Exp Brain Res (1986) 63: 1-20

Experimental Brain Research

Overview

The control of retinogeniculate transmission in the mammalian lateral geniculate nucleus

S.M. Sherman[1] and C. Koch[2]

[1] Department of Neurobiology and Behavior, Graduate Biology Building, State University of New York, Stony Brook, NY 11794-5230, USA
[2] Center for Biological Information Processing and Artificial Intelligence Laboratory, E 25-201, Massachusetts Institute of Technology, Cambridge, MA 02139, USA

Summary. In the mammalian visual system, the lateral geniculate nucleus is commonly thought to act merely as a relay for the transmission of visual information from the retina to the visual cortex, a relay without significant elaboration in receptive field properties or signal strength. However, many morphological and electrophysiological observations are at odds with this view. Only 10–20% of the synapses found on geniculate relay neurons are retinal in origin. Roughly half of all synapses derive from cells in layer VI of visual cortex; roughly one third are inhibitory and GABAergic, derived either from interneurons or from cells of the nearby perigeniculate nucleus. Most of the remaining synapses probably derive from cholinergic, noradrenergic, and serotonergic sites within the brainstem reticular formation. Moreover, recent biophysical studies have revealed several ionic currents present in virtually all thalamic neurons. One is a Ca^{2+}-dependent K^+ current underlying the afterhyperpolarization (or the I_{AHP}), which may last up to 100–200 ms following an action potential. Activation of the I_{AHP} leads to spike frequency adaptation in response to a sustained, suprathreshold input. Intracellular recordings from other neuronal preparations have shown that the I_{AHP} can be blocked by noradrenalin or acetylcholine, leading to an increased cellular excitability. Another ionic current results from a voltage- and time-dependent Ca^{2+} conductance that produces a low threshold spike. Activation of this conductance transforms a geniculate neuron from a state of faithful relay of information to one of bursting behavior that bears little relationship to the activity of its retinal afferents. We propose that state-dependent gating of geniculate relay cells, which may represent part of the neuronal substrate involved in certain forms of selective visual attention, can be effected through at least three different mechanisms: (1) conventional GABAergic inhibition, which is largely controlled via brainstem and cortical afferents through interneurons and perigeniculate cells; (2) the I_{AHP}, which is controlled via noradrenergic and cholinergic afferents from the brainstem reticular formation; and (3) the low threshold spike, which may be controlled by GABAergic inputs, cholinergic inputs, and/or the corticogeniculate input, although other possibilities also exist. Furthermore, it seems likely that gating functions involving the corticogeniculate pathway are suited to attentional processes within the visual domain (e.g., saccadic suppression), whereas brainstem inputs seem more likely to have more global effects that switch attention between sensory systems. In any case, it is now abundantly clear that geniculate circuitry and the intrinsic electrophysiological properties of geniculate neurons are no longer compatible with the notion that the lateral geniculate nucleus serves as a simple relay.

Key words: Lateral geniculate nucleus – Retinogeniculate gating – Attentional mechanisms – Neuronal integration – Thalamic function

Offprint requests to: S.M. Sherman (address see above)

I. Introduction

The mammalian visual system, and particularly the retino-geniculo-cortical component, has been a popular and fruitful subject of neurobiological enquiry. As a result, a great deal is known about its functional organization. The neuronal circuitry in the retina subserves changes in receptive field properties of single neurons at each synaptic level (Dowling 1970), and the same principle seems to apply to the visual cortex (Hubel and Wiesel 1977; Gilbert 1983). That is, the main functional significance of neural

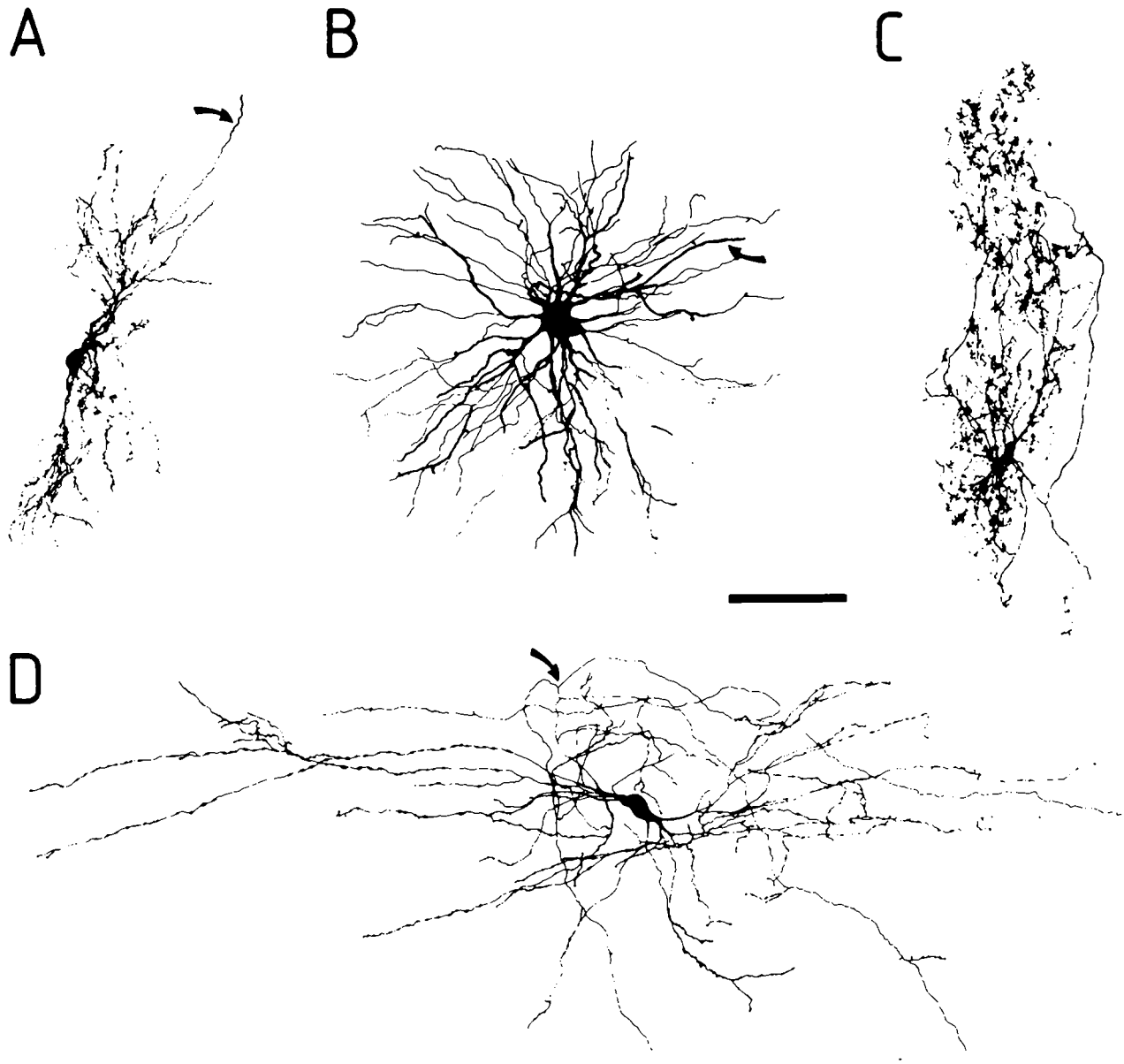

Fig. 1A–D. Reconstructions of four representative examples of the various neuronal types in the cat's lateral geniculate and perigeniculate nuclei; coronal views. The cells were physiologically identified and labeled with intracellular iontophoresis of horseradish peroxidase. The scale is 100 μm and applies to each of the reconstructions. Each of these cells has a myelinated axon, which is identicated by an arrow where evident; the cell in **C** has such an axon, but it cannot readily be picked out in the reconstruction due to the great complexity of the dendritic arbor. **A** Example of X relay cell from lamina A or A1. **B** Example of Y relay cell from lamina A or A1. **C** Example of putative interneuron from lamina A or A1. **D** Example of of perigeniculate cell. Although not evident from this drawing, the axon eventually courses ventrally to innervate the subjacent laminae A and A1 of the lateral geniculate nucleus. [**A** and **B** were redrawn from Friedlander et al. (1981); **C** was redrawn from Hamos et al. (1985); and **D** was drawn from the data of Cucchiaro et al. (1985)]

circuitry within these structures seems to be the elaboration of receptive field properties that allow the visual system to extract information about the visual stimulus. The lateral geniculate nucleus does not satisfy this generalization, because receptive fields of geniculate neurons are virtually identical to those of their retinal inputs, although some subtle differences have been noted (Hubel and Wiesel 1961; Singer and Creutzfeldt 1970; Cleland et al. 1971; Hoffmann et al. 1972; Shapley and Lennie 1985).

Since no obvious role for geniculate circuitry is evident with regard to elaboration of receptive field properties, confusion and speculation have characterized the discussion of geniculate function. The similarity of retinal and geniculate receptive fields argues in favor of the notion that geniculate neurons

act as mere relays of information from retina to visual cortex, and such a function for the lateral geniculate nucleus is often implied. However, numerous morphological and physiological observations, the summary of which forms the bulk of this paper, indicate that, in fact, the lateral geniculate nucleus has a more subtle and important function than to serve as a mere relay station. We suggest that one function of this thalamic nucleus is to gate or control the gain of signal transmission being relayed from retina to cortex. This gating or gain control, in the sense that we are using the terms, reflects the ability of retinal axons to drive geniculate relay cells. It can be operationally defined in terms of the number or frequency of action potentials seen in the geniculate neuron relative to that in its retinal afferents. This concept is what we mean when we refer below to the gain or efficacy of retinogeniculate transmission.

The notion that geniculate neurons can be gated in their relay of retinal information to cortex is certainly not new (cf. Singer 1977; Burke and Cole 1978; Crick 1984; Ahlsen et al. 1985), but it is a concept worth re-evaluating in the context of recent advances in our understanding of the innervation patterns and intrinsic electrophysiological properties of geniculate neurons. This paper explores some of the types of gating or gain control carried out by geniculate circuitry and suggests some specific biophysical mechanisms underlying them. We propose at least two gating operations. One involves traditional postsynaptic inhibition via pathways that use γ-aminobutyric acid (GABA) as a neurotransmitter (i.e., GABAergic pathways). The other involves intrinsic biophysical properties of geniculate neurons, which are expressed in the form of membrane conductance changes for specific ions. These conductance changes can greatly alter the gain of retinogeniculate transmission, and it is likely that they are controlled via nonretinal afferents to the lateral geniculate nucleus from the visual cortex and/or the brainstem reticular formation.

Unless otherwise explicitly noted, we shall confine ourselves in the present manuscript to anatomical and physiological data relevant to the cat. Several recent reviews can be consulted for details of the functional organization of the cat's central visual pathways (Singer 1977; Stone et al. 1979; Sherman and Spear 1982; Sherman 1985). Our reference to the lateral geniculate nucleus includes only the dorsal division, which projects to cortex: we are not concerned with the ventral division of the lateral geniculate nucleus, which has a different embryological origin and does not project to visual cortex. We shall concentrate in particular on laminae A and A1, which represent the dorsal laminae of the lateral geniculate nucleus, because these have been the most intensively studied. They form a reasonably matched pair receiving ocular input from either the contralateral nasal (lamina A) or ipsilateral temporal (lamina A1) retina. Much less is known about the physiology and intrinsic circuitry of other geniculate laminae. Intimately related to the laminae A and A1 is the perigeniculate nucleus, which lies just dorsal to lamina A above the lateral geniculate nucleus. The perigeniculate nucleus is often considered to be part of the reticular nucleus of the thalamus (see Singer 1977; Montero and Singer 1984), although some consider it to be a separate thalamic nucleus (e.g., Ahlsen et al. 1982). In any case, the perigeniculate nucleus represents an important contributor to geniculate circuitry (see Sect. II.C.2. below).

