Inhibition in the *Limulus* Lateral Eye *In Situ*

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ABSTRACT Inhibition in the *Limulus* lateral eye *in situ* is qualitatively similar to that in the excised eye. In both preparations ommatidia mutually inhibit one another, and the magnitude of the inhibitory effects are linear functions of the response rate of individual ommatidia. The strength of inhibition exerted between single ommatidia is also about the same for both preparations; however, stronger effects can converge on a single ommatidium *in situ*. At high levels of illumination of the retina *in situ* the inhibitory effects are often strong enough to produce sustained oscillations in the discharge of optic nerve fibers. The weaker inhibitory influences at low levels of illumination do not produce oscillations but decrease the variance of the optic nerve discharge. Thresholds for the inhibitory effects appear to be determined by both presynaptic and postsynaptic cellular processes. Our results are consistent with the idea that a single ommatidium can be inhibited by more of its neighbors in an eye *in situ* than in an excised eye. Leaving intact the blood supply to the eye appears to preserve the functional integrity of the retinal pathways which mediate inhibition.

INTRODUCTION

The detailed description of neural interactions in the *Limulus* retina has yielded a useful model of information processing for other sensory systems. In a pioneering series of experiments Hartline, Ratliff, and their co-workers demonstrated that the interactions among retinal units (ommatidia) in the *Limulus* eye are predominately inhibitory, and that the response of each ommatidium could be described by a set of piecewise-linear equations (for a review, see Hartline and Ratliff, 1972). More recent studies have shown that the equations can be revised to account for the result that ommatidia are more sensitive to lateral inhibition at some levels of excitation than they are at others (Lange, 1965; Barlow and Lange, 1974). Steady-state patterns of optic nerve activity computed from the revised set of equations match closely the Mach-band patterns recorded from the excised eye (Barlow and Quarles, 1975). The temporal properties of excitation and inhibition have also been studied in detail (Lange et al., 1966; Dodge et al., 1970; Knight et al., 1970; Ratliff et al., 1967, 1974).

Thus far, information about the properties of inhibition in the *Limulus* retina has been derived primarily from experiments on the excised eye.[1] This

[1] Biederman-Thorson and Thorson (1971) investigated some characteristics of excitation and inhibition in the *Limulus* eye *in situ*. Their study concentrated on the dynamic properties of the light-adapted retina. This paper discusses some of their results.

preparation, however, has at least one drawback: the sensitivity of ommatidia to light gradually declines after the eye is removed from the animal (Barlow and Kaplan, 1971). To overcome this problem, Barlow and Kaplan developed a technique for recording the responses of single optic nerve fibers without excising the eye or disrupting its blood supply. They found that the sensitivity of a single ommatidium *in situ* remains constant for periods of up to 5 days which is the maximum length of time they could record the impulses from a single optic nerve fiber. In addition, they found that a number of excitatory properties of the eye *in situ* differ from those of the excised eye. The most striking difference is the dynamic range of single receptors—10 log units of light intensity for ommatidia *in situ* vs. 5 log units for ommatidia in excised eyes (Barlow and Kaplan, 1971; Kaplan and Barlow, 1975).

Here we report that the inhibitory properties of the eye *in situ* are qualitatively similar to those of the excised eye, but there are important differences. The most striking difference is that the inhibitory effects are stronger in the eye *in situ*.

METHODS

Materials

The experiments were performed on large male horseshoe crabs (8–10 in. across the carapace) obtained from the Harborton Marine Laboratory, Harborton, Va. Females were avoided because eggs under the carapace interfered with the surgical procedures. The crabs were flown to Syracuse, placed in artificial seawater (Instant Ocean, Aquarium Systems, Inc., Eastlake, Ohio), and fed fresh clams on a regular schedule.

Preparation

The method of recording from single optic nerve fibers *in situ* is described in detail elsewhere (Barlow and Kaplan, 1971; Kaplan and Barlow, 1975). To summarize briefly, the animal was securely fastened to an elevated platform. A rigid state was attached to the dorsal carapace of the prosoma to support the recording electrodes and one optical stimulator. The platform carrying the animal was then placed in a small tank inside a lighttight, shielded cage. The gill structure was continuously bathed by aerated artificial seawater through slots in the platform. A small circular section of the shell (1.9 cm in diameter) was removed ~3 cm anterior to one of the lateral eyes, near the ophthalmic ridge. The optic nerve was exposed through the hole, dissected free of surrounding tissue, and cut. The cut end of the optic nerve coming from the eye was then drawn through an opening in a recording chamber which fit snugly in the hole in the shell. The chamber was filled with artificial seawater buffered to pH 7.3. The nerve was then dissected with fine glass needles into small strands of fibers. One strand containing a single active fiber was drawn into the tip of a glass suction electrode. When required, another strand of nerve containing a single active fiber from an ommatidium neighboring the first was drawn into a second suction electrode.

Stimulation

SINGLE-RECEPTOR ILLUMINATION Individual ommatidia were illuminated via fiber-optic light pipes (Barlow, 1967, 1969). A tungsten filament was focused on one end of a 70-μm light pipe with a ×45 microscope objective. At the maximum intensity of the optical system, the output of the other end of the light pipe was 10^{12} photons/s between 400 and 700 nm (measured with a calibrated photodiode, PIN 10D, United Detector

Technology Inc., Santa Monica, Calif.). This intensity is indicated as log I = 0 in the figures of this paper. The light intensity delivered to the ommatidium was set by neutral density filters and a circular wedge in the beam. Careful alignment of the optic axis of the light pipe with that of the test ommatidium restricted light scatter into neighboring ommatidia to 10^{-5} or less of the intensity incident on the test ommatidium.

FULL-EYE ILLUMINATION Diffuse illumination of the whole eye maximizes the inhibitory influences exerted on single ommatidia. Diffuse illumination was accomplished by placing a white Teflon screen in contact with the eye so that the plane of the screen was perpendicular to the optic axis of the test ommatidium. Light from a tungsten filament source was projected on the screen by a large fiber optic bundle. Control experiments showed that the diffuse light beam illuminated uniformly all but the most peripherally located ommatidia in the eye. To determine the incident light intensity, the eye was replaced by the calibrated photodiode. At the maximum setting of the optical system, the intensity incident on a single ommatidium was estimated to be 2.9×10^{11} photons/s which is about 3.4 times less intense than the stimulus delivered by the 70-μm light pipe. The data for full-eye illumination are therefore shifted to the left by 0.53 log units in Figs. 1, 5, 9, and 10.

Data Recording and Processing

Nerve impulses recorded from one or more optic nerve fibers were amplified and displayed on an oscilloscope. The amplified voltage signals were fed to an audio monitor and through an interface (Kletsky, 1971) to a Linc-8 computer (Digital Equip. Corp., Maynard, Mass.) for on-line data processing. The neural responses were also recorded on magnetic tape for further analysis at a later time.

