

## Dynamics of Skate Horizontal Cells

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**ABSTRACT** The all-rod retina of the skate (*Raja erinacea* or *R. ocellata*) is known to have the remarkable capability of responding to incremental flashes superimposed on background intensities that initially block all light-evoked responses and are well above the level at which rods saturate in mixed rod/cone retinas. To examine further the unusual properties of the skate visual system, we have analyzed responses of their horizontal cells to intensity-modulated step, sinusoidal, and white-noise stimuli.

We found that during exposures to mean intensities bright enough to block responses to incremental stimuli, decremental stimuli were also initially blocked. Thereafter, the horizontal cells underwent a slow recovery phase during which there was marked nonlinearity in their response properties. The cell first (within 2–3 min) responded to decrements in intensity and later (after >10 min) became responsive to incremental stimuli. After adaptation to a steady state, however, the responses to intensity modulation were nearly linear over a broad range of modulation depths even at the brightest mean levels of illumination. Indeed, examination of the steady-state responses over a 5-log-unit range of mean intensities revealed that the amplitude of the white noise-evoked responses depended solely on contrast, and was independent of the retinal irradiance as the latter was increased from 0.02 to 20  $\mu\text{W}/\text{cm}^2$ ; i.e., contrast sensitivity remained unchanged over this 1,000-fold increase in mean irradiance. A decrement from the mean as brief as 2 s, however, disturbed the steady state.

Another unexpected finding in this all-rod retina concerns surround-enhancement, a phenomenon observed previously for cone-mediated responses of horizontal cells in the retinas of turtle and catfish. While exposure to annular illumination induced response compression and a pronounced sensitivity loss in response to incremental light flashes delivered to the dark central region, the cell's sensitivity showed a significant increase when tested with a white noise or sinusoidally modulated central spot. Unlike horizontal cells in other retinas studied thus far, however, response dynamics remained unchanged.

Responses evoked either by a small spot (0.25-mm diam) or by a large field light covering the entire retina were almost identical in time course. This is in contrast

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with past findings from cone-driven horizontal cells whose response waveform (dynamics) was dependent upon the size of the retinal area stimulated.

#### INTRODUCTION

The retinas of some species of skate (*Raja erinacea* and *R. ocellata*) contain only rods, the photoreceptors for nocturnal vision (Dowling and Ripps, 1970; Brin and Ripps, 1977; Szamier and Ripps, 1983). These elasmobranchs are, however, quite active during daylight hours and electrophysiological studies have shown that their retinal neurons are capable of responding to modulation of a mean (background) illuminance far above the level at which the rod mechanism saturates in mixed (cone/rod) retinas (Dowling and Ripps, 1970, 1971, 1972; Green et al., 1975; Green and Siegel, 1975). However, light adaptation in the retina, measured with brief incremental flashes, is a very slow process (cf. Dowling and Ripps, 1972). For example, the horizontal cells lose their ability to respond to incremental stimuli for many minutes after a sudden increase in ambient illumination (Dowling and Ripps, 1971). But in the environment in which the skate must survive, sudden changes in illumination are rarely encountered. The fish's environment provides modulation of a mean illuminance that varies slowly throughout the day. It is expected, therefore, that the visual system of the skate has evolved to function optimally in such a photic environment.

Our recent studies on the cone horizontal cell in turtle and catfish (Chappell et al., 1985; Naka, 1985) have shown that the cell's modulation response is linearly related to the modulation of the mean illuminance, and that the "linear range" is much larger than had been found by other workers (Baylor and Hodgkin, 1973; Normann and Anderton, 1983). It was further shown that the incremental sensitivity as well as the response dynamics are different for different means. One of the basic functions performed by neurons in the outer retina is, therefore, to provide a piece-wise linearization and to produce an incremental response optimal to the prevailing mean levels. This is the field adaptation or parametric control of Rushton (1965). No comparable studies have been performed on rod horizontal cells, although Rushton's idea originated in his study on human rod vision. It should also be noted that measurement of a cell's sensitivity is straightforward when the cell's response is linearly related to the input modulation. Otherwise, the definition of sensitivity becomes problematical. It is important, therefore, to obtain a linear response in order to measure incremental sensitivity.

Accordingly, the principal goal of this study was to examine the response properties of skate horizontal cells at a steady dynamic state. The stimulus was a modulation of a mean irradiance by short steps, sinusoidal sweeps, or pseudo-random white-noise signals. The first two deterministic signals give results that can be related intuitively to the stimulus. On the other hand, white-noise modulation, a stochastic signal, produces responses that must be analyzed through some mathematical manipulation (Sakuranaga et al., 1986). Here we cross-correlated the white-noise modulation against resulting responses to obtain (Wiener) kernels that contain information on response dynamics; in addition, the analysis enabled us to assess the degree of linearity of the modulation response. White-noise analysis has been used extensively to study retinal neurons (Marmarelis and Naka, 1972; Chappell et al.,

1985; Naka et al., 1987) and the theoretical background has been fully described (Sakuranaga et al., 1986). We will discuss the results from the rod-driven skate horizontal cells in relation to results from the cone-driven horizontal cells.

## METHODS

### *Biological*

Conventional eyecup preparations were made from the posterior segments of eyes enucleated from skate (*R. erinacea* and *R. ocellata*). After removing most of the vitreous humor, the eyecup was placed in a lucite chamber under a continuous flow of oxygen; the scleral surface was in contact with a chlorided silver disc that served as a reference electrode. Intracellular recordings were made from horizontal cells in the tapetal region of the fundus, superior to the optic nerve head. The cells were impaled by 2 M potassium citrate-filled electrodes. Horseradish peroxidase was injected into 42 of the cells studied to verify that responses were recorded from horizontal cells. Light-evoked responses were fed to a unity gain electrometer (model 707; World Precision Instruments, New Haven, CT) and stored on analogue tape after amplification together with the light stimulus signal, which was monitored before it was attenuated by a series of neutral density filters (Fig. 1).

### *Stimulus*

Photic stimuli were produced by a dual-beam instrument similar to the one described by Dowling and Ripps (1971). One of two light sources of the instrument was replaced by a Sylvania glow modulator tube whose current (and hence light output) was controlled by a set of standard signals produced by a MINC-11 computer (Digital Equipment Corp., Marlboro, MA) through a D/A converter (Fig. 1). The modulated stimulus consisted of white noise, step increments and decrements, or a sinusoidal sweep from the glow tube in either spot (diameter, 0.25–1.9 mm) or full-field illumination (diameter, 3.2 mm); the second stimulus from a tungsten-iodide lamp was a steady annular adapting light. The standard stimulation protocol was a fixed sequence of pseudo-random signals, preceded by step increments and decrements; the first 9 s of a stimulus-response sequence is shown in Fig. 2. The fixed pseudo-random signal allowed us to compare white noise-evoked responses from different test runs. Other stimulus conditions included a series of test flashes in which the intensity of successive flashes was increased in linear fashion, and a sinusoidally modulated stimulus having a fixed mean irradiance.

The maximal mean retinal irradiance of the white-noise stimulus was  $20 \mu\text{W}/\text{cm}^2$  and the mean,  $I_0$ , and the modulation,  $I(t)$ , were reduced proportionally when the beam was attenuated by neutral density filters; however, the contrast,  $I(t)/I_0$ , remained unchanged. In Fig. 1 the probability density function (PDF) of the white-noise modulation signal is fitted by a Gaussian function (smooth line) with a standard deviation of  $6 \mu\text{W}/\text{cm}^2$ . Taking  $3\sigma$  as the dimmer and brighter limits of the light stimulus gives a modulation depth of 90%, the exception being the stimuli used in Fig. 6 in which the depth of modulation was changed by 6-db steps.