II. Morphological features of geniculate circuitry

A. Cell types

Figure 1 summarizes the four basic cell types found in laminae A and A1 and the adjacent perigeniculate nucleus. These can be distinguished on a number of morphological, physiological, and pharmacological grounds. They will be only briefly introduced here, because each is described in considerably more detail in the paragraphs below. Two distinct classes of geniculate neurons, called X and Y cells, project their axons to visual cortex (Fig. 1A, B). These are thus the relay cells of laminae A and A1. Also found in these laminae are a third class of cells that seem to be interneurons (Fig. 1C). Finally, the perigeniculate cells (Fig. 1D) lie in a thin tier just dorsal to lamina A. The interneurons and perigeniculate cells appear to be GABAergic and inhibitory (Singer 1977; O'Hara et al. 1980; Montero and Scott 1981; Fitzpatrick et al. 1984; Lindström 1982; Montero and Singer 1984; Hamos et al. 1985; Cucchiaro et al. 1985).[1]

1 Much of the evidence that these cells are GABAergic and inhibitory stems from two related observations. First, their somata and efferent terminals can be labeled with antibodies to GABA or glutamic acid decarboxylase (GAD), an enzyme involved in the final synthesis of GABA (Oertel et al. 1983; Fitzpatrick et al. 1984; Montero and Singer 1984). This is generally taken as evidence that the cell uses GABA as a neurotransmitter, and GABA is widely thought to be an inhibitory neurotransmitter. Second, the efferent terminals of these cells contain flattened or pleomorphic vesicles, and they form synapses with symmetrical thickenings around the pre- and postsynaptic membranes (see Sect. III.C.4; see also Guillery 1971; Montero and Scott 1981; Hamos et al. 1985; Cucchiaro et al. 1985). This, too, is generally taken as evidence of an inhibitory synaptic terminal. While these observations provide a strong case for the inhibitory and GABAergic function of these interneurons and perigeniculate cells, they stop short of unambiguous proof

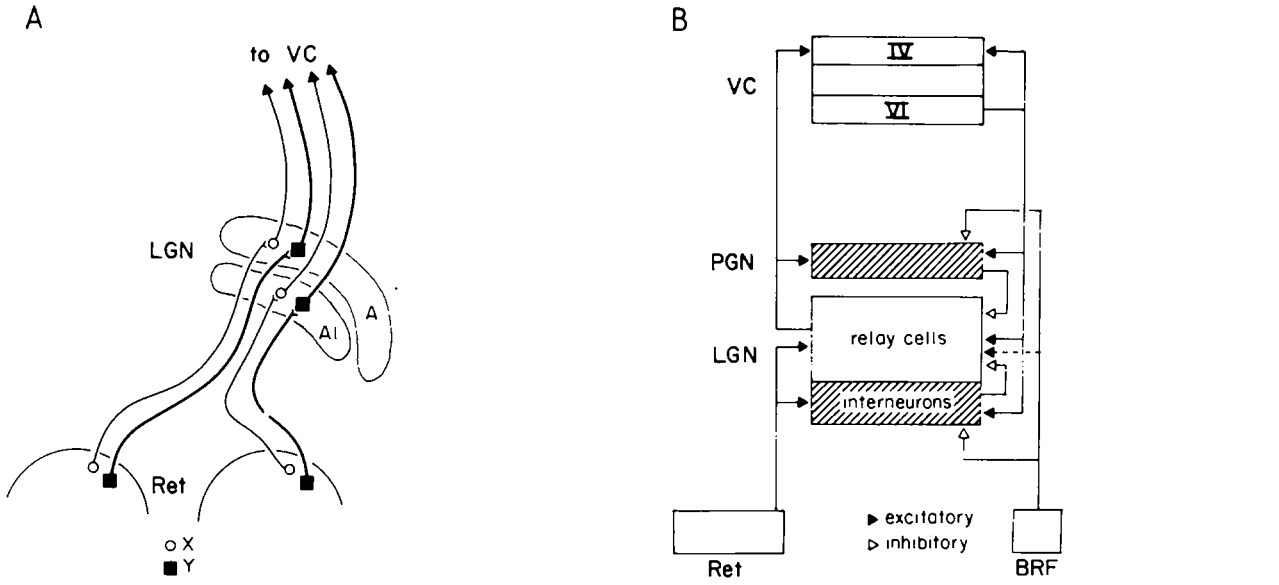

Fig. 2A and B. Schematic diagrams of the cat's retino-geniculo-cortical pathways. *Abbreviations*: *X*, X cell; *Y*, Y cell; *Ret*, retina; *LGN*, lateral geniculate nucleus; *A* and *A1*, geniculate laminae A and A1; *VC*, visual cortex; *BRF*, brainstem reticular formation (which includes midbrain and pontine components): *PGN*, perigeniculate nucleus (which, in the context of these diagrams, can be considered to be a portion of the reticular nucleus of the thalamus); *IV* and *VI*, cortical layers IV and VI. **A** Diagram illustrating the X and Y pathways from retina through the lateral geniculate nucleus to the visual cortex. **B** Schematic diagram illustrating the functional relationship between the various inputs to geniculate relay cells. The hatching highlights the inhibitory, GABAergic inputs to relay cells. Excitatory and inhibitory pathways are separately shown. The dashed line refers to the putative, long-lasting modulatory action of cholinergic and noradrenergic fibers from the brainstem reticular formation

B. X and Y pathways

As illustrated in Fig. 2A, a prominent feature of laminae A and A1 is their participation in two parallel, independent neuronal pathways from retina to cortex. These are the X and Y pathways, which involve the abovementioned X and Y relay cells, and each is thought to perform functionally distinct operations in the processing of visual information. It is beyond the scope of this paper to consider in detail the functional significance of these pathways, but one of us (Sherman 1979, 1985) has suggested that the Y pathway is involved in the primary analysis of basic form vision and that the X pathway is secondarily used to raise spatial resolution; other quite different hypotheses have also been suggested (Ikeda and Wright 1972; Stone et al. 1979).

The X and Y pathways begin in the retina. X and Y retinal ganglion cells form two physiologically distinct neuronal classes, and they correspond in the cat to the two morphological classes respectively termed β and α cells (Boycott and Wässle 1974). Every X and Y cell from the retina innervates lamina A or A1 of the lateral geniculate nucleus. Each geniculate cell receives all of its retinal input from one or very few retinal ganglion cells of the same type (on or off center, X or Y). *Thus, the receptive field of each geniculate cell is nearly (but not entirely) identical to that of its retinal input* (Hubel and Wiesel 1961; Singer and Creutzfeldt 1970; Cleland et al. 1971; Hoffmann et al. 1972; Shapley and Lennie 1985). There is no significant receptive field transformation in the relay of retinal information to the cortex. We can thus refer to geniculate cells as X or Y (e.g., Fig. 1A, B) in the same sense that these terms are used for the retina.

However, differences between the X and Y pathways are not limited to the retina and passively transmitted by the central pathways, because geniculate X and Y relay cells differ in morphology (Fig. 1A, B; see also Friedlander et al. 1981), synaptic inputs (Wilson et al. 1984; Hamos et al. 1985), and intrinsic response properties (Bloomfield et al. 1985). Essentially all geniculate cells innervated by retinogeniculate Y axons are Y relay cells, and most geniculate cells innervated by retinogeniculate X axons are X relay cells. However, some of the geniculate cells innervated by the X axons seem to be local inhibitory interneurons. These interneurons, which seem to be GABAergic (see Sect. II.A. above) and comprise perhaps 20–30% of the neurons in laminae A and A1, respond to visual stimulation much like the X relay cells (Friedlander et al. 1981; Hamos et al. 1985).

The question as to whether retinal Y axons, as well as X axons, innervate a subset of interneurons remains a point of controversy. Dubin and Cleland (1977) argued that interneurons could be distinguished from relay cells because the former could be *transsynaptically* activated from cortex, while the latter could only be *antidromically* activated from cortex (see also Lindström 1982; Ahlsen et al. 1982). By their criteria, Dubin and Cleland (1977) found geniculate cells of both X and Y classes that were identified as interneurons. However, Friedlander et al. (1981) demonstrated that these criteria did not always distinguish interneurons from relay cells, and, further, that no Y cell was sufficiently small to be an interneuron (cf. Fitzpatrick et al. 1984). An unambiguous physiological demonstration of interneurons remains to be seen. By other morphological criteria as well, including dendritic structure and the presence and nature of dendritic appendages, only a subset of geniculate cells innervated by retinogeniculate X axons have so far displayed morphological properties generally associated with interneurons (Friedlander et al. 1981; Hamos et al. 1985; Sherman, unpublished observations). Until we see convincing evidence to the contrary, we shall adopt the assumption that interneurons are mostly, if not exclusively, retinally innervated by X axons.

Differences are also evident in the geniculocortical termination patterns of X and Y cells from laminae A and A1 (Stone and Dreher 1973; Ferster and LeVay 1978; Humphrey et al. 1985a, b). Axons of both types innervate striate cortex (area 17) more densely in layer IV and less densely in layer VI. However, compared to the terminal arbors of geniculocortical X axons, those of Y axons are much more extensive and tend to be found more dorsally in layer IV. Also, whereas the X axons only innervate area 17, many Y axons innervate area 18, and some bifurcate to innervate both areas.

C. *Innervation patterns of geniculate neurons*

It is remarkable that, for both X and Y relay cells, retinal input represents a small minority (10–20%) of afferent synapses (for details, see Sect. II.C.4. below; see also Guillery 1971; Wilson et al. 1984). As noted above, these geniculate cells do not substantially alter the receptive fields of their retinal inputs in their relay to cortex. This implies that the nonretinal synapses on these cells, which represent 80–90% of all afferent inputs, are used for another purpose. One likely function of this massive nonretinal input is to gate or modify the retina-to-cortex relay. As the first central station in the processing of visual information en route to cortex, the lateral geniculate nucleus is strategically sited to control the flow of this input to cortex. Before any comprehension of this function can be realized, it is first necessary to understand the sources of extraretinal inputs to geniculate relay cells as well as the synaptic environment of these cells. Figure 2B schematically illustrates the known nonretinal afferents to relay cells of laminae A and A1.

1. The corticogeniculate pathway. A pronounced pathway originates among layer VI pyramidal cells of cortical areas 17, 18, and 19 (Guillery 1967; Jones and Powell 1969; Gilbert and Kelly 1975). Roughly half of these layer VI pyramidal cells contribute to the corticogeniculate pathway (Gilbert and Kelly 1975). From knowledge of the size of areas 17, 18, and 19 (Tusa et al. 1978; Orban 1984), the density of layer VI cells (Beaulieu and Colonnier 1983), and the number of geniculate relay cells (Bishop et al. 1953; Sanderson 1971), we estimate roughly that each geniculate relay cell receives convergent input from at least 10 cortical axons and probably from many more (see Appendix). The corticogeniculate axons monosynaptically excite geniculate relay cells (Ahlsen et al. 1982). Cross-correlation analysis between a visual cortex cell and a geniculate neuron reveals an excitatory pathway if the receptive field centers of both neurons are separated by less than 1.7° (Tsumoto et al. 1978). Larger separations produce inhibitory corticogeniculate interactions, presumably via pathways involving inhibitory interneurons or perigeniculate cells (see Fig. 2B and Sect. II.C.2. below). Conduction velocities of corticogeniculate fibers seem to be especially heterogeneous and include some quite slowly conducting axons (Tsumoto et al. 1978).

2. The perigeniculate pathway. The reticular nucleus of the thalamus is a sheet-like structure enveloping much of the dorsal thalamus (Scheibel and Scheibel 1966; Jones 1975; Steriade and Deschenes 1984), and the perigeniculate nucleus is functionally organized quite like this reticular nucleus. Indeed, the perigeniculate nucleus may well be a subregion of the thalamic reticular nucleus. All axons from the thalamus to the cerebral cortex pass through the thalamic reticular nucleus, as do all the reverse projections from the cortex to the thalamus. It is believed that most, if not all, of these axons passing in both directions through the reticular nucleus of the thalamus emit collaterals that make excitatory synaptic contacts there (Ide 1982). In particular, the perigeniculate nucleus receives collaterals from geniculate X and Y relay cells (Dubin and Cleland

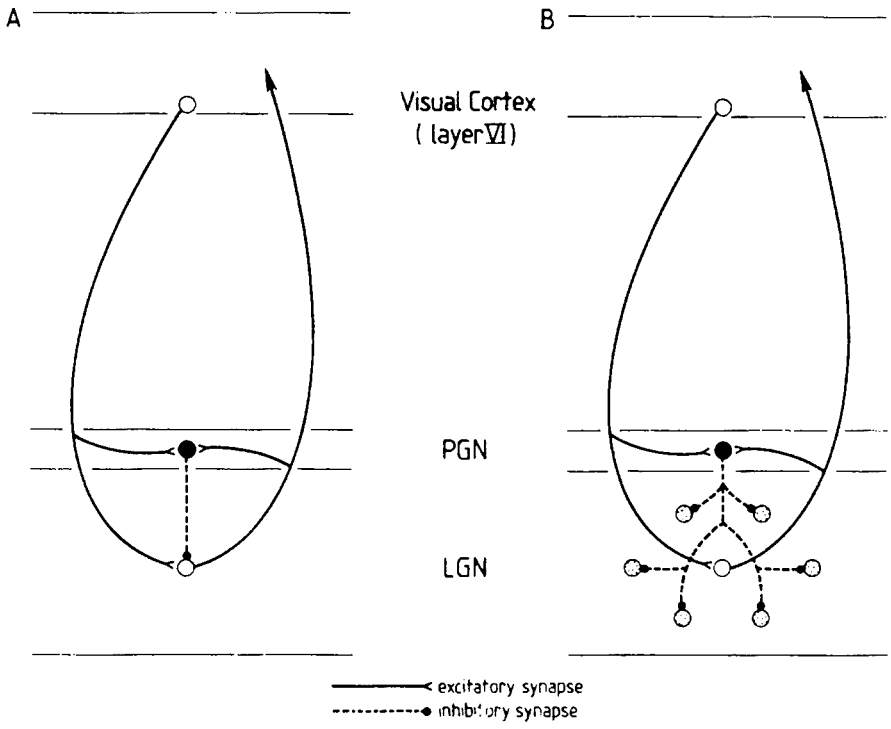

Fig. 3A and B. Schematic diagrams for two hypothetical circuits involving corticogeniculate cells, cells of the perigeniculate nucleus (*PGN*) and relay cells of the lateral geniculate nucleus (*LGN*). **A** Circuit illustrating true feedback inhibition at the single neuron level. Activity in the geniculate cell will subsequently lead to its own inhibition. Furthermore, activity in the corticogeniculate axon will cause excitation followed by inhibition in the geniculate cell. **B** Circuit illustrating more plausible connectivity than that illustrated in **A**. Here, activity in a geniculate cell (open circle) or its cortical afferent will lead to inhibition of the neighboring geniculate neurons (stippled), but such activity will not by itself lead to inhibition of the geniculate cell in question

1977; Friedlander et al. 1981; Ahlsen and Lindström 1982). As noted in Sect. II.A. above, the neurons in the perigeniculate nucleus (and in the thalamic reticular nucleus) appear to be GABAergic and thus inhibitory (Singer 1977; O'Hara et al. 1980, 1983; Montero and Scott 1981; Fitzpatrick et al. 1984; Lindström 1982; Montero and Singer 1984). Axons of the perigeniculate neurons enter laminae A and A1 to innervate geniculate cells there (Jones 1975; Cucchiaro et al. 1985). It is not yet clear whether perigeniculate cells innervate X and Y cells fairly equally (Lindström 1982; Ahlsen and Lindström 1982) or whether, as morphological data described below suggest, their innervation of Y cells tends to be somewhat heavier than it is for X cells.

