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Fast-Acting Compressive and Facilitatory Nonlinearities in Light-Adapted Fly Photoreceptors

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Abstract—Light-adapted fly photoreceptor cells were stimulated with brief positive and negative contrast flashes (contrast = $\Delta I/I$, I = intensity). Membrane potential responses to a wide range of flash intensities were well-fitted by a static nonlinearity followed by a compartmental model represented by a gamma function. However, the agreement improved if one parameter of the gamma function, n, varied quadratically with input light intensity. Response amplitude and time to peak were estimated from the fitted parameters. Response amplitude varied approximately linearly with contrast but showed nonlinear compression with the largest negative flashes. Reducing the background light level by 3 decades or hyperpolarizing the cell electrically produced stronger nonlinear compression with both contrast polarities. This is probably due to fast voltage-activated K^+ channels. Responses to double flashes with varying time separations were well-fitted by summed gamma functions, allowing separation of the individual flash responses. There was no detectable time-dependent interaction between paired positive flashes at all separations. However, the response to two negative flashes was greater than the linear prediction at short separations, and this facilitatory nonlinearity decayed with a time constant of about 1 msec. The facilitation is probably related to resonant behavior in light-adapted photoreceptors and may be due to an IP_3-induced intracellular Ca^{2+} release.

Keywords—Phototransduction, Light adaptation, Gamma function, Impulse response.

INTRODUCTION

Phototransduction in vertebrate and invertebrate eyes is a strongly nonlinear process because the gain of each photoreceptor must be adjusted over a wide range to cope with a similarly wide range of ambient light intensities. This gain control, or adaptation, includes several different processes with time courses varying from milliseconds to days (1,4,6,14). Dynamic nonlinear processes have been characterized in several dark-adapted insect photoreceptors (5,10,22) but light-adapted cells, which are much closer to the normal biological situation, are more difficult to study because they are less nonlinear (9,20,27) and because the popular methods of nonlinear analysis based on random (white noise) stimulation tend to linearize receptor responses (25). Therefore, different methods are needed to examine the nonlinear properties of fast light-adapted responses.

In recent work we used varying amplitude steps of light to obtain the first- and second-order Volterra kernels for phototransduction in blowfly photoreceptors (11). This characterization was used to develop a nonlinear cascade model consisting of static nonlinear, dynamic linear, and static nonlinear components, which gave a good fit to the behavior over a wide range of light intensities. Although this model was parametric, compared with the nonparametric Volterra series, the dynamic linear component, being an empirical result, contained a separate value for each discrete point in time, giving many parameters. Therefore, it could not be easily used to interpret the physical processes underlying transduction and adaptation.

In view of the ability of the nonlinear cascade model (11) to fit the responses of light-adapted fly photoreceptors over a wide range of light intensities, we have now developed a parametric nonlinear cascade model based on the gamma function. This enabled us to assess the nonlinearities in light-adapted photoreceptors with high precision. The model was able to fit the responses to a series of different amplitude dark and light flashes, and provided accurate measures of peak response and time to peak response as functions of flash intensity. The model was also able to fit the responses of photoreceptors to pairs of light and dark flashes separated in time. The analysis revealed several deviations from strictly linear summation of responses and provided increased understanding of the fast regulation of fly phototransduction.

METHODS

Animals, Stimulation, and Recording

Flies, *Calliphora vicina*, were obtained from a laboratory culture. Adults and larvae were fed on liver, yeast,

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and sucrose, and the stock was refreshed regularly with wild flies. Each fly was attached with beeswax onto a platform with a rotating Cardan arm, and a silver chloride reference electrode was mounted near the retina inside the head. Ventilation was maintained by leaving the abdomen intact with spiracles functioning normally.

Light stimuli were provided by a green emitting diode (Stanley HBG5666X, with peak emission at 555 nm) driven by a linearized voltage-to-current converter. The light stimulus was calibrated in effective photons (ep) by counting the voltage responses (single bumps) caused by the absorption of single photons. For this purpose, and for observing responses at different light adaptation levels, the intensity was attenuated with neutral density filters (Kodak, Rochester, NY). The stimulation protocols were produced by a computer program (17) using the ASYST programming language (Keithley). Dark-adapted flies were allowed to adapt to the mean light level being used for at least 2 min before beginning a recording.

Glass microelectrodes, filled with 3 M potassium acetate and 5 mM potassium chloride, had resistances of ~150 MΩ. Electrodes were mounted on a piezoelectric microtranslator (Burleigh PZ-550 inchworm controller) and entered the compound eye through small lateral hole that was sealed with high vacuum grease. Membrane potentials were recorded with an intracellular amplifier (SEC-1L, NPI Electronic, Germany) operating in the balanced bridge mode. In current injection experiments the single electrode (switched) current clamp (SECC) mode was used to avoid electrode voltage artifacts. Recordings were made from R1-6 photoreceptor somata, identified by criteria published previously (13,28). Responses having any trace of a "prespike" characteristic of photoreceptor axon responses (29) were discarded. Membrane potential responses were filtered at 500 Hz by the amplifier and sampled at 4 kHz. All experiments were performed at room temperature (21–23°C).

