

INHIBITORY MECHANISMS WITHIN THE RECEPTIVE FIELDS OF THE LATERAL GENICULATE BODY OF THE CAT

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Abstract. The spatiotemporal organization of receptive fields (RF) of neurons in lateral geniculate body (LGB) was analyzed using several experimental methods. The stimulation of the RF by two separate spots showed largely extended inhibitory field overlapping also the central region. The increase of light-adaptation or barbiturate anesthesia levels enhanced the effectiveness of RF inhibitory surround in qualitatively different manner. The correlated neurons pairs were found, showing the reciprocal arrangement of inhibitory and excitatory areas of their RFs. It was possible to identify some of these pairs as consisting of relay cell and intergeniculate interneuron. The neurons from perigeniculate nucleus were also investigated. They had a synaptic input from the retina and were not activated antidromically from the visual cortex. Their RFs were large with non-concentric ON-OFF type of organization. Both types of geniculate interneurons were used to propose a functional model of LGB circuitry reviewing the data of all presented experiments.

INTRODUCTION

The receptive field (RF) of the cell of lateral geniculate nucleus (LGN) is very similar to the retinal one (5, 6, 9, 11, 13, 16, 18). They

have approximately the same size and both of them are organized in two antagonistic concentric regions. Hubel and Wiesel (6) showed however, that the surround of the LGN-cell RF is more powerful in antagonizing the center response than the surround of the ganglion cell. This led these authors to put forth suggestion that the surround of geniculate RF results from the projection of the centers of retinal RFs. Many groups of authors, using different experimental methods, have corroborated the suggestion of Hubel and Wiesel. Stevens and Gerstein (13) introduced a new method, which represents the firing probability as a function of space and time. Their data induced them to propose that retinal excitatory surrounds rather than retinal centers generate the inhibitory surround of the LGN RF. This proposal agrees partially with a model of Dubin and Cleland (4), who moreover suggested the presence of a recurrent inhibitory influence from extrageniculate interneurons (1, 4, 8).

The present paper reviews our recent experiments in which we used the modified Stevens and Gerstein methods. Our data support the conclusions of Stevens and Gerstein (13) and of Dubin and Cleland (4). We have examined also the receptive fields of both intra- and extrageniculate interneurons, which fit well to the functional LGN model.

METHODS

The experiments were performed on adult cats in which the pretrigeminal section was performed. In a few experiments only local anesthetics were used, after protecting the animal from any other source of pain (see 13 and 19). Cats were immobilized by Flaxedil, therefore, artificial respiration was used. The CO₂ content in expiratory air was monitored and kept between 3.5 and 4%. Pupils were dilated with atropine, and refraction was corrected by +1D contact lenses.

Tungsten in lacquer microelectrodes were used for recording and marking the electrode position by means of electric current. The physiological data (10) and/or histology determined finally the recording points.

Stimuli were small bars of light ($0.25^\circ \times 0.75^\circ$ up to $2^\circ \times 4^\circ$ visual angle) of 5 cd/m² luminance projected onto a perimeter-like screen. Different light-adaptation levels were reached by means of another light bar ($0.5^\circ \times 2^\circ$) of varied luminance placed in RF center.

The cell's spatiotemporal firing pattern was analyzed in terms of "response planes (RPs)" and/or "contour planes" (13, 17). The response plane (Fig. 3, top row) is a stereoscopic view of 27 post-stimulus time histograms obtained "simultaneously" for cyclic stimulation of 27 sepa-

rate points spread over the RF axis by a small testing bar. The two-spot RP is similar, but with the second stimulating bar added at the center of the RF and switched on and off with different offset times in relation to the testing bar (Fig. 3, second row). The contour plane is a projection of response plane on the spatiotemporal plane as shown in Fig. 1.

The detailed method with the technique of response analysis is fully described in an earlier paper (17).