The connections involving geniculate relay cells, perigeniculate cells, and descending inputs from the visual cortex are retinotopically organized (Friedlander et al. 1981; Robson 1983; Cucchiaro et al. 1985). Furthermore, the reciprocal pathway between geniculate and perigeniculate cells (Fig. 2B) represents the morphological substrate for feedback inhibition described for geniculate relay cells (Dubin and Cleland 1977). However, it should be emphasized that this feedback inhibition need not represent a true feedback inhibition at the single cell level, as is illustrated in Fig. 3A. Indeed, the connections are more likely to be slightly offset, although still retinotopic, as is illustrated in Fig. 3B. This form of lateral inhibition implies that the activation of a geniculate relay cell serves to inhibit certain of its neighbors and is more consistent with physiological observations (e.g., Legendy et al. 1978) than is the circuitry shown in Fig. 3A. The physiological techniques generally employed to study inhibition of geniculate neurons by perigeniculate cells cannot distinguish between the alternatives of Fig. 3, because these techniques involve massive electrical stimulation of afferent pathways (e.g., Lindström 1982).

3. Pathways from the brainstem reticular formation. Morphological and electrophysiological studies indicate that both the lateral geniculate and perigeniculate nuclei receive input from several neuronal groups of the brainstem reticular formation, mostly from the caudal midbrain and rostral pons (Singer 1973; Foote et al. 1974; McBride and Sutin 1976; Hoover and Jacobowitz 1979; Moore and Bloom 1979; Sakai 1980; Kimura et al. 1981; Fibiger 1982; Ahlsen and Lo 1982; Ahlsen 1984; Hughes and Mullikin 1984). There is a corresponding plethora of effects on geniculate cells attributed to activation of brainstem neurons. These effects differ in their time courses, postsynaptic actions, and sites of origin.

Stimulating the brainstem reticular formation by brief electrical shocks typically eliminates hyperpolarizing potentials in cat geniculate relay cells

(Singer 1973; Fukuda and Stone 1976). It had previously been suggested that this disinhibition is due to brainstem-induced inhibition of the GABAergic interneurons (e.g., Singer 1973, 1977). Ahlsen et al. (1984) showed recently that, indeed, electrical stimulation of various brainstem sites causes large hyperpolarizing potentials in both perigeniculate neurons and geniculate interneurons. This inhibition has a latency of about 10–12 ms and a duration of about 100 ms. However, stimulation of some brainstem sites inhibits geniculate relay cells (Foote et al. 1974).

At least three components of the projection from the brainstem reticular formation to the lateral geniculate nucleus have been recognized. The best understood one consists of fibers originating in the locus coeruleus; these fibers contain noradrenaline (also know as norepinephrine) and provide a dense, uniform innervation of the lateral geniculate nucleus (Moore and Bloom 1979; Kromer and Moore 1980; Sakai 1980). In rats, a delayed but dramatic increase in the spontaneous firing rate of most geniculate neurons can be produced either by electrical stimulation of the locus coeruleus, by local application of glutamate (an excitatory amino acid) onto cell bodies in the locus coeruleus, or by direct iontophoretic application of noradrenalin onto the geniculate cells (Nakai and Takaori 1974; Rogawski and Aghajanian 1980; Kayama et al. 1982; Kayama 1985). If the optic nerve is sectioned to eliminate synaptic input from retina, neither direct application of noradrenalin nor electrical stimulation of the locus coeruleus activates geniculate neurons, although the same cells can easily be excited by iontophoresis of glutamate (Rogawski and Aghajanian 1980). In other words, the action of the pathway from the locus coeruleus onto geniculate relay cells is contigent upon prior or simultaneous excitation of the relay cells, a characteristic property of neuromodulatory substances.[2] Furthermore, this mechanism appears to affect the relay cells directly, since application of picrotoxin, which blocks the action of GABA, does not produce such a facilitation of the relay cell response (Rogawski and Aghajanian 1980). This would appear to exclude the possibility that noradrenalin excites the relay cells only by disinhibition (i.e., by inhibiting the inhibitory interneurons and perigeniculate cells).

The other two brainstem pathways to the lateral geniculate nucleus are less well understood. One is serotonergic and derives largely, but not completely, from the dorsal raphe nucleus (Pasquier and Villar 1982). Application of serotonin seems to have a depressant effect on geniculate neurons (Kemp et al. 1982), although electrical stimulation of the dorsal raphe nucleus may either excite or inhibit geniculate relay cells (Foote et al. 1974). The third pathway is cholinergic and, in the cat, seems to originate in the parabrachial nucleus (Sakai 1980; Kimura et al. 1981).[3] Iontophoretic application of acetylcholine produces increased activity among geniculate neurons (Kemp and Sillito 1982; Sillito et al. 1983). In the cat, acetylcholine seems to excite relay cells directly, in addition to or instead of disinhibiting them, because the effects of acetylcholine are not mimicked by application of bicuculline, which blocks GABAergic inhibition (Sillito et al. 1983). Recent evidence from the rat (McCormick and Prince 1986) indicates that acetylcholine may also directly hyperpolarize neurons of both the lateral geniculate and thalamic reticular nuclei. These different effects of acetylcholine seem to employ different postsynaptic receptors (see Sect. III.A.2. below).

In summary, neurons of the brainstem reticular formation can act in a variety of fashions to affect geniculate relay cells and thus alter retinogeniculate transmission. Two distinct actions exist. One is a short-latency, short-lasting effect inducing hyperpolarizing postsynaptic potentials in geniculate interneurons and perigeniculate cells. This seems to involve conventional synaptic processes. The other is a long-latency, long-lasting effect that modulates the excitability of geniculate relay cells through a direct pathway. This may result from unconventional synaptic processes involving neuromodulators that alter certain membrane conductances, such as a Ca^{2+}-dependent K^+ conductance. This latter possibility is discussed more fully in Sect. III.B.1. below.

4. Synaptology of laminae A and A1. The synaptology of geniculate X and Y cells has recently been described in some detail (Wilson et al. 1984; Hamos et al. 1985). Four major synaptic profiles exist (Guillery 1971), and for the most part their origins are reasonably well established. These synaptic terminals have been called *RLP* (for *r*ound vesicles,

2 A definition of neuromodulators, according to Barker (1978), is that they evoke no direct, independent change in the postsynaptic membrane potential but can alter the efficacy or the time course of neurotransmitter actions

3 There has been some confusion about the source of cholinergic inputs to the lateral geniculate nucleus from the brainstem reticular formation. In the rat, where these inputs were first described, they arise from a nucleus known as the cuneiform nucleus (Hoover and Jacobowitz 1979; Fibiger 1982). However, the area identified in the cat as the cuneiform nucleus contains cells that are neither cholinergic nor afferent to the lateral geniculate nucleus; only the parabrachial region of the cat fits this description. It may be that the terminology has obscured a genuine homology between the rat's cuneiform nucleus and the cat's parabrachial nucleus (for a discussion of this, see Kimura et al. 1981)

*l*arge profile, and *p*ale mitochondria), *RSD* (for *r*ound vesicles, *s*mall profile, and *d*ark mitochondria), and *F1* and *F2* (for *f*lattened vesicles).[4] Together, they comprise > 95% of the synaptic profiles present in laminae A and A1 (Guillery 1971). RLP terminals derive from retinal axons and form asymmetrical synapses. They are excitatory and comprise 10–20% of all synaptic profiles. RSD terminals derive mostly from areas 17, 18, and 19 of cortex. Synapses from these terminals are asymmetrical and excitatory, and they make up roughly 40–45% of all terminals present.[5] F1 terminals seem to derive mostly from perigeniculate cells (O'Hara et al. 1980; Montero and Scott 1981; Cucchiaro et al. 1985) and contribute roughly 20–25% of the synaptic terminals present; some F1 synapses seem to derive from the axons of geniculate interneurons (Hamos et al. 1985). Their symmetrical synapses appear to be inhibitory and to use GABA as their neurotransmitter (Lindström 1982; O'Hara et al. 1983; Fitzpatrick et al. 1984; Montero and Singer 1984). Finally, F2 terminals, which are thought to be GABAergic and inhibitory, derive from dendrites of X innervated interneurons (Fitzpatrick et al. 1984; Hamos et al. 1985), form symmetrical synapses, and contribute roughly 20–25% of the synapses present. Other rare terminal types (< 5% of the total) have also been described, and some of these might derive from the brainstem reticular formation (see, for instance, de Lima et al. 1985; see also Sect. III.B.1. below).

For both X and Y relay cells, cortical synapses represent slightly less than half of the total synaptic input and dominate the inputs to the distal dendritic shafts. Retinal synapses and synapses from both types of inhibitory profile (i.e., F1 and F2) terminate on proximal dendrites. However, the similarities between X and Y cells end here (Wilson et al. 1984). On X cells, retinal and F2 terminals form *triadic* synaptic arrangements on dendritic appendages or spines, such that the RLP terminal contacts the F2 terminal and both contact the same dendritic appendage. Relatively few F1 profiles are seen on X cells. On Y cells, retinal and F1 profiles terminate near one another on dendritic shafts without triadic circuitry, and few appendages or F2 terminals are found. Thus, inhibition on X cells tends to be of the *feedforward* type from geniculate interneurons, while that on Y cells tends to be of the *feedback* type from perigeniculate cells. This distinction is likely to be an oversimplification, since Lindström (1982) argues on physiological grounds that both types of inhibition are found in both X and Y cells. Indeed, Cucchiaro et al. (1985) provide evidence that some of the relatively few F1 terminals found on X relay cells derive from perigeniculate cells.

4 Several morphological features distinguish F1 from F2 terminals (Guillery 1971; Wilson et al. 1984; Hamos et al. 1985). F1 terminals are more densely filled with vesicles that tend to be flatter than is the case for F2 terminals. Also, F1 terminals are never postsynaptic to any other terminal, whereas F2 terminals are both presynaptic and postsynaptic structures. However, the distinction is not always easy to make

5 We shall often refer to RLP and RSD terminals as retinal and cortical terminals, respectively. Note, however, that some RSD terminals may derive from sources other than cortex (cf. Wilson et al. 1984)

III. Signal transmission through X and Y cells

By recording simultaneously from pairs consisting of a geniculate cell and its retinal afferent in the anesthetized cat, it is possible to account for every spike in the geniculate cell by an appropriately timed spike in the retinal afferent (McIlwain and Creutzfeldt 1967; Cleland et al. 1971). Thus each action potential in a retinal afferent produces no more than one spike in the postsynaptic geniculate X or Y cell. However, not every afferent spike leads to one in the postsynaptic cell. The gain of the retinogeniculate synapse is thus less than one. For a given geniculate neuron, this gain is state-dependent and can vary with the animal's level of arousal (Coenen and Vendrik 1972). Within the context of the known synaptic circuits and membrane conductances, we propose that there are at least three ways by which this gain can be changed, and these represent three different means of controlling gating in the lateral geniculate nucleus. One relies on conventional, GABAergic postsynaptic inhibition; the second involves the action of a Ca^{2+}-dependent K^+ conductance; and the third is based on a time- and voltage-dependent Ca^{2+} conductance.

A. Postsynaptic inhibition

1. GABAergic inhibition. Since X and Y relay cells exhibit large numbers of inhibitory terminals on their proximal dendrites, classic postsynaptic inhibition of these neurons can obviously reduce the gain of retinogeniculate transmission. The nearly exclusive source of these synapses are the dendritic appendages of interneurons and axon terminals of these same interneurons plus those of perigeniculate cells. The inhibitory outputs of each of these neurons are organized in a retinotopic fashion and are thus limited in extent within the lateral geniculate nucleus (cf. Hamos et al. 1985; Cucchiaro et al. 1985). This implies that the resultant inhibition can be quite specific and localized within the nucleus.