Responses were obtained to brief increases or decreases in light intensity (light or dark flashes) from a constant adapting light intensity. All flashes were of 1 msec duration, unless otherwise indicated. Flash amplitudes were measured in contrast (dimensionless) units by dividing the change in light intensity during the flash by the constant adapting light intensity. Thus, the largest available negative contrast flash was a change to total darkness giving a contrast value of -1. To reduce the signal-to-noise level of the recordings, flash responses were averaged to repeated presentations of identical stimuli, with an interstimulus interval of 150–300 msec. Similar procedures were followed for double flash experiments, except that pairs of flashes with variable separation in time were used.

The Model

The nonlinear cascade model used to fit combined flash responses is shown in Fig. 1. The input signal, $x(t)$, measured the amplitude of the contrast flash stimulus as a function of time, t, where contrast is defined as $[I(t) - I_0]/I_0$, where $I(t)$ is light intensity and I_0 is the constant adapting stimulus intensity. The first component was a static nonlinearity consisting of a fifth-order polynomial in contrast:

$$u(t) = c_1x(t) + c_2x(t)^2 + c_3x(t)^3 + c_4x(t)^4 + c_5x(t)^5. \quad (1)$$

No zero-order term was included because, for simplicity, the mean value of the cell output before each flash was subtracted from the entire response. This amounts to an assumption that all internal processes within the cell would return to their resting state at a sufficiently long time (~150 msec) after each flash. This is justified because all experiments were done with (controllably) light-adapted flies, and stimulation was performed with only very short flashes.

The output of the first component of the cascade was convolved with the gamma function:

$$\Gamma(t,n,\tau) = \frac{1}{n!\tau}(t/\tau)^n e^{-t/\tau}, \quad (2)$$

where the number of hypothetical stages in the sequence of filters is $n + 1$, and the time constant of the filters is τ (30).

This model was modified for the present special case of impulsive stimuli by allowing the parameter n of the gamma function to vary with the amplitude of the contrast flash, x_0 to become:

$$n = n_0 + \alpha x_0 + \beta x_0^2 \quad (3)$$

The model was fitted to the data using the Levenberg–Marquardt general nonlinear technique (24). The model of Fig. 1 was used as the nonlinear function, and the parameters to be fitted consisted of n_0, α, β (defining n), τ, and the coefficients of the polynomial, c_i. The algorithm al-

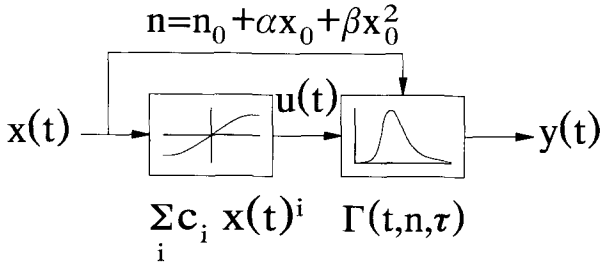

FIGURE 1. The nonlinear cascade model of phototransduction. The discrete light input signal, $x(t)$, first passed through a fifth-order polynomial static nonlinearity with coefficients, c_i to give an intermediate signal, $u(t)$, and then through a gamma function, $\Gamma(t,n,\tau)$ to produce the output membrane potential, $y(t)$. Parameter n of the gamma function was a quadratic function of the input, as indicated by the direct pathway from the input to the gamma function.

ways converged successfully. The mean square error (mse) of the fitted model was obtained from

$$mse = 100\frac{\overline{(y - y')^2}}{\overline{y^2} - \overline{y}^2}, \quad (4)$$

where y' is the model estimate of the output y.

The peak amplitude, p, and time to peak, t_p of the fitted gamma distributions were obtained by differentiating Eq. 2 to give:

$$p = \frac{e^{n\log n - n}}{\tau n!} \quad (5)$$

$$t_p = n\tau$$

RESULTS

Responses to a Series of Contrast Flashes

Responses to incremental or decremental 1 msec flashes in light adaptation were in good agreement with an earlier report (16). Thus, the contrast gain (as maximum response per unit contrast) increased with increasing light adaptation, from 0.2 mV/contrast us with a background of 500 photons/se to about 2 mV/contrast us with 10^6 photons/sec. The contrast gain was also nearly symmetrical (but see below).

