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THE MECHANISM OF DARK ADAPTATION
A Critical Resumé

BY

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IT is a familiar experience that the eyes take some minutes or even hours to accustom themselves to a very low illumination after having been exposed to a high one. Few realise that the increase in sensitivity may be 10,000 fold. If, for example, an illumination of 0·1 metre candle (m.c.) is just visible immediately after switching off a very bright light, an hour or so later in the dark the necessary illumination may have fallen to 0·00001 m.c. Not all scientists working on this and related subjects realize that the process continues for at least an hour, and, according to Achmatov (1927) for at least 24 hours. To measure the least visible illumination of a test surface at various times after going into the dark seems a simple problem, but there are many complicating factors (Phillips, 1939) which have served as traps for the unwary. In this paper, however, we shall not criticize the technique of measurements, but test the adequacy of the physiological theories used to explain the results. The subject now concerns not only a few specialists but also workers from other fields, since it has become generally realized that deficiency of vitamin A may produce faulty dark adaptation.

In times of peace town dwellers never need to use their eyes at the low illuminations encountered in the country at night. Owing to the " black-outs " and the increase in night operations in the services it will not be possible to delay for very much longer a serious study of the problems.

Dual mechanism of dark adaptation.—The curve in Fig. 1 shows the change in visual threshold with time in the dark measured from the time when the observer had been plunged into darkness. He had previously looked at a brightly illuminated
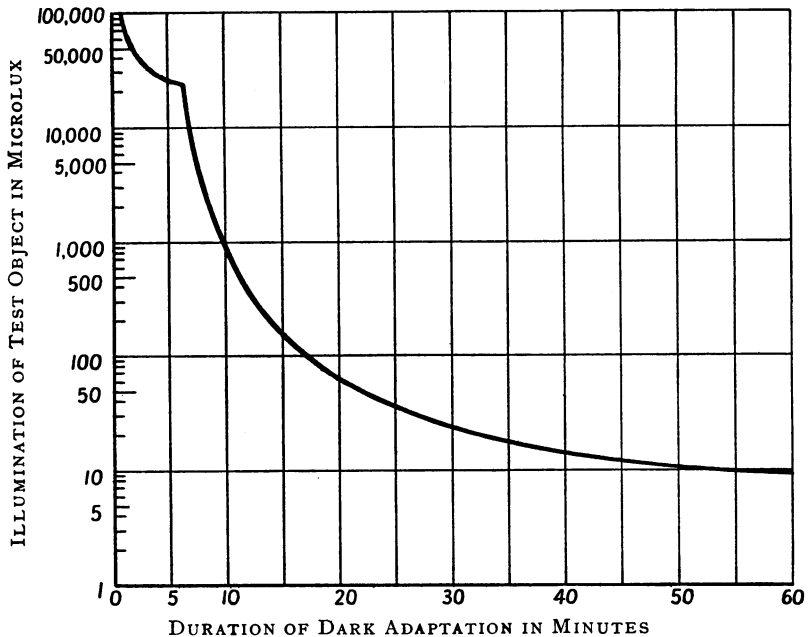
FIG. 1.

Horizontally: Duration of dark adaptation in minutes. Vertically:
The smallest visible illumination in microlux (1,000,000 microlux=
1 m.c.). (After Kohlrausch, *Handb. norm. Path. Physiol.*, 1931;
see Wright and Granit, *Brit. Jl. Ophthal.*, Monograph Supple-
ment IX, 1938.)

screen for some minutes. It will be seen that the smallest detect-
able illumination became progressively less during the 60 min.
of the test. With a higher initial light adaptation and with
greater speed in taking the first reading, a greater increase in
sensitivity could have been obtained. The important point to
notice is that the curve is divided into two parts which form a
kink at their intersection. The dual nature of the curve suggests
that two mechanisms are involved and that they adapt at different
rates. (Kohlrausch, 1922, Hecht, 1929.) The generally accepted
explanation is that the first part of the curve, lasting 6-11 min.,
reveals the adaptation of the photopic mechanism of vision, which
is mediated by the retinal cones. The second part of the curve
reveals the adaptation of the scotopic mechanism, which is
mediated by the retinal rods and their visual purple. The scotopic
mechanism, although capable of a very great increase in sen-
sitivity, seems to exhibit an initial delay in adaptation. As a
result, only test-patch illuminations which are sufficiently high
to stimulate photopic vision can be seen during the early stage of

adaptation.   Photopic vision is completely adapted in about 6 min. (Hecht, 1921), and a little later, scotopic vision becomes sufficiently sensitive to appreciate illuminations which are now too low to stimulate photopic vision.   This view is based on the alteration in the relative prominence of one or other part of the curve when the experiment is conducted with light of different wave-lengths, and with observation by different parts of the retina (Kohlrausch, 1922, Hecht, 1937).

Our belief in a dual mechanism of vision is also based on experiments in which some visual function, such as visual acuity, is measured over a wide range of illuminations.   As the illumination is raised from a low value, visual acuity improves at one rate up to a certain illumination.   Up to this point scotopic vision is being stimulated.   Beyond it visual acuity improves at another rate corresponding to the activity of the photopic mechanism (König, 1897, Shlaer, 1937).

Duplicity Theory.—This theory states that photopic and scotopic vision are mediated by the cones and the rods respectively.   It is based on a large amount of circumstantial evidence. As an example we may mention the similarity between the phenomena of scotopic vision and the properties of visual purple. This substance, which is found only in the rods, can be brought into solution, and its properties can be accurately investigated. It is found, for instance, that wave-lengths around 502 mμ appear the brightest in scotopic vision, that is, when the spectrum looked at is of low intensity.   This wave-length is also that at which visual purple absorbs most of the incident light (König, 1894, Dartnall and Goodeve, 1937, Lythgoe, 1937), and it is also the wave-length which is most capable of bleaching visual purple (Trendelenburg, 1904, Schneider, Goodeve and Lythgoe, 1939). When the spectrum is brighter, maximum luminosity is at about 555 mμ, but we cannot explain photopic vision, which is now being stimulated, in terms of the properties of any known substance in the retina.

