

Intracellular and extracellular in vivo recording of different response modes for relay cells of the cat's lateral geniculate nucleus

F.-S. Lo, S.-M. Lu, and S.M. Sherman

Department of Neurobiology, State University of New York, Stony Brook, NY 11794-5230, USA

Received April 9, 1990 / Accepted July 30, 1990

Summary. Prior studies of thalamic neurons have demonstrated that they exhibit at least two response modes: a *relay mode* and a *burst mode*. During the relay mode, sensory information is faithfully relayed to cortex; during the burst mode, which is caused by a voltage-dependent Ca^{2+} conductance, this relay of sensory information is interrupted. We began in vivo studies of these response modes in neurons from the lateral geniculate nucleus of anesthetized, paralyzed cats. Each of the 9 X and 10 Y cells we recorded intracellularly displayed voltage-dependent, low threshold spikes that were presumably the Ca^{2+} spikes described from in vitro recording. These spikes were triangular in waveform and typically had 2–7 fast action potentials (interspike intervals of 1.2–4 ms) riding its crest. Furthermore, the cell's membrane had to be hyperpolarized to *de-inactivate* the low threshold spike before a depolarization could then *activate* it. We could activate these low threshold spikes in Y cells from EPSPs, whether spontaneous or evoked from activation of the optic chiasm. However, in only one of the X cells could we activate low threshold spikes from chiasm shock; in the remainder, we could activate low threshold spikes only via depolarizing current pulses, possibly because the EPSPs of these X cells were too small to activate these spikes. We also used extracellular recording to study spontaneous activity and responses to chiasm shock from 114 geniculate neurons and, as a control, 57 optic tract axons. We concentrated on periods of bursty responsiveness signifying the burst mode. We define a burst as 2–7 action potentials with interspike intervals ≤ 4 ms, and the bursts are separated by > 100 ms; from our intracellular recording, we know that such bursts signify low threshold spikes. We found that, during extracellular recording, 20 of the 39 X cells and each of the 75 Y cells displayed evidence of the burst response mode, although burst periods were rare in X cells. Electrical activation of the optic chiasm greatly enhanced the burstiness of Y cells for periods of 500 ms or more. We also electrically stimulated the parabrachial

region of the midbrain, which provides a mostly cholinergic innervation to the lateral geniculate nucleus. Although parabrachial activation by itself had no detectable effect on Y cell response modes, prior parabrachial activation prevented the enhanced burstiness caused by chiasm stimulation. This parabrachial effect lasted for roughly 500 ms after stimulation. Neither chiasm nor parabrachial stimulation, singly or in combination, had a noticeable effect on the bursting activity of X cells. Finally, none of the extracellularly recorded retinogeniculate axons (23 X and 34 Y) showed any evidence of burst responses. This supports the conclusion that the burst responses we found for geniculate neurons represent an emergent property of the lateral geniculate nucleus, and this burstiness reflects an interruption of retinogeniculate transmission. We conclude that geniculate X and Y cells do indeed show evidence during extracellular recording of maintaining two very different response modes and that, under our recording conditions, Y cells are much more prone to burst activity than are X cells.

Key words: Lateral geniculate nucleus – Low threshold spike – Retinogeniculate gating – Thalamic response modes – Cat

Introduction

We now know that the mammalian lateral geniculate nucleus is not a simple, machine-like relay of retinal information to cortex (cf. Singer 1977; Burke and Cole 1978; Sherman and Koch 1986, 1990; Steriade and Llinás 1988). Instead, geniculate cells receive the vast majority of their synaptic input from nonretinal sources, and these influence geniculate neurons to control the gain of retinogeniculate transmission (reviewed in Sherman and Koch 1986, 1990). These nonretinal afferents include local inhibitory inputs, afferents from the visual cortex, and inputs from various regions of the brainstem. The local inhibitory inputs use γ -amino-butyric acid (GABA)

as their neurotransmitter, and most important among the brainstem inputs are axons that emanate from the mid-brain parabrachial region and use acetylcholine (ACh) as their neurotransmitter (Sillito et al. 1983; De Lima et al. 1985; De Lima and Singer 1987; McCormick and Prince 1987; Smith et al. 1988; Steriade et al. 1988; reviewed in Sherman and Koch 1986, 1990; Steriade and Llinás 1988).

An important element in the control of retinogeniculate transmission by nonretinal afferents is their influence on the variety of membrane conductances exhibited by thalamic relay cells. These conductances greatly affect the responses of these cells to sensory inputs. One of the most dramatic of these conductances is the low threshold Ca^{2+} spike (Jahnsen and Llinás 1984a, b). This is a voltage-dependent increase in conductance to Ca^{2+} , which leads to a spike-like depolarization of the cell. It is called "low threshold", because its initiation threshold is lower than that of a conventional action potential. However, when the membrane is kept more depolarized than roughly -65 mV, this Ca^{2+} conductance becomes *inactivated*; the membrane must be hyperpolarized below this level for at least 50–100 ms to *de-inactivate* the conductance so that the next sufficiently large depolarization will *activate* it. This low threshold spike typically has a high frequency burst of 2–7 conventional action potentials riding on its peak.

When the cell does not display these low threshold spikes, it is said to be in the *relay mode*, because it is then capable of faithfully relaying sensory input to cortex. However, these low threshold spikes, once initiated, tend to occur at more or less regular intervals and produce high frequency bursts of several conventional action potentials; the low threshold spikes and associated bursts of action potentials are separated by silent periods of 100 ms or more (Jahnsen and Llinás 1984a,b; Sherman and Koch 1986, 1990; Steriade and Llinás 1988). Under these conditions, the cell is said to be in the *burst mode*, and it cannot faithfully relay sensory information to cortex, because the bursts no longer reflect the firing pattern of the neuron's sensory afferents. Thus the presence or absence of low threshold spikes would greatly affect the transmission of sensory signals through thalamus to cortex.

Phenomena that we can, in retrospect, attribute to low threshold spikes have an extensive history for thalamic neurons, including those of the lateral geniculate nucleus. Thus burstiness associated with sleep or low levels of arousal has been repeatedly described from extracellular recording of geniculate neurons for some time (Hubel 1960; Hubel and Wiesel 1961; McCarley et al. 1983). Also, it now appears that the "delayed depolarizing potential" reported by McIlwain and Creutzfeldt (1967) from "quasi-intracellular" recording was, in fact, the low threshold spike. More recently, low threshold spikes have been recorded in vitro from the lateral geniculate nuclei of rodents and cats (Jahnsen and Llinás 1984a,b; McCormick and Prince 1987; McCormick and Pape 1988; Crunelli et al. 1989), and in vivo in cats from a variety of thalamic nuclei, including the lateral geniculate nucleus (cf. Deschênes et al. 1984; Hu et al. 1989a–c;

reviewed in Steriade and Llinás 1988). We are also beginning to learn something about the control of low threshold spiking in thalamic neurons. McCormick and Prince (1987) demonstrated in vitro that ACh can regulate the low threshold spike. The main cholinergic input to geniculate relay cells in the cat emanates from the parabrachial region of the midbrain, and Hu et al. (1989a–c) have recently provided in vivo examples in which parabrachial activation can inhibit low threshold spikes of geniculate relay cells.

However, there has not yet been a systematic in vivo description of these properties for geniculate relay cells. We thus sought to initiate a systematic study of these phenomena of low threshold spiking and possible control from parabrachial afferents in an in vivo preparation of the cat's lateral geniculate nucleus. A further rationale for our approach derives from the fact that the cat's visual pathways from the retina through the lateral geniculate nucleus to visual cortex are organized into two fairly independent neuronal streams known as the X and Y pathways (Lennie 1980; Stone 1983; Sherman 1985; Shapley and Lennie 1985), and the mechanisms and substrates underlying retinogeniculate transmission differ between these X and Y pathways (reviewed in Sherman and Koch 1986, 1990; see also Lo and Sherman 1989). We thus paid particular attention to any differences between geniculate X and Y cells in terms of low threshold spikes and their control from the parabrachial region of the midbrain.

