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COMMON NOISE IN THE FIRING OF NEIGHBOURING GANGLION CELLS IN GOLDFISH RETINA

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SUMMARY

1. Pairs of goldfish retinal ganglion cells with overlapping receptive fields were recorded during stimulation with repeated light flashes. Cross-correlation histograms for 'maintained' discharge, 'on' responses, and 'off' responses were computed with a correction for the systematic responses to the stimuli; cross-covariances were derived from these. If stimulus-induced signals and noise combine linearly, then the cross-covariances are independent of differences in mean firing rate.

2. Cross-covariances of pairs of cells with the same response polarity displayed a positive peak near zero lag; pairs with complementary responses showed a negative peak. 'On–off' cells could generally be classified as on-like or off-like, based on the plateau of firing during a prolonged flash and the relative magnitudes of the on and off peak responses; the cross-covariances of these cells were as one would predict if they were pure on- or off-centre neurones.

3. The cross-covariances derived from the on period usually differed in magnitude from those derived in the dark (either maintained or off response). In general, cross-covariances for off responses were nearly identical to those for the maintained discharges of the same pair, although the mean rates at off were usually quite different from the maintained. The change in magnitude of the cross-covariances from on responses therefore appears to be a non-linear effect of light, and not of the changes in firing rate induced by the light.

4. Other features of the cross-covariances were not affected by stimulation. The general shapes remained fairly constant, and the lags at which the peaks occurred were not consistently affected.

5. We estimated the variance of the firing rate of each unit in three ways, and used two methods of portioning the variance implied by the cross-covariances; from these estimates, we obtained an upper bound for the proportion of the variance of firing of a cell which is due to the common noise that affects both members of a pair. We found that the common influence accounts for less than 20% of the total variance. During stimulation, both the magnitude of the cross-covariance and the variance of the rates change; however, the percentage of total variance contributed by the common noise source is constant.

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6. We conclude that light has the effect of changing the gain of the pathway after the introduction of both the common and unshared (private) noise sources but before the ganglion cell. One way this might be achieved, in spite of the likelihood that the common noise enters distally in the network while the private noise enters proximally, is that both noise sources may be injected within a closed feed-back loop. The gain of the loop would be adjusted by a light-mediated effect upon the feed-back element.

INTRODUCTION

The action potential (spike) discharge of ganglion cells in the vertebrate retina is quite variable; the source of this variability is unknown. One means of tracking down the source is to study statistical dependencies in spike discharge between neighbouring ganglion cells by generating cross-correlation histograms (Perkel, Gerstein & Moore, 1967). With this method, statistical dependencies between ganglion cells have been demonstrated in goldfish (Arnett, 1978; Levine & Johnsen, 1982; Johnsen & Levine, 1983), rabbit (Arnett & Spraker, 1981) and cat retinae (Rodieck, 1967; Mastronarde, 1983*a*). The type of dependency observed in these studies was related to the functional types of the ganglion cells in the pair; ganglion cells with the same types of centre processes tended to fire in synchrony, while those with complementary centre processes were likely not to fire together. The peak (positive or negative) of the cross-correlation did not in general occur at zero lag, the point representing simultaneous events in the two cells (Arnett & Spraker, 1981; Johnsen & Levine, 1983).

There are two possible ways to account for these statistical dependencies: either a common noise source is affecting more than one ganglion cell, or there is a functional interaction between ganglion cells (Perkel *et al.* 1967). In light of anatomical and certain physiological considerations, the latter possibility has generally been discarded in favour of the common noise hypothesis (Rodieck, 1967; Arnett, 1978; Johnsen & Levine, 1983), although Mastronarde (1983*c*) demonstrated a small direct interaction between certain Y-cells.

In the past, the search for dependencies between ganglion cells has been limited to data taken during periods of maintained discharge, either in the dark or in steady diffuse illumination (Rodieck, 1967; Arnett, 1978; Arnett & Spraker, 1981; Mastronarde, 1983*a*). Mastronarde (1983*b*) reported the only study in which the same pairs of cells were observed at different mean illuminations. His Fig. 1 reveals little difference in cross-correlation for changes of about a log unit in mean lighting. He reported that the magnitudes of the cross-correlations did vary somewhat with mean illumination, but the shapes were relatively invariant (except at extremely low levels, where individual quantal events contributed more to the cross-correlation).

In order to discover whether the mechanisms responsible for the observed dependencies between ganglion cells are altered by the processes associated with the responses of the cells, we wanted to study statistical dependencies during periods of active response to stimulation. With time-dependent stimulation, predictable changes occur in the mean firing rates of ganglion cells; however, the variability does not disappear. The question arises as to what changes will occur in the contribution of the common noise to the noise in ganglion cell firing. In particular, does the common

noise add, in a linear fashion, a fixed amount to the noise of ganglion cell firing regardless of the mean rate of the cell, or does the amount of noise depend on either the mean rate or the presence of light? In this study, we estimated the variability of goldfish ganglion cell firing due to the common noise source, both in the dark and during stimulus flashes.

METHODS

Experimental methods

Goldfish (*Carassius auratus*) were maintained at room temperature in large uncrowded aquaria on a 12 h light/12 h dark cycle. Each fish was placed in the dark for one-half hour or more before its retina was isolated by the procedure of MacNichol & Svaetichin (1958). The prepared retina was placed, receptors up, in an isolation chamber. Pure humid oxygen flowed over the retina; the chamber volume was replaced a few times per minute. A vitreous-soaked wick was draped around the retina; it contacted a chlorided silver wire to secure an indifferent (signal ground) connexion. The active electrode was made of platinum–iridium wire insulated with glass (Wolbarsht & Wagner, 1963).

The signal from the electrode was amplified, fed to an audio monitor, and converted to pulses representing the two spike trains. It was generally not difficult to detect two neuronal spike trains simultaneously with one electrode. Only neurone pairs were recorded for which the electrode could be positioned to detect spikes from one neurone at about twice the amplitude of spikes from the other.

We devised a time and amplitude discrimination scheme to optimize separation of the two spike trains. Two threshold discriminators were combined with logic circuitry to operate as follows: the signal from the electrode, consisting of two superposed spike trains, passed to each of the two discriminators. Discriminator A produced a pulse whenever a large-amplitude spike occurred. This discriminator detected signal transitions on their leading edges, but produced its output pulse after a delay set by the experimenter to equal the expected duration of a large-amplitude spike. Discriminator B was set to trigger at the level of the lower-amplitude spike. Unlike discriminator A, it produced its pulse when the input signal amplitude re-crossed the threshold while returning toward zero, i.e. on the trailing edge of any spike, large or small amplitude. Since discriminator B detected the trailing edge of a spike and A was triggered with a delay, both discriminators produced pulses at the same time when there was a large-amplitude spike; in this case, the output of B was suppressed by the simultaneous pulse from A.

