J. Physiol. (1965), **179**, *pp.* 518–537
With 1 *plate and* 11 *text-figures*
Printed in Great Britain

THE SPATIAL PROPERTIES OF THE HUMAN ELECTRORETINOGRAM

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(*Received* 22 *January* 1965)

Cooper, Creed & Granit showed in 1933 that the electroretinogram produced by a flash of light that is imaged on the macula lutea differs slightly from that produced by a similar flash imaged on peripheral retina. In the following 25 years a number of attempts were made (for example, Monnier & Boehm, 1947; Crampton & Armington, 1955) to examine in more detail the relation between the position of a stimulus in the visual field and the electroretinogram that it produces. But in none of these attempts was the electrical activity of a clearly defined region of the retina recorded, since in none were any precautions taken to prevent light scattered within the eye from stimulating a much larger area of retina than that on which the geometrical image of the stimulus fell. The necessity of such precautions was first made probable by the experiments of Fry & Bartley (1935) on rabbits. It was conclusively established when, in 1951, Asher in England and Boynton & Riggs in America observed that a stimulus whose geometrical image falls wholly on the head of the human optic nerve (blind spot) gives an electroretinogram almost indistinguishable from that given by an otherwise similar stimulus whose image falls on functioning retina—indeed Asher found the blind spot to give a slightly larger response, perhaps owing to its higher reflectance.

The first investigation in which precautions were taken against unintentional stimulation of retina outside the geometrical image was that of Armington, Tepas, Kropfl & Hengst (1961). They superimposed the stimulus on a steady background illuminating most of the retina, but excluding the region of the stimulus, in the hope that the stray light from the stimulus would be weak compared with the background, and, falling below the electroretinographic Weber fraction, would therefore produce no electroretinogram. The hope seems not to have been fulfilled, for they, like Asher, found that a stimulus whose image fell on the blind spot produced a slightly larger response than one that lay a little nasal or temporal to it.

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In the experiments of the present paper we chose steady backgrounds much stronger than those used by Armington and his collaborators, and obtained clear evidence that such backgrounds are effective in eliminating the effects of stray light. We are therefore able to describe the electroretinograms characteristic of the various regions of the retina, to examine the degree to which the electroretinogram is spatially additive, and to establish electroretinographic perimetry as a technique available for the investigation of local disorders of the retina.

METHODS

Recording. A silver-wire electrode was embedded in the ocular surface of a scleral contact lens of which all but the pupil area was made opaque with black paint so as to screen the silver wire from the stimulating light. This sufficed to prevent photo-electric artifacts in controls where the subject was replaced by wet blotting paper. The conjunctival sac was anaesthetized with Pontocaine hydrochloride 0·5 % (tetracaine hydrochloride U.S.P.) for insertion of the contact lens, which was carefully selected to give the subject as good visual acuity as possible at the working distance (31 cm), and was kept free from scratches and blemishes. Nevertheless, acuity was always worse by a factor of about 1·2 than with the naked eye, and there was a perceptible veiling, black objects in a mainly bright field appearing slightly less black than they should.

The indifferent electrode was a circular silver plate 1·5 cm in diameter, thickly smeared with electrode jelly and strapped to the forehead.

The signal from the electrodes was fed into a Grass P 5 capacitance-coupled preamplifier adjusted so that its gain was 3 db down at 1·5 c/s and at 2000 c/s (see calibrations in the Text-figs.). The subject, the preamplifier, and the optical stimulator ('electroretinographic perimeter') of Pl. 1 *a–c* were placed in a screened room. All other equipment was outside the screened room. The amplified signal was displayed on a cathode-ray oscilloscope, and was also fed into an 'Enhancetron' electronic digital summing device (Nuclear Data Inc., Palatine, Ill., U.S.A.). This instrument converts into digital form the output of the preamplifier at each of 1024 or 512 instants during a single sweep (we always used 512), and adds together the outputs at corresponding instants of successive sweeps. In this way the noise from the electrodes and amplifier, and from irrelevant muscular, electroencephalographic and other biological activity, which should be proportional to the square root of the number of presentations, is reduced in comparison with the signal, which is directly proportional to the number of presentations. The electroretinogram of an area as small as those from which we recorded may be as little as a microvolt in amplitude, and without such a device would be lost in the noise. With fairly large areas we found that the sum of 50 or 100 responses gave satisfactory records (Text-figs. 1–4 and 6); from smaller areas we needed several thousand responses. The output of the 'Enhancetron', which represented the sum of the responses since the previous erasure of its memory, was displayed on one beam of the oscilloscope. The text-figures of this paper are photographs of these oscilloscope traces, except that Text-fig. 3 shows beneath each sum a single record typical of the fifty from which the sum was made.

