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Spike timing and visual processing in the retinogeniculocortical pathway

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Although the visual response properties of neurons along the retinogeniculocortical pathway have been studied for decades, relatively few studies have examined how individual neurons along the pathway communicate with each other. Recent studies in the cat (*Felis domestica*) now show that the strength of these connections is very dynamic and spike timing plays an important part in determining whether action potentials will be transferred from pre- to postsynaptic cells. This review explores recent progress in our understanding of what role spike timing has in establishing different patterns of geniculate activity and how these patterns ultimately drive the cortex.

Keywords: retina; thalamus; visual cortex; multielectrode; spike timing; synchrony

1. INTRODUCTION

The LGN of the thalamus is the primary source of visual input to the cerebral cortex. Neurons in the LGN receive visual information directly from retinal ganglion cells—the output cells of the retina—and, in turn, give rise to axons that terminate in the primary visual cortex. The LGN exhibits a tremendous range of shapes and sizes across species (figure 1). Despite differences between species in the morphology of the LGN, one property appears common to all geniculate nuclei: LGN neurons have receptive fields that are remarkably similar to those of their retinal afferents (Hubel & Wiesel 1961; Levick *et al.* 1972; Usrey *et al.* 1999). Even the name given to LGN projection neurons—relay cells—implies that these neurons do little more than simply pass the baton of visual activity from the retina to the primary visual cortex. Given the tremendous similarity of receptive fields encountered in the retina and LGN, the question often arises of what purpose the LGN serves. An answer to this question can be found by examining the activity patterns of monosynaptically connected retinal ganglion cells and LGN neurons. While receptive fields do not change dramatically between retina and LGN, the LGN can and does transform the temporal structure of activity that it receives from the retina. Thus, the LGN is able to filter and restructure the patterns of activity that encode the visual information. This review explores the nature and range of geniculate responses to retinal input with an emphasis placed on what effect different patterns of LGN activity have on driving cortical responses.

2. DYNAMICS OF RETINOGENICULATE COMMUNICATION

Two properties of visual responses in the retina and LGN are worth noting before discussing the role of spike timing for visual processing in the LGN. First, retinal ganglion cells typically fire action potentials at higher rates than their geniculate targets (Hubel & Wiesel 1961; Levick *et al.* 1972; Kaplan *et al.* 1987; Usrey *et al.* 1999). In other words, not all retinal spikes trigger geniculate action potentials. Second, the latency of visual responses in the LGN is not simply the latency of retinal ganglion cell responses plus the delay imposed by spike transfer from retina to LGN, but rather, a value greater than the sum of the two. This second point can be quantified by simultaneously recording the responses of a retinal ganglion cell and one of its monosynaptic target neurons in the LGN (Levick *et al.* 1972; Mastronarde 1987; Usrey *et al.* 1999). For a pair of Y cells, it generally takes *ca.* 2.5 ms for a retinal spike to travel to the LGN and trigger a postsynaptic spike (figure 2). By contrast, the difference in time-course to visual response is generally *ca.* 10 ms. This timing difference indicates that early retinal responses to a visual stimulus do not trigger geniculate action potentials. Thus, the spiking activity of geniculate neurons depends on the history of afferent activity from the retina.

A number of recent studies in the cat have examined the relationship between retinal spike history and geniculate spike production by looking at the effect of retinal interspike interval on the probability that a retinal spike will elicit a geniculate spike (Mastronarde 1987; Usrey *et al.* 1998; Levine & Cleland 2001; Rowe & Fischer 2001). For a pair of retinal spikes from a single ganglion cell with a very short interspike interval, *in vivo* experiments demonstrate that the second spike of the pair is much more likely than the first (about four to six times more likely) to drive a geniculate spike (figure 3). This increased efficacy of second spikes declines as interspike intervals increase from values just greater than the ganglion cell's refractory period to *ca.* 30 ms. At interspike intervals greater than 30 ms, second retinal spikes are equal to first spikes in their probability of triggering a geniculate spike (Mastronarde 1987; Usrey *et al.* 1998; Levine & Cleland 2001; Rowe & Fischer 2001). This paired-spike effect

One contribution of 22 to a Discussion Meeting Issue 'The essential role of the thalamus in cortical functioning'.