There are very few visual judgments which show marked changes both during adaptation to darkness and also as a result of increasing the illumination.   The perception of flicker is an exception, since it is peculiarly sensitive to changes in both these conditions.   Above about 0·1 m.c. the critical frequency of flicker varies approximately as the logarithm of the illumination (Porter, 1902, etc.).   Suppose we have a small test-patch in which darkness and an illumination of 1·48 m.c. alternate for equal intervals of time.   If we increase the rate of alternation, all sensation of flicker will vanish at 19·2 flashes per sec.   If now we use ten times the brightness, 30·1 (19·2 + 10·9) flashes a second will be necessary to abolish flicker, whilst if we again increase it ten fold, 41·0 (30·1

+ 10·9) flashes will be necessary. This applies only to illumina-
tions above 0·1 — 0·2 m.c. Below this value scotopic vision is in
action and a quite different relation holds (Porter, 1902, Lythgoe
and Tansley, 1929a, Hecht and Verrijp, 1933). We may notice
in passing that there is no scotopic component when the relation
is investigated by red light longer than a certain wave-length.
This observation is in conformity with the fact that this wave-
length is not absorbed by, nor does it bleach visual purple. The
distinction between scotopic and photopic vision is most marked
with a blue of short wave-length.

The behaviour of the critical frequency of flicker during dark
adaptation is best investigated by measuring the fusion frequency
whilst the illumination of the flash is kept constant. This method
gives us a fresh means of studying dark adaptation. Normally
we measure the least perceptible brightness at different times,
first the photopic and then the scotopic mechanism being stimu-
lated. In the experiments with flicker, however, the brightness
can be maintained at such a level as to stimulate the photopic
mechanism or only the scotopic mechanism throughout dark
adaptation. In a typical experiment the observer would sit inside
a whitened cube with brightly lighted walls. Through a small
hole (1°) in the cube he would see the flashing test-patch and he
could then increase the rate of alternation of light and dark until
the test-patch ceased to flicker. The light in the cube would then
be extinguished, and the observer would repeat the setting at
regular intervals, during which period he would see the small
illuminated test-patch in dark surroundings. For illuminations
which are too low to stimulate any but the scotopic mechanism,
the fusion frequency rises during dark adaptation (Fig. 2A). For
illuminations high enough to stimulate the photopic mechanism,
the fusion frequency actually falls during dark adaptation, show-
ing that the eye is becoming progressively less sensitive to flicker.
Here for the first time we meet a visual judgment which is
performed less well by the dark-adapted eye. For intermediate
illuminations of the test-patch there is a fall followed by a rise in
the critical frequency (Lythgoe and Tansley, 1929a), revealing the
dual nature of dark adaptation. These experiments show that
dark adaptation is not a process manifested only by a progressive
lowering of the light threshold, but that throughout its course
there is some fundamental change which causes the perceptions
of both scotopic and photopic vision to be modified.

For the sake of completeness we may mention here that there
is an area in the centre of the retina subtending about 3° where
there are no rods and where the phenomena of scotopic vision are
absent. Peripheral to this area the density of the cone population

falls off, but that of the rods increases up to a ring of retina which subtends an angle of about 20° to the fixation point, whence it falls off slowly. As is to be expected, the photopic parts of our curves become progressively less evident, and, in general, the contributions of the scotopic portion increases with the increase in rods (Lythgoe and Tansley, 1929b, p. 87, l. 22, Hecht, 1937, p. 262, l. 1).
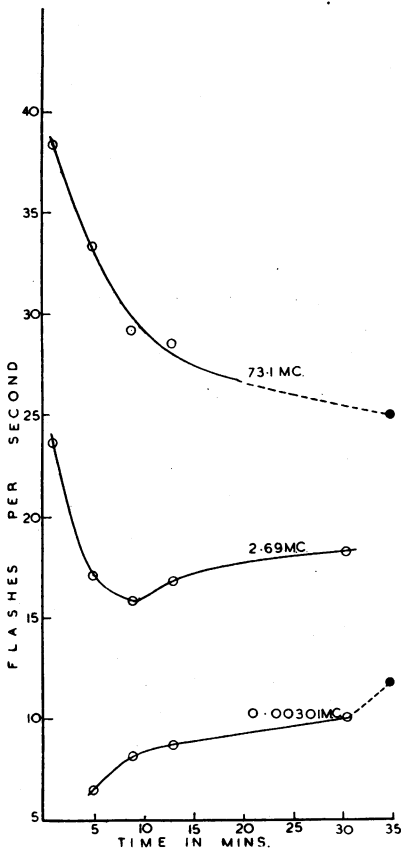

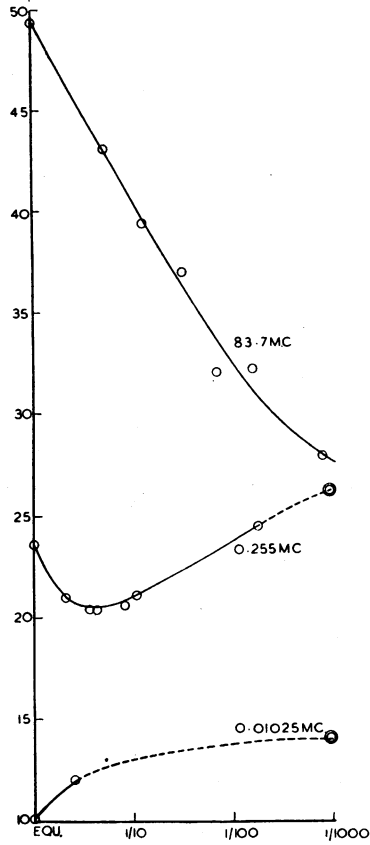
FIG. 2A.   FIG. 2B.

To show the similarity between the changes in the critical frequency of flicker (1) during dark adaptation (figure to left) and (2) as a result of changing the brightness of the field surrounding the test-patch (figure to the right). For any one curve the illumination of the test-patch was unaltered (see values set against each curve). All observations were made with 10° of eccentric vision. In the figure to the right the values equ. 1/10, 1/100, etc., refer to conditions where the surrounding field of vision was equally bright, one-tenth as bright and one-hundredth as bright as the test-patch, respectively. ● After 60 mins. in the dark. ◎ Surrounding field of vision completely dark.