Measuring Inhibitory Coefficients

The inhibitory coefficient is a measure of the strength of inhibition exerted by one ommatidium on another (Hartline and Ratliff, 1957). It is defined as the slope of the line relating the decrease in firing of one unit to the rate of firing of the other. The coefficient was determined directly by recording the activity of two neighboring ommatidia and illuminating each of them via separate light pipes. One of the ommatidia was designated as the test unit 1 and the other as the inhibiting unit 2. The response of 1 to a 10-s light stimulus was recorded while the rest of the eye remained in darkness. This response (e_1) is termed the uninhibited response rate or excitation of 1. After ~15 min in darkness for 1 to recover its normal level of spontaneous activity, the stimulus to 1 was repeated with a concurrent light stimulus to 2. Runs with and without inhibition were alternated and sets of runs with different intensities of illumination on 2 were carried out. During the last 5 s of the 10-s light stimulus, after all transient effects had died out, the response rates of 1 and 2 were recorded. These rates, r_1 and r_2, are termed the inhibited response rates. The Hartline-Ratliff equation relates e_1, r_1, and r_2 as follows:

$$e_1 - r_1 = k_{12}(r_2 - r_{12}^0). \tag{1}$$

k_{12} is the coefficient of the inhibitory interaction of 2 on 1 and r_{12}^0 is the threshold response which 2 must exceed to inhibit 1. If e_1 is held constant, the decrease in firing rate of 1 is linearly related to the suprathreshold response rate of 2 (Barlow and Lange, 1974). The coefficient k_{12} is then the slope of function relating $(e_1 - r_1)$ to r_2. In most experiments the intensity of illumination on 1 was adjusted to produce an e_1 of about 25 impulses/s. This procedure minimized the nonlinear inhibitory effects described by Barlow and Lange (1974).

The strength of inhibition exerted by one ommatidium on another was often too weak to be measured with precision. Therefore, in a number of experiments a small cluster of

four ommatidia was used for the source of inhibition. The small cluster was illuminated through a fiber optics bundle (type LGM-1, American Optical Corp., Buffalo, N. Y.). The response of only one of the four ommatidia in the cluster was recorded on the assumption that all four units responded alike. The assumption seems valid because equally illuminated receptors in the same eye respond with nearly identical firing rates. The inhibitory coefficient for the effect of the cluster on the test unit was divided by four to provide an estimate of the strength of inhibition exerted by a single unit. We assumed that each of the four units in the cluster behaves in a similar fashion and that the cluster was small enough to approximate a point source of inhibition (Barlow, 1969). These assumptions are substantiated by the measurements of coefficients from single pairs of ommatidia.

RESULTS

Fig. 1 gives the steady-state responses of a single, dark-adapted ommatidium *in situ* over a 10-log unit range of light intensity when singly illuminated and when the entire eye is diffusely illuminated. The intensity function for the singly illuminated ommatidium contains a plateau which is characteristic of receptors *in situ* (Barlow and Kaplan, 1971, 1977; Kaplan and Barlow, 1975). Under full-eye illumination the plateau region appears broadened. At high levels of illumination, inhibition from surrounding ommatidia caused a substantial

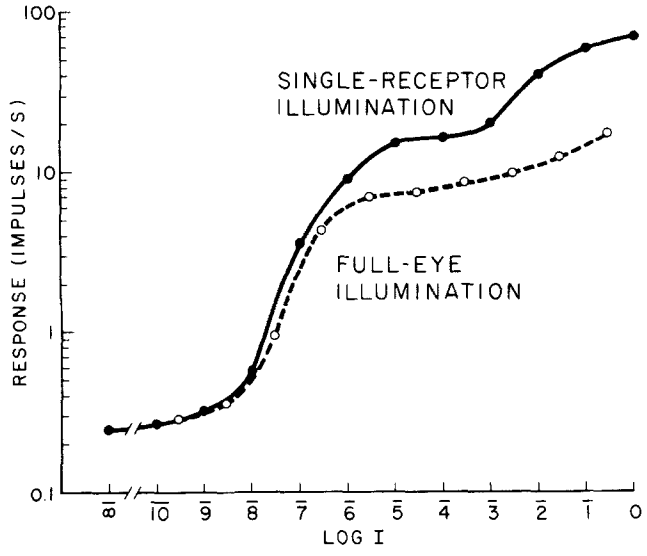

FIGURE 1. Intensity functions of the steady-state response of a single ommatidium in a *Limulus* eye *in situ*. The steady-state response is generally defined as the mean firing rate in the last 5 s of a 10-s flash, although at low intensities the flash duration and the count interval were often increased to compensate for variability in the spike discharge. Light was delivered to the single ommatidium via a fiber optic light pipe. At log I = 0 the quantal flux at the cornea was $\sim 10^{12}$ photons/s between 400 and 700 nm. The whole eye was uniformly illuminated by placing a Teflon diffusing screen over the eye. The screen was then illuminated via a large bundle of fiber optics. All data were recorded under dark-adapted conditions. Spread of data is within the size of the data points.

decrease in the response of the recorded unit. At log I = −1 the firing rate was reduced by a factor of about 4, from 60 to 14 impulses/s, which is a significantly stronger effect than that measured for excised eyes (Barlow and Lange, 1974). Such strong inhibitory effects can lead to an interesting phenomenon which is described below. Fig. 1 also shows that lateral inhibition was effective at low levels of illumination. The two curves separate at about log I = −8 which corresponds to a mean response rate below one impulse/s. This result indicates that under full-eye illumination the mean response rate required for exerting detectable inhibitory effects is about one impulse/s.

Strength of Inhibition Exerted by Many Ommatidia

The total strength of inhibition exerted on a single ommatidium can be estimated from the data in Fig. 1 following the method of Barlow and Lange (1974). The response rate r_p of the pth ommatidium in an array of n units is given by the revised form of the Hartline-Ratliff equations (Lange, 1965):

$$r_p = [e_p - (1 + ae_p) \sum_{\substack{j=1 \\ j \neq p}}^{n} k'_{pj}(r_j - r^o_{pj})_+]_+, \; p = 1, 2, \ldots, n, \tag{2}$$

where the subscript + is an operator defined by

$$\alpha_+ = \begin{cases} \alpha \text{ for } \alpha \geq 0 \\ 0 \text{ for } \alpha < 0 \end{cases}.$$

Barlow and Lange (1974) describe in detail the notations and restrictions for Eq. 2. As explained above, all ommatidia in the eye respond at nearly the same rate under conditions of diffuse illumination, and thus we shall assume that the response rate of each receptor is equal to r_p. We shall also assume that the thresholds (r^o_{pj}) are zero. This assumption appears justified for the conditions of whole-eye illumination (see Fig. 1 and Discussion). Eq. 2 now becomes

$$\Sigma k_{pj} = (1 + ae_p) \Sigma k'_{pj} = \frac{e_p}{r_p} - 1, \tag{3}$$

where the value of Σk_{pj} is a measure of the total strength of inhibition exerted on the pth unit. For a given intensity of illumination the value of e_p can be read from the "single-receptor" curve in Fig. 1 and the value of r_p from the "full-eye" curve.

Fig. 2 gives the values of Σk_{pj} computed for the data in Fig. 1 from an eye *in situ* and also for a typical set of data from an excised eye. The peak value of Σk_{pj} for the eye *in situ* is 3.0 which is more than double the maximum value of 1.1 for the excised eye. Stronger levels of inhibition were observed in other experiments. In about one-third of the eyes examined *in situ*, the peak values of Σk_{pj} exceeded 6.0, which is more than twice the value shown in Fig. 2. Consequences of such strong levels of inhibition are considered below.