Material and methods

We recorded intracellularly and extracellularly from neurons of the cat's lateral geniculate nucleus and from retinogeniculate axons, using techniques that were slightly modified from our previous descriptions (Bloomfield et al. 1987; Bloomfield and Sherman 1988; Lo and Sherman 1989). The cats were initially anesthetized either with barbiturate (33 mg/kg i.p.) or with 4% Halothane in a 50/50 mixture of $\text{N}_2\text{O}/\text{O}_2$ for all surgery, including the introduction of venous and tracheal cannulae and the formation of craniotomies. We then paralyzed and anesthetized the cats for the remainder of the recording session. For paralysis, we administered 5 mg gallamine triethiodide followed by 3.6 mg/h gallamine triethiodide plus 0.7 mg/h of d-tubocurarine. For anesthesia, we used a 70/30 mixture of $\text{N}_2\text{O}/\text{O}_2$ supplemented with either the addition of 1 mg/kg/h Nembutal to the intravenous infusion or with 0.3–1.0% Halothane. Supplemental Nembutal was used only in cats that were initially induced with Nembutal. This variation in anesthesia was used as a partial control for the effects of anesthesia on retinogeniculate transmission (see Results). The cats were artificially ventilated. End-tidal CO_2 was monitored and kept near 4%, and body temperature was monitored and kept near 37° C. Heart rate and EEG were also monitored throughout.

We used fine-tipped micropipettes filled with 3 M NaCl or KAc to record extracellularly and/or intracellularly from the geniculate neurons. For experiments aimed at intracellular recording, we beveled these electrodes to a final impedance of 30–60 M Ω at 100 Hz, and for extracellular recording, we beveled to a somewhat coarser tip (i.e., 10–30 M Ω at 100 Hz). We recorded electrophysiological activity through a high-impedance amplifier equipped with a bridge and current injection circuitry. When performing intracellular studies, we deemed a neuronal impalement suitable for further analysis if we observed a rapid DC drop to a resting membrane potential of -50 mV or more negative, a stable resting membrane potential, and a neuronal input resistance of $\geq 10\text{M}\Omega$ (Bloomfield and Sherman

1988); we also required that spontaneously occurring action potentials be typically ≥ 40 mV, although we noted that action potential amplitude was somewhat variable during a given penetration and that it often became temporarily smaller, particularly during periods of high responseiveness or when action potentials rode large depolarizations like the low threshold spike (see Results). All recordings were displayed on an oscilloscope and stored on an FM tape recorder for off-line analysis and possible computer averaging.

We inserted one pair of bipolar stimulating electrodes into the brain to straddle the optic chiasm, and in most experiments, we also placed several pairs of such electrodes into the visual cortex. We applied single pulses (0.1 ms duration, 100–500 μ A, < 1 Hz) across these electrodes. The optic chiasm electrodes were used to activate geniculate cells orthodromically from the optic tract; the cortical electrodes were used to activate these cells antidromically and thereby identify relay cells. For the extracellular recording experiments, we also inserted a pair of stimulating electrodes into the brainstem at A:0, L:2–4, and D:–19, an area representing the midbrain parabrachial region (Uhlrich et al. 1988). We stimulated this parabrachial region with square-wave pulse trains (100–500 μ A at 330 Hz and 50–80 ms duration) to activate its ascending input to the lateral geniculate nucleus (for reviews of the latter, see Singer 1977; Burke and Cole 1978; Sherman and Koch 1986, 1990; Steriade and Llinás 1988).

We presented flashed or moving targets on a frontal tangent screen to map neuronal receptive fields. We also introduced contrast modulated sinusoidal gratings into the receptive field to assess the spatial and temporal linearity of summation for the recorded neurons. The gratings were generated on a cathode ray tube with a maximum contrast of 0.6, a space average luminance of 40 cd/m², a modulation rate of 2 Hz, and a spatial frequency that could be continuously varied. All of the cells reported here were located in the A-laminae of the lateral geniculate nucleus (for an analogous report of C-laminae neurons, see Lo and Sherman 1990). For each of these cells, we identified the neuronal class (X or Y cell, on or off center). The X/Y identification was based on a battery of tests, including linearity of summation in response to the grating stimuli, receptive field center size, and response latency to optic chiasm stimulation (Lennie 1980; Stone 1983; Sherman 1985; Shapley and Lennie 1985).

Results

Overall, we recorded from a total of 133 geniculate neurons, 19 intracellularly and 114 extracellularly. The intracellular recording included 9 X and 10 Y cells, and the extracellular recording included 39 X and 75 Y cells. We also recorded extracellularly from 57 retinogeniculate axons, including 23 X and 34 Y cells. The intracellular and extracellular data were obtained from separate experiments using slightly different techniques (see Materials and methods). These geniculate neurons and retinogeniculate axons exhibited on or off center receptive fields in the expected proportions, but since we detected no other response property that correlated with on or off center type, we pooled across these center types for data analysis.

Intracellular responses of geniculate neurons

Our requirements for successful intracellular recording as described in Materials and methods were met for 19 neurons of the lateral geniculate nucleus, 9 X cells and 10 Y cells, all recorded in the A-laminae. We investigated each of these cells for the presence of electrical behavior

reflecting low threshold Ca²⁺ spikes. It is important to emphasize that, due to the nature of our *in vivo* recording, it was not possible to reveal the ionic basis of any recorded neuronal responses. Consequently, we could not demonstrate that the membrane voltage changes we observed were based on a conductance change to Ca²⁺ or any other specific ion. We instead relied on previously published criteria from *in vitro* recording (Jahnsen and Llinás 1984a,b; McCormick and Prince 1987; Crunelli 1989) to determine the presence of voltage behavior indicative of low threshold Ca²⁺ spikes (see also Deschênes et al. 1894; Hu et al. 1989a–c). Such spikes exhibit a triangular depolarization of 10–20 mV in amplitude and roughly 40 ms in duration. They occur with nearly all-or-none behavior and a threshold somewhat below that for a conventional action potential. A burst of 2–7 action potentials with interspike intervals of ≤ 4 ms typically rides on its crest. Finally, the low threshold spike displays a voltage dependency such that membrane voltages more depolarized than about –65 mV inactivate it, and only a depolarization from more hyperpolarized levels can activate it. We shall thus refer to these voltage responses simply as “low threshold spikes” and shall reconsider their relationship to low threshold Ca²⁺ spikes in Discussion.

Every one of the geniculate cells we studied exhibited low threshold spikes. It is also interesting in the context of the extracellular data presented below that burstiness in the action potential discharges of these neurons recorded intracellularly appeared *only* in association with low threshold spiking. In our description of these extracellularly recorded data, we note that occasional bursts of action potentials are characterized by interspike intervals of ≤ 4 ms followed by silent periods of > 100 ms. During intracellular recording, we *never* observed such short interspike intervals separated by silent periods except for action potentials riding the crests of low threshold spikes; we did observe such short interspike intervals during occasional epochs when a neuron's membrane potential was artificially depolarized by current injection, but the silent periods characteristic of the burstiness were not then evident. We thus conclude that the burstiness we recorded extracellularly reflects low threshold spiking.

Fig. 1 illustrates a typical low threshold spike recorded from a Y cell. In this case the membrane was held at –80 mV, which was a sufficiently hyperpolarized level to de-inactivate the spike. Also, at this level, the excitatory postsynaptic potential (EPSP) evoked monosynaptically by electrical stimulation of the optic chiasm was sufficient to trigger the low threshold spike roughly half the time. When this spike was not activated, only the evoked EPSP was clearly seen. At a membrane potential of –80 mV, the inhibitory postsynaptic potential (IPSP), which begins soon after the EPSP, was very close to its reversal potential and thus could not be clearly seen (Eysel 1976; Bloomfield and Sherman 1988). Fig. 1A shows two superimposed traces: the thicker trace (labeled a) shows a low threshold spike, and the thinner trace (labeled b) shows only the evoked EPSP. Notice that the threshold for the low threshold spike (*horizontal*

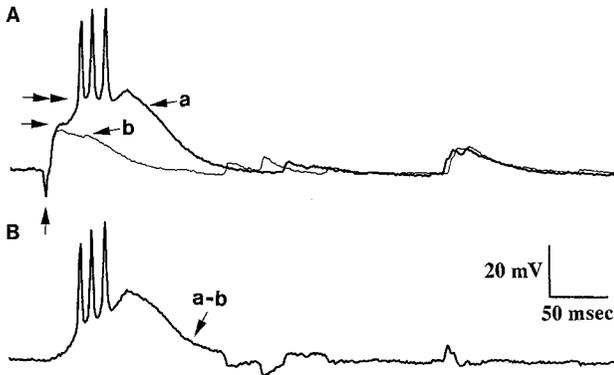


Fig. 1A, B. Example of a low threshold spike recorded from a geniculate Y cell. Action potentials in this figure, and others, are slightly clipped due to digitization of the recorded data. The cell membrane was held at -80 mV. At this membrane level, the low threshold spike was de-inactivated, and stimulation of the optic chiasm produced an EPSP that was sufficiently large to activate this spike roughly half the time. **A** Two superimposed traces showing responses to activation of the optic chiasm (vertical arrow). A low threshold spike is evoked in the thicker trace (a), with three action potentials riding its crest. In the thinner trace (b), only an EPSP is evoked from chiasm shock. The threshold for activation of the low threshold spike (horizontal arrow with single head) is 5–10 mV more hyperpolarized than the threshold for action potentials (horizontal arrow with double head). **B** Low threshold spike in isolation, achieved by subtracting the two traces (b from a) in **A**

arrow with single head) is roughly 10 mV below that for the action potentials (horizontal arrow with double head). Fig. 1B, which represents the difference between traces a and b in Fig. 1A, shows the low threshold spike somewhat more clearly by isolating it from the shock artifact and EPSP.

