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16. On making these identifications, it becomes possible to reinterpret the initial observations of the response discovered by Arden, Ikeda, and Siegel (*13*). These authors assumed that the fast, negative response they observed was a single response generated by both meta I and meta II. However, they observed this response in two different types of experiments. In one experiment, the eye was cooled to −1°C and then exposed to tungsten light; in the other, the eye was exposed to light before it was cooled. In both cases, on delivering the first stimulus flash, they observed a fast negative response. It now appears, from my results, that in the first case only response A should have been present, whereas, in the second case, response C should have been predominant. Since both response A and response C are fast negative responses, it would be difficult to distinguish between them with these experiments. In addition, response B, which is positive, would not be distinguished from R1.
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Rhodopsin: Responses from Transient Intermediates Formed during Its Bleaching

Abstract. *Fast electrical responses elicited from the transient intermediates in the bleaching of rhodopsin have been investigated in the retina of the albino rat. In the experiments we used two-flash stimuli triggered sequentially with a continuously variable time delay between them. At room temperature the potential is biphasic in wave-form. The dominant, corneal-positive component is preceded by a small, corneal-negative component. Cooling the retina to about 0°C suppresses the positive component and isolates the faster, negative component. Experiments with color filters show that these two components display different spectral sensitivities and, hence, suggest that each of them is produced by a different photoproduct of bleaching.*

The early receptor potential is a fast electrical response elicited from the vertebrate retina if the retina is presented with an intense flash stimulus (*1, 2*). The potential originates in the photoexcitation of visual pigment molecules and consists of two separate components of opposite polarity (*2, 3*). These two components display different temperature dependencies and the earlier, positive component can be isolated by cooling (*3*). Recently Arden and Ikeda (*4*) reported that in a rat eye which has been illuminated with tungsten light still another response is observed. The response is corneal negative and precedes the positive component of the early receptor potential. This potential is associated with photoregeneration of the visual pigment from one or more of the intermediates in the bleaching of rhodopsin. They suggested that both metarhodopsin I and II are involved in the production of this potential, although the contribution of metarhodopsin I apparently is relatively small (*5*). We now present evidence that a similar potential obtained from the rat retina by quite different techniques displays a biphasic wave form at room temperature and that each component of the potential appears to originate from a different photoproduct of bleaching.

The stimulus source consisted of two 60-joule xenon lamps (Honeywell Strobonar 65C) triggered sequentially with a continuously variable time delay between the two flashes. The two flashes were focused on the retina by simple lens arrangements, the optic axes forming an angle of about 24° with each other. This arrangement allowed investigation of the potential associated with photoregeneration at precisely timed intervals following the bleaching flash (first flash).

Throughout this study the eyes of the albino rat (Wistar strain from Purdue colony) were used. The eyes were enucleated from fully dark-adapted animals and hemisected around the equator. The vitreous half of the eye was discarded, and experiments were performed on the posterior half spread on a piece of moist filter paper.

If the hemisected eye is exposed to a series of two-flash stimuli (bleaching and test flashes), the response to the second flash (test flash) in the two-flash sequence takes on a distinct wave-form. The responses to the two-flash stimuli obtained at 23° and 0°C are displayed in Fig. 1. The response to the test flash (second flash) elicited at room temperature is biphasic (Fig. 1A). Cone (*6*) was the first to note that a biphasic potential of polarities opposite to those of the early receptor potential can be elicited from a thoroughly light-adapted eye. In contradistinction to the early receptor potential, the dominant component of this response is corneal positive with a small corneal-negative component preceding the positive component. Apparently the faster, corneal-negative component corresponds to the "photoreversal potential" reported by Arden and Ikeda (*4*). Arden and Ikeda (*4*) and Arden, Ikeda, and Siegel (*5*) have demonstrated that the negative component of this potential is associated with photoregeneration from photoproducts of bleaching. Our observations suggest that both components are associated with photoregeneration. For convenience we shall refer to the response as the "reverse potential."

The reverse potential displays a temperature dependence similar to that of the early receptor potential. With a flash separation of about 12 msec the positive component of the potential can be observed conveniently if a bleaching flash is delivered to the retina about 1 minute before the administration of the two-flash sequence (*7*). At a temperature of 23°C the potential obtained in this way is clearly biphasic (Fig. 1A). On the other hand, if a similar sequence of operations is performed at about 0°C, only the fast negative component is present (Fig. 1B). Indeed the initial bleaching flash is not needed to produce the negative component of sizable amplitude. It is readily produced when the two-flash stimuli are delivered to a completely dark-adapted eye at 0°C, providing the flash interval does not exceed about 100 msec. The responses obtained from a dark-adapted eye with a flash separation of 12 msec are shown in Fig. 1C. Thus, at about 0°C the slower positive component is abolished, and the negative component is isolated. At physiological temperature, on the other hand, Arden, Ikeda, and Siegel have shown that the presence of the reverse potential manifests itself

only through the much steeper initial slope of the negative peak of the early receptor potential (*4, 5*). Our results confirm their observations. Apparently the reverse potential can be readily observed only if the amplitude of the early receptor potential elicited in the same flash is very small.