To interpret the results, the cascade model of Fig. 1 was selected after preliminary experiments using both the gamma function (30) and the log-normal (21) models for the dynamic linear component. Additionally, the modeling was tested with the static nonlinearity either preceding or succeeding the dynamic linear component, as suggested by our earlier findings (11). All of these configurations gave relatively good fits to the experimental data, but models with the static nonlinearity at the start of the cascade gave a lower mean square error (mse) by about 0.5–1%. It was more difficult to choose between the log-normal and gamma function–based dynamics. However, the gamma function has a simpler mathematical structure and usually gave lower values of mse. For both types of model, a significant improvement in the mse could be obtained by allowing one parameter to vary with input light intensity. For the gamma function model, the best improvement in mse with the addition of two parameters was achieved by replacing the parameter n with a quadratic function (Eq. 3).

Figure 2 shows the membrane potential changes in a dark-adapted fly photoreceptor produced by 10 flashes of different amplitude contrast, ranging over approximately ±1 contrast units, with the fitted model from Eqs. 1–3. The calculated fit is shown by a thicker line superimposed on the original data. The fit gave a mean square error of 2.4%, with very good correspondence to the peak responses. Examples of the fitting to individual light and dark flashes are shown inset. Most of the mean square error was caused by the inherent noise present in the recordings after 200 averages and also by a small overshoot at the end of each response, which was usually seen with both negative and positive responses (8).

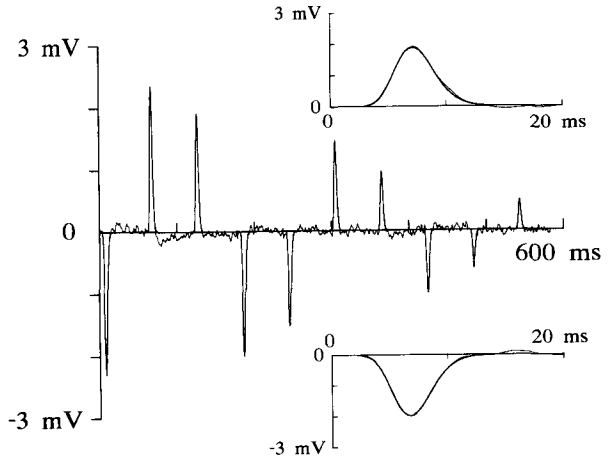

FIGURE 2. Comparison of the predictions of the model of Fig. 1 with a set of 10 flash responses in a light-adapted fly photoreceptor. The mean light level was 1,250,000 ep/sec and the contrast values of the flashes (from left to right) were −0.994, 1.043, 0.85, −0.87, −0.671, 0.64, 0.43, −0.45, −0.22, and 0.22. Note that each of the flash responses was obtained separately by averaging 200 presentations, and they were then combined numerically before fitting. Expanded views of part of the data and the model predictions are shown in the inset for the third (upper) and fourth (lower) responses. The mean square error of the fitted model was 2.4%.

The averaged fitted parameters from 14 receptor cells (fitted as in Fig. 2) are shown in Fig. 3. The time to peak parameter, t_p, did not vary significantly between cells and

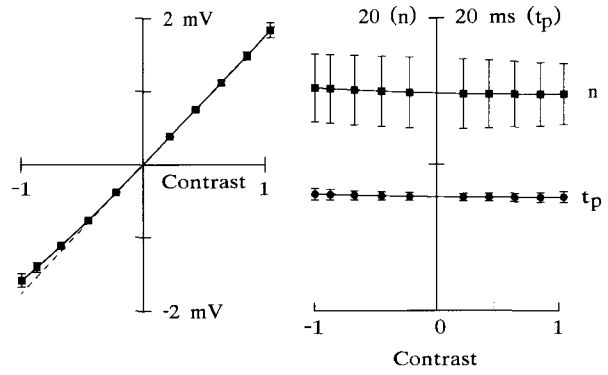

FIGURE 3. Peak response amplitude, p, parameter, n, and the time to peak, t_p, as functions of flash contrast. The data are mean values from 14 different receptor cells, fitted as shown in Fig. 2. Bars indicate standard deviations. The mean square errors for the 14 fits ranged from 0.98 to 4.25% with a mean of 2.25%. The peak responses (left) deviated from linearity during negative contrast flashes. A straight line (dashed) has been drawn through the origin and the data point from the highest positive contrast. The negative contrast flash responses deviate positively from this line by approximately 2 standard deviations. The parameter n and the time to peak, t_p, both decreased slightly with contrast.

had an interpolated value of 7.8 msec at zero contrast and a small tendency to increase at negative contrasts. The parameter n was more variable from cell to cell, with a value of 15 at zero contrast and also a tendency to increase with negative contrast flashes. The peak response, p, was a linear function of contrast intensity for positive flashes but demonstrated nonlinear compression for negative contrast flashes. At a background light level of 1,250,000 ep/sec this intensity dependence was close to linear for all experiments, but reducing the background intensity to 1,250 ep/sec caused the function to become nonlinear, showing saturation, or compression, of the response to larger contrast flashes. This was particularly true for negative flashes, as shown in Fig. 4. This nonlinearity could be caused by the voltage-dependent properties of the photoreceptor membrane (19,28). On the basis of this hypothesis we determined the 1 msec contrast response function with the full background intensity of 1,250,000 ep/sec while hyperpolarizing the cells (with SECC) close to the resting potential with current injection (Fig. 4). The change in membrane potential caused a similar change from linear to saturating nonlinear peak amplitude.