For several reasons, we interpret the larger evoked depolarization of Fig. 1 as a low threshold spike and not an EPSP component that is occasionally evoked. First, this larger depolarization shows a fairly sharp voltage dependency for de-inactivation and activation (see above), which is not characteristic of EPSPs. Second, the amplitude and time course of the larger depolarization, especially as revealed in Fig. 1B, is identical to the low threshold spike evoked by current injection (see below) and quite different from any EPSP seen. Third, the burst of action potentials riding the crest of the larger depolarization is a signature of low threshold spikes and was never seen in association with EPSPs. Thus by adjusting the membrane potential in this way in other neurons to the point at which EPSPs were evoked in isolation on some trials and low threshold spikes on others, we could readily identify the evoked low threshold spikes.

X cells. All 9 X cells were tested for the presence of low threshold spikes in the manner depicted by Fig. 2, and each of these exhibited such spikes. Fig. 2 shows the voltage dependency for the low threshold spike in a typical X cell. At membrane potentials more depolarized than about -65 to -70 mV for this cell, which had a resting potential of -60 mV, no low threshold spike was seen to the depolarizing current pulses (Fig. 2A,B). When

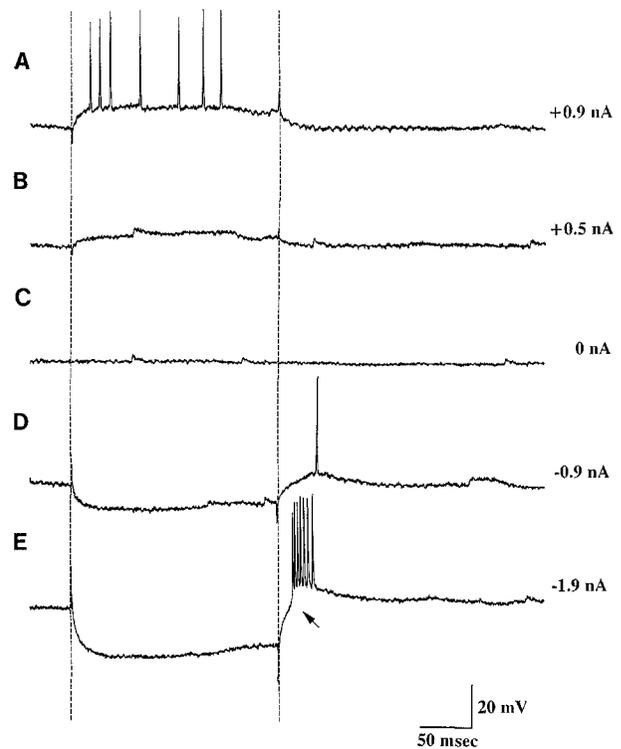


Fig. 2A–E. Demonstration of voltage dependency to de-inactivate the low threshold spike for an X cell. Current was injected into the cell during the time between the dashed vertical lines, and the amount of current injected is indicated to the right of each trace. **A–C** Failure to de-inactivate the low threshold spike. Depolarizations of the membrane by injected current or action potentials failed to elicit a low threshold spike, because the membrane had not been sufficiently hyperpolarized to de-inactivate it. **D** Near threshold for de-inactivation of the low threshold spike. Repolarization following cessation of the current pulse leads to a small overshoot that might represent a small low threshold spike. **E** Unambiguous de-inactivation of the low threshold spike. Thus passive repolarization of the membrane after cessation of the current pulse activates a low threshold spike (arrow)

hyperpolarized to -70 mV (Fig. 2D), the subsequent repolarization led to a small overshoot that might have been a small low threshold spike. However, if the 200 ms hyperpolarizing current pulse was large enough to hyperpolarize the cell to -82 mV (Fig. 2E), it reliably de-inactivated the low threshold spike so that the subsequent repolarization activated it (arrow).

Despite the fact that we could routinely elicit low threshold spikes in each of the 9 X cells by intracellular current injections, in which we first hyperpolarized the cell to de-inactivate the spikes and then activated them by releasing the hyperpolarizing current, we found such low threshold spikes to be extremely rare for recording epochs during which injected currents were held constant. That is, if spontaneous or evoked EPSPs were the only depolarizing events present, threshold was rarely reached and low threshold spikes were thus rarely activated. In fact, for 8 of the 9 X cells, even when their membrane potentials were at a level to de-inactivate low threshold spikes, as determined by current injection, chiasm stimulation never activated a low threshold spike. As noted below, this contrasts with the behavior of Y

cells, for which low threshold spikes were routinely activated from chiasm shock.

The one exceptional X cell is illustrated in Fig. 3, which shows responses to chiasm stimulation as a function of membrane potential. At a membrane potential of -55 mV (Fig. 3A), chiasm shock regularly elicits an EPSP that produces an action potential at a latency of 2.1 ms. At -70 mV (Fig. 3B), which is slightly too depolarized to de-inactivate the low threshold spike, an EPSP is evoked by chiasm activation, and occasionally this EPSP produces an action potential. At -80 mV (Fig. 3C), which de-inactivates the low threshold spike, the EPSP evoked from chiasm stimulation reliably ac-

tivates a low threshold spike, and riding on each is a brief, high frequency burst of action potentials. The other 8 X cells, when tested similarly, never responded with a low threshold spike to chiasm stimulation and instead simply produced fewer action potentials as their membrane potentials were increasingly hyperpolarized.

Y cells. As did the X cells, every one of the 10 Y cells tested displayed clear evidence of low threshold spikes. Fig. 4 shows the voltage dependency of the low threshold spike for a representative Y cell. The resting membrane potential for this cell was -55 mV. As in Fig. 2 for the X cell example, a depolarization activates a low threshold spike in this Y cell only if the membrane is sufficiently hyperpolarized prior to the depolarization (Fig. 4E).

A key difference between the X and Y cells in our sample is found in the ability of chiasm stimulation to activate low threshold spikes. For only 1 of the 9 X cells could such an ability be demonstrated, and this cell is illustrated in Fig. 3. However, for each of the 10 Y cells, chiasm shock reliably activated low threshold spikes. This difference between X and Y cells is statistically significant ($p < 0.001$ on a χ^2 -test).

Fig. 5 illustrates a typical example for the Y cell population, and it is comparable to the illustration of the X cell in Fig. 3. At a membrane level of -50 mV (Fig. 5A), no low threshold spikes were evident, and the cell responded 1.3 ms after every chiasm shock with an action potential that was then followed by an IPSP. At a polarization level of -60 mV (Fig. 5B), the cell produced no

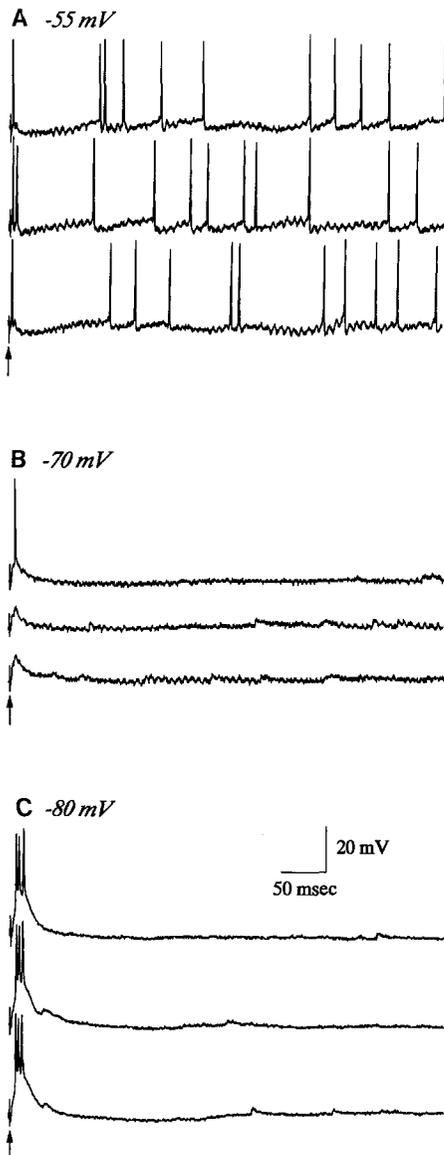


Fig. 3A–C. Effects of membrane voltage on responses to activation of the optic chiasm in an X cell. The shock artifacts are indicated by the arrows, and the membrane was held at different voltage levels by intracellular current injection prior to chiasm shock. **A** Membrane voltage level of -55 mV. **B** Membrane voltage level of -70 mV. **C** Membrane voltage level of -80 mV. In this cell, -80 mV reliably de-inactivated the low threshold spike, and chiasm shock at this membrane voltage level reliably activates low threshold spikes

