SECTION II

The Properties of Rods and Cones. Variations in Area, Intensity and Duration of the Stimulus in Dark and Light Adaptation. ‘Flicker’

Johannes von Kries, who realized the importance of the anatomy of the retina in considering the physiology of vision more clearly than any of his contemporaries, must indeed have felt the need for objective data if one can judge from the following quotation. It must be added that his own contributions have certainly not provoked the anticipated laughter of the next generation!

Chapter VII

The Duplex Nature of the Retina as Reflected in the Electroretinogram

The Duplicity Theory

The substance of the duplicity theory is well known. The concept of a duplex retina goes back to a generalization, made by the German anatomist Schultze in 1868, that the vertebrates can be divided into two groups, diurnal and nocturnal, corresponding to the predominance of cones or rods in their retinas. Parinaud’s (1898) work connecting night blindness with a deficiency in the rod mechanism also deserves its place in the fundamental investigations on which the theory is based. v. Kries (1904) gave the duplicity theory its final shape. He collected a large number of experimental arguments in its favour and summarized them in 1929, shortly before his death. The duplicity theory is undoubtedly correct in stating that scotopic, or twilight, vision is mediated by the rods and that the cones, responsible for photopic vision become active when the illumination is increased. Most of the old work on the sensory phenomena in this field has been repeated, confirmed and extended by Hecht and his collaborators. The reader is referred to his review (1937) for a presentation of the arguments based on experiments other than electrophysiological ones.

Briefly, the theory states that the rods are low threshold sensory cells which mediate vision at intensities of illumination below about 0.1 m.c. The threshold of the cones is at about this brightness and, on increasing the illumination, the two types of receptor at first operate simultaneously. If the illumination is increased still further, however, the cones alone become responsible for the sensation. The colour sense is dependent on cone activity, the rods being colour blind (v. Kries). The low threshold of the rods is due to a highly light-sensitive substance, visual purple, which is present in them, as well as to the fact that several rods are connected to one bipolar cell and several bipolars to one ganglion cell and so to one optic nerve fibre. It is not necessary to go into the details of the histology of the
retina here, particularly since it has recently been described in
great detail by Polyak (1942) and Walls (1942) in books of
which the former is largely devoted to the subject. We must,
however, mention one point from Polyak’s important work,
namely that some bipolar cells are connected both to rods and
cones. A relatively high degree of potential isolation of the cone
pathways is only found in and around the fovea (in the chim-
panzee) and even here there may be connexions with the rod
pathways through the amacrine cells. In the rest of the retina
rods alone as well as rods and cones together may converge on to
a single ganglion cell and thus on to the same fibre of the optic
nerve. Polyak’s work was done on monkeys possessing a definite
macular region and it is doubtful whether isolated cone path-
ways are ever present in the common laboratory animals. When
one is recording the activity of optic nerve fibres, therefore, one
must always reckon with the probability that, after some dark
adaptation, one is dealing with a dominating rod response in
the same fibre that, in the light adapted state, was activated by
a cone. As we shall see in the last section of this book, all the
experimental work confirms this suggestion.

In formulating the duplicity theory, which has, hitherto, been
based chiefly on sensory or behaviourist data, one is now forced
to define a rod as a visual receptor which contains visual purple
(Granit, 1936). This is because the only reliable experimental
criterion of a rod phenomenon is its association with the spectral
absorption curve of visual purple. Since this substance absorbs
very little light of wavelengths longer than 0.620 μ (red) and
since the cones are relatively insensitive to the shorter wave-
lengths (violet) and are much more sensitive than the rods to
red light, it is often possible to separate rod from cone phe-
nomena by selecting weak lights of suitable wave-lengths as the
stimulus. But such a procedure immediately defines a rod as an
element containing visual purple, a connexion which was hist-
ologically strengthened by Tansley’s (1933b) revealing dis-
covery that, in the developing rat retina, visual purple appears
in parallel with the outer limbs of the rods.

For the histologist the definition of rod and cone is not so
clear unless it is restricted to the mammals where all rods end
on the bipolar cells in knobs and all cones in dendrites (Detwiler,
Franz, 1934, Greef, 1900, Pütter, 1912, Ramon y Cajal, 1894,
The duplex nature of the retina (1933, Rochon Duvigneaud, 1934). In frogs, on the other hand, all the receptors—both rods and cones—have dendritic terminations on their bipolar cells. A form criterion requires that rods should be long and slender, cones short and cone-like, but in the human fovea the cones are long and slender and look like rods.

The physiologist, defining his organs according to their reactions and not, in the first instance, capable of finding functional equivalents for the form of the retinal receptors or of their connexions with the bipolar cells, has to begin by making the presence or absence of visual purple his starting-point. His difficulties begin when the visual purple has been, to some extent, destroyed by light. What happens then? Are the rods now blind, do they still behave like rods, or have they been transformed into some kind of cone by the light? And how do isolated rods and cones react? The answers to some of these questions can be obtained by electrophysiological methods and will be considered later in Chapter IX and in the sections dealing with visual purple and with colour reception. Here we shall confine ourselves to the question of how the duplex nature of the retina is expressed in the electroretinogram.

The Purkinje shift

One easy way of demonstrating the difference between rod and cone reactions is by recording the size and shape of the electroretinograms of a light and of a dark-adapted eye using the wave-lengths of an equal energy spectrum as stimuli. As far back as 1901, Himstedt and Nagel—although they did not use an equal energy spectrum—demonstrated a Purkinje shift in the frog retina by this method. They found that, during dark adaptation and using weak stimuli, maximum electrical responses were elicited by light of a wave-length of 0.544 μ, while after adaptation to bright sunlight the maximum response had shifted to 0.590 μ and much stronger stimuli had to be used. These results were confirmed for frogs and extended to other mixed eyes by Piper in 1905. The slow instruments then in use could not distinguish between different phases of the electroretinogram, but when Brossa and Kohlrausch repeated the experiments in 1913 using a string galvanometer, they were able to show that it is the b-wave which is affected.
by the state of adaptation (see also Kohlrausch, 1931). Chaffee and Hampson (1924) were the first to use an equal energy spectrum, but they did not compare the two states of adaptation. In an otherwise well-controlled investigation, Smit (1934) unfortunately did not systematically measure the \( b \)-wave.

This was the situation in 1937 when the following investigation of the Purkinje shift in the frog’s eye was undertaken in this laboratory. Such experiments are a necessary preliminary to any investigation of colour reception by the electrophysiological method. In Figure 67 the size of the \( b \)-wave is plotted against the wave-length of the stimulating light; the rod curve is that obtained from dark-adapted eyes responding to low-intensity stimuli, the cone curve that from well-lighted animals stimu-

![Figure 67](image-url)
lated by bright spectral lights (the intact bulb was always used). It will be seen that the rods give the biggest response to a wave-
length of about 0.510 \( \mu \), the cones to one around 0.560 \( \mu \). The double contour of the rod curve indicates the range of variation. The cone results showed much less variation, there being only an asymmetrical expansion into the violet (shorter wave-
lengths) which was sometimes present and sometimes not (the dotted extension). Therman (1938) found that the size of the isolated PII potential also reflects the Purkinje shift, showing that, although this component is more marked in cone eyes, it is also a feature of the rod system.

The significance of the Purkinje shift from the point of view of visual purple as well as colour reception will be discussed later in the relevant sections where the results obtained with animals other than the frog, both with the micro-electrode technique and by recording the electroretinogram will be dealt with in detail. The experiment just described is mentioned in order to illustrate the way in which the rod and cone responses can be separated from one another by a proper choice of the stimulating wave-length and a suitable state of adaptation. It is possible to find states of adaptation in which both types of receptor function together, giving a maximum response within a spectral range from 0.460-0.600 \( \mu \) so long as the equal energy stimuli are strong enough, and there are also interesting cases in which a rod curve can be obtained if weak stimuli are used and a relatively pure cone curve when the strength of the stimuli is increased (Granit and Wrede, 1937).

Given enough experience, it is not difficult, by looking at a series of frog electroretinograms taken during the early stages of dark adaptation, to decide the point at which the eye begins to show signs of rod activity. The following criteria are helpful in making such a decision. First of all there is a second rise of PI, recorded as a \( e \)-wave, and then the off-effect often becomes diphasic, showing an initial, small and rapid phase followed by a slow rise, part of which may appear to be a continuation of the \( e \)-wave. Thus, if, during dark adaptation, one compares the response to a stimulus of wave-length 0.620 \( \mu \) with that to 0.470 \( \mu \) the secondary slow rise of the \( e \)-wave, as well as that of the off-effect, may be absent in the former case and large in the latter at a time when the difference in size and rate of rise
of $b$-waves (cf. below) are not yet easily detectable (Granit and Wrede, 1937).

It is much more difficult to compare the effect of light and dark adaptation on the electroretinogram of the E-retina because the fact that the positive potentials developed in these eyes are largely due to the rods (see below) means the virtual disappearance of the $b$-wave when the animal is thoroughly light adapted (Charpentier, 1936, Granit, 1935, Karpe, 1945). Recently Adrian (1945) has shown that in man short wave-lengths (violet) stimulating the rods, elicit a typical E-electroretinogram with an easily measurable $b$-wave and a small or non-existent $a$-wave, whereas wave-lengths from the red end of the spectrum, stimulating the cones, produce an electroretinogram characterized by a well-marked $a$-wave followed by a small $b$-wave. Adrian’s results provide further support for the point which has already been made, and which will be further emphasized later, namely that PIII is much better developed in the cone than in the rod pathways. The fact that marked differences in the electroretinogram of mixed retinas result from the use of wave-lengths from different parts of the spectrum should not necessarily be taken as indicating the presence of special colour receptors. Such effects should be regarded merely as further evidence for the duplicity theory. We shall return to the differences between rod and cone electroretinograms later.

In discussing the possibility of a real selective effect of the wave-length of the stimulating light on the shape of the electroretinogram, Gotch (1904), Brossa and Kohlrausch (1913), Kohlrausch and Brossa (1914), and Smit (1934) have all pointed out that the $b$-wave rises faster when short than when long wave-lengths are used as the stimulus. Careful analysis of this claim (Granit and Munsterhjelm, 1937, Granit and Wrede, 1937) has led us to the conclusion that, in the frog, the difference in the rates of rise of the $b$-wave only occurs in the dark-adapted eye and may thus be considered as a third criterion of incipient rod activity. If the frog eye is thoroughly light adapted so that it behaves as a cone eye, there is no such effect of wave-length. Kohlrausch (1918) made a similar claim for the pigeon eye, but Graham and Riggs (1935) have since concluded that all the alleged specific effects of wave-length on the responses of this eye may be imitated by a proper choice of the intensity of
the stimulus. In this eye there are also enough rods to give an electrically demonstrable Purkinje shift (Granit, 1942 b)—a fact already suggested by Laurens’ (1932) studies of its pupil reactions—so that here too the state of adaptation may easily have been an uncontrolled variable in the early electrophysiological work (summarized by Kohlrausch in 1931).

*The General Effect of the Intensity of the Stimulus on the Electoretinogram*

The most obvious effect of increasing the intensity of the stimulus is a general increase in the size of the electoretinogram, but besides this there is an increased differentiation of the responses of the various retinal processes which leads to a greater distinction of the changes at ‘on’ and ‘off’ and, at least in the mixed and rod retina, to the appearance of the c-wave; the a-wave also becomes more marked. If the isolated receptor layers of *Limulus*, *Dytiscus* and the cephalopods are used, an increase in the stimulus merely increases the size of the electoretinogram with an accentuation of its initial phase, which corresponds to an initial increase of frequency in the optic nerve discharge followed by a silent period. In the *Dytiscus* electoretinogram taken at high intensities, there is also a slow secondary rise, reminiscent of the c-wave of the vertebrate, which may or may not be due to PI. The figures in Chapters II and III should be consulted for graphic illustrations of these phenomena.

In many ways the change in the electoretinogram of the E-retina with illumination presents a simpler picture than does that of the I-retina. Within limits the b-wave increases with intensity in the same way as does that of the initial peak in *Limulus*, but at very high intensities of stimulation the b-wave sometimes, and the c-wave always decreases again. In the cat, the small off-effect, which at lower intensities appears as a retardation of the drop at ‘off’, may at high intensities manifest itself as a small hump.

The electoretinograms of pure cone retinas of the I type are characterized by the prominence of the negative processes, as has been shown by Meservey and Chaffee (1927) who compared such records, from the chameleon, horned toad, and turtle, with those from the frog (cf. also Chaffee and Sutcliffe, 1930)
and by Bernhard (1942) who studied the tortoise and grass snake. The negative trend of the electroretinogram between the large on- and off-effects, which is emphasized by the lack of PI in spite of dark adaptation, indicates a dominance of PIII activity in all these eyes. In fact, the off-effect is often actually larger than the on-effect. Bernhard proved that this generally negative reaction was due to PIII when he changed it into a positive one by the application of alcohol (Fig. 68).