The temperature studies suggest that, as in the case of the early receptor potential, the reverse potential consists of at least two separate components, each of which displays independent temperature dependence. The fact that the potential is observed in response to the second flash in a two-flash sequence suggests that its generation is closely linked with photostimulation of the photoproducts of bleaching, and the fact that photoregeneration accompanies the production of this response suggests that the photoproducts from which the response is generated are one or more of the transient intermediates over which rhodopsin bleaches. A question arises as to which of the intermediates might be involved in the production of this potential and whether or not the same intermediate produces both components of the potential. Perhaps the most direct way of identifying the intermediates responsible for the responses is to compare the action spectra of the responses with the absorption spectra of the intermediates. Unfortunately, however, the amplitudes of the responses were too small to carry out action spectra of the responses with any great accuracy. Instead the spectral sensitivities of the responses were determined by interposing Corning color filters in the stimulus light path. The results obtained at room temperature are shown in Fig. 2. If a filter transmitting at about 360 nm with a one-half transmission bandwidth of about 70 nm [color specification (CS) number 7-51] is introduced in the light path of the test flash (the second flash), only the slower positive component can be observed (Fig. 2B). The amplitude of the response is small, probably due to attenuation in intensities. No indication of the negative component can be seen.

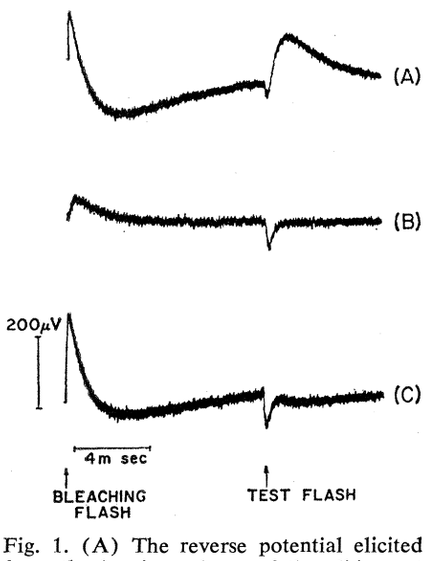

Fig. 1. (A) The reverse potential elicited from the hemisected eye of the albino rat at 23°C. The potential was produced in response to the "test flash" which followed the delivery of the "bleaching flash" by about 12 msec. The two-flash sequence followed the delivery of still another bleaching flash by 1 minute. (B) The potentials obtained by following the same sequence of operations at 0°C. (C) The potentials obtained from a dark-adapted retina at 0°C in response to two flashes separated by 12 msec.

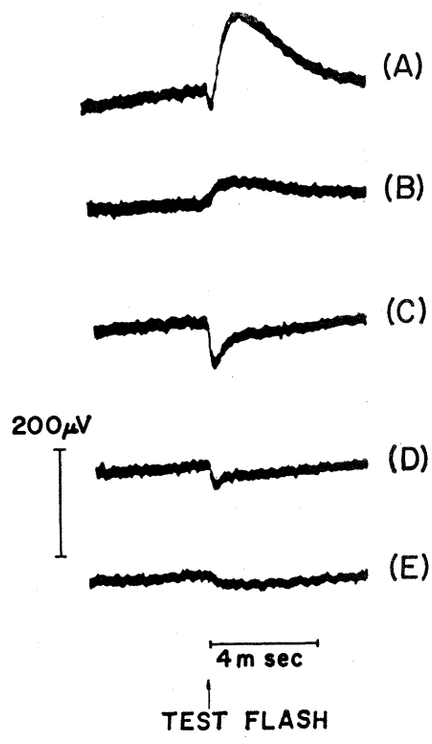

Fig. 2. (A) The reverse potential obtained at 23°C with a white flash. (B) The same response obtained with an ultraviolet transmitting filter (Corning color filter, CS number 7-51) in the light path of the test flash. (C) The same response obtained when wavelengths below about 435 nm are excluded by the introduction of a yellow cutoff filter (CS number 3-72) in the light path. (D) The same potential obtained with a cutoff filter excluding wavelengths below about 470 nm (CS number 3-71) in the light path. (E) The same response obtained when wavelengths below about 500 nm are excluded from the test flash with a cutoff filter (CS number 3-70).

A cutoff filter excluding wavelengths below about 435 nm (10 percent transmission at 435 nm, CS number 3-72) will almost completely abolish the positive component. On the other hand, the faster negative component appears accentuated (Fig. 2C). The negative component is still produced even if the test flash does not contain wavelengths below about 470 nm (Fig. 2D). If wavelengths below about 500 nm were excluded by introduction of a filter having CS number 3-70 (10 percent transmission at 500 nm), even the negative component of the reverse potential is largely absent (Fig. 2E). The negative component isolated at lower temperatures displays spectral sensitivity similar to that at room temperature. Indeed, the spectral sensitivities of these components do not appear to change appreciably as the temperature of the retina is varied.