### *Data analysis*

Analogue data were digitized at a rate of 500 Hz and stored in the memory of the MINC-11 computer for preliminary on-line processing. Cross-correlation was made between the modulation signal before attenuation,  $nI(t)$ , and the modulation response,  $v(t)$ , where  $n$  is the attenuation factor of the neutral density filter. For 0 log (no filter)  $n$  is 1, and for 1 log attenuation  $n$  is 10. This process produced kernels whose amplitudes were scaled as contrast sensitivity

with units of  $\text{mV} \cdot \text{s}$  (Fig. 1). Kernels on a contrast sensitivity scale can be converted to an incremental sensitivity scale by multiplying the scale by the attenuation factor  $n$ . Algorithms for computing the first order kernel, model predictions (convolution), and mean square errors (MSEs) were described previously (Chappell et al., 1985; Sakuranaga and Ando, 1985). Analyses were performed on data transferred subsequently to the memory of a VAX 11/780 computer (Digital Equipment Corporation) at the National Institute for Basic Biology

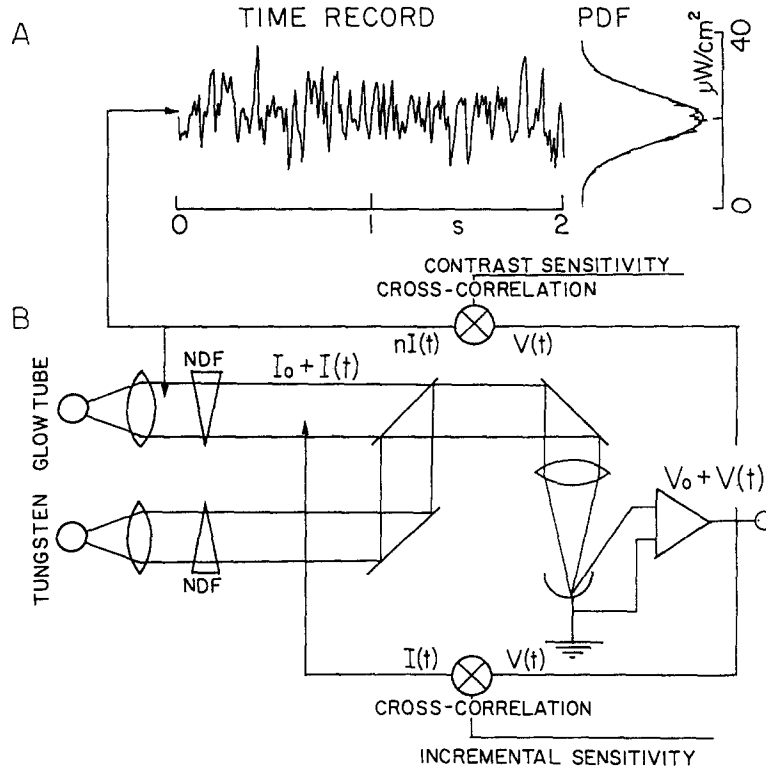


FIGURE 1. (A) The initial segment of a white noise-modulated light stimulus. Its probability density function (PDF: noisy line) was computed for a 60-s period and is fitted with a Gaussian distribution (smooth line) having a SD of  $6 \mu\text{W}/\text{cm}^2$ . (B) A schematic of the experimental set-up. The two-channel photostimulator provides light stimuli from two sources: a glow modulator tube and a tungsten-halogen lamp. The photic stimuli are directed to preparation after the attenuation by neutral density filters (NDF). Cross-correlation between the original light signal ( $nI(t)$ ) and response ( $V(t)$ ) yields the contrast sensitivity; correlation between the attenuated light signal ( $I(t)$ ) and response ( $V(t)$ ) produces the first-order kernel or incremental sensitivity of the system.

(NIBB), Okazaki, Japan using a software system (STAR) that was implemented on the VAX computer in combination with a 120B array processor (Floating Point System, Portland, OR). The system was developed at the NIBB by M. Sakuranaga and Y.-I. Ando.

#### TERMINOLOGY

Although formal definitions of terms have been fully described (Chappell et al., 1985); a few salient features are summarized below. A light stimulus,  $L(t)$ , can in

general be considered to consist of two parts (Fig. 2, upper trace):

$$L(t) = I_o + I(t) \tag{1}$$

where  $I_o$  is the steady mean irradiance and  $I(t)$  is its modulation around the mean. The corresponding responses,  $V(t)$ , from retinal neurons can also be separated into two components (Fig. 2, lower trace):

$$V(t) = V_o + v(t), \tag{2}$$

in which  $V_o$  is the mean membrane potential produced by  $I_o$ , and  $v(t)$  is the voltage fluctuation around the mean elicited by  $I(t)$ . In the simplest case, the stimulus ( $I_o$ ) without any modulation produces a steady polarization ( $V_o$ ) and the cell's static or DC sensitivity is given by:

$$Ss = V_o/I_o, \tag{3}$$

Traditionally,  $V_o$  is evoked by a brief step of light ( $I_o$ ) of increasing intensity in the dark (Figs. 2 and 3). For graded potentials of photoreceptors and horizontal cells in a wide range of

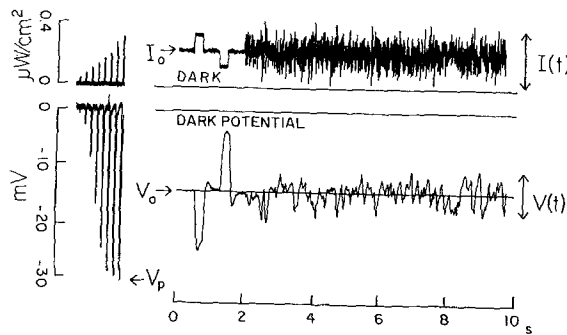


FIGURE 2. Horizontal cell responses to light flashes of increasing intensity, and to incremental and decremental steps followed by the initial 8 s of 100 s of white noise. On the left side are the series of step-evoked responses that eventually saturate at the peak potential,  $V_p$ . The relationship between  $V_o$  and  $I_o$  is used to describe the static (DC) sensitivity of the cell. The relation-

ship between  $I(t)$  and  $V(t)$  gives the dynamic (AC) incremental sensitivity, i.e., the first-order kernel. Note that the two step-evoked responses were nearly mirror images of each other, and analysis of the incremental and decremental responses to the modulated stimuli indicated that the system responded linearly. Modulated responses were recorded after a 1-h field adaptation to a mean retinal irradiance of  $0.2 \mu\text{W}/\text{cm}^2$ .

