SM. 2004. Interneurons and triadic circuitry of the thalamus. *Trends Neurosci.* 27:670–75

Sillito AM, Jones HE. 2008. The role of the thalamic reticular nucleus in visual processing. *Thalamus Related Syst.* 4:1–12

Simoncelli EP, Olshausen BA. 2001. Natural image statistics and neural representation. *Annu. Rev. Neurosci.* 24:1193–216

Sincich LC, Adams DL, Economides JR, Horton JC. 2007. Transmission of spike trains at the retinogeniculate synapse. *J. Neurosci.* 27:2683–92

Sincich LC, Horton JC, Sharpee TO. 2009. Preserving information in neural transmission. *J. Neurosci.* 29:6207–16

Smith SL, Hausser M. 2010. Parallel processing of visual space by neighboring neurons in mouse visual cortex. *Nat. Neurosci.* 13:1144–49

So YT, Shapley R. 1981. Spatial tuning of cells in and around lateral geniculate nucleus of the cat: X and Y relay cells and perigeniculate interneurons. *J. Neurophysiol.* 45:107–20

Stepanyants A, Hirsch JA, Martinez LM, Kisvarday ZF, Ferecsko AS, Chklovskii DB. 2008. Local potential connectivity in cat primary visual cortex. *Cereb. Cortex* 18:13–28

Steriade M, McCormick DA, Sejnowski TJ. 1993. Thalamocortical oscillations in the sleeping and aroused brain. *Science* 262:679–85

Swadlow HA, Gusev AG. 2001. The impact of 'bursting' thalamic impulses at a neocortical synapse. *Nat. Neurosci.* 4:402–8

Szentágothai J, Hamori J, Tombol T. 1966. Degeneration and electron microscope analysis of the synaptic glomeruli in the lateral geniculate body. *Exp. Brain Res.* 2:283–301

Taniguchi H, He M, Wu P, Kim S, Paik R, et al. 2011. A resource of Cre driver lines for genetic targeting of GABAergic neurons in cerebral cortex. *Neuron* 71:995–1013

Tavazoie SF, Reid RC. 2000. Diverse receptive fields in the lateral geniculate nucleus during thalamocortical development. *Nat. Neurosci.* 3:608–16

Troyer TW, Krukowski AE, Priebe NJ, Miller KD. 1998. Contrast-invariant orientation tuning in cat visual cortex: thalamocortical input tuning and correlation-based intracortical connectivity. *J. Neurosci.* 18:5908–27

Uhlrich DJ, Cucchiaro JB, Humphrey AL, Sherman SM. 1991. Morphology and axonal projection patterns of individual neurons in the cat perigeniculate nucleus. *J. Neurophysiol.* 65:1528–41

Usrey WM, Reppas JB, Reid RC. 1998. Paired-spike interactions and synaptic efficacy of retinal inputs to the thalamus. *Nature* 395:384–87

Usrey WM, Reppas JB, Reid RC. 1999. Specificity and strength of retinogeniculate connections. *J. Neurophysiol.* 82:3527–40

Usrey WM, Sceniak MP, Chapman B. 2003. Receptive fields and response properties of neurons in layer 4 of ferret visual cortex. *J. Neurophysiol.* 89:1003–15

Vaingankar V, Soto-Sanchez C, Wang X, Sommer FT, Hirsch JA. 2012. Neurons in the thalamic reticular nucleus are selective for diverse and complex visual features. *Front. Integr. Neurosci.* 6:118

Van Horn SC, Erisir A, Sherman SM. 2000. Relative distribution of synapses in the A-laminae of the lateral geniculate nucleus of the cat. *J. Comp. Neurol.* 416:509–20

Vigeland LE, Contreras D, Palmer LA. 2013. Synaptic mechanisms of temporal diversity in the lateral geniculate nucleus of the thalamus. *J. Neurosci.* 33:1887–96
Wang S, Bickford ME, Van Horn SC, Erisir A, Godwin DW, Sherman SM. 2001. Synaptic targets of thalamic reticular nucleus terminals in the visual thalamus of the cat. *J. Comp. Neurol.* 440:321–41
Wang X, Hirsch JA, Sommer FT. 2010. Recoding of sensory information across the retinothalamic synapse. *J. Neurosci.* 30:13567–77
Wang X, Sommer FT, Hirsch JA. 2011a. Inhibitory circuits for visual processing in thalamus. *Curr. Opin. Neurobiol.* 21:726–33
Wang X, Vaingankar V, Sanchez CS, Sommer FT, Hirsch JA. 2011b. Thalamic interneurons and relay cells use complementary synaptic mechanisms for visual processing. *Nat. Neurosci.* 14:224–31
Wang X, Wei Y, Vaingankar V, Wang Q, Koepsell K, et al. 2007. Feedforward excitation and inhibition evoke dual modes of firing in the cat's visual thalamus during naturalistic viewing. *Neuron* 55:465–78
Wässle H, Peichl L, Boycott BB. 1983. Mosaics and territories of cat retinal ganglion cells. *Prog. Brain Res.* 58:183–90
Werblin FS. 2010. Six different roles for crossover inhibition in the retina: correcting the nonlinearities of synaptic transmission. *Vis. Neurosci.* 27:1–8
Westheimer G. 1975. Visual acuity and hyperacuity. *Invest. Ophthalmol.* 14:570–72
Wiesel TN. 1959. Recording inhibition and excitation in the cat's retinal ganglion cells with intracellular electrodes. *Nature* 183:264–65
Wilson J. 1989. Synaptic organization of individual neurons in the macaque lateral geniculate nucleus. *J. Neurosci.* 9:2931–53
Wolfe J, Palmer LA. 1998. Temporal diversity in the lateral geniculate nucleus of cat. *Vis. Neurosci.* 15:653–75
Xue JT, Carney T, Ramoa AS, Freeman RD. 1988. Binocular interaction in the perigeniculate nucleus of the cat. *Exp. Brain Res.* 69:497–508
Yeh CI, Stoelzel CR, Weng C, Alonso JM. 2009. Functional consequences of neuronal divergence within the retinogeniculate pathway. *J. Neurophysiol.* 101:2166–85
Ziburkus J, Lo FS, Guido W. 2003. Nature of inhibitory postsynaptic activity in developing relay cells of the lateral geniculate nucleus. *J. Neurophysiol.* 90:1063–70

Annual Review of Neuroscience

Volume 38, 2015

Contents

Indexes

Errata

An online log of corrections to *Annual Review of Neuroscience* articles may be found at http://www.annualreviews.org/errata/neuro