Transient Responses to Sudden Illumination in Cells of the Eye of *Limulus*

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ABSTRACT Responses recorded from visual cells of *Limulus* (presumably eccentric cells) following abrupt and maintained illumination consist of depolarization with superimposed spikes. Both the depolarization and the frequency of firing are greater at the beginning of the response than later on. Frequency of firing decreases with time also during stimulation with constant currents, but the decay is then less than it is during constant illumination. Early and steady-state responses do not increase in the same proportion following illumination at different intensities. Membrane conductance is higher during the early peak of the response than in steady state. Early and late potential changes appear to tend to the same equilibrium value. The results support the assumptions that: (*a*) discharge of impulses is the consequence of depolarization of a specialized "pacemaker region" in the axon; (*b*) depolarization induced by light is the consequence of increase of membrane conductance. The major conductance changes occurring during constant illumination may be due to corresponding changes of the "stimulus" supplied by the photoreceptor or to changes of sensitivity of the eccentric cell's membrane to this stimulus. Some accessory phenomena may be the consequence of regenerative properties of the nerve cell itself.

Many receptor organs respond to a suddenly applied and steadily maintained stimulus (a step function) with a discharge of impulses which decrease in frequency with time. It seems important to inquire about the causes of this decay (usually called adaptation), not only because its clarification is a necessary preliminary to the study of other problems, but also because its understanding may further our insight into the basic functions of receptor organs.

The present article is an analysis of the changes occurring with time in the responses evoked by a step of light in cells of the eye of *Limulus*. Findings

obtained in previous work (Fuortes, 1959), in which the action of light was studied several seconds after the beginning of the illumination (when the responses had reached conditions approaching steady state), were interpreted on the basis of the model reproduced in Fig. 1. It is assumed in this model that the primary effect of illumination upon the eccentric cell is to increase

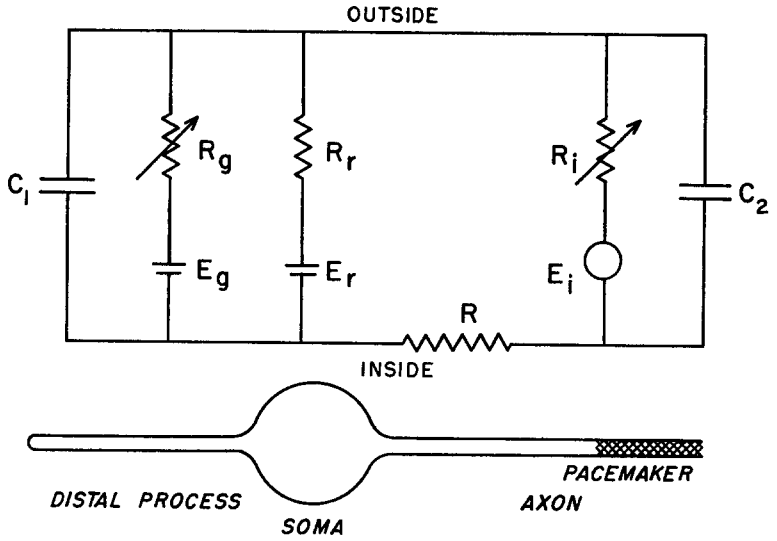

FIGURE 1. Electrical circuit to illustrate properties of eccentric cells. The diagram is essentially identical with those of Figs. 11 and 12 in Fuortes, 1959. A resistance R has been explicitly included to represent separation of pacemaker region from soma. R_g and E_g represent resistance and electromotive force of those parts of the eccentric cell's membrane which are responsible for production of generator potentials; R_r and E_r, of the parts which maintain resting values; and R_i and E_i, of the membrane areas subserving generation of impulses. R_g is supposed to decrease with light, possibly owing to the action of a chemical transmitter. R_g and R_r are thought to be insensitive to the voltage across the membrane, except under special circumstances briefly mentioned under Discussion (electrically inexcitable membrane according to Grundfest, 1959). R_i and E_i are represented as single elements for simplicity but should be imagined to include all mechanisms required for impulse production. Their value is, therefore, supposed to change as a function of the voltage across the membrane.

conductance of part of its membrane: the increase of conductance brings about depolarization and this depolarization is the cause of firing. This same model will be applied to the interpretation of the results obtained in the present study. It will be seen that the initial response to a step of light, as well as the transition from early to "steady state" response, is a disappointingly complex process. Some of these complications should be expected if responses to light are a consequence of the processes implied in the model proposed

above; others seem to depend upon features which are not explicitly included in the original model.

METHODS

The lateral eye of *Limulus* was used for these experiments. The eye was sectioned in two and placed in sea water at constant temperature (6°C to 20°C in different experiments). A glass micropipette was introduced in one ommatidium and moved by means of a micrometric screw until satisfactory evidence of penetration of the electrode tip into a cell was obtained. The responses analyzed in this study were taken exclusively from cells which could be identified as eccentric cells according to the criteria proposed in a previous paper (Fuortes, 1958, p. 219).

The techniques used for recording potentials and for applying currents were essentially the same used by previous authors (Hartline, Wagner, and MacNichol, 1952; MacNichol, Wagner, and Hartline, 1953; MacNichol, 1956) and have been described in a former article (Fuortes, 1959). The stimulating light was focused on the lens of the penetrated ommatidium and care was taken to avoid illumination of neighboring ommatidia.

The analysis of the results included measurement of potential differences and of frequency of firing. In most cells considered in this study, resting membrane potentials of between 45 and 55 mv were measured either upon penetration or when the electrode was withdrawn, at the end of the experiment. Potential changes developing during activity were measured with respect to this resting potential. As was done in previous studies (Fuortes, 1958, 1959), in the presence of firing of impulses, the measurement of membrane potential was taken in the intervals between successive spikes.