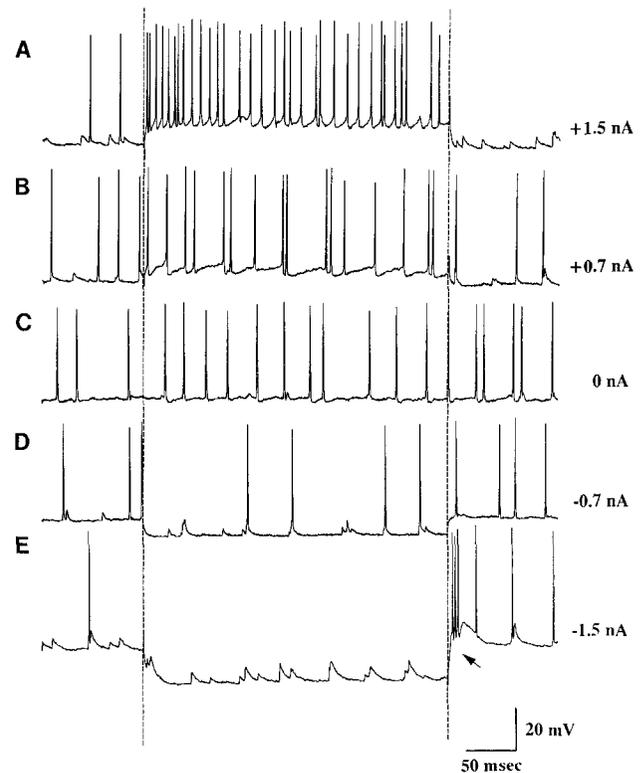


Fig. 4A–E. Demonstration of voltage dependency to de-inactivate the low threshold spike for a Y cell; conventions as in Fig. 2. Only in **E** was sufficient hyperpolarizing current injected into the neuron to de-inactivate the low threshold spike (arrow) reliably

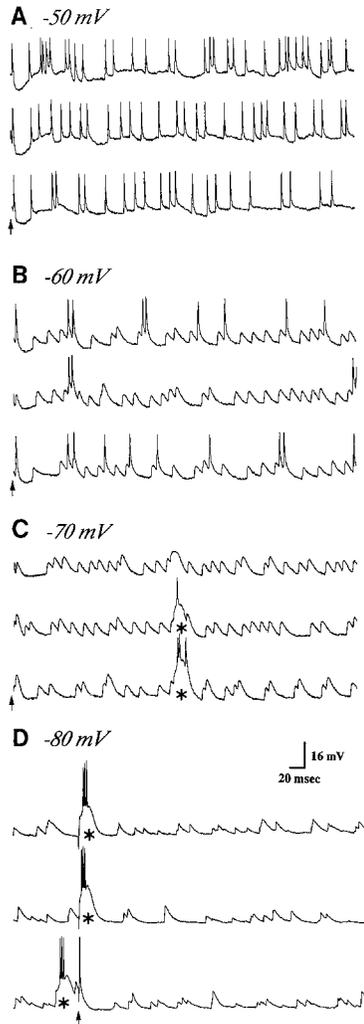


Fig. 5A–D. Effects of membrane voltage on responses to activation of the optic chiasm in a Y cell; conventions as in Fig. 3. The amplitude of action potentials was particularly variable during this recording (see Materials and methods). **A** Membrane voltage level of -50 mV. **B** Membrane voltage level of -60 mV. **C** Membrane voltage level of -70 mV. This membrane voltage was close to the level needed to de-inactivate the low threshold spike, and such spikes were commonly activated (*asterisks*), but only 50–250 ms after the chiasm shock (see text for details). **D** Membrane voltage level of -80 mV. At this membrane voltage, low threshold spike were reliably de-inactivated, and the EPSP evoked from chiasm shock activates them in the top two traces (*asterisks*). An exception to this is seen in the bottom trace due to a prior spontaneous low threshold spike (*asterisks*), because these spikes never occurred with an interval of less than 100 ms between them

clear low threshold spikes, and an action potential plus IPSP sequence usually began 1.3 ms after the chiasm shock, although occasionally only the EPSP and subsequent IPSP were seen. Fig. 5D shows that, if the cell is further hyperpolarized to -80 mV, thus de-inactivating the low threshold spike reliably, chiasm shock fairly regularly activates a low threshold spike from the monosynaptic EPSP.

Although we have not yet had the opportunity to study it systematically, we found in a number of our intracellular recordings of Y cells that, if we hyperpolarized the cell to a potential very close to that needed

to de-inactivate the low threshold spike, such spikes could often be activated by spontaneous EPSPs. An example of this phenomenon is shown in Fig. 5C after the cell was hyperpolarized to -70 mV. Low threshold spikes were evoked in the two lower traces (*asterisks*) at a relatively constant interval after the chiasm stimulation. In this example, the EPSP evoked monosynaptically from the chiasm shock failed to evoke a low threshold spike, possibly because the ensuing IPSP was needed to de-inactivate the spike more completely; in other examples (not illustrated), the monosynaptic EPSP as well as subsequent spontaneous EPSPs could activate low threshold spikes.

Fig. 5D illustrates another interesting phenomenon. Although chiasm shock regularly evoked low threshold spikes when the cell was hyperpolarized to -80 mV, such spikes spontaneously activated by EPSPs at other times are exceedingly rare at this membrane potential. However, an example of such a spontaneously occurring low threshold spike is shown in the bottom trace of Fig. 5D just before the chiasm shock, and, for this neuron, this was the only example out of more than 20 recorded chiasm shocks that failed to evoke a low threshold spike from the monosynaptic EPSP. This suggests that low threshold spikes may have a functional “refractory period” that limits their frequency of occurrence (see also Jahnsen and Llinás 1984a,b), and we never saw two such spikes separated by less than 100 ms in any responses from our neuronal sample.

Extracellular responses of geniculate neurons

Typical examples of X and Y cell responses. As noted in Introduction, geniculate neurons can display one of two response modes: *relay mode or burst mode*. We operationally defined the burst mode as noted above (i.e., epochs of 2–7 action potentials with interspike intervals of ≤ 4 ms, with the burst epochs separated by silent periods of > 100 ms). These different modes have very different consequences for retinogeniculate transmission (Sherman and Koch 1986, 1989; Steriade and Llinás 1988; Hu et al. 1989a–c; see also Discussion). Figs. 6 and 7 illustrate for a typical geniculate X and Y cell the major observations of our extracellular recording in this study, and most of the remainder of Results is devoted to further documentation of these observations.