As noted above in Sect. II.A. and II.C.4., these inhibitory synapses of the interneurons and perigeniculate cells appear to be GABAergic. GABAergic synapses are generally thought to operate via the classic, bicuculline-sensitive, $GABA_A$ postsynaptic receptors by increasing a chloride conductance (Curtis and Johnston 1974; Dingledine and Langmoen 1980; Segal and Barker 1984). The resultant inhibitory postsynaptic potential (IPSP) does not markedly hyperpolarize the cell, since the equilibrium potential for Cl^- is generally between -60 and -75 mV and is thus close to the resting membrane potential of the cell. In other words, activation of the $GABA_A$ receptor, which we shall refer to as "$GABA_A$ inhibition", mediates a *silent* or *shunting* inhibition, increasing the membrane conductance at that location and thus reducing the cell's input resistance. This occurs without any pronounced hyperpolarization or depolarization of the cell, and it shunts or short-circuits any excitatory input that arrives during the increased Cl^- conductance. Computer simulation of synaptic inputs in branched dendritic trees have shown that $GABA_A$ inhibition can be very effective in reducing excitatory potentials (EPSPs) if the inhibition is on the direct path between the excitatory synapse and the soma; if off the direct path by about 10 μm or more, this $GABA_A$ inhibition is ineffective (Koch et al. 1982). The proximal location of most inhibitory synapses on geniculate relay cells is consistent with such a process.

A different GABAergic effect has been described that acts via a distinctly different type of postsynaptic receptor, the $GABA_B$ receptor (Bowery et al. 1981; Bowery et al. 1983; Simmonds 1983; Bowery et al. 1984; Bowery et al. 1985; Newberry and Nicoll 1984, 1985). This receptor binds the GABA agonist baclofen but is resistent to the action of bicuculline. Newberry and Nicoll (1984, 1985) describe such a receptor on hippocampal cells, arguing that the receptors control K^+ channels. Since the equilibrium potential for K^+ (roughly -90 to -100 mV) is much more negative than the cell's resting potential, activation of $GABA_B$ receptors (i.e., $GABA_B$ inhibition) results in significant hyperpolarization. Moreover, $GABA_B$ inhibition seems to produce less of a membrane conductance increase, and thus less of a decrease in neuronal input resistance, than does $GABA_A$ inhibition. $GABA_B$ inhibition also has a longer time course than does $GABA_A$ inhibition. Computer simulations show that $GABA_B$ inhibition reduces EPSPs with little regard for the relative positions within the dendritic arbor of the inhibitory and excitatory synapses (Koch et al. 1982; O'Donnell et al. 1985). This is quite different from the abovementioned spatial requirements of $GABA_A$ inhibition. Thus, whereas $GABA_A$ inhibition can be quite strong and nonlinear, $GABA_B$ inhibition acts much more linearly, inhibiting the electrical activity of the neuron by offsetting EPSPs with an hyperpolarization.

Our understanding of the action and distribution of the $GABA_B$ receptor is just beginning. The conclusion that the $GABA_B$ receptor is much less commonly distributed in the mammalian brain than is the $GABA_A$ receptor seemed safe until quite recently. It is still probably wise to view the bulk of the GABAergic inhibition in the cat's lateral geniculate nucleus as acting via the $GABA_A$ receptor, or in other words, as silent or shunting inhibition, until we have firm evidence to the contrary. This is supported by evidence that IPSPs mediated by geniculate interneurons can easily be reversed by an injection of Cl^- ions into the cell (Lindström 1982; see also McIlwain and Creutzfeldt 1967) and that local application of bicuculline leads to a loss of inhibitory mechanisms in geniculate neurons (Sillito and Kemp 1983; Berardi and Morrone 1984). However, recent evidence from the rat suggests that $GABA_B$ receptors may be fairly common in mammalian brain, including the thalamus and lateral geniculate nucleus (Bowery et al. 1984, 1985). If both $GABA_A$ and $GABA_B$ inhibition exist in the cat's lateral geniculate nucleus, it is of obvious interest to determine how these relate to X and Y cells, to perigeniculate and interneuronal outputs, to F1 and F2 terminals, etc.

A final point regarding postsynaptic inhibition involves an interesting difference between X and Y cells. As noted above, the inhibitory input to Y cells, which is predominantly of the F1 type, occurs primarily on proximal dendritic shafts, whereas the inhibitory input to X cells, which is predominantly of the F2 type, occurs primarily on dendritic appendages in triadic arrangements with retinal synapses. One of us (Koch 1985) has recently modeled the significance of this morphological difference. Due to the proximal location of F1 terminals on Y cells, inhibition from these terminals will tend to reduce both retinal and cortical inputs more or less equally. For X cells, the morphology of the appendage serves to isolate the inhibitory effect of GABAergic terminals there from the dendritic shaft and the soma (Koch and Poggio 1983), thereby limiting its action to shunting local retinal input to the same appendage. The cortical input to X cells, which dominates the distal dendritic shafts, would be relatively unaffected by these inhibitory inputs located on the appendages. Moreover, increased activity in the retinal afferent (e.g., from appropriate visual stimuli) will lead to increased amounts of inhibition at the geniculate relay cell. The

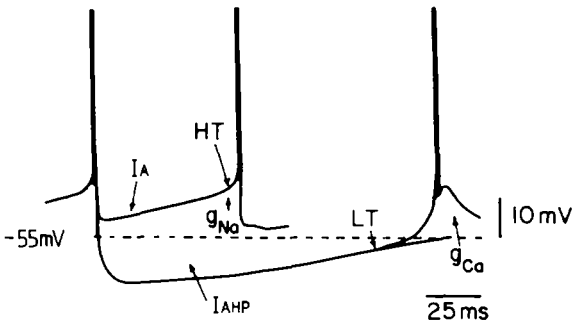

Fig. 4. Schematic summary of various active processes for thalamic neurons. At a resting membrane potential of −55 mV, depolarization leads to a conventional, fast action potential with a relatively high threshold (*HT*) due to an increase in a Na^+ conductance (g_{Na}). Following the action potential, there is a rapid repolarization and subsequent hyperpolarization (I_A) due to increases in two voltage-dependent K^+ conductances, one of which repolarizes the neuron after the action potential and the other of which leads to a moderate afterhyperpolarization. A third, Ca^{2+}-dependent, K^+ conductance (I_{AHP}), which is under transmitter control, may also occur and thereby dramatically enhance the afterhyperpolarization. Finally, if the cell is sufficiently hyperpolarized for a long enough period, a low-threshold (*LT*) Ca^{2+} conductance (g_{Ca}) is de-inactivated and can subsequently be triggered. This is because the g_{Ca} becomes inactive when the membrane is maintained in a sufficiently depolarized state, and the membrane must then be hyperpolarized for 100 ms or more to de-inactivate the g_{Ca} so that it can be initiated with a subsequent depolarization. It is thus possible that the I_{AHP} serves to de-inactivate the g_{Ca}, and repolarization following the I_{AHP} triggers an LT spike. [Redrawn with modifications from Fig. 12 of Jahnsen and Llinas (1984b)]

local nature of inhibition for X cells is only conserved in the model, however, if the reversal potential of the inhibitory synapses is equal or near to the resting potential of the cell. That is, the inhibition is specific and localized if it is $GABA_A$ inhibition, but not if it is $GABA_B$ inhibition. If this inhibition onto X cells is indeed $GABA_A$ inhibition, then the local circuit that consists of the appendage and triadic synaptic arrangement is functionally equivalent to presynaptic inhibition, even though the locus of inhibition is postsynaptic (Koch 1985).

2. Other inhibition. As noted above in Sect. II.C.3., some hyperpolarizing input to relay cells may be induced directly by axons of the brainstem reticular formation. In particular, studies of rats have shown that acetylcholine can hyperpolarize thalamic neurons by increasing a K^+ conductance (McCormick and Prince 1986). Application of acetylcholine results in inhibition of spontaneous activity and an increase in periods of high frequency burst discharges, behavior reminiscent of the low threshold spike seen in thalamic neurons (Jahnsen and Llinas 1984a, b) and described below in Sect. III.B.2. This effect may be quite similar to that described above for $GABA_B$ inhibition. It thus seems that cholinergic input from the parabrachial nucleus can directly modulate geniculate neurons via this conductance change. There is also evidence that acetylcholine can increase excitability by reducing a K^+ conductance (see Sect. III.B.1. below), and that these different cholinergic effects operate via different muscarinic receptors (McCormick and Prince 1986; Egan and North 1986). Cholinergic decreases of a K^+ conductance operate via an M_1 muscarinic receptor, while K^+ conductance increases result from action of an M_2 muscarinic receptor. Finally, it is not known whether other putative neurotransmitters from the brainstem reticular formation (i.e., noradrenalin and serotonin) can directly inhibit geniculate neurons.

B. Voltage- and time-dependent conductances in thalamic neurons

Recent biophysical studies emphasize that the integrative properties of thalamic neurons can be very nonlinear. Jahnsen and Llinas (1984a, b) used an in vitro thalamic slice preparation to show that nearly all thalamic (including geniculate) neurons of the guinea pig exhibit a rich variety of time- and voltage-dependent conductances plus one dependent solely on Ca^{2+}. Figure 4 schematically summarizes some of these conductances. Four of the conductances lead to inward currents: a fast Na^+ conductance underlying the conventional action potential, a slow Na^+ conductance that produces a steady plateau of depolarization, a low threshold Ca^{2+} conductance underlying the low threshold (LT) spike, and a high threshold Ca^{2+} conductance that may be generated in the dendrites. Three K^+ conductances lead to outward current: one is voltage-dependent and repolarizes the cell following the action potential, and two are responsible for the spike afterhyperpolarization. The components of the afterhyperpolarization are a transient voltage-dependent K^+ conductance (the I_A) and a slower K^+ conductance that depends only on Ca^{2+} and not explicitly on the membrane potential (I_{AHP}).

Most or all of these conductances seem to exist for neurons of the cat's thalamus, at least for the ventroanterior and ventrolateral thalamic nuclei (Deschenes et al. 1984; Roy et al. 1984). While all of these conductances may contribute to the gating properties of thalamic neurons, we shall examine in more detail only the conductances subserving the spike afterhyperpolarization and the LT spike, because these are likely to play a major role in gating of retinogeniculate transmission. However, the others may also prove quite important in this gating.

1. The spike afterhyperpolarization

The hyperpolarization following a conventional action potential is important for the integrative properties of a neuron, since the strength and duration of this afterhyperpolarization control the extent to which the neuron adapts to long-lasting excitatory inputs. Results from the guinea pig thalamic slice preparation (Jahnsen and Llinas 1984a, b) and the cat's in vivo ventroanterior and ventrolateral thalamic nuclei (Deschenes et al. 1984) indicate that action potentials are followed by a prolonged afterhyperpolarization with an overall duration of 25–45 ms or longer, the basis of which is an increased K^+ conductance. Removing the Ca^{2+} from the bathing solution or intracellular injection of EGTA, a Ca^{2+} chelator, abolishes the afterhyperpolarization, strongly implicating a Ca^{2+}-dependent K^+ conductance.

Studies of bullfrog sympathetic ganglion cells (Pennefather et al. 1985) and of rodent hippocampal neurons (Adams and Lancaster 1985; Lancaster and Adams 1986) has established two distinct Ca^{2+}-dependent K^+ conductances underlying the spike afterhyperpolarization. One conductance, termed the I_C, depends on both intracellular free Ca^{2+} and membrane voltage while the second conductance, termed the I_{AHP}, depends only on Ca^{2+}. The time course of the I_C is at least an order of magnitude faster than that of the I_{AHP}. Moreover, the I_{AHP} can be blocked by acetylcholine in bullfrog sympathetic ganglion cells and by both noradrenaline and acetylcholine in rodent hippocampal neurons, while the I_C is blocked by neither substance.

This last property of the I_{AHP} gives rise to a physiological mechanism by which the gain of thalamic neurons can be altered. When a prolonged depolarizing current pulse is injected into a hippocampal pyramidal cell, the cell responds with an initial spike or burst of spikes, after which time it remains silent for the duration of the pulse. This spike frequency adaptation or accommodation is markedly attenuated by local application of noradrenalin and/or acetylcholine, which causes the cell to fire throughout the depolarizing current pulse (Madison and Nicoll 1982, 1984, 1986a,b; Cole and Nicoll 1984; Madison et al. 1985). The basis of this striking modification of spike frequency adaptation involves the blockage of the I_{AHP} subsequent to Ca^{2+} entry into the cell. It thus seems plausible that the activation of cholinergic fibers from the parabrachial nucleus and/or noradrenergic fibers from the locus coeruleus increases the excitability of geniculate relay cells by a similar mechanism. That is, noradrenaline and acetylcholine can each inhibit a long-lasting Ca^{2+}-dependent K^+ current, similar to the I_{AHP}, and this modifies the response of the cell to long-lasting depolarizing inputs. For noradrenaline (and possibly also for acetylcholine), the action is mediated by a second messenger, which is cyclic AMP (Madison and Nicoll 1986b). This presumed action of cholinergic input, which results in a reduced K^+ conductance, differs from the cholinergic action described above in Sect. III.A.2., which results in an increased K^+ conductance. Furthermore, the different conductance changes represent the action of different muscarinic receptors, since an M1 receptor is implicated in the decreased K^+ conductance and an M2 receptor is implicated in the increased K^+ conductance (McCormick and Prince 1986; Egan and North 1986).