Nonlinearity of the Inhibitory Effects

Fig. 2 shows that the total strength of inhibition (Σk_{pj}) was dependent on the uninhibited response rate (e_p) of the test ommatidium. In effect, the test

ommatidium was more sensitive to lateral inhibition at some levels of excitation than at others. This result may be represented by the introduction of a nonlinearity in the Hartline-Ratliff system of equations (Barlow and Lange, 1974). The data in Fig. 2 show that the nonlinear effect is more pronounced in the eye *in situ*. The values of Σk_{pj} for the eye *in situ* are directly proportional to e_p in the range from ~10 to 45 impulses/s. The revised, nonlinear set of equations (Eq. 2) applies in this range. Below this range ($e_p < 10$ impulses/s) the strength of inhibition is not strongly dependent on the level of excitation, a

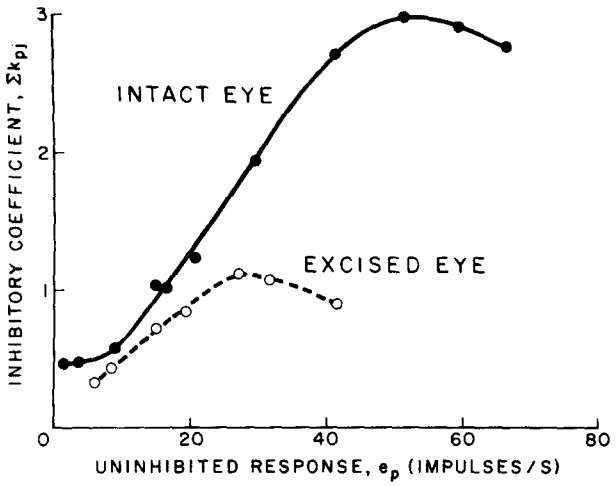

FIGURE 2. The total strength of inhibition, Σk_{pj}, as a function of the uninhibited response rate of a single ommatidium in an excised eye and in an eye *in situ*. Ordinate values were calculated from the intensity functions in Fig. 1 using Eq. 3. These sets of data are typical of intact and excised eyes. Differences between the curves for response rates below 15 impulses/s are not significant. The data show that the inhibition exerted on an ommatidium is dependent on the level of excitation of that ommatidium in both preparations, but that the total strength of inhibition is greater in the intact eye.

result originally described for the excised eye (Hartline et al., 1956). The piecewise-linear form of Eq. 2 ($a = 0$) applies in this range (Hartline and Ratliff, 1958). At high levels of excitation ($e_p > 45$ impulses/s), the data for the eye *in situ* deviate from both the original and revised formulations. Similar deviations from theory were found for the excised eye at lower levels of excitation ($e_p > 25$ impulses/s). Barlow and Lange (1974) noted that the results for the excised eye varied considerably from one ommatidium to another and that no general rule could be given. We found, however, that the data recorded from ommatidia *in situ* at high levels of excitation are generally consistent with those in Fig. 2, a result which may reflect uniformity in the physiological properties of unexcised eyes.

Strength of Inhibition Exerted by a Single Ommatidium

The sum of the inhibitory coefficients, Σk_{pj}, is a measure of the strength of inhibition exerted on a single ommatidium by a group of receptors. What are

the contributions of the individual members of the group, that is, what are the values of the individual inhibitory coefficients, k_{pj}? As described in Methods, individual inhibitory coefficients were measured in two ways: first with inhibition exerted by a single ommatidium, and second with inhibition provided by a small cluster of ommatidia.

A word about notation. In Eq. 1 the inhibitory coefficient for the action of ommatidium 1 on 2 is designated by k_{12}. In Eq. 2 the notation is modified to include nonlinear effects (Barlow and Lange, 1974); however, the notation in Eq. 2 is simply related to that in Eq. 1. For example, in the case of just two interacting receptors, 1 and 2, $k_{12} = (1 + ae_1)k'_{12}$ and $k_{21} = (1 + ae_2)k'_{21}$. The measured values of the inhibitory coefficients presented here follow the notation in Eq. 1.

Fig. 3 A gives the decrease in response of ommatidium 1 as a function of the response rate of a single inhibiting ommatidium 2. Fig. 3 B gives the decrease in response of one ommatidium as a function of the response rate of one ommatidium in a cluster of four inhibiting units. Data are given in Fig. 3 B and 10 units for as many eyes. The slopes of the lines give the values of the inhibitory coefficients (see Methods). In Fig. 3 A the slope is 0.03, and in Fig. 3 B the average slope is 0.037 ± 0.005 (after performing the appropriate division by four). The two methods yield approximately the same results. Comparison of the slopes in A and B is justified inasmuch as both types of experiments were carried out with ommatidia separated by about five to seven ommatidial diameters. We have not yet measured the spatial distribution of the inhibitory coefficients in the eye *in situ* because of the technical difficulties introduced by the high levels of spontaneous optic nerve activity recorded from dark-adapted ommatidia. The saturation of inhibition reported by Johnstone and Wachtel (1976) was not detected in our experiments.

The value of 0.037 for the inhibitory coefficient agrees well with the value of 0.036 measured by Biederman-Thorson and Thorson (1971) for the light-adapted eye *in situ*. The exceptionally good agreement, however, may be fortuitous. Published values for excised eyes include 0.06 ± 0.02 (Barlow, 1967) and 0.1–0.2 (Hartline and Ratliff, 1957).[2] Thus, if appears that although the total strength of inhibition (Σk_{pj}) is much greater in unexcised eyes, the values of the individual coefficients (k_{pj}) are comparable in both preparations.

The data in Fig. 3 show that the inhibitory interactions in the eye *in situ* are characterized by discrete thresholds and that the magnitude of inhibition is directly proportional to the response of the inhibiting receptors. Mutually inhibitory effects were also observed in the eye *in situ* although the results are not displayed in Fig. 3. These basic properties of inhibition (Hartline et al., 1956; Hartline and Ratliff, 1957, 1958) do not appear to be altered by excision of the lateral eye.

Oscillations in the Optic Nerve Responses

Intense illumination of a large region of the eye *in situ* often elicits oscillations in

[2] Experiments on excised eyes generally have been carried out only with preparations exhibiting substantial levels of inhibition. As a consequence, the inhibitory coefficients reported for excised eyes tend to bias high values. No similar selection process took place in our experiments on the eye *in situ*.