The rôle of visual purple in dark adaptation.—Any animal
which has rods will be found to have visual purple in its retina
(in the rods) if the animal has been kept in the dark for an hour
or so before the retina is removed. On bringing the retina to
the light the visual purple will be bleached, and instead of being
a bluish-red, it will become orange, yellow or almost colourless
according to the conditions of the experiment. If the bleached
retina of a frog is again put into the dark some visual purple is
" regenerated." In the mammal it is essential to replace the
retina in contact with living pigment epithelium before regenera-
tion will occur, and with the frog also there is much more
regeneration if this is done.

The bleaching of visual purple in the light and its subsequent
regeneration in the dark give us a physical basis for the
phenomena of dark adaptation, since by photochemical reasoning
we can say that, in order to produce a minimal stimulus, a constant
amount of visual purple must be broken down, and the more
visual purple there is, the less will be the illumination necessary
to produce this amount of breakdown. This simple theory can
be stated thus: For a threshold stimulus, ILLUMINATION ×
CONCENTRATION OF VISUAL PURPLE = A CONSTANT, provided the
density of visual purple is small. It must be emphasized that
in the orthodox statement of the duplicity theory, visual purple
is responsible only for vision at low illuminations, both when a
steady state has been reached and during the later part of dark
adaptation.

Criticism of the Orthodox Statement of the Duplicity Theory

Although the duplicity theory is the greatest generalization in
sensory physiology we shall render it a disservice by giving it
nothing but uncritical attachment. Some points of criticism are
given in the following sections; others have been published
elsewhere (Lythgoe, 1938a).

The fate of the rods and visual purple at higher illuminations.—
In the investigation of a visual function over a wide range of
illuminations there is, as mentioned earlier, one relation between
function and illumination for low, and another for higher
illuminations. The change occurs at about 0·1 m.c., an illumina-
tion approximately equal to that given by a ¾ full moon on the
earth. By the use of light of different wave-length, by observa-
tions made with the peripheral retina and by correlating the
habit of a species with its retinal histology, we know that the rods
are mainly responsible for vision below 0·1 m.c., and the cones for
higher illuminations. We do not know whether vision above and

below this illumination is wholly due to the cones and rods respectively. Our first concern is with the fate of the rods at high illuminations. In curves relating visual function and illumination we can find no trace of a scotopic component at the higher illuminations, and, if the term " rod vision " is synonymous with " scotopic vision," we should say that the rods are playing no part in the visual processes. On general grounds this is surprising, since rods are far more numerous than cones both in number and in the area of retina occupied, and if the rods play no part in vision above 0·1 m.c. it means that they are functionless over the greater part of the scale of illuminations met by the eye (Parsons, 1927).

This objection acquires greater force when we consider the visual purple content of eyes which have been subjected to illuminations above 0·1 m.c. for a considerable time. Even with albino rats placed in an illumination of 2,000 m.c. for a long period, the visual purple is not quite completely bleached (Tansley, 1931). We should expect to find visual purple at much higher illuminations in pigmented eyes. I have exposed Hungarian frogs to the illumination of a lightly-clouded mid-summer sky (say 50,000 m.c.) for 40 min. At the end of the period only ¾ of the visual purple had been bleached. Since in frogs visual purple may be protected from the light by migrating pigment epithelium, Granit's experiments on cats probably give a truer picture of what is happening in man (Granit, Munsterhjelm and Zewi, 1939). The experiments showed, primarily, that during dark adaptation the electrical response of the retina is very small if the concentration of visual purple is less than 50 or 60 per cent. of its final value, but they also demonstrated conclusively that there must be considerable quantities of visual purple in eyes which have been exposed to illuminations some 10,000 times 0·1 m.c. If the rods and their visual purple play no part at these higher illuminations we must conclude with Granit that the visual purple which is present, although bleachable by light, can produce no stimulus to the optic nerve, and, therefore, no sensation of light.

Complicating factors in the explanation of early dark adaptation. —The terms " photopic and scotopic vision " are purely descriptive and apply, first, to the distinctive phenomena of vision at high and low illuminations respectively. Secondly, the terms apply to the early and late parts of the curve depicting the course of dark adaptation. Although there is little doubt that the adaptation of the cones is mainly responsible for the early or photopic part of the curve, there is some evidence that another mechanism is playing a part. This second mechanism may be

that of scotopic vision or it may be a phenomenon of nervous adaptation, which will be considered later.

As a first approximation it can be said that for photopic vision, visual acuity varies as the logarithm of the illumination. It follows that during the early stage of dark adaptation this relation should also hold if, as is usually stated, vision is then entirely photopic. Recently Dr. A. J. Marshall and I have conducted a series of experiments to test this point (unpublished observations). The observer was given a standard period of light adaptation, and the minimum illumination needed to see a large grating test-object was measured at different times of dark adaptation, the size of grating remaining constant. The grating size was then changed and the experiment repeated. A series of curves relating minimum illumination and time in the dark was thus obtained, one curve for each size of grating. By taking a cross-section at any one time it was possible to construct a second graph, relating visual acuity and illumination for any desired time. The graph so made closely resembles Fig. 3 which was obtained by Hecht and Shlaer (1936). The descriptions are not comparable, since fusion frequency is replaced by visual acuity, and the various traces for decreasing wave-length are replaced by traces for increasing time in the dark. A further difference is that, even for time 60 sec. after the onset of dark adaptation, the derived curve did not show the simple logarithmic relation between grating size and illumination, and the deviation became progressively greater until the final curve obtained after some 15 min. of dark adaptation. The conclusion to be drawn from this experiment is that scotopic vision, or some other phenomenon, is playing a part in early dark adaptation which is usually thought to be exclusively photopic.