![Diagram](image)

**Figure 68.** The effect of alcohol on the electroretinogram of the tortoise. *A:* normal response to illumination, largely negative. *B:* the effect of 10 per cent alcohol. The negative reaction, due to PIII, has been removed. Time marking: 1/5 sec. (Bernhard, 1941, Acta Physiol. Scand., 3)

![Diagram](image)

**Figure 69.** Electroretinogram of a cold-blooded cone retina (the horned toad). (Chaffee and Sutcliffe, 1930, Amer. J. Physiol., 95)

Figure 69 shows a record from the retina of the horned toad, taken by Chaffee and Sutcliffe (1930). These electroretinograms vary a good deal according to the exact position of the electrode on the retina, but the two figures may be taken as indicating the limits of variation found in cone I-retinas. In cold-blooded animals the records from cone eyes indicate a faster a-wave,
THE DUPLEX NATURE OF THE RETINA

$b$-wave, and off-effect with shorter latent periods than do those from mixed eyes (frog). The threshold in the dark-adapted cone eye is also higher. Meservey and Chaffee (1927) give the ratio of the thresholds for frog, turtle, and horned toad as 1:500: 80,000.

If one electrode, preferably a large cotton pad, is placed behind the bulb, movements of the other across the retina would be expected to produce some variation in the size and shape of the record. Unfortunately, work on these lines has been relatively unsystematic. In the horned toad a complication is introduced by the extremely thin sclera which makes it doubtful whether the back of the bulb can be regarded as an equipotential surface. Keeler (1930) obtained different types of electroretinogram from different regions of this retina and tried to correlate them with structural differences, but his results were vitiated by the use of the optic nerve for his reference electrode since this must have introduced serious and quite unnecessary complications due to the electrotonic potential.

Figure 70. Effect of increasing the intensity of the stimulus on the off-effect in a cone retina. Curves (1) 0.6 secs. exposure; (2) 10.2 secs. exposure; (3) 8.5 secs. exposure; (4) and (5) 7.10 secs. exposure. Ordinates: curves (1-4) off-effect in millivolts (R), curve (5) log R. Horned toad. (Meservey and Chaffee, 1927, J. opt. Soc. Amer., 15)
and the nerve impulses, both of which would distort the electroretinogram.

Up to a point the changes at 'on' and 'off' are also emphasized by increasing the stimulus in pure cone eyes (all of which are of the I-type) but the off-effect decreases again if the stimulus is very strong (Fig. 70). This effect has already been discussed in Chapter V in connexion with the corresponding change in frequency in the optic nerve discharge.

The effect of an increase in the intensity of the stimulus on the electroretinogram of the mixed I-retina is best considered together with the influence of the state of adaptation, since, in these eyes, strong stimuli produce changes which depend on the transition from rod to cone activity. One might go so far as to say that light adaptation transforms the appearance of the retinal response from an E-type in the dark with weak stimuli to an extreme I-reaction at higher intensities.

*The Influence of the State of Adaptation*

The analysis of the electroretinogram into its components has compelled us to make use of a number of facts which must now be recalled and combined to form a coherent picture of the way in which the form of the retinal response alters with adaptation. We can first of all dismiss the I-retina of the *pure cone* type since in these retinas adaptive changes are, on the whole, negligible. Light adaptation diminishes the response.

In the E-retina light adaptation leads to the partial or complete disappearance of PI, the component potential responsible for the c-wave, so that, for this reason alone, the electroretinogram taken at high intensities is much altered. In these retinas, all mammalian and all dominated by rods, PI is also very sensitive to the state of adaptation and its activity is greatly decreased by stimuli strong enough to light adapt the eye. This sensitivity of PI to light results in an electroretinogram with hardly any b-wave at all (Granit, 1935, 1944), but with an immediate negative deflection (produced by PII) which gradually returns to the base-line, the b-wave being so small that it is completely swamped by the a-wave. However, after some time (or immediately if there has only been moderate light adaptation), a small positive hump indicating PII activity will appear, to be followed by a negative phase which, in its
turn, slowly passes into a fresh positive reaction sometimes ending in an off-effect. The quantitative aspect of this return of PII activity after light adaptation will be dealt with in Chapter XVII when we shall consider its relation to visual purple regeneration.

In the mixed I-retina, PII appears to be more resistant to light adaptation than it is in the E-retina. But even in these eyes, of which that of the frog may be taken as typical, light adaptation is followed by a great reduction of PII activity and, therefore, of the b-wave (Wrede, 1937, Riggs, 1937, Therman, 1938). Examination of the electroretinogram of the light-adapted frog shows that, except that the negative phase between the on- and off-effects is usually less definite, it bears a close resemblance to that of the pure cone eye illustrated in Figure 69. Dark adaptation of the frog eye results in very great changes in the electroretinogram. The appearance of PI activity adds a slow positive change (c-wave) and the off-effect is much diminished, the amount depending on the duration of the stimulus. In addition the b-wave increases and may start earlier so as to cut short the a-wave, making it relatively smaller. In fact the mixed I-retina during dark adaptation behaves as though it were changing into an E-retina.

We can make a very interesting comparison between the changes in the electroretinograms of two birds, the pigeon and owl, both with I-retinas containing the two types of receptor (Franz, 1904), but the former dominated by cones and the latter by rods. The electroretinogram of the pigeon, despite a pronounced Purkinje shift (Granit, 1942 b), is relatively independent of the state of adaptation, but that of the owl varies from a dark-adapted form which could be mistaken for a cat record to one, after light adaptation, which looks as if it had been taken from a frog (Granit, 1935). Since the electroretinogram represents an average record of changes in the receptors and their connexions with the optic nerve, it will of course reflect the majority response of the retinal units.

The marked depression of the off-effect which follows the dark adaptation of a mixed retina of the I type is most easily demonstrated if the stimulus is kept short, less than a few seconds. This is probably because long stimuli themselves tend to light adapt the eye. However, when a thoroughly dark-
adapted eye of this type is stimulated with short exposures, the off-effect is more marked if the stimulus is of low intensity. This, at first sight contradictory finding, suggests that intense activation of the retina by light is followed by post-excitary inhibition (extinction) which helps to cut down the off-effect. These points are illustrated in Figure 52B (low intensity electro-retinogram of the frog) and Figures 28 and 35 (high intensity responses).

**PIII and the State of Adaptation**

In order to understand the effect of the state of adaptation of a mixed eye of the I type on the appearance of its electro-retinogram it is necessary to consider the effect on the component potential PIII in more detail than we have done hitherto. It is clear that PII activity varies in a simple manner with the adaptive condition of the retina. Light adaptation always diminishes it and the more rods there are the more marked is this effect.

The process responsible for the PIII potential never seems able to respond as actively in an E- as in an I-retina. We have already shown (see Fig. 42) that, in the frog, a second flash of light, superimposed on the off-effect, produces an abnormally large second a-wave (due to PIII). When a similar experiment is performed on the E-retina of the cat (Fig. 71), the second stimulus is found to be incapable of producing a new a-wave. All that appears is a second b-wave. This difference between the two types of retina, which was first noticed by Piper (1911), is very striking and indicates the slowness of PIII as well as the small extent to which it develops in the E-retina.

At this point one should remember that, in the frog retina, the negative potential (PIII) increases as the duration of the stimulus is increased and also that at least part of this potential vanishes very quickly when the light is cut off. On the other hand, there is also the 'remnant negativity' (p. 55) indicative of a slower disappearance of part of the total negative potential. The question as to whether the potential we have called PIII is produced by one process or whether it is, in reality, made up of two components, one responsible for the quick disappearance (swing-back) of negativity at 'off', the other for 'remnant negativity' is, as yet, unsolved. The fast fraction of PIII does not pos-
Figure 71. Effect of increasing the interval between two stimuli on the electroretinogram of different types of retina. A. frog; B. pigeon; C. owl; D. cat. Uppermost curve of each series shows the uninterrupted off-effect, short vertical lines indicate the beginning of the second stimulus. Time marking: 1/10 sec. (Granit, 1935, J. Physiol., 85).
scess the property of 'refractoriness' which is characteristic of PII. On the contrary, the PIII potential, as we have already seen, can be immediately re-established by a fresh stimulus. Somehow, then, it seems as though light adaptation in a mixed I-retina paves the way for the appearance of PIII (see also Chap. VIII).

The effect of light adaptation in enhancing PIII is shown by the experiment illustrated in Figure 72. This is an electroretinogram which was made partially negative by Waller's

![Electroretinogram](image)

**Figure 72.** The effect of adaptation on PII and PIII in the frog. A. electroretinogram taken after thorough light adaptation; B. after 5 mins. dark adaptation; C. after renewed light adaptation for 2 mins. The size of the b-wave remains fairly constant, indicating little effect on PII, but dark adaptation decreases the negative deflection, indicating a reduction in the PIII potential. Duration of stimulus: A. 1.8 secs., B. 2 secs., C. 2.1 secs. Dotted line: base-line of galvanometer. (Granit and Riddell, 1934, J. Physiol., 81)

(1900) method of massaging the bulb. The first record (A) was taken after thorough light adaptation, the second (B) after 5 minutes of dark adaptation, and the third (C) after a renewed light adaptation lasting 2 minutes. It will be seen that the size of the b-wave remains pretty constant throughout the experiment showing that there has been relatively little change in PII. The effect of the state of adaptation on PIII, on the other hand, is most marked, there being a large negative deflection with a quick return at 'off' in A, but after 5 minutes of dark
adaptation the deflection is much smaller and the return at ‘off’ very slow. The brief light adaptation which preceded the taking of the last record (C) was sufficient to increase both the negative deflection and the rate of return.

If we compare these results with those of Bernhard and Skoglund (1941) on the effect of alcohol (Fig. 38), we find that this effect is exactly similar to that of dark adaptation (sometimes it is even more marked); the total level of positivity increases and the off-effect and \( a \)-wave are diminished. In fact, it would be impossible to distinguish the high intensity electroretinogram of a completely dark-adapted eye from that of a light-adapted eye treated with alcohol. All this suggests that, at least in a mixed retina, light adaptation can actually increase \( \text{PIII} \). It is certainly relatively greater than \( \text{PII} \) in the photopic state whatever the type of retina. When we consider the close connexion between \( \text{PIII} \) and inhibition this can only mean that, in one sense at least, a light-adapted eye is relatively more inhibited than one which is dark adapted.

The facts dealt with in this chapter indicate the possibility of finding a correspondence between the shape of the electroretinogram and the type of receptor dominating the retina from which it is taken. We may hope to find a relationship that goes further than the general statement that \( \text{PIII} \) is characteristic of cone retinas and \( \text{PII} \) of rod ones. Of course, both processes are present in all types of retina. Before making a final effort to elucidate this problem we must inquire more fully into the significance of the curious changes of the electroretinogram of a mixed I-retina with its state of adaptation. In addition, it is necessary to study the effect of adaptation on the optic nerve discharge: These matters will be discussed in the next two chapters.
Chapter VIII

DIFFERENTIATION VELOCITY AS A FUNCTION OF THE STATE OF ADAPTATION. THE RESPONSE TO INTERMITTENT ILLUMINATION

The Response to Continuous Stimulation

One of the most characteristic effects of dark adaptation on PII is that its response (the b-wave) is followed by a long period of 'refractoriness'. The following type of experiment demonstrates not only this phenomenon but also the gradual changes which take place during light adaptation. A beam of light is passed through an arrangement of prisms so that two equal stimuli can be simultaneously applied to the same opened and dark-adapted frog's eye. One light elicits a large b-wave of some 0.5 mV. and is then left shining to adapt the eye. The second light is now used as a test stimulus which can be flashed in at frequent intervals in order to determine how soon the eye is capable of responding with a second b-wave. When the eye is fully dark adapted some minutes must elapse before the test stimulus becomes effective and it is clear that some adaptive change must have occurred when the test flash at last succeeds in producing a small b-wave on top of the level of potential kept up by the continuous illumination. That this is, in fact, the explanation can be shown by cutting off the continuous stimulation and repeating the experiment after a brief interval, sufficient to rest the eye but not long enough to destroy its light adaptation. The test flash now evokes a b-wave of its own within a fraction of a second, in fact, as soon as that produced by the adapting light has subsided. Thus, whereas the scotopic retina was sluggish and incapable of discriminating between a test light and the general level of excitation set up by the adapting light, some light adaptation sufficed to enable the eye to record the added energy as a separate b-wave, signifying a fresh burst of impulses through the optic nerve' (Granit, 1938). It is as though light adaptation were somehow able to reset the retinal recording instrument from 'slow' to 'fast'.