When a large and a small spike occurred at about the same time, both A and B produced pulses, but not simultaneously. Thus, with two spikes superposed the output of B was not suppressed by A, and spikes were registered on both recording channels. This method represented the two spike trains as nearly independently as possible, although on rare occasions a pair of simultaneous spikes was erroneously registered or omitted. This error affected the cross-correlation function (described below) only at lags of 1 ms or less.

Once a cell-pair was isolated, an H-P 2100A minicomputer timed and supervised the experiment. Spike activity was recorded as times of occurrence (1 ms resolution), and shipped to a PDP-11/03 computer. The PDP-11 did a brief summary analysis of the data between records; it also stored all raw data on floppy disk media for off-line analysis.

The optical stimulator had three independent channels, two with tungsten halogen sources under feed-back control and one with a highly stable compact xenon arc source. Each had a monochromator, electromagnetic shutter, and bank of colour-neutral attenuating filters. Each channel imaged a field stop at 10:1 minification on the retina.

The stimuli were spots of light of 710 nm, within 2 log units of the maximum available retinal irradiance, $1{\cdot}46 \times 10^{12}$ quanta cm^{-2} s^{-1}. The spots were 0·32–1·00 mm diameter as measured at the retina. If the diameter of a receptive field is measured with a small (about 0·1 mm diameter) probing spot, most ganglion cells give a 'centre' response over a range of at least 1 mm (e.g. Daw, 1968). Therefore, our stimuli were effectively confined to the central area of the receptive field. The form of this central response for all cells recorded here was 'on' (excited at onset of a light flash), 'off' (inhibited at the onset of a light flash), or 'on–off' (excited at both onset and offset of a light flash).

In several experiments, the relationship between the receptive field central area and the electrode position was checked with a small probing spot. The position at which each cell responded

maximally to the spot corresponded closely with the electrode axis; in fact, to the accuracy obtainable, both cells had receptive fields concentric with the electrode. (This concurrence of neighbours is not surprising given the large field sizes compared to the spacing between ganglion cells.) It was concluded from this that centring a small spot about the electrode tip was sufficient to secure stimulation effective for the centre region of the receptive field of each cell.

Each cell-pair was recorded in discrete periods (gates) of 9–30 s each, separated by at least 10 s. Pairs of cells were recorded for eight to 108 successive gates (with only six exceptions, there were at least thirty gates in an experiment). The light stimulation was identical in all gates of an experiment; in most cases, each gate consisted of a 3 s dark period ('maintained' period), followed by a 3 s light flash ('on' period), followed by another 3 s in the dark ('off' period). In the remaining cases, one or more of the periods exceeded 3 s, but only the first 3 s of each were included in the analyses (except as noted).

All experiments were inspected for non-stationarities (gate-to-gate trends) by plotting the rates in successive gates as a function of time. This was done separately for the maintained, on, and off periods. Sometimes there was a weak trend (increasing, decreasing, or cyclic) in the mean rates of the cells in the dark; often there was a trend in the sizes of the responses to light (Levine & Shefner, 1977*a*). Although weak trends would have only small effects on the cross-correlation estimates to be reported here, strong trends would be unacceptable, and only sequences of gates lacking strong trends were used.

Analytical methods

The cross-correlation function for two spike trains represents the probability of firing by one unit as a function of the time, τ, before or after the occurrence of a spike in the other unit (Perkel *et al.* 1967). This can be estimated by:

$$c(\tau) = \frac{\Delta t}{\bar{r}_a T} \sum_{t=1}^{T/\Delta t} r_a(t) \cdot r_b(t+\tau) \qquad (1)$$

in which $c(\tau)$ is the cross-correlation histogram, Δt is the bin width, T is the total sample time, and $r_a(t)$ and $r_b(t)$ are the firing rates of the two units at time t. If the times of occurrence of spikes produced by the two units are independent of each other (as at large τ), the expected value of this function is $\bar{r}_b$, the mean firing rate of unit b.

This cross-correlation estimate is meaningful only if the two spike trains are stationary. We wanted to compare cross-correlations between the maintained period and each of the two response periods, during which there is an obvious and repeatable pattern of firing following onset or offset of a stimulus. Two units, even if completely independent statistically (for example, in separate retinae), would show some cross-correlation in the on period because they are being driven by the common influence of the stimulus. We wished to remove the influence in the cross-correlation of the response to stimulation, and examine only the intrinsic common stochastic influences on the two units (the only component present in the maintained period).

To do this, we used a procedure devised by Perkel *et al.* (1967). It was assumed in this procedure that influences due to the stimulus add linearly to and are independent of the processes responsible for the maintained activity of the cell. We calculated the ordinary cross-correlation histogram, which is the average of the estimates obtained by applying equation (1) to the two spike trains in the appropriate periods in gate 1, gate 2, etc. This cross-correlation shows common influences on the two cells which are intrinsic to the retina, as well as effects due to the common stimulus, if any. We also obtained an alternate-gate cross-correlation, in which the spike train of unit a was recorded in gate 1, but the spike train of unit b was that from gate 2; this was averaged with train a of gate 2 cross-correlated with train b of gate 3, and so forth. For this estimate of the cross-correlation, the only common influences that can be imparted are due to the responses to the common stimulus. We then subtracted the alternate-gate cross-correlation from the ordinary cross-correlation, leaving only that component due to common influences not induced by the stimulus. Because differencing the two functions also removed the asymptotic level, it was restored (for consistency with equation (1)) by adding the constant $\bar{r}_b$. We calculated all cross-correlations as the difference between the ordinary and the alternate-gate cross-correlation, with $\bar{r}_b$ restored.

The cross-correlations estimated for the three different periods, although all representing intrinsic common noise, would still appear different merely because $\bar{r}_b$ generally differed among the three periods. We wanted a function which is independent of mean rate; this function would be identical

among the three periods, assuming a linear model for common noise. This provided a test for the linear model.