Double Flash Experiments

To test the linearity of the flash responses and the speed of nonlinear interaction further, cells were stimulated with pairs of identical contrast flashes separated in time, and the responses were fitted with the gamma function model. Separate parameters were used for each of the two responses, except for n, which depended on the input (Eq. 3) and was identical for both responses. The individual flashes were each of 0.5 contrast units and 1 msec duration. Figure 5 shows four examples of such experiments

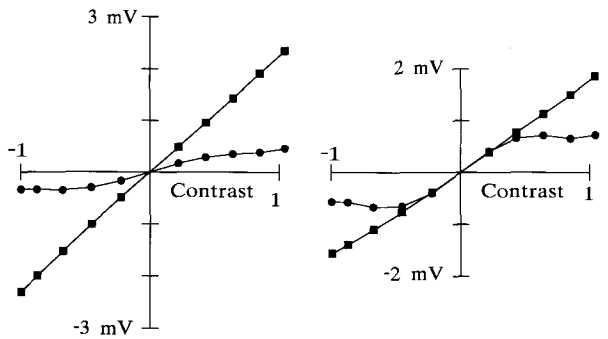

FIGURE 4. Peak responses, p, as a function of flash contrast. Left: squares show data from the fit of Fig. 2 to responses in a cell at a background level of 1,250,000 ep/sec. Circles show data from a similar fit, but at a background level of 50 ep/sec, using 400 averages. Note the very linear behavior at the higher light level, compared with the strongly nonlinear behavior at the low light level. Right: a normal (squares) and hyperpolarized (circles) cell receiving a background intensity of 1,250,000 ep/sec. Note the nonlinearity induced by the hyperpolarization. The current of −3 nA produced a membrane potential change of −15 mV.

with both positive and negative contrast flashes and flash separations of 4 and 7 msec. The fitting algorithm assumed that the response was made up of a sum of two gamma functions and allowed the parameter τ and the amplitude of the response to be variable for each of the two flashes. From the six fitted parameters, the peak amplitude, p, and time to peak, t_p, were calculated, as well as the sum of the two peak amplitudes. It can be seen that the model gave an excellent fit to the total response from the paired flashes.

The peak amplitudes of the fitted responses and their sums are shown as functions of flash separation in Fig. 6. Two deviations from linear summation of the flashes were seen in these experiments. The peak amplitudes of the two flash responses were generally indistinguishable, but the amplitudes of the negative flash responses tended to increase at separations below 10 msec. The time-course of this interaction is shown clearly in the individual and summed values in Fig. 6. As an additional test of the phenomenon, Fig. 7 includes the peak amplitudes of the gamma distribution fitted to single flashes of 0.5 contrast units and 2 msec duration, corresponding to paired 1 msec flashes with a separation of 1 msec. The peak of the single negative response was similar to the summed responses of widely separated paired flashes, as would be predicted by a linear model, but smaller than the summed responses to paired flashes at short separations. The speed of decay of this enhancement effect was measured in four receptors by fitting a single exponential function to the data (Fig. 7). The four time constants obtained were 1.74, 1.72, 0.64, and 0.48 msec. The enhancement of the response to paired flashes at short separations was never seen in the positive flash response.

A second deviation from linearity is shown by the decrease in response to both positive and negative flashes at a separation of 5 msec in Fig. 6. Although this effect looks like a random variation in one set of data, it was seen in most data sets as a significant increase or decrease in response at only one separation and in either the positive or negative flash responses. When present, it always occurred at a flash separation below 10 msec. Time to peak, t_p, values of the fitted gamma distributions were generally consistent throughout the full range of separations and flash amplitudes. Figure 8 shows the values of t_p produced by the experiments of Fig. 6. The value of t_p produced by single flashes of 2 msec duration was also in good agreement with these results, and the value for such a flash of 0.5 contrast units is shown as a single point on the figure.

DISCUSSION

Linearity and Nonlinearity of the Contrast Responses

In this work we carefully tested the linearity of light-adapted fly photoreceptors and found two new and distinct