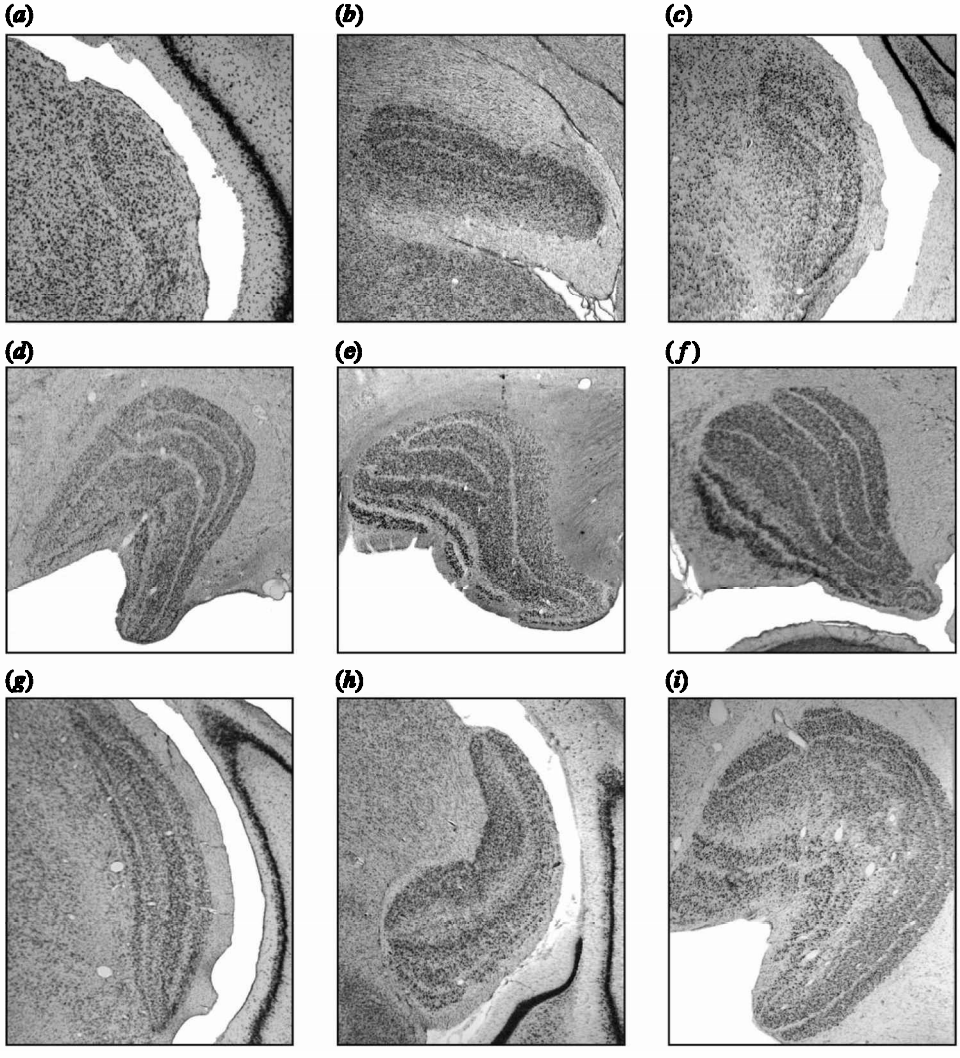

Figure 1. Photomicrographs of Nissl-stained sections of thalamus showing the LGN in nine different animals. (*a*) Rat (*Rattus norvegicus*), (*b*) cat (*Felis domestica*), (*c*) flying fox (*Pteropus poliocephalus*), (*d*) macaque monkey (*Macaca mulatta*), (*e*) human (*Homo sapiens*), (*f*) chimpanzee (*Pantroglodytes*), (*g*) tree shrew (*Tupai belangeri*), (*h*) galago (*Galago senegalensis*), (*i*) cebus monkey (*Cebus capuchinus*). The LGN is often referred to as a relay nucleus because LGN neurons receive direct input from the retina and provide direct output to the primary visual cortex. The brain sections were kindly provided by E. G. Jones. The images are not to scale.

does not depend on the overall strength of connection between retinal and geniculate cells, as cell pairs that are strongly connected (high probability of spike transfer) display the same degree of paired-spike enhancement as cell pairs that are weakly connected.

The relationship between retinal interspike interval and spike efficacy has been documented in both anaesthetized cats (Mastronarde 1987; Usrey *et al.* 1998; Levine & Cleland 2001; Rowe & Fischer 2001) and, more recently, alert cats (Weyand 2000). The dynamics of retinogeniculate transmission can also be studied using brain slices that include the LGN and cut retinal axons (Chen *et al.* 2002; Lo *et al.* 2002). This *in vitro* approach has the advantage that the mechanism(s) underlying the dynamic properties of synaptic transmission can be studied. Using this *in vitro* approach, Chen *et al.* (2002) have recently shown that retinogeniculate synapses undergo paired-pulse depression. This depression appears to rely, in large part, on postsynaptic mechanisms including desensitization of AMPA receptors and saturation of NMDA receptors. The finding that retinogeniculate synaptic transmission undergoes synaptic depression *in vitro*, while spike transfer between the retina and LGN is enhanced *in vivo*, is an interesting issue and further experiments need to be performed to correlate the *in vivo* and *in vitro* results.

