purely probability considerations, and the question requires further investigation. Recently we have found a limited number of irradiated females in which both loci were apparently simultaneously affected, resulting in patches of whitened ommatidia, identical with those found in the male, superposed upon the dark eosin background. Such occurrences are very infrequent, so that the examination of an extremely large quantity of material is required for their study. A statistical investigation has been undertaken of the distribution of these "double-white" mutations in diploid stock, and of their occurrence in triple-X stock, and may shed some light on this phase of the question.

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DARK ADAPTATION AFTER VARYING DEGREES OF LIGHT ADAPTATION

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The photosensitive system of a photoreceptor must involve at least two processes, a light-sensitive process and a recovery process. Arnold and Winsor (1934) have shown that the validity of Talbot's law implies that the velocity of the light-sensitive process is directly proportional to light intensity.

In the further analysis of the photosensitive system the most direct line of attack seems offered by a study of dark adaptation. One adapts the eye to a given intensity of light, extinguishes the adapting light, and then determines the threshold intensity as a function of time in the dark. If the threshold intensity is a measure of the concentration of photosensitive material present, we have a means of studying the recovery process. Unfortunately, we do not know the nature of the relation between threshold and concentration of photosensitive material; but even without such knowledge some progress is possible.

We may write the equation for the rate of change of the photosensitive material S in the form

$$\frac{ds}{dt} = -I\phi, (s, x, y \dots) + \phi_2 (s, x, y \dots) \qquad (1)$$

in which the first term on the right represents the light-sensitive process, and the second the recovery process. The variables $(x, y \dots)$ we assume to be completely determined by the distribution of material in the photosensitive mechanism at any time; or, we may take $(x, y \dots)$ to be actually the values of the various concentrations.

Let us now assume further that a cyclic mechanism will describe the system, in which some fixed amount of material is distributed between various states, of which $(s, x, y \dots)$ are the amounts. Evidently, then, if there are n states, there will be $(n - 1)$ variables entering in the right-hand side of (1); and, in general, we shall require $(n - 1)$ differential equations for a complete description of the system.

The theoretical treatment of photoreception given by Hecht (1934) assumes that only two states exist; that the photosensitive substance S is broken down to P, and that S is reformed directly from P. In this case (1) simplifies to

$$\frac{ds}{dt} = - I\phi_1(s) + \phi_2(s). \qquad (2)$$

If now we consider the course of dark adaptation subject to (2) we have

$$\int_{s_0}^{s} \frac{ds}{\phi_2(s)} = t - t_0. \qquad (3)$$

From (3) it appears that recovery curves for a single receptor element, or for a homogeneous population of elements, from different initial conditions will differ only in their position on the time axis. If, then, one light-adapts to a series of different intensities, one should obtain a series of dark adaptation curves starting at different levels, but superimposable by a shift on the time axis.

Experiments of this kind have been reported by Blanchard (1918) for the eye as a whole, and by Fedorova (1927) and Johannsen (1934) for the fovea. In all cases the curves differ in shape for different initial adapting intensities. In the belief that possibly the experimental technique hitherto used was not completely satisfactory, experiments have been undertaken to test the point.

The observer was light-adapted for five minutes by an opal glass field 18 × 24 cm., about 4 cm. from the eyes; the illumination on the adapting field was from a 1000w projection lamp, variable in position to regulate the adapting intensity. To provide greater range in the adapting intensity, a screen with a smaller opening covered with opal glass was inserted in front of the adapting screen.

Threshold measurements were made on a circular test patch subtending, in one series 1.3° of visual angle, in a later series 0.44°. A fixation point was located at 9.8° from the center of the test patch. Observations were made monocularly with the natural pupil; provision was made in the apparatus for observation with either eye, and as a general rule the course of adaptation in both eyes was followed. The test patch was exposed through a camera shutter operated by the observer, set at $^1/_{50}$ second. The illumination on the test patch was provided by the adaptometer described by Derby, Chandler and Sloan (1929), which we calibrated over a range of intensities from 0.22 ml. to 0.000075 ml. (For the use of this instrument we are indebted to the kindness of Dr. J. Herbert Waite.)

A typical set of curves is shown in figure 1. It will be noted that at the highest intensity there is a clear separation into cone and rod adaptation curves, as has been found by Kohlrausch (1922, 1931), Hecht, Haig and Wald (1935) and Hecht and Haig (1936). We may here confine ourselves to the rod curves (the lower portions, subsequent to the break). It is apparent that the curves are of markedly different shapes, and that they are not superimposable by any shift on the time axis. Figure 2 shows curves in which the two eyes were simultaneously adapted to different levels, by the use of a filter covering one eye during adaptation. Here again the difference in shape is evident.