These proposed effects of noradrenergic and cholinergic fibers on geniculate relay cells represent processes with fairly long time courses on the order of seconds or minutes. This cannot be the entire story, because electrophysiological studies have shown that electrical activation of the brainstem reticular formation produces relatively fast inhibition of interneurons and perigeniculate cells with rapid excitation or disinhibition of geniculate relay cells (Singer 1973; Ahlsen et al. 1984). At least some of the afferents from the brainstem reticular formation must thus employ fairly conventional synaptic mechanisms. Furthermore, we have not suggested a specific role for the serotonergic input to the lateral geniculate nucleus from the dorsal raphe nucleus. In this context, it is interesting that Stockmeier, Martino, and Kellar (1985) suggest that serotonergic axons regulate β-adrenergic receptors on a long time scale.

We wish to address two additional qualifications to the above hypothesis. First, many electrophysiological data have been interpreted to mean that fibers from the brainstem reticular formation do not directly innervate geniculate relay cells but that they instead innervate interneurons and perigeniculate cells; the effect of these fibers on the relay cells is thus indirect (Singer 1973; Lindström 1982). However, evidence presented above in Sect. II.C.3. indicates that geniculate relay cells can be directly excited by noradrenalin and acetylcholine, and that acetylcholine can also directly hyperpolarize geniculate neurons. Furthermore, de Lima et al. (1985) have recently demonstrated that cholinergic synapses are formed directly on the dendrites of geniculate relay cells. These are likely to derive from cells in the brainstem reticular formation, because we know of no other cholinergic neurons that produce synaptic terminals in the lateral geniculate nucleus. Perhaps much of the electrophysiological data requires re-

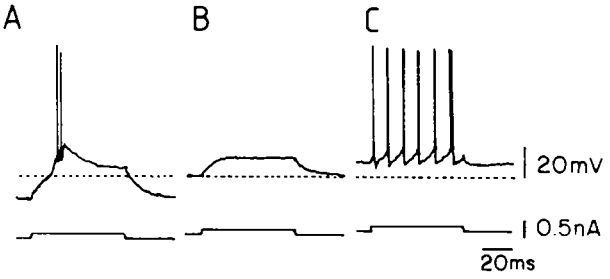

Fig. 5A–C. Examples of LT spike properties from a mammalian thalamic neuron recorded intracellularly in vitro; shown are the cell's responses to three identical depolarizing current injections. **A** LT spike activation. The LT spike has been de-inactivated by maintaining the cell's resting membrane potential at −70 mv. A small depolarizing current pulse (bottom trace) can thus trigger the LT spike upon which rides a brief burst of conventional action potentials. **B and C** LT spike inactivation. The LT spike has been inactivated by maintaining the resting potential at too depolarized a level for the Ca^{2+} conductance underlying the LT spike. The same current injections that in **A** fired an LT spike now fail to do so. If the cell is not sufficiently depolarized (**B**), a subthreshold passive response is evoked by the current injection. If the cell is sufficiently depolarized before the current injection (**C**), a tonic stream of conventional action potentials are discharged in a relatively linear fashion. [Redrawn from Fig. 2 of Jahnsen and Llinas (1984a)]

interpretation, especially since the non-classical postsynaptic effects that we suggest are produced by these noradrenergic and cholinergic afferents would be difficult to detect with conventional electrophysiological techniques. Second, evidence from rats indicates that noradrenaline excites geniculate neurons via α-adrenergic receptors (Rogawski and Aghajanian 1980; Kayama et al. 1982), but the abovementioned blockage of the I_{AHP} in hippocampal cells seems to involve β-adrenergic receptors (Madison and Nicoll 1986a,b). It is thus not clear the extent to which the otherwise similar responses of hippocampal and geniculate neurons to noradrenaline and acetylcholine share the same underlying properties.

2. The LT spike

a. Properties of the LT spike. Figure 5 summarizes many of the principal features of the LT spike. The Ca^{2+} conductance that underlies the LT spike becomes *inactive* when the cell's membrane is more depolarized than about −60 mV. At normal resting levels (−55 to −60 mV), the LT spike is thus blocked. The cell then responds to depolarizing current injection or excitatory synaptic input with a fairly linear depolarization (Fig. 5B) that, if large enough, can discharge a tonic stream of fast, conventional Na^+ action potentials (Fig. 5C). When the membrane potential is hyperpolarized beyond about −60 mV to −65 mV for at least 100 ms (the actual voltage- and time-dependencies may vary from cell to cell), the Ca^{2+} conductance is *de-inactivated* and the LT spike can be *activated* by a small depolarization such as an EPSP (Fig. 5A).

The overall LT response is usually composed of two distinct parts. Frist is the LT spike proper, which is a slowly rising and falling triangle-like potential. The LT spike has a rather low threshold firing level and results from movement of Ca^{2+} into the cell. Second, a rapid succession of 1 to 4 fast Na^+ spikes (> 300 Hz) usually rides on the crest of the slower LT spike. The upward stroke of the LT spike is followed by the afterhyperpolarization, which lasts for about 100–200 ms. Subsequently, another LT spike can start a new cycle, and this process can be repeated many times.

Thalamic cells therefore exhibit two distinct response modes to afferent input: a tonic, faithful "relay" mode at resting levels, and a bursting, nonlinear mode if hyperpolarized. The latter blocks the normal relay of information to the cortex and thus may be an important cellular mechanism in the overall gating by geniculate neurons of the retina-to-cortex signals. This dual transmission mode not only exists in vitro for the guinea pig thalamus, but similar behavior has also been documented in vivo for the cat's ventroanterior and ventrolateral thalamic nuclei (Deschenes et al. 1984), and preliminary evidence extends this to cells of the cat's lateral geniculate nucleus recorded in vivo (Bloomfield and Sherman, unpublished observations). Interestingly, McIlwain and Creutzfeldt (1967) described what they called "delayed depolarizing potentials" in neurons of the cat's lateral geniculate nucleus, and these potentials seem remarkably similar to the LT spikes described by Jahnsen and Llinas (1984a, b). Also, many geniculate cells in unanesthetized cats exhibit periods of bursty firing reminiscent of LT spikes, and these bursty firing periods correlate with various phases of alertness (Bizzi 1966; McCarley et al. 1983). Electrical stimulation of the brainstem reticular formation can lead to such bursty behavior in geniculate neurons (Singer 1973). Responses consistent with LT spikes thus seem ubiquitous for mammalian thalamic neurons.

b. Physiological mechanisms for controlling the LT spike. Clearly, the LT spike can be an important means of regulating the state of a geniculate relay cell. It thus becomes crucial to understand how the brain controls LT spike activation (i.e., depolarizing the cell once the Ca^{2+} conductance is de-inactivated), inactivation (i.e., establishing membrane levels more depolarized than about −55 mV), and de-inactiva-

tion (i.e., establishing membrane levels more hyperpolarized than about −60 mV for 100–200 ms).

i. Activation. As Jahnsen and Llinas (1984a,b) have shown, synaptic activation is sufficient to trigger LT spikes, if the underlying Ca^{2+} conductance is de-inactivated. Since retinal input is a potent source of EPSPs in geniculate cells (Singer and Creutzfeldt 1970; Eysel 1976), retinal activity, whether spontaneous or visually elicited, is a plausible candidate for triggering LT spikes and the subsequent interruption of normal retino-geniculo-cortical transmission. EPSPs from corticogeniculate axons are another possible source of LT spike activation. However, since any form of depolarization is a plausible candidate for triggering an LT spike once the cell is in a de-inactivated state, it may be that dis-inhibition can also activate an LT spike. That is, release from an hyperpolarizing input, which in itself might de-inactivate the LT spike, could discharge this spike. It is for this reason that the LT spike can become cyclical, since the ensuing afterhyperpolarization can de-inactivate the Ca^{2+} conductance and the cessation of the afterhyperpolarization can activate a new LT spike (Jahnsen and Llinas 1984a, b).

ii. Inactivation. To inactivate the Ca^{2+} conductance underlying the LT spike, it is sufficient to prevent the cell from becoming hyperpolarized more than about 5–10 mV from its "normal" resting level, normal being operationally defined as that level most often seen with good intracellular impalements, for more than 100 ms or so.[6] For thalamic neurons this normal resting level is typically between −55 and −65 mV. It may be that the cell's true resting membrane potential (i.e., in the absence of all synaptic input) is sufficiently depolarized to inactive the Ca^{2+} conductance mediating the LT spike. Conversely, it may be that, in the absence of synaptic bombardment, the cell's resting potential is sufficiently hyperpolarized to de-inactivate the LT spike and that tonic activity among some of the cell's excitatory inputs maintains it in a sufficiently depolarized state to inactivate the LT spike. The distinction between these possibilities is reconsidered below.

iii. De-inactivation. While physiological inactivation and activation of the Ca^{2+} conductances underlying the LT spike may perhaps be readily explained, de-inactivation is more complex. Both Jahnsen and Llinas (1984a,b) and Deschenes et al. (1984) used only hyperpolarizing current injection from the intracellular recording electrode to control this de-inactivation. We may now ask, "How does the neural circuitry of the lateral geniculate nucleus *physiologically* hyperpolarize geniculate relay cells to accomplish de-inactivation of the Ca^{2+} conductances and LT spike?" Three quite different mechanisms for the hyperpolarizing de-inactivation are considered here.

First, inhibitory synaptic inputs may sufficiently hyperpolarize the relay cell to de-inactivate the Ca^{2+} conductance. This straightforward explanation suggests that perigeniculate cells or geniculate interneurons control the inactivation and de-inactivation of the LT spikes, and thus gating. Crick (1984) has proposed that such a scheme, with the requisite hyperpolarization controlled from the reticular nucleus of the thalamus, is the biophysical mechanism underlying certain forms of attention to sensory stimuli. Unfortunately, there is a problem with this hypothesis. If the inhibition is GABAergic and acts via $GABA_A$ receptors, and thus via a Cl^- conductance increase, then such inhibition cannot hyperpolarize the cell beyond the equilibrium potential for Cl^- (roughly between −60 and −75 mV; see Sect. III.A.1.); this limited hyperpolarization may be insufficient to de-inactivate the Ca^{2+} conductance underlying the LT spike. Also, effective shunting of the excitatory synaptic input during de-inactivation might prevent any EPSPs from triggering the LT spike (e.g., Koch et al. 1983). However, GABAergic inhibition via $GABA_B$ receptors and a K^+ conductance increase might be compatible with needs for hyperpolarization and maintained neuronal input resistance for de-inactivation of the Ca^{2+} conductance. It should also be noted that such de-inactivation has a long time dependency, because the hyperpolarization must be maintained for 100 ms or more. Although there is no evidence that the IPSPs generated in geniculate cells of the cat are sufficiently long-lasting to accomplish this (McIlwain and Creutzfeldt 1967; Singer and Creutzfeldt 1970; Singer 1973; Eysel 1976; Lindström 1982), it can be accounted for via maintained activity in the inhibitory GABAergic afferents.

Second, some of the inputs onto geniculate cells may act in an unconventional manner. The most likely unconventional candidate for a controlling mechanism of the LT spike was recently demonstrated in an in vitro study of the rat's thalamic reticular and lateral geniculate nuclei by McCormick and Prince (1986). They demonstrated that application of acetylcholine, which increases a hyperpolarizing K^+ conductance, can induce LT spikes. Unconventional synaptic activation may also include some of the inhibitory (i.e., F1 or F2) terminals, some of

6 The LT spike can also be inactivated if the membrane potential becomes more hyperpolarized than about −80 to −85 mV (Jahnsen and Llinas 1984a, b). However, since such hyperpolarization is rarely if ever seen during physiological conditions, we shall disregard this possible means of LT spike de-inactivation for the remainder of this paper

the presumed cortical (i.e., RSD) terminals, or, perhaps, the few (5%) synaptic terminals that cannot be classified and that may derive from the brainstem reticular formation. These terminals may discharge neurotransmitters or co-factors that hyperpolarize the cell for > 100 ms through some as yet undetermined receptor/conductance mechanism.[7] However, except for the recent but preliminary report of McCormick and Prince (1986), studies of unconventional transmitter-induced conductance changes have just begun, and they have concentrated on other neuronal systems (Belcher and Ryall 1977; Madison and Nicoll 1982, 1984, 1986a,b; Jan and Jan 1983; Cole and Nicoll 1984; Madison et al. 1985).