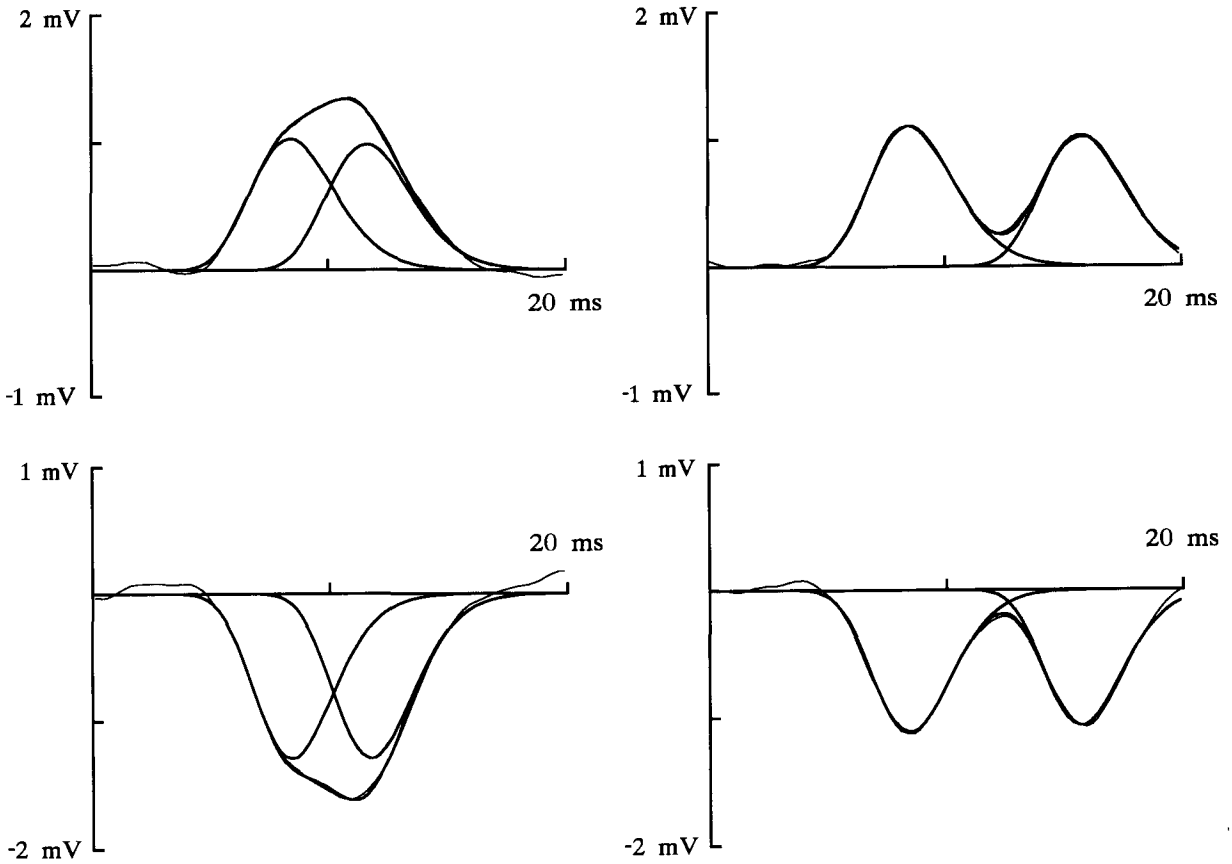

FIGURE 5. Responses of a photoreceptor cell to paired flashes of ±0.5 contrast, 1 msec duration, with variable separation. Each example shows the original membrane potential recording (thin line), the two fitted flash responses from the model of Fig. 1, and their sum. The upper two figures show responses to positive contrast flashes, and the lower two figures show responses to negative flashes. Two flash separations of 3 msec (left) and 7 msec (right) are shown.

deviations from linearity: a fast compression with single flashes and a facilitatory interaction between pairs of negative contrast flashes. Photoreceptor voltage responses would be expected to behave approximately linearly with small stimuli, because a linear estimation generally fits any data quite well when only a small piece of its nonlinear characteristic is explored. This is especially true with light-adapted photoreceptor cells, since their sensitivity is reduced and their voltage responses to similar stimuli are smaller than in the dark-adapted state. In addition to this linear approximation, light-adapted invertebrate photoreceptors also respond more linearly than dark-adapted receptors because their membrane potentials are depolarized from the resting potential. This means that positive and negative contrasts can elicit voltage responses of approximately the same amplitude, above and below the depolarized level. Taking this into account, the nonlinearities we have found represent an important deviation from the known behavior of invertebrate photoreceptors.

With a sufficiently long step change in light intensity, even light-adapted photoreceptors can behave quite nonlinearly (11,16). On a fast time scale, using brief contrast flashes, such nonlinearity is not easily detected. However, under the detailed inspection that we used here, light-adapted photoreceptor responses contained clearly nonlinear dynamics, which could be successfully modeled by a nonlinear cascade model. This model was derived from one that we developed previously on the basis of parallel cascade analysis (11). The model contained a dynamic linear component sandwiched between two static nonlinearities. On the fast time-scale used here, it was possible to ignore the output nonlinearity and to simplify the model to a static nonlinearity followed by a dynamic linear component (Fig. 1). The main value of the model here was to provide accurate measures of the amplitudes and time courses of photoreceptor responses under different conditions.

