whereas novobiocin itself absorbs at 311 mμ at *p*H 10 and 308 mμ at *p*H 7. No peak is obtained when $CaCl_2$ is substituted for $MgCl_2$.

3) Potentiometric titrations of 0.01*M* solutions of novobiocin in the presence and absence of 0.02*M* $MgCl_2$ revealed a small but definite and reproducible alteration in the titration curve brought about by magnesium ions.

Binding studies with tritium-labeled novobiocin revealed that the antibiotic is bound quickly to bacterial cells, even at 0°C. If it is assumed that novobiocin is distributed equally throughout the cells, calculations reveal that concentrations of $10^{-2}M$ are obtained when the external concentration is $10^{-3}M$. If the antibiotic is bound preferentially to surface components of the cell, the local concentration may be considerably higher than $10^{-2}M$. Since complexes of magnesium ions and novobiocin form with $10^{-2}M$ novobiocin in solution, it seems reasonable to assume that such complexes may also occur within the cell.

There seems to be no specificity in the binding of novobiocin, since sensitive and resistant bacteria as well as serum albumin and other proteins bind it equally well. The selectivity of novobiocin action must therefore have some other basis. Novobiocin is more effective against Gram-positive than Gram-negative bacteria, and Webb (*3*) has shown that Gram-positive bacteria have much larger magnesium requirements than Gram-negative bacteria. Thus the selectivity of the antibiotic may be due to the varying requirements of organisms for magnesium. Residual growth occurs in the presence of low concentrations of novobiocin. This lag in the effectiveness of the antibiotic is not due to slow uptake of the antibiotic, for novobiocin is bound very rapidly. Similar residual growth occurs when cells are transferred to a magnesium-deficient medium. Therefore, the residual growth observed in novobiocin-treated cells probably occurs at the expense of uncomplexed magnesium ions, and growth ceases when these are diluted out.

Since novobiocin forms insoluble salts with many metals, it may be that other essential metals—such as iron, copper, and zinc—are also bound by the antibiotic in the bacterial cell. However, magnesium is quantitatively the most important metal in the cell, and it is reasonable that the effects of novobiocin would first resemble a magnesium deficiency. Recently there has been much interest in intracellular magnesium levels, because of the stabilization of ribosomes by this metal. Novobiocin may induce ribosome degradation and thus bring about a number of indirect effects on protein synthesis.

I recognize the difficulty of proving with complete certainty that the primary action of novobiocin is to induce an intracellular magnesium deficiency. Reversal studies with magnesium may be misleading, and all of the other evidence is indirect. However, because of the large number of points of correspondence between the effects of novobiocin action and the effects of magnesium deficiency, the present conclusions seem justified (*4*).

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20 November 1961

Chromatic Response Mechanisms in the Human Fovea as Measured by Threshold Spectral Sensitivity

Abstract. Threshold sensitivity was measured with 40-degree surrounds of 5.3 and 800 trolands of white, and 509, 580, and 690 mμ spectral light. With the brighter white surround there appeared peaks at 550, and 570 and a shoulder at 600 mμ. These were selectively eliminated by the spectral surrounds.

The so-called humps and notches in the luminosity curve have received increasing attention in the past 10 years. Although their existence is no longer questioned, there has been little more than speculation to relate them to visual functioning. They are presumed related to cone vision, since they do not appear in the fully dark-adapted "rod" sensitivity curve (*1, 2*). Thomson (*3*) established by statistical tests that they are not merely random fluctuations of sensitivity. Stiles and Crawford (*4*), in an early study, found three submaxima at 440, 540, and 600 mμ, which they could selectively eliminate by adapting to bright, broad-band colors in the blue, green, and red parts of the spectrum.

Although our data show humps in the blue region of the spectrum, the emphasis of our work here is on the occurrence of similar but much larger dips and humps in the long wavelength side of the visible spectrum. Sloan (*5*) first showed a notch in the spectral sensitivity function at 580 mμ. This notch appears from time to time in subsequent determinations (*2–7*). Sperling and Lewis (*6*) and Sperling (*8*), by using a stimulus of 45 minutes in diameter in a dark surround, have shown that the notch at 580 mμ goes from a deep cleft at absolute threshold to an almost smooth curve at high brightness. They discuss their results in terms of variable summation between underlying red and green receptor mechanisms.

In the present experiments we have introduced a light surround field which is variable in luminance and spectral color. The apparatus was in all details similar to that of Sperling and Lewis (*6*). A D246 Hilger and Watts double monochromator fitted with glass prisms was used. A 6-volt, 18-ampere ribbon filament source provided sufficiently intense spectral light over the wavelength range from 410 to 670 mμ to allow threshold determinations under all conditions of surround with bandwidths no wider than 4 mμ. A maxwellian view and an artificial pupil 2 mm in diameter were used. The relative energy content of the stimuli was determined by direct nonselective radiometry using a 0.75 mm^2 platinum black thermocouple in place of the artificial pupil. The surround field was provided by an integrating sphere 1 foot in diameter and an intense projector system which was adapted to accommodate interference filters. The stimulus filled a 20-minute diameter circle cut out of the 40° surround field and viewed at 62 cm. The eye was held behind the artificial pupil by fixing the head by means of a dental impression mounted on a three-way micromanipulator. The stimulus was of 40 msec duration as produced by a sector disc rotating in an image of the exit slit. A calibrated neutral density wedge and filters were used to reduce the stimulus to threshold. Fixation of the observer's eye was achieved by instructing him to look at the center of the small circular stimulus. Between trials he was instructed to fixate a point on the sur-

round. Our procedure was the threshold method of limits with wedge steps of 0.05 density. A complete curve was obtained each session, greatly reducing variability over previous studies which have explored only parts of the curve in single sessions.