In the linear model, the firing rate of each unit is determined by the sum of a parameter that determines mean rate ($\bar{r}_a$ for unit a, $\bar{r}_b$ for unit b), plus disturbances from a common noise source affecting both units (N_c), plus disturbances from a 'private' noise source affecting only the one unit (N_a or N_b). This model appears in Fig. 1. We assumed the noise sources have a mean of zero (any non-zero component can be subsumed in the mean rate parameters), and are independent of each other. The mean rate is determined by intrinsic properties of the cell and by the time-varying response to stimulation. The firing rates of the two cells in a pair at any time t are given by

$$r_a(t) = \bar{r}_a + a \,.\, N_c(t) + N_a(t), \tag{2a}$$

$$r_b(t) = \bar{r}_b + b \,.\, N_c(t-\omega) + N_b(t), \tag{2b}$$

where the constants a and b allow for the differential effectiveness of N_c on the two units, and ω allows for a difference in conduction times from N_c to the two units. (The mean rates, $\bar{r}_a$ and $\bar{r}_b$, can be treated as constants since any time dependency during a period will have been removed by the correction for the presence of light stimulation.)

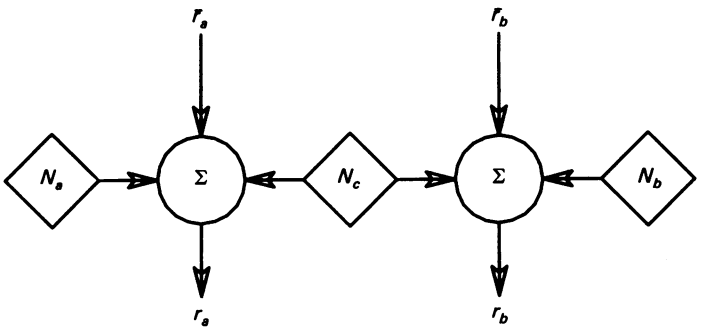

Fig. 1. Linear addition of noise sources (diamonds) and signals in a pair of ganglion cells to determine the observed firing rates, r_a and r_b. Common noise N_c contributes to both units; private sources (N_a and N_b) contribute to each, along with the mean firing levels, $\bar{r}_a$ and $\bar{r}_b$.

The cross-correlation histogram expected from the linear model can be found by substitution of equations (2) into equation (1), yielding nine summed terms. However, many of these terms have an expected value of zero; terms involving the product of an $\bar{r}$ and a single N vanish because the N have zero mean, while cross products of different N are zero because the N are independent. All that remains is

$$c(\tau) = \bar{r}_b + \frac{a \,.\, b}{\bar{r}_a}\left(\frac{\Delta t}{T}\sum_{t=1}^{T/\Delta t} N_c(t) \,.\, N_c(t-\omega+\tau)\right). \tag{3}$$

Notice that the private noise sources N_a and N_b, although they may reduce the precision of the cross-correlation estimate (and certainly do contribute to the variability of the firing of the cells), do not appear in the cross-correlation function.

In order to generate a function that is independent of the mean rates of the two cells, we multiplied the cross-correlation by $\bar{r}_a$ and subtracted the product of the mean rates, $\bar{r}_a \,.\, \bar{r}_b$; for the linear case, this gave the cross-covariance of N_c:

$$C(\tau) = \bar{r}_a \,.\, c(\tau) - \bar{r}_a \,.\, \bar{r}_b. \tag{4}$$

(Note this estimates $E((r_a - \bar{r}_a)(r_b - \bar{r}_b))$, the familiar definition of cross-covariance.) $C(\tau)$ should reach a maximum (or a minimum) of $a \,.\, b$ at $\tau = \omega$, and approach zero for large τ. It is in units of (spikes $s^{-1})^2$. a and b, which we treated as constants, may themselves be functions of time, allowing for temporal filtering in the pathways to the two units; with this assumption, $C(\tau)$ would not have to be symmetric about $\tau = \omega$. Mastronarde (1983*a*) has pointed out that the temporal

properties of the two units in a pair can also account for the 'side dips' often evident near the main peak of a cross-correlation. Figs. 2–6 in this paper show cross-covariances generated according to equation (4), applied to cross-correlation histograms (equation (1)) corrected for the response pattern as described above. For clarity of presentation, the histogram bins were rounded at the corners.

To assess the statistical significance of our estimates of the cross-covariance functions, we followed Arnett & Spraker (1981), who provided a simple expression for the standard deviation of a function related to our cross-correlation histogram. Their derivation (based on Johnson & Kiang, 1976) assumed independence of the two spike trains. We translated their expression into the units of our cross-covariance, including a correction for the fact that our cross-correlation histograms are the difference of two effectively independent histograms (ordinary and alternate-gate) and thus have twice the variance. Our estimate of the standard deviation of the cross-covariance is

$$\sigma_c \cong \sqrt{(\bar{r}_a . \bar{r}_b / T\Delta t)}. \tag{5}$$

Note that the derivation of equation (5) assumed the independence of the two spike trains; it therefore only is valid for testing for differences from zero. We have used this estimate to indicate two standard deviations on our cross-covariances. To apply this estimate to distinguish non-zero cross-covariances, one would have to assume the variability of the cross-covariance is the same at those values of τ where the spike trains are not independent. Nevertheless, σ_c can serve as a rough metric for the variability of the cross-covariance function as a whole.

The total variance of the firing of either unit is the sum of the variance of the common noise plus the variance of the private source:

$$\sigma^2_{r_a} = a^2 + \sigma^2_{N_a}, \tag{6a}$$

$$\sigma^2_{r_b} = b^2 + \sigma^2_{N_b}, \tag{6b}$$

where σ^2_r is the variance. From equations (6), we determined what portion of the variance of firing is attributable to N_c, and what portion is due to the private noise, N_a or N_b. However, we first had to obtain estimates of a or b and σ^2_{ra} or σ^2_{rb}.

We cannot know a and b individually without a further assumption. If we assume that $a = b$ (that is, the common noise contributes an equal amount of variance to each of the two units), the value of the cross-covariance function at $\tau = \omega$ is $a^2 (= b^2)$, the variance of N_c, as viewed from either cell. One alternative assumption is that the common noise represents the same fraction of the total variance for each of the two units. It can be shown that this assumption yields the lowest possible average percentage contribution of the common noise; since we wished to obtain an upper bound, we did not consider this possibility. A third possible assumption is that the common noise contributes to the variability of each unit in the same proportion that light-induced signals from the receptors contribute to changes in the firing rates of the two cells, that is

$$a/b = \hat{r}_a/\hat{r}_b, \tag{7}$$

so

$$a^2 = a . b . \hat{r}_a/\hat{r}_b, \tag{8a}$$

and

$$b^2 = a . b . \hat{r}_b/\hat{r}_a. \tag{8b}$$

Here, $\hat{r}_a$ and $\hat{r}_b$ are the peak responses of the cells. They were obtained by taking the maximum of each averaged response histogram (peri-stimulus time, p.s.t. histogram, 2 ms bin width) after convolving it with a dome-shaped pattern approximating a γ distribution truncated to be 26 ms wide (see Johnsen & Levine, 1983).