Third, LT spike de-inactivation may be effected by disfacilitation of a tonic excitatory input. The corticogeniculate pathway seems an ideal candidate for this. As noted above in Sect. II.C.4., the majority of excitatory inputs onto geniculate relay cells derive from cortex. We estimate (see Appendix) that each geniculate relay cell receives convergent input from at least 10, and most likely many more, corticogeniculate neurons. Furthermore, the corticogeniculate input is heterogeneous with respect to conduction velocity and may thus be heterogeneous with respect to latency as well (Tsumoto et al. 1978). Unlike the retinal input that innervates each geniculate cell from a few axons of equal conduction velocity and thus excites the geniculate cell synchronously (Singer and Creutzfeldt 1970; Cleland et al. 1971; Hoffmann et al. 1972; Eysel 1976), the cortical input almost certainly arrives asynchronously. This, plus the distal dendritic location of corticogeniculate synapses, a location that tends to spread out the cortically induced EPSPs in time, suggests that activity in corticogeniculate fibers can maintain a steady depolarization in geniculate relay cells. Perhaps when one records a −60 mV "resting" potential, this actually indicates a true resting potential of, say, −75 mV that is tonically depolarized to −60 mV by activity among corticogeniculate fibers. Phrased differently, prolonged inactivity (> 100 ms) in the corticogeniculate fibers can de-inactivate the Ca^{2+} conductance and permit the next retinal (or even cortical) EPSP to trigger the LT spike.

7 It is interesting in this regard that, within the cerebral cortex, all synaptic terminals found to contain neuropeptides also contain GABA (Hendry et al. 1984). Neuropeptides are thought to act frequently as neuromodulators rather than as conventional neurotransmitters. Perhaps some of the GABAergic terminals in the lateral geniculate nucleus also contain neuropeptides or analogous substances that function as neuromodulators to produce long-lasting hyperpolarization. The recent observation that the neuropeptide, somatostatin, is co-localized with GABA in neurons of the thalamic reticular nucleus (Oertel et al. 1983) renders this suggestion somewhat more plausible

One requirement of this hypothesis is a reasonable level of maintained activity among the corticogeniculate neurons. Unfortunately, published data suggest that only a subset of these cells has any detectable spontaneous activity (Gilbert 1977; Harvey 1980). Of course, one would like to know the response properties of these neurons in cats during different physiological states of attention, and it is not clear how large a subset of these cells must be active to control LT spikes in the manner suggested. It is possible that one or several of the proposed mechanisms, such as hyperpolarizing synaptic input from perigeniculate cells and lack of excitatory input from corticogeniculate fibers, must act in conjunction in order for LT spike de-inactivation to occur.

In any case, our hypothesis that the corticogeniculate pathway serves to control the LT spike is inexplicable if single cortical axons monosynaptically excite geniculate neurons and disynaptically inhibit them through the action of perigeniculate neurons. This would prevent the corticogeniculate pathway from exerting a pronounced and prolonged depolarization of geniculate cells. However, the neuronal circuit summarized in Fig. 3B is consistent with the sort of role we have suggested for the corticogeniculate pathway. We have discussed the evidence for this circuitry above in Sect. II.C.1.

Despite many experimental attempts to elucidate some important function for the anatomically massive corticogeniculate pathway, only subtle changes in response properties of lateral geniculate neurons have been described following manipulation of the corticogeniculate projection (e.g., Kalil and Chase 1979; Schmielau and Singer 1977; Geisert et al. 1981). Note, however, that these experiments have always been performed on anesthetized animals. Our suggestion at least provides a role for the corticogeniculate pathway that is commensurate with its anatomical size. Furthermore, since the cells of origin of the corticogeniculate pathway lie in visual cortex (i.e., areas 17, 18, and 19), gating decisions are the direct result of visual cortical processing. In fact, corticogeniculate fibers may be regarded as a sort of "final common pathway" that conveys gating decisions made as a result of cortical processing and efficiently enforces them at the bottleneck of retinogeniculate circuitry.

IV. Conclusion and summary: the lateral geniculate nucleus as a gate to the visual cortex

The main purpose of this paper is to focus attention on the function of the cat's lateral geniculate nucleus

(and, in a more general sense, the mammalian thalamus). Although the receptive field approach has suggested no major function for geniculate circuitry beyond a fairly simple relay of retinal signals to cortex, three lines of enquiry paint a different picture. First, retinal synapses form a small minority of inputs to geniculate relay cells. Second, activation of inputs to the general region of the lateral geniculate nucleus from as yet poorly defined regions in the brainstem reticular formation can alter the gain of retinogeniculate transmission. Third, biophysical studies of thalamic neurons reveal a rich array of transmitter-, voltage-, and time-dependent conductances than can significantly alter the transmission of retinogeniculate signals. This paper has focused on biophysical mechanisms possibly subserving gating and the different anatomical pathways over which these mechanisms may be controlled.

Three quite different gating mechanisms are proposed. These are conventional GABAergic inhibition (whether via $GABA_A$ or $GABA_B$ receptors), noradrenergic or cholinergic control of the I_{AHP}, and control of the LT spike. The time courses of these mechanisms vary enormously, from several ms for GABAergic inhibition through 100–200 ms for the LT spike to seconds or minutes for noradrenergic or cholinergic control of the I_{AHP}. Furthermore, quite different afferent pathways, from visual cortex and from the brainstem reticular formation, appear to subserve these gating mechanisms. In this last section, we shall briefly summarize these topics and consider some of their possible functional roles.

A. GABAergic inhibition

One process of retinogeniculate gating is based on conventional inhibition of geniculate relay cells via GABAergic synapses. Both corticogeniculate axons and fibers from the brainstem reticular formation appear to innervate the GABAergic interneurons and perigeniculate cells (Singer 1973; Lindström 1982; Ahlsen et al. 1984, 1985). Thus both pathways have access to this fastest of the gating processes. GABAergic inhibition leads to an increase in either a Cl^- or K^+ conductance, depending on whether the postsynaptic receptor is $GABA_A$ or $GABA_B$. The two classes of geniculate relay cell, X and Y, seem to have different circuits involving different types of GABAergic terminals. For Y cells, these are predominantly F1 terminals from perigeniculate cells, and these terminals form synapses onto dendritic shafts; for X cells, these are predominantly F2 terminals from interneurons, and these terminals form synapses onto dendritic appendages in triadic arrangements with retinal terminals. F1 terminals from perigeniculate cells also provide limited innervation of X cells. The possible functional significance of these different circuits has been outlined above in Sect. III.A. (see also Koch 1985).

B. The afterhyperpolarization

A second mechanism possibly employed for retinogeniculate gating involves control of the geniculate cell's accommodation in response to a maintained excitatory input. Under normal conditions of accommodation, many cells respond to such a maintained input with a few action potentials at the start of the excitatory input; removal of this accommodation leads to a maintained output of action potentials throughout the duration of the input. In mammalian hippocampal pyramidal cells, the accommodation is due to a voltage-insensitive, Ca^{2+}-dependent K^+ current, the I_{AHP} (Madison and Nicoll 1984), and direct application of noradrenaline or acetylcholine blocks the I_{AHP}. The acetylcholine effects are elicited via an M_1 muscarinic receptor. Since it is plausible that this Ca^{2+}-dependent K^+ current is present in cat geniculate cells, we propose that much of the excitatory action of noradrenergic fibers from the locus coeruleus and cholinergic fibers from the parabrachial nucleus is due to blockage of the I_{AHP}. This type of excitation is effected by using noradrenaline and acetylcholine as neuromodulators rather than as conventional neurotransmitters. Caveats to this hypothesis were emphasized above in Sect. III.B.1.

C. The low threshold spike

The third putative gating mechanism involves activation of the Ca^{2-} conductance underlying the LT spike. Physiological control of the LT spike is mostly a matter of speculation as noted above in Sect. III.B.2.b., although an excellent candidate for its control via cholinergic input and M_2 muscarinic receptors has recently been nominated. In addition, it is far from clear what, if any, is the physiological significance of the LT spike. The simplest hypothesis we can advance is that the LT spike and the accompanying long-lasting hyperpolarization shuts down geniculate input to visual cortex. Thus, if the LT spike is inactivated, the lateral geniculate nucleus will transmit information from the retina more or less faithfully, subject to the modulation by cortical and brainstem afferents. Once an LT spike has been initiated, it will block retinogeniculate transmission for at least 100 to 150 ms.

A more complex proposition has been advanced by Crick (1984). He suggests the possibility that the bursting response (i.e., the conventional action potentials riding the crest of an LT spike) in a particular subset of geniculate relay cells temporarily enhances certain related synaptic circuits; this may be the neurophysiological substrate of the behavioral fact that the observer, whether cat or primate, currently *attends* to an object at that particular receptive field position. Our suggestion, which emphasizes the reduction of retinogeniculate transmission following the burst of action potentials, is so different from Crick's (1984) that the contrast between them serves as an effective reminder of our present uncertainty about the specific functional role of the LT spike.

D. Different roles of afferents from brainstem reticular formation and from cortex

In the above paragraphs, we have suggested a number of different mechanisms involving several different neuronal circuits by which gating of retinogeniculate transmission could be effected. It seems likely that this gating is important to attentional mechanisms related to visual stimuli. Two major nonretinal pathways, from brainstem reticular formation and from the visual cortex, are involved in the control of this gating, and it is likely that these afferent pathways are employed in quite different forms of visual attention.

1. Afferents from the brainstem reticular formation. The afferents from the brainstem reticular formation may be used to direct attention more globally to a specific sensory modality as may occur, for instance, when we block out extraneous sounds while reading. These afferents may also be important in the overall changes of geniculate cell responsiveness during sleep and arousal (Singer 1977). Livingstone and Hubel (1981) report that geniculate neurons exhibit increased spontaneous firing rates and enhanced responses to optimal visual stimuli during arousal (see also Coenen and Vendrik 1972; McCarley et al. 1983). Furthermore, neurons in both the dorsal raphe nucleus and locus coeruleus fire more briskly during periods of increased alertness, such as arousal, and they fire less briskly during paradoxical sleep (Chu and Bloom 1973; Foote et al. 1980). These brainstem afferents may thus modify retinogeniculate transmission during different levels of arousal (see also Harth and Unnikrishnan 1985).

Another potentially interesting phenomenon related to afferents from the brainstem reticular formation may be the time course of their effects on retinogeniculate transmission. For instance, activation of the locus coeruleus increases the excitability of geniculate neurons for many seconds (e.g., Kayama et al. 1982; Kayama 1985). Also, application of acetylcholine to thalamic neurons induces a hyperpolarization with a latency of > 100 ms that lasts for many seconds (McCormick and Prince 1986), and the only known cholinergic input to thalamic cells derives from the brainstem reticular formation. These observations suggest that at least some of the afferents from the brainstem reticular formation are not directly involved in a fast selection of visual targets within the visual scene, such as occurs during selective visual attention, but rather that they modulate retinogeniculate gating as a function of the animal's level of arousal. Also, many afferent fibers from the brainstem reticular formation have diffuse, widely distributed terminal arbors in the lateral geniculate nucleus (Uhlrich et al. 1985). Thus the temporal and spatial resolution of this pathway may be quite coarse.

2. Afferents from the visual cortex. The purely visual nature of the corticogeniculate pathways implies that it is involved in attentional phenomena within the visual sense. The pathway is arranged in a precise retinotopic fashion. This suggests that retinogeniculate gating controlled by the corticogeniculate pathway could vary across the visual field to permit changes in fixation or attention to different visual objects. The pathway might also play a crucial role in such attentional processes as elevated visual thresholds during saccadic eye movements (Helmholtz 1866; Burr et al. 1982), and evidence exists for suppressed firing of many geniculate cells during such eye movements (Noda 1975). Finally, if populations of corticogeniculate fibers differentially innervate X and Y relay cells, a plausible possibility yet to be experimentally tested, the cortex would be able to gate these cell classes differentially. This would permit the input lines to cortex to be dominated by one or the other pathway. During fast-paced activity when high acuity is not essential, such as playing basketball, it might be beneficial to open the gates of the general purpose Y pathway and close those of the X pathway; conversely, during reading, the high-acuity X pathway might be favored, and the gates would be set accordingly (cf. Sherman 1979, 1985).

It is clear from physiological studies that the corticogeniculate fibers access GABAergic circuits in the lateral geniculate and perigeniculate nuclei. We have also suggested above in Sect. III.B.2.b.iii. that the corticogeniculate pathway might be involved in control of the LT spike. However, we see no reason

to suppose that this pathway also controls the I_{AHP} in geniculate relay cells, because there is no evidence that corticogeniculate axons utilize the appropriate transmitters (i.e., acetylcholine or noradrenaline). We thus suggest that the corticogeniculate pathway employs two of the three proposed methods of gating retinogeniculate transmission.

E. Conclusions

We have proposed three different biophysical mechanisms by which retinogeniculate transmission can be altered or gated. These involve conventional GABAergic inhibition (via interneurons and perigeniculate cells), the LT spike, and the I_{AHP}. GABAergic inhibition is quite fast (with a time course of 10 ms or less), the LT spike is intermediate in speed (with a time course of 100–200 ms), and control of the I_{AHP} can produce quite prolonged excitability changes (lasting seconds or minutes). GABAergic inhibition, especially if it acts via $GABA_A$ receptors to shunt excitatory inputs, can be quite selective in reducing or abolishing the contribution of specific afferents to the output of the relay cell. By inhibiting a specific set of geniculate interneurons or perigeniculate cells, it may be possible to promote high levels of retinogeniculate transmission through specific patterns of input lines from the retina (Koch 1985). Conversely, control of the LT spike and the I_{AHP} affect the postsynaptic geniculate cell's responsiveness to all excitatory inputs, including all retinal afferents.