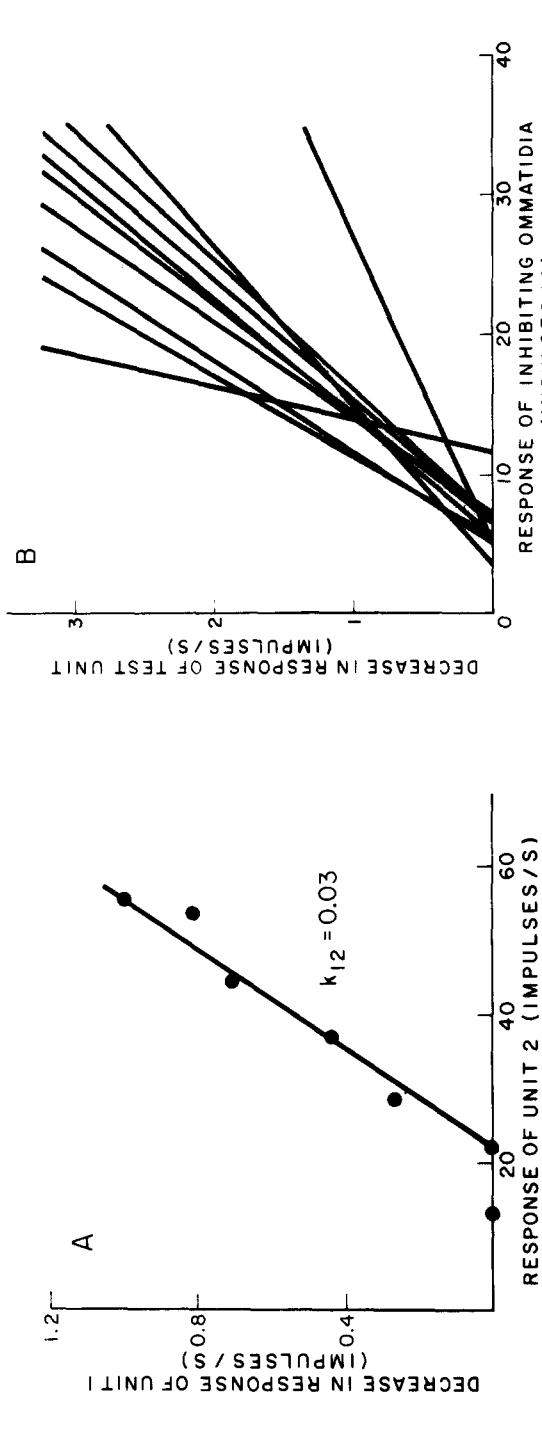

FIGURE 3. (A) The decrease in firing of one ommatidium as a function of the mean response rate of a nearby ommatidium. Both units were singly illuminated by fiber optic light pipes. The two units were separated by five ommatidia. (B) The decrease in firing of a single ommatidium as a function of the response rate of one of a cluster of four inhibiting ommatidia. Results are given for 10 experiments on as many eyes. In each experiment the single ommatidium was illuminated by a light pipe, and the inhibitory cluster was illuminated with a bundle of light pipes. The mean uninhibited firing rate of the test receptors, e_p, was 23 impulses/s for the experiments shown in A and B.

the optic nerve discharge. If the appropriate conditions are met, every optic nerve fiber fires in near synchrony one or more impulses every 200 ms or about five times/s. Fig. 4 gives the result of an experiment designed to determine the role of lateral inhibition in the oscillatory behavior. When the eye was diffusely

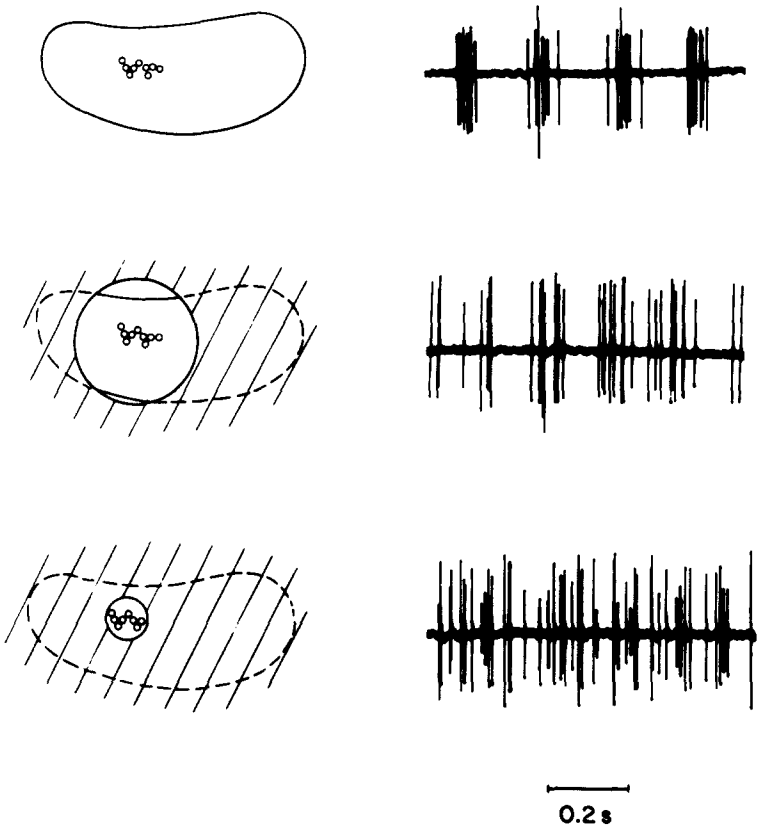

FIGURE 4. An illustration of the oscillations in the optic nerve discharge of a *Limulus* eye *in situ*. Simultaneous optic nerve recordings from nine ommatidia located in a central region of the retina are displayed on the right. The position of the ommatidia is illustrated on the left. Time marker indicates 200 ms. (Top) Uniform illumination of the entire eye produced pronounced oscillations in the optic nerve discharge. (Middle) Masking half the eye reduced the periodicity of the discharge. (Bottom) Restricting the illumination to the region of the receptors abolished the oscillations.

illuminated (top record), nine centrally located ommatidia elicited synchronous bursts of spikes about five times/s. Partially masking the eye (middle record) reduced the magnitude of the oscillations. Restricting the area of illumination to the region immediately surrounding the recorded ommatidia (bottom record) abolished the oscillations. Inasmuch as the oscillations were most pronounced when the number of inhibiting ommatidia was greatest, it would appear that strong lateral inhibitory effects produced the optic nerve oscillations.

Strong inhibition is characteristic of lateral eyes *in situ*, but not all eyes display oscillatory behavior. For example, the data in Figs. 1 and 2 were recorded from an eye *in situ* which did not produce detectable oscillations. The maximal strength of inhibition, Σk_{pj}, for this eye was 3.0. Fig. 5 gives a similar set of data for an eye which yielded pronounced oscillations. Our experiments on unexcised eyes yielded values of Σk_{pj} ranging from 2.3 to 8.5. We stress that no oscillations were observed for levels of illumination which elicited uninhibited response rates (e_p) below 30 impulses/s even when the area of illumination extended over the entire retina. Oscillations were generally produced when the level of whole-eye illumination exceeded log I = −2.0. Higher intensities were required for smaller areas of illumination. Oscillations were generated when Σk_{pj} exceeded a value of ~5.0 regardless of how that level of inhibition was achieved.

Sustained oscillations could often be elicited by a small increment in light intensity. For example, whole-eye illumination of the preparation in Fig. 4 with log I ≤ −2.5 elicited no detectable oscillations, but a gradual increase in intensity above log I = −2.5 yielded small amplitude oscillations, and further increases produced more pronounced oscillations. When the intensity reached log I = −2.0 the oscillations consisted of synchronous bursts of impulses separated by silent periods (Fig. 4, top). The oscillations were sustained for the entire duration of the light stimulus which exceeded 2 h in this experiment.