We estimated σ^2_r in three ways for each cell. One estimate of σ^2_r may be obtained directly from the spike train, if it is partitioned into bins of the same width as those used to derive the cross-covariance of N_c. It is assumed here that it will be rare for more than one spike to fall within a single 5 ms bin, the width actually used; the variance is therefore approximately

$$\sigma^2_r = \bar{r}\left[\frac{1}{\Delta t} - \bar{r}\right]. \tag{9}$$

Alternatively, we can estimate σ^2_r from the equation

$$\sigma^2_r = \sigma^2_{\text{i.s.i.}} \mu^{-3}_{\text{i.s.i.}} \Delta t^{-1}, \tag{10}$$

where $\mu_{i.s.i.}$ is the mean of the distribution of intervals between successive spikes, $\sigma^2_{i.s.i.}$ is the variance of that distribution, and Δt is the sample period, here 5 ms (see Levine, 1980). (Note that if $1/\Delta t$ is very large compared to $\bar{r}$, equation (10) is approximately equation (9) multiplied by the square of the coefficient of variation of the intervals, $\sigma_{i.s.i.}/\mu_{i.s.i.}$.) However, this relationship assumed a renewal process. Our third estimate takes into account the fact that the maintained discharge of goldfish retinal ganglion cells is not well described by a renewal process, at least in the range from 200 ms to 1 or 2 s (Levine, 1980, 1982). A better estimate for σ_r^2 comes from

$$\log \sigma_r = A + m \cdot \log \Delta t, \tag{11}$$

where the parameters A and m are obtained by fitting a straight line on a double logarithmic plot of σ_r *vs.* Δt. To obtain the third estimate of σ_r^2, we extrapolated a regression line to $\Delta t = 5$ ms (the bin width) and squared the obtained value.

RESULTS

We recorded from thirty-one pairs of ganglion cells in twenty-eight separate retinae. The cross-covariances from five of those pairs showed no significant peak; these pairs were deemed unusable and will not be considered further. All of the fifty-two cells included in our sample were active in the dark; the mean maintained discharge was 24·75 spikes s^{-1} (standard deviation = 15·30 spikes s^{-1}).

We confirmed the observations cited in the Introduction that when both units in a pair are of like response type (both cells on-centre or both off-centre), they show an increased probability of firing in synchrony or near synchrony (positive peaks in cross-covariance), and that when they are of complementary types they tend not to fire in proximity (negative peak in cross-covariance). However, twenty of our cells produced 'on–off' responses; 'on–off' cells have not heretofore been examined for cross-correlation with unitary responders. We observed that most of these on–off cells produced a response that could be categorized as more like that of an on-centre cell or more like that of an off-centre cell; the features we considered were the plateau level of firing after the stimulus had been present for one or more seconds (greater or less than 'maintaned' discharge), and whether the peak of the response to stimulus onset was greater or less than the peak of the response to stimulus offset. When these features taken together indicated the cell was more 'on-like' (as in Fig. 2) or 'off-like' (as in Fig. 3; see also Figs. 5 and 6), the direction of the cross-covariance with the second unit of the pair was as one would predict from the response types of the two cells. It seems unlikely that the on–off nature of the response was caused by intrusion of the surround, because these cells were often stimulated with spots considerably smaller than the receptive field centre. We also note that in all but two of these cases, the on–off cells were paired with unitary (pure on-centre or pure off-centre) cells; it seems unlikely that a stimulus could generally cause surround intrusion in only one of the two cells in a pair. We thus believe these were genuinely on–off cells, and that they participate in the same cross-correlations as the purely on-centre and off-centre cells.

A cross-covariance estimate was obtained for each of the twenty-six cell-pairs that had a significant cross-covariance. When the estimates obtained for maintained discharge were compared with those obtained for on and off responses, the most striking differences noted among these functions were in magnitude. Sixteen pairs had a different cross-covariance at on than they had for maintained discharge. In

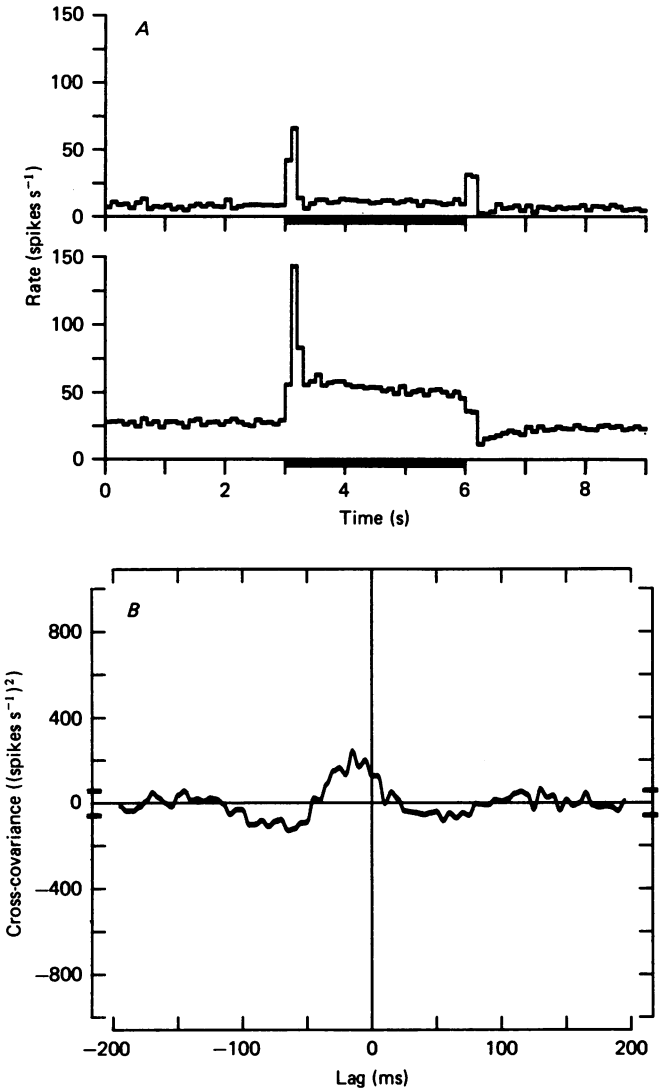

Fig. 2. Cross-covariance of an on-like 'on–off' unit with an on-centre neurone. Note the positive peak for cells of similar type. *A*, p.s.t. histograms, 100 ms bin width. *B*, cross-covariances, 5 ms bin width (maintained discharge only). Mean rates: $\bar{r}_a = 8{\cdot}29$ spikes s^{-1}, $\bar{r}_b = 27{\cdot}41$ spikes s^{-1}. Thirty-four gates. $2\sigma_c$ is shown by ticks on the ordinates; except for the peak, nearly all points lie within the $2\sigma_c$ range.

four of these sixteen pairs the cross-covariance at on had the largest peak (Fig. 4), while in twelve pairs the peak was the smallest for on (Fig. 5). In six cases, the function at off also differed from that for maintained (Fig. 6); however, the difference between the function for maintained discharge and that for on was always as great or greater than between cross-covariances for maintained and off. Ten of the twenty-six pairs showed little difference in cross-covariance among the three functions corresponding to maintained, on or off. There seems to be no consistent rule relating the cell types in a pair and the magnitude of the cross-covariance for on relative to that for the maintained (see Table 1).