A Fast Compressive Nonlinearity with Single Flashes

A compression of the contrast responses was seen with both positive and negative contrasts, but it depended on the background intensity used. It was difficult to detect at near daylight backgrounds, but was distinct at dimmer

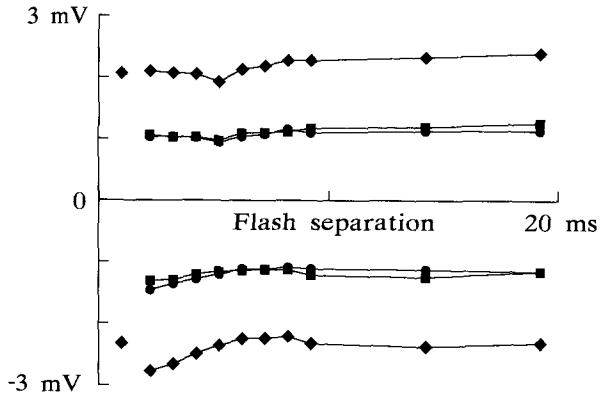

FIGURE 6. The peak amplitudes, *p*, of the fitted double flash responses from the same experiment as in Fig. 5 as a function of flash separation. Responses to positive contrast flashes are upper and negative lower. In each case the amplitude of the first flash is shown by a square symbol, the second flash by a circle symbol, and their sum by a diamond symbol. Also shown, as separate diamonds, are the fitted responses to single flashes of 0.5 contrast units and 2 msec duration, corresponding to paired flashes of 1 msec duration with a separation of 1 msec.

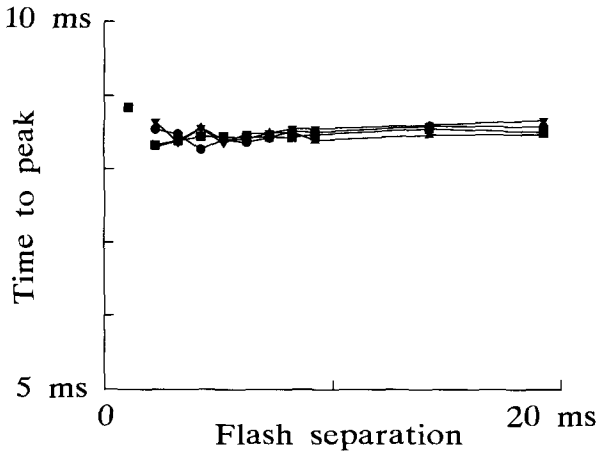

FIGURE 8. The time to peak values, t_p, of the paired flash responses from Fig. 7. The four traces are: first positive flash (inverted triangles), second positive flash (upright triangles), first negative flash (squares), and second negative flash (circles).

levels. The dependence of the compression on membrane potential rather than on contrast (Fig. 4) suggests that it was caused by the voltage dependence of the membrane. Two types of K^+ channels ("fast" and "slow") have been described in blowfly photoreceptors (28). The slow type was probably unimportant with the short contrast steps used here, because it had an activation time constant of ~30 msec at voltages near the resting potential where the compressive nonlinearity was pronounced (17,28). However, the fast channels were almost totally activated at 20 mV above the resting potential, while being continually activated and deactivated near the dark-adapted membrane potential. Modulation of these channels by the voltage response would cause compression of the response on a fast time scale. This fast compression at low backgrounds would therefore resemble the slow compression at near-daylight backgrounds, caused by the slow channels (17). The function of the fast compression may also be similar, namely restricting the membrane potential to a range that is too small to saturate the high-gain synapse (18) between photoreceptors and first-order interneurons.

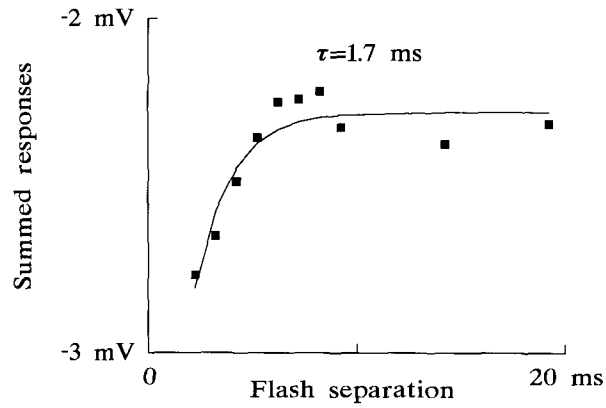

FIGURE 7. The sums of the paired negative flash responses from Fig. 7 (squares) fitted with a single exponential function (solid line). The time constant of the exponential was 1.7 msec.