Our experiments thus far indicate that levels of inhibition corresponding to $\Sigma k_{pj} \geq 5$ are sufficient to induce oscillations in the optic nerve discharge. Such levels of inhibition were found in about one-third of the eyes examined *in situ* and in no eyes tested after excision. Σk_{pj} for excised eyes is typically <2.3 (Barlow and Lange, 1974), although higher values have been observed on occasion (Barlow and Quarles, 1975). The high values of Σk_{pj} measured in eyes which exhibited oscillations strengthens the notion that strong lateral inhibition produced the oscillations.

Responses were recorded from several omatidia in Fig. 4 to demonstrate the oscillatory behavior because the oscillations are not readily apparent in the discharge of a single unit. When oscillations occur, records from single ommatidia normally consist of regular trains of impulses with interspike intervals of 200 ms.[3] Fig. 6 displays the results of an experiment in which the optic nerve discharge from a group of ommatidia A located in a restricted region of the eye was recorded on one electrode and the discharge from a single member B of the group was recorded on a second electrode. Under whole-eye illumination, ommatidium A responds with a regular train of impulses which is nearly synchronous with the bursts fired by the neighboring ommatidia in B.

Do widely separated ommatidia also respond in phase during oscillation? To answer this question the responses of two separate groups of ommatidia were recorded with suction electrodes. The records in Fig. 7 show that the optic nerve responses from both groups were nearly synchronous when the eye was

[3] Although a train of impulses with uniform interspike intervals of 200 ms is normally recorded from a single ommatidium when the eye is in oscillation, we have occasionally recorded bursts of two or three impulses fired at 200-ms intervals. Such bursts require the highest levels of excitation and inhibition.

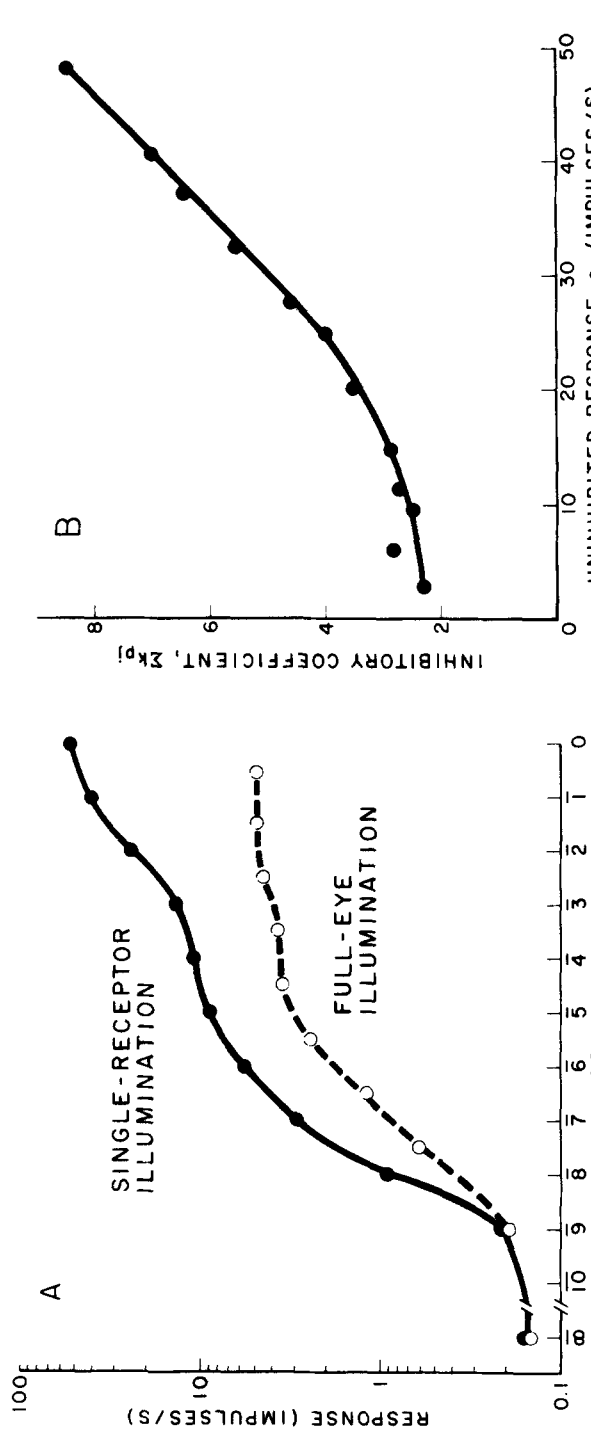

FIGURE 5. Data from a *Limulus* eye *in situ* which exhibited oscillations in the optic nerve discharge. (A) Intensity functions of a single ommatidium with and without the effects of inhibition. The data were obtained in the manner described for Fig. 1. Spread of data is within the size of the data points. (B) The total strength of *inhibition*, $\sum k_{pj}$, as a function of the uninhibited response rate of the test ommatidium, e_p, calculated with Eq. 3 from the intensity functions in A.

diffusely illuminated. More widely separated groups of receptors yielded similar results. These results suggest that, when appropriate conditions exist, all ommatidia in the retina can fire impulses in near synchrony every 200 ms.

Threshold for Inhibition

Discrete thresholds characterize the inhibitory interactions among ommatidia in the lateral eye *in situ*. In Fig. 3 A the threshold for the action of unit 2 on 1 was 22 impulses/s, that is, 2 had to fire >22 impulses/s to inhibit the response of 1.

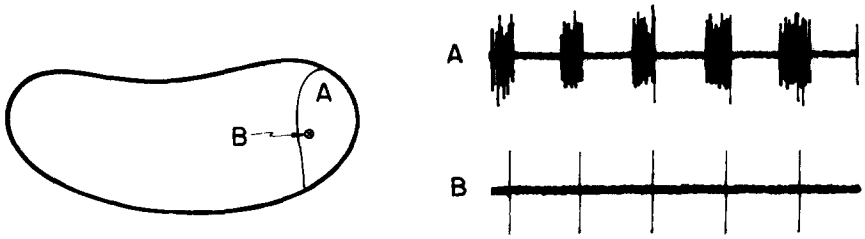

FIGURE 6. Record A is the discharge of a group of ommatidia recorded in response to full-eye illumination. Record B is the response of a single ommatidium from the same region of the eye as indicated in the schematic drawing on the left (top, dorsal; right, anterior). Note that the regular firing of the single unit is in phase with the periodic bursts from the group.

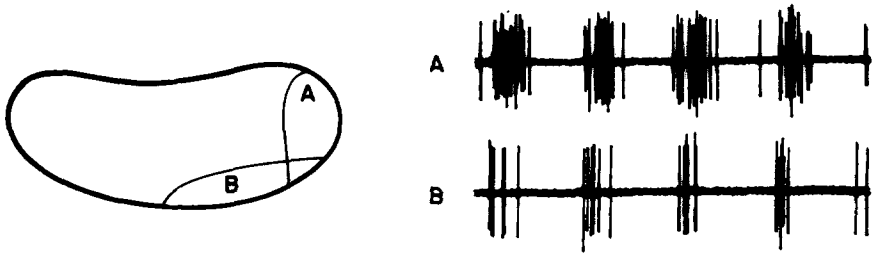

FIGURE 7. Records A and B are from two different groups of ommatidia located in separate regions of the eye. Two of the recorded ommatidia were located in the region of overlap between A and B. The responses were elicited by full-eye illumination as in Fig. 6. The synchronous oscillation of both A and B implies that all ommatidia in the eye can oscillate in phase.