These results show that the two components of the reverse potential display different spectral sensitivities, indicating that they originate from substances having different absorption spectra. Apparently the intermediate responsible for the production of the positive component absorbs strongly in the near ultraviolet, but not very significantly at wavelengths above 435 nm. The only intermediate which absorbs strongly in the near ultraviolet and from which photoregeneration to rhodopsin can occur is metarhodopsin II (*8*). Thus, it is very likely that the positive component is produced primarily from metarhodopsin II, while the role of metarhodopsin II in the production of the negative component is relatively insignificant. The intermediate product responsible for the generation of the negative component, on the other hand, absorbs strongly in the region between 420 nm and 500 nm. Either metarhodopsin I or lumirhodopsin could be responsible for the response. In flash-photolysis studies of cattle rhodopsin (*9*) and of the frog retina (*10*) at temperatures between 4° and 37°C the first detectable intermediate is metarhodopsin I, even though the technique allows time resolution of about 20 μsec. It is therefore not likely that there would be a significant amount of lumirhodopsin left to produce the response 12 msec after the flash illumination of rhodopsin. The most likely intermediate from which the negative component of the reverse potential is produced appears to be metarhodopsin I.

Thus, at room temperature at least, metarhodopsin I appears to be involved mainly in the production of the negative component of the reverse potential, while metarhodopsin II contributes primarily to the positive component. These conclusions are supported by our experiments in which the time interval between the bleaching flash and the test flash is varied. At short intervals between flashes (approximately 1 msec) the negative component predominates; at longer intervals (100 to 1000 msec), on the other hand, the positive component is the dominant potential.

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Selection of Social Partners as a Function of Peer Contact during Rearing

Abstract. *Three groups of monkeys were raised with different degrees of contact with their peers. The first group was allowed no contact, the second only visual and auditory contact, and the third was allowed complete and normal contact with their peers. Animals of all three groups were allowed to interact socially; they were then tested for their preference for monkeys raised under the same conditions or for monkeys raised under different conditions. Monkeys raised under the same conditions preferred each other, even if the stimulus animals were completely strange to the test monkey.*

The early experiences of primates often have profound consequences on later behavior. In rhesus monkeys exploratory, maternal, sexual, and social behaviors appear extremely vulnerable to early social and sensory restriction (*1*). Monkeys reared in isolation tend to withdraw from other animals and huddle by themselves in social situations prefer each other to monkeys interact with more normal monkeys, they may not be effectively exposed to the stimuli which might lead to some degree of social adjustment. The fact that socially normal monkeys may avoid contact with monkeys reared in isolation further retards rehabilitation. We varied the amount of peer contact during rearing and investigated its effect on physical approach to a social partner, in order to determine whether monkeys reared under identical conditions prefer each other to monkeys reared under different conditions.

Three groups of rhesus monkeys were reared from birth in the laboratory without mothers. Each group contained four males and four females. Sets of three animals were matched across groups for age, sex, and test experiences after rearing was complete. The first group (A) was reared from birth to 9 months in individual closed cages. On the first 5 to 7 days they experienced physical, but minimal visual, contact with a human during feeding. No other physical or visual contact with humans or live monkeys occurred during rearing. Changing visual experiences throughout rearing were limited to presentation of pictures of monkeys engaged in various behaviors and pictures of people and inanimate objects (*2*). From months 9 through 18 the monkeys in group A were housed individually in bare wire cages from which they could see and hear other isolates and humans, but physical contacts were unavailable.

Subjects in the second group (B) were reared individually in a large nursery room in bare wire cages from birth to 9 months. Other monkeys and humans could be seen and heard, but physical contact was not available. From month 9 through 18 the monkeys in group B were housed in the same room as the monkeys in group A; they were in wire cages where they could see and hear, but not touch, one another.

The third group (C) lived in wire cages in peer groups of varying sizes during the first 18 months of life. Rearing conditions and social behavior tests provided physical peer contact during this period. In summary, group A had no early contact with live peers, group B had visual and auditory but no physical contact with peers, and group C had complete peer contact during the rearing period.

When they were 18 months old, sets of monkeys from all groups interacted during social behavior tests in a large playroom (*3*). Each animal was tested weekly for 12 weeks in three 30-minute sessions. In one weekly session a constant set of one group A, one group B, and one group C monkey of the same sex interacted together; the same animals were always tested together. On the two other weekly sessions constant pairs of groups A and B, A and C, and B and C subjects interacted in groups of four monkeys. After social testing, each subject had received equal playroom exposure to one monkey from its own rearing condition and to two monkeys from each of the other rearing conditions. After playroom testing was completed, the monkeys were tested for their preference for other monkeys reared under the same conditions or for those reared under different conditions.

Testing was done in the "selection circus" (Fig. 1), which consists of a central start compartment that bounds the entrances to six adjoining choice compartments. Wire-mesh cages for the stimulus animals were attached to the outside of appropriate choice compartments. The front walls of the stimulus cages, the outside walls of the choice compartments, and the guillotine doors separating choice compartments from the start compartment were all made of clear plexiglas.

For the testing, the subject was placed in the center start compartment with the plexiglas guillotine doors down for a 5-minute exposure period. The subject could see and hear the stimulus animals, but could not enter the choice compartments near them. Unused choice compartments were blocked off by plywood walls inserted in place of