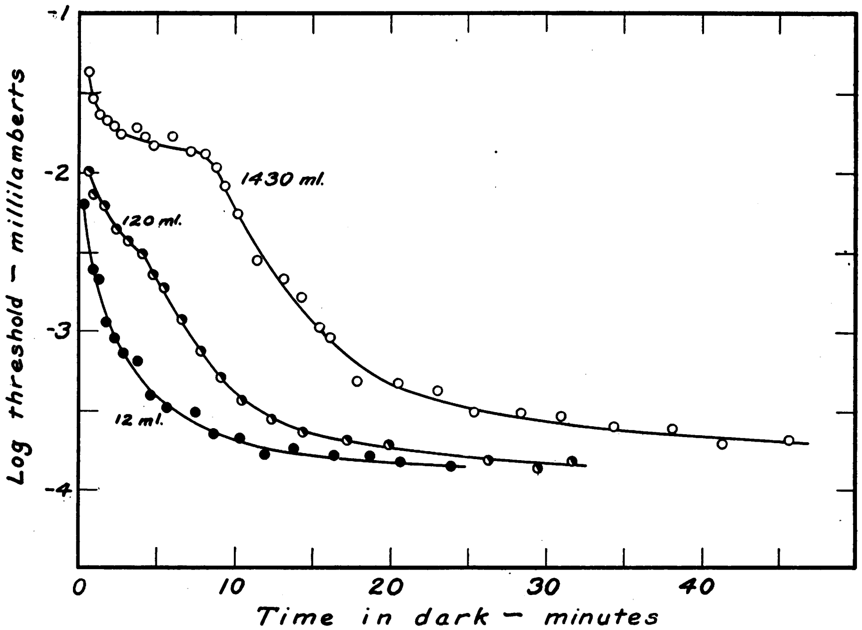
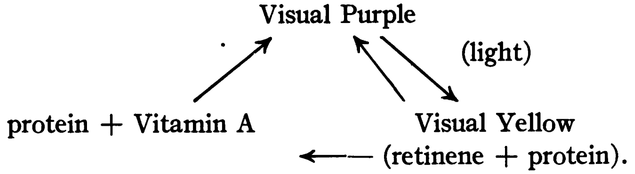


FIGURE 1

Dark adaptation following 5 minutes light adaptation to indicated intensities. (Curves obtained on left eye of C. P. W.; test field 1.3° visual angle.)

It is thus apparent that equation (2) cannot be adequately descriptive of the facts. Of the assumptions involved, the most obviously questionable seems to be that of the existence of only two states for the photosensitive material. Wald (1935a, b) has given strong reasons for supposing that the chemistry of the visual purple cycle involves at least three substances, in the form:



(4)

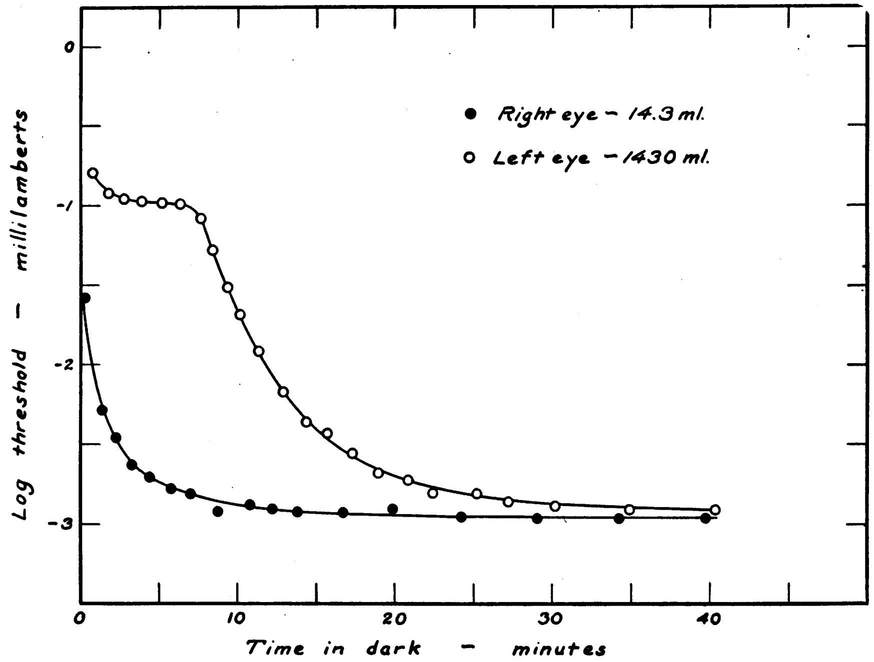


FIGURE 2

Dark adaptation following simultaneous light adaptation of right and left eyes to indicated intensities. (Observer A. B. C.; test field 0.44° visual angle.)

It is clear that if (4) represents the chemical situation, our equation for rate of change of S cannot be written as in (2), but must be written

$$\frac{ds}{dt} = -I\phi_1(s, x) + \phi_2(s, x) \tag{5}$$

since now three states rather than two are involved.

Further, the course of recovery will depend not only on the total amount of visual purple which has been changed, but on its distribution between visual yellow and vitamin A; and this distribution need not be independent of the adapting intensity.

Attention should here be called to experiments by Wald and Clark (1936) in which differences in the form of the dark adaptation curve are obtained by varying the *time* of light adaptation. These differences are in complete agreement with what would be predicted from the chemical scheme (4).

No attempt is here made at a further analysis of the curves obtained, because, in the absence of independent evidence as to the orders of reaction and the magnitudes of the velocity constants, the possibilities available are so wide as to render any curve fitting a meaningless procedure. It is, however, quite possible that a suitable experimental procedure would separate the reactions and enable one to obtain curves in which a single reaction predominated.

Summary.—The shape of the human dark adaptation curve changes with changes in the degree of initial light adaptation. The changes are inconsistent with the assumption of a mechanism in which the active material exists in only two states. The results are consistent with Wald's mechanism in which three states are postulated.

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