These changes in the speed of action of the retina may be
Differentiation Velocity

summarized in the general statement that ‘whatever happens in the dark-adapted eye, whether it be an effect at “on” or at “off”, it will always be a far more drawn-out affair than in the light adapted state’ (Granit, 1938). This fact is well illustrated

![Diagram A](image1)

**Figure 73.** Effect of a short dark interval on the b-wave produced by re-illumination in the frog. A. original electroretinogram. B. b-wave produced by a flash superimposed on the off-effect. C. b-wave produced by the same flash 10 secs. after the end of the off-effect. Time marking: 1/2 sec. (Granit and Riddell, 1934, J. Physiol., 81)

![Diagram B](image2)

**Figure 74.** The effect of the state of adaptation on the size of the a-wave produced by re-illumination in the frog. A. dark adapted, interval before flash 120 msecs.; B. dark adapted, interval before flash 270 msecs.; C. light adapted, interval before flash 120 msecs.; D. light adapted, interval before flash 290 msecs. Duration of original stimulus 1.3 sec. except in C where it was 1.6 sec. Duration of flash 35 msecs. Calibration to 0.673 mV. (Granit and Riddell, 1934, J. Physiol., 81)

in Figure 73 where the retina is stimulated by a flash following the cessation of an earlier stimulus of the same intensity. If the second flash is put in on top of the off-effect, the b-wave (B) is rapid with a sharp peak, but if as little time as 10 seconds is allowed to elapse after the off-effect, the same flash produces a
large b-wave (C) with a rounded top (in the figure the difference is slightly over-emphasized by a small increase in the speed of the film, cf. time marking).

It has already been pointed out that, in the frog’s eye, the off-effect becomes small and slow as a result of dark adaptation (Figs. 28, 35). Figure 74 shows that there is a very direct correlation between the state of adaptation and the size of the second a-wave (due to PIII) which follows a flash superimposed on the off-effect. Records A and B show the effect of such a flash in the completely dark-adapted eye, C and D the corresponding effect after the eye had been subjected to the same light (1,800 m.c.) for some time. After light adaptation there is a large, fast off-effect and a large, fast a-wave as well. In an eye treated with potassium chloride in order to isolate the component PIII the negative potential, due to PIII, returns very slowly to the baseline at the end of stimulation in the dark-adapted eye and much more quickly after light adaptation. In the former case (dark adaptation) a flash inserted at ‘off’ when the record is returning to the baseline, either has no effect at all or, at most, a very small one. In the latter (light adaptation) the negative potential is quickly re-established by the flash.

Thus, in addition to establishing a preponderance of PIII over PII, light adaptation causes both forms of potential change to become faster. Since these results were all obtained with a mixed retina of the I-type (frog) it is natural to ask whether a change-over from rod to cone activity would account for them. If this were indeed the explanation it is difficult to understand why the faster cones did not take part in the retinal reactions from the beginning in spite of dark adaptation, for the stimuli were all far above the cone threshold. Thus, if we were dealing with nothing but a simple change-over from rods to cones it would be necessary to introduce the additional assumption that in the dark-adapted state the rods are somehow able to inhibit the cones.

The Response to an Intermittent Stimulus in the E- and I-retina

The use of an intermittent light stimulus provides a convenient means of studying how far a retina is capable of following rapid changes of illumination. In Figure 75, taken from an experiment on the frog’s eye, the uppermost curve (A) shows
that the dark-adapted retina reacts so slowly that it cannot follow the individual light flashes (marked below the electroretinogram). Record B shows that a complete change in the general response follows 5 minutes' adaptation to the stimulating light (1,800 m.c.). There are now brisk wavelets synchronized with the individual stimuli which follow one another much more quickly than they did in A. Record C begins with the off-effect of an earlier period of illumination followed by

![Electroretinograms](image-url)

**Figure 75.** Effect of adaptation on the response of the frog retina to intermittent stimulation. *A.* electroretinogram of the completely dark adapted eye; *B.* and *C.* after light adaptation. Max. *b*-wave about 1.0 mV. Intensity of stimulus, 1,800 m.c. (Granit and Riddell, 1934, J. Physiol., 81)

the effect of intermittent stimulation by the same light. The first of these flashes produces a typical negative *a*-wave (coinciding with inhibition in the optic nerve), and then the whole curve swings up and down in time with the stimulation frequency. The fusion frequency under these conditions was 13 flashes per second, but after 15 minutes' dark adaptation it fell to 7 flashes per second, quickly returning to its former value on re-adaptation to light.
In this experiment the eye is seen fulfilling one of the essential tasks for which it was constructed, that of discriminating between light and darkness. The dark adapted eye is highly sensitive and slow, like a ballistically recording galvanometer, integrating the total quantity of energy reaching it. After adaptation to light the retina is less sensitive, but very much faster and capable of differentiating between light and darkness (Granit, 1938) much better than before.

Since the response of the I-retina to intermittent stimulation begins with a manifestation of PIII activity (the a-wave) it is interesting to consider the effect of treating the eye with alcohol which diminishes PIII. Figure 76, from Bernhard and Skoglund's paper, shows that the fusion frequency drops after alcohol treatment, being 17 in the upper record (before treatment) and 13 in the lower (after treatment). Also the curve does not follow the stimulus as closely after treatment as it does before. Again, alcohol has the effect of imitating dark adaptation because they both diminish PIII.

Thus, at least in the frog with its I-type retina, the ability to follow rapid changes of illumination is dependent on the presence of the retinal component PIII as a briskly active mechanism. An accurate response to flicker entails a quick alternation of pre-excitatory inhibition and excitation which is possible because the PIII reaction is always there ready to
manifest itself as an excitatory off-effect rapidly cut off by the next flash. What might, perhaps, be called ‘the re-setting of the visual instrument’ by light adaptation is obviously largely due to a change-over from rod to cone dominance, but light adaptation must clearly have done more than simply remove the rods from the scene of activity. We have seen above that, in the dark-adapted retina, the rods must in some way be capable of damping cone activity, possibly by taking over the cone pathways as in the auditory ‘masking’ of one tone by another in the acoustic nerve (Davis, 1935). In addition it is possible that light adaptation actually speeds up the retinal mechanisms, perhaps by increasing the accommodative resistance of the neurones. Somehow PIII seems to be an essential factor in these processes.

**Figure 77.** Response of an E-retina (cat) to intermittent stimulation. Intensity of stimuli 110 millilamberts. Positive deflection in the middle of the record is an artefact. Time in 100 msecs. (Creed and Granit, 1933, J. Physiol., 78)

As one would expect in a retina whose reaction to re-illumination is a sub-normal b-wave (Fig. 71), an E-retina responds to intermittent stimulation with repeated b-waves (Piper, 1911, Creed and Granit, 1933). A record of the response of the cat’s eye to flicker is given in Figure 77 and it will be seen that the only sign of a counter-process such as might correspond to the well-marked a-wave of the I-retina, was a lengthening of the latent period of the ‘flickering’ b-waves. Once again it is necessary to emphasize that the electroretinogram records an ‘average’ of the responses of many receptors and that each individual will react according to the properties of its type.

*The Factors which Determine the Differentiation Velocity*

In considering the general problem of what I shall call the
'differentiation velocity' of the retina in the light or the dark-adapted state there are three questions which I shall try to answer on the evidence now available to us. Are there good reasons for assuming that the cones react faster than the rods? Do relatively pure rod or cone responses become faster after light adaptation or is the change in the speed of the response of mixed retinas wholly due to the change-over from rod to cone dominance? What information can we obtain from the optic nerve? The terms 'rod' and 'cone' are used here to include both the receptor and its synaptic path in the retina.

The first of these problems was attacked by Piper in 1911. His experiments with cats, dogs, rabbits, and monkeys did not provide a satisfactory answer since the cats showed a fusion frequency of about 25 flashes per second while the monkey (Macacus) had one of only 17 per second in spite of the fact that it is fairly safe to assume that the monkey eye is better provided with cones than the cat eye; in general the results showed that the fusion frequency of the E-retina is low. The warm-blooded I-retinas examined by Piper all belonged to birds and were of the mixed type. In the hen and buzzard (Falco buteo) dominated by cones, in the owl (Surnia aluco) by rods. The first two eyes showed maximum fusion frequencies of 35 and 40 respectively, the third one of only 20. These results on birds provide positive evidence that the rods as such respond more slowly than the cones. Further evidence on this point will be found in Chapter IX.

Piper did not discover that remarkable change produced in certain mixed retinas of the I type (frog, owl) by a change in the state of adaptation which has been described and analysed in this and the preceding chapter. I, therefore, repeated his experiments with such animals as were available to me (1935), first with the eyes dark adapted and again after light adaptation to 620 m.c. My results are set out in Table II.

<table>
<thead>
<tr>
<th>Animal</th>
<th>Fusion frequency</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Scotopic</td>
</tr>
<tr>
<td>Pigeon</td>
<td>40</td>
</tr>
<tr>
<td>Owl</td>
<td>22</td>
</tr>
<tr>
<td>Cat</td>
<td>26</td>
</tr>
<tr>
<td>Rabbit</td>
<td>30</td>
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DIFFERENTIATION VELOCITY

The greatest difference was found in the I-retina of the owl which also, like that of the frog, has an electroretinogram which changes from an E-like type in the scotopic state to an I-type in the photopic state. Those retinas in which the electroretinogram remains of the same type whatever the state of adaptation also vary less in their fusion frequency. The measurement of fusion frequency in light adaptation may be rather difficult if the $b$-wave is much reduced. This was the case in the cat and the difference may, therefore, be somewhat larger than is shown in the table. In the rat (Charpentier, 1936) the $b$-wave becomes so small after light adaptation that fusion frequencies cannot be measured at all. None of these eyes has a pure rod or a pure cone retina, but a comparison of the results obtained on the owl and on the pigeon certainly supports the view that cone dominance is associated with higher fusion frequencies than rod dominance.

The best material for comparative work on these lines is found among the eyes of cold-blooded animals. Thus, Meservey and Chaffee (1927) found that the responses of the cone eyes of two lizards, the chameleon, and horned toad, were shorter and quicker than those of the mixed eye of the frog. They did not measure any fusion frequencies.

We can, therefore, conclude that a cone retina is actually faster than a rod retina whether its owner is warm- or cold-blooded. Further support for this conclusion is provided by the results obtained on the human eye which will be discussed in the next chapter.

Work on the electroretinogram provides no evidence which can help us to answer the question as to whether light adaptation can increase the differentiation velocity of a retina which is homogeneous with respect to its receptors. It is, however, possible to draw some conclusions from the results obtained on the optic nerve. For instance, Hartline and his collaborators (1941) found that light adaptation reduced the total number of impulses in the optic nerve of Limulus (cf. the effect on the guinea pig eye (Fig. 65b) which possesses a retina with a large number of on-elements behaving in a way reminiscent of primary sense cells). The shorter discharges from light-adapted cells should enable them to follow faster frequencies of stimulation even though, according to Hartline, the latent period is
but little affected by the state of adaptation. This change in differentiation velocity can, however, only be small since the fusion frequency is so little influenced in, for instance, the pigeon (and even in this eye part of the effect may be due to a transition from mixed vision to a more nearly pure cone vision). In mixed eyes, therefore, the turn-over from rod to cone vision and vice versa must be the central and most important factor in the great variation of differential velocity with state of adaptation which is characteristic of just those eyes in which such a transition involves a large number of both kinds of receptor.

Work on the Human Eye

This effect of adaptation on the speed of the visual response has also been brought out in investigations of human visual sensation. Thus, Schaternikov (1902), working in v. Kries’ laboratory, found that light adaptation raised the subjective fusion frequency. A very complete study of the effect of both the state of adaptation of the eye and of background brightness was made by Lythgoe and Tansley in 1929 and their results were later supplemented by Enroth and Werner’s (1936) observations on some pathological cases. The effect of light adaptation in raising the fusion frequency is very marked in the mixed peripheral retina and much less prominent in the pure cone fovea. In fact, fovea and periphery behave as though the retina of a pigeon (fovea) were surrounded by that of an owl (periphery). Yet the human retina belongs to the E type (see Appendix II). Discussing this problem in 1940, Lythgoe suggested that, during light adaptation, some reorganization of the neural connexions takes place resulting in a dissociation of the individual pathways which, in the dark, interact and co-operate to a much greater extent. Electrophysiological analysis, beginning at the other end of the chain of visual events, has revealed the properties of PIII and has shown what actually happens in the retina itself. At present it is not possible to decide whether or not the retinal changes thus discovered would lead to the net result postulated by Lythgoe, but there is nothing inherently improbable in his theory.