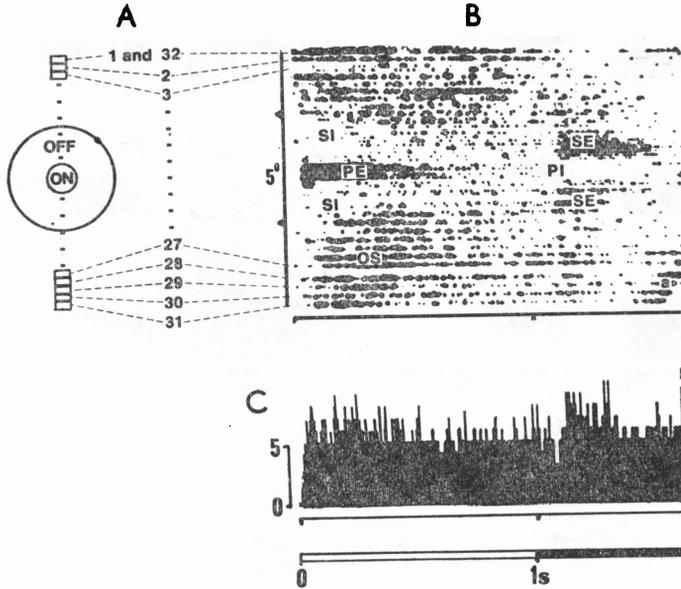


Fig. 1. *A*, the classic plot of the ON-center LGN-cell receptive field with 31 points of stimulation along the RF axis. Stimulus: $1^\circ \times 0.5^\circ$ bar of light of 5 cd/m^2 luminance, *B*, contour plane of the field shown in *A*. 31 lines show the cell responses to stimulation of appropriate points on RF axis. Two repetitions of the stimulus in every point. Each dot represents one spike. The calibration in visual degrees to the left. Dark and white domains formed on the plane are marked as follows: PE, (primary excitatory) describes spatiotemporal characteristic of center response; SE, (secondary excitatory) refer to opposite type excitatory surround; SI, (secondary inhibitory) can be considered as a result of activation of inhibitory surround; PI (primary inhibitory) correspond partially to centrally induced reciprocal inhibition (12, 18); OS, low strength tertiary domains; most probably refer to the outer surround described by Hammond (5); a, artificial intensification of the oscilloscope screen. *C*, sum-PST-histogram representing integrated in space spikes from all responses shown in *B*. Same time axis as in *B*, white bar, stimulus ON-time; dark bar, stimulus OFF-time. 2 ms bin width. Calibration of number of impulses to the left.

RESULTS

The potentiation of inhibition in the LGN-cell RF in relation to the retinal one. Figure 2 shows data obtained during simultaneous recording of activity of a pair of units: afferent retinal fiber (A) and its target,

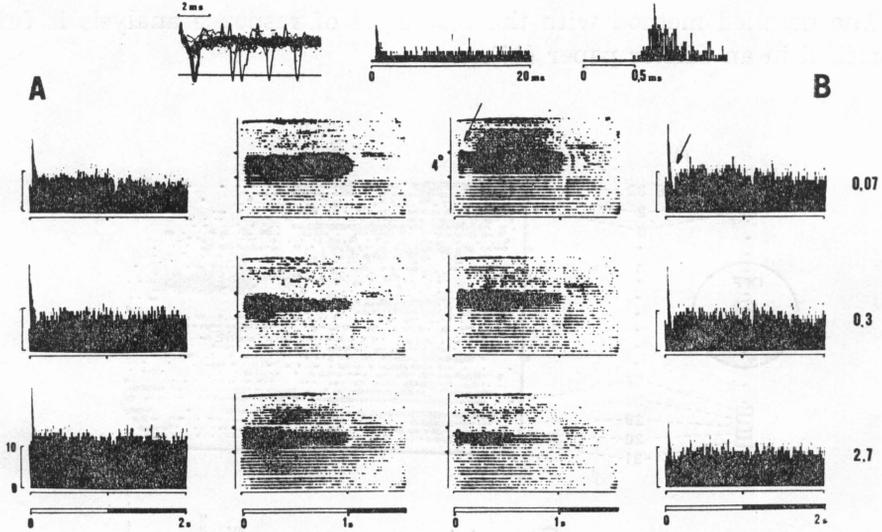


Fig. 2. Analysis of double recording of OT (A) and LGN-cell (B) spikes. Top row, left side: oscilloscope trace showing OT fiber spikes (up-going, negative pulses) and LGN-cell action potentials; both retouched. Several superimposed sweeps triggered by retinal spikes. To the right: cross-correlograms $A \rightarrow B$; same data, different magnification of time base. A, (left two columns) PST-sum-histograms and corresponding contour planes of retinal RF in three light adaptation levels. B, (right two columns) contour planes and appropriate PST-sum-histograms of LGN cell RF. Stimulus: bar of light $0.5^\circ \times 1^\circ$ of 5 cd/m^2 luminance. Six repetitions of the stimulus in each point. Background luminance values in od/m^2 noted on the right side of each row.