Results from other experiments on the *in situ* preparation indicate that in general thresholds between pairs of ommatidia are >20 impulses/s. We note that similar threshold values were obtained from experiments on the excised eye employing the same fiber-optics illumination system;[4] however, somewhat lower values have been reported for experiments utilizing different techniques of optical stimulation (Hartline and Ratliff, 1957; Ratliff et al., 1963; Johnstone and Wachtel, 1976).

Increasing the number of inhibiting ommatidia lowers the threshold for inhibition. In Fig. 3 B a cluster of four inhibiting ommatidia produced a mean threshold of 6.3 ± 2.3 impulses/s for the eye *in situ*. Under the same experimental conditions, excised eyes yielded thresholds ranging from 4 to 11 impulses/s with a mean value of 8.3 ± 3.6 (Barlow and Lange, 1974).[4] The thresholds were

[4] Barlow, R. B. Unpublished observations.

lowered significantly when the number of inhibiting ommatidia was increased (Figs. 1 and 5). In both experiments inhibition of the spike discharge was detected at mean firing rates of <1.0 impulses/s. Experiments on excised eyes for the same condition of whole-eye illumination yielded a mean threshold of 2.0 ± 1.1 impulses/s (Barlow and Lange, 1974).[4] This result is consistent with the low threshold values which are generally found when inhibition is exerted by a large number of ommatidia (Hartline et al., 1961; Purple, 1964; Lange et al., 1966; and Knight et al., 1970). We note that Hartline et al. (1961) ruled out the possibility that increasing the number of ommatidia lowers the inhibitory threshold even though it is the simplest explanation for their results.

The spontaneous activity of dark-adapted ommatidia *in situ* can also lower the threshold for inhibition. This result is demonstrated in Fig. 8 by an experiment

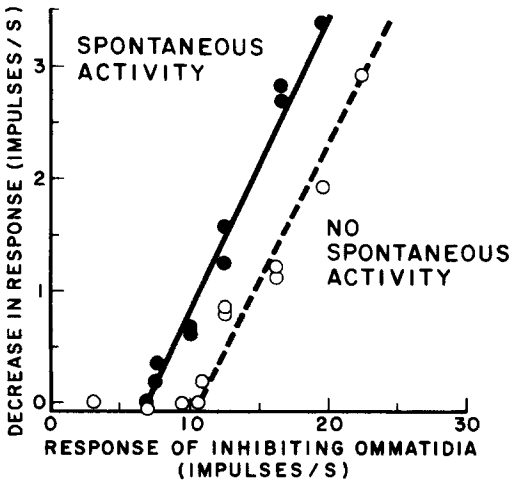

FIGURE 8. The effect of spontaneous activity on inhibitory threshold. Decrease in firing of a test ommatidium is plotted as a function of the response rate of one of a cluster of four ommatidia which provide the inhibition. Filled circles were measured when the eye was fully dark adapted between experimental runs so that all receptors reached a steady level of spontaneous activity. Unfilled circles were taken when spontaneous activity was eliminated by light adaptation. The shift to the right with mild light adaptation indicates that elimination of spontaneous activity increases the inhibitory threshold.

which measured the inhibition exerted on a single ommatidium by a small cluster under two conditions: first, with the surrounding ommatidia spontaneously active as a result of dark adaptation and, second, with the spontaneous activity of surrounding units silenced by the effects of light adaptation. Elimination of spontaneous activity increased the inhibitory threshold (x-intercept) without significantly influencing the inhibitory coefficient (slope). Apparently the summation of subthreshold inhibitory effects from nearby spontaneously active ommatidia with the inhibitory input from the cluster can lower the effective threshold of action on the test receptor.

To sum up, thresholds of similar magnitude characterize inhibitory interactions in excised and unexcised eyes. In both cases an ommatidium may be inhibited either by a neightboring unit responding in excess of some fixed rate

(threshold) or by a cluster of units firing at lower rates. These results suggest that subthreshold inputs from a cluster of ommatidia can add postsynaptically at a nearby ommatidium to exceed the threshold of action on that unit. The experiments by Graham et al. (1973) demonstrate on the other hand that subthreshold inputs from widely separated ommatidia within the inhibitory field of a centrally located unit cannot add together to reach the threshold of that unit. In such cases presynaptic mechanisms appear to predominate. We conclude that both presynaptic and postsynaptic mechanisms determine the threshold values and that for a given ommatidium the predominant mechanism is governed by the spatial distribution of ommatidia exerting inhibition.

Variability of the Spike Discharge

Lateral inhibition reduces both the rate and the variability of the spike discharge of single optic nerve fibers *in situ*. Fig. 9 gives the variance of the instantaneous firing rate (reciprocal of the interspike interval) from a single optic nerve fiber in the absence of inhibition (single-receptor illumination) and in the presence of

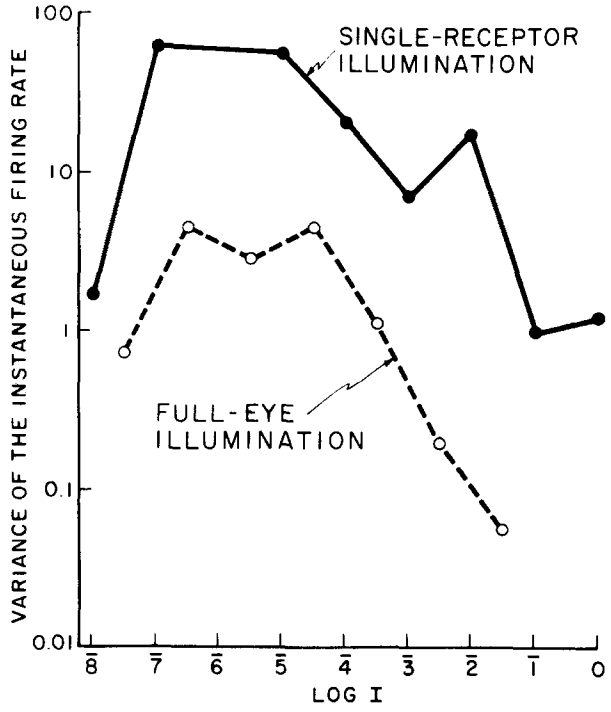

FIGURE 9. The variance in the instantaneous firing rate of a single ommatidium plotted as a function of light intensity. Variance (V) was calculated from 100 consecutive interspike intervals at each light intensity with the formula; $V = \sum_i^n (T_i - m)^{-2} n^{-1}$ where T_i is the interspike interval, m is the mean firing rate, and n is the number of intervals. The variance was measured when the ommatidium was singly illuminated (without inhibition) and when the eye was uniformly illuminated (with inhibition). Lateral inhibition decreased the variance of the instantaneous firing rate throughout the intensity range.

maximal inhibition (full-eye illumination). The results in the absence of inhibition agree with those of Kaplan (1973), namely, the variability in the impulse train approximates an inverted U-shaped function of light intensity. In the presence of inhibition the variance is reduced over the entire range of test intensities but the general shape of the curve is unchanged.