Working with the human electroretinogram, Sachs (1929) claimed that the subjective fusion frequency was the same as
DIFFERENTIATION VELOCITY

that noted on the electroretinogram. This, however, is not so. The fusion frequency of the electroretinogram always remains a great deal below that at which flicker disappears (Cooper, Creed, and Granit, 1933; Bernhard, 1941). The explanation of this discrepancy must lie in the ‘average’ nature of the electroretinogram where the dominant rods are likely to determine the result while the actual sensation experienced is guided by cone activity. But it is also possible that the rotation of activity (p. 98) which, although sometimes seen in the electroretinogram (Granit and Munsterhjelm, 1937), is particularly well marked in micro-electrode records from the optic nerve (Fig. 63) may be partly responsible. Rotation of activity in the nerve may maintain an intermittent stimulation of the cortical structures at a rate above that which can be recorded on the electroretinogram. Bartley (1937, 1939) in attempting to analyse these factors in the electroretinogram has emphasized the significance of the neural aspects in explaining flicker. The mechanism whereby the electroretinogram record of flicker is produced has not yet been properly worked out, but we do know that, just as the subjective fusion frequency for the human eye increases with an increase in the intensity of the stimulus, so also does the fusion frequency recorded electrically from the retina and optic nerve (Adrian and Matthews, 1928, Creed and Granit, 1933).

The Adaptive Effect of Light and the Differentiation Velocity

From the facts discussed in this chapter and the last it is clear that light, as well as affecting the concentration of such photochemical substances as visual purple, also has a remarkable effect on the general properties of the retina which can be said to acquire new constants after stimulation. Not only are the receptor processes speeded up in a manner which recalls an increase of accommodative resistance (Chapter I), but both PII and PIII become faster, the latter also increasing relative to the former and perhaps becoming actually larger than before. After light adaptation the retinal reactions to the onset and cessation of illumination come to the fore, an effect which is accentuated by the shorter discharges during stimulation. These effects are especially obvious in mixed retinas where they involve a transition of activity from the rod to the conc
system. The total result of this transformation is, as it were, a resetting of the retinal instrument from slow to fast, from integration to differentiation.

It is a sound principle to use the duality theory as far as possible in seeking explanations of the phenomena of visual physiology. This procedure also serves to reveal the shortcomings of the theory and we have here a case where it fails at one important point. Granting that the cone system is faster than the rod system, there still remains the riddle of why the stimuli (well above the cone threshold) which were used in all the experiments described in this chapter and the last, were not able to activate the cone system of the scotopic eye. What has happened to the cone response? According to the orthodox theory its presence or absence is solely a matter of threshold. I have already tried to get the duality theory out of this difficulty (Granit, 1935) firstly by extending the definitions of rod and cone to include their synaptic pathways and secondly by assuming that the cones cannot function as a fast system in the dark because they are ‘inhibited’ by the slower rods. This ‘inhibition’ was tentatively described (Granit, 1938) as a type of ‘masking’ comparable to Davis’s ‘auditory masking’ or to the ‘occlusion’ of the Sherrington school, the rods using all the available pathways and thereby excluding the cones. On this view a depression of the activity of the rods by light adaptation is enough to release the neural paths for the use of the cones. Cone activity is associated with a large PIII potential which can be diminished by the use of alcohol, the result being a state of ‘artificial dark adaptation’ independent of changes in the sensitivity of the receptors. Therman (1939) has shown that dark adaptation not only increases the size of the b-wave elicited by blue light (which affects visual purple and so stimulates the rods), but also reduces that elicited by red light (which stimulates the cones but not the rods). It is difficult to explain these results on any other hypothesis than that the active rods suppress cone activity.

The assumption that the rods can suppress cone activity has been made before in work on human visual sensation. G. E. Müller (1924) used it to explain a type of inhibition which may be exerted by the peripheral on the central retina (v. Liebermannsche Hemmung) and Granit (1927) as well as Creed and
Granit (1928) also explained certain of their sensory results along the same lines. However, Göthlin (1917) appears to have been the first to produce reliable sensory evidence in favour of an inhibitory or depressive effect of the rods on the cones and to put the suggestion forward in unmistakable terms.
Chapter IX

QUANTITATIVE EFFECTS OF VARIATIONS IN THE STRENGTH OF THE STIMULUS

The Size of the Electroretinogram as a Function of the Intensity of the Stimulus

Most workers, from Dewar and McKendrick (1876) to the present time, have found the size of the electroretinogram to be roughly proportional to the logarithm of the strength of the stimulus. The most complete measurements of the early period were those of de Haas (1903), though the slow recording instruments available at that time were not capable of dividing the positive deflection into a $b$-wave and a $c$-wave.

Later we have the exhaustive investigation of the frog's eye from this point of view carried out by Chaffee and Hampson (1942) using the string galvanometer. They concluded that, at low intensities, the height of the $b$-wave was proportional to the square root of the stimulus while, at high intensities, it was proportional to the logarithm. The precise laws of correspondence can be of little theoretical significance since the electroretinogram only represents the sum of opposite component potentials. In any case we can now use the more suitable technique of recording directly from the optic nerve.

The fact that Chaffee and Hampson found the relationship between the size of the positive retinal response and the stimulus intensity to differ according to whether a high- or low-intensity range was used is of great interest since it suggests that rod and cone dominance are characterized by different quantitative relations between stimulus and effect. If the size of the response in Chaffee and Hampson's experiments is plotted against the logarithm of the intensity the resulting curve is steeper for the cone than for the rod region, just as all the results on human sensation, from those of König and v. Kries would lead one to expect. To discuss the various interpretations of this curve (see e.g. Hecht, 1937; Crozier and Holway, 1940) is beyond the scope of this book.

Before we consider the curves relating impulse frequency to
the intensity of the stimulus in the cat, it may be of interest to glance at Figure 78 where several aspects of the response of this eye (dark adapted), including the height of the $b$-wave, are plotted against the logarithm of the stimulus intensity.

![Figure 78. Effects of increasing the intensity of the stimulus on the electrical reactions of the cat retina. $\circ$-$\circ$ size of $b$-wave; $\ldots$ rate of rise of $b$-wave; $\ldots$ reciprocal of latent period; $\times$-$\times$ size of $c$-wave. Abscissae: log $I$. Ordinates: response as percentage of the maximum. (Granit, 1932, Report Physiol. Opt. Soc. Discussion on Vision, London)](image)

Comparison of the Optic Nerve Discharge in Pure Rod and Mixed Mammalian Eyes

We have already shown (Chaps. II, V, VI) that, where the optic nerve derives directly from the primary sense cells as in *Limulus*, the discharge in it is very simple and like that from any other sense organ, but that as soon as there are even two layers of interfering structures interposed, as in *Pecten*, the nervous response becomes very complicated. The main complication introduced by the interposition of secondary neurones is due to the appearance of elements which are wholly or partially inhibited by the effects of illumination and which, therefore, become active when the stimulation stops. One might say that
the activity of certain of the retinal cells is not only blocked by light, but that these cells seem capable of storing up this activity during continued stimulation so that they respond at 'off' roughly in proportion to the amount of activity they have developed. The activity released from such cells may sometimes be recorded directly (pure off-fibres) or, more often, it is combined with that of the ordinary on-fibres in varying proportions leading to mixed on-off-effects in the optic nerve fibre on to which both have converged. Thus, 'the retina as a sense organ cannot be identified with the rod-cone receptor system. The synaptic apparatus continuously modifies the primary response' (Granit, 1933) coming from the sensory cell. This is a new and central fact which has been established by electrophysiological research and which, for the first time, enables us to go beyond the elementary duplicity theory which, based on sensation, was forced to rely on the properties of visual purple as its criterion of rod effects and to ascribe everything else to the cones. In the first place it has become necessary to extend the theory, as I have done, to embrace the synaptic patterns which they activate as well as the receptors.

Let us now compare the effect of changing the stimulus intensity on the discharge in the optic nerve fibres of two types of E-retina: the pure rod type represented by the guinea pig and the mixed type represented by the cat. The guinea pig eye is the purest rod eye of the E-type systematically studied in this laboratory and shows no Purkinje shift (Granit, 1942 a), a phenomenon which is found as soon as an eye has even a moderate number of cones. The cat retina is a mixed one and although the number of cones is not very great there are enough to produce a Purkinje shift in about 36 per cent of the elements studied from this point of view (Granit, 1943 c).

The most striking difference between the optic nerve fibres of these two eyes has already been mentioned, that in the rod eye of the guinea pig the majority of the elements whose response is isolated by the use of micro-electrodes are of the simple on-type, whereas in the mixed eye of the cat the majority belongs to the on-off-type. Figures 65 and 79 illustrate typical responses from the guinea pig retina, those with and those without an after-discharge, Figure 17 the very similar type of response from Limulus. It is as though, in the guinea pig, the
response from the primary sense cell were passed through the retinal system of synapses without significant modification, although it is true that a small number of isolated elements, particularly in the central retina, respond in the on-off fashion characteristic of those from mixed or pure cone eyes. Their presence is easily demonstrated with a coarse micro-electrode. The guinea pig would, therefore, seem to be the ideal animal for those interested in developing photochemical equations from sensory or behaviourist data.

Figure 79. Effect of increasing the intensity of the stimulus on the response of an isolated retinal element of the guinea pig. Relative energy values of stimuli (from above downwards): 1 (threshold), 1.3, 1.48, 2.22, 3.91, 9.31. Wave-length of stimulus, 0.530 μ. Time marking: 1/50 sec. (Granit, 1942, Acta Physiol. Scand., 3)

Figure 80 is an analysis of the reactions of four typical one-elements, from four different guinea pigs, to increasing in-
tensions of stimulus during dark (filled circles) and light (open circles) adaptation. All the curves, with the exception of the lower one in A, illustrating the discharge frequency in the later stage of stimulation, are plots of the initial maximum frequency against the logarithm of the stimulus intensity. After the dark-adapted responses had been recorded, the adapting light (2,400 m.c.) was kept on all the time, only being interrupted for short intervals while the tests with different intensities were performed. The most characteristic change is the shift in threshold of the elements C and D between 3 and 3.5 log units. For these two elements too the curve rises more steeply after light adaptation. This change in slope is less obvious in B where the records marked by ‘circle with cross’ were taken 1 second, and those by ‘open circle’ 2 seconds after stimulation with 2,400 m.c. In C and D the final frequency is the same both for the scotopic and the photopic eye but, in the latter, it is reached at a higher level of stimulus intensity.

These results indicate that, on an average, the curves of a large number of these elements may rise rather more steeply after light adaptation. The main effects of light adaptation, however, are the decrease in the total number of impulses (duration of the discharge) produced by each stimulus (Fig. 65b) and the increase in the threshold.

Another general property which distinguishes the discharge of a rod retina from that of a mixed one is its failure to reach the final high frequency which is characteristic of the latter (cf. Fig. 80 with Figs. 81-83 from the cat). The maximum frequency attained in the fibres of the guinea pig eye is never much above 100 per second while values as high as 400 per second have been seen in the cat. This is not merely a matter of the type of receptor present since even the few on-off-elements in guinea pigs only show a maximum frequency of 100 per second and pure on-elements in the cat may produce frequencies of 200. In Limulus (Hartline and Graham, 1932) too, the isolated receptor discharge, also a pure on-effect, only reaches a maximum figure of about 100 impulses per second, but the agreement with the figure for the guinea pig may, of course, be pure coincidence.

There are other differences between cats and guinea pigs which appear to be due to the fact that the one has a retina
Figure 80. Effect of increasing the intensity of the stimulus on the frequency of the discharge in four isolated elements of the guinea pig retina in light and dark adaptation. A: dark adapted, • initial frequency, ○ frequency after silent period; B: • dark adapted, ○ 1 sec., + 2 secs. after light adaptation (initial frequency); C and D: • dark adapted, ○ light adapted (initial frequency). Continuous line parallel to abscissa (in B and C), frequency of spontaneous discharge during dark adaptation. Interrupted line parallel to abscissa (C), frequency of spontaneous discharge during light adaptation. Light adaptation, at least 10 mins. to 2,400 m.c. Ordinates: impulses per sec. (Granit, 1944, J. Physiol, 103.).
dominated by on-off-elements, the other one dominated by on-elements. The pure on-elements in both types of retina remain on-elements whatever the intensity of the stimulus, but the on-off-elements vary a great deal with different intensities,

**Figure 81.** Effect of increasing the intensity of the stimulus on the frequency of the discharge in two isolated on-off elements of the dark adapted cat. ○ frequency of on-discharge; ● frequency of off-discharge. Double horizontal line in B indicates frequency of spontaneous discharge. Initial frequencies only. Ordinates: impulses per sec.

appearing sometimes as on-off-elements, sometimes as off-elements and sometimes as on-elements apparently according to rules of interaction between excitation and inhibition which have, so far, been impossible to unravel. Figures 81-3 illustrate the bewildering changes of behaviour shown by isolated on-off-elements of the cat’s eye for different intensities of stimulation.
Figure 82. Effect of the state of adaptation on the responses of two isolated on-off elements of the cat to increase in stimulus intensity. ○ on-discharge during dark adaptation; ● off-discharge during dark adaptation; ○ on-discharge during light adaptation; ◇ off-discharge during light adaptation. Light adaptation, at least 10 mins. to 2,400 m.c. Initial frequencies only. In B, continuous horizontal line indicates frequency of spontaneous discharge during dark adaptation, broken horizontal line frequency during light adaptation. (Granit, 1944. J. Physiol., 103.)
The filled circles show the response of the off-component of an on-off discharge and the semi-filled circles that of its on-component in the dark-adapted eye, while the open circles and those with a double margin indicate the responses of these components during light adaptation.