the LGN-cell (B). The following differences can be observed between the A- and B-unit firing patterns: (i) reduction of the frequency of firing irrespective of the light-adaptation level as shown in consecutive rows by total number of spikes counted in PST-sum-histograms; (ii) narrowing of the primary excitatory domains as seen on contour planes taken in mesopic adaptation levels; (iii) simultaneous potentiation of inhibitory surround (see also 17 and 18); (iv) appearance of post-phasic inhibitory period (arrows) seen in LGN-cell ON-responses in all adaptation levels; (v) appearance of oscillations for turning OFF the stimulus in the central region of the LGN-cell RF (well seen in scotopic level of adaptation).

These observations point out to an increased inhibitory action taking place on the LGN-cell level, as discussed in the previous paper (18) and by other authors (5, 6, 8, 9, 11, 16).

The strength and spatial extent of inhibitory influences. Figure 3 shows the results of a two-spot type experiment as recorded on one ON-center LGN-cell (19, Wróbel and Gerstein, in preparation). The top response planes in Fig. 3 are control ones, obtained as described in the

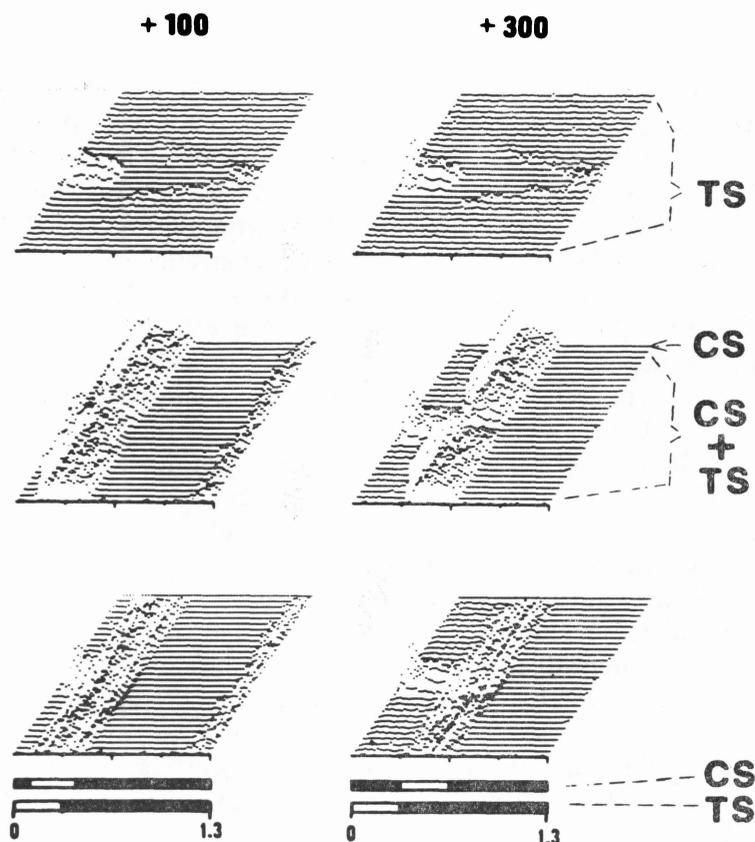


Fig. 3. Response planes as recorded from one ON-center LGN-cell. Top row: control response planes obtained by stimulation of the RF in 27 points along its axis. Stimulus (TS): $0.25^\circ \times 0.75^\circ$ bar of light of 6 cd/m^2 intensity. 16 repetitions of the stimuli in each point. Middle row: two-spot response planes. Despite the testing stimulus (TS) the RF was stimulated in the center by separate conditioning stimulus (CS). The time offset between stimuli was 100 and 300 ms, as indicated above. The uppermost histograms of these planes show cell responses to conditioning stimulus alone. Base row: The result of algebraic subtraction of the CS histogram from all others of two spot planes. The observed valleys represent spike deficit within the CS "bar of activity" as seen in appropriate two-spot response planes. See text for details.