The lower limit of photopic vision.—We have seen that the change-over from scotopic to photopic vision occurs at an illumination of about 0·1 m.c. When, however, observations are made with a small centrally fixated field whose image falls on central cones only, it can be shown that the mediating mechanism of photopic vision is sensitive to an illumination as low as 0·0034 m.c. (Hecht, 1921, Sharpley, 1936). Without making any reference to rods and cones, it is clear from an ordinary dark adaptation graph that the first loop of the curve, which is associated with photopic vision, is maintained to an illumination as low as 0·004 m.c. (The kink is at a higher illumination in Fig. 1. The lower value has been found by several authors.) When observations are being made under a steady illumination between 0·004 and 0·1 m.c., there should be enough light to stimulate the photopic mechanism, but scotopic vision seems to be

dominant and there is no trace of a photopic component. Photopic vision seems to become dominant quite suddenly when the illumination is raised above 0·1 m.c., thereafter revealing no scotopic component.

An argument similar to that used in the last section shows that there is probably more than one receptive mechanism in action at illuminations just below 0·1 m.c., that is to say, at illuminations which are generally supposed to be just insufficient to stimulate
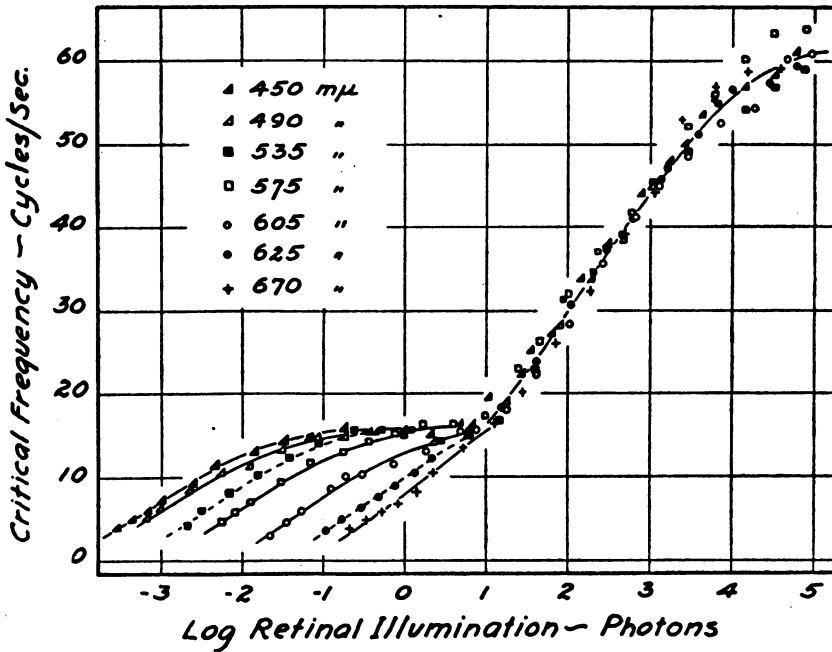

FIG. 3.

The relation between the critical frequency of flicker and illumination expressed in terms of photons.
(A perfectly diffusing white screen illuminated by 3 m.c. and seen through 1 sq. mm. of pupil gives a retinal illumination of about 1 photon.) (Hecht and Shlaer, 1936.)

the cones. This is shown by the experiments of Hecht and Shlaer (1936), where the critical frequency of flicker is plotted against illumination for a number of wave-lengths (Fig. 3). A critical fusion frequency of about 15·6 was obtained at a number of wave-lengths (450, 490, 535, 575 mμ) with a retinal illumination of about 1 photon (that the retinal illumination is the same for all wave-lengths is not significant). If only one receiving mechanism were at work we should expect to find that the values of the fusion frequency would be again equal to one another if the retinal

illumination were reduced to one hundredth. The values were, in fact, about 13·2, 11·5, 10·0 and 7·0 for the 4 wave-lengths respectively.

Concentration of visual purple and threshold stimulation.—Very serious difficulties arise when we attempt a quantitative interpretation of the decrease in the light threshold during dark adaptation in terms of the increasing concentration of visual purple. We saw earlier that for a threshold stimulation we should expect the product of the illumination and the concentration of visual purple to be a constant,· provided the concentration is not too large. We must also confine our attention to the increase in sensitivity occurring after the first 10 min. or so in the dark, since visual purple does not seem to play an important rôle during the first part of the curve. There are no figures for the concentration of visual purple in the human retina at different periods of dark adaptation, but we will assume that the figures of Granit *et al.* (1939) for the cat are applicable to man. Between the 10th and 30th min. the concentration of visual purple increases from 57 to 95 per cent. of its final value, and according to the simple theory, the visual threshold should be divided by about one half (57/95) during this period, whereas it is, in fact, divided by about 1,000. In other words the increase in concentration is not nearly enough to account for the great increase in sensitivity.

Concentration of visual purple and threshold stimulation in deficiency of vitamin A.—A further difficulty occurs when we attempt a quantitative explanation of the night blindness found in serious deficiency of vitamin A. Holm (1925) and Tansley (1931) have shown that in this condition there is both a lowering of the light threshold and a retarded regeneration of visual purple, a conclusion which has been confirmed by Charpentier (1936) who used an electro-physiological method. At first sight this illustrates strikingly the essential part played in scotopic vision by visual purple, but quantitatively there is a serious discrepancy. Tansley's rats had been kept without vitamin A for so long that their weights had begun to fall. Man with an equal degree of deficiency would have had a light threshold about 1,000 times normal, and we should expect the concentration of visual purple, both in man and in Tansley's rats, to be about 1/1,000 normal. This means that no visual purple could have been detected by the method of estimation used, whereas there were appreciable quantities in all experiments but one.

Too much emphasis cannot be laid on this argument, however, since deficiency of vitamin A leads to other retinal changes, such as a progressive atrophy beginning with the outer limbs of the rods (Tansley, 1933, Johnson, 1939) and a degeneration of the

nervous elements having its principal effect on the ganglion cells (Mellanby, 1934). The degeneration of the rods may be connected with the paucity of visual purple, since both Granit (1938) and I (1938) think it probable that visual purple is related to the surface of the rod, whilst Schmidt (1938) has put forward evidence that visual purple forms part of the structural framework of the rods. If this view is correct it is not difficult to see that deficiency of vitamin A would produce poor night vision, both by reducing the concentration of visual purple and by damaging its seat of action.