The two anatomical sources of gating control, corticogeniculate fibers and afferents from the brainstem reticular formation, may have quite different roles to play in retinogeniculate gating. Cortical areas 17, 18 and 19, being exclusively concerned with vision, may control transfer of attention within the visual sense. Conversely, the brainstem reticular formation, most of the cells of which respond to all sensory modalities, may serve to gate visual inputs to cortex from the lateral geniculate nucleus in the context of activity in other sensory pathways.

While we believe we have advanced plausible hypotheses in this paper, much more research needs to be directed at the putative mechanisms underlying gating of retina-to-cortex transmission. We do not even have a clear idea as to what specific visual function is subserved by this gating, beyond the general and rather hazy notion that it is related to visual attention (see also Singer 1977; Burke and Cole 1978; Crick 1984; Ahlsen et al. 1985). Only with much more research directed at these questions can we truly begin to appreciate the functional significances of the lateral geniculate nucleus and other thalamic nuclei.

Appendix

The number of corticogeniculate neurons can be estimated as follows. These cells derive from layer VI of cortical areas 17, 18, and 19, and roughly half of these layer VI cells innervate laminae A and A1 (Gilbert and Kelly 1975). Beaulieu and Colonnier (1983) estimate the density of cells in layer VI of area 17 to be roughly 17,000 cells per mm^2 of surface area. Since the surface area for area 17 is 380 mm^2 (Tusa et al. 1978), layer VI there contains roughly 6.5×10^6 cells, of which about 3.2×10^6 innervate laminae A and A1. Area 18 and 19 are each about 1/6 as large in surface area as is area 17 (Orban 1984). If a similar layer VI density exists for these areas (published data on layer VI density are presently unavailable for these areas, but the assumption seems reasonable), then roughly an additional 1.1×10^6 corticogeniculate cells innervate laminae A and A1. Overall, then, roughly $4.0–4.5 \times 10^6$ cortical cells innervate laminae A and A1 for each hemisphere. Sanderson (1971) points out that the total number of cells in the lateral geniculate nucleus is approximately 4.5×10^5 (see also Bishop et al. 1953). In very rough terms, laminae A and A1 contribute approximately 1/2 to 2/3 of this number. Taken together, this implies that the corticogeniculate cells innervating laminae A and A1 outnumber these geniculate cells by 10–20 to 1. However, since Robson (1983) points out that corticogeniculate axons have widespread arbors that cross laminar borders, each axon must consequently diverge to innervate several geniculate cells. As the divergence factor (i.e., the number of geniculate cells innervated by each corticogeniculate axon) increases, so must the convergence factor (i.e., the number of corticogeniculate axons that innervate each geniculate cell). In fact, the convergence factor is the product of the divergence factor and the ratio of corticogeniculate axons to postsynaptic geniculate cells. As noted, this latter ratio is 10–20 and if the divergence ratio is, say 5–10, then the convergence ratio would be roughly 100. That is, on the average, each geniculate cell receives some input from about 100 cortical cells.

Acknowledgements. The laboratory of SMS is supported by USPHS grants EY03038 and EY03604. CK is supported by the Sloan Foundation and by a grant from the Office of Naval Research, Engineering Psychology Division. We thank S.A. Bloomfield, J. Cucchiaro, E. Hildreth, B. Lancaster, J. Maunsell, T. Poggio, and D.J. Uhlrich for critically reading of the manuscript.

References

Adams PR, Lancaster B (1985) Components of Ca-activated K current in rat hippocampal neurones in vitro. J Physiol (Lond) 362: 23

Ahlsen G (1984) Brain stem neurones with differential projection to functional subregions of the dorsal lateral geniculate complex in the cat. Neuroscience 12: 817–838

Ahlsen G, Grant K, Lindström S (1982) Monosynaptic excitation of principal cells in the lateral geniculate nucleus by corticofugal fibers. Brain Res 234: 454–458

Ahlsen G, Lindström S (1982) Excitation of perigeniculate neurones via axon collaterals of principal cells. Brain Res 236: 477–481

Ahlsen G, Lindström S, Lo F-S (1982) Functional distinction of

perigeniculate and thalamic reticular neurons in the cat. Exp Brain Res 46: 118–126

Ahlsen G, Lindström S, Lo F-S (1984) Inhibition from the brain stem of inhibitory interneurones of the cat's dorsal lateral geniculate nucleus. J Physiol (Lond) 347: 593–609

Ahlsen G, Lindström S, Lo F-S (1985) Interaction between inhibitory pathways to principal cells in the lateral geniculate nucleus of the cat. Exp Brain Res 58: 134–143

Ahlsen G, Lo F-S (1982) Projection of brain stem neurones to the perigeniculate nucleus and lateral geniculate nucleus in the cat. Brain Res 238: 433–438

Barker JL (1978) Evidence for diverse cellular roles of peptides in neuronal function. Neurosci Res Prog Bull 16: 535–555

Beaulieu C, Colonnier M (1983) The number of neurons in the different laminae of the binocular and monocular regions of area 17 in the cat. J Comp Neurol 217: 337–344

Belcher G, Ryall RW (1977) Substance P selectively blocks nicotinic receptors on Renshaw cells: a new concept of inhibitory synaptic interaction. J Physiol (Lond) 272: 105–119

Berardi N, Morrone MC (1984) The role of γ-aminobutyric acid mediated inhibition in the response properties of cat lateral geniculate nucleus neurones. J Physiol (Lond) 357: 505–524

Bishop PO, Jeremy D, McLeod JG (1953) The phenomenon of repetitive firing in the lateral geniculate nucleus of the cat. J Neurophysiol 16: 437–447

Bizzi E (1966) Discharge patterns of single geniculate neurons during the rapid eye movements of sleep. J Neurophysiol 16: 437–447

Bloomfield SA, Hamos JE, Sherman SM (1985) Passive electrical properties of X- and Y-cells in the cat's lateral geniculate nucleus. Soc Neurosci Abstr 11: 232

Bowery NG, Doble A, Hill DR, Hudson AL, Shaw JS, Turnbull MJ, Warrington R (1981) Bicuculline-insensitive GABA receptors on peripheral autonomic nerve terminals. Eur J Pharmacol 71: 53–70

Bowery NG, Hill DR, Hudson AL (1983) Characteristics of $GABA_B$ receptor binding sites on rat whole brain synaptic membranes. Br J Pharmacol 78: 191–206

Bowery NG, Hudson AL, Price GW (1985) Comparative autoradiographic studies with [^{3}H]-GABA and [^{3}H]-(−)-baclofen in rat brain in vivo. Br J Pharmacol 85: 234

Bowery GP, Price GW, Hudson AL, Hill DR, Wilkin GP, Turnbull MJ (1984) GABA receptor multiplicity. Visualization of different receptor types in the mammalian CNS. Neuropharmacology 23: 219–232

Boycott BB, Wässle H (1974) The morphological types of ganglion cells of the domestic cat's retina. J Physiol (Lond) 240: 397–419

Burke W, Cole AM (1978) Extraretinal influences on the lateral geniculate nucleus. Rev Physiol Biochem Pharmacol 80: 105–166

Burr DC, Holt J, Johnstone JR, Ross J (1982) Selective depression of motion sensitivity during saccades. J Physiol (Lond) 333: 1–15

Chu N-S, Bloom FE (1973) Norepinephrine-containing neurons: changes in spontaneous discharge patterns during sleeping and waking. Science 179: 908–910

Cleland BG, Dubin MW, Levick WR (1971) Sustained and transient neurones in the cat's retina and lateral geniculate nucleus. J Physiol (Lond) 217: 473–496

Coenen AML, Vendrik AJH (1972) Determination of the transfer ratio of cat's geniculate neurons through quasi-intracellular recordings and the relation with the level of alertness. Exp Brain Res 14: 227–242

Cole AE, Nicoll RA (1983) Acetylcholine mediates a slow synaptic potential in hippocampal pyramidal cells. Science 221: 1299–1301

Cole AE, Nicoll RA (1984) Characterization of a slow cholinergic postsynaptic potential recorded in vitro from rat hippocampal cells. J Physiol (Lond) 352: 173–188

Crick F (1984) The function of the thalamic reticular complex: the searchlight hypothesis. Proc Natl Acad Sci USA 81: 4586–4590

Cucchiaro J, Uhlrich DJ, Hamos JE, Sherman SM (1985) Perigeniculate input to the cat's lateral geniculate nucleus: a light- and electron microscopic study of single, HRP-filled cells. Soc Neurosci Abstr 11: 231

Curtis DR, Johnston GAR (1974) Amino acid transmitters in the mammalian central nervous system. Ergebn Physiol Biol Chem Exp Pharmakol 69: 97–188

Deschenes M, Paradis M, Roy JP, Steriade M (1984) Electrophysiology of neurons of lateral thalamic nuclei in cat: resting properties and burst discharges. J Neurophysiol 51: 1196–1219

Dingledine R, Langmoen IA (1980) Conductance changes and inhibitory actions of hippocampal recurrent IPSPs. Brain Res 185: 277–287

Dowling JE (1970) Organization of vertebrate retinas. Invest Ophthalmol 9: 655–680

Dubin MW, Cleland BG (1977) Organization of visual inputs to interneurons of lateral geniculate nucleus of the cat. J Neurophysiol 40: 410–427

Egan TM, North RA (1986) Acetylcholine hyperpolarizes central neurones by acting on an M_2 muscarinic receptor. Nature 319: 405–407

Eysel UTh (1976) Quantitative studies of intracellular postsynaptic potentials in the lateral geniculate nucleus of the cat with respect to optic tract stimulus response latencies. Exp Brain Res 25: 469–486

Ferster D, LeVay S (1978) The axonal arborization of lateral geniculate neurons in the striate cortex of the cat. J Comp Neurol 182: 923–944

Fibiger HC (1982) The organization and some projections of cholinergic neurons of the mammalian forebrain. Brain Res Rev 4: 327–388

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: 1809–1829

Foote SL, Aston-Jones G, Bloom FE (1980) Impulse activity of locus coeruleus neurons in awake rats and monkeys is a function of sensory stimulation and arousal. Proc Natl Acad Sci USA 77: 3033–3037

Foote WE, Maciewicz RJ, Mordes JP (1974) Effect of midbrain raphe and lateral mesencephalic stimulation on spontaneous and evoked activity in the lateral geniculate of the cat. Exp Brain Res 19: 124–130

Friedlander MJ, Lin C-S, Stanford LR, Sherman SM (1981) Morphology of functionally identified neurons in the lateral geniculate nucleus of the cat. J Neurophysiol 46: 80–129

Fukuda Y, Stone J (1976) Evidence of differential inhibitory influences on X- and Y-type relay cells in the cat's lateral geniculate nucleus. Brain Res 113: 188–196

Geisert EE, Langsetmo A, Spear PD (1981) Influence of the corticogeniculate pathway on response properties of cat lateral geniculate neurons. Brain Res 208: 409–415

Gilbert C (1977) Laminar differences in receptive field properties of cells in cat primary visual cortex. J Physiol (Lond) 268: 391–421

Gilbert C (1983) Microcircuitry of the visual cortex. Ann Rev Neurosci 6: 217–247

Gilbert CD, Kelly JP (1975) The projections of cells in different layers of the cat's visual cortex. J Comp Neurol 163: 81–106

Guillery RW (1967) Patterns of fiber degeneration in the dorsal lateral geniculate nucleus of the cat following lesions in the visual cortex. J Comp Neurol 130: 197–222

Guillery RW (1971) Patterns of synaptic interconnections in the dorsal lateral geniculate nucleus of the cat and monkey: a brief review. Vision Res Suppl 3: 211–227

Hamos JE, Van Horn SC, Raczkowski D, Uhlrich DJ, Sherman SM (1985) Synaptic connectivity of a local circuit neuron in the cat's lateral geniculate nucleus. Nature 317: 618–621

Harth E, Unnikrishnan KP (1985) Brainstem control of sensory information: a mechanism for perception. Int J Psychophysiol 3: 101–119

Harvey AR (1980) A physiological analysis of subcortical and commissural projections of area 17 and 18 of the cat. J Physiol (Lond) 302: 507–534

von Helmholtz H (1866) Handbuch der physiologischen Optik. Translated by Southall JP. Dover, New York, 1925

Hendry SHC, Jones EG, DeFelipe J, Schmechel D, Brandon C, Emson PC (1984) Neuropeptide-containing neurons of the cerebral cortex are also GABAergic. Proc Natl Acad Sci USA 81: 6526–6530

Hoffmann K-P, Stone J, Sherman SM (1972) Relay of receptive-field properties in dorsal lateral geniculate nucleus of the cat. J Neurophysiol 35: 518–531

Hoover DB, Jacobowitz DM (1979) Neurochemical and histochemical studies of the effect of a lesion of nucleus cuneiformis on the cholinergic innervation of discrete areas of the rat brain. Brain Res 170: 113–122

Hubel DH, Wiesel TN (1961) Integrative action in the cat's lateral geniculate body. J Physiol (Lond) 155: 385–398