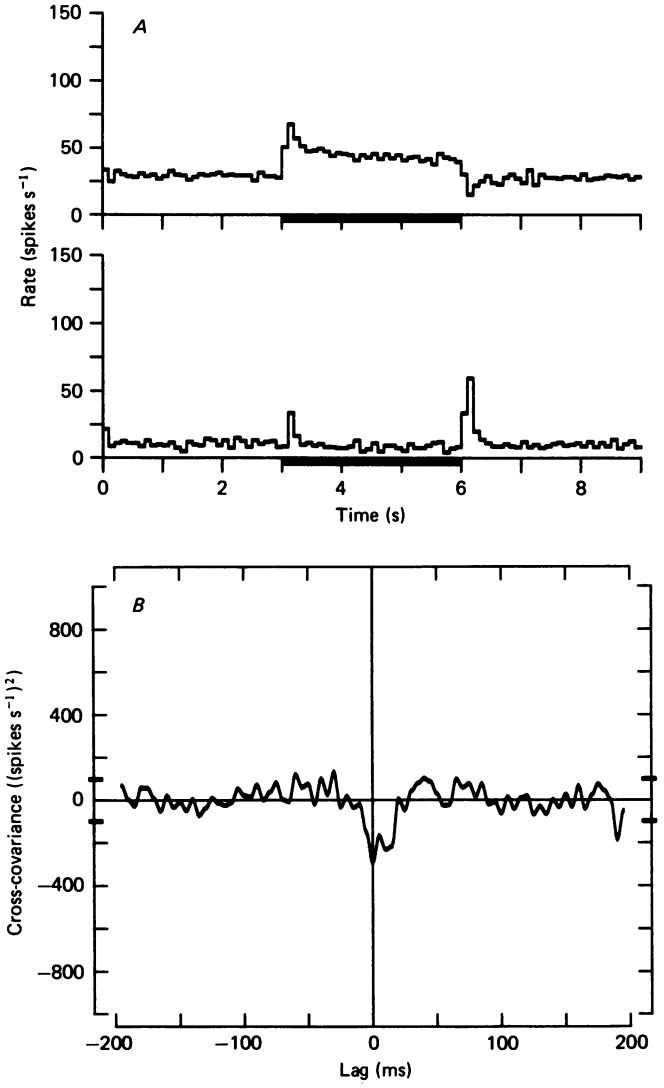

Fig. 3. Cross-covariance of an off-like 'on–off' unit with an on-centre neurone. Note the negative peak for cells of opposite type. Conventions as in Fig. 2. Mean rates: $\bar{r}_a = 29{\cdot}49$ spikes s^{-1}, $\bar{r}_b = 11{\cdot}19$ spikes s^{-1}. Eighteen gates.

It is clear that the magnitude of the contribution of common noise to ganglion cell variability usually differs during light stimulation; this is not consistent with the linear model shown in Fig. 1. Although our cross-covariance does not depend on firing rates, the question may be raised as to whether the changes in variability are induced specifically by the presence of light and hold only when it is present, or are related mainly to the changes in the firing rate caused by light. This question cannot be answered with certainty, but we can make the following observation: some cells, particularly off-centre cells, show the greatest changes in firing rate at light offset; in these cases, the cross-covariances for on were nevertheless the most disparate. If the changes in the cross-covariance were mainly due to rate changes, these pairs ought to show the greatest change in cross-covariance at off. Several cells that were

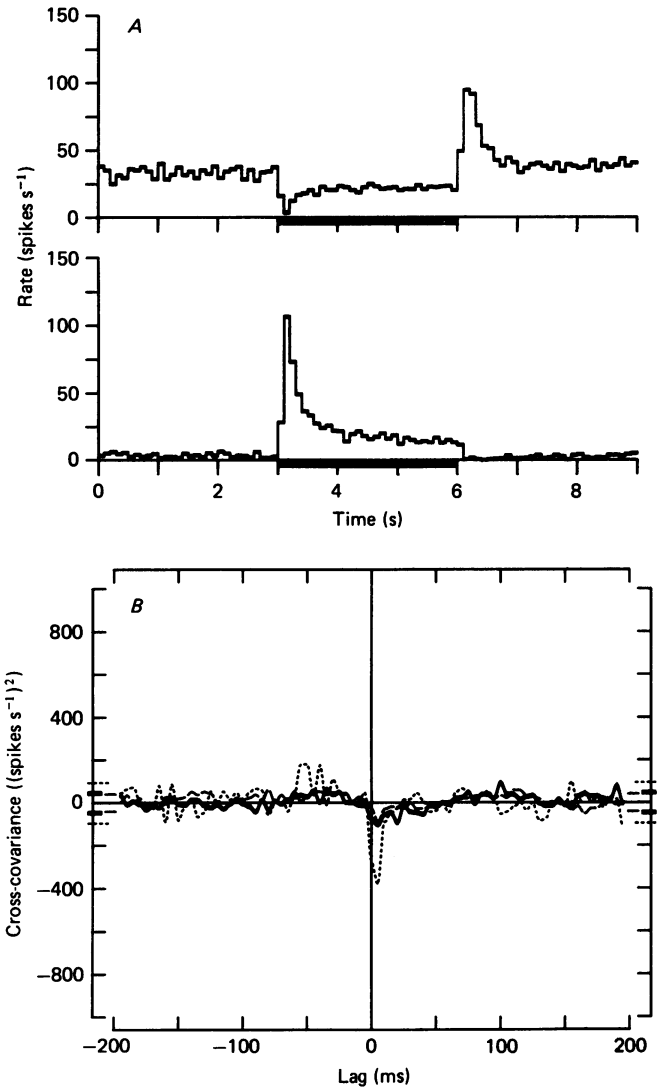

Fig. 4. Effect of stimulation on cross-covariances, showing a larger negative cross-covariance at on. *A*, p.s.t. histogram derived from each unit; conventions as in Fig. 2*A*. *B*, cross-covariances for maintained discharge (heavy continuous line), on response (dotted line), and off responses (dashed line); 5 ms bin width. Mean maintained rates: $\bar{r}_a = 33{\cdot}54$ spikes s^{-1}, $\bar{r}_b = 3{\cdot}60$ spikes s^{-1}. Thirty gates; 0·56 mm spot at 0·0 log attenuation. For all three function, $2\sigma_c$ is shown on the ordinates with ticks of corresponding line types.

particularly strongly excited at off did not show any differences between the off cross-covariance and that for maintained. Therefore, it can be concluded that even though a light flash causes a change in firing rate after the light is extinguished, there is an influence on the cross-covariance due specifically to the presence of light which does not survive termination of the stimulus.