Dark adaptation curves do not retrace one another's paths.— The bleaching and subsequent regeneration of visual purple are more complicated than a simple chemical reaction performed in a test-tube. Let us suppose that we have two test-tubes each containing an equal concentration of a substance which is decomposed by light into two or more substances, or suffers some tautomeric change in the light. Let us further assume that all the breakdown products are stable and recombine in the dark to form the original light-sensitive substance. If the original substances in the test-tubes are bleached, one more than the other, then the recombination in the test-tube which has suffered the greater breakdown will proceed until it has reached the state of breakdown originally found in the less bleached test-tube. If the retinal rods are no more than test-tubes full of visual purple, the bleaching and subsequent regeneration of this substance should behave in the way just described. Assuming both that the final concentration of visual purple is always the same in a given retina, and that the breakdown products are not lost, then regeneration from any given stage of breakdown should always follow the same course, however that stage had been reached. Furthermore, if the same visual threshold is always associated with a given concentration of visual purple, then one curve could describe the course of dark adaptation under all conditions. The same threshold and, presumably, the same concentration of visual purple might be attained at different times in two experiments on an observer, but after equality had been reached the two curves should follow the same course. It has been shown experimentally that this is not so. It is also known that a short flash of light, such as is produced by striking a match in the dark, has only a transitory effect on the process of dark adaptation.

General Conclusions.—Our conclusion, both from a study of the course of dark adaptation and of the nature of the curves relating visual function to illumination, is that the sharp division into photopic and scotopic components does not correspond to a sharp division into cone and rod function. The cones can function at

a lower illumination than is usually stated and they are probably in action for part of the curve conventionally marked scotopic. Similarly, certain phenomena suggest that the rods may play some part in photopic vision, although we shall see later that a nervous change is probably also active in the early stages of dark adaptation. If this view is accepted we shall be entitled to retain the terms " photopic " and " scotopic vision," but we must make it clear that they do not refer to vision which is due exclusively to the cones or to the rods, respectively.

There are still more serious difficulties in the quantitative interpretation of the phenomena of scotopic vision in terms of visual purple. The aim of the rest of this article will be to examine some possible causes of our difficulties.

Regeneration of Visual Purple

According to Kühne (1879) and Hecht (1919-20), visual purple is bleached by light, but simultaneously it is regenerated from its breakdown products, although at a rate which may not be the same as the rate of bleaching. In Hecht's original analysis the breakdown of the light-sensitive substance was directly proportional to its concentration and to the light intensity falling on it. Regeneration was said to occur from two breakdown products and to conform to the equation for a reaction of the second order. The derived equation satisfactorily explained a number of visual relations, such as that found for the discrimination of brightness differences at various illuminations, but it was not satisfactory when given the crucial test of explaining the rate of dark adaptation. It is possible, however, that the assumption of other types of reaction kinetics would have done equally well over a limited range of illuminations. Wright (1935, 1936) found that the hypothesis was inadequate to explain the perception of brightness difference when high illuminations were used. Furthermore, although the rate of regeneration of visual purple may follow faithfully the equation for one of the commoner types of chemical change, it does not follow that what we are observing is primarily determined by a chemical reaction. Physical factors, such as the diffusion of metabolites, may set the pace, whilst the chemical change may occur only when the ground has been prepared for it.

The increase in sensitivity during dark adaptation does not follow an equation either of the first or second order, and from this point of view there are few grounds for thinking that the underlying chemical change is unimolecular or bimolecular. Tansley's (1931) figures, however, did hold out some hope that the increase in the concentration of visual purple with time in the dark might one day be expressed in a simple formula. Granit

and his colleagues have shown, however, that under most, if not all conditions, there is a delay in the regeneration of visual purple. Although this observation may explain the delayed adaptation of the scotopic component of dark adaptation, it adds considerably to the difficulty of a biochemical explanation of regeneration.

If either the increase in sensitivity or the increase in concentration of visual purple during dark adaptation could be adequately described by an equation representing one of the well-known types of chemical reaction, we should have a clue to the nature of the regenerative process. Since no such equation has been found we must do what should have been done before, namely, first study the chemical processes themselves, and secondly explain the time course of the increased sensitivity during dark adaptation.

Course of bleaching of visual purple.—Kühne gave the first account of the colour changes observable when visual purple is bleached by light. Subsequent quantitative work has confirmed the accuracy of his observation. Kühne said that visual purple is bleached by light to form visual yellow, and that the latter subsequently breaks down to visual white. We see at once that bleaching occurs in at least two stages, and that regeneration might be possible from either. Kühne also recognized other colour changes, but he thought they were produced by mixtures of visual purple and visual yellow, and he did not assume the existence of an intermediate link to explain them. My own view, based on a study of the absorption curves at different stages of bleaching, is that light acting on visual purple first produces a distinct chemical compound which I call " transient orange." The latter is very unstable and decomposes thermally in the dark to form " indicator yellow " which, in its turn, forms a colourless compound, especially in weakly acid solutions (Lythgoe, 1937). When Kühne writes of " visual yellow " one can tell only by the context whether he means " transient orange " or " indicator yellow," but it is usually the latter, since special precautions have to be taken to demonstrate the presence of the former substance. My reasons for dropping the term " visual yellow " are, first, that it would be used to describe two substances without any indication of which was meant. Secondly, the term implies that the substance forms a direct link in the chain of events leading to a visual sensation. This is no longer believed. The term " indicator yellow " is used to describe the most obvious character of the chemical substance in question, namely, that it is yellow and that its yellowness changes with acidity (Chase, 1936, Lythgoe, 1937). Transient orange is an unstable substance which always appears orange and whose absorption curve is very little affected by acidity (Lythgoe and Quilliam, 1938b). In this I differ from Wald (1938). I have been unable to find any other intermediate stage.