vertebrate species (cf. Witkovsky, 1980) the relationship between  $I_o$  and  $V_o$  is approximated by the Naka-Rushton equation (Naka and Rushton, 1966) from which the static sensitivity is given by:

$$V_o/I_o = V_{\text{max}}/(I_o + \sigma), \tag{4}$$

where  $V_{\text{max}}$  is the cell's maximum (saturation) response to a very bright flash of light and  $\sigma$  is the intensity at which  $V_o$  equals one-half  $V_{\text{max}}$ . Static sensitivity is a function of  $I_o$ . Responses produced by flashes given in the dark, however, do not represent a cell's static steady state because the initial part of the response is transient (nonstationary), and consequently may be nonlinear (cf. Figs. 2 and 5). We note that most of the cells in which the equation has been applied did not produce a steady response to a steady illumination and  $V_o$  is often replaced by  $V_p$ , the transitory peak response. A cell's dynamic steady state response can be measured by adapting the retina to a steady mean irradiance ( $I_o$ ) and then observing the cell's response to intensity modulation ( $I(t)$ ) around that mean. When a cell is in a steady state, its mean membrane potential ( $V_o$ ) is held at a constant level so that static sensitivity is also held constant. The only meaningful measure of sensitivity at this state is the relationship between  $I(t)$  and the

resulting response,  $V(t)$ . This relationship gives the AC or incremental sensitivity. For a given  $I_o$ , the value of  $V_o$  is much smaller than that of  $V_p$  as is shown in Fig. 2. This is because the membrane potential gradually depolarizes during field adaption (see Fig. 4 in Dowling and Ripps, 1971). Experimentally, the mean irradiance can be modulated by such deterministic signals as step increments or decrements, or by sinusoidal modulation (cf. Tranchina et al., 1981). If the response to modulation is linear or quasilinear, measurements of a cell's incremental sensitivity is straightforward. On the other hand, if a cell's modulation response is nonlinear, such measurements become complex. For example, if a cell produces responses of different amplitudes for step increments and the corresponding decrements, it may have two incremental sensitivities, one for increments and the other for decrements (Fig. 4, B2 and 3). A more general approach to sensitivity measurement is the use of a (stochastic) white-noise modulation of a mean illuminance. Cross-correlation between the modulation input,  $I(t)$ , and the resulting response,  $v(t)$ , produces a series of (Wiener) kernels. Since cross-correlation extracts the linear components of the response, the first-order kernel gives the cell's response (or the best linear approximation thereof) to a brief flash of light superposed on a steady mean irradiance. The first-order kernel reconstructs the cell's response produced by a white-noise stimulus as a convolution integral:

$$v'(t) = \int_0^{\infty} h(\tau; I_o) \cdot I(t - \tau) d\tau, \quad (5)$$

where  $v'(t)$  is the reconstructed (predicted or model) response,  $h(\tau; I_o)$  is the first-order kernel at a mean  $I_o$ , and  $I(t)$  is the white-noise modulation. The MSE gives a measure of the difference between the real ( $v[t]$ ) and the predicted ( $v'[t]$ ) responses. So far, studies made on modulation responses for turtle cones (Naka et al., 1987) and horizontal cells (Chappell et al., 1985), and catfish (Naka et al., 1975; Sakai and Naka, 1987); and dogfish (unpublished observation) horizontal cells have determined that the first-order kernels from these cells predicted white noise-evoked responses with MSEs of ~10%, showing that modulation responses were linearly related to white-noise modulation and the first-order kernels were a good approximation of the impulse response. Kernels in units of  $\text{mV} \cdot \text{s} / \mu\text{W}/\text{cm}^2$  may be used as a measure of a cell's incremental sensitivity (Naka et al., 1979; Sakuranaga and Ando, 1985). As in the case of the static sensitivity, incremental sensitivity is a function of the mean irradiance. When the mean changes, the first-order kernels may change in amplitude as well as in dynamics (waveform). These parametric changes are often referred to as field adaption (Rushton, 1965) and represent a piece-wise linearization. In this paper, first-order kernels will be referred to simply as kernels.

## RESULTS

### *The Intensity-Response Relation (Flash Stimuli)*

The static sensitivity of a cell is derived usually from its response to a range of stimulus intensities presented in the dark. Fig. 3 shows the responses of a horizontal cell (A, lower trace) to a series of 14 brief flashes ( $t = 20$  ms) in which successive stimuli increased linearly in intensity (A, upper trace). As shown in Fig 3 B, the relationship between the flash intensity ( $I_o$ ) and the peak amplitude ( $V_p$ ) of the resulting response is described by Eq. 4':

$$V_p / V_{\max} = I_o / (I_o + \sigma). \quad (4')$$

The experimental points (filled circles) fit well with the theoretical function (continuous line) although there is a slight discrepancy in the low-intensity region. Dowling

and Ripps (1971) reported earlier that flash-evoked responses were fitted by Eq. 4' using  $I_0$  to the 0.7 power for the best fit.

#### *Responses to Intensity-Modulated Stimuli*

Fig. 4 shows the results of an experiment in which the mean irradiance was increased suddenly (arrow on stimulus trace) by a 1-log-unit step from 0.2 to 2.0  $\mu\text{W}/\text{cm}^2$ . (Note a brief depolarization before the increase due to beam occlusion by the filter housing as the filter was removed.) Immediately thereafter, the standard modulation sequence was repeated three times for periods of 100 s each (1, 2, and 3 in Fig. 4 A). The initial 3 s of each sequence is shown on an expanded time scale in Fig. 4 B. Note that the onset of the step increase in mean irradiance produced a

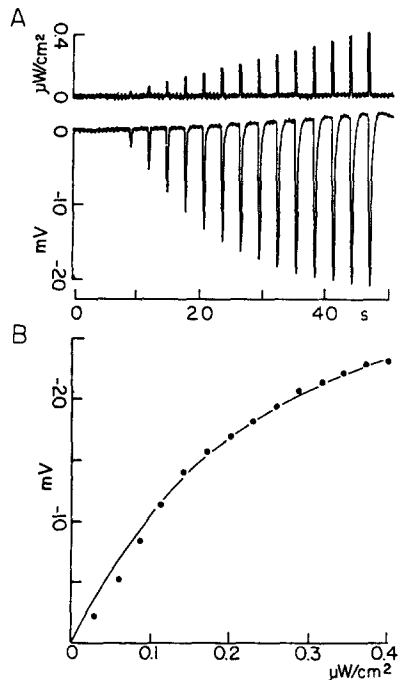


FIGURE 3. The responses in A (lower trace) were evoked by a series of 14 steps (given in the dark) whose amplitudes were increased in a linear fashion (upper trace). In B, the peak amplitudes (filled circles) are shown along with a curve obtained from the Naka-Rushton equation (continuous line).

membrane hyperpolarization of  $\sim -7$  mV from the level observed before the increase in the mean, and that over the next 20 s (Fig. 4 A) the membrane potential hyperpolarized to a plateau of  $\sim -30$  mV (see also Dowling and Ripps, 1971). During this period the cell did not respond to stimulation, but  $\sim 50$  s after the change-over, the membrane potential depolarized slightly and soon thereafter the cell became responsive to the decremental components of the white-noise stimulus. Indeed, the step decrement given at the start of the second and third stimulus trains evoked large depolarizations of  $>20$  mV, whereas the step increments that followed did not produce any visible response (Fig. 4 B, traces 2 and 3). A similar situation was obtained with white-noise stimuli through the remainder of the test period shown in Fig. 4; i.e., the responses to decrements grew in amplitude until the mod-

ulation responses were a series of depolarizing transients. This is evident in the record between 200 and 300 s in Fig. 4 A, where there is no sign of a response to increments, while many depolarizing transients exceeded 15 mV.