method section. The planes shown in the second row (and build up simultaneously with control ones) are the result of the cell responses to two stimuli switched on and off with 100 and 400 ms time offset. The first of the stimuli (TS-testing spot) was switched on and off in all positions along the RF axis as during generating the regular control plane. The second, (CS-conditioning spot), stimulated always the RF center and evoked a central type of response on each from the 27 histograms. The cell responses for that stimulus appeared on a response plane as a bar of increased probability of firing, parallel to the space axis. This bar is depressed in the central region. It means that the cell excitatory response for CS and TS stimuli, when both are placed near the RF center, is weaker than for one of them (CS). The degree of the observed depression is presented in the third row in Fig. 3. The planes shown in this row were obtained algebraically by subtracting the histogram of the cell response, as obtained by stimulating the RF by the conditioning spot (CS) only, from all other histograms seen on the second row planes (CS + TS). The resulting valleys seen in the third row planes illustrate the deficiency of the expected cell firing, i.e. an intrinsic inhibitory action within RF. After a close inspection, two depressions on +100 ms plane can be seen, both running along the whole investigated distance, but deepest in the central region of the field. The earliest of them is observed during ON-time of both stimuli, the second, during the time when they are out of phase. Adapting Singer and Creutzfeldt (11) terms, both depressions might partially refer to "synergistic" and "antagonistic" inhibition respectively.

The inhibitory influences which we observed during ON and OFF-time of the stimulus extend over the whole field, far beyond its central region. Further investigation is needed to find out how closely they could be compared to the "suppressive field" found by Levick et al. (8). Our experiment has also shown that the synergistic inhibition is most potent in the field center, as is the antagonistic one. That suggestion was postulated by many investigators, both for the retinal and geniculate RFs.

The potentiation of inhibition within LGN-cell RF. We have found that at least three factors influence the RF organization by suppressing the cell responses in space and/or time. They are: (i) light-adaptation level; (ii) thiopental anesthesia and (iii) electrical stimulation of the visual cortex. The examples of such reorganizations produced by the first two factors are presented in Fig. 4. The set of four contour planes shown in two middle columns of this figure are taken during analysing the responses of the same cell under different physiological conditions. The enhancement of light-adaptation level (second column of Figs. 4A

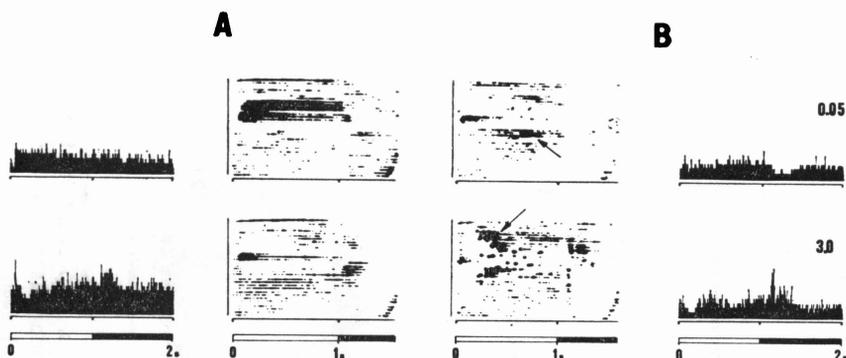


Fig. 4. The organization of RF of one LGN-cell in different light adaptation (rows), and barbiturate anesthesia (columns) levels. A pretrigeminal preparation. A, awake animal; B, spindle-like sleep evoked by 5 mg/kg dose of nembutal. Background luminance values in cd/m^2 are indicated on the right side of appropriate rows. Stimulus: $0.5^\circ \times 1^\circ$ bar of light of 5 cd/m^2 luminance. Four repetitions of stimulus in each point.

and 2B) increased the spatiotemporal extent of inhibitory surround. This type of inhibitory potentiation was discussed in the previous paper (17). The same receptive field was further investigated after injecting intravenously a low dose of nembutal (5 mg/kg), which evoked spindles in EEG activity (Wróbel, Sarna and Dec in preparation). The spatiotemporal organization of the RF was markedly changed under such conditions (Fig. 4B). The inhibitory surround increased spatially and new postinhibitory responses appeared (as indicated by arrows). These types of tertiary responses of much lower strength were observed before in awake animals (13, 17). The examination of contour planes of Fig. 4 indicated qualitative differences between the patterns of inhibitory surround enhancement evoked by light-adaptation and tiopenthal anesthesia. The mechanism of RF reorganization under barbiturate anesthesia is still not sufficiently known (3) and has to be studied further.

Finally, the preliminary results (Wróbel and Tarnecki, in preparation) seem to indicate that electrical stimulation of the visual cortex suppresses the LGN-cell light-evoked responses in the whole RF area. This finding is in agreement with the experiment of Kalil and Chase (7).