Chemistry of visual purple and its products of bleaching.—It now seems clear that visual purple is made up of a chromophore attached to a protein. This chromophore, or its bond with the protein, is responsible for the characteristic absorption curve. Chemically it is probably a carotenoid which is closely related to vitamin A. If this is so, absence of the vitamin will probably lead to a shortage of visual purple in the retina. The general nature of the chemical changes involved in bleaching have been worked out by Wald (1936). Light causes a loosening of the bond between the protein and its chromophore, so rendering the latter more freely soluble in organic solvents. The substance extracted is called retinene. It behaves like a carotenoid compound, but nothing is known of its structural chemistry. Wald originally seems to have thought that light could split off the chromophore from the protein, and that visual yellow (indicator yellow) was retinene itself. Recently he seems to have modified this view (1938). There are some grounds for thinking that indicator yellow is itself a conjugated protein. We are justified in saying no more than that light weakens the chemical link which is responsible for the characteristic absorption curve of visual purple. It is possible that the essential chemical change is one of hydrolysis (Lythgoe and Quilliam, 1938a, Dartnall, Goodeve and Lythgoe, 1938).

The changes just described can be demonstrated either in solution or in the whole retina, but when bleaching has occurred in the retina itself there is a further chemical change. It is found that if the whole retinae are left for some time after bleaching, organic solvents now extract vitamin A itself, indicating that this substance has been formed from retinene. Krause and Sidwell (1938) deny that this is so, finding on the contrary that there is less vitamin A after bleaching than before. If true, this means that in their experiments vitamin A was continuously destroyed, and, since this would apply both to the original and to any newly-formed vitamin A, all we can conclude from their experiments is that this substance is more rapidly destroyed than it is formed, if it is formed at all.

Caution is needed in the interpretation of experiments on solutions of visual purple since these usually contain large quantities of impurities extracted simultaneously from the retina. This criticism applies *a fortiori* to experiments on whole retinae.

A general criticism of Wald's chemical explanation of the bleaching of visual purple and of its regeneration, is that there is no place in it for the action of the carotenoid, xanthophyll, which is known to be present in large quantities in some retinae.

Precursors of regenerated visual purple.—Wald believes that

visual purple can be regenerated from the vitamin A stage in its breakdown. This we can readily understand if at this stage both vitamin A and the protein are present. In deficiency of the vitamin we presumably have the protein alone, and visual purple can be reformed if vitamin A is supplied. Visual purple can certainly be regenerated from solutions of indicator yellow (Ewald and Kühne, 1878, Hecht, Chase, Shlaer and Haig, 1936, Lythgoe, 1937). It is probable that some of the regeneration in the intact retina is from indicator yellow (Boll, 1876, Kühne, 1878, 1879, 1882, and many others). Regeneration from this stage in the breakdown is explained by Wald (1936) as a recombination of protein and retinene, or, according to my reading of his later writings (1938), as a strengthening of the bond between the protein and the chromophore.

Transient orange is an intermediate link in the formation of indicator yellow from visual purple, and recently I have found that under certain conditions regeneration can also occur from this stage in solution. The regenerated substance, although sensitive to light, is slightly different from the original visual purple.

In vitro visual purple can be regenerated from any one of its breakdown products, namely, from transient orange, indicator yellow or visual white. We do not yet know which mechanism normally occurs *in vivo*. We are suffering from an *embarras de choix*. Many workers have shown that the course of dark adaptation varies in kind as well as in degree with the conditions of the previous exposure to light. Wald and Clark (1937) have suggested that the stage of breakdown reached depends on the duration of light adaptation, and that the differences in dark adaptation depend on the rate of regeneration from the various stages. Caution is necessary in accepting this explanation in view of the discrepancy between the concentration of visual purple in the retina and the sensation evoked. Furthermore, the explanation does not take into account the acceleration of regeneration produced by irradiation of the breakdown products. This remarkable phenomenon will now be described.

Factors influencing regeneration (a) Light.—It is thought that in the intact animal, regeneration is constantly occurring during the whole time that light is falling on the retina (Kühne, 1879, Cobb, 1916, Hecht, 1918, etc.). This we should expect for that part of the regenerative process which is chemical and obeys the law of mass action. Bauer's (1911) experiments showed, however, that the concentration of visual purple depends largely on the previous exposure to light, being *greater* in animals which had been irradiated for the longer period. These experiments have

been put on a firm quantitative basis by Zewi (1939), and it is now
clear that previous exposure of the whole retina to light acts as a
stimulus to regeneration.   Under many conditions, moreover,
visual purple does not begin to regenerate immediately the
adapting light is switched off. This delay is absent in those animals
pre-exposed to light of high intensity or for a long duration.   If
an observer has been exposed to bright sunlight during the lunch
hour the later stage of dark adaptation in all the afternoon runs
is retarded, but the early stage of adaptation is found to be quicker
(Dr. A. J. Marshall, unpublished work).   The pre-exposure to
bright light might have caused an accelerated regeneration of
visual purple (especially the early phase), and so quickened initial
adaptation.

   Chase (1937) found that if a solution of visual yellow (indicator
yellow) was irradiated strongly there was some regeneration of
visual purple which would not otherwise have occurred.   I have
confirmed this observation, and find that regeneration also occurs
under certain conditions from the intermediate transient orange,
provided it has been strongly illuminated.   It is surprising that
the absorption curve and other properties of the regenerated sub-
stance are not quite the same as those of the parent visual purple.
One cannot help wondering whether the photosensitive substances
responsible for day vision are formed in this way : the bright light
may be the essential agent in the preparation of the visual purple
for the reception of high illuminations.

   Factors influencing regeneration (b) The healthy retina.—
Although irradiation can stimulate the regeneration of visual
purple in the frog's retina it does not follow that it is an essential
factor without which there can be no regeneration. It is certainly
not the only factor in regeneration. Tansley (1933) has shown that
regeneration is possible in tissue culture, but only in a healthy
retina.   Zewi has shown conclusively that in the whole retina,
regeneration depends on the oxygen supply.   Regeneration is
greatest when the retina is in contact with a choroid, whose blood
circulation is intact, and is least when the retina is isolated,
especially if it is put into an atmosphere of nitrogen.   According
to McFarland and Evans (1939), anoxaemia slows the process of
dark adaptation.   Phillips (1939) has found that dark adaptation
is much slower in old people.   Both these observations show that
something more than a simple reunion of breakdown products
forms the chemical basis of dark adaptation.

   It seems possible that we have two methods for the regeneration
of visual purple.   Regeneration from its breakdown products
almost certainly involves the addition of energy to the system,
and this energy can be provided either by the absorption of light
or by a chemical process needing oxygen.