Calibration. Rectangular pulses of a few microvolts were fed into the preamplifier through a resistance equal to that of the subject. Sums were obtained of a number of these pulses equal to the number of presentations of the light stimulus. These sums are directly comparable with the summed electroretinographic records, since the signal passed through the same sequence of operations, starting with the preamplifier and ending with the photography of the summed output from the 'Enhancetron'.

Stimulation. Plate 1*a*, *b* and *c* shows the stimulator ('electroretinographic perimeter') that was used in the experiments of Text-figs. 1–4 and 6. It consisted of a cluster of nine truncated pyramids painted white inside. Each pyramid had a 4 or 18 W electric light bulb near its apex, and its base was covered with a diffusing panel of tracing paper. The bases were of such shapes and sizes that when fitted together they formed a roughly hemispherical bowl of radius 31 cm. The eye's view of the electroretinographic perimeter is plotted in perimetric co-ordinates in the inset to Text-fig. 3. Sheets of black cardboard projected from the borders of the panels towards the eye. Four of these are shown in Pl. 1*c*. They prevented reflexion of light from panel to panel. The central pyramid (whose panel was square and is numbered 1 in the inset to Text-fig. 3) contained two electric light bulbs. One of these was in the main cavity of the pyramid. The other was in a separate compartment at the extreme apex, separated from the main cavity by a camera shutter. In the experiments of Text-figs. 1, 2 and 6, the stimulus was presented by opening this shutter. A small photocell monitored the light that entered the pyramid, and served to trigger the oscilloscope and the 'Enhancetron'.

In the experiments of Text-figs. 3 and 4, panels other than the central square were used for stimulating. In these experiments each stimulus was produced by switching on the appropriate lamp or lamps. The sudden change in the potential difference across the lamp was used to trigger the oscilloscope and 'Enhancetron'. Because of the time taken for the filament of the lamp to become hot, the stimulus began less suddenly than in the experiments of Text-figs. 1, 2 and 6, and its beginning coincided less exactly with the trigger; but comparison of (for example) Text-fig. 2 with Text-fig. 3 suffices to show that this defect is not important for the purpose of the present paper.

Variations in luminance of the panels were achieved by changes in the voltage supplied to the lamps. Luminance measurements were made with a S.E.I. photometer.

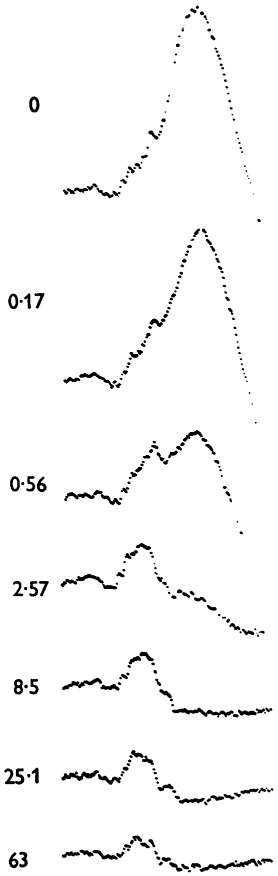
In the experiments of Text-fig. 6, a grating of eighteen vertical strips of white cardboard, each subtending 50 minutes of arc at the eye and separated from its neighbours by a gap also 50 minutes of arc wide, was mounted 6 cm in front of the central square panel (1 of Text-fig. 3). The cardboard strips could be illuminated by means of a lamp above the subject's head which was masked so that it shone on nothing else. Between the strips, the subject saw the tracing paper of the central panel, whose luminance could be controlled in the usual manner.

For the experiments of Text-figs. 5, 7, 8, 10, and 11 we used a simpler method of stimulation, which is illustrated in Pl. 1*d*. It consisted of a lens of focal length 25 cm which formed an image of the filament of a car headlamp bulb within the subject's pupil. The subject bit on a wax impression to fix his head. This Maxwellian system provided uniform retinal illumination in a region of the visual field up to 12° in diameter. The lens was mounted in the middle of a large sheet of white cardboard which was illuminated by two lamps placed beside the subject's head. Opaque white masks with holes in them could be placed over the lens to make the stimulus smaller, and fixation points were marked on the cardboard sheet wherever required. Neutral filters and a rotating sectored disk between the lamp and lens allowed the luminance to be varied and the stimulus to be made regularly intermittent. A photocell triggered the sweep of the 'Enhancetron' and oscilloscope at the beginning of the light portion of each cycle.