In Figure 81, record A illustrates the reactions from a scotopic eye which showed no spontaneous activity, record B those of a dark-adapted element with a level of spontaneous frequency indicated by the double line running parallel to the abscissa.

Figure 82 shows the reactions of two elements (A and B) each studied first of all during dark adaptation and then after light adaptation to 2,400 m.c. The curves for B are particularly interesting. They illustrate the responses of a spontaneously active element, and some of the original records are reproduced in Figure 84. For this element the frequency of the scotopic off-effect (filled circles) is well marked at low intensities, reaches a maximum and is then inhibited at a stimulus intensity of about 1 m.c., but rises a second time only to suffer a second inhibition at 1,000 m.c. The presence of spontaneous activity is very helpful, since its suppression, as in this experiment, reveals inhibitory effects which would otherwise escape notice.

In Figure 83 the two upper curves in A illustrate the frequency variations of an element in the photopic eye, that with double circles representing the off-response and the other the on-response of this element. The appearance of the actual discharge can be seen in the inset in this figure. In B the curves for an element with a very high frequency off-effect and low frequency on-effect in both states of adaptation are shown.

We see, therefore, that in the cat, just as in the guinea pig, the effect of light adaptation is to raise the threshold and to curtail the discharge. The actual increase in frequency of any given element is but little influenced by light adaptation, but since the low threshold part of the response is removed leaving only the high threshold fraction which, for a large number of elements, is characterized by a quicker rise in frequency, the average effect will be a steeper rise in the curve relating frequency to the logarithm of the illumination.

The great variations in the responses of individual fibres of the cat's optic nerve make any sweeping generalizations out of
Figure 83. Effect of increasing the stimulus intensity on the frequency of discharge of isolated elements of the cat retina. 
A: light adapted, ○ on-discharge, ◊ off-discharge. Ordinates of two lower curves: total number of impulses in off- (upper) and on-discharge (lower curve). The actual oscillogram (much diminished) inset. B: dark adapted, • frequency of off-discharge, ○ frequency of on-discharge; light adapted, ◊ frequency of off-discharge, ○ frequency of on-discharge.
the question at the present time. Much work will have to be
done on different mammals before this new field, opened out
by the micro-electrode technique, can be said to have been
adequately surveyed. Even the first generalization that one
would like to make, that the differences between the reactions

![Figure 84. Effect of different stimulus intensities on the dis-
charge of an isolated, spontaneously active, dark adapted
element of the cat retina (whose reactions are illustrated in
Fig. 82B). Figures give density of the combination of wedge
and filter inserted into the beam of the 892 m.c. stimulating
light. Note that the frequency at 'on' increases with the stimulus
intensity whereas that at 'off' first decreases, then increases and
then decreases again. (Granit, 1944. J. Physiol., 103.)

of the cat and guinea pig are due to the cones in the eye of the
former (seen e.g. by Züll, 1902; Chievitz, 1889; Granit, 1933),
is not without its difficulties. This suggestion implies that a rod
retina is more likely to produce simple on-responses with a
relatively low range of frequencies, a cone retina much more
complex on-off-discharges reaching high frequencies at high
intensities. Also, since cone retinas show off-effects, pre-
excitatory inhibition must be developed in them.

It will be obvious to anyone acquainted with the sensory
aspect of visual research that these differences between rod and
cone retinas show excellent agreement with the results of work
on visual sensation. It is true that the interpretations outlined
above assume that the synaptic organization of the retina
contributes to the differentiation of the response and that they
thus go far beyond the simple concepts of the orthodox dupli-
city theory. The rods give rise to long trains of impulses at a
low frequency and only follow changes of intensity with an
increased frequency within narrow limits. As soon as cones
appear on the scene (even the modest numbers present in the
cat) we encounter a mechanism of differentiation capable of
responding to a large range of stimulus intensity with variations
of both frequency and impulse pattern. This response occurs
both at the onset and at the cessation of illumination so that the
slightest change in the stimulus situation is translated into a
new type of message to the brain. So we find that the fusion
frequency of flicker, visual acuity and intensity discrimination
are poor for rod vision (low intensities) but improve for cone
vision (high intensities) and that the curves relating these
visual functions to the logarithm of the intensity of the illu-
mination rise slowly in the rod and steeply in the cone region
(below and above 0.1 m.c.).

These conclusions are suggested by our work on the retinas
of cats and guinea pigs with the micro-electrode technique and
are, on the whole supported by that of Hartline (1938) on the
optic nerve of the frog (Fig. 64) since this eye may be regarded
as a further development in the direction of cone dominance.
It is necessary, however, to add a word of caution to this tempt-
ing generalization extending the duplicity theory. The experi-
ments on guinea pigs were carried out under rather deep
anaesthesia (urethane 4-6 c.c. depending on size and individual
resistance) whereas the cats were decerebrate and only had
some 10 c.c. urethane to prevent eye movements. I doubt
whether the extra anaesthetic could account for all the differ-
ences noticed, but it is probable that it could cut down the
frequency range of the receptors and thus greatly over-
emphasize a real difference between cats and guinea pigs. On
the other hand it seems doubtful whether, in the guinea pigs, the deep anaesthesia could have acted selectively on the off-discharge leaving the on-discharge intact. This is quite unlike the usual effect of such agents which, in the electroretinogram, tend to remove the on-effects some time before the off-effect shows any sign of disappearing. I believe, therefore, that, at least in this respect, the difference between the response of the cat and guinea pig eyes is due to a genuine difference in the synaptic organization of rod and cone retinas. The following experiment confirms this view. A retinal element giving an on-off-response was isolated in each of three rats all similarly anaesthetized with urethane. A further administration of three times the normal dose of the drug failed to eliminate the off-response. It seems, therefore, that the small number of isolated on-off-elements found in the retinas of both rats and guinea pigs (the number is rather larger in the rat) is not due to the use of an anaesthetic, but is in fact characteristic of these animals.

I do not wish to give the impression that pure on-elements are only to be obtained from rods and on-off-effects only from those synapses on to which cones converge, because we have found in our work on adaptation and colour reception (see Chaps. XVII, XIX-XXI) that it is difficult to avoid the conclusion that the difference between a rod and a cone is not so rigid as current theories would lead one to suppose. But I do think that in general the synaptic organization of the rods tends to be less able to develop pre-excitatory inhibition, with consequent off-effects, than that of the cones. More work on more animals, both mammals and other vertebrates, is necessary before these questions can be definitely answered.

In view of the great variability of the on-off patterns obtained from the cat retina, one has difficulty in deciding which type of response may be considered typical and which exceptional. My impression is that the great majority of the elements are of the type which is affected by pre-excitatory inhibition at 'on' when the stimulus is strong (see Figs. 61, 81A and 82A) and that, on the whole, off-effects are more prominent at high intensities—another consequence of an increase in pre-excitatory inhibition. This view agrees very well with Adrian's (1941) finding that, in the cat, bright light tends to produce a brief
discharge followed by inhibition both in the optic nerve and in the visual cortex. It also agrees with the fact that, on the electroretinogram, strong stimuli elicit small $b$-waves followed by marked negative waves (PIII) and off-effects. In the monkey the optic nerve and visual cortex respond better to high intensities (Adrian, 1941).

If we now return to Figure 78 which illustrates the relation between the logarithm of the intensity of the stimulus and the size of the $b$-wave we find that, just as for the frequency of impulses, the curve rises less steeply at the lower intensities (rod region) than at the higher (cone region). This similarity between the relation of the $b$-wave and the frequency to the intensity of the stimulus supports the view, several times stated above, that the $b$-wave represents the average frequency of the response which is higher and rises more steeply at high than at low intensities.

It has already been shown that, in the cat, light adaptation greatly diminishes PII. How can we explain then that, in spite of this, very high frequencies can be recorded from this eye if the electrodes are rightly placed? It looks as though a different synaptic system were activated in the photopic state, a system with a reduced capacity for evoking PII and with a new relation between PII and impulse frequency. The small size of PII may be connected with the fact that, under these conditions, the number of active receptors is decreased due to the loss of visual purple from some of the rods which thereby lose their capacity to react. Such a loss of active receptors would not be shown up by the micro-electrode method, but would become evident in an average response such as that recorded on the electroretinogram. It is also possible that, in a photopic eye, PII is produced in a different system, perhaps with a less favourable orientation towards the electrodes used for recording the electroretinogram. Where the truth lies we do not know, but we do know that when, in a scotopic eye, the cones play an important part at higher intensities they can evoke PII in proportion to the increase in impulse frequency as if they were rods, for the size of the $b$-wave increases with the frequency of the discharge. The same phenomenon occurs in the frog, but here it is independent of the state of adaptation. The frog's eye, which shows a larger PII than the cat's after light adaptation,
also has a larger number of cones. So the number of cones may, after all, be the decisive factor although it is perhaps not the only one responsible for the diminished size of PII in the light-adapted eye of the cat.

It has already been pointed out that Hartline (1938), working on single fibres of the frog optic nerve, found that, whatever their type, these were stable in their reactions. This is not the case in the mammalian eye where only the pure on-elements are stable while the on-off-elements undergo curious transformations when the strength of the stimulus is altered. Pure off-elements, common in the frog, are very rare in mammals. It is particularly interesting that, in such mammals as the cat, pre-excitatory inhibition is strong enough at high intensities to remove (in some elements) practically the whole of the on-response. Post-excitatory inhibition may also remove the off-response with certain strengths of stimulus, but it disappears again as the strength is increased as though it might have been overcome by the pre-excitatory inhibition since it is at these intensities that an off-effect appears (see Figs. 81 and 84). It is as though these two types of inhibition were in continuous rivalry in the cat retina, and it seems as if the synaptic apparatus of this retina were less definitely fixed in a given pattern than is the case with the frog. Both types of inhibition are present in the frog’s eye too with pre-excitatory inhibition particularly well developed as shown by the prominent off-effects obtained from this eye, while post-excitatory inhibition probably accounts for the depression of the off-effects at higher intensities (Fig. 64). We have, as yet, no explanation of the marked rivalry between excitation and the different forms of inhibition in the mammalian retina.
Chapter X

The Duplicity Theory from the Electro-Physiological Point of View. E- and I-retinas Defined. Summary of Chapters VII-IX

E- and I-retinas, Rods, and Cones

We are now in a position to consider both how the different electroretinograms, first of E- and I-retinas and then of rod and cone retinas are related to the discharge in their optic nerves, and the effect of the state of adaptation, both on the electroretinogram and on the optic nerve discharge of the different types of retina. There is, of course, still much to be done before this very new field can be said to have been properly surveyed but, even at this stage, an attempt may be made, by gathering up the available data, to discover how far an extended version of the duplicity theory can cover the facts. In the first instance we may inquire how far the E- and I-electroretinograms represent the responses of retinas dominated by rods and cones respectively.

We find that the electroretinogram of an I-retina is characterized by:

1. A relatively large and brisk off-effect, due to renewed PII activity.
2. Supernormal negative a-waves (‘notches’) elicited by flashes falling on the eye during the off-effect.
3. The reaction to fast intermittent stimulation: positive off-effects, elicited by the dark intervals, cut short by the negative a-waves caused by the flashes.
4. The fact that, when the type of reaction changes as a result of light adaptation, the change is more marked at ‘off’ than at ‘on’ tending to make the features summarized above more obvious in light than in dark adaptation.
5. A rather high fusion frequency in the photopic state as the negative ‘notches’ or a-waves, which play such an important part in the reaction to intermittent light, coincide with volleys of (pre-excitatory) inhibition interrupting the rebound of excitation at ‘off’.

The E-electroretinogram differs from the I-type as follows:
1. A small and slow off-effect.
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(2) A subnormal positive b-wave elicited by a flash falling on the eye during the off-effect (such waves are not preceded by a negative notch).

(3) The reaction to intermittent stimulation: repeated subnormal b-waves elicited by the flashes.

(4) The fact that, when the type of reaction changes after light adaptation, the change is more marked at 'on' than at 'off'.

(5) A rather low fusion frequency in the photopic state. Since the subnormal b-waves coincide with volleys of impulses in the nerve, this type of retina may be said to respond to flicker primarily with volleys of excitation (Granit, 1935).

The above statements, of course, refer to the average retinal response. The individual elements respond with excitation or pre-excitatory inhibition according to the type to which they belong.

If one uses the discharge of impulses in the optic nerve as a criterion, the typical I-retina of the frog may justly be said to react mainly to changes in the general level of illumination, the optic nerve responses corresponding to the large retinal reactions at 'on' and 'off'. When, during dark adaptation, the reactions of this mixed eye, in common with all others, become more E-like, it tends to produce more drawn-out discharges in the optic nerve without losing its capacity of responding to the onset and cessation of illumination. The large and active a-waves produced by PIII, particularly those caused by re-illumination on top of the off-effect, as well as the off-discharge in the nerve can be referred to the fact that the frog retina possesses up to 30 per cent of elements which are completely inhibited by light and set free, to produce a vigorous off-effect, when illumination ceases. Such elements have been very rare in the E-retinas studied. Pre-excitatory inhibition (the type that is associated with PIII) is thus particularly prominent in the I-retina.