There are a number of possible explanations for the difference between the *in vivo* and slice results. The first possibility is based on the amount of circuitry available in the two preparations. In the *in vivo* experiments, all of the inputs and outputs of the LGN are intact and second spikes might have an increased probability of driving geniculate responses because first spikes trigger a polysynaptic circuit that could potentially bring the geniculate cell closer to threshold. Second, it has been suggested that polysynaptic inhibition may be greater than monosynaptic excitation at low levels of retinal activity and that the balance of inhibition and excitation shifts towards excitation as retinal activity increases (Crunelli *et al.* 1988; Ziburkus 2001). Finally, LGN cells might simply behave differently when stimulated with natural patterns of retinal activity over long periods of time compared with short patterns of electrical stimulation. In the Chen *et al.* (2002) study, reti-

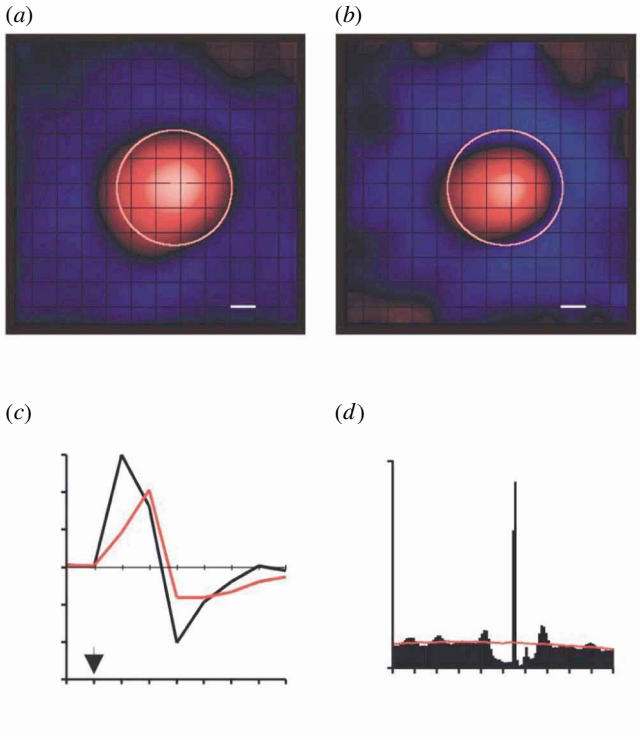

Figure 2. Receptive fields (*a*,*b*), impulse responses (*c*), and cross correlogram (*d*) of a pair of monosynaptically connected neurons in the retina (*a*) and LGN (*b*). White-noise receptive field maps (see Reid *et al.* (1997) for method) show the receptive fields of a retinal ganglion cell (*a*) and LGN cell (*b*) recorded simultaneously. *On* regions indicated in red, *off* in blue. The thin circle in both panels corresponds to a fit of the centre of the retinal ganglion cell's receptive field (1.75 σ, or standard deviations, from the peak of the best fitting Gaussian). The impulse response (*c*) shows the time-course of visual response for the retinal ganglion cell (black line) and LGN cell (red line). The peak of the visual response of the LGN cell is *ca.* 15.5 ms slower than the peak response of the retinal ganglion cell. The cross correlogram (*d*) shows the relative activity of the two cells. Retinal spikes occur at time zero and the short-latency peak to the right of zero indicates that many retinal spikes trigger a spike in the LGN cell with a latency of *ca.* 2.5 ms. This peak provides evidence that the retinal ganglion and LGN cells are monosynaptically connected. (Modified from Usrey *et al.* (1999).)

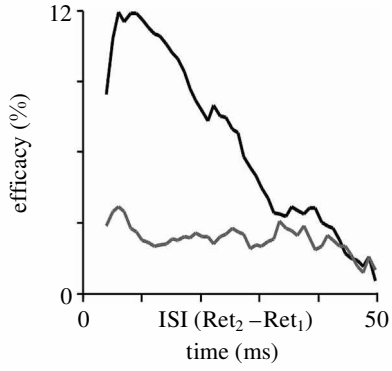

Figure 3. Plot showing the average efficacy of two retinal spikes (Ret_1 and Ret_2) as they occur with an increasing interspike interval (ISI) ($n = 12$ pairs of monosynaptically connected retinal ganglion cells and LGN cells recorded *in vivo*). Efficacy is equal to the percentage of retinal spikes that elicit a geniculate spike. The second retinal spikes (black) are much more effective than the first retinal spikes (grey) at very short interspike intervals. As the interspike interval increases, the efficacy of the second retinal spikes decreases until *ca.* 30 ms, when the second spike efficacy is approximately the same as the first spike efficacy. (Modified from Usrey *et al.* (1998).)

nal axons were stimulated electrically every 2 min with patterns that mimicked an *in vivo* response to a single flash of light. Given the power of *in vitro* techniques for addressing mechanistic questions about synaptic dynamics, it will be interesting to see how LGN neurons respond to longer trains of electrical stimuli that better approximate retinal responses to dynamic visual stimuli.