Fig. 6 shows the responses of an X cell. During spontaneous activity (Fig. 6A), the neuron fired action potentials at fairly random intervals. Stimulation of the optic chiasm (Fig. 6B) usually resulted in an action potential with a latency of 1.8 ms, and after a variable refractory silent period of 100 ms or so, presumably due to an IPSP following the evoked action potential (see Eysel 1976; Bloomfield and Sherman 1988), the neuron’s firing pattern became indistinguishable from its pattern before chiasm shock. Stimulation of the midbrain parabrachial region, with or without subsequent chiasm activation (Fig. 6C,D), seemed not to affect the response properties of this cell. In other X cells, we did often see an elevated discharge rate after parabrachial activation

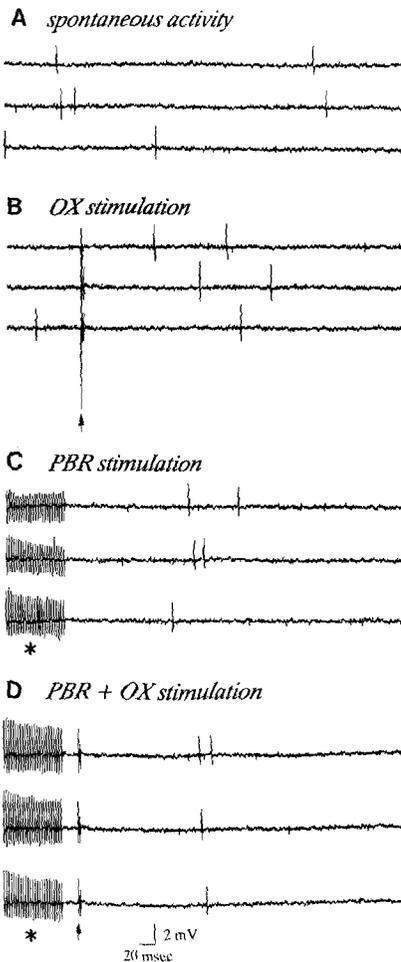


Fig. 6A–D. Traces of extracellular recording from a geniculate X cell during four different response periods. The *arrows* point to the shock artifacts following activation of the optic chiasm, and the *asterisks* indicate the shock artifacts due to activation of the parabrachial region. **A** Spontaneous activity. **B** Stimulation of the optic chiasm. **C** Stimulation of the parabrachial region. **D** Stimulation of the parabrachial region followed by optic chiasm shock. Although it is difficult to see at this time base, the cell responded to chiasm shock in both **B** and **D** with a latency of 1.8 ms

(Bloomfield et al. 1988; Uhlrich et al. 1989), but never did such activation induce bursty firing in these cells. In any case, the X cell shown in Fig. 6 showed no evidence of bursting under any of the illustrated conditions and seemed to remain in the relay mode throughout.

As Fig. 7 illustrates, the Y cell's responses were quite different. Fig. 7A shows no evidence of burstiness during spontaneous activity, although, as noted below, most Y cells exhibited limited periods of burst activity during spontaneous firing. However, chiasm activation, in addition to evoking an action potential with a latency of 1.2 ms, also caused the cell to enter the burst response mode in the ensuing 500 ms (Fig. 7B). Interestingly, although parabrachial activation alone had no discernible effect on the Y cell's response pattern (Fig. 7C), activation of this midbrain region beginning 100 ms before chiasm stimulation prevented the latter from increasing the neuron's burstiness (Fig. 7D). Thus the Y cell can be at least partly switched from the relay mode

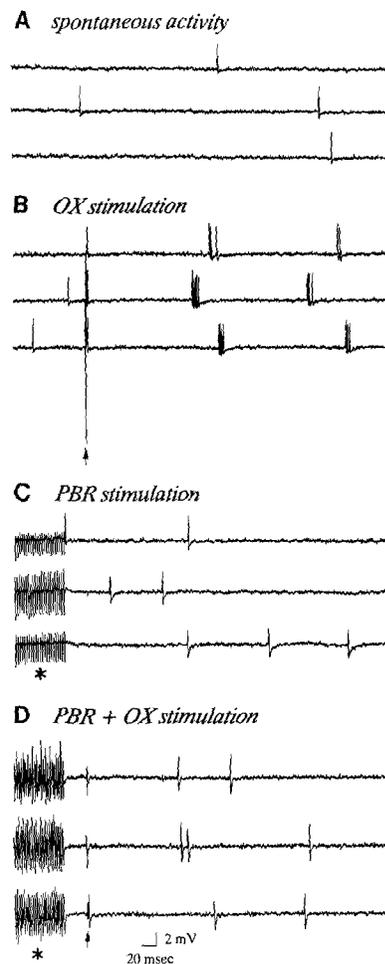


Fig. 7A–D. Traces of extracellular recording from a geniculate Y cell; conventions for **A–D** as in Fig. 6. The cell responded to chiasm stimulation in both **B** and **D** with a latency of 1.2 ms

to the burst mode by activation of the optic chiasm, but prior stimulation of the parabrachial region blocks this chiasm-induced phenomenon.

We did not systematically test each Y cell for the effect on these burst periods of varying the interval between parabrachial and chiasm stimulation. We concentrated instead on ensuring that every cell was tested with a standard 100 ms interval between the onset of the parabrachial activation and the chiasm shock. However, we did occasionally vary this interval for 6 of the Y cells, and from this we conclude that the effects of parabrachial stimulation (i.e., its ability to counter the tendency for chiasm stimulation to evoke burst responses from Y cells) last for roughly 500 ms.

Responses of the X and Y cell populations. To evaluate the generality of the X and Y cell examples illustrated in Figs. 6 and 7, we constructed interspike interval histograms for individual neurons and pooled them as follows. Each histogram represents the average of six 500 ms sampling periods chosen during the different conditions shown in Figs. 6B, D and 7B, D, which corresponds to the response to activation of the optic chiasm alone and the response to this activation when it occurs

100 ms after stimulation of the parabrachial region of the midbrain. Thus all interspike intervals ≤ 20 ms were determined, and the ordinates of the resultant histograms were divided by six to obtain an average histogram of interspike intervals for one 500 ms period. We recorded the interspike intervals following optic chiasm stimulation (as in Figs. 6B and 7B) for every one of the 39 X and 75 Y cells, and for a subset of 17 X and 25 Y cells we also recorded these intervals following stimulation of both the parabrachial region and optic chiasm (as in Figs. 6D and 7D).

Fig. 8 shows population histograms derived from pooling the interspike interval histograms from individual cells as follows. The average histogram for each cell provided a single value for each interspike interval, and the population histograms reflect the mean \pm standard error for each interval. Note that, while the burst periods are represented by interspike intervals of ≤ 4 ms, it is possible that some of these short interspike intervals do not reflect bursts as we have defined them, because

these histograms do not reflect the other feature of bursts: the lengthy silence between bursts. Nevertheless, our qualitative observation is that such short interspike intervals rarely occur outside of bursts under our recording conditions.

Fig. 8 reveals little evidence of bursting in response to chiasm stimulation for the X cell population. That is, interspike intervals of ≤ 4 ms represented few of those for X cells (8% of the intervals in Fig. 8A, 15% in Fig. 8B, and 15% in Fig. 8C). Also, Fig. 8B, C shows that the additional parabrachial activation caused no statistical difference in the occurrence of shorter intervals following chiasm shock ($p > 0.1$ on a χ^2 -test). Y cells, however, were induced to burst by chiasm shock (Fig. 8D, E), but prior activation of the parabrachial region strongly countered this inducement to burst (Fig. 8F). Interspike intervals of ≤ 4 ms were much more common in Y cells responding to chiasm shock alone than to chiasm shock after parabrachial activation (57% of the intervals in Fig. 8D, 55% in Fig. 8E, and only 27% in Fig. 8F), and