#### Steady State Responses

The results of Fig. 4 reveal a gross nonlinearity in the response of the skate horizontal cell during the early stage of field adaption produced by a sudden increase in the mean irradiance by 1 log unit. However, when sufficient time was allowed for the retina to adapt to a given mean, two sets of identical stimuli given in succession produced almost identical responses; i.e., the retina had reached a dynamic steady state (cf. Fig. 5). We have not tested systematically the times required to reach a steady state for various levels of mean irradiance, but it is much less for dimmer

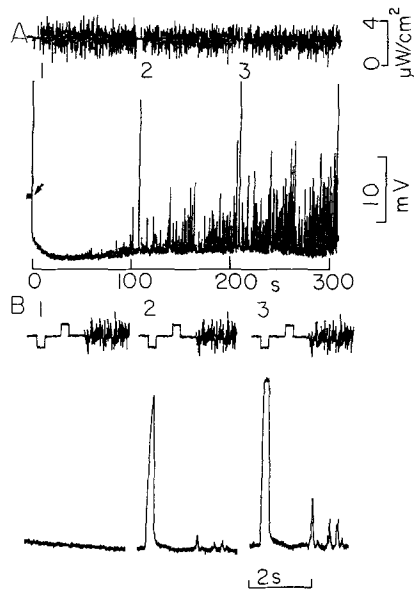


FIGURE 4. The early phase of light adaptation is shown in the responses to modulated stimuli after a sudden increase in the mean irradiance from 0.2 to 2  $\mu\text{W}/\text{cm}^2$ . Immediately after the increase, indicated by the membrane hyperpolarization (arrow), the standard modulation stimulus (mean of 2  $\mu\text{W}/\text{cm}^2$ , upper trace) was repeated three times. The early parts of the modulation stimulus and response are expanded in B1, B2, and B3, which correspond to 1, 2, and 3 in A. See text for details.

than for brighter mean irradiance (i.e., 2  $\mu\text{W}/\text{cm}^2$ ), where nearly an hour may be needed.

Examples of the results obtained under steady state conditions are illustrated in Figs. 5 and 6 A. Fig. 5 shows responses elicited by step increments and decrements, and white-noise stimuli having a mean retinal irradiance of 0.02  $\mu\text{W}/\text{cm}^2$ , which was 2 log units above the threshold irradiance for the skate horizontal cell under our experimental conditions (cf. Fig. 9). Two sets of records taken 120 s apart are superposed in Fig. 5, and it is clear that except for a minor difference in the responses to step changes, the two traces, including the DC levels, are matched exactly. At this low mean level, the step increment produced a somewhat larger response than the step decrement (13 and 8 mV, respectively). At all mean irradiance levels ( $2 \times 10^{-4}$ –20  $\mu\text{W}/\text{cm}^2$ ) used in this experiment a steady state as shown in Fig. 5 was always achieved when the retina was exposed to the irradiance for a sufficiently long period of time.



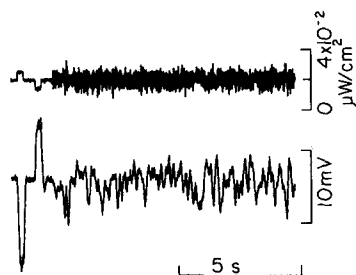


FIGURE 5. Responses evoked by the standard modulation stimulus under steady state conditions. Recordings were obtained after a 1-h exposure to the mean retinal irradiance of  $0.02 \mu\text{W}/\text{cm}^2$ . Two response sequences evoked by stimuli given 2 min apart are shown; only a shift in the DC level of 1 mV was required to superpose the two traces, which then matched exactly except that incremental and decremental steps produced slightly different responses.

If the modulation response is linearly related to stimulus modulation, the kernels should be able to reconstruct the original response produced by a white-noise stimulus as in Eq. 5. A measure of the degree of accuracy of this reconstruction is the MSE, the difference between the original and reconstructed responses in a mean square sense. Table I gives the MSEs of the reconstructed response at six levels of mean irradiance. The responses were linear in the sense that  $\sim 90\%$  of their response was accounted for by the linear component. An exception is the response evoked around a very low mean irradiance ( $0.0002 \mu\text{W}/\text{cm}^2$ ). At this mean the small response amplitude made the signal-to-noise ratio very low, which resulted in a large MSE. Horizontal cells in other retinas, catfish (Naka et al., 1975), turtle (Chappell et al., 1985), and dogfish (unpublished results) also had MSEs of  $\sim 10\%$ . Fig. 6 shows that response linearity under steady dynamic conditions is not limited to low mean irradiances. In this experiment, the mean retinal irradiance, like that of Fig. 4, was 2

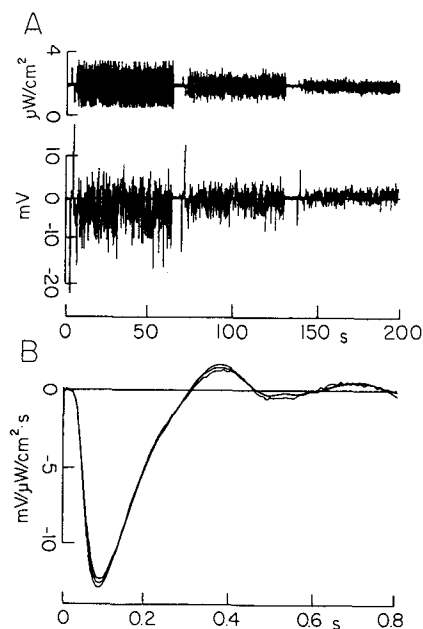


FIGURE 6. (A) Responses to white-noise stimuli that had a constant mean retinal irradiance ( $2.0 \mu\text{W}/\text{cm}^2$ ) but different depths of modulation. Note that the mean level of hyperpolarization (lower trace) remained unchanged for modulation depths of 0,  $-6$ , and  $-12$  db, and that incremental and decremental steps produced responses of similar amplitude but opposite polarity. (B) The three kernels computed from the three white-noise segments in A. The kernels were identical, which indicates that the cell's incremental sensitivity was independent of the depth of modulation; i.e., the response was linear.

$\mu\text{W}/\text{cm}^2$ , and, in addition, the depth of modulation of the white-noise stimulus, as well as the step increment and decrement, were decreased from 0 to  $-12$  db in 6-db steps. Changes in the modulation depth did not produce any change in the mean hyperpolarization,  $V_o$ , indicating that it was produced by the mean irradiance,  $I_o$ . The modulation responses ( $v[t]$ ) including the ones produced by step increments and decrements, were symmetric around the mean,  $V_o$ , although a slight asymmetry is seen in the responses evoked by the 0-db signal. The first-order kernels computed from the three segments are almost identical; i.e., incremental sensitivity as well as dynamics do not depend upon the depth of modulation. This is what we expect from a linear system.