Based on the dynamics of synaptic interactions at the retinogeniculate synapse, one might expect tremendous variability in geniculate responses to a repeated visual stimulus. By contrast, Kara *et al.* (2000) have recently shown in anaesthetized cats that geniculate responses are much less variable than that of a Poisson process. These results are similar to the remarkable degree of synaptic reliability obtained in both LGN and hippocampal slices using short segments of natural stimulus trains (Dobrunz & Stevens 1999; Chen *et al.* 2002). Taken together, these results provide support for the idea that the dynamics of retinogeniculate interactions are repeatable and consistent.

3. RETINAL DIVERGENCE AND LGN SYNCHRONY

The pathway from retina to LGN is both convergent and divergent. Studies exploring convergent connections have shown that while some LGN neurons receive all of their retinal input from just one retinal ganglion cell, most LGN neurons receive convergent input from a small number of ganglion cells with partially overlapping receptive fields (Levick *et al.* 1972; Mastronarde 1987; Usrey *et al.* 1999). How individual LGN neurons integrate these convergent inputs is an open question and one that deserves future attention. By contrast, the effects of divergent connections have been more thoroughly explored (reviewed in Usrey & Reid 1999). Some years ago, Cleland (1986) proposed the idea that retinal ganglion cells with divergent axons should induce synchronous responses among target LGN neurons. The first evidence of this synchrony was observed from multielectrode recordings of LGN neurons in the cat with overlapping receptive fields (Alonso *et al.* 1996). Confirmation that this geniculate synchrony is the result of common retinal input (figure 4) was later demonstrated from simultaneous recordings of individual retinal ganglion cells along with multiple postsynaptic target neurons in the LGN (Usrey *et al.* 1998). Synchrony resulting from anatomical divergence in the LGN is both strong and fast—up to 30% of the spikes from two LGN cells that receive input from the same retinal ganglion cell can occur within less than 1 ms of each other.

There is a strong relationship between synchronous geniculate activity and retinal interspike interval. For a pair of retinal spikes with interspike intervals of less than 30 ms, *in vivo* recordings show that second retinal spikes are up to 12 times more likely than first spikes to drive