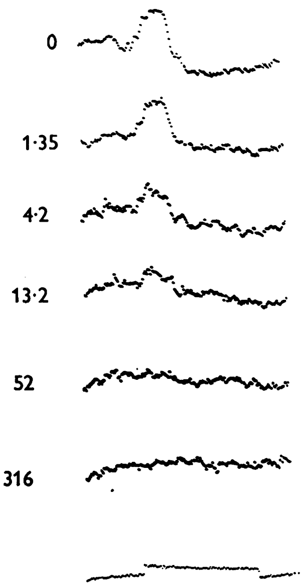
RESULTS

Suppression of stray light

The top record in Text-fig. 1 shows the sum of 100 responses obtained when the central panel of the electroretinographic perimeter—a centrally fixated square of side 30°—was flashed on with a luminance of 129 cd/m². The surrounding eight panels of the perimeter were dark. The e.r.g. has



Text-fig. 1



Text-fig. 2

Text-fig. 1. The effect of surround luminance on the electroretinographic response to a constant stimulus. The stimulus was a centrally fixated square of side 30° (1 in inset to Text-fig. 3; centre panel in Pl. 1*c*). Its luminance was 129 cd/m², and it was flashed on for 310 msec every 2·5 sec. Each record is a sum of 100 responses. The surround occupied regions 2–9 in the inset to Text-fig. 3, i.e. all the visual field except the stimulus area. Its luminance in cd/m² is given at the side of each record. The calibration given in Text-fig. 2 holds also for Text-fig. 1. In all records of this paper the beginning of each flash coincides very nearly with the beginning of the oscilloscope sweep. In Text-figs. 3 and 4 this coincidence is only approximate (see p. 519); elsewhere it is at least as exact as the photographic reproduction of the records.

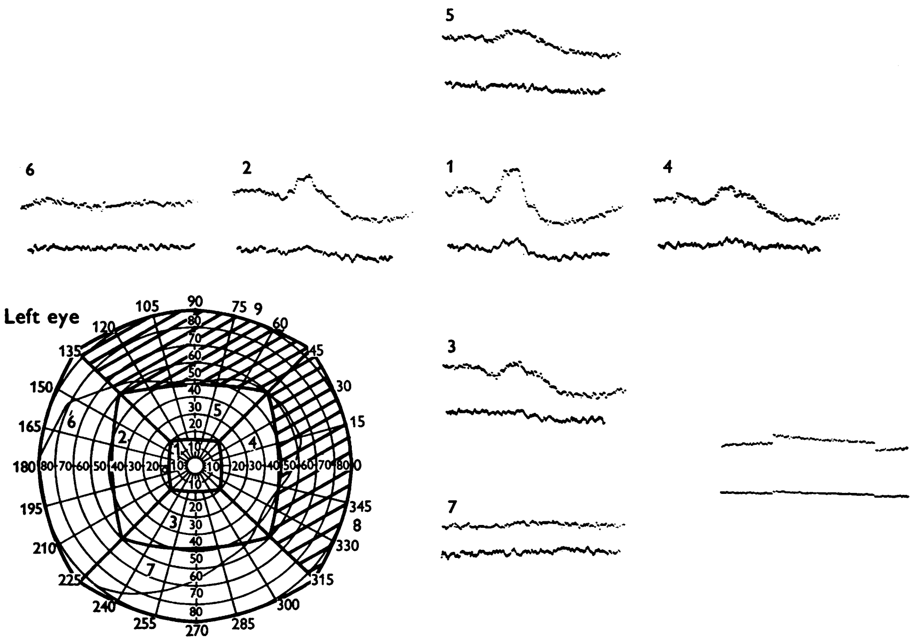
Text-fig. 2. The effect of superimposed background on the electroretinographic response to a constant stimulus. The stimulus was a centrally fixated square of side 30° (1 in the inset to Text-fig. 3; centre panel in Pl. 1*c*). Its luminance was 129 cd/m², and it was flashed on for 310 msec every 2·5 sec. Each record is a sum of 100 responses. The stimulus was superimposed on a background whose luminance (in cd/m²) is shown at the side of each record. The rest of the visual field (2–9 in the inset to Text-fig. 3) was steadily illuminated at 8·5 cd/m². The calibration below shows the sum of 100 rectangular pulses of amplitude 5·5 μV and duration 100 msec applied to the preamplifier.

a small *a* wave and a very prominent *b* wave with an amplitude of about $110 \mu V$. On the rising phase of the *b* wave there is a small subsidiary peak. The other records in the same figure were obtained with an identical stimulus, except that the 8 surrounding panels were now steadily illuminated at successively higher luminances from 0·107 cd/m² in the second record to 63 cd/m² in the bottom record. It can be seen that the electroretinogram changes greatly as the surround luminance increases: the main peak of the *b* wave decreases and then disappears. The small subsidiary peak on its rising phase persists and becomes the most conspicuous feature of the response. An obvious interpretation of these findings (an interpretation in whose favour we shall give further evidence) is that the main peak of the *b* wave in the record obtained with the surround dark is due to stray light falling on retina outside the geometrical image of the central panel. With increasing surround luminance, a stage is reached when the stray light falls below the incremental electroretinographic threshold for the surround, and we are left with a response which is substantially that of the region of the retina on which the geometrical image of the stimulus falls. This occurs when the surround luminance is about 8·5 cd/m². The reduction of the electroretinogram for the same stimulus with higher surround luminances is probably due to the desensitization of the central region of the retina by stray light derived from the surround.