In the former work, in which only steady-state conditions were considered, frequencies were measured by counting the number of impulses discharged in a convenient time unit, but in the present study, dealing with rapidly changing responses, frequencies were measured as the inverse of the intervals between successive impulses. These intervals were recorded on analog magnetic tape, measured by means of a time interval digitizer, and punched on paper tape by means of a high speed perforator. Since the data analyzed here were not recorded originally on magnetic tape, photographic records were transferred onto tape by moving the film at uniform speed and projecting the enlarged records on a photocell provided with a black screen which left only a slit of about 0.5 mm exposed to light. When the shadow of a spike passed the slit, a sharp electrical transient was generated and recorded on the magnetic tape. The results obtained with this method were checked on occasion by direct measurements on the film record, and were found to be satisfactory.

RESULTS

Responses to Lights of Different Brightness A series of responses to lights of different intensities is shown in Fig. 2. The voltage change underlying the

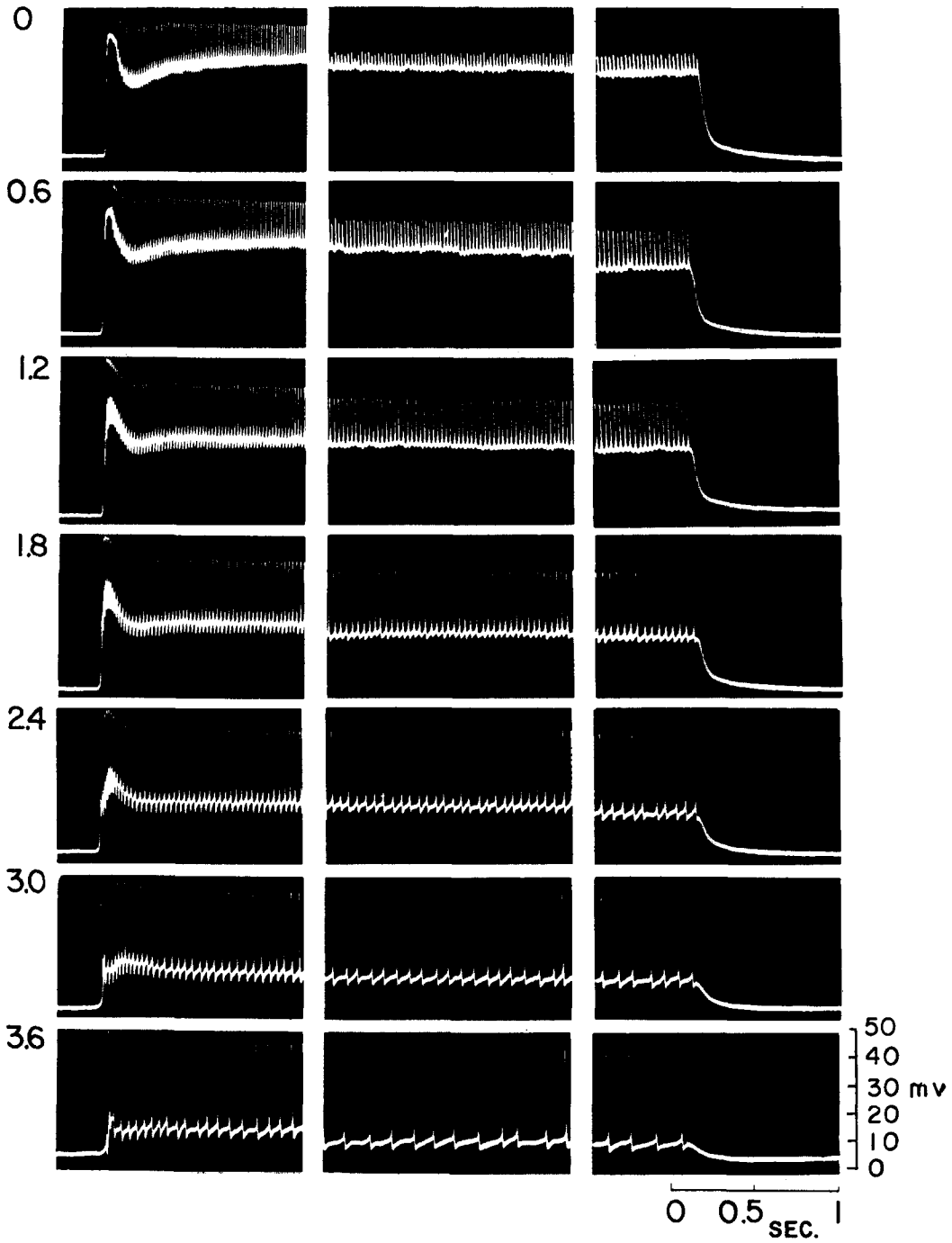

FIGURE 2. Responses to steps of light. Unit 3358 (same cell as in Figs. 3 and 6 through 10). Figures at left indicate attenuation of light intensity in logarithmic scale. Steps of light lasted 20 seconds. Gaps between the three records in each row are 8.4 seconds each. The stimuli were applied in order of increasing intensity and were separated by 20 second intervals. Temperature, 18°C.

impulses is retraced in the inset of Fig. 3, while the graph in this figure shows the relation between voltage change and intensity of stimulation. Voltage was measured at the peak of the early response and 20 seconds after onset of the illumination. This late condition is referred to as "steady state" although slow changes still occur at this time.