Features of the cross-covariance other than their magnitudes did not differ among maintained, on and off stimulus conditions. The direction (positive or negative) of the cross-covariance peak (which depends on the pairing of cell response types) never

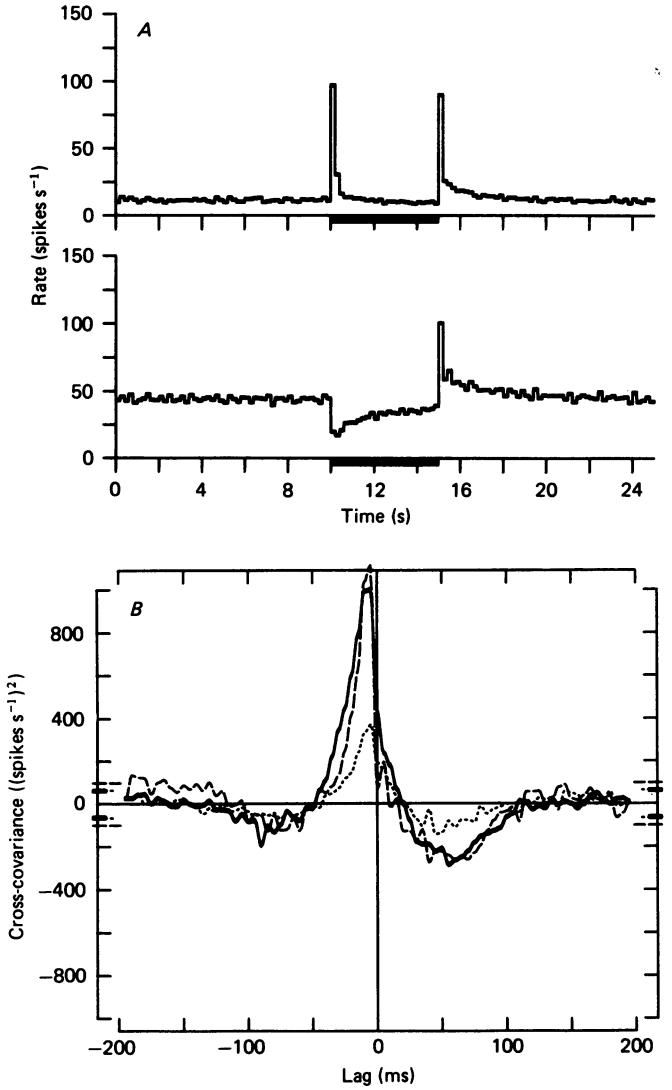

Fig. 5. Effect of stimulation on cross-covariances, showing a smaller positive cross-covariance at on. *A*, p.s.t. histograms, 200 ms bin width. *B*, cross-covariances; conventions as in Fig. 4*B*. Mean maintained rates: $\bar{r}_a = 11{\cdot}46$ spikes s^{-1}, $\bar{r}_b = 44{\cdot}41$ spikes s^{-1}. Seventy gates; 0·56 mm spot at 0·5 log attenuation.

changed, although in a few cases the on peak became so small as to be buried in the noise of the estimate. The lag at which the peak occurred in a given cell pair (ω) was also hardly disturbed. The lag of the peak during maintained activity was correlated with the lag of the peak at on and off with correlation coefficients of 0·88 and 0·91, respectively. We plotted the measured values of the lags during the stimulus *vs.* the corresponding lags for the maintained discharge; the slope of the best-fit line through the origin was 0·92. We also noted that with only two exceptions, the onset or offset of a light stimulus made little or no qualitative alteration in the shape of the cross-covariance.

Thus far, we have examined properties of the noise common to both ganglion cells

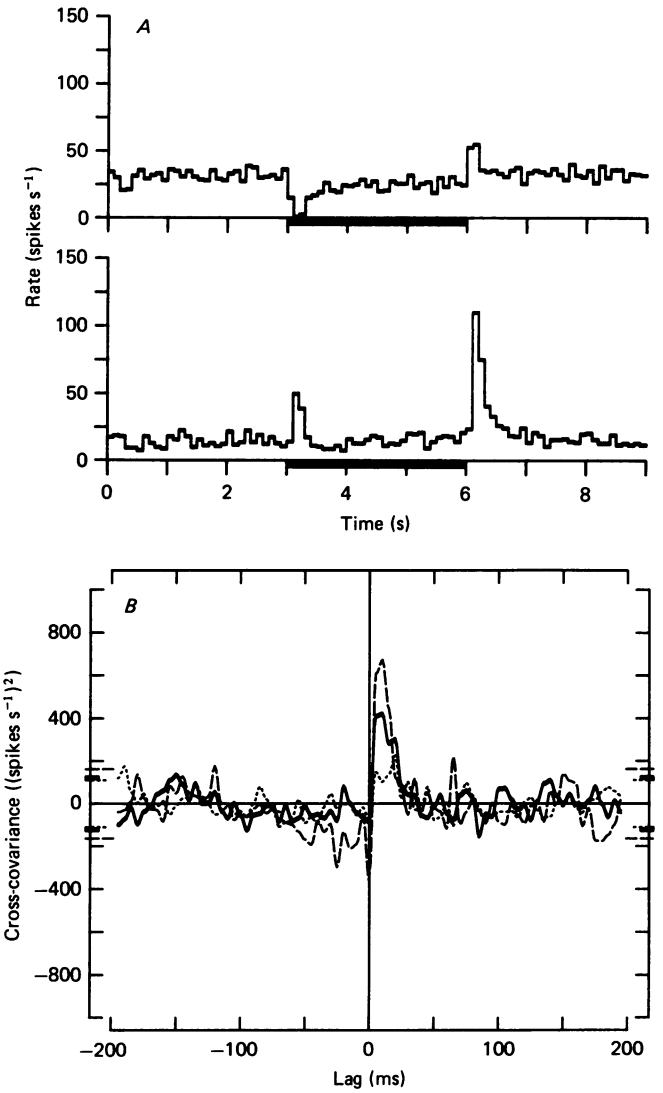

Fig. 6. Effect of stimulation on cross-covariances, showing cross-covariances of different magnitudes at on and off. Conventions as in Fig. 4. Mean maintained rates: $\bar{r}_a = 31{\cdot}43$ spikes s^{-1}, $\bar{r}_b = 14{\cdot}48$ spikes s^{-1}. Sixteen gates; 0·56 mm spot at 2·0 log attenuation.