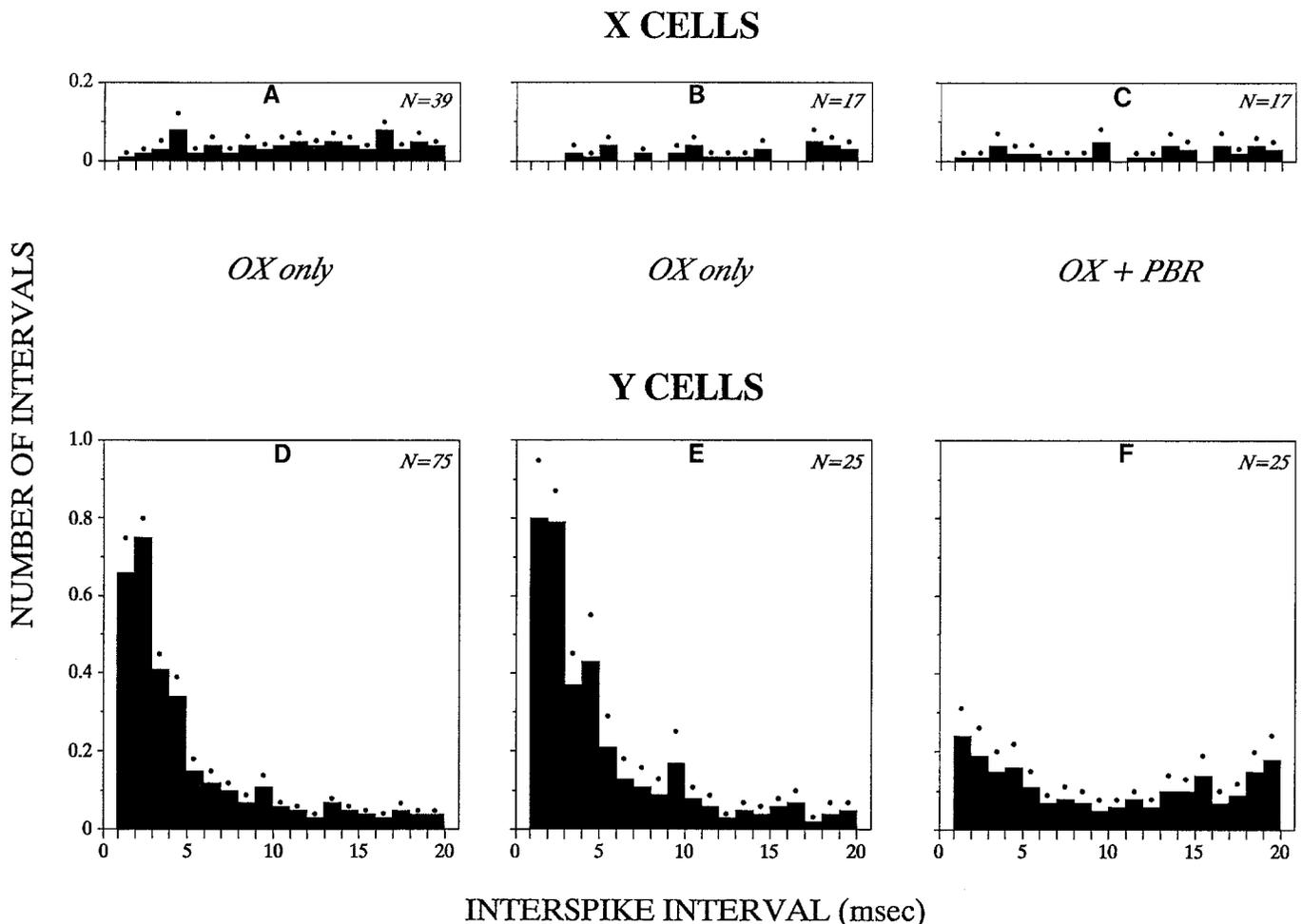


Fig. 8A-F. Frequency histograms of interspike intervals for geniculate X and Y cell populations. Each of these histograms represents an average of pooled data from individual cells (see text for details), and the ordinates of the resultant histograms have been adjusted to represent the interspike intervals for an "average" cell during a 500 ms period. Thus each cell contributes a single datum for each interspike interval, and the distance of the dot above each bar

represents the standard error of these measurements. **A-C** X cells. The average histogram for all 39 neurons following stimulation of the optic chiasm only (OX only) is shown in **A**, and for a subset of 17, these histograms are shown both for chiasm stimulation alone in **B** as well as for chiasm plus parabrachial activation (OX + PBR) in **C**. **D-F** Y cells; conventions as in **A-C**

these differences are statistically significant ($p < 0.001$ on a χ^2 -test). Finally, while chiasm stimulation by itself generated a higher proportion of these shorter interspike intervals in Y cells compared to X cells ($p < 0.001$ on a χ^2 -test), the addition of prior parabrachial stimulation removes this difference between cell classes ($p > 0.1$ on a χ^2 -test).

We further characterized the response properties of these cells by computing the probability of detecting a burst discharge in a given 500 ms sampling period, using the abovementioned definition for a burst response. The burst probability assigned to a given sampling period was 0 or 1, and these were averaged across at least six randomly chosen sampling periods for each of the conditions tested (no stimulation or various stimulation combinations of the optic chiasm and parabrachial region). A probability of burst discharge was thus computed for each cell in the different stimulation conditions, and these data are summarized in Fig. 9. We found that, by our criteria, every single Y cell showed at least some

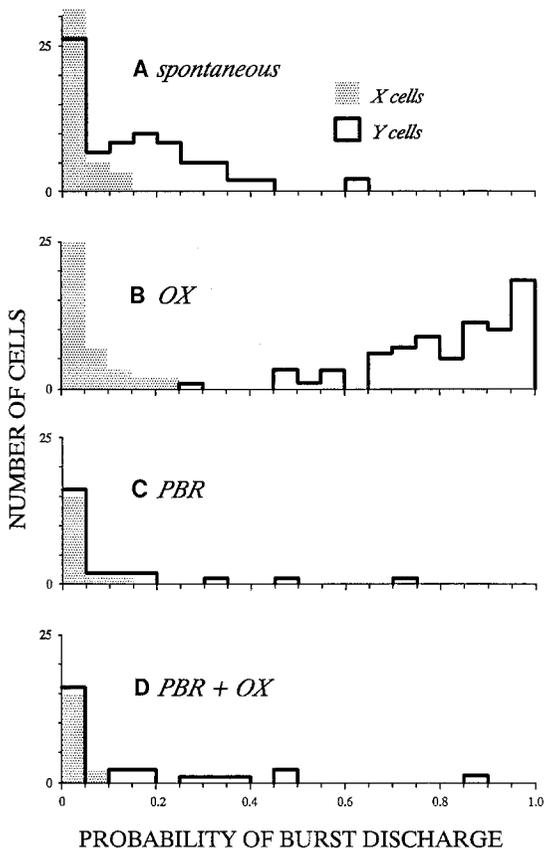


Fig. 9A–D. Frequency histograms of the probability of burst discharge for geniculate X and Y cells. These probabilities were computed for each cell and stimulus condition shown. A probability of 0 means that the cell never exhibited interspike intervals ≤ 4 ms during any of the 6 or more 500 ms sampling periods; a probability of 1 means that every sampling period included at least one such interspike interval; and an intermediate probability represents the fraction of sampling periods during which at least one such interspike interval occurred (see text for details). **A** Burst probabilities during spontaneous activity. **B** Burst probabilities following activation of the optic chiasm. **C** Burst probabilities following parabrachial activation. **D** Burst probabilities evoked by activation of the parabrachial region plus the optic chiasm

periods of bursting, particularly in response to chiasm activation, but 19 of the 39 X cells failed to exhibit a single such epoch of burstiness during any response period. This difference between cell types is statistically significant ($p < 0.001$ on a χ^2 -test).

The probability of burst discharges was low for X cells in all four stimulus conditions illustrated in Fig. 9, and no statistically significant differences were seen among these X cell distributions. The mean probabilities for the X cells were 0.03 for spontaneous activity, 0.05 following chiasm stimulation, 0.01 after parabrachial stimulation, and 0.01 after parabrachial stimulation followed by chiasm shock. These values for Y cells were, respectively, 0.15, 0.83, 0.09, and 0.13.

We draw several conclusions from these comparisons. First, in the conditions without parabrachial stimulation (Fig. 9A, B), Y cells were more likely to burst than were X cells ($p < 0.001$ on the Mann–Whitney U-test during both spontaneous activity and after chiasm shock). Second, parabrachial stimulation (Fig. 9C, D) made the burst probabilities much more similar between these cell types, although the Y cells remained slightly more bursty ($p < 0.05$ for both comparisons on the Mann–Whitney U-test). Third, as expected from the analyses of interspike intervals, chiasm shock made the Y cells much more likely to burst ($p < 0.001$ on the Mann–Whitney U-test). Fourth and finally, although parabrachial stimulation by itself had little effect on Y cell burst probabilities, it counteracted the effects of chiasm shock so that parabrachial plus chiasm stimulation produced a probability of burst discharge in Y cells that was less than that evoked by chiasm shock alone ($p < 0.001$) and not different from that seen during spontaneous activity ($p > 0.1$; Mann–Whitney U-test for both comparisons).

As seen from Fig. 9, there was considerable variability among neurons regarding their likelihood of bursting. However, we found no correlation between this variable and any other feature that we recorded for these cells, including receptive field center size, the on or off nature of the center response, or the response latency to activation of the optic chiasm. We also sought to determine if the probability of burst discharge correlated for individual neurons between the two conditions of spontaneous activity and response to chiasm stimulation. Both cell classes displayed a weak but significant correlation, but, curiously, this correlation was *positive* for X cells ($r = +0.57$; $p < 0.001$) while it was *negative* for Y cells ($r = -0.26$; $p < 0.05$). This difference in correlation coefficient between X and Y cells is statistically significant ($p < 0.001$). In other words, X cells most likely to burst during spontaneous activity remain so in response to chiasm shock, but the reverse is true for Y cells. Whatever the explanation for this, it suggests that the mechanisms controlling the relay versus burst response modes may be quite different for these two cell classes.