Text-figure 2 shows the effect of adding background to the stimulus. As in Text-fig. 1, the stimulus was a 30° centrally fixated square flashed on at 129 cd/m². All eight surround panels remained on continuously at 8·5 cd/m² to eliminate the effects of stray light. The individual records in Text-fig. 2 differ one from another in the amount of steady light that was added as a background to the central square. In the top record there is no such background. In successive lower records, brighter and brighter background in the central square decreases the amplitude of the response until there is no detectable response when the background is 316 cd/m². This is the human counterpart of any column (e.g. column 4) of Fig. 1 of Brindley (1956) for the frog, or Fig. 1C of Cone & Platt (1964) for the rat, and allows the Weber fraction for the human electroretinogram to be assessed. In support of the interpretation of Text-fig. 1 already given, it shows that a steady luminance of 8·5 cd/m², which abolishes the main peak of the *b*-wave when placed in the whole visual field except the stimulus area, has almost no further effect when added to the stimulus area as well; whereas a steady luminance of 52 cd/m², whose effect on the early peak of the *b*-wave is small when it is placed in the whole visual field except the stimulus area, abolishes the response almost completely when placed in the stimulus area.

Large-scale electroretinographic perimetry

It appears from Text-fig. 1 that a surround whose luminance is one fifteenth of that of the stimulus suffices to suppress the stray light electroretinographic response of adjoining areas; and that if the surround luminance is much greater than this, it reduces the response of the central



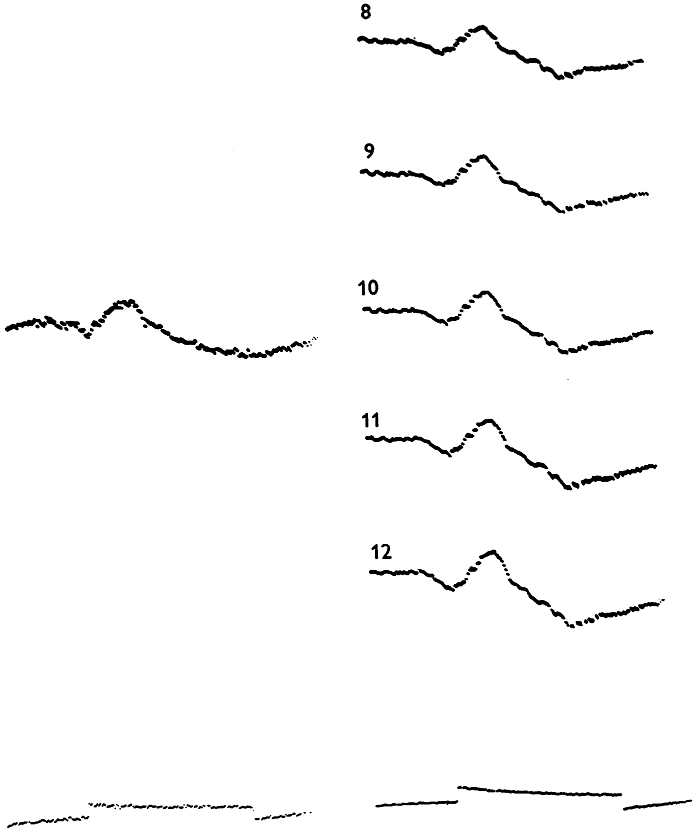
Text-fig. 3. Electroretinograms produced by stimuli in different parts of the visual field. Each record shows a single response and above it, at reduced amplification, the sum of 50 responses, when one of the seven regions of the visual field shown unshaded in the inset was suddenly illuminated for about 500 msec every 2·5 sec at luminance 52 cd/m². The whole visual field, except for the region flashed, was always steadily illuminated at 8·5 cd/m². The calibration shows records of a single pulse, and above it the sum of 50 pulses, of amplitude 5·5 μV and duration 100 msec. As can be seen the vertical scales for single records and sums differ by a factor of about 15. In this Text-fig. and in Text-fig. 4 the onset of the stimulus coincided with the beginning of the sweep except for the time taken for the filament of the lamp to become hot; this can be seen by comparison with Text-fig. 2 to be almost negligibly short.

area. In examining regional variations of the electroretinogram (Text-fig. 3) we used a surround whose luminance was one-sixth of that of the stimulus, and hence fully enough to eliminate the effects of stray light if our interpretation of Text-fig. 1 is correct. Of the panels 1–7, all but one were kept on steadily, and 50 flashes of the remaining one were summed on the 'Enhancetron'. Regional variations are quite prominent: the central panel gives the largest response although it has the smallest area, the inner temporal panel (2) gives a higher amplitude than any other panel of the inner ring (3–5), and the outer panels (6 and 7) give almost no responses. The areas covered by panels of the three kinds (central, inner peripheral, and outer peripheral) are in the ratio of 1:3:6. The great reduction of the amplitude of the electroretinogram as one goes from the centre to the periphery of the visual field is brought out in further detail in Text-figs. 8–10.