As shown in Figs. 5 and 6, the skate horizontal cells produce, when the retina is fully field-adapted, a response that is linearly related to the input modulation, and the same stimulus repeated twice evokes exactly the same response. In skate, this steady state can easily be upset by briefly dimming the mean irradiance, i.e., the skate horizontal cell is very sensitive to the changes in the mean irradiance. It took from a few to tens of minutes to regain the steady state (the time it took was depen-

TABLE I  
*Mean Square Errors at Various Levels of Mean Retinal Irradiance*

Mean retinal irradiance $\mu\text{W}/\text{cm}^2$	$n$	Mean square error
20	8	$11.5 \pm 1.7$
2	6	$10.9 \pm 1.3$
0.2	13	$11.2 \pm 1.3$
0.02	8	$10.2 \pm 1.3$
0.002	8	$12.8 \pm 1.6$
0.0002	4	$16.3 \pm 4.2$

$n$  is the number of experimental runs for a given stimulus condition and values are mean  $\pm$  SD (%).

dent, of course, upon the duration of dimming as well as the magnitude of mean illumination). One example is shown in Fig. 7. The retina was fully field-adapted to a mean irradiance of  $2 \mu\text{W}/\text{cm}^2$  and the mean was modulated by two sinusoidal sweeps after a brief 0.2-s decrement. The two responses are shown on an expanded time scale in Fig. 7 B. Although the cell's static sensitivity increased somewhat, as seen from the larger static response  $V_o$ , the modulation responses were symmetrical, which shows that the cell's modulation response was linear. The retina was then exposed to a decrement of intensity that lasted 2 s. The cell's static sensitivity increased, as seen from the larger  $V_o$ , and the modulation responses evoked by the same sinusoidal sweeps were no longer symmetric; the depolarizing phase was much smaller and the hyperpolarizing phase became slightly larger (Fig. 7 C). Similar but more dramatic changes were shown in Fig. 4. To study the incremental response of skate horizontal cells, it was necessary to keep the mean as steady as possible; otherwise the steady state could easily be disrupted.

#### *The Weber-Fechner Relationship*

Fig. 8 shows responses evoked by three incremental and decremental steps (superposed in the figure to facilitate comparison at three levels of mean illumination.

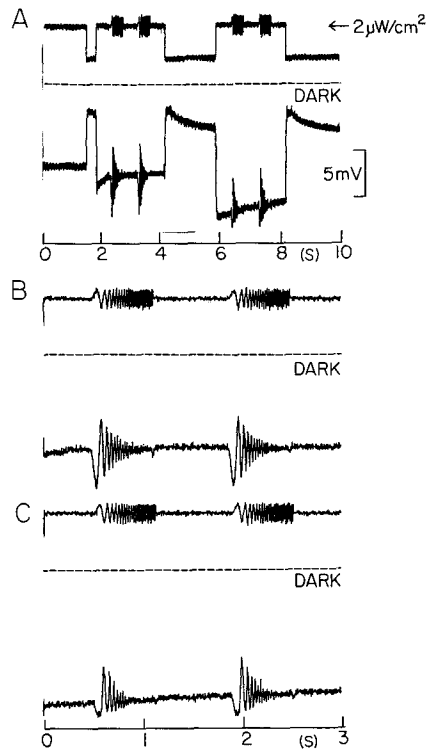


FIGURE 7. Steady state conditions around a mean can be altered by very short decrements in the mean. Here, the horizontal cell potential recovers quickly toward its original steady state potential after a decrement lasting  $<1$  s, and the responses to frequency-swept sinusoids (shown on an expanded scale in *B*) are symmetrical around the mean. A slightly longer decrement (2 s), however, results in a potential shift of several mV and the response becomes nonlinear as indicated by its asymmetry shown on expanded scale in *C*.

Note that (a) the incremental and decremental steps produced almost symmetrical responses, b) the response amplitudes were comparable, and (c) the responses became longer in duration for the brightest mean. The first two observations were made despite the 100-fold change in the absolute amplitudes of the mean as well as the modulation. This shows that, under steady state conditions, the most important parameter in generating the horizontal cell responses in the skate was the contrast

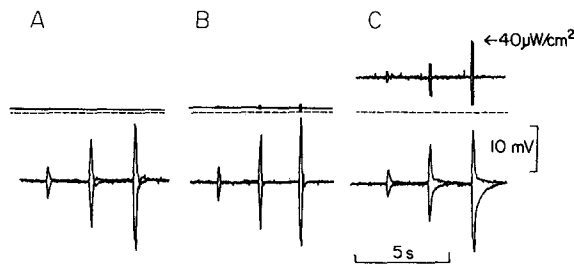


FIGURE 8. Incremental and decremental responses evoked at three mean levels,  $0.2 \mu\text{W}/\text{cm}^2$  in *A*,  $2 \mu\text{W}/\text{cm}^2$  in *B*, and  $20 \mu\text{W}/\text{cm}^2$  in *C*. Step modulations of three different amplitudes were given and traces for the incremental and decremental inputs as well as responses are superposed at each intensity for purposes of comparison. Note the almost symmetrical responses to the modulations of opposing polarity and the comparable response amplitudes for the three mean levels.

because among the three sets of stimuli used in Fig. 8, only the contrast remained unchanged to account for the modulation responses of comparable amplitudes.

To examine this question in more detail we have evoked responses using a white noise-modulated stimulus. Fig. 9 shows a series of steady state responses generated by the standard stimulus sequence of six levels of mean irradiance, from  $2 \times 10^{-4}$  to  $20 \mu\text{W}/\text{cm}^2$ . For dim mean irradiance, with the cell near its resting (dark) potential, step increments produced larger responses than step decrements (Fig. 9, *A* and *B*); while at the highest mean irradiance, the step decrements produced a larger response than the step increments (Fig. 9 *F*). The peak-to-peak amplitudes of the

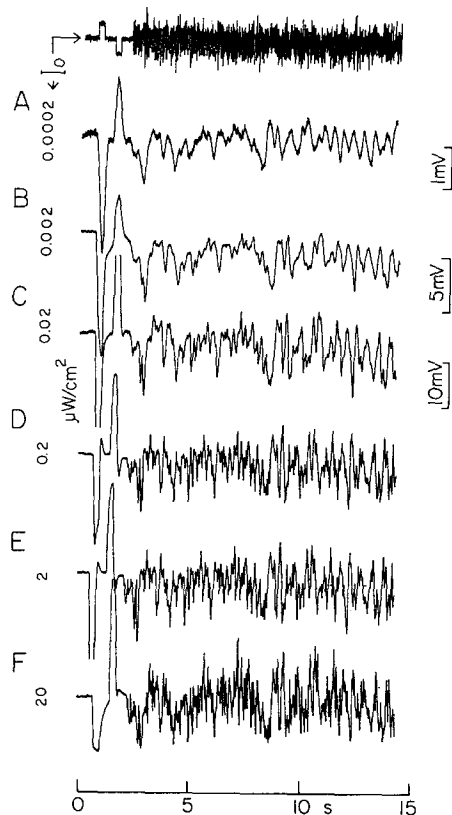


FIGURE 9. The initial 13-s segments of responses evoked by the standard stimulus sequence (upper trace) at mean retinal irradiances ranging from  $2 \times 10^{-4}$  to  $20 \mu\text{W}/\text{cm}^2$ . The 10-mV scale applies to traces *C-F*. A 1,000-fold increase in both mean irradiance ( $0.02$ – $20 \mu\text{W}/\text{cm}^2$ ) and modulation depth produced responses of similar amplitudes. Note, however, the discrepancy between the white-noise responses (which are linear) and step-evoked responses (some of which showed nonlinearity in amplitude and waveform). See text for details.

responses evoked by white-noise stimulation remained roughly constant when the mean irradiance was increased in 1-log-unit increments from  $0.2$  to  $20 \mu\text{W}/\text{cm}^2$  (Fig. 9, *C-F*); i.e., the response amplitudes were similar despite a 1,000-fold-increase in the mean irradiance as well as in absolute amplitude of the modulation. This indicates that over a large range of ambient illumination, a 10-fold increase in the mean retinal irradiance produced a 10-fold decrease in the cell's incremental sensitivity; this is the Weber-Fechner relationship (see also Fig. 11 *B* and Naka, 1985). However, with mean irradiances of  $<0.02 \mu\text{W}/\text{cm}^2$ , response amplitudes became much smaller than that accounted for by the Weber-Fechner relationship: a 1-log-unit decrease in the mean irradiance did not result in a 10-fold increase in the incremental sensitivity (note change of scale on the right side of Fig. 9, *A* and *B*).