Effects of anesthesia on response modes. A striking finding noted above for Y cells is the effect that activation of the parabrachial region can have on the cell's tendency to respond in its relay versus burst firing mode. Since the

ascending pathways from the brainstem to thalamus have been implicated in various forms of arousal, attention, and wakefulness (Burke and Cole 1978; Livingstone and Hubel 1981; Sherman and Koch 1986, 1990; Steriade and Llinás 1988), we wondered what affect different conditions of anesthesia might have on these response modes. Although this might yield interesting results, we were not prepared to test the effects of differing levels of anesthesia, because we always maintained our preparations under constant and fairly deep anesthesia. However, we did vary the type of anesthesia between Halothane and barbiturate (see Materials and methods). For 7 of the tested X cells and 15 of the Y cells, Halothane was the anesthetic; for the remaining 32 X and 60 Y cells, barbiturate was used. We found no discernible difference made by the anesthetic on any of our tests for relay versus burst response modes.

Extracellular responses of optic tract axons

It is clear from the above that geniculate neurons can often exhibit periods of bursting activity, that the tendency to burst is much greater among Y cells than among X cells, and that different stimulus conditions (such as optic chiasm and/or parabrachial stimulation) can alter the probability of a neuron being in its relay or burst response mode. As noted earlier, these response modes have very different and dramatic effects on retinogeniculate transmission (Sherman and Koch 1986, 1990; Steriade and Llinás 1988). If this interpretation were correct, then the sort of bursting responsiveness described here should be an emergent property of geniculate neurons and not be seen among their retinogeniculate afferents.

To document this, we analyzed the extracellularly recorded responses of retinogeniculate X and Y axons. These axons were recognized on the basis of several criteria: they followed optic chiasm stimulation with virtually no latency jitter; the response latencies to such stimulation (0.6–1.1 ms for X axons and 0.3–0.8 ms for

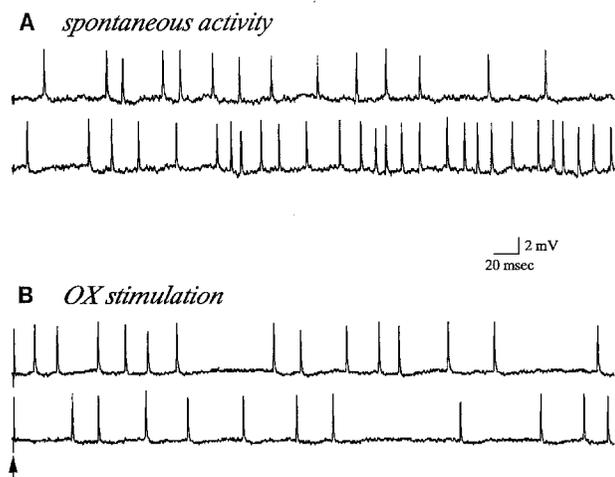


Fig. 10A, B. Traces from extracellular recording of a retinogeniculate X axon in the optic tract. **A** Spontaneous activity. **B** Stimulation of the optic chiasm. The shock artifact (*arrow*) obscures the action potential evoked at a latency of 0.8 ms

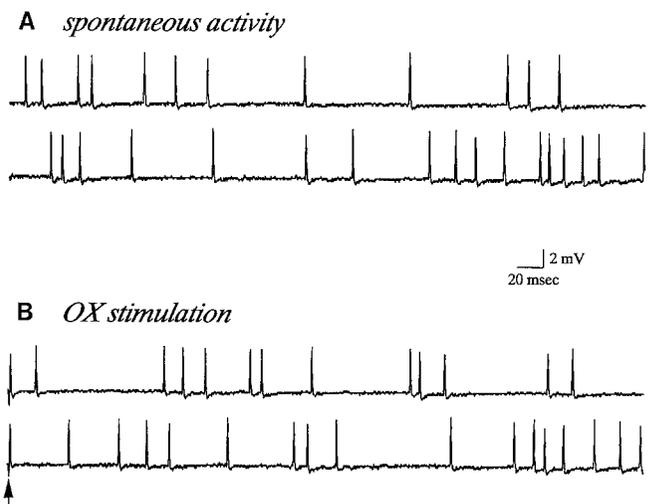


Fig. 11A, B. Traces from extracellular recording of a retinogeniculate Y axon in the optic tract; conventions as in Fig. 18. The response latency to chiasm stimulation was 0.3 ms

Y axons) were typically at least 0.5 ms shorter than that of the corresponding class of geniculate neuron (in our sample of geniculate neurons, 1.6–2.4 ms for X cells and 0.8–1.5 ms for Y cells); and they could never be antidromically activated from cortex. Also, most retinal axons were recorded in the optic tract subjacent to the lateral geniculate nucleus. As noted below, the response properties of these retinal axons differed in several ways from those of their corresponding class of geniculate cell.

Figs. 10 and 11 show recordings from a typical X and Y axon. These figures illustrate the complete lack of burstiness among these retinogeniculate axons, and none of our sample of these axons displayed any evidence of burst responses. That is, we never saw a single interspike interval ≤ 4 ms in any of our 500 ms sampling periods for the retinogeniculate axons. This is particularly notable for the Y axons following chiasm stimulation (e.g., Fig. 11B), given the observation that chiasm shock typically evokes burstiness in geniculate Y cells. We frequently recorded these axons in electrode tracks from which we had previously recorded geniculate neurons with evidence of burst response periods. It thus seems clear that the evidence for burst response modes that we often saw in geniculate neurons, particularly in Y cells, is a property not seen among retinogeniculate afferents.

Discussion

Geniculate circuitry acts on the intrinsic functional properties of relay cells to control the gain of retinogeniculate transmission (Singer 1977; Burke and Cole 1978; Sherman and Koch 1986, 1990; Steriade and Llinás 1988). On the one hand, these relay neurons have a multiplicity of active conductances that greatly affect their mode of response to retinal input. On the other hand, the vast majority (80–90%) of synaptic input formed onto these relay cells is nonretinal in origin, and these nonretinal inputs regulate the active conductances to modulate retinogeniculate transmission. Perhaps the most striking of the active conductances in thalamic

neurons is the voltage-sensitive, low threshold, Ca^{2+} conductance, or low threshold spike, which leads to brief periods of high frequency action potentials. Jahnsen and Llinás (1984a,b) proposed that this conductance can switch the neuron's response mode from the *relay mode*, during which sensory (e.g., retinal) information is relayed fairly faithfully to cortex, to the *burst mode*, during which little or no such sensory information can be relayed, and the cell discharges mainly in high frequency bursts. Such low threshold spikes and/or their associated burst discharges have been repeatedly demonstrated for relay cells in many thalamic nuclei, including the cat's lateral geniculate nucleus (Hubel 1960; Hubel and Wiesel 1961; McIlwain and Creutzfeldt 1967; McCarley et al. 1983; McCormick and Prince 1987; McCormick and Pape 1988; Crunelli et al. 1989; Hu et al. 1989a–c).

In this study, we have been able to demonstrate that both X and Y cells of the cat's lateral geniculate nucleus are able to express low threshold spikes, although there seem to be subtle differences in this spiking between cell classes. Because our intracellular recording indicates that the high frequency bursts of action potentials occur only during low threshold spikes, we conclude that these bursts, which we commonly observed in geniculate neurons, especially in Y cells following activation of the optic chiasm, reflect such low threshold spikes. Since such a response mode is never seen in retinogeniculate axons, this bursting indeed reflects a property of retinogeniculate transmission, during which the geniculate neuron has slipped from its relay response mode to its burst mode. Finally, we provide evidence that activity in the input to the lateral geniculate nucleus from the parabrachial region may help to prevent this bursting and thus promote the relay response mode in geniculate cells. This last conclusion is in agreement with recent proposals suggesting that cholinergic input from the parabrachial region of the midbrain can control low threshold spikes, and thus the response mode, in thalamic neurons (McCormick and Prince 1987; see also Hu et al. 1989a–c).

Differences between X and Y cells

We noted obvious differences between geniculate X and Y cells in terms of their low threshold spikes and burst responses. During intracellular recording, Y cells, when their low threshold spikes were de-inactivated, readily activated these spikes from EPSPs. However, for X cells, analogous EPSPs that occurred during de-inactivation of the low threshold spike generally seemed too small to achieve such activation. Although we did not systematically measure such EPSP amplitudes for the present study, our clear impression was that EPSPs of Y cells were larger than those of X cells, which is consistent with a similar conclusion reported by Bloomfield and Sherman (1988).

This difference between X and Y cells during intracellular recording was paralleled by a related difference seen during extracellular recording. Although both neuronal populations exhibited some periods of burstiness, which was never seen in their retinogeniculate

afferents, these periods were significantly more common for Y than for X cells. Every Y cell showed some evidence of burst response modes, but only slightly more than half of our X cell population (20 of 39) did so. This difference between cell types was relatively small during spontaneous activity but much more marked in response to activation of the optic chiasm; such activation greatly enhanced the periods of burstiness for Y cells and had little effect on X cells. Thus, under our recording conditions, Y cells are much more likely to generate low threshold spikes and are more likely to enter their burst response mode than are X cells.