Spatial additivity of the electroretinogram

In the frog, Brindley (1956, 1957) was able to show that the sum of the electroretinograms produced by several retinal regions is equal to the single electroretinogram produced when all these regions are stimulated simultaneously. Text-figure 4 shows a test to see whether such additivity holds for the human eye. Ten flashes were delivered to each of panels 1–5 (see inset to Text-fig. 3) in succession, and the sum of the responses to these fifty stimuli was recorded. This is shown on the left side of Text-fig. 4. Then panels 1–5 were flashed simultaneously twelve times. The sums of 8, 9, 10, 11 and 12, responses are shown on the right side of Text-fig. 4. In this experiment, all the panels that were not flashed remained on constantly. If there is additivity, the sum of ten responses to panels 1–5 flashed simultaneously will be equal to the sum of 50 responses produced by flashing each of panels 1–5 separately ten times. The good agreement between the record on the left side of Text-fig. 4 and the middle record (representing 10 flashes) of the right side shows that spatial additivity holds for these large regions of the visual field of the human eye. The calibration records show that the associative law holds between summation and size of signal, i.e. that the sum of $n.a$ responses of voltage V yields the same record as the sum of n responses of voltage $a.V$.

The retinal regions covered by the stimuli in Text-fig. 4 are large. Text-figure 5 shows a test of additivity for smaller retinal regions. The stimulus situation was the second one described in the Method section (p. 520; Pl. 1*d*). The electroretinograms of small regions have low amplitudes, and very many responses must be summed to obtain usable records. A high frequency of stimulation was therefore used. The records shown are all sums of a large number of flashes given at a repetition frequency of 14·3 c/s. The number of flashes was chosen to make the product of number of flashes and area stimulated a constant, because if additivity holds, the summed e.r.g. should then be constant. The records of Text-fig. 5 show that this is very nearly true. Since the amount of noise is smaller the smaller the number of responses summed (and should ideally be proportional to the square root of that number), the scatter of the dots decreases from left to right of the figure.

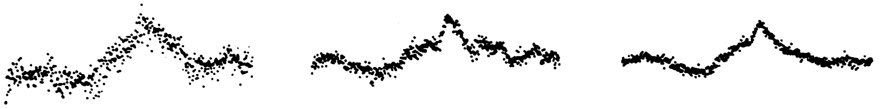


Text-fig. 4. Additivity of the electroretinogram. On the left is shown the sum of ten responses to the illumination of each of the panels 1 to 5 of the inset to Text-fig. 3 (50 responses in all). The stimuli were of luminance 52 cd/m² and duration about 500 msec, and were delivered regularly every 2·5 sec. Those panels from 1 to 5 which were not flashed were steadily illuminated at 8·5 cd/m², and the outer panels (6–9) were steadily illuminated at 25·7 cd/m². On right are the sums of 8, 9, 10, 11, and 12 responses to the illumination of panels 1–5 simultaneously for about 0·5 sec every 2·5 sec at 52 cd/m² while the remainder of the field (panels 6–9) remained steadily illuminated at 25·7 cd/m². The extent to which the record on the left matches the middle one of the records on the right indicates the spatial additivity of the e.r.g. for these large fields. Calibration records: left, sum of 50 rectangular pulses of 5·5 μV and 100 msec; right, sum of 11 rectangular pulses of 25·3 μV and 100 msec. The similarity of these two records shows that summation on the 'Enhancetron' obeys the associative law with respect to size of signal.

Experiments with a grating as stimulus

We tried to answer the following questions, which are not wholly independent of each other.

1. Does the spatial additivity already demonstrated on a large and on a moderately small scale hold also on a very small scale?



Text-fig. 5. Additivity of the electroretinogram on a smaller scale. The stimulus was a circular field of luminance 339 cd/m^2 centred on a point 27° from the fixation point. A surround extending beyond 60° in all directions was steadily illuminated at 17·0 cd/m^2. The stimulus was flashed on for 7 msec every 70 msec; thus the *mean* luminance of the stimulus was 33·9 cd/m^2. Left: field 4° 30′ diameter, sum of 2856 responses. Middle: field 7° 22′ diameter, sum of 1070 responses. Right: field 11° 34′ diameter, sum of 322 responses. The product of area and number of responses is a constant for all three records; thus the degree to which they are similar (except in the amount of noise) indicates the spatial additivity for these relatively small fields. The records in this Text-fig. and in Text-figs. 7, 8, 10 and 11 are 62·5 msec in length.