The greater the relative number of rods in an E-retina the less prominent is pre-excitatory inhibition. The relatively pure rod retina of the guinea pig, for instance, is dominated by elements which respond with a prolonged discharge to the onset of illumination, whereas the E-retina of the cat, with a small number of cones, while also discharging a prolonged volley of impulses, shows a predominance of the reaction both
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at 'on' and at 'off'. In the majority of the elements in the cat the typical pre-excitatory inhibition of the off-effect by a new flash takes the form of a very brief interruption of the discharge. In the electroretinogram it coincides with a slight increase in the latent period of the $b$-wave and is not accompanied by the large $a$-wave characteristic of an I-retina.

If we ascribe the differences between the reactions of the pure rod retina of the guinea pig and the mixed retina of the cat to the cones present in the latter (as, in my opinion, we must so long as it is impossible to account for them in other ways), it is clear that the distinction between the responses of rods and cones (with their synapses) carries us beyond the division of retinas into an E-type and an I-type, and that this division merely serves as a first means of differentiation based only on the electroretinogram. In point of fact, the nomenclature of these two types was deliberately chosen in order to avoid any theoretical implication but rather to indicate that excitation is of relatively more importance in the former, pre-excitatory inhibition in the latter. If we remember that the electroretinogram represents an average reaction reflecting the properties of the dominant retinal receptor system, it is still possible to regard the guinea pig as one extreme, the cat as intermediate, the frog as a further development in the direction of an I-retina and the cold-blooded animals with pure cone retinas (tortoise, snake, turtle, horned toad) as the other extreme. Before it is possible to take up a final stand on this question the reactions of a mammalian pure cone eye as well as those of the pure rod eyes of cold-blooded animals and birds will have to be analysed. Until such investigations have been carried out there is always the possibility that the possession of an E-retina distinguishes mammals from the other vertebrate species.

Unfortunately this problem cannot be solved by using small areas of the human retina where one might hope to be able to compare the response of an area dominated by cones (fovea) with that of one dominated by rods in the same eye. The responses from the human eye are small and do not lend themselves well to analyses of this kind and, in addition, the on- and off-effects of any eye are greatly decreased if the area stimulated is diminished. Actually Cooper, Creed, and Granit (1933)
found that electroretinograms taken from the periphery of the human retina did not differ significantly from those taken from the fovea although the peripheral area used was at 7° where the rods should be in the majority. Karpe (1945) has since conclusively demonstrated that the b-wave of the human electroretinogram is chiefly due to the rods (cf. also Adrian, 1945).

However, the fact that the large on- and off-effects disappear from any eye if stimulation is restricted to a small area seems to be of great importance in the interpretation of the connexion between the electroretinogram and the nerve discharge. The responses of a single fibre do not alter in type when the stimulated area is cut down even though the reactions to onset and cessation of illumination become smaller (see next chapter). Thus it seems that, before an eye can produce an off-effect on its electroretinogram, it must be able to mobilize a certain number of off-elements in order to prevent the effect being smothered. This provides a potent argument in favour of the view that E- and I-responses are, in fact, typical of retinas dominated by rods and cones respectively. It suggests further that pure off-elements are particularly well able to demonstrate their presence by producing off-effects on an electroretinogram.

Even in 1933, when we were still using needle electrodes, I found a definite off-effect when recording from the cat’s optic nerve although the electroretinogram only revealed a very small off-effect if any. Similar experiments recently performed by Bartley and Bishop (1940) on the rabbit gave the same results and we have seen that the micro-electrode technique has amply confirmed this finding for E-retinas in general. This discrepancy between the occurrence of an off-effect on the electroretinogram and in the optic nerve of E-retinas may be regarded as a special case of the effect of area if we assume that, in these eyes, the number of pure off-elements is too small to produce a good off-effect on the electroretinogram. In the I-retina there is a large number of pure off-elements which can, therefore, make themselves felt on the electroretinogram. A final solution of this and related problems must await the analysis of many more different types of retina.

Turning from the average retinal response to the results of the detailed analysis of impulse activity in separate fibres, it is clear that these can be interpreted on the basis of the duplicity
theory so long as this is extended to include the synaptic organization of the rod and cone systems. From this point of view the results may be summarized in a general statement to the effect that a cone system is a mechanism for differentiation, a rod system one for integration. The properties of a rod system do not differ very much from those of an isolated receptor. The extensive convergence of a large number of receptors on to one final common path seems to be the main feature of the organization of a rod system and this is of obvious importance in the integration of the feeble stimuli characteristic of the scotopic eye. The cone system, on the other hand, seems to be organized for the interpretation of changes in the visual field, changes of illumination, of the area stimulated, of 'locus' in the field as a whole and, as we shall see in Section IV, of colour. The off-effect, together with the frequency range, plays the major part in the interpretation of such changes since it is faster than the on-effect and can be quickly inhibited when necessary. It is probable that there are forms intermediate between the most highly organized cone systems and the primitive rod systems and it may not always be possible to distinguish these from one another either histologically or functionally, the less so since, apparently, they often converge on to the same ganglion cell. But the general trend of development from the extreme rod to the extreme cone system goes from simple to complex responses, from integration to differentiation.

From the histological point of view the difference between the synaptic apparatus of rods and cones lies in the presence of the amacrine cells in the latter. The hypothesis, suggested by Graham and Granit in 1931 (before inhibition had been demonstrated in the optic nerve), that the amacrine cells distribute inhibition, is, therefore, still worth considering since pre-excitatory inhibition appears to be one of the main contributions of the cone system to the visual instrument. It seems, therefore, that the nature of its whole synaptic organization may be more important in defining a cone than the shape of the receptor or the way in which it makes connexion with its bipolar cell.

Sensory Discrimination

If, for the moment, we neglect the main anatomical factor
in discrimination, i.e. the size of the ‘receptor unit’ (larger for the rods because of the greater number attached to one ganglion cell), and restrict our attention to the question of impulse activity, there would seem to be two properties of the cone system which determine its discriminative power. First we have the cones’ capacity for responding, within a large range, to changes of illumination with changes in the frequency of the discharge, a capacity much less well developed in the rods, and secondly there are the complicated patterns of impulses put out by the cones in contrast to the more uniform rod patterns. It appears, therefore, that discrimination (see Wright, 1937; Wright and Granit, 1938) is a function of both the frequency and the pattern of the optic nerve discharge and that both contribute to the final result. The significance of the pattern of the discharge is now being, although gradually, realized by investigators studying discrimination by means of human sensation or animal behaviour (Anderson and Weymouth, 1923; Crozier and Holway, 1940; Berger and Buchtal, 1938; Bartley, 1941). Frequency must be of particular importance for the discrimination of changes of stimulus intensity, pattern not only for this task but for the recognition of spatial phenomena such as the dominance of contour and ‘local sign’.

Wright and Granit (1938), in discussing Wright’s (1937) pattern theory have already drawn attention to the many factors which interfere with the precise definition of the retinal image. These include the general defects of the eye as an optical instrument, the anatomical shortcomings of the retina as a focusing screen and last, but not least, the rapid movements of the eyeball, also emphasized by Weymouth (1928). Granting that the fineness of the retinal ‘grain’ is the primary condition of good discrimination, whether it be visual acuity or brightness discrimination, these defects must, nevertheless, lead to a considerable amount of overlapping of adjacent retinal images. Under such circumstances the high degree of differentiation of which the cone system is capable can only be explained on a pattern theory. The accurate appreciation of contour, in particular, must be due to minute fluctuations of the eyeballs resulting in on- and off-effects as well as sudden inhibitions of the latter. Even if it were possible to keep the eye absolutely still every sharp intensity gradient must give rise to very com-
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complicated excitation inhibition patterns tending to emphasize the gradient and giving the higher centres a cue for discrimination.

All the work on sensation from the days of König (1906), and v. Kries, up to the present time, is in agreement with the view that the rods cannot follow a large range of intensities with equivalent changes in the frequency of the impulses discharged. All the curves which have been constructed relating various aspects of discrimination (visual acuity, etc.) to the intensity of illumination are flatter in the rod than in the cone region. The electrophysiological results reported in Chapter IX show that the frequency of the discharge must have a central place in any interpretation of these phenomena in preference to such alternative explanations as variations in threshold.

Frequency must also be the main factor in the perception of brightness, but this property must also be considered in relation to the sensitivity of the different receptive elements to changes in the wave-length of the stimulating light (Section IV). However, the initial rise and fall of the frequency at the onset

![Graph](image-url)
of illumination is obviously reflected in the concurrent change in the sensation of brightness (see Broca and Sulzer, 1902; Granit and Hammond, 1931; and Adrian, 1928, whose comparison of the time course of the frequency changes in the optic nerve with the sensation changes is illustrated in Fig. 85).

*Sensory Work on Inhibition*

Very little of the work that has been done on visual sensation can profitably be correlated with the electrophysiological observations on pre-excitatory inhibition and extinction in the retina. Such work is urgently needed. Schouten (1937) showed that illumination of a given retinal area produced what he called alpha-adaptation, a depression of sensitivity spreading almost instantaneously to adjacent areas as if it were caused by an electrical potential. He compared the time course of alpha-adaptation with that of the retinal potential PIII. Important work on alpha-adaptation has recently been carried out by Pitt (1939) as well as by Schouten and Ornstein (1939).
Chapter XI

INTERACTION, AREA, DURATION AND INTENSITY OF THE STIMULUS AS INTERCHANGEABLE VARIABLES

The Effect of the Duration and Area of the Stimulus on the Electroretinogram

When only a small spot on the retina is illuminated an electroretinogram can be recorded from areas outside that stimulated. This is due both to physical and physiological (electrotonic) causes. Unfortunately we have very little precise electrophysiological information about this spread of the effect of localized stimulation except in the case of Octopus (Fröhlich, 1914) and more work using the highly developed micro-electrode technique of to-day is much to be desired. Fröhlich's results, such as they are, indicate that the electrical potential recorded from a small illuminated spot (1·5 m.m. in diameter) on the retina falls off sharply in the surrounding area. It must be remembered, however, that the cephalopod retina does not contain lateral connexions, nor are there secondary and tertiary neurones to be influenced by electrotonic spread as in the vertebrate retina.

It has been shown that, in vertebrates, the size and shape of the electroretinogram is affected by decreasing the retinal area stimulated in the same way as by decreasing the intensity of the stimulus, and the same relation holds for the simple retinas of the cephalopods (Fröhlich, 1928) and Limulus (Graham, 1932). In view of the well-known fact that, at the threshold of perception, the effects of alteration of area and intensity are interchangeable (see p. 178) it is unfortunate that the quantitative relationship between these two factors has never been worked out for a mammalian eye so that one might know to what extent and within what limits the total quantity of excitation must be kept constant if a constant response is to be obtained. Such data are only available for Limulus (Graham, 1932) in which, as might be expected, the electroretinogram over a considerable range is simply proportional to the number
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of ommatidia stimulated. In this case, therefore, there is no interaction.

The best evidence that, in the vertebrate eye, interaction between adjacent retinal elements plays an important part in vision comes from work on the optic nerve and, for this reason, we shall only deal briefly with the less easily interpreted results on the electroretinogram.

Gotch (1903, 1904), using the capillary electrometer, was the first to produce accurate measurements of the latent period. He showed that the latent period of the retinal response de-

**Figure 86.** Effect of stimulus intensity and area on the cat electroretinogram. A: variation of latent period of b-wave; B: reciprocals of values in A; C: variations of latent period from another experiment. Vertical lines, intensity values; crosses, areas (max. 1,660 mm.²). Abscissae: log I in milli-lamberts and log area in arbitrary units. (Creed and Granit, 1933, J. Physiol., 78)

creased when the intensity of stimulation was increased. Although this finding has since been confirmed by every worker on the subject, the only quantitative measurements over a large range of intensities (Fig. 86) are those of Creed and Granit (1933) of the b-wave of the cat electroretinogram. Einthoven and Jolly (1908) confined their attention to measurements of the extreme values at maximal and minimal intensities. They found, in the frog, that the a-wave could be elicited after as little as 10 msecs. if the stimulus was strong enough, but that values around 40 msecs. were more common. At such high
interactions the appearance of the $a$-wave masks that of the $b$-wave. The longest latent period obtained by these workers for very weak stimuli was 2.2 secs.