Reciprocal inhibitory interactions between LGN-cells. Stevens and Gerstein (14) have reported pairs of LGN-neurons with an inhibitory deep in the center of spontaneously taken cross-correlogram. They have postulated intrageniculate interneurons which would reciprocally potentiate the inhibitory surround of LGN-cell in relation to the retinal one. Our previous results (18) have strongly supported this model. Figure 5 presents the responses of two LGN-cells recorded simultaneously by one

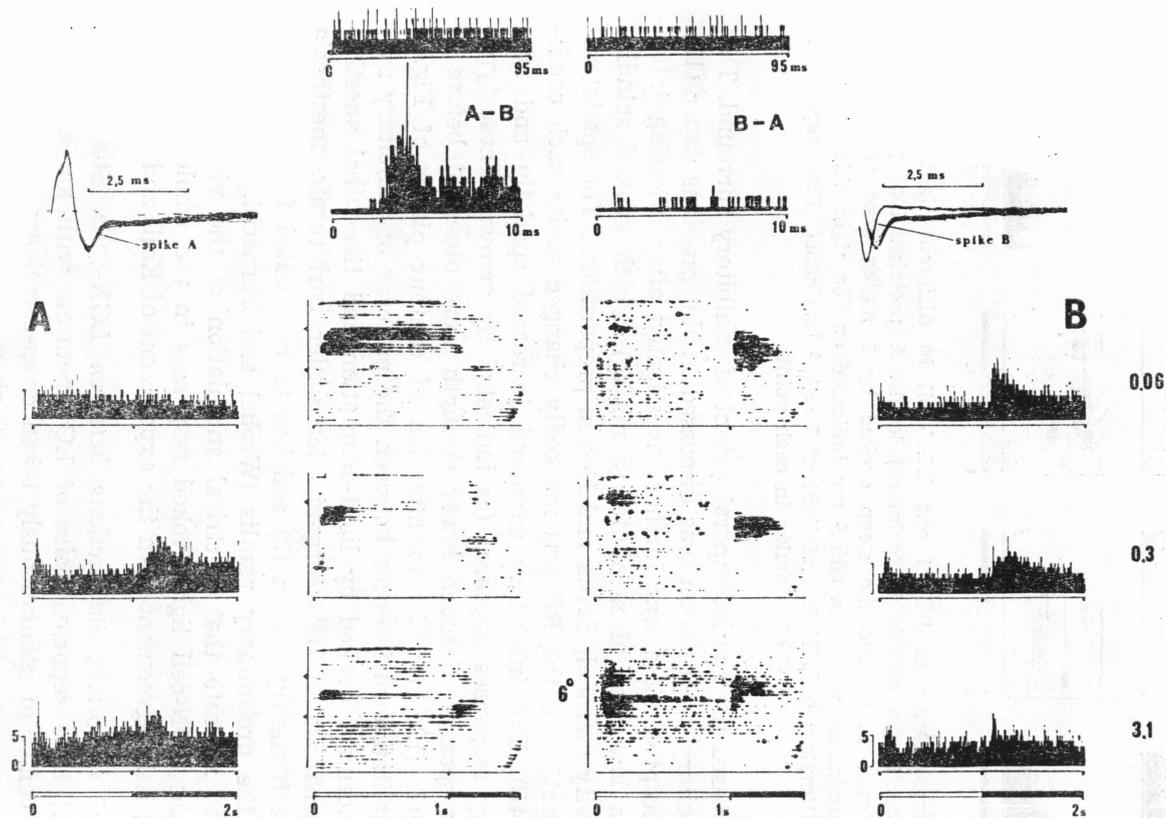


Fig. 5. Organization of RFs of simultaneously recorded spikes (*A* and *B*) of two LGN neurons. Top rows in the middle: cross-correlograms of both spike trains (*A* to *B* and *B* to *A*). Two analyses with different time bases (tb) for each half of cross-correlation histogram. 1024 counts of source spikes for histograms with 95 ms tb and 1536 counts for 10 ms tb. *A* (two left columns), PST-sum-histograms and corresponding contour planes of unit *A*. *B* (two right columns), similar data of unit *B*. Stimulus: $0.5^\circ \times 1^\circ$ bar of light of 5 cd/m^2 luminance. Four repetitions of the stimulus in each point. Three levels of light-adaptation (in cd/m^2) are marked on right side of each row.