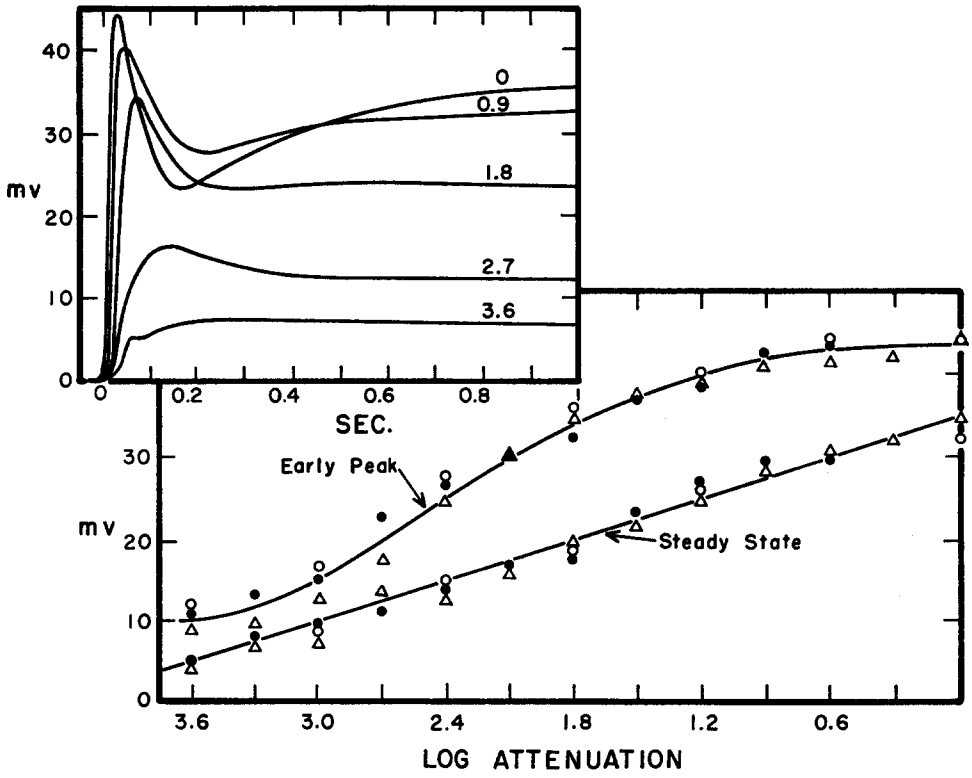

FIGURE 3. Height of responses as a function of light intensity and of time. Unit 3358. Data from three experiments as illustrated in Fig. 2, all from the same unit. The graph shows the value of the depolarization recorded at the beginning of the response (*Early Peak*) and after 20 seconds (*Steady State*), for different attenuations of light intensity, as indicated in abscissa. Tracings of the voltage changes evoked by light are superimposed in the inset.

It is seen both in the tracings and in the graph that the various phases of the responses do not change in the same proportion with different intensities. In steady state, the voltage displacement is an approximately linear function of the logarithm of the intensity of illumination (MacNichol, 1956; Fuortes, 1958), but an S-shaped relation is found for the early peak, so that the difference between peak and steady-state potentials is largest for responses to moderate light intensities.

The course of decay from early to steady-state responses is in general quite complex, although it may fit a simple exponential function for responses to stimuli of moderate intensity (*e.g.* 2.7 in the inset of Fig. 3).

Some of these features may be explained assuming that "saturation" of

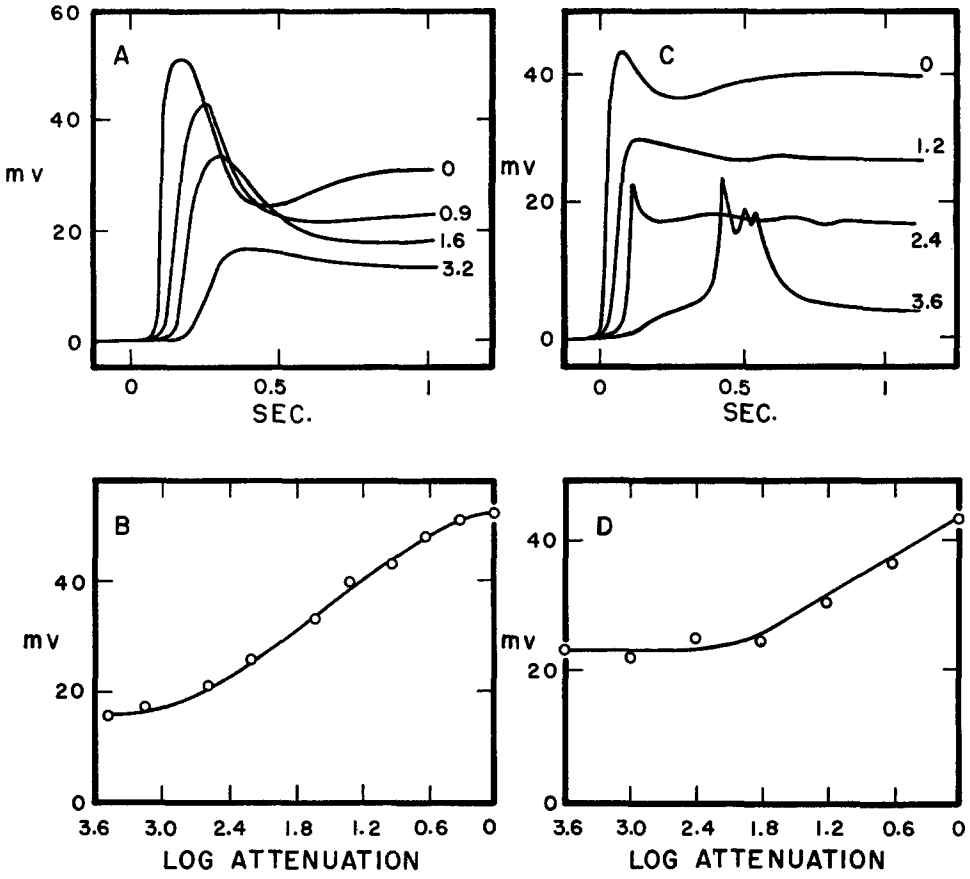

FIGURE 4. Responses to light in two different cells. Tracings and plots like those of Fig. 3, but omitting graph of steady-state responses. The cell of A and B (unit 11157) gave results similar to those of Fig. 3. The responses of the cell of C and D (unit 42358) showed instead sharp transient waves of depolarization which, in the lowest tracing, appeared to originate abruptly from a slower response. In both cases, temperature was about 20°C.

one of the processes leading to depolarization of the eccentric cell occurs following stimulation with bright lights, but early responses may be complicated also by other processes, as revealed by findings to be mentioned in the following section.

Oscillations and Sharp Transients in Early Responses to Steps of Light Fig. 4 shows tracings and plots of the early potential changes recorded from two

different cells, following stimulation with steps of light of different intensity.

In the unit of Fig. 4 A and B, the potential change follows a smooth course for all light intensities used, and the height of the early peak grows progressively with increasing light intensity. The superimposed tracings of Fig. 4 A illustrate that the responses to bright light do not fall gradually from the early peak, but go through a minimum, from which they rise again to steady-state level. This is seen clearly also in the unit of Figs. 2 and 3, but is much less apparent in that of Fig. 4 C.