By proving that the retinal-nerve interval (from the beginning of the $a$-wave to the appearance of the optic nerve discharge) is constant and so showing that the latent period of the nerve discharge can be decreased by increasing the retinal area stimulated, Adrian and Matthews (1927) were the first fully to realize the significance of area as a factor in the electrical response. Of course other aspects of this problem were quite familiar to many of the workers on visual sensation, but Adrian and Matthews’ results provided the opportunity for attacking it without the complications added by possible specific integrations in the higher centres. The effect of area on the electroretinogram has since been confirmed by a number of workers (Fry and Bartley, 1935; Creed and Granit, 1933; Granit, 1933. For measurements over large ranges see Granit, 1933, and Creed and Granit, 1933; also Fig. 86). The effect is the same whether the $a$- or the $b$-wave is used as an index. Further, even if two stimuli are applied at some distance from one another their influence must spread because the combined effect is to decrease the latent period of the $b$-wave below that produced by either stimulus alone (Adrian and Matthews, 1928; Granit, 1933).

What is the significance of this effect? According to Fry and Bartley (1935) and Bartley (1941) it is wholly due to stray light. In my opinion, however, it cannot be explained on these lines although, no doubt, stray light may modify a genuine area effect. It appears that Bartley’s point (1941) is that the alternative explanation, assuming the presence of some sort of interaction, is based on the reactions of the optic nerve and not of the retina. On the other hand, since he believes that the $b$-wave is produced by the reactions of the neural layers of the retina where interaction must take place if it is to affect the optic nerve at all, why cannot interaction be indicated by the $b$-wave? Fry and Bartley quote the following experiment in answer to this question. In a rabbit eye two adjacent stimuli produced potentials ($b$-waves) $a$ and $b$ when used separately so that a rapid alternation of the two was expected to produce $a$ and $b$ potentials of partly overlapping sequence. Actually
only the first stimulus gave its response (a), the response b being occluded. Their explanation is that the focal light only elicits a negligible fraction of the electrical response which they hold to be mainly due to scattered light, leaving the retina refractory to the second stimulus. This explanation is probably correct for strong stimuli. Granit, Rubinstein, and Therman (1935) repeated the experiment using an excised and opened frog eye, a lens of good optical properties and two light spots about 0.4 mm. across, thrown 0.3 mm. apart on the retina. These stimuli were made weak enough to elicit retinal responses of about 50 μV. each. With such a preparation the two stimuli together produced a response about 10-15 per cent less than the theoretical value a + b. Scattered light, therefore, could not account for more than 10-15 per cent of the combined response. When, however, the second stimulus followed the first after a brief interval of darkness it was unable to elicit its own b-wave. Therefore it seems that adjacent neurones must be influenced by some kind of physiological spread of the electrical response from the stimulated area.

Even though it is certain that scattered light excites receptors outside the area of stimulation, particularly when the stimulus is strong, it is not clear why just the closely adjacent receptors should have especially short latent periods. They have, after all, received a weaker stimulus than those in the focal area. The effect of area on the latent period of the retinal response can hardly be explained by such arguments alone. If Adrian and Matthews are right in concluding that the retinal-nerve interval is constant, a further argument against the 'stray light hypothesis' is to be found in their demonstration that, within limits, the nerve responds with a shortening of its latency to the integrated product of area and intensity. This shortening must then be due to a shortened retinal latency.

Let us now investigate the possibility of finding a physiological explanation of the shortening of the latent period of the a- and b-waves of the electroretinogram when the retinal area stimulated is increased. In order to understand how the effect of area and intensity can be interchangeable one must imagine some process whereby a reinforcement of excitation can be caused by increasing the number of neurones activated. There are two possible mechanisms both of which are known to occur
in other parts of the nervous system; first, facilitation by transmission across synapses and second, further stimulation by the electrical field set up within the illuminated area. Probably both mechanisms play their part. Some ten years ago, when the problem first arose, there was no direct experimental evidence in support of the second alternative and so the first only was considered. This naturally led to the suggestion that the whole electroretinogram was the result of post-synaptic reactions (Adrian and Matthews, 1928; Granit, 1933). To-day, knowing as we do, that the electrical field around a group of active neurones can excite other neurones (see e.g. a summary by Gerard, 1942), the question of the localization of the various retinal processes reflected in the electroretinogram are better discussed in the light of other evidence (see Chap. VI).

The duration of the illumination has long been recognized to be one of the factors determining its effect, whether in the production of a sensation (Bloch, 1885), a nerve response (reflex temporal summation) or a photochemical reaction (Bunsen-Roscoe law). Using the ballistically recorded electroretinogram as an index, de Haas (1903), in a quantitative study, found that the size of the response was constant so long as the product of intensity and time of illumination was kept constant and that this law held for durations up to as long as 8 seconds, suggesting that the effect is not a purely photochemical one. De Haas’ results were confirmed by Hartline’s (1928) investigation of the electroretinograms of various insect eyes. Further discussion of this question in the light of evidence obtained from the examination of the optic nerve response will be deferred until later (p. 177).

‘Duration’ and ‘Area’ as Factors in Excitation. Studies on the Whole Optic nerve

Adrian and Matthews (1927a) directed the analysis of these questions into new channels when they demonstrated that the latent period of the discharge in the eel optic nerve can be decreased by increasing either the intensity, area or duration of the stimulus. These three factors are thus, within limits, interchangeable and the end effect determined by their total product. This relation was found to be approximately valid so long as the retinal area was not more than 1 mm. in diameter.
When the duration of the stimulus was the variable factor it was found that, for any given intensity, there was an optimal duration at which the stimulus has a maximal effect in shortening the latent period of the nerve discharge. If the exposure is reduced, not only does the latent period increase, but there is a reduction both in the frequency and number of impulses so that the reciprocal of the latent period is a good measure of the average activity in the nerve. Obviously the effect of the duration of the stimulus on the latent period cannot extend beyond the moment at which the discharge first appears. Hence, as a determinant to latency, duration can never exceed a critical value somewhat less than the latent period determined by the intensity and area used.

Adrian and Matthews pointed out that the spatial effect must be explained on some such assumption as ‘that the total effect of the light is transmitted to some region whose extent is independent of the area illuminated’. They discuss the two explanations already mentioned in connexion with the electroretinogram: electrical spread and transmission across converging synapses. They also realized that, if the retinal-nerve interval is constant, the latter alternative implies a postsynaptic localization of the reactions responsible for the electroretinogram.

An important contribution to this problem was provided by Graham’s (1932) demonstration that the size of the area stimulated has no effect on the latent period of the nerve discharge in Limulus. In this preparation the latent period is simply determined by the particular ommatidium which first activates its nerve fibre. Even in a retina of this type, lacking, as it does, the synaptic apparatus of the vertebrate eye, there is still ample scope for electrical spread so that Graham’s results imply that the spatial effect in vertebrates depends on synaptic convergence.

The Effect of ‘Duration’ Studied in Isolated Fibres

The single, non-synaptic receptor unit of Limulus is an ideal preparation for studying the photochemical aspect of the problem of the effect of the duration of illumination on the response and it has been used by Hartline (1934) for this purpose. The effect of alternately varying the duration and inten-
sity of the stimulus is illustrated in Figure 87 (taken from Hartline’s paper). He found that, for short exposures, the expected reciprocal relation between duration and intensity held good. In Figure 88 the logarithm of the product of duration and intensity necessary to produce a constant response is plotted against the duration, and the point at which the discharge first appears is marked by the arrows. It will be seen that the critical duration (indicated by the horizontal part of

![DURATION Diagram](image-url)

**Figure 87.** Effect of intensity and duration of the stimulus on the frequency of the discharge in a single optic nerve fibre of *Limulus*. Relative intensity for each horizontal row on right \((1.0 = 3 \times 10^6 \text{ m.c.})\). Duration of stimulus (in sec.) for each vertical column at top. Light flash blackens the white line above the time marker (arrows mark the position of the flash for very short durations). Time marking: 1/5 sec. (Hartline, 1934, J. Cell. comp. Physiol., 5)

the curve) is a little shorter than the latent period. Afterwards the curve rises, in accordance with the fact that the frequency is now dependent on intensity alone. In the two curves of Figure 88 the response used as an index was an initial frequency of 40 per second for the upper and a maximum frequency of 56 per second for the lower. If, instead, the total number of impulses produced by the stimulus is used as an index, the
reciprocality relation holds for even longer durations. It must, of course, finally break down whatever criterion is used both because of the linear relation between frequency and the logarithm of the intensity and because of the existence of a threshold intensity below which no impulses can be elicited however long the exposure (Fig. 87, bottom record).

It is interesting to compare these results with what is known of human vision in experiments in which it has been usual to take the absolute threshold as an index instead of a constant response of the nerve. Bloch (1885) discovered the original reciprocal relation of intensity and duration and later workers (Piéron, 1920; Blondel and Rey, 1912; and many others) found it to fit very well for short exposures up to about 30

![Figure 88. Relation of the energy of a stimulus necessary to produce a constant response in a single optic nerve fibre of Limulus to its duration. Abscissae: log (base 10) duration (secs.). Ordinates: log (base 10) energy (1 unit of energy = \(3 \times 10^3\) m.c. secs.). The upper curve shows the energy necessary to produce an initial frequency (first three impulses) of 40 per sec.; the lower the energy necessary to produce a maximum frequency (three impulses) of 56 per sec. The time of appearance of the impulses concerned is indicated by the arrows marked with the number of the impulse. (Hartline, 1934, J. Cell. comp. Physiol., 5)
Figure 89. Relation of the logarithm of the product of duration and intensity at the threshold at 15 degrees in man to the logarithm of the duration. The curves are for different areas of the sizes marked. (Graham and Margaria, 1935, Amer. J. Physiol., 113)
mscs. Blondel and Rey found that for longer exposures a better
fit was given by the equation:

\[ it = a + bt \]

where \( i \) is the intensity, \( t \) the duration and \( a \) and \( b \) constants. This equation is illustrated by the dotted line in Figure 88, asymptotic to Hartline's two intersecting lines. According to Braunstein (1923) the reciprocal relation between duration and intensity holds good up to about 10 msecs. exposure, but only if the area stimulated is small. For an account of much valuable work on the reflex reactions of lower animals Hecht's summary (1929) should be consulted (cf. also Piéron, 1941).

Because of the part played by spatial interaction in the vertebrate eye it is always advisable, when working on sensation, to use retinal areas of several different sizes for stimulation. When Graham and Margaria did this (Fig. 89) they found that with a small area (2') their results were similar to Hartline's (cf. top curve in Fig. 89 to Fig. 88), but that with larger areas, where there is more spatial interaction, they fitted Blondel and Rey's equation better. They pointed out that, in accordance with the laws enunciated by Riccò (1887) and Piper (1903), the absolute threshold is lower the greater the area stimulated and that for small areas and short exposures it is determined by the total quantity of energy received.

The reciprocity relation for short exposures is no doubt determined by the fundamental photochemical process and so obeys the Bunsen-Roscoe law. Unfortunately we have no data, either for isolated receptors or for the retina; on the time course of the summation of subliminal stimuli so that we do not know the limits within which temporal summation can occur. Using sensory criteria, Richet and Bréguet (1880) showed that subliminal stimuli are summed in the human eye, and Granit and Davis (1931) measured the times within which two subliminal stimuli could summate to produce a threshold sensation (Fig. 90). In this figure the fall of the curve represents the way in which the level of the excitatory remainder of a flash (capable of pushing a second subliminal stimulus up to the threshold value) decreases with time. The initial, flatter, part of the curve probably indicates the time during which the straightforward reciprocal relationship between duration and intensity holds. The longest interval for the summation of
subliminal stimuli was between 130 and 140 msecs. These results were held to imply that the time relations of excitation are determined by temporal summation in the synapses as well as by photochemical processes.

![Graph](image)

**Figure 90.** Temporal course of the excitatory remainder caused by a subliminal flash into the human eye. Abscissae: interval between first, subliminal, flash and second, test, flash. Ordinates: duration of second flash necessary to push excitatory remainder of first over threshold in percentage of duration of first flash (upper curves) and absolute value in msec. (lower curves). Dotted line: 10°, other curves: fovea. (Granit and Davis, 1931, Amer. J. Physiol., 98)

**Analysis of the Area Effect**

In order to analyse the spatial effect Adrian and Matthews (1928) used four spots of light so far apart that all together gave the same latent period before the appearance of the optic nerve discharge as any one of them alone. They found that the addition of strychnine, a drug which is known to increase synaptic interaction, resulted in a shortening of the latent
period when all four areas were stimulated together. The
possibility of using an absolute measure such as the latent
period, gives the objective methods used by Adrian and
Matthews a distinct advantage over sensory methods in which
one must use a comparison with a standard intensity if one
is to exclude the effects of integration in the higher centres
(Riccó, 1887; Piper, 1903).