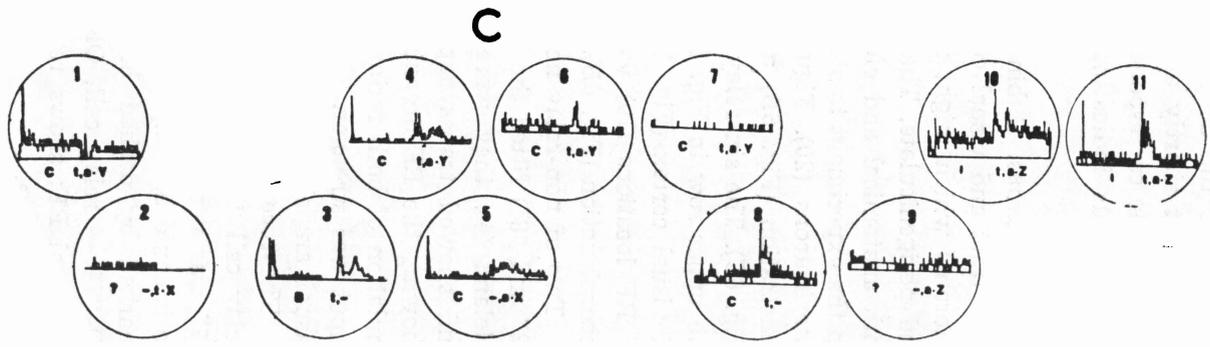
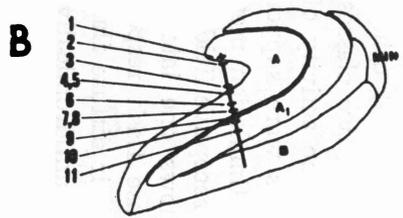
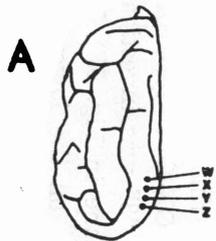
electrode. The cross-correlograms shown in the top row of this figure indicate the dependence of B-spike firing probability in relation to A-spike appearance. The dead time of the correlation is lower than 1 ms. Since the deep in A-B cross-correlogram lasts 2.5 ms, one can assume that shortly after A-cell fired, the probability of B-spike was lowered. The corresponding RFs of both cells show the reciprocal arrangement, thus indicating the inhibitory interaction between A and B cells.

Interneurons. Dubin and Cleland (4) using electrical stimulation of optic tract and visual cortex, found two classes of cells without cortical efferents which might influence the activity of LGN relay cells: intra- and perigeniculate. Their findings were supported by Ahlsen et al. by both anatomical and electrical stimulation methods (1, 2). We have set up the experiment to study the receptive field of both kinds of postulated interneurons (20). Figure 6 shows one lateral geniculate body (LGB) penetration (Fig. 6B) and diffuse flash responses of 11 recorded cells (Fig. 6C). The six relay cells (their diffuse flash responses are shown in the upper row in Fig. 6C) were antidromically activated by stimulation of visual cortex (Fig. 1A). The expected ocular inputs and progression of RF locations (10) were in a good agreement with anatomical track reconstruction (Fig. 6B).

Two of non-relay neurons found in this penetration (Fig. 6, numbers "3" and "8") fitted the criteria of interneurons postulated by Dubin and Cleland (4): they were not activated by stimulation of visual cortex and showed transsynaptic input from the retina. The contour planes showing the RF organization of cell "3" are presented in Fig. 6D. Stimulation of both retinae evoked responses of cell "3", but contralateral input was stronger. The RF of this cell is very large (exceeding 30° of visual angle) and shows the ON-OFF type of organization (17).

The receptive field of cell "8" was investigated simultaneously with relay cell "7" (top contour plane in Fig. 6E). The activity of relay cell "7" was very small, as shown on the lower contour plane in Fig. 6E, so it could be simply followed on the corresponding "7 + 8" plane (areas marked by dashed lines). The organization of both receptive fields: (i) "7" — relay cell, ON-center RF and (ii) "8" — OFF center, interneuronal RF; shows reciprocal spatiotemporal arrangement as was discussed before.

The above described data gave further support to the postulated model (18) of LGN functional circuitry.