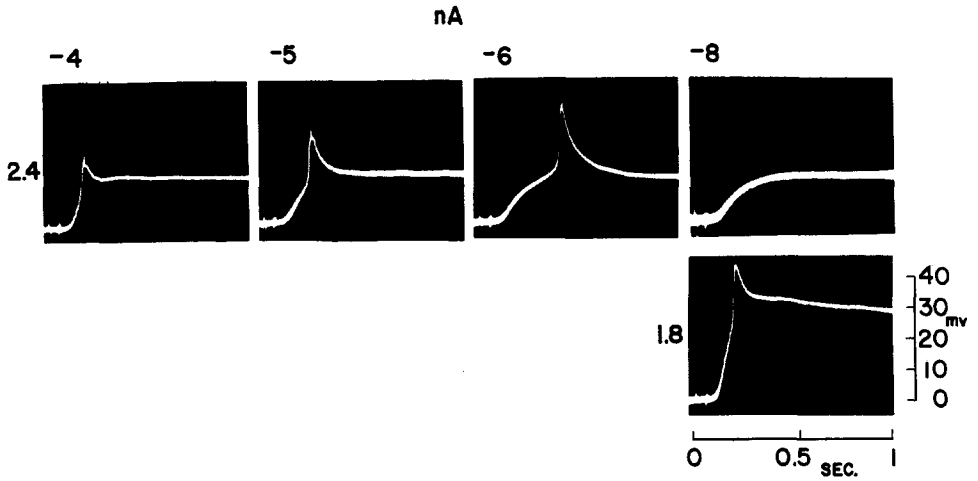

FIGURE 5. Action of hyperpolarizing currents on sharp transients. Unit 71359. The upper row illustrates responses to steps of light of constant intensity (attenuation 2.4) applied while the cell was hyperpolarized by constant currents of different values (indicated by figures above each record). Currents cause delay and finally abolition of depolarizing transient. However, early transient is restored in the presence of strong hyperpolarizing current if light intensity is increased (lower record, attenuation 1.8). Temperature, 18°C. 1 nA = 10^{-9} amp.

In the cell of Fig. 4 C and D, the response to a light attenuated by 3.6 logarithmic units shows sudden sharp transients superimposed upon a more gradually developing response. The sharp initial peak of the response to illumination attenuated by 2.4 resembles the first delayed transient of the bottom tracing and might be due to the same process. The graph of peak height as a function of light intensity (Fig. 4 D) shows that peak height does not change appreciably for attenuations between 3.6 and 1.8. These observations suggest that the early response to a step of light may include two components. The process giving rise to the fast transient does not appear to increase systematically with increasing light intensity and is predominant in the responses to weak lights. The slower component grows as light intensity is increased and becomes predominant with bright lights. When the sharp

transient is small or absent, the shape of the response will be controlled by the slower process and results such as are illustrated in Fig. 4 A and B will be obtained.

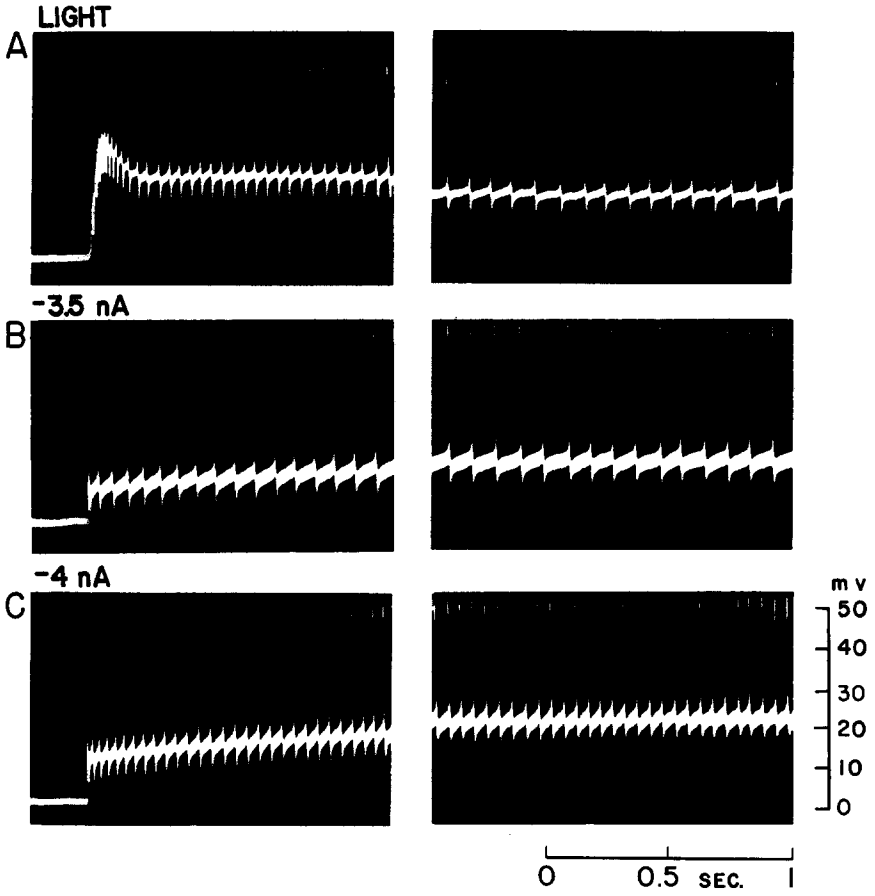

FIGURE 6. Frequency of firing in responses evoked by light or by currents. Unit 3358. A: response to a step of light of moderate intensity. B and C: responses to currents of intensity as indicated. Left and right hand records are separated by an interval of 8.5 seconds. The slow drift of the baseline in B and C is probably due to changes of electrode resistance and does not indicate changes of membrane resistance or membrane potential (see Frank and Fuortes, 1956). Temperature, 18°C.