Nonlinear Interactions between Pairs of Flashes

Under dark-adapted conditions, an initial flash suppresses the response to a test flash, *i.e.*, light adapts the photoreceptor. This effect is present at very low light intensities, even with flashes containing only one photon (10). Here, light-adapted photoreceptors were used, and no such effects were found with positive contrast flashes, presumably because the brief changes in light intensity were not enough to change the adaptation state measurably. Instead, negative double flashes revealed a facilitatory process, with a time constant of ~1 msec. This facilitation might be responsible for one of the main features of the frequency responses of light-adapted fly photoreceptors, namely their underdamped resonance behavior. The time constant of 0.5–2 msec for the decay in facilitation is in good agreement with the time constants of the resonance terms (~1 msec) obtained from white noise analysis (7,8).

What is the physical basis of the facilitatory response? A voltage-dependent enhancement mechanism in fly photoreceptor axons (29) can be disregarded, because axon or near axon recordings can easily be distinguished, even in the dark adapted state, by a small "prespike." A similar kind of facilitation has recently been reported in honeybee drone photoreceptors (26). Although those results were obtained under dark-adapted conditions and with incre-

mental flashes, their physical basis could well be the same. The light-gated channels in invertebrate photoreceptors are probably regulated by the intracellular concentration of calcium, $[Ca^{2+}]$, released from internal stores by an IP_3-mediated mechanism (15). In other preparations, this Ca^{2+} release had a bell-shaped dependence on the free $[Ca^{2+}]$ in the cytoplasm (3) increasing at low levels but saturating and decreasing at higher levels. The increased or decreased IP_3 stimulation would then be either depressed or facilitated by additional phototransduction, depending on the cell's working position along the $IP_3 - Ca^{2+}$ release function. In the honeybee drone, the facilitation under near dark-adapted conditions could have been caused by a shift along the curve upward toward the top of the bell-shaped function where the Ca^{2+} released by IP_3 is at its maximum. If the light-adapted operating point of this function lies near the top of the bell, then small decremental responses would transiently reduce the free $[Ca^{2+}]$ and cause a larger hyperpolarization than expected, *i.e.*, a deviation from linear dependence on light.

The lack of facilitation seen with a continuous 2 msec flash (Fig. 6) contrasts strongly with the facilitation produced by two 1 msec flashes only 1 msec apart. This suggests that the facilitation depends critically on the dark period between the flashes, even if it is short. Any future model of the facilitatory process must take this into account.

Transduction Modeling

An early parametric model of flash responses in *Limulus* photoreceptors (12) consisted of a sequence of simple exponential low-pass filters. Although linear in its basic form, this model was modified to account for changes in behavior at different backgrounds by adding feedback from the output to control the time constants of the filters. The physical analogy of this model was proposed to be a similar sequence of chemical reactions, although the number of such reactions was large (>10). Similar nonlinear models were subsequently used to model photoresponses in other invertebrates (23) and vertebrates (2). A normalized form of the model, a gamma function, has also been used to model single photon responses of *Limulus* photoreceptors (30). An elaboration of this approach was the inclusion of second-order underdamped filters and a pure time delay, or dead-time (7,8) that was able to explain the resonances in fly photoreceptor frequency responses and to reduce the number of components in the sequence to ~5. A different approach to the problem used a log-normal distribution to fit flash responses from a range of dark-adapted insect photoreceptors (21). The physical basis of this model was suggested to be an approximately logarithmic dependence of some internal transmitter on light intensity, coupled to a normally distributed sensitivity of ion channels to the transmitter. However, in spite of their different physical interpretations, both the gamma function (30) and the log-normal model gave similarly good fits to the flash responses, and both used two parameters.

Linear models cannot cope with the nonlinearities of phototransduction, but the relatively simple nonlinear cascade (11), and the present model, with only a few adjustable parameters, were able to fit the responses accurately. The results of this modeling exercise suggest that there is very fine tuning of several processes in the photoreceptors under physiological illumination conditions. The fine tuning of the membrane voltage dependence by K^+ channels was the subject of a recent comparative paper (19) and the present work gives more weight to the arguments presented there. Vision is the primary sensory system for many aspects of insect behavior. For small insects, phototransduction demands such a high metabolic expense that its components must be accurately and efficiently matched. Detailed nonlinear analysis of the type presented here allows these interactions to be explored.