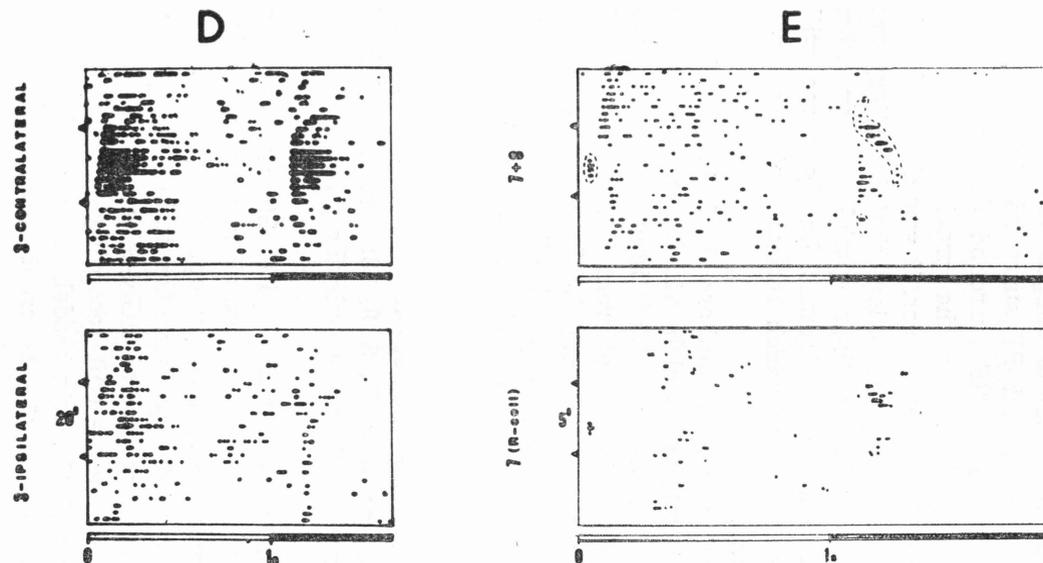


Fig. 6. A, the points where stimulating electrodes entered the visual cortex; B, the histological identification of the microelectrode penetration through the LGB. The points from which the appropriate cell responses were recorded are marked and numbered. C, the diffuse flash (of 10 cd/m² intensity) responses of the cells found during penetration. The first half of the histograms correspond to ON-time, the second to the OFF-time of the stimulus. The probability axis magnification of histograms 3, 4 and 5 is lowered twice in relation to all others. Histograms in the upper row show the responses of relay cells. In the lower row the responses of other neurons are shown. Notation letters: B, C, I, binocular, contralateral and ipsilateral inputs from retinae; t, transsynaptic response, a, antidromic activation from points W, X, Y, Z as indicated in A. The OT and visual cortex patterns of responses are separated by comma. D, the contour planes of responses of neuron "3" as obtained by stimulating contra- and ipsilateral retinae respectively. Stimulus: 2° × 4.5° bar of 5 cd/m² luminance, E, lower contour plane shows the RF organization of relay cell "7". The upper contour plane summates the responses of both units: "7" and "8" (interneuron). Dashed lines limit the spatiotemporal areas of activity of cell "7". Stimulus: 0.5° × 1° bar of 5 cd/m² luminance. Two repetitions of the stimulus in each point of the RFs shown on D and E contour planes.

DISCUSSION

The aim of this paper was to review our study on the inhibitory mechanisms within the LGN-cell receptive field. The reinforcement of surround inhibition in LGN-cell RF in relation to the retinal one was reported by several authors (5, 6, 8, 9, 11–13, 16, 17). Maffei and Fiorentini (9) in conformity with the original suggestion of Hubel and Wiesel (6), questioned the role of retinal RF surrounds in this reinforcement on the basis that geniculate RF surround does not vanish during dark adaptation. It was shown in the previous paper (17) that it is not true for many LGN-cells. Moreover, it was shown therein (compare also Figs. 2B and 4 in this presentation) that inhibitory and antagonistic excitatory surrounds change their spatial position when light-adaptation level is changed. These findings hardly agree with a model by Maffei and Fiorentini (9), in which retinal centers are responsible for geniculate surround.

On the other hand, several groups of authors (1, 4, 8, 11, 12, 18) have postulated the recurrent pathway which, via interneuron, would be able to inhibit the geniculate relay cells. Such interneuron was supposed to get inputs from many geniculate efferent fibers of both ON- and OFF-center characteristics, thus deepening the LGN-cell RF in the so called "inhibitory pool" (12) or "suppressive field" (8). It is not obvious, however, how to explain, with such model alone, the strong reduction of inhibitory surround of LGN-cell RF which takes place under scotopic condition, as shown in our previous paper (17, compare also Figs. 2B and 4). In scotopic conditions the retinal ganglion cells respond still vigorously to stimulus presentation (5, 6, 9, 18; Wróbel and Kruk in preparation) and should activate via relay cells the postulated interneurons.