Effects of Currents on the Sharp Transients Evoked by Steps of Light Fast transients can be separated from the slower component of the early response to a step of light by means of hyperpolarizing currents through the microelectrode. Fig. 5 shows responses recorded when a step of light of moderate intensity (attenuation 2.4 log units) was applied while constant currents of different intensity were passed through the cell's membrane. The hyper-

polarizing current increased both the size and the delay of the sharp transient, and separation of the two components of the early response became more and more obvious as current intensity was increased. In the experiment considered, the sharp transient was suddenly abolished when current intensity reached 8 nA. However, with this current intensity, the sharp transient could again be evoked if light intensity was increased (attenuation 1.8).

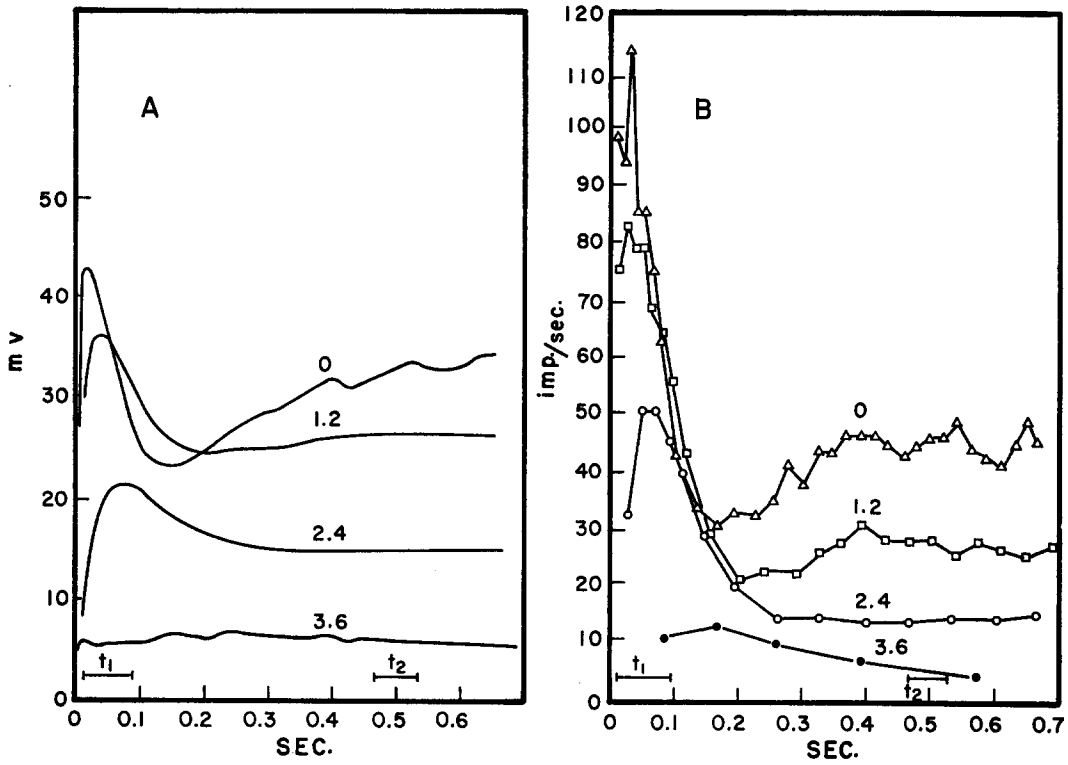

FIGURE 7. Voltage and frequency changes evoked by steps of light at different intensities. Unit 3358. A: tracings of voltage changes as in inset of Fig. 3. Numbers near tracings indicate light attenuation. B: Plots of reciprocals of intervals between successive impulses in responses traced in A. Both in A and B, zero in the abscissa indicates time of firing of first impulse. The points in B are placed at the end of each interval so that they indicate time of firing of following impulses.

In certain experimental conditions (different light intensities applied during flow of constant current), these sharp transients were generated when a critical value of membrane voltage was reached. However, under other conditions it could be shown that these transients do not necessarily originate when the same critical membrane voltage is attained. For instance, only very rarely could sharp transients be evoked when membrane voltage was displaced by currents in the absence of illumination.

Frequency of Firing in Responses to Constant Lights or Constant Currents Hartline, Coulter, and Wagner (1952) stated that frequency of impulses decays in similar manner in responses to steps of light or to steps of depolarizing current applied with external electrodes. This was observed, in the present investigation, only for weak stimuli, when the initial transient of responses to light is

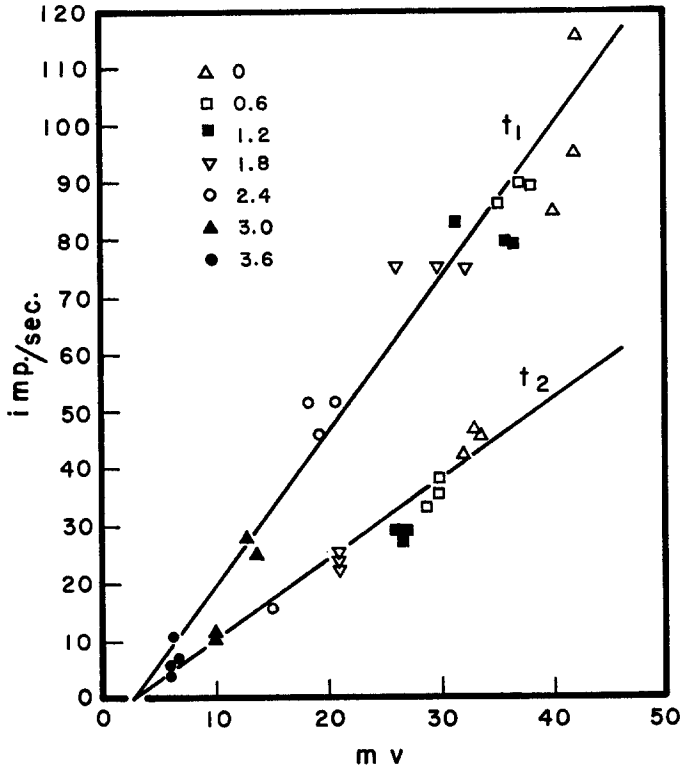

FIGURE 8. Relation between voltage and frequency of firing at different times. Unit 3358. Data taken from experiment of Fig. 7 but including other measurements from same cell. One to three intervals were measured within the period t_1 (indicated by the short horizontal line in Fig. 7) and corresponding voltages were measured from the tracings at the mid-point of each interval. Three measurements within the period t_2 were taken graphically from plots such as those of Fig. 7 B. The different symbols refer to measurements taken at different light intensities, as indicated.

small (see bottom tracings of Figs. 2, 4 A, and 7 A). In general, however, frequency decays more rapidly during constant illumination than during stimulation with constant currents, as illustrated in Fig. 6.