Fig. 10 plots the relative variability (coefficient of variation) for the data in Fig. 9. The coefficient of variation is defined as the ratio σ/m, where σ is the square root of the variance (ordinate in Fig. 9) and m is the mean instantaneous firing rate. The results for single receptor illumination are similar to those

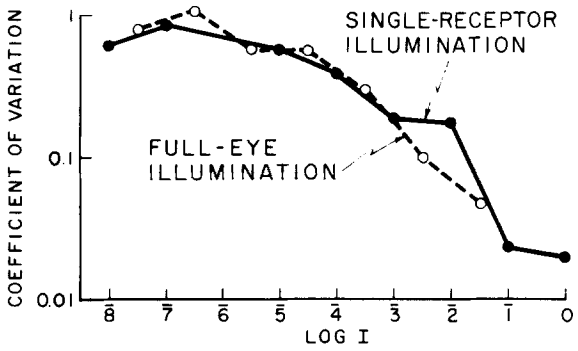

FIGURE 10. The relative variability of the instantaneous firing rate of a single ommatidium plotted as a function of light intensity. Relative variability is defined as the coefficient of variation, σ/m, where $\sigma = \sqrt{V}$ and m is the mean instantaneous firing rate. The coefficients of variation were calculated from the data of Fig. 9. Relative variability declines with increasing light intensity. Apparently high levels of excitation reduce relative variability, but inhibition has no measurable effect.

reported by Kaplan and Barlow (1975). Note that the coefficient of variation is not changed by lateral inhibitory inputs. This result was found both for eyes in which the strength of inhibition was high enough to produce sustained oscillations in the impulse discharge (Figs. 4, 6, and 7) and for eyes in which no oscillations were detected. Apparently inhibition not only decreases the rate of spike discharge of an ommatidium but also reduces in proportion the variability of the discharge.

DISCUSSION

Inhibition in the *Limulus* lateral eye *in situ* is qualitatively similar to that in the excised eye. In both preparations ommatidia mutually inhibit one another, and the magnitude of the inhibitory effect is a linear function of the response rate above threshold. In spite of these similar properties, there are important differences.

Strength of Inhibition

Excising the lateral eye of *Limulus* reduces the total strength of inhibition exerted on a single ommatidium. Excision does not, however, reduce the maximal levels of inhibition that can be exerted between single ommatidia. We therefore conclude that excision decreases the number of ommatidia which can

inhibit each receptor in the eye. A possible explanation is that the inhibitory pathways in the eye are impaired by the process of excision. Collateral fibers and (or) synapses which mediate inhibition in the lateral plexus (Hartline et al., 1961) may be susceptible to the mechanical forces created during excision.[5] Even in the absence of mechanical damage, inhibitory pathways are subject to the same ischemic conditions after excision as are the receptor cells. In view of the detrimental effects ischemia has on the excitatory properties of the receptors (Barlow and Kaplan, 1971), it is indeed possible that comparable damage is exerted on the inhibitory pathways.

In retrospect, it appears that the decrease in the efficacy of inhibition after excising the eye may be correlated with the "holes" in the inhibitory field reported by Barlow (1967). He defined a hole as an ommatidium located in the inhibitory field of another receptor but incapable of inhibiting that receptor. From measurements of the configuration of the inhibitory field in the excised eye, Barlow (1967) estimated that with no holes in the field the maximum strength of inhibition converging on a single ommatidium would be equivalent to a value of Σk_{pj} of ~7.0. This value would yield about a 90% reduction in the firing rate of a single ommatidium for whole-eye illumination. Values of Σk_{pj} for excised eyes typically range from ~0.5 to 2.5 which corresponds to only a 30–70% reduction in firing rate (Barlow and Lange, 1974). Barlow attributed the large difference in the estimated and measured values of Σk_{pj} to the presence of holes in the inhibitory field. It is interesting to note that the estimated value of 7.0 for Σk_{pj} for an excised eye without holes is within the range of the measured values for the eye *in situ* (Fig. 5). It is thus possible that holes do not exist in inhibitory fields of the lateral eye *in situ* but appear only after the eye is excised. If this is the case, then inhibitory fields have a more uniform configuration in the eye *in situ*. As we noted earlier, the detailed configuration of the inhibitory field has not yet been measured in the unexcised eye.

Threshold for Inhibition

The threshold for inhibition is the response rate which one ommatidium must exceed to inhibit the discharge of another (Hartline and Ratliff, 1957). Previous work has generally supported the view that there is a separate threshold for each inhibiting ommatidium. This view is incorporated in the original steady-state equation (Hartline and Ratliff, 1958) as well as in the revised form (Eq. 2). Eq. 2 indicates that the action of each inhibiting ommatidium j is characterized by a separate threshold r^o_{pj} rather than one threshold which the sum of the inhibitory effects on ommatidium p must overcome. Data supporting this scheme are derived from experiments on interactions exerted by several neighboring ommatidia (Hartline and Ratliff, 1957, 1958; Ratliff and Hartline, 1959; Ratliff et al., 1963; Barlow, 1967; Barlow and Lange, 1974) and by widely separated groups of ommatidia (Graham et al., 1973).

[5] In this regard we note that stripping the cornea off the eye may exert substantial mechanical forces on the retina, which could account for the difference between some of the results obtained with the "stripping" technique (Johnstone and Wachtel, 1976) and those reported here for the eye *in situ*.

The results presented in this paper indicate that under some experimental conditions the threshold depends in part on the number of ommatidia exerting inhibition. For example, inhibition exerted by a single nearby ommatidium is generally characterized by thresholds exceeding 20 impulses/s although lower values have been reported (see Results). Increasing the number of inhibiting ommatidia to four lowers the threshold to about six impulses/s in the eye *in situ*. When the number of inhibiting ommatidia is large as in full-eye illumination (Figs. 1 and 5), the threshold is generally less than one impulse/s. Similar data have been reported for the excised eye, although Hartline et al. (1961) ruled out the possibility that increasing the number of inhibiting ommatidia lowers the threshold (see Results).

We suggest that the threshold for inhibition depends on the number of inhibiting ommatidia and on their location relative to each other and to the inhibited ommatidium. These properties undoubtedly reflect to some extent the anatomy of the inhibitory pathways. For example, the effects from widely separated ommatidia cannot sum to overcome the inhibitory threshold of a centrally located ommatidium (Graham et al., 1973). This result suggests that the corresponding inhibitory pathways do not interact but rather synapse on functionally separate regions of the inhibited ommatidium, which is consistent with the tiered model of the lateral plexus proposed by Gur et al. (1972). An adequate description of this situation requires separate thresholds as in Eq. 2. The values of the separate thresholds appear to be determined by cellular processes which are presynaptic to the inhibited ommatidium.

On the other hand, the inhibitory effects from a cluster of ommatidia can sum to reach the threshold of a nearby unit. This result indicates that subthreshold inhibitory postsynaptic potentials sum to exert suprathreshold effects on neighboring units. This situation can be represented by replacing the individual thresholds, r_{pj}^{o}, in Eq. 2 with a single threshold, T_p:

$$r_p = \left\{ e_p - (1 + ae_p) \cdot k_p' \left[\left(\sum_{\substack{j=1 \\ j \neq p}}^{n-1} r_j \right) - T_p \right]_+ \right\}_+, \; p = 1, 2, \ldots\ldots n. \tag{4}$$

The n-1 ommatidia in the cluster will inhibit the nearby pth ommatidium when the sum of their responses exceeds the fixed threshold, T_p, of that unit. Each unit in the cluster is assigned the same coefficient, k_p'. Eq. 4 describes well the inhibitory effects exerted by a cluster for $n \leq 7$. Other cases have not been tested; however, it may be possible to extend this relationship to include several clusters of neighboring ommatidia. Experiments utilizing large clusters of ommatidia ($n > 30$) yield thresholds which are generally small fractions of the response rates of the inhibiting units, r_j. Such cases are adequately described by Eq. 3. They support the often-used assumption that inhibitory thresholds can be neglected when the number of inhibiting units is large (Barlow and Lange, 1974; Barlow and Quarles, 1975).