2. Does the activity of the retina that is revealed in the electroretinogram depend on spatial contrast of illumination, as the activity of ganglion cells does, or only on how much light is received by the illuminated areas?

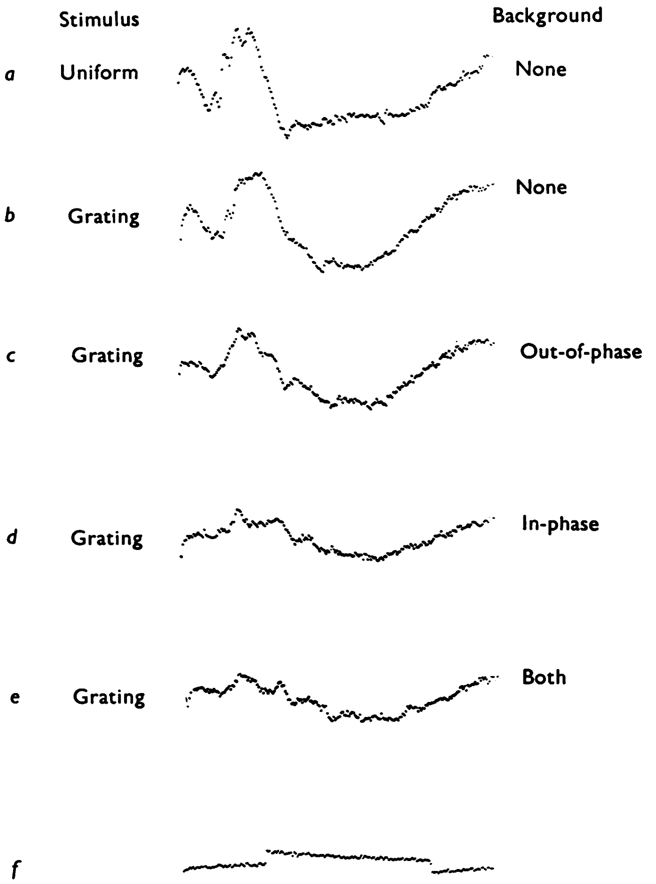
3. Does steady illumination of a region of the retina affect the electroretinographic response to an additional stimulus only if this (or part of it) falls on the same region of the retina, or also if it falls on neighbouring retina?

Text-figure 6 illustrates the relevant experiment. All the five records in it are sums of the same number of responses (50) with the same luminances of stimulus (107 cd/m^2) and of steady surround (19 cd/m^2). In *a* the stimulus was a uniform square of side 30°; in *b* to *e* it was the same 30° square covered with a grating of period 1° 40′ consisting of alternating opaque and transparent strips of equal width. The stimulating flashes appeared in the transparent strips. They were superimposed on a steady background of 33·9 cd/m^2 appearing in the opaque strips (*c*), the transparent strips (*d*), both (*e*), or neither (*b*).

The answers given to our questions by the experiment are:

1. Since record *c* resembles record *a* but is of about half its amplitude, spatial additivity holds approximately on this small scale. In fact, *c* slightly exceeds half *a*. This suggests a small departure from additivity, an 'occlusion' in the Sherringtonian sense, but it does not suffice to prove it, for our controls against stray light are not stringent enough to exclude

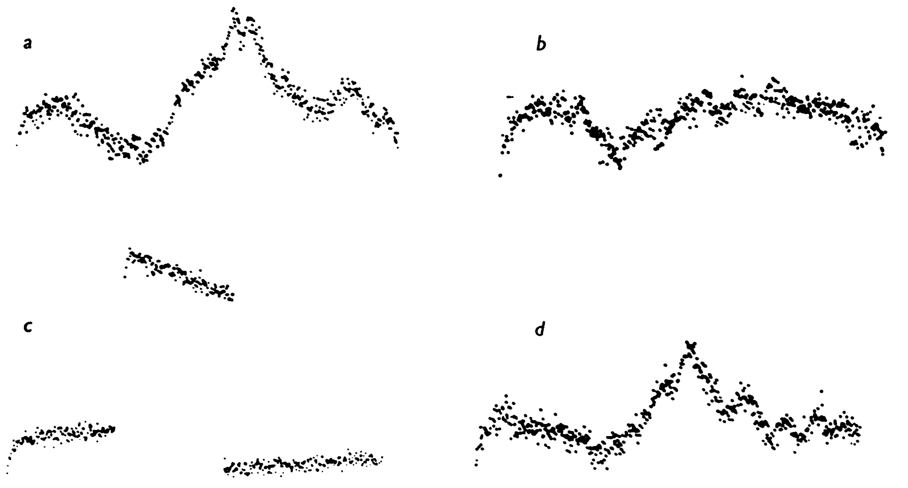
responses to the very strong stray light that must (see Westheimer, 1963) be present within a few microns of the boundaries of the geometrical image of the stimulus.