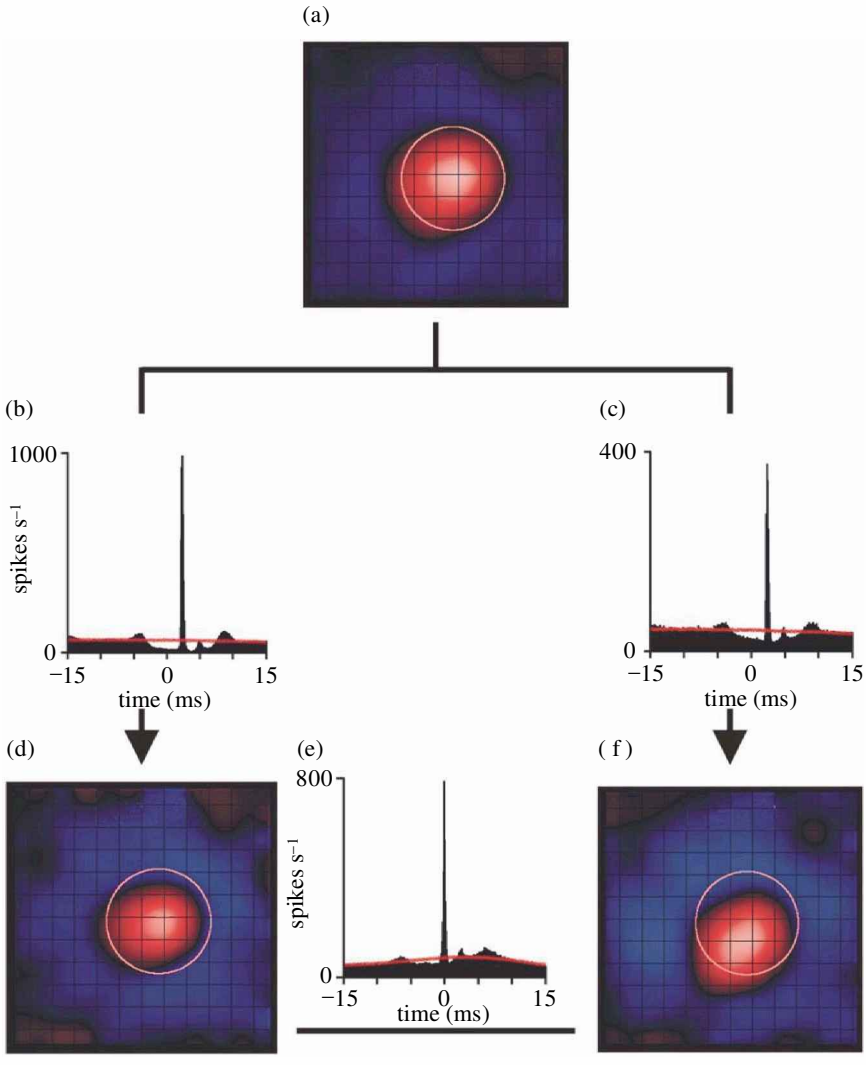

Figure 4. Receptive fields (*a*,*d*,*f*) and cross correlograms (*b*,*c*,*e*) of two LGN neurons that receive common input from a retinal ganglion cell (all cells recorded simultaneously). LGN neurons that receive common retinal input fire many synchronous spikes. The receptive fields were mapped using a white-noise stimulus. The *on* responses are shown in red and the *off* responses in blue. The circle over all the receptive fields corresponds to a Gaussian fit of the centre of the retinal cell's receptive field. The correlograms at the sides of the figure have short latency (*ca*. 2.5 ms) peaks indicating that the retinal ganglion cell provided monosynaptic input to both the LGN neurons. The peak in the correlogram in (*e*) shows that the two LGN cells fire many spikes simultaneously (less than 1 ms). The red traces superimposed on the correlograms correspond to the stimulus-dependent firing of the cells (shuffle correlogram). (*a*) Retina, (*b*) ret → LGN A, (*c*) ret → LGN B, (*d*) LGN A, (*e*) LGN A−LGN B, (*f*) LGN B. (Modified from Usrey *et al.* (1998).)

synchronous responses (Usrey *et al.* 1998). Thus, if the firing rate of an individual retinal ganglion cell rapidly increases, as occurs with an appropriate visual stimulus, the occurrence of synchronous LGN spikes increases dramatically. In other words, there is a partial transformation in information coding from a single-cell rate code to a population temporal code (Dan *et al.* 1998). The key to whether or not these synchronous geniculate spikes play a major part in visual processing lies in whether or not there is a cortical mechanism for preferentially detecting coincident spikes (see § 5).

4. NON-RETINAL INFLUENCES ON GENICULATE ACTIVITY

LGN neurons receive non-retinal input from a variety of sources including the thalamic reticular nucleus and various regions of the brainstem. The major source of non-retinal input to the LGN, however, comes from neurons in layer 6 of the visual cortex (Gilbert & Kelly 1975; Lund *et al.* 1975; Hendrickson *et al.* 1978; Katz 1987; Fitzpatrick *et al.* 1994; Murphy & Sillito 1996; Usrey & Fitzpatrick 1996). Although this feedback projection is numerically strong—feedback axons provide approximately five times more synapses onto LGN neurons than retinal axons (Guillery 1969; Erisir *et al.* 1997*a*,*b*)—we lack a firm understanding of what role corticogeniculate feedback plays in vision. As LGN receptive fields are very similar to those of their retinal inputs and bear little relation to those of their layer-6 input, it seems likely that cortical feedback serves to influence the temporal properties or gain of LGN responses rather than the structure of LGN receptive fields. A number of functions of corticogeniculate feedback have been proposed over the years.

Three prominent views of feedback are:

(i) adjusting the gain or timing of geniculate responses to retinal input (Schmeliau & Singer 1977; Tsumoto *et al.* 1978; Molotchnikoff *et al.* 1984; Gulyas *et al.* 1990; Funke *et al.* 1996; Rao & Ballard 1999; Przybyszewski *et al.* 2000);
(ii) shifting geniculate neurons between burst and tonic modes of firing (Sherman 1996, 2001); and
(iii) increasing the correlated activity of LGN neuron ensembles (Sillito *et al.* 1994; see also Weliky 1999; Jones 2001).

The first proposal—feedback serves to adjust the gain or timing of LGN responses to retinal input—is not without experimental support. For instance, experiments in the cat (*Felis domestica*) indicate that cortical feedback can increase the magnitude of LGN responses to moving patterns and textures (Gulyas *et al.* 1990). Along these lines, a number of laboratories have noted that the percentage of retinal spikes that evoke LGN spikes increases when cells are stimulated with patterns more appropriate (i.e. drifting gratings) for driving cortical neurons (Levick *et al.* 1972; Usrey *et al.* 1999). With respect to timing, a recent study has shown that cortical feedback may play a role in sharpening the interspike interval distribution of LGN responses (Funke *et al.* 1996). If so, then cortical feedback could serve to improve the temporal accuracy of signal transmission.