Fig. 7 shows the time course of the voltage displacement (A) and of the rate of discharge (B) evoked in one cell by lights of different intensities. The curves in the two figures present a general resemblance, but they cannot be

superimposed by scaling because frequency decays more sharply with time than voltage does.

In Fig. 8, the same data are plotted to show the instantaneous relation between voltage and frequency at selected times (t_1 and t_2 in Fig. 7). These measurements are subject to large errors since both voltage and frequency change rapidly and it is quite difficult to synchronize the measurements with

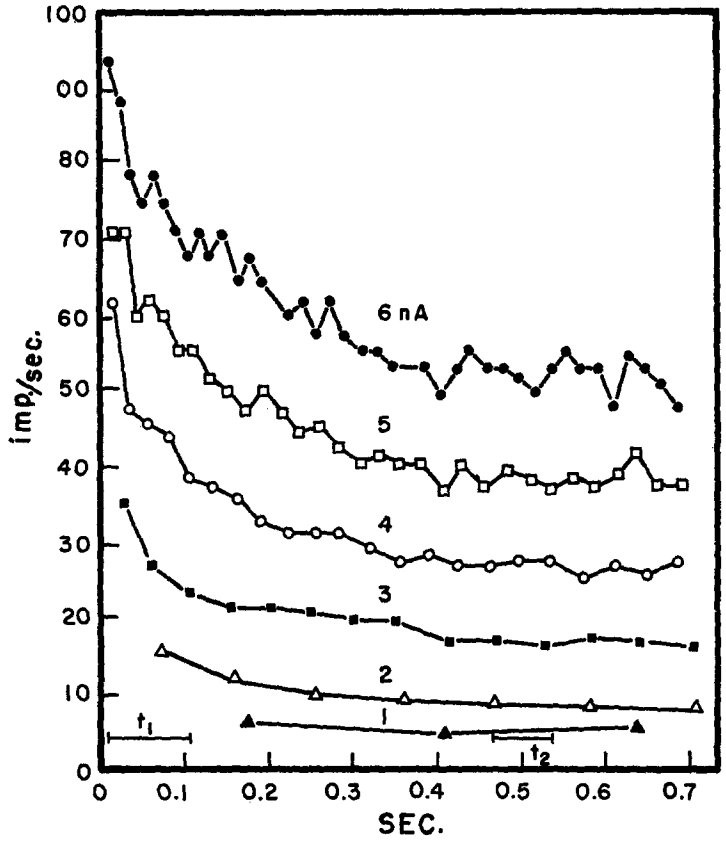

FIGURE 9. Decay of frequency during stimulation with constant currents. Unit 3358. Plots of reciprocals of intervals between successive impulses in responses elicited by depolarizing current steps of intensity as indicated.

accuracy. Still, the data taken at t_1 and t_2 could both be roughly fitted by straight lines, and there is little doubt that the slope of the line was steeper for the measurements taken at the earlier time.

The same type of analysis was then performed for the responses elicited in the same cell by steps of current, and the results illustrated in Figs. 9 and 10 were obtained. It is seen in these plots that frequency decays smoothly with time during flow of a constant current. Comparison of the frequency-in-

tensity plots of Fig. 10 with the frequency-voltage plots of Fig. 8 shows that the slope changes with time in the same manner. This would be expected if the stimulus responsible for generation of impulses were constant during constant current stimulation but changed as the voltage recorded across the soma membrane during illumination.

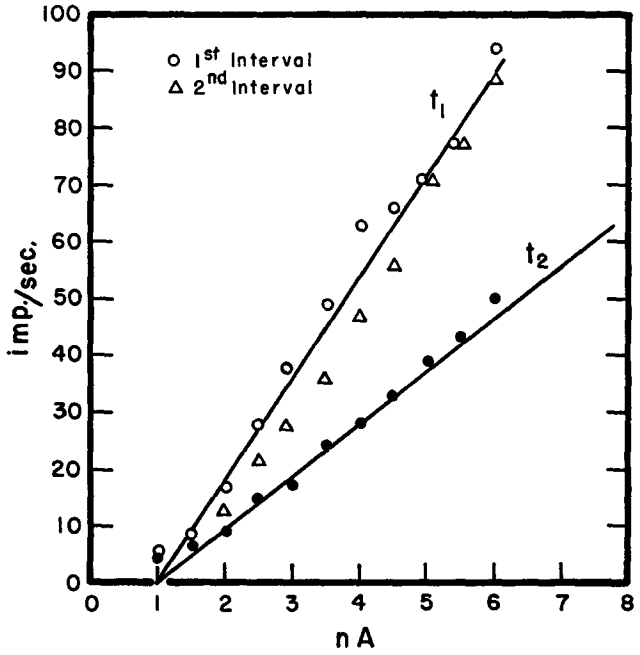

FIGURE 10. Relation between current intensity and frequency at different times. Unit 3358. Reciprocal of intervals measured at an early time t_1 or at a later time t_2 (see short horizontal lines in Fig. 9) after onset of stimulation, plotted as a function of intensity of the stimulating current. Points around the line t_1 measure inverse of first and second intervals in the trains of impulses elicited by each current intensity used. Points around the line t_2 are the average of as many measurements as could be taken within the period t_2, as shown in Fig. 9. The straight lines t_1 and t_2 have slopes in the same ratio as those of the corresponding lines in Fig. 8.