Hubel DH, Wiesel TN (1977) Functional architecture of the macaque monkey visual cortex. Proc R Soc B 196: 1–59

Hughes HC, Mullikin WH (1984) Brainstem afferents to the lateral geniculate nucleus of the cat. Exp Brain Res 54: 253–258

Humphrey AL, Sur M, Uhlrich DJ, Sherman SM (1985a) Projection patterns of individual X- and Y-cell axons from the lateral geniculate nucleus to cortical area 17 in the cat. J Comp Neurol 233: 159–189

Humphrey AL, Sur M, Uhlrich DJ, Sherman SM (1985b) Termination patterns of individual X- and Y-cell axons in the visual cortex of the cat: projections to area 18, to the 17–18 border region, and to both areas 17 and 18. J Comp Neurol 233: 190–212

Ide LS (1982) The fine structure of the perigeniculate nucleus in the cat. J Comp Neurol 210: 317–334

Ikeda H, Wright MJ (1972) Receptive field organization of sustained and transient retinal ganglion cells which subserve different functional roles. J Physiol (Lond) 227: 769–800

Jahnsen H, Llinas R (1984a) Electrophysiological properties of guinea-pig thalamic neurones: an in vitro study. J Physiol (Lond) 349: 205–226

Jahnsen H, Llinas R (1984b) Ionic basis for the electroresponsiveness and oscillatory properties of guinea-pig thalamic neurones in vitro. J Physiol (Lond) 349: 227–247

Jan YN, Jan LY (1983) A LHRH-like peptidergic neurotransmitter capable of "action at a distance" in autonomic ganglia. Trends Neurosci 6: 320–325

Jones EG (1975) Some aspects of the organization of the thalamic reticular complex. J Comp Neurol 162: 285–308

Jones EG, Powell TPS (1969) An electron microscopic study of the mode of termination of cortico-thalamic fibres within the sensory relay nuclei of the thalamus. Proc R Soc B 172: 173–185

Kalil RE, Chase R (1970) Corticofugal influence on activity of lateral geniculate neurons in the cat. J Neurophysiol 33: 459–474

Kayama Y (1985) Ascending, descending and local control of neuronal activity in the rat lateral geniculate nucleus. Vision Res 25: 339–347

Kayama Y, Negi T, Sugitani M, Iwama K (1982) Effects of locus coeruleus stimulation on neuronal activities of dorsal lateral geniculate nucleus and perigeniculate reticular nucleus of the rat. Neuroscience 7: 655–666

Kemp JA, Roberts H, Sillito AM (1982) Further studies on the action of 5-hydroxytryptamine in the dorsal lateral geniculate nucleus of the cat. Brain Res 246: 334–337

Kemp JA, Sillito AM (1982) The nature of the excitatory transmitter mediating X and Y cell inputs to the cat dorsal lateral geniculate nucleus. J Physiol (Lond) 323: 377–391

Kimura H, McGeer PL, Peng JH, McGeer EG (1981) The central cholinergic system studied by choline acetyltransferase immunohistochemistry in the cat. J Comp Neurol 200: 151–201

Koch C (1985) Understanding the intrinsic circuitry of the cat's LGN: electrical properties of the spine-triad arrangement. Proc R Soc B: 391–398

Koch C, Poggio T (1983) A theoretical analysis of electrical properties of spines. Proc R Soc 218: 455–477

Koch C, Poggio T, Torre V (1982) Retinal ganglion cells: a functional interpretation of dendritic morphology. Philos Trans R Soc 298: 227–264

Koch C, Poggio T, Torre V (1983) Nonlinear interactions in a dendritic tree: localization, timing, and role in information processing. Proc Natl Acad Sci USA 80: 2799–2802

Kromer LF, Moore RY (1980) A study of the organization of the locus coeruleus projections to the lateral geniculate nuclei in the albino rat. Neuroscience 5: 255–271

Lancaster B, Adams PR (1986) Calcium-dependent current generating the afterhyperpolarization of hippocampal neurons. J Neurophysiol (in press)

de Lima AD, Montero VM, Singer W (1985) The cholinergic innervation of the visual thalamus: an EM immunocytochemical study. Exp Brain Res 59: 206–212

Lindström S (1982) Synaptic organization of inhibitory pathways to principal cells in the lateral geniculate nucleus of the cat. Brain Res 234: 447–453

Livingstone MS, Hubel DH (1981) Effects of sleep and arousal on the processing of visual information in the cat. Nature 291: 554–561

Madison DV, Lancaster B, Nicoll RA, Adams PR (1985) Voltage clamp analysis of slow cholinergic synaptic transmission in the hippocampus. Soc Neurosci Abstr 11: 466

Madison DV, Nicoll RA (1982) Noradrenalin blocks accommodation of pyramidal cell discharge in the hippocampus. Nature 299: 636–638

Madison DV, Nicoll RA (1984) Control of the repetitive discharge of rat CA1 pyramidal neurones in vitro. J Physiol (Lond) 354: 319–334

Madison DV, Nicoll RA (1986a) Actions of noradrenaline recorded intracellularly in rat hippocampal CA1 pyramidal neurones, *in vitro*. J Physiol (Lond) 372: 221–244

Madison DV, Nicoll RA (1986b) Cyclic adenosine 3', 5'-monophosphate mediates β-receptor actions of noradrenaline in rat hippocampal pyramidal cells. J Physiol (Lond) 372: 245–259

McBride RL, Sutin J (1976) Projections of the locus coeruleus and adjacent pontine tegmentum in the cat. J Comp Neurol 165: 265–284

McCarley RW, Benoit O, Barrionuevo G (1983) Lateral geniculate nucleus unitary discharge in sleep and waking: state- and rate-specific aspects. J Neurophysiol 50: 798–818

McCormick DA, Prince DA (1986) Acetylcholine induces burst firing in thalamic reticular neurones by activating a potassium conductance. Nature 319: 402–405

McIlwain JT, Creutzfeldt OD (1967) Microelectrode study of synaptic excitation and inhibition in the lateral geniculate nucleus of the cat. J Neurophysiol 30: 1–21

Montero VM, Scott GL (1981) Synaptic terminals in the dorsal lateral geniculate nucleus from neurons of the thalamic reticular nucleus: a light and electron microscopic autoradiographic study. Neuroscience 6: 2561–2577

Montero VH, Singer W (1984) Ultrastructure and synaptic relations of neural elements containing glutamic acid decarboxylase (GAD) in the perigeniculate nucleus of the cat. Exp Brain Res 56: 115–125

Moore RY, Bloom FE (1979) Central catecholamine neuron systems: anatomy and physiology of the norepinephrine and epinephrine systems. Ann Rev Neurosci 2: 113–168

Nakai Y, Takaori S (1974) Influence of norepinephrine-containing neurons derived from the locus coeruleus on lateral geniculate neuronal activities of cats. Brain Res 71: 47–60

Newberry NR, Nicoll RA (1984) A bicuculline-resistant inhibitory postsynaptic potential in rat hippocampal pyramidal cells in vitro. J Physiol (Lond) 348: 239–254

Newberry NR, Nicoll RA (1985) Comparison of the action of baclofen with γ-aminobutyric acid on rat hippocampal pyramidal cells in vitro. J Physiol (Lond) 360: 161–185

Noda H (1975) Depression in the excitability of relay cells of lateral geniculate nucleus following saccadic eye movements in the cat. J Physiol (Lond) 249: 87–102

O'Donnell P, Koch C, Poggio T (1985) Demonstrating the nonlinear interaction between excitation and inhibition on dendritic trees using computer-generated color graphics: a film. Soc Neurosci Abstr 11: 465

Oertel WH, Graybiel AM, Mugnaibi E, Elde RP, Schmechel DE, Kopin IJ (1983) Coexistence of glutamic acid decarboxylase- and somatostatin-like immunoreactivity in neurons of the feline nucleus reticularis thalami. J Neurosci 3: 1322–1332

O'Hara PT, Lieberman AR, Hunt SP, Wu J-Y (1983) Neural elements containing glutamic acid decarboxylase (GAD) in the dorsal lateral geniculate nucleus of the rat: immunohistochemical studies by light and electron-microscopy. Neuroscience 8: 189–211

O'Hara PT, Sefton AJ, Lieberman AR (1980) Mode of termination of afferents from the thalamic reticular nucleus in the dorsal lateral geniculate nucleus of the rat. Brain Res 197: 503–506

Orban GA (1984) Neuronal operations in the visual cortex. Springer Berlin Heidelberg New York Tokyo

Pasquier DA, Villar MJ (1982) Specific serotonergic projections to the lateral geniculate body from the lateral cell groups of the dorsal raphe nucleus. Brain Res 249: 142–146

Pennefather P, Lancaster B, Adams PR, Nicoll RA (1986) Two distinct CA-dependent K currents in bullfrog sympathetic ganglion cells. Proc Natl Acad Sci USA 82: 3040–3044

Robson JA (1983) The morphology of corticofugal axons to the dorsal lateral geniculate nucleus in the cat. J Comp Neurol 216: 89–103

Rogawski MA, Aghajanian GK (1980) Modulation of lateral geniculate neurone excitability by noradrenalin microiontophoresis or locus coeruleus stimulation. Nature 287: 731–734

Sakai K (1980) Some anatomical and physiological properties of pontomesencephalic tegmental neurons with special reference to the PGO waves and postural *atonia* during paradoxical sleep in the cat. In: Hobson JA, Brazier MAB (eds) The reticular formation revisited. Raven Press, New York, pp 427–447

Sanderson KJ (1971) Visual field projection columns and magnification factors in the lateral geniculate nucleus of the cat. Exp Brain Res 13: 159–177

Scheibel ME, Scheibel AB (1966) The organization of the nucleus of the reticularis thalami: a Golgi study. Brain Res 1: 43–62

Schmielau F, Singer W (1977) The role of visual cortex for binocular interactions in the cat lateral geniculate nucleus. Brain Res 120: 354–361

Segal M, Barker JL (1984) Rat hippocampal neurons in culture: properties of GABA-activated Cl^- ion conductance. J Neurophysiol 51: 500–515

Shapley R, Lennie P (1985) Spatial frequency analysis in the visual system. Ann Rev Neurosci 8: 547–583

Sherman SM (1979) The functional significance of X- and Y-cells in normal and visually deprived cats. Trends Neurosci 2: 192–195

Sherman SM (1985) Functional organization of the W-, X-, and Y-cell pathways: a review and hypothesis. In: Sprague JM, Epstein AN (eds) Progress in psychobiology and physiological psychology, Vol 11. Academic Press, New York, pp 233–314

Sherman SM, Spear PD (1982) Organization of the visual pathways in normal and visually deprived cats. Physiol Rev 62: 738–855

Sillito AM, Kemp JA (1983) The influence of GABAergic inhibitory processes on the receptive field structure of X and Y cells in the cat dorsal lateral geniculate nucleus (dLGN). Brain Res 277: 63–77

Sillito AM, Kemp JA, Berardi N (1983) The cholinergic influence on the function of the cat dorsal lateral geniculate nucleus (dLGN). Brain Res 280: 299–307

Simmonds MA (1983) Multiple GABA receptors and associated regulatory sites. Trends Neurosci 6: 279–281

Singer W (1973) The effect of mesencephalic reticular stimulation on intracellular potentials of cat lateral geniculate neurons. Brain Res 61: 35–54

Singer W (1977) Control of thalamic transmission by corticofugal and ascending reticular pathways in the visual system. Physiol Rev 57: 386–420

Singer W, Creutzfeldt OD (1970) Reciprocal lateral inhibition of On- and Off-Center neurones in the lateral geniculate body of the cat. Exp Brain Res 10: 311–330

Steriade M, Deschenes M (1985) The thalamus as a neuronal oscillator. Brain Res Rev 8: 1–63

Stockmeier CA, Martino AM, Kellar KJ (1985) A strong influence of serotonin axons on β-adrenergic receptors in rat brain. Science 220: 323–325

Stone J, Dreher B (1973) Projection of X- and Y-cells of the cat's lateral geniculate nucleus to areas 17 and 18 of visual cortex. J Neurophysiol 36: 551–567

Stone J, Dreher B, Leventhal A (1979) Hierarchical and parallel mechanisms in the organization of visual cortex. Brain Res Rev 1: 345–394

Tsumoto T, Creutzfeldt OD, Legendy CR (1978) Functional organization of the corticofugal system from visual cortex to lateral geniculate nucleus in the cat. Exp Brain Res 32: 345–364

Tusa RJ, Palmer LA, Rosenquist AC (1978) The retinotopic organization of area 17 (striate cortex) in the cat. J Comp Neurol 177: 213–236

Uhlrich DJ, Cucchiaro JB, Sherman SM (1985) Terminal patterns of the brainstem projection to the lateral geniculate nucleus in the cat: an anterograde tracer study using *Phaseolus vulgaris* leucoagglutinin (PHA-L). Soc Neurosci Abstr 11: 232

Wilson JR, Friedlander MJ, Sherman SM (1984) Ultrastructural morphology of identified X- and Y-cells in the cat's lateral geniculate nucleus. Proc R Soc B 221: 411–436

Received December 4, 1985 / Accepted March 27, 1986