*Response Dynamics*

The responses to white-noise stimulation (shown in Fig. 9) shows that the waveforms at various levels of irradiance were different. At low mean levels ( $0.0002$  and  $0.002 \mu\text{W}/\text{cm}^2$ ), the modulation responses were small, very sluggish, and did not follow high-frequency components in the white-noise stimulus. Even in the range of irradiances over which response amplitudes were comparable (i.e.,  $0.02$  to  $20 \mu\text{W}/\text{cm}^2$ ), the cell responded to faster components of the white-noise stimulus as the mean irradiance was increased.

Observations made in Fig. 9 were confirmed by computing kernels. Fig. 10 shows kernels from four white noise runs at each mean irradiance level scaled as contrast sensitivity; the four kernels are superposed to illustrate the stability of the recording.

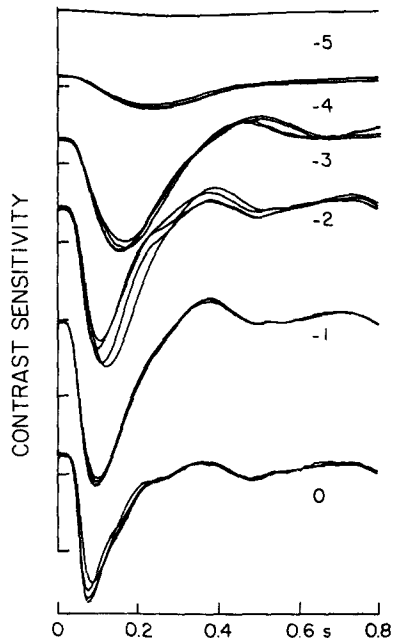


FIGURE 10. Contrast sensitivity measured at six levels of mean irradiance. The numbers below each kernel indicate  $\log I_0$ , where  $I_0 = 20 \text{ mW}/\text{cm}^2$  for the kernel marked 0. Cross-correlation was performed between  $nI(t)$ , the light signal monitored before attenuation, and  $V(t)$ , the cellular response (cf. Fig. 1). Note that the amplitudes of the kernels plotted on the contrast sensitivity scale are similar for irradiances greater than  $0.002 \mu\text{W}/\text{cm}^2$  (i.e., kernels labeled  $-3$  to 0). However, the waveform of the kernels changed significantly as the mean was increased; the initial slope became steeper and the time-to-peak shortened, indicating that the responses followed faster components of the white-noise stimulus train.

Kernels at each mean have almost identical amplitude as well as waveform. As the mean irradiance was increased, the kernels became sharper, which confirmed that the cell followed progressively faster components of the stimulus. It is also apparent that although contrast sensitivity was not significantly different for the three highest values of mean irradiance, it was reduced by  $\sim 30\%$  when the average irradiance of the test beam was attenuated by 3 log units, and was markedly depressed at the lowest irradiance levels ( $-4$  and  $-5$  log units). Given the attenuation factor of the neutral density filters, the incremental sensitivity (i.e., incremental and decremental sensitivity for quasi-linear responses) can be computed from the contrast sensitivity data of Fig. 10. The resultant kernels (Fig. 11 A) show that as the mean irradiance increased, the incremental sensitivity decreased, the peak response times became shorter, and the half-width of the kernels narrowed. In Fig. 11 B the incremental sensitivity as defined by the peak amplitude of the kernel is plotted against  $I_0$  (open circles). The data show the range of irradiance (4 log units) over which the Weber-

Fechner relationship held (straight line of unit slope) and the departure from this relationship at the lower mean irradiance as sensitivity approached its "absolute" level. Also shown is the striking similarity between the skate data and those obtained by Blakemore and Rushton (1965) on a rod monochromat; i.e., an individual whose retina, like that of the skate, lacks cones.

It has been shown in both turtle and catfish horizontal cells that the dynamics of the cell's modulation responses were dependent upon the size of the retinal area stimulated. A small spot of light produced a very sluggish response, whereas a large spot (or field) of light of the same illuminance produced a much faster response (Fig. 1 in Marmarelis and Naka, 1973; Fig. 13 in Chappell et al., 1985). In skate

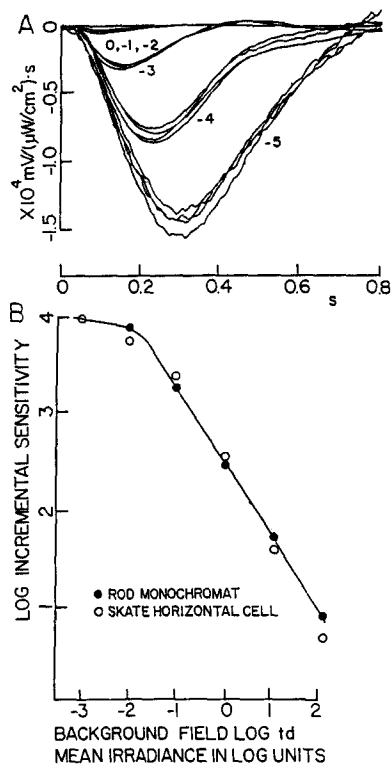


FIGURE 11. (A) Kernels are shown on an incremental sensitivity scale; they were obtained by multiplying the kernels in Fig. 10 by the attenuation factor corresponding to the neutral density filter used. At each mean level, four kernels from four white-noise runs are shown. (B) The amplitude of the kernels is plotted (open circles) against the mean of the stimulus,  $I_0$ . The data is of two parts: one described by the Weber-Fechner line (unit slope) and the other approaching absolute sensitivity. Data for a rod monochromat plotted for comparison (filled circles) were modified from the original data in Blakemore and Rushton (1965).

horizontal cells, on the other hand, we found that response dynamics were independent of stimulus size for spot diameters  $>0.2$  mm. Fig. 12 shows responses evoked by four steps of light, given in the dark, whose magnitude was increased from 0.15 to  $0.2 \mu\text{W}/\text{cm}^2$ . Light stimuli were in the form of spots whose diameters were 0.5, 1, and 1.9 mm. Responses evoked by these three spots were normalized in their amplitudes. The smallest spot produced the noisy trace and the largest spot produced responses with a slow return to the baseline, which deviated somewhat from the other two traces. The main parts of the responses, however, are nearly superposed on top of each other which shows that the response dynamics remained unchanged. This observation was confirmed with the use of white noise-modulated spots and by computing the kernels. Fig. 13 A shows five kernels produced by spots whose diam-

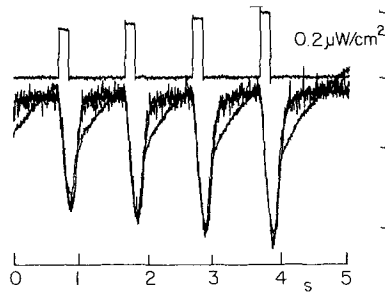


FIGURE 12. Step responses to a series of four steps of light of increasing intensity ( $0.15\text{--}0.2\ \mu\text{W}/\text{cm}^2$ ) given in the dark. At each intensity, responses were elicited with spot stimuli of 0.5, 1.0, and 1.9 mm in diameter. Traces for the three spot diameters are superposed and their peak amplitudes were normalized. Note that the responses show nearly identical time courses for the three

stimulus diameters. Calibration bar to the right of these responses represents 5 mV for the largest spot, which has the slow return to the baseline, 2.4 mV for the intermediate spot, and 1 mV for the smallest spot.

eter increased from 0.25 to 3.2 mm in diameter. As one would expect from the lamina (S-space of Naka and Rushton, 1967) formed by the horizontal cells, the larger spot produced larger kernels. On the other hand, the five normalized kernels showed an exact superposition, indicating that the dynamics were identical and independent of the size of the area stimulated (Fig. 13 B).