Text-fig. 6. Electroretinogram for grating stimuli. All records are sums of 50 responses. (*a*) A centrally fixated square of side 30° and luminance 107 cd/m² was flashed on for 310 msec every 2·5 sec. The remainder of the visual field (panels 2 to 9 inclusive) was steadily illuminated at 19·1 cd/m². (*b*) Conditions as in (*a*) except that the flashing stimulus field consisted of eighteen bars, each 50 min of arc wide and 107 cd/m² in luminance, separated by bars 50 min of arc wide which remained dark throughout. (*c*) Conditions as in (*b*), except that those bars of the grating in which the stimulus *did not* appear were steadily illuminated at 33·9 cd/m². (*d*) Conditions as in (*b*), except that those bars of the grating in which the stimulus *did* appear were steadily illuminated at 33·9 cd/m². (*e*) Conditions as in (*b*), (*c*) and (*d*), except that the whole of panel 1, both the bars where the stimulus appeared and those where it did not, was steadily illuminated at 33·9 cd/m². (*f*) Calibration: sum of 50 rectangular pulses of 5·5 μV and 100 msec.

2. Since record *b* is smaller than record *a*, spatial contrast of illumination evidently makes no large contribution to the electroretinogram. We cannot tell whether it may make a small one.

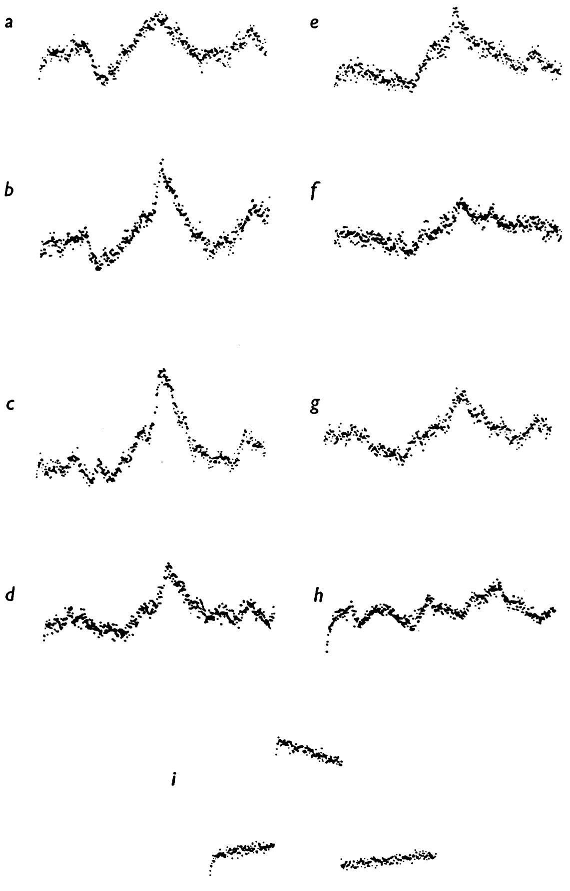
3. The very clear difference between *c* and *d*, taken with the similarity between *c* and half *a*, shows that a steady light that is strong enough to depress greatly the sensitivity of the regions of the retina on which it falls does not depress substantially the sensitivity of closely neighbouring regions. This is in contrast, but not in conflict, with the observations of Rushton & Westheimer (1962) on visual thresholds; the spatial interaction that they observed appeared clearly only with gratings nearly twice as fine as that of Text-fig. 6.



Text-fig. 7. Electroretinogram for stimuli falling on the blind spot. The stimulating field was a circle of diameter 7° 22′ and luminance 339 cd/m², and was flashed on for 7 msec every 70 msec. It was surrounded by a steady field of luminance 17·0 cd/m² extending to at least 60° in all directions. Each record is a sum of 1428 responses. Location of flashing field: (*a*) temporal retina in a position equivalent to blind spot; (*b*) nasal retina, centred on blind spot; (*d*) nasal retina, 30° from fixation point, and hence peripheral to blind spot. (*c*) Calibration: sum of 1428 rectangular pulses 5·5 μV in amplitude and 20 msec in duration.