In an attempt to discover how far human visual sensations
are dependent on interaction in the retina I repeated Adrian
and Matthews' experiment using the fusion frequency of
flicker as an index of effect (Granit, 1930). This also gives an
absolute value known to increase with the intensity of the
stimulus according to a definite law (Ferry-Porter law). The
test-object consisted of a four-spot pattern (each spot 1° in
diameter and placed on the circumference of an imaginary
circle 3° in diameter) which could be viewed either with the
peripheral (10°) or the central retina. The background was
illuminated to collect and neutralize scattered light. When
fixation was peripheral and the intensity of the stimulus 94 m.c.
the fusion frequency was significantly higher when the four
points were used than when one was used alone (39'8 compared
to 45'5). With central fixation, on the other hand, the effect was
small and at an intensity of 0'94 m.c. was absent altogether.
The greater capacity for summation shown by the periphery
in this experiment must be due to the greater amount of con-
vergence on to the ganglion cells characteristic of this region
as compared to the centre. Strychnine increased the spatial
effect (Granit, 1932a). This work was developed into an ex-
tensive analysis of spatial effects by the flicker method (Granit and
Ammon, 1930; Granit and Davis, 1931; Granit and Hammond,
1931; Granit and Harper, 1930) and need not be reviewed
here since good summaries are available in works devoted to
visual sensation (Graham, 1934; Bartley, 1941). Figure 91A
illustrates the apparatus used for this type of experiment; some
of the curves obtained are shown in Figure 91B. These and
many more experiments of the same type have proved conclu-
sively that interaction at the retinal level does play an important
part in our visual sensations. In the peripheral retina interaction
seems generally to produce summation of excitation; at the
fovea the effects are usually more complex (Graham and Granit,
Figure 91. A: apparatus for experiments on the effect of the distance apart on the interaction of two flickering stimuli. B: relation between separation and fusion frequency at 0° and 10° when one (S) or both (D) areas are flickering. (Granit, and Harper, 1930, Amer. J. Physiol., 95)
and suggest inhibition. Graham and his collaborators, also using sensory methods, have since published several important contributions to the elucidation of these problems (Beitel, 1936; Graham and Bartlett, 1939-40; Graham, Brown, and Mote, 1937; cf. also Rubinstein and Therman, 1935).

Hartline (1940 a and b) has recently used his single fibre preparation with a micro-illuminator to study the area effect due to anatomical convergence in the frog retina. He has called that part of the retina from which stimulation elicits a discharge

![Figure 92](image_url)

**Figure 92.** Chart of the receptive field of a single optic nerve fibre of the frog. Each line encloses a retinal region within which the exploring spot light (relative size shown above left), of an intensity of which the log is given on the line, produced a response from the fibre. On each line the indicated intensity was the threshold; the set of curves constitutes a contour map of the distribution of the retinal sensitivity to light with reference to this particular fibre. (Hartline, 1940, J. Opt. Soc. Amer., 30)

in a given fibre, the 'receptive field' of the fibre. Figure 92 illustrates the extent and sensitivity (in log units of the illumination necessary to produce a response) of such a receptive field. The receptive field is most sensitive in the centre and is smallest (0.50 m.m. in diameter) when a threshold stimulus is used. With intensities of 100-1,000 times the threshold it may increase to twice its original size (cf. Adrian and Matthews, 1928, and p. 175). The greatest response with the shortest
latent period is always obtained by stimulation of the centre of the field.

Within the receptive field area and intensity are interchangeable whether the length of the latent period or the frequency of the impulses elicited in the fibre is used as an index. This interchangeability, however, only holds up to a certain point above which the ganglion cell behaves as though it were 'overloaded' (cf. the results on the cat illustrated in Fig. 84 where intensity was the variable factor). The less sensitive parts of the field, along its edges, contribute less to the spatial effect and those outside it not at all. Summation was also found when four separate points within the field were stimulated simultaneously. As is the case for neurones in other parts of the central nervous system, so also in the retina is it necessary for a number of impulses to converge on to a ganglion cell from different terminals before a response can occur in the nerve fibre (Hartline).

So far, in considering Hartline's results, we have only dealt with summation of excitation. He has also shown that summation of pre-excitatory inhibition takes place in those fibres whose discharge is inhibited by illumination and which respond to its cessation with an off-effect. In such fibres there is an increased off-effect when the stimulated area is increased or when several points within the receptive field are illuminated at once, and the off-response can be inhibited by reillumination of a point within the field. It is well known, from work on the nervous system, that inhibitory as well as excitatory influences show summation. As Sherrington has aptly said, inhibition shows all the properties of excitation, but with the opposite sign.

We have pointed out more than once that, when an eye has to produce a quick reaction, the off-effect is of particular importance. Thus, if a pencil is passed through the beam of light illuminating a frog's eye, its passage is at once recorded by a brief off-discharge in the optic nerve (Granit and Therman, 1935). With the single fibre preparation, the shadow of a thin wire will produce a response every time it is moved within the receptive field (Hartline), and even if the light is only shifted outwards, to fall on the less sensitive parts of the field, an off-effect can be obtained from its centre. It is clear, therefore, that the spatial effect cannot be due to scattered light.
Receptive fields overlap one another considerably so that illumination of any given point on the retina may activate several fibres. In so far as such fibres may be of different types and combined in different ways it is clear that form discrimination and ‘local sign’ can be developed to a very high degree of perfection by such a mechanism (cf. Chap. IX).

When Adrian and Matthews first demonstrated that the interaction which is to be expected from the retinal structure actually does exist, they were puzzled as to how to reconcile it with the high degree of isolation which is necessary to give, for instance, the visual acuity of which the human eye is capable. I found myself in the same difficulty during my early work on flicker (Granit and Harper, 1930). It has been shown (Chap. IX) that such difficulties do not exist to-day. The highly differentiated responses obtained from adjacent retinal areas, further differentiated as they are by minute changes in area and intensity, give a retina which is adequately supplied with cones extreme efficiency in transforming a visual field into complex excitation patterns to be relayed to the higher centres. Bartley (1941) still refers to the co-existence of interaction and insulation in the retina as a ‘major puzzle’ in the physiology of vision. This outlook can only be due to lack of penetration into the electrophysiological reactions of the retina since these have provided the solution of the mystery. Indeed, if the clues for such experiences as ‘form’, ‘colour’, and ‘visual acuity’ are not provided by the retina they can never be created out of nothing by the higher centres.

Thanks to the presence of a nervous centre in the eye, next to and in the same plane as the receptor layer, the retina is able to operate as though it were a highly differentiated ‘electrical feeler’ responding with patterns of sparks (impulses) and thus interpreting the distribution of luminous flux in the universe around us.

We are still far from understanding the mechanisms of excitation and inhibition in the neural layers of the retina. Summation of excitation and inhibition is a matter of convergence, but we do not know to what extent it is merely a question of several rods and cones connected to one bipolar cell and several of these to one ganglion cell or how far it is dependent on horizontal and amacrine cells serving as internuncial neu-
rones for adjacent fields. Nor do we know what part, if any, the electrical field set up by a stimulus plays in interaction.

According to Greef (1900) the number of horizontal connexions in the retina increases with the developmental stage of an animal. If this is so one would expect interaction to increase in importance as one passes from the lower vertebrates to the higher mammals. The cones, which seem to be a more highly developed product, functionally, than the rods, are each supplied with a separate amacrine cell in the human fovea.

Considering the rapid advances made in the analysis of retinal physiology by electrical methods, we are, perhaps, safe in relying on further progress in this field. It is still true that 'more work with the retina rather than sensations would appear to be necessary for the establishment of a retinal physiology on a sufficiently broad and unprejudiced basis' (Granit, 1933), but the progress made during the ten years that have elapsed since those words were written has amply justified the hopes entertained by the writer at that time.
Chapter XII

SOME OTHER FORMS OF INTERACTION. SYNCHRONIZATION

Synchronization of the Response from Large Areas

Owing to the complexity of the excitation patterns set up in the optic nerve by illumination of the retina, records from the whole nerve appear, for purely statistical reasons, in the form of irregularly synchronized beats of grouped impulses and similar beats are also superimposed on the retinal records, particularly on those from opened eyes. Such beats are more prominent when the record is made from the nerve. In addition to this type of synchronization, which has no biological foundation, there is a true physiological interaction between large adjacent retinal areas. This phenomenon was first observed in the cef’s eye by Adrian and Matthews (1928) who found that an essential condition for obtaining large regular waves of excitation in the optic nerve, at about 25 per second, was even illumination of the whole retina. The frequency of these waves increased somewhat when high light intensities were used.

In this respect the retina behaves like other massed ganglia in the nervous system and elsewhere, and the essential similarity of all such reactions is emphasized by their response to strychnine which can start rhythmic beats both in the central nervous system and in the optic nerve of an eye kept in the dark (Adrian and Matthews, 1928). We have already shown that spontaneous activity is not uncommon in the retina and it appears that the interaction of adjacent regions may develop as a result of gradually increasing spontaneous activity creating electrical fields capable of synchronizing the discharges from different retinal areas (see Chap. V on the rotation of activity).

It is doubtful whether the production of such large synchronized beats is, in fact, a normal form of retinal activity since Adrian’s later work, (1932, 1937) on the optic ganglion of Dytiscus showed that they were encouraged by abnormal conditions. For instance, ageing of the preparation seemed to be essential for the production of large rhythmic beats and the
same finding was reported by Bernhard (1942) in other insects as well as in Dytiscus. (For further work on insects see Roeder, 1939, 1940.)

An interesting feature of this rhythmic activity in the optic nerve is the presence of two types of rhythm, called by Adrian 'dark rhythms' and 'bright rhythms'. As these names imply the first is obtained from eyes completely shielded from light, the second as a result of illumination. The beautiful example of a 'bright rhythm', shown in Figure 93, is taken from an unpublished experiment of Bernhard's on the eye of the common house-fly; this preparation includes both the retina and optic ganglion. In this record two sets of frequencies, apparently of

![Image](image_url)

**Figure 93.** 'Bright rhythms' in the optic ganglion of the house fly. Time marking: 1/5 sec.

![Image](image_url)

**Figure 94.** 'Dark rhythms' in the optic ganglion of the wasp. Note their inhibition by illumination. Time marking: 1/5 sec.

110 and 115 per second, seem to be interfering with one another. An example of a 'dark rhythm', also obtained by Bernhard from a similar preparation of the wasp eye, is given in Figure 94. It will be seen that illumination completely destroys the rhythmic character of the record. This effect was also noticed by Adrian in *Dytiscus* and is characteristic of 'dark rhythms'. Bernhard has shown that, in insects, these rhythms originate in the optic ganglion; they are not produced by the isolated receptors of, for example, *Dytiscus*.

Crescitelli and Jahn (1939) have reported similar rhythmic activity in the grasshopper eye and have found that it is favoured by raising the temperature. It is most easily obtained by intermittent stimulation with brief flashes of light, and there
is then an optimum frequency of stimulation at which the rhythm is most prominent.

All these observations confirm Adrian and Matthews’ original suggestion that the normal response to ‘flicker’ may play upon tendencies to rhythmic activity in large groups of neurones. Even when isolated elements are used a dormant tendency to rhythmic activity can be aroused by intermittent illumination. A ‘flickering’ stimulus may also force its rhythm on a spontaneously active element for a time before the latter is able to regain its own frequency (Granit, 1941b).

Synchronization at ‘On’ and ‘Off’

Most text-books on vision devote considerable space to such phenomena as ‘recurrent images’, ‘ghosts’, and spontaneously appearing and disappearing after-images, phenomena which have been responsible for a large number of observations, measurements and theories. All that we now know from work on the optic nerve suggests that many of these effects must originate in the retina (cf. Kohlrausch, 1925, for rhythmic electroretinograms after short exposures), although, of course, recurrent excitation is also quite common in the higher centres (cf. Bartley, 1941). The off-effect, in particular, is liable to set off rhythmic beats (Granit and Therman, 1935; Hartline, 1938; Wilska, 1939b), but they are sometimes produced by the on-effect as well, especially after short exposures. Recurrent images could also be due to a temporary extinction of activity (cf. Fig. 84) such as so often follows high frequency discharges or results from ‘silent periods’. Recent experiments performed by Craik (1940), who temporarily blinded an observer’s eye by pressure and still found recurrent images when the pressure was released, are certainly in favour of a peripheral localization of such phenomena.

Interaction Between the Two Eyes

Cajal (1894) believed that the optic nerve contains efferent fibres. The electrophysiological method would seem to be the natural one for discovering whether, in fact, reactions in one eye can affect the other by way of such fibres. Engelmann and Grijns (1891, 1898) have claimed that such effects do occur. They found that illumination of one eye in the frog produced
a response from the other when it was kept dark, and that the response was diminished by section of the optic nerve. Part of the effect was found to be due to skin reactions, but some of it was held to be genuine. Work along these lines should be repeated with the more satisfactory modern methods.

Since antidromic stimulation of the optic nerve has been shown to have no effect on the retinal response (Granit and Helme, 1939) one is inclined to doubt the existence of an interretinal reflex concerned with the electrical reactions to light. However, centrifugal effects may well arise elsewhere in the central nervous system and take effect peripheral to the 'locus' responsible for the electroretinogram. This is a problem which should undoubtedly be investigated.