Each point in Fig. 1 is the average of 24 threshold determinations combined from two observers. Superimposed on the dimmer (5.3 trolands) white surround curve (Fig. 1*a*) is shown the threshold curve obtained by Sperling and Lewis (*6*) for a completely dark surround by the same techniques. It is clear from this comparison that the secondary peak is reduced to a shoulder in the presence of the light surround, while the main peak retains almost the same shape up to 580 mμ where the second peak begins. The brighter white surround (800 trolands) in Fig. 1*b* shows an additional feature. A hump appears between 560 mμ and 590 mμ, which was never seen in the Sperling and Lewis dark surround data. It is clearly a regular feature of light surround data, as shown by a glance at *b*, *c*, and *e* of Fig. 1.

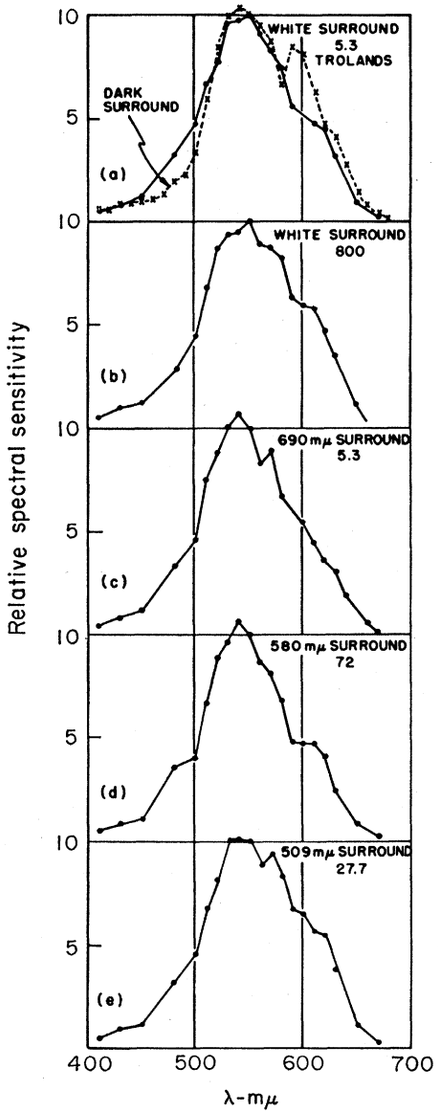

Fig. 1. Relative spectral sensitivity of the fovea for different conditions of surround adaptation: *a*, 5.3 troland white; *b*, 800 troland white; *c*, 5.3 troland 690 mμ red; *d*, 72. troland 580 mμ yellow; *e*, 27.7 troland 509 mμ green. Superimposed on *a*, as shown by crosses and dashed line, are the results obtained by Sperling and Lewis (*6*) with a completely dark surround.

Figure 1*c* shows the effects of red adaptation. The shoulder seen with the white surround from 590 to 670 mμ almost completely disappears, as had been found by Stiles and Crawford (*4*). The hump at 560 to 590 mμ becomes a more distinct peak. Of great interest is the fact that with a narrow waveband surround from the yellow region (580 mμ) the hump at 560 to 590 mμ is practically eliminated (Fig. 1*d*), while the shoulder at 590 to 670 mμ remains and is possibly exaggerated. In Fig. 1*e* are shown data taken with a 509 mμ narrow-band green surround. Here both the 560 to 590 and 590 to 670 mμ humps are retained. The main peak, however, appears somewhat reduced in the region of 540 mμ.

Our results thus indicate the presence of three humps or peaks in the green through red regions of the spectrum, one at 540 to 550 mμ in the green, one at 560 to 590 mμ in the yellow, and one from 580 to 590 mμ through the extreme red end of the spectrum. The "green" peak is slightly reduced by adaptation to the 509 mμ surround; the yellow is virtually eliminated by adaptation to 580 mμ; and the red, by adaptation to 690 mμ. Thus we have not only shown that the humps in the green-to-red part of the spectrum exist and are repeated from one set of data to another on the same observers, but also that they are produced by underlying processes which have maximum sensitivities at different places in the spectrum, since we can reduce or eliminate them by adaptation to narrow wavebands from those regions without any appreciable effect on the adjacent processes.

We conclude that it is most likely that the spectral sensitivity or luminosity function is a combination of the overlapping sensitivity functions of different chromatic receptor groups which appear to greater or less degree as humps in the composite curve. Of additional interest, it is probable that the dark-adapted sensitivity of the yellow process is lower. Hence, the yellow (560 to 590 mμ) hump does not appear at dark or dim surround levels but appears when brighter adaptation levels force more intense stimuli in order to reach threshold.

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14 February 1962

Dilute Locus and Audiogenic Seizures in Mice

Abstract. Evidence which indicates a positive relationship between susceptibility to audiogenic seizure and dilute coat color in mice is presented, and a possible mechanism for this relationship is discussed.

Susceptibility to audiogenic seizures has been demonstrated in mice with various coat colors. The character appears to be controlled by a quantitative genetic mechanism (*1*), and it is also influenced by many environmental conditions (*2*). Recently an analysis by Coleman (*3*) of biochemical activity of alleles at the dilute locus in various mouse strains has provided a plausible basis for implication of this locus with seizure susceptibility as well as coat color. He has demonstrated decreased phenylalanine hydroxylase activity in mice with dilute phenotypes. The reduced activity results in inhibition of tyrosine production and in formation of abnormal breakdown products from the accumulated phenylalanine. These products are inhibitors of decarboxylase reactions, including those concerned with the production of serotonin and γ-aminobutyric acid, compounds thought to be involved in normal brain metabolism. Therefore Coleman suggests that the influence of the dilute gene on phenylalanine hydroxylase activity may