TABLE 1. Numbers of pairs showing a larger cross-covariance at on, little or no difference among the cross-covariance functions, or a smaller cross-covariance at on, according to the types of units comprising the pair

Magnitude of on cross-covariance	Both cells on-like	Both cells off-like	Complementary
Larger than maintained	—	—	4
Same as maintained	3	3	4
Smaller than maintained	1	7	4

of a pair, both in the dark and during the responses to light. We next address the question of how much of the variability of firing of each unit is attributable to the common noise, and how much is generated by the private source; that is, we want to know the percentage of the total variance of rate represented by a or b.

We estimated the total variance of the firing in the dark using the three estimates given by equations (9), (10) and (11). Since we sought an upper limit on the contribution of the common noise, we chose the minimum of the three estimates for each unit. However, for thirteen of the fifty-two units the plot of standard deviation of rate *vs.* sample duration was unsuitable for estimating σ_r^2 from equation (11). For these units, the slope was considerably shallower than $-\frac{1}{2}$, and the observed standard deviation of rate greater than would be predicted by equation (10) for samples of at least 200 ms. This could be due to slow oscillations of the rate (on the order of seconds), or a slight drift in the mean rate. In these cases, the variance of rate was taken as the lesser of the estimates from equations (9) and (10). In all, twenty-six of the estimates came from equation (9), seventeen from equation (10), and nine from equation (11).

The percentage contribution of the common noise to the maintained firing was estimated twice for each unit: once using the assumption that $a = b$ ($a^2 = b^2 = a.b$), and once using the assumption of proportional contributions expressed by equations (8). The means of these estimates were 16·32 and 16·26 %, respectively, with standard deviations of 14·67 and 17·35 % ($n = 52$). It thus seems reasonable to conclude that the common noise responsible for the cross-correlation between units contributes somewhat less than 20 % of the total variance of the maintained firing of each unit.

We also wanted to know what percentage of the variance of firing is contributed by the common noise during a response to light, when the magnitude of the common noise is different. Because we cannot estimate the variance of rate if the firing is not stationary, we only considered the firing during the steady plateaus, not the peaks. In nineteen of the cell pairs, the firing rate of both cells during the stimulus stabilized to steady plateaus that were maintained for at least 1·5 s before stimulus offset; in all but three of these, the stable plateau was maintained for at least 2 s. In those cases for which there was a plateau, the percentage contribution of the common noise was estimated just as for the maintained firing, using only the data from as long a plateau period during stimulation as was available. As before, σ_r^2 was taken as the least of the estimates given by equations (9), (10) or (11) (in twelve of the thirty-eight cases, equation (11) could not be applied), $a.b$ was measured from the cross-covariance, and percentages were calculated both by assuming $a = b$ and from equations (8). In twenty-three of the thirty-eight cells, the equation that gave the minimum estimate for maintained also provided the minimum for on. The mean percentage contributions of the common noise during the response plateaus were 15·10 and 14·54 % by the two methods, with standard deviations of 13·80 and 12·10 % ($n = 38$). These means are not significantly different from each other (paired t test), nor are they significantly different from the means found for the maintained discharge.

The preceding analyses gave an upper bound for the percentage contribution of the common noise to the variance of firing. In order to ensure that the similarity of percentage contributions was not affected by the choice of equations, we recalculated the means using the average of the two lowest estimates (with the same two equations

used for maintained and on in each cell). As before, there was no significant difference between the mean percentages for maintained and for on (for $a = b$, maintained was 11·75 %, S.D. = 8·50 %; on was 11·01 %, S.D. = 9·92 %. For proportional contributions, maintained was 12·13 %, S.D. = 11·19 %; on was 11·01 %, S.D. = 9·73 %).

Not only were the mean percentage contributions of the common noise the same in light and dark, but the estimates for maintained and the estimates during the plateau were quite highly correlated (for $a = b$, $r = 0{\cdot}67$, $n = 38$, $P < 0{\cdot}0001$; for a and b in proportion to peak responses, $r = 0{\cdot}78$, $P < 0{\cdot}0001$). The average slope of the principal component relating maintained to on was 0·96, which is extremely close to the unity slope expected if there is no difference in percentage contributions. These relationships indicate that while the presence of a stimulus might change the mean firing rate, the variability of firing, and the magnitude of the cross-covariance, the common noise always contributes the same percentage of the variance of firing.

In order for the percentage contribution of the common noise to remain constant, the magnitude of the private noise source must change in proportion to any change in common noise between maintained and on. To show that this did occur, we correlated the difference in common noise (change in $a.b$) with the difference in private noise (from equations (6), with σ_r^2 given by the same mean of two estimates as in the previous two paragraphs). The correlation was positive ($r = 0{\cdot}44$, $P < 0{\cdot}01$), indicating that despite the considerable variability in our measures of variances, the private source covaried with the common source. Moreover, the principal component of a scatter plot relating these changes in variances had its intercept very near zero and a slope of 4·14; with the principal component constrained to pass through the origin, the slope was 4·33. This slope is what would be expected if the percentage contribution of the common noise were held constant at 18·8 %. These and other statistics relating percentage contribution to rates, variances, coefficients of variation, or ratios of these quantities during the plateau to those in the dark convince us that the percentage contribution of the common noise is not altered during stimulation.

DISCUSSION

The cross-covariances observed during a stimulus generally differed from those observed in the periods before or immediately after it. The cross-covariances in the period immediately after light offset did not generally differ from those derived from the maintained firing, even though the off response often exceeded the on response in magnitude. We have therefore concluded that the observed non-linear effect upon the cross-covariance at on is not due simply to a change in firing rate wrought by the stimulus. How then can we explain it?

We can propose three plausible explanations. The first is that the common noise source (the only possible contributor to a non-zero cross-covariance) is replaced by a different common noise source when a light is present. This kind of substitution might be related to the 'on' and 'off' processes described by Levine & Shefner (1975, 1977*a*) as being responsible for long-term variability of firing rates. In the model they proposed, the firing rate during the stimulus reflects variability inherent in depolarizing distal neurones, while the variability in darkness is governed by hyperpolarizing distal neurones (which depolarize in the dark). When the one class is active (depolarized),

the other is virtually ineffective, for its hyperpolarized state would halt essentially all transmitter release. Thus, the variability in the presence of light differs from that in the dark, regardless of whether the dark precedes or follows a stimulus flash. The direction of the difference would depend upon which noise source happened to have the larger variance for those cells.