The proposal that cortical feedback plays a part in determining the mode of LGN activity—burst mode or tonic mode—is based on an understanding of the cellular basis of the low threshold Ca^{2+} spike that is common to thalamic neurons (Jahnsen & Llinás 1984*a*,*b*; Lo *et al.* 1991; Huguenard & McCormick 1992; McCormick & Huguenard 1992). This low threshold spike requires de-inactivation of T-type Ca^{2+} channels. At membrane potentials more positive than *ca.* −60 mV, T-type Ca^{2+} channels are inactivated and suprathreshold depolarization results in a tonic mode of firing. At potentials below −60 mV, T-type Ca^{2+} channels are de-inactivated and suprathreshold depolarization results in a Ca^{2+} spike and a burst of action potentials. According to the model proposed by Sherman (1996, 2001), input from corticogeniculate axons does not directly drive LGN action potentials, but rather depolarizes LGN neurons above the inactivation potential for T-type Ca^{2+} channels thereby shifting LGN cells into a tonic mode of firing. Without layer-6 input, LGN cells hyperpolarize and T-type Ca^{2+} channels become de-inactivated allowing LGN cells to fire a burst of spikes the next time the membrane crosses the threshold. Although the burst mode has traditionally been viewed as a mode that occurs in animals that are asleep, drowsy or inattentive, recent studies have shown not only that thalamic bursts occur in alert animals, but that bursts can carry high amounts of sensory information (Guido & Weyand 1995; Reinagel *et al.* 1999; Ramcharan *et al.* 2000; Fanselow *et al.* 2001; Weyand *et al.* 2001).

Finally, Sillito *et al.* (1994) indicated that cortical feedback serves to increase the degree of correlated activity between LGN neurons (Sillito *et al.* 1994). By recording from pairs of LGN cells with nearby receptive fields, they found that the correlated activity between the cells was both increased and sharpened during visual stimulation when the corticogeniculate pathway was intact compared with when it was inactivated by cortical aspiration. These correlations were faster (25–200 ms) than expected, but slower than those described above (figure 4) resulting from divergent retinal axons (less than 1 ms). The proposal that layer-6 feedback serves to synchronize LGN responses has been controversial. Using a two-neuron model, Brody (1998) has demonstrated that during stimulus-driven conditions, slow (tens of seconds) covariations in the resting potential of two cells can lead to fast (25–200 ms) correlations.

5. CORTICAL RESPONSES TO DIFFERENCE PATTERNS OF LGN ACTIVITY

With the increasing use of multielectrode recording techniques to study monosynaptically connected neurons in the brain (Kralik *et al.* 2001), researchers are beginning to answer questions about how the thalamus communicates with the cerebral cortex *in vivo*. Multielectrode-recording techniques have been applied successfully to study thalamocortical connections in the visual (Tanaka 1985; Reid & Alonso 1995; Alonso *et al.* 1996, 2001; Usrey *et al.* 2000), auditory (Miller *et al.* 2001*a*,*b*) and somatosensory systems (Roy & Alloway 2001; Swadlow & Gusev 2001). In so doing, researchers have examined the specificity and strength of thalamic connections as well as what role spike timing of thalamic afferents has in driving cortical responses.

Neurons in the LGN give rise to axons that terminate primarily in layer 4 of the primary visual cortex. In the cat, these layer-4 neurons, called simple cells, have receptive fields with elongated and adjacent *on* and *off* subregions and respond best to oriented bars or edges of light (Hubel & Wiesel 1962). Simultaneous *in vivo* recordings from monosynaptically connected LGN neurons and layer-4 simple cells have demonstrated the tremendous specificity of connections between the two cells (Tanaka 1985; Reid & Alonso 1995; Alonso *et al.* 2001). With very few mistakes, neurons in the LGN provide input to simple cells when their receptive fields are appropriately overlapped and matching in response sign (*on* or *off*).