REFERENCES

1. Autrum, H. Light and dark adaptation in invertebrates. In: Handbook of Sensory Physiology VII/6C, edited by H. Autrum. New York: Springer-Verlag, 1981, pp. 1–91.
2. Baylor, D. A., A. L. Hodgkin, and T. D. Lamb. The electrical responses of turtle cones to flashes and steps of light. *J. Physiol.* 242:685–727, 1974.
3. Bezprozvanny, I. Bell-shaped calcium-response curves of Ins(1,4,5)P3- and calcium-gated channels from endoplasmic reticulum of cerebellum. *Nature* 351:751–754, 1991.
4. Classen-Linke, I., and H. Stieve. The sensitivity of the ventral photoreceptor of Limulus recovers after light adaptation in two phases of dark adaptation. *Z. Naturforsch.* 41c:657–667, 1986.
5. Dubs, A. Non-linearity and light adaptation in the fly photoreceptor. *J. Comp. Physiol.* A 144:53–59, 1981.
6. Fein, A., and E. Z. Szuts. Photoreceptors: Their Role in Vision. Cambridge: Cambridge University Press, 1982, 212 pp.
7. French, A. S. Phototransduction in the fly compound eye exhibits temporal resonances and a pure time delay. *Nature* 283:200–202, 1980.
8. French, A. S. The linear dynamic properties of phototransduction in the fly compound eye. *J. Physiol.* 308:385–401, 1980.
9. French, A. S., and M. Järvilehto. The dynamic behaviour of photoreceptor cells in the fly in response to random (white noise) stimulation at a range of temperatures. *J. Physiol.* 274:311–322, 1978.
10. French, A. S., and J. E. Kuster. Nonlinearities in locust photoreceptors during transduction of small numbers of photons. *J. Comp. Physiol.* A 156:645–652, 1985.
11. French, A. S., M. Korenberg, M. Järvilehto, E. Kouvalainen, M. Juusola, and M. Weckström. The dynamic nonlinear behaviour of fly photoreceptors evoked by a wide range of light intensities. *Biophys. J.* 65:832–839, 1993.
12. Fuortes, M. G. F., and A. L. Hodgkin. Changes in time

scale and sensitivity in the ommatidia of *Limulus*. *J. Physiol.* 172:239–263, 1964.
13. Hardie, R. C. Electrophysiological analysis of fly retina. I: Comparative properties of R1-6 and R7 and 8. *J. Comp. Physiol.* A 129:19–33, 1979.
14. Hardie, R. C. Functional organization of the fly retina. In: Progress in Sensory Physiology, Vol. 5, edited by D. Ottoson. New York: Springer-Verlag, 1985, pp. 1–79.
15. Hardie, R. C. Whole-cell recordings of the light-induced current in dissociated *Drosophila* photoreceptors: evidence for feedback by calcium permeating the light sensitive channels. *Proc. R. Soc. Lond.* B 245:203–210, 1991.
16. Juusola, M. Linear and nonlinear contrast coding in light adapted blowfly photoreceptors. *J. Comp. Physiol.* A 172: 511–521, 1993.
17. Juusola, M., and M. Weckström. Band-pass filtering by voltage-dependent membrane in an insect photoreceptor. *Neurosci. Lett.* 154:84–88, 1993.
18. Laughlin, S. B., J. Howard, and B. Blakeslee. Synaptic limitations to contrast coding in the retina of the blowfly. *Calliphora*. *Proc. R. Soc. Lond.* B 231:437–467, 1987.
19. Laughlin, S. B., and M. Weckström. Fast and slow photoreceptors—a comparative study of the functional diversity of coding and conductances in the *Diptera*. *J. Comp. Physiol.* A 172:593–609, 1993.
20. Leutscher-Hazelhoff, J. T. Linear and non-linear performance of transducer and pupil in Calliphora retinula cells. *J. Physiol.* 246:333–350, 1975.
21. Payne, R., and J. Howard. Response of an insect photoreceptor: A simple log-normal model. *Nature* 290:415–416, 1984.
22. Pece, A. E. C., and A. S. French. Sublinear summation of responses in locust photoreceptors. *J. Comp. Physiol.* A 170:729–738, 1992.
23. Pinter, R. B. Sinusoidal and delta function responses of visual cells of the *Limulus* eye. *J. Gen. Physiol.* 49:565–593, 1966.
24. Press, W. H., B. P. Flannery, S. A. Teukolsky, and W. T. Vetterling. Numerical Recipes in C. Cambridge: Cambridge University Press, 1990, 735 pp.
25. Spekreijse, H., and H. Oostings. Linearizing: A method for analysing and synthesizing non-linear systems. *Kybernetik* 7:22–31, 1970.
26. Waltz, B. Enhancement of sensitivity in photoreceptors of the honey bee drone by light and by Ca^{2+}. *J. Comp. Physiol.* A 170:605–613, 1992.
27. Weckström, M., E. Kouvalainen, and M. Järvilehto. Nonlinearities in response properties of insect visual cells: An analysis in time and frequency domains. *Acta Physiol. Scand.* 132:103–113, 1988.
28. Weckström, M., R. C. Hardie, and S. B. Laughlin. Voltage-activated potassium channels in blowfly photoreceptors and their role in light adaptation. *J. Physiol.* 440:635–657, 1991.
29. Weckström, M., M. Juusola, and S. B. Laughlin. Presynaptic enhancement of signal transients in photoreceptor terminals in the compound eye. *Proc. R. Soc. Lond.* B 250: 83–89, 1992.
30. Wong, F., B. W. Knight, and F. A. Dodge. Dispersion of latencies in photoreceptors of Limulus and the adapting bump model. *J. Gen. Physiol.* 76:517–537, 1980.