*The Effect of Surround Illumination*

Little is known about the center-surround organization of neurons in the all-rod retina of the skate. Although we have not investigated this phenomenon systematically, preliminary experiments indicate that response enhancement occurs with appropriate stimulus parameters. For example, under steady state conditions engendered by prolonged exposure to a sinusoidally modulated spot stimulus, response enhancement is produced by the addition of a steady annular field. In Fig. 14 A the mean retinal irradiance of the sinusoidal spot stimulus ( $0.2\ \mu\text{W}/\text{cm}^2$ ) induced a DC shift in membrane potential of  $\sim -4$  mV around which the recurrent stimulus produced fluctuations in potential  $< 1$  mV in amplitude. In the presence of surround illumination there was a further hyperpolarization of  $\sim 7$  mV, and the peak-to-peak amplitudes of the response to the sinusoidal input exceeded 3 mV. The response

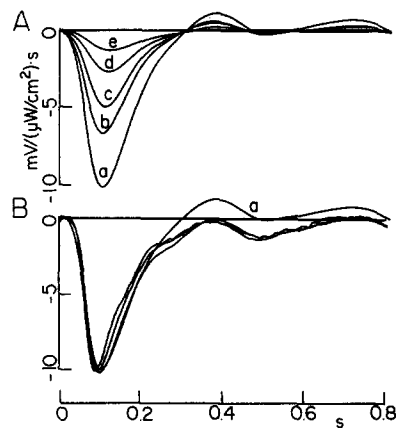


FIGURE 13. Kernels for horizontal cell responses on spots of decreasing diameters (a through e for 3.2, 1.9, 1.0, 0.5, and 0.25 mm, respectively) shown in A are normalized in B to show that they follow an identical time course. The trace marked a was obtained in response to the field (3.2 mm in diameter) of light in both A and B.

waveform, however, was no longer sinusoidal. Due apparently to the greater enhancement of the depolarizing components of the response, the potentials appeared to be half-wave rectified and nonlinear. Similar experiments with white noise-modulated stimuli (not shown) also showed response enhancement. The steady annular field increased the amplitude of the kernel; i.e., the surround increased the impulse sensitivity of the cell. The waveform of the kernels remained unchanged, as would be expected from the results shown in Fig. 13.

On the other hand, when this interactive property was tested in the usual manner, i.e., with brief test flashes, the presence of the surround caused a depression in response amplitude. Fig. 14 *B* provides a comparison of the results obtained with and without the annulus, for spot stimuli presented as brief-duration flashes increasing linearly in intensity. Note that at all stimulus intensities the flash-evoked responses were of smaller amplitude in the presence of the annular field. With the

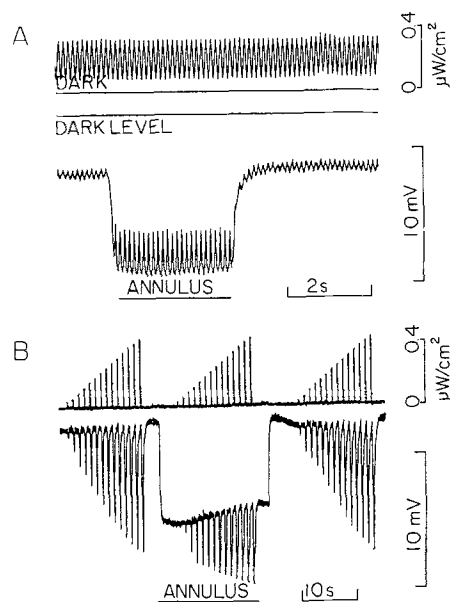


FIGURE 14. Responses to sinusoidal stimulation. The onset of a small (0.5 mm) diameter stimulus hyperpolarized the resting potential  $\sim 4$  mV, about the level at which the responses were modulated. The addition of a steady annular field (0.8-mm inner diameter; 3.5-mm outer diameter) induced a further hyperpolarization of the membrane potential, and a large increase in the responses to sinusoidal stimulation. (*B*) Responses to brief steps of light of increasing intensity obtained using the small-diameter stimulus are decreased in amplitude by the addition of the annular field. Note that in the presence of the annulus, the response to the weakest step was not detectable above the noise level of the recording.

higher intensity flashes, the responses approached saturation (owing to the initial hyperpolarization induced by the surround) and the reduced amplitudes were probably due in part to response compression, but no such explanation can be invoked to account for the lower amplitudes obtained with dimmer flashes.

#### DISCUSSION

A sudden increase in ambient illumination brings forth a change in the response properties of the skate horizontal cell, which is referred to as light or field adaptation (Rushton, 1965). The adaptation consists of three stages: the initial, the nonlinear, and the linear. As already described by Dowling and Ripps (1971), the initial stage of field adaptation is a sustained hyperpolarization during which the cell is not responsive to any modulation and its response is described completely by the steady



membrane potential ( $V_o$  in Eq. 3). This was referred to as the "silent period" by Dowling and Ripps. This initial stage is not a simple saturation since the modulation response begins to appear without any appreciable change in the cell's membrane potential. The initial stage gradually transforms into the nonlinear stage, during which the cell begins to respond to the decremental step. Although we have not made any systematic study of the time course of this recovery, it was surely longer for the brighter means and shorter for the dimmer mean. In Fig. 4, in which the mean was increased from 0.2 to 2.0  $\mu\text{W}/\text{cm}^2$ , the cell took nearly 80 s to respond to stimulus modulation.

The first response to appear is the depolarization produced by a decremental step. As shown in Fig. 4, such a response could be quite large, often exceeding 20 mV in amplitude, whereas an incremental flash of similar amplitude failed to evoke any response. The cell's response was very nonlinear and the cell could have two sensitivities: the low incremental sensitivity as described by Dowling and Ripps (1971), and a high decremental sensitivity. Had they used a decremental step they might also have observed a large depolarizing response. If the mean is kept unchanged, the cell eventually reaches a steady state in which the cell responds linearly to intensity modulation around the mean irradiance. Dowling and Ripps' results show that the progress in the field adaptation was accompanied by a slow depolarization, a decrease in  $V_o$ . Their records show that the cell's membrane potential was still depolarizing after a 35-min exposure to a steady mean irradiance. In this experiment it took more than 1 h to reach a steady state in the presence of a steady mean of 20  $\mu\text{W}/\text{cm}^2$ . When the steady state was reached, the membrane potential stayed at a given level and two identical series of modulated stimuli produced almost identical responses (Fig. 5).