Membrane Resistance during Illumination A relation was found in a previous paper between voltage displacement evoked by light and conductance of the eccentric cell's membrane. This relation was the basis for the model proposed to interpret the mechanisms of responses to light in the eye of *Limulus* (Fig. 1). The measurements performed in the older work in "steady state" conditions (Fuortes, 1959) have been applied in this research to the early phases of the response. Steady currents were passed through the microelectrode, and for each current intensity used, responses to steps of light of different intensities were recorded. The potential drop recorded through the

Wheatstone bridge in each condition was measured at the peak of the initial response and 1.5 seconds after start of the illumination. The results of this experiment are illustrated in Fig. 11. Membrane resistance in darkness was

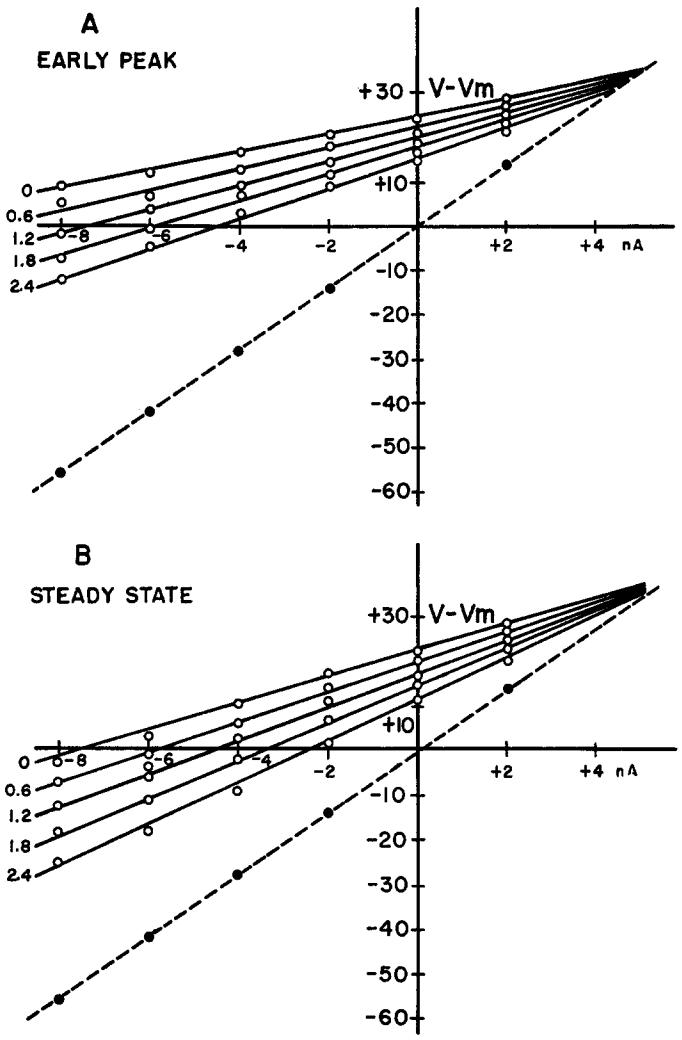

FIGURE 11. Potentials resulting from the combined action of lights and currents. Unit 72059. The dashed lines were drawn to have a slope corresponding to a resistance of 7 MΩ, presumed to measure membrane resistance in darkness (see text for explanation). The vertical distances between dashed lines and open circles measure the potential changes evoked by lights of five different intensities (light attenuation indicated by figures at left) applied during flow of constant currents of the intensities shown in abscissa. Hyperpolarizing and depolarizing currents are indicated by minus and plus signs respectively. Ordinate measures the difference between internal potential and resting potential ($V - Vm$).

determined using the postulation proposed in a former article (Fuortes, 1959) that frequency of firing is determined exclusively by membrane voltage. This resistance was calculated to be 7 MΩ. The voltage displacement evoked by currents could not be measured in the records, because the bridge was balanced for currents applied in darkness, but if the resistance value calculated indirectly is correct, then currents of −8, −6, −4, −2, 0, and +2 nA will change membrane potential by −56, −42, −28, −14, 0, and +14 mv respectively. These values are marked in the plot by solid circles joined by the dashed line. The potential changes evoked by illumination are then measured in the records and are plotted starting from these levels of membrane potential. The open circles in the upper graph (A) in Fig. 11 measure the height of the transient phase of the response to light; the lower graph (B) measures the height of the response 1.5 seconds after start of illumination. It is seen that in either case, the measurements obtained with a given illumination fall on a straight line (see Fuortes, 1959, Figs. 6 and 7). Under some assumptions (mentioned in previous work), the slopes of the lines in this plot measure membrane resistance in darkness (dashed line) and at different intensities of illumination. It follows that membrane resistance is decreased by light and that the resistance change is greater at the beginning of the response than later on.

The lines traced through the experimental points of both plot A and plot B in Fig. 11 converge around a point corresponding to about +35 mv. This value is about 10 mv negative with respect to the outside potential and is approximately the same value obtained in previous experiments (Fuortes, 1959; Rushton, 1959). According to the model presented in Fig. 1, this value represents the equilibrium potential for the changes evoked by light. The results indicate, therefore, that this equilibrium point is the same at the beginning and at a later stage of the response, and that the decay of potential is due to a decrease of membrane conductance rather than to a change in the electromotive force.

DISCUSSION

According to the interpretation advanced in previous work, the essential processes leading to generation of impulses following photic stimulation in the eye of *Limulus* are as follows: (*a*) light is absorbed in a specialized portion of the retinula cells, adjacent to the distal process of the eccentric cell; (*b*) following absorption of light, a chemical (transmitter) substance is liberated by the retinula cells and diffuses to the eccentric cell; (*c*) the transmitter substance combines with the membrane of the eccentric cell process, evoking

increase of its conductance and decrease of its potential;[1] (*d*) depolarization of the distal process is accompanied by a current which tends to depolarize soma and proximal portions of the axon of the eccentric cell; impulses are generated in a localized region of the axon (pacemaker region, see Tomita, 1957) as a consequence of this depolarizing current. These suggested mechanisms are largely analogous to those which are supposed to operate in transmission of excitation across the central synapses and at the neuromuscular junctions.

If these are the processes which operate in the transformation of light into nerve impulses, it is clear that a large number of factors may influence the relations between the original stimulus (light) and the final response (discharge of impulses).