However, the above conclusions are based on spontaneous activity and the responses to electrical activation, not responses to effective visual stimuli. Thus the EPSPs we recorded tended to be individual events with virtually no temporal summation. With visual stimulation that strongly activates geniculate neurons, the EPSPs can arrive at sufficiently high frequency to sum temporally, thus producing a much larger depolarization than the individual EPSPs can create (our unpublished observations). Thus, it is possible that, while Y cells can readily activate a low threshold spike with both spontaneous and visually driven EPSPs, X cells can do so only with the latter. This needs to be tested with intracellular recording during visual stimulation.

Nevertheless, our data suggest that Y cells are more readily switched into the burst response mode than are X cells, and that parabrachial activation can keep Y cells in the relay mode (see also below). We also obtained indirect evidence that the mechanisms controlling response modes for geniculate neurons might be very different for X and Y cells. The weak *negative* correlation for Y cells in the probability of bursting between periods of spontaneous activity and those following chiasm stimulation suggest that such stimulation fundamentally alters response modes for these cells. Conversely, the *positive* correlation for X cells suggests very little effect of chiasm shock on response modes for these cells. This, in turn, suggests the possibility that the physiological mechanisms and neuronal pathways controlling these response modes differ between X and Y cells, although we have only begun to investigate this question.

Effects of parabrachial activation

Another possible difference between X and Y cells relates to the effects of parabrachial activation. Such activation essentially countered the effect of chiasm stimulation for Y cells but had no detectable effect on burstiness in X cells. Should X cells exhibit low threshold spikes and bursty responses to visual stimulation (see above), it would then be interesting to explore the effects of parabrachial activation on these responses.

The mechanism of the parabrachial effect on Y cells has yet to be determined, since we have not yet adequately studied this phenomenon with intracellular recording. However, parabrachial stimulation does depolarize most relay cells (Bloomfield et al. 1988; Hu et al. 1989b), and this may promote inactivation of the low threshold spike. Also, evidence from *in vitro* studies (McCormick and

Prince 1987) indicates that ACh, which is the neurotransmitter for most parabrachial axons (De Lima and Singer 1987; Smith et al. 1988), prevents the occurrence of low threshold spikes.

Implications for retinogeniculate transmission

Prior *in vitro* studies (McCormick and Prince 1987) demonstrate that practically every geniculate relay cell in the cat exhibits low threshold spikes with the accompanying high frequency bursts of action potentials indicative of the burst response mode. This in turn suggests that, under the proper conditions, every relay cell can alternate between the relay and burst response modes. We can now generally extend this conclusion to the *in vivo* preparation, although it is not yet clear from our data that every X cell can readily enter the burst mode under physiological conditions. Because the shift between these response modes dramatically alters the gain of retinogeniculate transmission, this demonstrates that the combination of extraretinal inputs to geniculate relay cells plus certain intrinsic properties of these cells can strongly influence the extent of retinal information relayed to cortex.

Acknowledgements. This work was supported by USPHS research grant EY03038 and postdoctoral fellowship EY06082.

References

- Bloomfield SA, Hamos JE, Sherman SM (1987) Passive cable properties and morphological correlates of neurones in the lateral geniculate nucleus of the cat. *J Physiol (Lond)* 383: 653–692
- Bloomfield SA, Sherman SM (1988) Postsynaptic potentials recorded in neurons of the cat's lateral geniculate nucleus following electrical stimulation of the optic chiasm. *J Neurophysiol* 60: 1924–1945
- Bloomfield SA, Uhlrich DJ, Sherman SM (1988) The effects of brainstem stimulation on neurons in the cat's lateral geniculate nucleus. *ARVO Abstr* 29: 295
- Burke W, Cole AM (1978) Extraretinal influences on the lateral geniculate nucleus. *Rev Physiol Biochem Pharmacol* 80: 105–166
- Crunelli V, Lightowler S, Pollard CE (1989) A T-type Ca^{2+} current underlies low-threshold Ca^{2+} potentials in cells of the cat and rat lateral geniculate nucleus. *J Physiol (Lond)* 413: 543–561
- 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
- De Lima AD, Singer W (1987) The brainstem projection to the lateral geniculate nucleus in the cat: identification of cholinergic and monoaminergic elements. *J Comp Neurol* 259: 92–121
- Deschênes 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
- Eysel UTh (1976) Quantitative studies of intracellular potentials in the lateral geniculate nucleus of the cat with respect to optic tract stimulus response latencies. *Exp Brain Res* 25: 469–486
- Hu B, Steriade M, Deschênes M (1989a) The effects of brainstem peribrachial stimulation on perigeniculate neurons: the blockage of spindle waves. *Neuroscience* 31: 1–12
- Hu B, Steriade M, Deschênes M (1989b) The effects of brainstem peribrachial stimulation on neurons of the lateral geniculate nucleus. *Neuroscience* 31: 13–24
- Hu B, Steriade M, Deschênes M (1989c) The cellular mechanism of thalamic ponto-geniculo-occipital waves. *Neuroscience* 31: 25–35
- Hubel DH (1960) Single unit activity in lateral geniculate body and optic tract of unrestrained cats. *J Physiol (Lond)* 150: 91–104
- Hubel DH, Wiesel TN (1961) Integrative action in the cat's lateral geniculate body. *J Physiol (Lond)* 155: 385–398
- Jahnsen H, Llinás R (1984a) Electrophysiological properties of guinea-pig thalamic neurones: an *in vitro* study. *J Physiol (Lond)* 349: 205–226
- Jahnsen H, Llinás R (1984b) Ionic basis for the electro-responsiveness and oscillatory properties of guinea-pig thalamic neurones *in vitro*. *J Physiol (Lond)* 349: 227–247
- Lennie P (1980) Parallel visual pathways. *Vision Res* 20: 561–594
- Livingstone MS, Hubel DH (1981) Effects of sleep and arousal on the processing of visual information in the cat. *Nature* 291: 554–561
- Lo F-S, Sherman SM (1989) Dependence of retinogeniculate transmission on membrane voltage in the cat: differences between X and Y cells. *Eur J Neurosci* 1: 204–209
- Lo F-S, Sherman SM (1990) *In vivo* recording of postsynaptic potentials and low threshold spikes in W cells of the cat's lateral geniculate nucleus. *Exp Brain Res* 81: 438–442
- 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, Pape H-C (1988) Acetylcholine inhibits identified interneurons in cat lateral geniculate nucleus. *Nature* 334: 246–248
- McCormick DA, Prince DA (1987) Actions of acetylcholine in the guinea pig and cat medial and lateral geniculate nuclei, *in vitro*. *J Physiol (Lond)* 392, 147–165
- 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
- Shapley R, Lennie P (1985) Spatial frequency analysis in the visual system. *Ann Rev Neurosci* 8: 547–583
- 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. Elsevier, pp 233–314
- Sherman SM, Koch C (1986) The control of retinogeniculate transmission in the mammalian lateral geniculate nucleus. *Exp Brain Res* 63: 1–20
- Sherman SM, Koch C (1990) Thalamus. In: Shepherd GM (ed), *Synaptic organization of the brain*, 3rd edn. Oxford University Press, New York, pp 246–278
- 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
- Singer W (1977) Control of thalamic transmission by corticofugal and ascending reticular pathways in the visual system. *Physiol Rev* 57: 386–420
- Smith Y, Paré D, Deschênes M, Parent A, Steriade M (1988) Cholinergic and non-cholinergic projections from the upper brainstem core to the visual thalamus in the cat. *Exp Brain Res* 70: 166–180
- Steriade M, Llinás RR (1988) The functional states of the thalamus and the associated neuronal interplay. *Physiol Rev* 68: 649–742
- Steriade M, Paré D, Parent A, Smith Y (1988) Projections of cholinergic and non-cholinergic neurons of the brainstem core to relay and associational thalamic nuclei in cat and monkey. *Neuroscience* 25: 47–67
- Stone J (1983) *Parallel processing in the visual system*. Plenum, New York
- Uhlrich DJ, Cucchiari JB, Sherman SM (1988) The projection of individual axons from the parabrachial region of the brainstem to the dorsal lateral geniculate nucleus in the cat. *J Neurosci* 8: 4565–4575
- Uhlrich DJ, Tamamaki N, Murphy PC, Sherman SM (1989) Brainstem modulation of geniculate cells in cats. *Soc Neurosci Abstr* 15