Simultaneous recordings from monosynaptically connected geniculate neurons and layer-4 simple cells in the cat have also been used to examine the effects of geniculate spike timing on cortical responses. In particular, these studies have examined what effect interspike interval has on the probability of evoking a cortical spike. Similar to results from the retinogeniculate pathway, recent studies have shown that geniculate spikes show paired-spike interactions, whereby second spikes of a pair have an increased probability of driving a cortical spike (Usrey *et al.* 2000). This enhanced probability is greatest at the shortest interspike intervals measured (less than 1 ms) and decreases with interspike intervals up to *ca.* 15 ms when second spikes become equal to first spikes in their probability of driving a cortical spike. As with the retinogeniculate pathway, *in vitro* studies have shown that the geniculocortical pathway to layer 4 undergoes paired-pulse depression (Stratford *et al.* 1996; see also Gil *et al.* 1999; Chung *et al.* 2002). As *in vivo* studies indicate that second geniculate spikes have an increased probability of

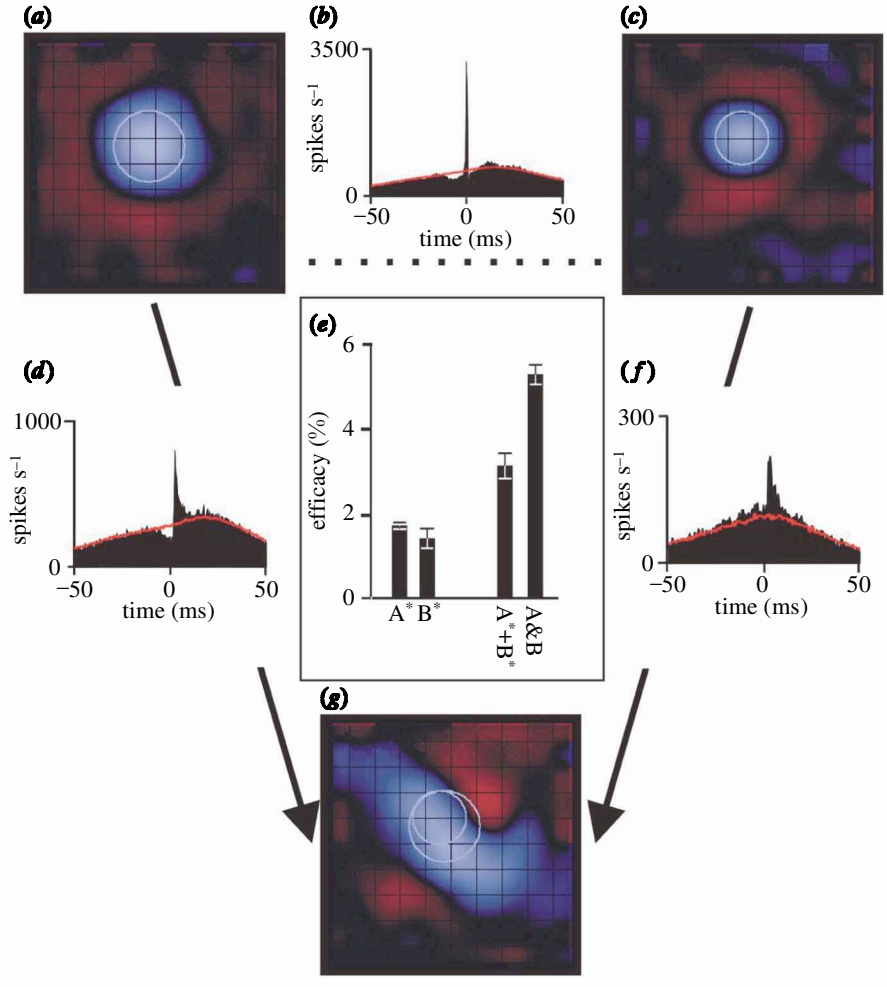

Figure 5. Receptive fields (*a*,*c*,*g*) and cross correlograms (*b*,*d*,*f*) of two LGN neurons that provide convergent input to a common cortical neuron (all cells recorded simultaneously). LGN inputs that arrive simultaneously at a cortical neuron interact synergistically to drive a cortical response. The receptive fields were mapped using a white-noise stimulus. The *on* responses are shown in red and the *off* responses in blue. The circle over the cortical cell's receptive field corresponds to Gaussian fits of the centres of the LGN neurons' receptive fields. The correlograms in (*d*) and (*f*) show that both LGN neurons provide monosynaptic input to the cortical neuron. (*a*) LGN cell A, (*b*) A–B, (*c*) LGN cell B; (*d*) A–C; (*f*) B–C; (*g*) cortex cell C. (*e*) To examine the interactions of the converging inputs, the geniculate spikes were divided into three groups: LGN spikes that occurred within 1 ms of each other (A and B), LGN spikes that occurred in cell A but not in cell B (A*), and LGN spikes that occurred in cell B but not in cell A (B*). The efficacy (percentage of spikes that drive a cortical spike) of the simultaneous LGN spikes (A and B) is 70% greater than that expected if the LGN spikes interact in a linear fashion (A* + B*). (Modified from Alonso *et al.* (1996).)

driving cortical spikes, while *in vitro* studies show that second geniculate spikes are depressing, future studies are warranted to better understand this synaptic connection. For instance, it is important to know the extent to which polysynaptic circuits influence paired-spike interactions measured *in vivo*, as well as how natural patterns of electrical stimulation influence synaptic currents *in vitro*. Finally, with the increasing use of whole-cell recordings from cortical neurons *in vivo*, a more complete understanding of the role of thalamic spike timing on cortical responses should be revealed (Hirsch *et al.* 1995; Ferster *et al.* 1996; Azouz & Gray 2000; Chung *et al.* 2002).