The processes controlling the relations between depolarizing currents and frequency of firing can be best analyzed by examining responses to currents applied through the microelectrodes. It was stated in an earlier paper (Fuortes, 1959) that resistance of the eccentric cell's membrane does not change appreciably owing to flow of current, except when impulses are discharged. Thus, a constant stimulating current will produce (in the interval between impulses) a constant potential drop across the soma membrane and an approximately constant current through the pacemaker region of the axon, where impulses are generated. To this constant current, the pacemaker region responds with decreasing frequency of firing, owing to changes occurring there in the stimulus-response relations (Fuortes and Mantegazzini, 1962). These changes occur also when firing is evoked by light, but in addition, constant illumination produces a decaying potential drop across the soma membrane and thus a decaying current through the pacemaker region. The decrease of frequency occurring during constant illumination can be explained as being due to the decrease of voltage at the soma membrane and to changes occurring at the pacemaker region, presumed to be situated in the axon. (See Tomita, 1956, 1957; Fuortes, 1960.)

But while analysis of responses to currents may be useful for understanding the features of firing, it cannot explain the features of the potential changes evoked by light, since these are presumably the consequence of a chemical action.

[1] The assumption of a chemical transmission between rhabdome and eccentric cell was proposed to explain conductance changes following illumination but not following application of currents (Fuortes, 1959; Rushton, 1959). Dr. H. K. Hartline has pointed out to us that conductance changes can be explained without invoking a chemical transmitter, if one assumes (*a*) that the membrane ot the rhabdome is very close to the membrane of the eccentric cell, and (*b*) that the membrane of the rhabdome changes conductance with illumination. An analogous interpretation had been advanced a few years ago by Dr. Jerry Lettvin as an alternative explanation of results obtained on spinal motoneurones. Both suggestions seem to fit equally well the data obtained so far, and a choice can be postponed until the need arises.

Experiments such as those described here were performed with the hope that the electrical changes recorded from eccentric cells would furnish rather direct clues for identifying the processes initiated by light in photoreceptors, but it appears that such inference may be instead quite indirect. Clearly, the course of the nerve cell's response should not be expected to reproduce the course of the "stimulus" supplied by the photoreceptor changes, since the ability of the nerve cell's membrane to respond to the stimulus may change with time. For instance, the decay of voltage recorded from eccentric cells during constant illumination might be due to decreased concentration of the postulated transmitter agent, or to decreased sensitivity of the eccentric cell to the transmitter. Such decrease of response due to "desensitization" has been observed in the neuromuscular junction by Katz and Thesleff (1957).

Moreover, it is possible that voltage changes across the eccentric cell's membrane may develop independently both of transmitter concentration and of chemical sensitivity of its membrane, and there are reasons for considering that the sharp, transient potential waves illustrated in Figs. 3 C and 5 may be the consequence of regenerative properties of the eccentric cell's membrane. It has been seen that production of these transients is affected by currents through the eccentric cell's membrane. Depolarization of the eccentric cell does not seem to be sufficient to evoke them, because only rarely could they be produced by means of depolarizing currents in the absence of light, but depolarization to a certain level appears to be required for their production, since they are retarded or abolished by hyperpolarizing currents.

It will be noted that the sharp transients described here have features similar to those of the transient potential changes which sometime occur in dark-adapted preparations, following illumination with dim lights (Yeandle, 1958). To explain production of Yeandle's potentials, it has been suggested that the "transmitter substance" may be liberated in the form of discrete packages, and the effects of currents on Yeandle's potentials were tentatively interpreted assuming that the transmitter carries a negative charge (Fuortes, 1960). It appears difficult, however, to apply these suggestions to the present results. One of the major difficulties is raised by the observation that currents which drastically affect the sharp transients do not influence other components of the generator potential in a comparable way. It is possible, therefore, that the transients described here are due not to discontinuities of transmission but to some process originating in the nerve cell itself when a certain membrane voltage is reached, provided that some other condition (perhaps a certain membrane conductance) is also attained.

A further complication is revealed by the "undershoot" which follows the early peak of responses elicited by bright lights (see Figs. 2, 3, and 4 A). This phenomenon has been ascribed by Jones, Green, and Pinter (1962)

to an autocatalytic process, but it is not clear what reactions may be involved. Inhibition due to scattered light falling upon ommatidia adjacent to the one impaled by the microelectrode (Hartline, Wagner, and Ratliff, 1956) may contribute to the decrease of frequency; however, it is unlikely that it may explain the fall of voltage, since only minor voltage changes are usually associated with this type of inhibition (Fuortes, 1960; Hartline, Ratliff, and Miller, 1961, Fig. 10).

It must be concluded that several unknown processes affect the early responses to a step of light and may be responsible for the finding that the early response is not proportional to the response recorded in steady state.

Despite the complex nature of early responses evoked by a step of light, the relation between voltage displacement and conductance was found to be very similar at the peak of the early transient and in steady state.

According to the results of Fig. 11, illustrating the changes of response induced by currents through the eccentric cell's membrane, the equilibrium potential (represented by the value of the battery, *Eg* in Fig. 1) is approximately the same for early and steady-state responses. Apparently, the early voltage change is large because conductance is high, and decays later because conductance decreases.

Benolken (1961) has recently described results showing that the membrane potential of cells in the eye of *Limulus* may be reversed during the early phase of responses to bright lights and has proposed that the model represented in Fig. 1 should be modified to take this reversal of potential into account. It should be pointed out, however, that the early reversal of membrane potential has been observed by Benolken in cells which could not be classified as eccentric cells according to the criteria proposed in previous work (Fuortes, 1958). In these cells (presumed to be retinula cells), an early reversal of potential had already been reported (Fuortes, 1958, Fig. 2), but the model discussed in this and in preceding papers was proposed to explain the features of responses of presumed eccentric cells, in which potential reversal has not been observed so far.

The results described in this paper on the early phases of responses to steps of light are consistent with the model proposed in a previous article (Fuortes, 1959) and reproduced in Fig. 1. It appears that both the voltage changes occurring during the early phase of visual responses and those occurring in steady state can be ascribed to changes of the resistance represented by R_g in Fig. 1. But the model says nothing about the processes controlling the resistance R_g, and the results described here indicate only that the changes of the value of R_g follow a complex course, being probably controlled by a variety of factors which remain largely unknown at present.

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