On the basis of the spatiotemporal study of RF, Stevens and Gerstein (13, 14) have postulated the interneuron-like elements of geniculate origin which would "reciprocally" antagonize the opposite types of LGN RFs; which means that retinal excitatory surrounds rather than retinal centers generate the inhibitory surround of LGN-cells receptive field.

Our results obtained with double — unit recordings (Figs. 5 and 6) strongly support the Stevens and Gerstein model. On the other hand, some of our data suggest also the separate recurrent inhibitory mechanism. Such mechanism could provide a base for the following observed features: (i) the strongest inhibitory action in the RF center and its large spatial extent (Fig. 3); (ii) oscillations evoked in LGN cell after stimulation of its RF center and absence of such oscillations in the activity of its retinal input (Fig. 2, see also 11).

Our analysis of receptive fields is in agreement with the LGN-cell

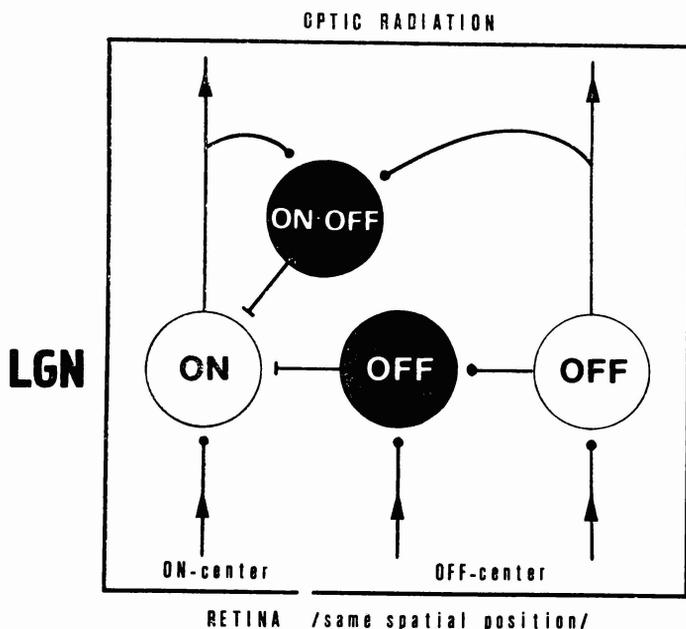


Fig. 7. Functional model of connections between LGB-cells. White circles, represent relay cells; black circles, represent interneurons. See text for details.

wiring model based on electrical stimulation method (4). This model can be used to explain our observation on LGN-cell RF organization as shown in the Fig. 7. The ON-center retinal RF (being central in the scheme) is transferred by LGN relay cell to the cortex. Two separate connections produce the inhibitory influences on that pathway. One of them starts from OFF-center retinal RF of the same spatial position and via intrageniculate interneuron "contrasts" ON-center RF of LGN relay cell (Fig. 6E). The second consists of many recurrent geniculate efferent collaterals which converge on perigeniculate interneuron constituting its large receptive field of the ON-OFF type (Fig. 6D). Such interneuron via inhibitory synapse would produce the LGN-cell "suppressive field".

Our double-unit recordings (Figs. 5 and 6E) supply a strong evidence of the first inhibitory connection. The participation of perigeniculate interneurons with ON-OFF receptive field organization (as shown in Fig. 6D and in the previous papers 17, 20) in the second connection, was postulated by other authors (1, 4, 8, 12).

It should be noted that experimental data of Levick et al. (8) suggest the convergence of several retinal fibers with overlapping RFs in the geniculate relay cell. For the sake of simplicity only single lines were drawn on the scheme in Fig. 7, since it presents the functional model rather than the accurate anatomical reality. The retinal input to intra-

geniculate interneuron has been drawn in Fig. 7 after Dubin and Cleland (4), since it is not contradictory to our experiments.

Our data seem to integrate themselves into a promising entity. We are convinced, however, that they should be supported by more precise and/or different methods. The role of other types of neurons which were found in the geniculate body and in the interlaminar nuclei (e.g. cells "5" and "9" in Fig. 6) in geniculate circuitry remains still unknown.

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