The *in vivo* finding that spikes from an individual LGN axon have an increased probability of driving a cortical spike when they follow a previous spike by less than 15 ms indicates that cortical neurons should be able to respond well to bursts of LGN spikes. Although untested in the visual system, Swadlow & Gusev (2001) have recently demonstrated in the somatosensory system that thalamic bursts are extremely effective at driving cortical responses. As mentioned above (§ 4), one proposed function of the feedback pathway from the cerebral cortex to the thalamus is to shift thalamic neurons between burst and tonic modes of firing (Sherman 1996, 2001). While this potential function of feedback is currently an area of active research, the results thus far support the idea that thalamic bursts are effective at driving the cortex.

Neurons in layer 4 of the visual cortex receive convergent input from several LGN neurons. While the number of convergent inputs probably varies in a species-specific fashion, estimates based on data from the cat indicate that individual layer-4 neurons receive convergent input from *ca.* 30 LGN neurons (reviewed in Peters & Payne (1993) and Reid *et al.* (2001)). Recent *in vivo* studies in the cat have examined how cortical neurons respond to these convergent inputs by simultaneously recording from two LGN neurons and a monosynaptically connected layer-4 cell (Alonso *et al.* 1996; Usrey *et al.* 2000) (figure 5). Simi-

lar studies have been performed to examine the effect of convergent inputs from the ventrobasal complex of the thalamus to the somatosensory cortex (Roy & Alloway 2001). Both studies demonstrate that convergent inputs interact in a reinforcing fashion over very brief windows of time to drive cortical spikes. Reinforcement is at a maximum for spikes that arrive within 1 ms of each other. Interactions then decrease until *ca*. 7 ms (*ca*. 2.5 ms time constant) when spikes from two separate LGN cells appear independent of each other. As mentioned above (§ 3), LGN neurons that receive divergent input from a common retinal ganglion cell fire a large percentage of their spikes synchronously (less than 1 ms) (Alonso *et al.* 1996; Usrey *et al.* 1998). Results from geniculocortical recordings now show that layer-4 neurons have the means to respond selectively to these coincident events. There has been an ongoing debate over the years as to whether or not the precise timing of presynaptic inputs plays a significant part for sensory processing in the cerebral cortex (Softky & Koch 1993; Shadlen & Newsome 1994, 1998; Konig *et al.* 1996; Stevens & Zador 1998; Gray 1999; Shadlen & Movshon 1999; Jones 2001; Salinas & Sejnowski 2001). While the debate is likely to continue for intracortical connections, results from the experiments described in § 5 indicate that spike timing is very important for thalamocortical connections. Finally, one of the proposed functions of corticogeniculate feedback (described in § 4) is to increase the correlated activity among LGN neurons (Sillito *et al.* 1994). If indeed cortical feedback serves this role, then these correlations should increase the probability that LGN neurons will drive layer-4 neurons.

6. CONCLUSIONS AND FUTURE DIRECTIONS

The LGN has long been considered a simple relay for transferring activity from the retina to the primary visual cortex. Results from recent experiments, however, are beginning to call this view into question. For instance, we now know that the responses of LGN neurons are determined largely by the temporal history of afferent activity in the retina (Mastronarde 1987; Usrey *et al.* 1998; Levine & Cleland 2001; Rowe & Fischer 2001). Similarly, we also know that spike timing plays a crucial part in the transfer of activity from the LGN to the primary visual cortex (Alonso *et al.* 1996; Usrey *et al.* 2000; see also Roy & Alloway 2001; Swadlow & Gusev 2001). While these results demonstrate the importance of timing for visual processing in the early visual pathway, they create more questions than they provide answers. For instance, in awake animals, what effect does behavioural state, attention, statistics of the visual stimulus, or eye-movement history have on the dynamics of synaptic interactions between LGN neurons and their pre- and postsynaptic partners? Similarly, what effect does cortical feedback have in awake animals on the timing of LGN responses and the nature of thalamocortical transmission? These are difficult questions to address, but with the increasing combined use of multielectrode recording techniques and alert primates we are in a position to begin obtaining answers.

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GLOSSARY

LGN: lateral geniculate nucleus