To sum up, interactions among widely separated ommatidia are characterized by inhibitory thresholds with presynaptic properties and can be represented by Eq. 2. Inhibition exerted by small clusters of ommatidia exhibits subthreshold summation, and special cases can be described by Eq. 4. At the present time the

spatial pattern of retinal illumination must govern the appropriate theoretical treatment of steady-state inhibitory interactions.

Variability in the Spike Discharge

Lateral inhibition reduces the variability in the spike discharge of single optic nerve fibers *in situ* (Fig. 9). Because the decrease in variability is proportional to the decline in mean firing rate at all test intensities, inhibition does not change the relative variability in the impulse train (Fig. 10).

Shapley (1971) investigated the effect of inhibition on the fluctuation of the spike discharge in excised eyes. He found that lateral inhibition could either increase or decrease the variance of the firing rate but always increased its relative variability because the reduction in mean firing rate exceeded the change in variance. Frequency spectra of the firing rate variance calculated by Shapley showed that inhibition decreased the high-frequency variance and increased the low-frequency variance. Variance spectra of our data agree qualitatively with those of Shapley. The only significant difference is that lateral inhibition in the eye *in situ* reduced the absolute level of the variance at all frequencis.

The possibility that fluctuations in neural activity code sensory information has been discussed by several investigators. Some have suggested that the variability in spike discharge could function as an intensity code (Burkhardt and Whittle, 1973; Sanderson et al., 1973), and others noted that the variability could convey information about the state of adaptation of the eye (Chung et al., 1970; Kaplan and Barlow, 1975). In the *Limulus* lateral eye the instantaneous response rate is a highly ambiguous function of light intensity. For a given intensity the firing rate of a single optic nerve fiber can vary widely depending on its state of adaptation and on the amount of inhibition received from its neighbors.

Kaplan and Barlow (1975) demonstrated that variability and mean firing rate together supply enough information to signal the incident light intensity and the state of adaptation of an ommatidium in the absence of lateral inhibition. Our data show that in the presence of lateral inhibition the relative variability of the optic nerve discharge remains an unambiguous function of light intensity when the state of adaptation is held fixed (Fig. 10). This relationship appears to break down when the state of adaptation is changed. Preliminary results indicate that increasing the level of light adaptation decreases variability more than the mean firing rate and thus reduces the relative variability of the spike discharge. Further investigation is required for a better understanding of the effects of light intensity, lateral inhibition, and state of adaptation on the temporal properties of optic nerve activity *in situ*.

Oscillations in the Optic Nerve Discharge

Lateral inhibition, under the appropriate conditions, can produce sustained oscillations in the spike discharge *in situ* (Figs. 4, 6, and 7) which, under normal conditions, are not observed in excised eyes. The common finding for the excised eye is that the onset of a diffuse, large-field stimulus evokes transient oscillations which have been attributed to the time delay to the onset of lateral inhibition (Hartline et al., 1961). However, we note that Adolph (1973) was able

to generate sustained oscillations in responses recorded from excised eyes by increasing the ambient temperature to 25°C. The period of oscillation was ~100 ms.

The sustained oscillations in the optic nerve discharge reported here appear to result from the interplay of excitatory and inhibitory influences. The observed effects could be explained by the following scheme. The onset of a bright, large-field stimulus generates a strong transient discharge in the optic nerve fibers and in their collateral branches in the plexus behind the eye. After a delay of ~130 ms (Ratliff et al., 1967),[4] the transient excitatory response evokes a synchronous inhibitory signal which is sufficiently strong to silence the discharge of each illuminated ommatidium. Once the optic nerve activity has ceased no further inhibitory signals are generated, and the inhibitory effects elicited by the preceding excitaton begin to decay. When the effects decay below some threshold level, the inhibition is abolished and the silent period ends with a burst of impulses generated by the steady light stimulus. The synchronous burst of excitatory activity elicits a second inhibitory signal, and the sequence of events then repeats itself.

This scheme for generating the oscillatory responses is consistent with our observation that such synchronous bursts of impulses require strong inhibitory interactions. The scheme is also consistent with the observation that the period of oscillation of ~200 ms is longer than the delay time to the onset of lateral inhibition. The length of the period is probably set by the delay time of 130 ms plus some fraction of the decay time for lateral inhibition, which is ~500 ms (Ratliff et al., 1966 and 1974). The fact that the sustained oscillations are spatially synchronous is further evidence that the delay time for the onset of inhibition is not a strong function of the distance separating the interacting receptor units (Ratliff et al., 1974).

The period of oscillation must indeed reflect the dynamic properties of both lateral inhibition and self-inhibition (Stevens, 1964; Purple and Dodge, 1965; Lange et al., 1966), but we make no attempt here to determine the relative contributions. Several theoretical aspects of the oscillatory responses have been investigated by Coleman and Renninger (1974, 1976, 1977). The response patterns they computed from a nonlinear integral equation agree qualitatively with the physiological results reported here.

The synchronous discharge of every optic nerve fiber may have important consequences for the animal. For example, under conditions which produce oscillations, the entire population of receptors yields no more information than that provided by a single receptor (see also Knight, 1972). On the other hand, such a repetitive, synchronous volley of nerve impulses would appear to provide an extraordinary input to the brain. Not only does intensity coding break down under such conditions, but information about any graded sensory stimuli is abolished. Oscillations in the optic nerve discharge must indeed represent a unique physiological state of the visual system.

It is interesting to note that similar oscillations were recorded from the optic nerve of the Conger eel by Adrian and Matthews in 1928. The waves of activity which they noted had a frequency of about 5/s and required diffuse illumination of the whole retina. Their paper also describes earlier work by Fröhlich (1913)

who reported similar oscillations in the optic nerve response of a cephalopod. More recently Glantz and Nudelman (1976) described oscillations in the steady-state discharge of the sustaining fibers of the crayfish optic nerve. The period of these oscillations was 100 ms, and intense, large-field illumination was required. Such optic nerve oscillations may prove to be a more widespread phenomenon once the appropriate experimental conditions are met.

CONCLUSIONS

Properties of lateral inhibition in the *Limulus* eye *in situ* were examined. The main finding is that an ommatidium is subject to inhibition from more of its neighbors before excision than after. Under certain stimulus conditions the inhibitory interactions can produce sustained, synchronous oscillations in the optic nerve discharge. Thresholds for inhibition appear to be determined by both presynaptic and postsynaptic events. Inhibition was found to reduce the variance in the impulse discharge of optic nerve fibers in proportion to the reduction in mean firing rate.The relative variability of the spike train is therefore not changed by inhibition, a result which may play a role in intensity coding.

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