The skate horizontal cell is characterized by the extremely slow progress of field adaptation. In the cone-driven turtle horizontal cells, a steady state was reached in a few seconds after the onset of an intensity-modulated stimulus that had a mean irradiance of 50  $\mu\text{W}/\text{cm}^2$  (Fig. 2 in Chappell et al., 1985). When fully field adapted, the skate horizontal cell response could be reconstructed by the first-order kernels with a MSE of  $\sim 10\%$ . This value is similar to those found for turtle and catfish horizontal cells (Naka et al., 1975; Chappell et al., 1985), and turtle cones (Naka et al., 1987). The linear range response in skate was  $>10$  mV peak-to-peak, a response amplitude comparable to those found for the turtle and catfish horizontal cells. This observation can be appreciated by comparing the results in Fig. 6 that were obtained by changing the depth of modulation of a white-noise stimulus and those from turtle horizontal cells shown in Fig. 9 of Chappell et al. (1985). As such comparison shows, the linear-range response is a common feature seen in the outer layer of lower vertebrate retinas. On the other hand, the linear-range response obtained by using flashes was  $<1$  mV in amplitude (Baylor and Hodgkin, 1973; Normann and Ander-ton, 1983). The linear range of the response produced by flashes given in the dark is naturally limited because such responses are transient and inherently nonlinear. The skate lives in an environment in which a sudden change in the mean irradiance is rarely encountered and the linear modulation response must be typical of the normal response of skate horizontal cells. In most of the past studies on retinal neurons, no test had been performed to assure that the cell was in a steady state and to assess the degree of linearity of the cell's modulation response.

In the skate horizontal cell, the incremental sensitivity indexed by the amplitude of the kernel is fit exactly by the Weber-Fechner function over a range of 4 log units. A similar relationship was found previously for the skate receptor and horizontal cell (Dowling and Ripps, 1971, 1972), as well as for the human rod monochromat (Blakemore and Rushton, 1965). In both of those cases, however, the measure of sensitivity was a threshold or a given amplitude response, whereas in the present study we have shown that the function held over a large response amplitude not limited by these constraints. It is interesting to note that the Weber-Fechner function also held for the cockroach ocellar neuron's modulation response over 4 log units and for turtle receptor and horizontal cells over 2 to 3 log units (Mizunami et al., 1986). On the other hand, in catfish horizontal cells the incremental sensitivity was the local slope of the Naka-Rushton equation (Naka et al., 1979). In skate the static sensitivity of the horizontal cell is the Naka-Rushton function, whereas its incremental sensitivity is described by the Weber-Fechner function instead of being the local slope of the Naka-Rushton function, as it is in catfish. There must be, therefore, some mechanism to produce the Weber-Fechner function. A lateral shift of the Naka-Rushton function is one possible mechanism.

In all visual cells we have analyzed, the cells followed a faster input frequency at brighter means although the incremental sensitivities were lower. Conversely, at low mean irradiance the incremental response is sluggish but the cell has a higher sensitivity (Naka et al., 1979, 1987; Chappell et al., 1985). This phenomenon functions to optimize the cell's response to the prevailing mean luminance and is referred to as field adaptation by Rushton (1965). It is likely there is a parametric control to achieve this optimization. Although we have no data to indicate the origin of this mechanism, there are at least two pieces of evidence to show that it is in the photoreceptors themselves. The first evidence is from Dowling and Ripps (1972) who showed in the skate that the main feature of the adaptation process found in horizontal cells originated in the photoreceptors. A second piece of evidence is provided by Naka et al. (1987), who showed that in the turtle, the receptors themselves were the site of parametric control. The peak response time of a kernel is an indication of the cell's frequency response. In skate, the peak response time of the kernel at the brightest mean irradiance was ~100 ms, whereas in both turtle and catfish it was 50 ms for a comparable mean irradiance. The corner frequency of the response power spectra was <5 Hz for the skate, but slightly >10 Hz in both turtle and catfish horizontal cells.

There is one important difference between the horizontal cells in the skate and those in the turtle and catfish retinas, where an incremental response evoked by a small spot of light was much slower than that produced by a large spot of light (Marmarelis and Naka, 1973; Chappell et al., 1985). Although the early catfish studies suggested that the spot response was made faster by the presence of annular illumination or by the stimulation of a large field, recent evidence suggests that the receptors produce the same incremental responses to both small and large fields of light, and show that the fast (receptor) spot response becomes slower when the signal is transmitted to the horizontal cells. In skate horizontal cells, on the other hand, the horizontal cell dynamics were the same whether the responses were evoked by a small or a large field of light. This was true for the responses evoked by steps given in the dark (Fig. 12) or by a modulation of a mean illuminance (Fig. 13). This can be

seen by comparing results in Fig. 13 with those shown in Fig. 13 of Chappell et al., 1985. This suggests that there is no significant transformation during signal transmission from the receptor to the horizontal cells. We do not know whether this is a characteristic of rod systems in general or if it is simply a property of the skate retina.

Prior studies of cone-driven horizontal cells in catfish (Naka, 1985) and turtle (Chappell et al., 1985) have shown that the responses of luminosity-type horizontal cells to an intensity-modulated spot stimulus are significantly enhanced by the addition of an illuminated surround. Our findings (Fig. 14) extend this observation to the horizontal cells of an all-rod retina. Despite the fact that the annular field produced a further hyperpolarization of the horizontal cell membrane as its effect spread through the electrically coupled S-space (Naka and Rushton, 1967), it induced a large increase in the transient voltage generated by the sinusoidal stimulus. A similar effect was seen with white-noise stimuli. In the other retinas, however, the increase in response amplitude was accompanied by faster response dynamics, which are shown by the faster time to peak of the first-order kernel; in the skate, response dynamics remained the same. Surprisingly, the annular surround had the reverse effect when the central stimulus field was presented as light flashes of increasing intensity; over the entire range of intensities, response amplitudes were diminished.

The invariance of the response dynamics of the spot response with or without enhancement of the response by surround illumination is consistent with the fact that the dynamics of the first-order kernel of the spot response are invariant with spot diameter up to and including full field illumination (kernel *a* in Fig. 13 *B*) even though amplitude increases substantially with diameter. This is demonstrated by the nearly exact superposition of normalized step responses of a horizontal cell to spots of three different diameters (three traces superposed) in Fig. 12. Note the nonlinearity of the recovery phase of the response to the largest spot, as shown by the slower return to baseline, comparable to the asymmetry introduced in the response during annular illumination of Fig. 14 *A*.

It is difficult to account for the apparent difference in center-surround organization demonstrated by annular illumination around a modulated mean, as opposed to steps given in the dark. Naka et al. (1987) contend that response enhancement of modulated stimuli occurs postreceptorally, and is not a consequence of a horizontal cell-photoreceptor "feedback" mechanism (Baylor et al., 1971). Recording intracellularly from turtle cones, Naka et al. (1987) observed that the dynamics of the cone responses were not altered by levels of surround illumination that markedly enhanced the amplitude and dynamics of the horizontal cell responses. The results on skate tend to support their conclusion in that the skate retina contains only rods (Szamier and Ripps, 1983), and feedback to rods for more proximal elements has not been demonstrated in other vertebrate retinas. In any event, it is clear that a center-surround organization that leads to the enhancement phenomenon observed in horizontal cells is not unique to the cone system.

Supported by the Herbert W. Rand Fellowship of the Marine Biological Laboratory (to K. I. Naka), by National Science Foundation grant BNS-8304932 (to K. I. Naka and R. L. Chappell) and by National Institutes of Health grants EY-00777 (to R. L. Chappell) and EY-06516 (to H. Ripps).

*Original version received 29 December 1986 and accepted version received 21 June 1988.*

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