Possible Nervous Changes during Dark Adaptation

We cannot seriously doubt that the basic physiological change in dark adaptation is a reaction in which visual purple is regenerated, but it is questionable whether this is the only change. There are reasons for thinking that nervous influences are also at work.

Most of what we have said so far has been exclusively concerned with adaptation to low illuminations after exposure to high ones. It is now being realized, however, that dark adaptation is only a special case of a fundamental change which is always occurring when the eyes are being used. The term adaptation is now used to mean the adjustment of the retinal mechanism to the general prevailing brightness of objects in the field of view. By " adaptation " we now mean either the process of adjustment or the final " stationary state " (Hecht) after adjustment is complete. In my opinion something has been learnt of the special case of dark adaptation by studying adaptation in general. Let us imagine that an observer is seated inside a whitened cube, the illumination on whose walls is gradually reduced. The observer's eyes are then being adapted to progressively lower brightnesses. There is a small opening in the cube which is normally closed, but can be opened to afford a short view of some visual test-object which may not be illuminated to the same extent as the walls of the cube. The observer will be performing a visual task at one illumination with eyes adapted to another. Complete darkening of the walls of the cube gives a special case in a wide range of conditions. It has been found that the state of adaptation of the eye, as determined by the brightness of the cube, has a profound influence on the performance of a visual task seen through the hole.

Fig. 2B shows that the perception of flicker is very susceptible to changes in adaptation (Lythgoe and Tansley, 1929a). Starting with a high brightness in the cube one first measures the fusion frequency for a flickering light of a slightly lower brightness. Keeping the brightness of the test-patch constant, the brightness of the walls of the cube is progressively reduced until they are equally bright and later less bright than the test-patch. For photopic vision the perception of flicker is best when the test-patch is of the same brightness as the walls of the cube, or, in other words, when the eyes are adapted to the same brightness as that at which they are required to make their judgment. (Readings where the cube was brighter than the test-patch are not recorded on the graph.) The eyes must be allowed time in order to become adapted to each new illumination : in the same way it takes time for the eyes to adapt to complete darkness. Using as a criterion the perception of differences of brightness, Craik (1938) found

that visual perception is at its best when the eyes have been pre-adapted to the illumination at which they will subsequently make their judgment. This appears to be a general law for photopic vision. For scotopic vision, on the other hand, the most favourable condition seems to be dark adaptation, that is when the walls of the cube are completely dark. This is shown by experiments on flicker (Lythgoe and Tansley), to some extent by experiments on the difference threshold (Craik), and by the fact that the perception of small feebly illuminated objects improves during the course of dark adaptation.

The changes in the fusion frequency of flicker during the course of dark adaptation (Fig. 2A) are similar to those found when the adaptation of the eye is changed slowly and progressively by lowering the brightness of the cube's walls (Fig. 2B). Sometimes, as in the measurement of visual acuity, the change during the course of dark adaptation is both too small and too rapid to be measured accurately by the usual method, but by taking readings at progressively lower brightnesses of the cube's walls we can virtually slow the process of dark adaptation and study its phenomena at leisure (Lythgoe, 1932). In much the same way small cinematograph projectors can be stopped to allow a closer view of any one frame.

The finer visual judgments during dark adaptation.—The increasing sensitivity of the eye during dark adaptation is shown not only by the lowering of the light threshold but also by the progressive improvement in performance of visual tasks needing only low illuminations, namely, those calling for only coarse judgments. The finer visual judgments, for which higher illuminations are necessary, behave otherwise and, as we have seen, show a progressive deterioration during dark adaptation. If one adopts a purely chemical outlook on the stimulation of the retina by light, one would expect visual performance to be at its highest when the image of the test object falls on a part of the retina containing a maximum quantity of visual purple or other light-sensitive substance, and not on a retina which had been partially bleached by lighted surrounds.

Nervous interaction.—Adrian has proved that nervous inter-action can occur in the retina (Adrian and Matthews, 1928), although its presence had been suspected for a long time. Nervous interaction between those parts of the retina receiving the image of the lighted cube and the fovea, affords the most likely explanation of the influence of the surrounding field on central vision. Recent experiments by Schouten (1937), and Schouten and Ornstein (1939), even make such an explanation probable. We shall see that it is also probable that a nervous change plays a part in the ordinary process of adaptation to darkness. By the

method of binocular matching (*e.g.*, Wright) Schouten made a
quantitative record of the apparent brightness of a patch of light,
when there was exhibited near it another source of light, which
for convenience we will call the glaring source. Everyday obser-
vation has taught us that " When the moon shone, we did not see
the candle . . . . so doth the greater glory dim the less " (Merchant
of Venice). Experiment is necessary, however, to demonstrate
the time course of the phenomenon and the great extent to which
the apparent brightness of the test-light is depressed by a neigh-
bouring source of glare. The reduction in the apparent brightness
took place in about 1/10 sec., and the value so reached was main-
tained for the duration of the experiment. This process of
a-adaptation, as it is called, cannot possibly be photochemical in
origin, both because it takes effect so quickly, and because the
effect is exercised at a distance. Much the most likely explanation
is that glare produces its effect by some variety of nervous inter-
action. Our concern, however, is with the recovery from the glare
which resembles part of the process of dark adaptation. We have
seen that glare reduces the apparent brightness of the test-patch.
Removal of the glare causes a restoration of the original bright-
ness, but this process takes considerably longer than 1/10 sec.
Since the original suppression of brightness was due to nervous
interaction, we may assume that some part of the recovery from
the glare is also due to a nervous change. The uniformly lighted
field of view, such as is used for the preliminary light adaptation
in experiments on dark adaptation, may be regarded as made up
of a multitude of contiguous glare sources. Each one of these
will produce an effect on the test-patch and some part at least of
the recovery from the effects of high illumination, or, as we call
it, the process of dark adaptation, will have a nervous component.

By means of the Pulfrich rotating pendulum I have shown
(Lythgoe, 1938*b*) that a glaring source of light *shortens* the latent
period of vision for another light exhibited nearby. A uniformly
lighted field of vision has the same effect. The phenomenon can
be explained best by assuming that some sort of nervous inter-
action is taking place in the retina. It is mentioned here to show
that changes in the adaptation of the eye produce many and varied
effects.