A difficulty for this explanation is the observation that despite the changes in cross-covariance, the common noise provides the same percentage of the total variance of firing during the stimulus as before it. If the change in cross-covariance during the light were the result of substituting a different common noise source with a different variance, there would have to be a concomitant change in the variances of the private noise sources. However, it is likely that at least a fair portion of the noise enters at a proximal level (Schellart & Spekreijse, 1973), while the common noise seems to be fairly distal (the sign of the cross-covariance is determined by the response types of the two cells in the pair; see also Arnett & Spraker, 1981). It is difficult to imagine a likely mechanism for changing a proximal private noise source in the correct proportion to account for the different variance of the distal common source which is effective during the on response.

A second possible explanation is that the presence of the light has a direct non-linear effect upon the common noise source. This was proposed by Arnett & Spraker (1981), who suggested that the common noise might be receptoral, and should therefore be decreased by illumination (Lamb & Simon, 1977; Zeevi & Mangoubi, 1978). It is true that a smaller cross-covariance at on was our most common outcome. However, when we averaged the magnitudes of the cross-covariances across all pairs, we found no significant decrease in the cross-covariance during illumination; individual pairs showed either increases or decreases. This hypothesis is also hard to reconcile with the fact that the common noise represents a constant percentage of the total variance; as with the first proposal, we would have to explain why the private noise is proportionally affected.

The third, and most likely, explanation is that the presence of illumination affects the transmission properties of the pathway from the common noise source to the ganglion cells. In this non-linear effect of light, the gain of the retinal pathway is changed. A decrease is gain might well represent the portion of retinal adaptation that occurs within about 1 s after a change in the light. Given that the gain was often less during illumination (i.e. the cross-covariance for on was usually the one with the smallest magnitude), this may be what normally occurred. It is surprising, however, that the gain was not always decreased during illumination. Perhaps part of the on response in on–off- and on-centre cells is associated with a gain increase.

This proposal can easily explain the fact that the common noise represents a constant percentage of the variability of firing. It is only necessary that the gain which is affected by illumination lies proximal to both the common and the private noise sources. In analysing the noise of individual ganglion cells, Levine (1982) concluded that some signal processing (high-pass filtering) must occur proximal to the noise source; it is possible that the gain change due to light occurs at this same stage.

A gain change at the most proximal level can also explain the observation that noisiness and mean firing rate are related. The variance of the firing is larger for cells with higher firing rates (the correlation between mean rate and variance of rate is

0·81, $P < 0·0001$). There is essentially no change in relative noisiness when the mean rate changes; in fact, there was no significant change in the coefficient of variation of rate, $\sigma_r/\bar{r}$, for maintained *vs.* the on plateau either for cells with elevated plateaus or cells with depressed plateaus (relative to the mean maintained). There was also no significant difference in the coefficient of variation of the intervals, $\sigma_{\text{i.s.i.}}/\mu_{\text{i.s.i.}}$, for either cell type (see also Levine & Shefner, 1977*b*).

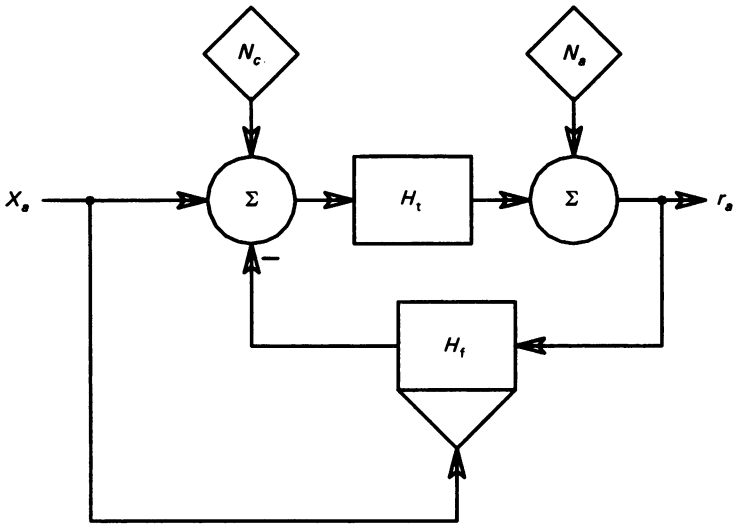

Fig. 7. Schematic of a feed-back gain-control model in which the percentage contribution of common noise would be constant despite a difference in the locus at which common and private noise sources enter the processing network. H_t is the forward element acting on the sum of photic (X_a) and common noise (N_c) signals; H_f is feed-back. Private noise (N_a) enters the loop after H_t. See text.

There is an intriguing variation upon this gain-change model which also is consistent with the notion of common noise well distal to private noise: we may postulate that both sources enter the processing network within a closed feed-back loop. A representation of this model is shown in Fig. 7. The signal engendered by stimulation, X_a, enters at the left, and is summed with the distal common noise, N_c, and a feed-back signal (which might come from interplexiform cells, horizontal cells, or, if all of the noise sources are in the inner plexiform layer, amacrine cells). H_t represents whatever processing properties are applied in the retinal pathway until N_a, the more proximal private noise, is added. The sum of N_a and the output of H_t control the rate signal, r_a, the firing of the ganglion cell. This sum, processed by H_f, provides the feed-back. The firing rate, r_a, is determined by the input (light) and the two noise sources according to

$$r_a = \frac{H_t . X_a + N_c . H_t + N_a}{1 + H_t . H_f}. \tag{12}$$

If we assume the effect of light is to change H_f (presumably by a feed-forward process, or H_f would be affected by the changes in firing at offset as well as onset), the effectiveness of N_c and N_a will be equally adjusted, and their ratio

remain constant despite the fact that H_t operates after the introduction of N_c, but before the injection of N_a.

This feed-back model is similar to a model proposed for contrast gain control in the cat retina by Shapley & Victor (1981). They modelled the signal-processing path in the retina as a cascade of low-pass filters followed by a high-pass filter; the high-pass filtering is achieved by constructing a closed feed-back loop in which the feed-back element is a low-pass filter. They proposed that the product of gain and band width of the feed-back element is changed by contrast. We also propose that the feed-back element is altered, in this case by illumination *per se* (a similar modification of the Shapley & Victor model was proposed by Frishman & Levine, 1983).

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