*Dark adaptation as a combination of both chemical and nervous
changes.*—I look on dark adaptation as a complex phenomenon in
which the eye both becomes more sensitive to light and performs
better the grosser types of visual judgment where the recognition
of the presence or absence of light is the most important factor.
Simultaneously the eye becomes progressively less able to perform
the finer visual tasks. The lowering of the light threshold is due
mainly to the regeneration of visual purple: the increased
sensitivity of the photopic mechanism (Hecht, 1921, Wright, 1937)

is probably due to a similar change. The decreasing ability to perform the finer visual judgments may be due to synaptic rearrangements, which make the retinal elements more capable of initiating an impulse, but less capable of performing fine judgments. The sort of change I envisage is shown in Fig. 4. During complete light adaptation let us consider a number of visual elements, each one of which is served by a separate nerve fibre. During dark adaptation each fibre serves several elements
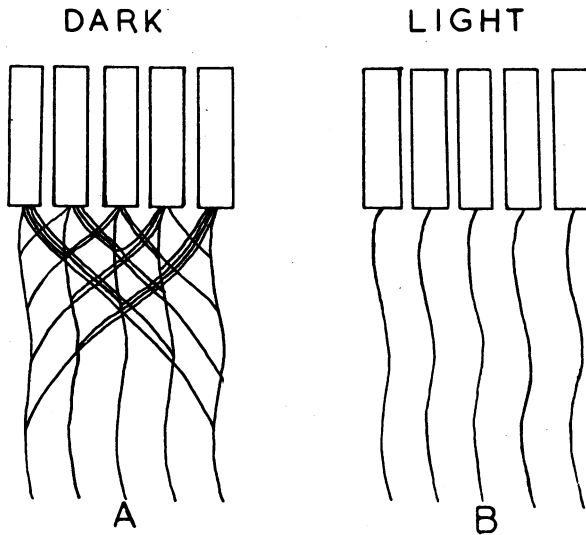
DARK   LIGHT

FIG. 4.

Illustrates the suggestion made in the text that there is more over-lapping of the nerve supply to the rods and cones during dark adaptation than during light adaptation.

by a spread of its synaptic connections. This would reduce the fineness of discrimination but it would probably improve the retinal sensitivity to light since it is known that although an image of a certain brightness falling on one rod (or cone) may produce no sensation of light, a larger image of the same brightness falling on two or more rods (or cones), may do so. Such an integration may be possible only when several rods connect with one nerve fibre (Fig. 4A) and not in the light-adapted arrangement (Fig. 4B).

If we regard the process of dark adaptation as one in which, *inter alia,* the rods or cones acquire progressively more nerve fibres in common, we must regard the process of light adaptation as one in which the rods or cones become progressively more segregated in their nervous connections. If this were so it would explain

the improvement in visual acuity with illumination, a phenomenon which has proved very difficult to explain. One would explain the improvement in visual acuity produced by a surrounding visual field of suitable brightness by saying that it induces the discrete arrangement of cones and nerve fibres at the fovea.

Although in this way we can explain the change in performance of those visual tasks which are dependent on the spatial selectivity of their central representation, we have difficulty in explaining the change in the discrimination of brightness differences with adaptation. One cannot say whether it would be explained by the rearrangement of nerve fibres shown in Fig. 4. If the cones to the left hand of Fig. 4A or 4B were more highly illuminated than those to the right hand, then the corresponding nerve fibres on the left would discharge more rapidly than those on the right. The transition from fast to slow would be more abrupt in the fibres from the discretely represented cones in Fig. 4B which represents light adaptation, than in Fig. 4A which represents dark adaptation. A blunt edge to the comparison fields is known to affect adversely the discrimination of brightness differences, but it is questionable whether the apparently blunt edge which would be seen in Fig. 4A would explain the poor discrimination of brightness by the dark adapted eye.

Many of the difficulties in accepting a purely photochemical explanation of the phenomena of dark adaptation have been taken from the work of Granit, Holmberg and Zewi (1938a, b). These authors have shown that the electrical response of the retina is not solely dependent on the concentration of visual purple. The virtual absence of an electrical response may occur in spite of a relatively high concentration of visual purple. These authors suggest that part of the visual purple may be inactive physiologically, although capable of being bleached by light. I have a bias against any view which assumes that visual purple is being bleached to no purpose. Although it may not be so for other physiological activities, the sense organs usually work most economically. I prefer to think of each molecule of visual purple as being a potential initiator of a nerve impulse when broken down by light, but that the final electrical response of the retina and optic nerve is determined by the existing synaptic arrangements. I feel that Granit is right, however, to stress the view that visual purple is closely connected with a surface in the rods. If the rod is a nerve cell one is much inclined to the view that when light bleaches a molecule of visual purple lying in the surface, an electrical disturbance is initiated at that spot which may be able to start an impulse in an optic nerve fibre.

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SPHERO-CYLINDRICAL CONTACT LENSES—
A PRELIMINARY NOTE

BY

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SOME two years ago, one of us was examining a patient who had
been fitted with contact lenses and was disappointed to find that
visual acuity with the contact lens was less good than with
ordinary glasses. The spherical element was checked by the
duochrome test and appeared to be right, so retinoscopy was per-
formed and it was discovered that there was some residual
astigmatism. When the correcting cylinder was placed in a trial
frame in front of the eye wearing the contact lens an immediate
improvement in visual acuity became manifest. It was then
suggested that an endeavour should be made to grind the
cylindrical correction on to the contact lens, but this could not be
done with the machinery available at that time. Recent improve-
ments in the technique of contact lens manufacture have now
rendered this possible, however, and although only four cases
have so far been treated in this manner, we felt that the results
were sufficiently good to warrant the issuing of a preliminary
report.

Before coming to the clinical aspect of this work it is not out
of place to consider the theoretical side. When contact lenses
were first produced, it was assumed that a cylindrical correction
was unnecessary because astigmatism was entirely due to
aberrations in the anterior surface of the cornea, and was therefore
neutralised by covering the aspherical surface with a thin layer
of saline and a spherical shell of glass. Perhaps this was making