Electroretinographic detection of the blind spot

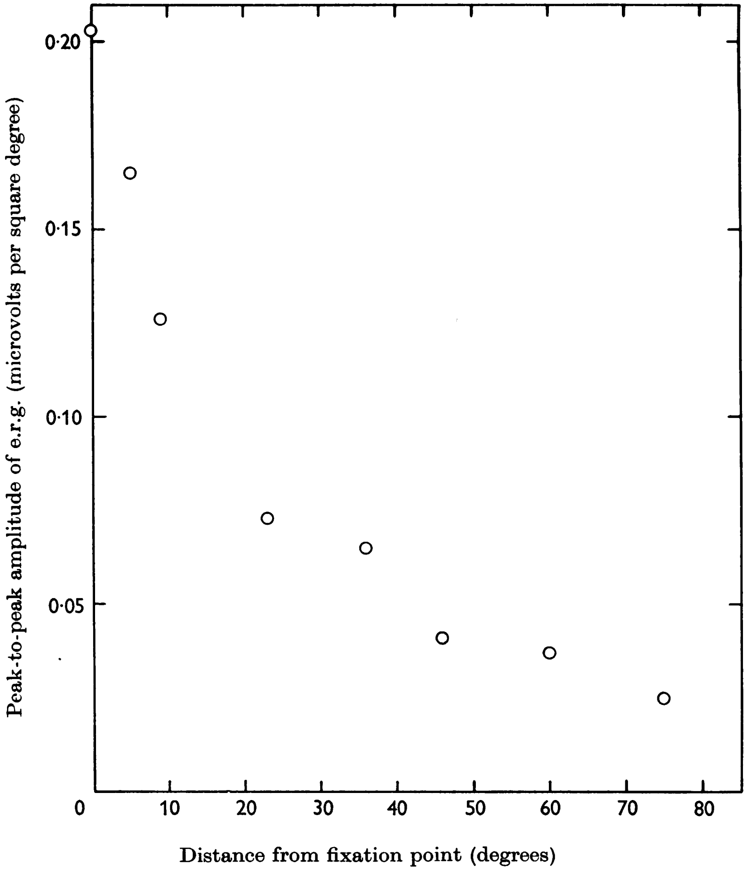
One of the clearest pieces of evidence that our backgrounds suffice to eliminate nearly all the effects of stray light comes from the experiment of Text-fig. 7. A stimulus very slightly larger than the blind spot was presented either centred on the blind spot (record *b*), or peripheral to the blind spot (record *d*), or as far to the nasal side of the fixation point as the blind spot is to its temporal side (record *a*). When centred on the blind spot it gave a small response of unusual shape; when it fell wholly on retina at equal (*a*) or greater (*d*) eccentricity, it gave a much larger response of the shape typical of extrafoveal retina under such conditions (cf. Text-figs. 5 and 8*a*–*g*).



Text-fig. 8. Electroretinograms produced by different parts of the visual field. Circular stimuli of various diameters, placed at various distances from the fixation point along the temporal horizontal meridian, were flashed on for 7 msec every 70 msec. The luminance of each flash was 339 cd/m^2. A steady surround of 17·0 cd/m^2 extended to at least 60° in all directions. (*a*) 11° 34′ diameter, 75° eccentricity, sum of 1428 responses. (*b*) 11° 34′ diameter, 60° eccentricity, sum of 1428 responses. (*c*) 11° 34′ diameter, 46° eccentricity, sum of 1428 responses. (*d*) 7° 22′ diameter, 36° eccentricity, sum of 1428 responses. (*e*) 7° 22′ diameter, 23° eccentricity, sum of 1428 responses. (*f*) 4° 30′ diameter, 9° eccentricity, sum of 1428 responses. (*g*) 4° 30′ diameter, 5° eccentricity, sum of 1428 responses. (*h*) 2° diameter, 0° eccentricity, sum of 2856 responses (displayed at 1/2 gain). (*i*) Calibration: sum of 1428 rectangular pulses of amplitude 5·5 μV and duration 20 msec.

Small-scale electroretinographic perimetry

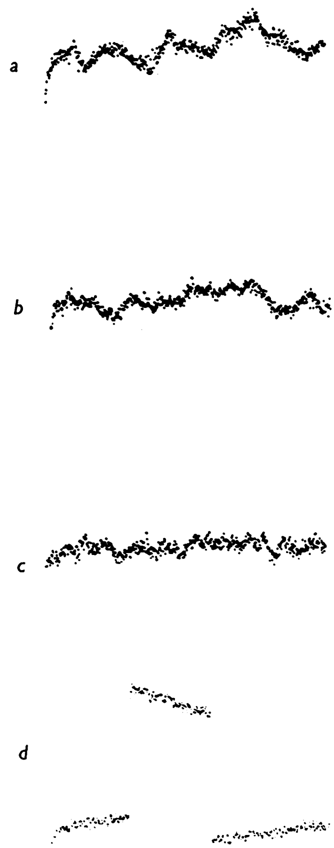
It has already been seen from the experiment of Text-fig. 3 that the amplitude of response for a stimulus subtending a given solid angle at the eye decreases with increasing distance from the fixation point. Text-figure 8 shows this in more detail. We did not here attempt to use stimuli of constant angular subtense, for if such stimuli had been large enough to



Text-fig. 9. Peak-to-peak amplitude of electroretinogram (μV per square degree of stimulus), plotted as a function of eccentricity of stimulus in degrees. The amplitudes are measured from the records shown in Text-fig. 8.

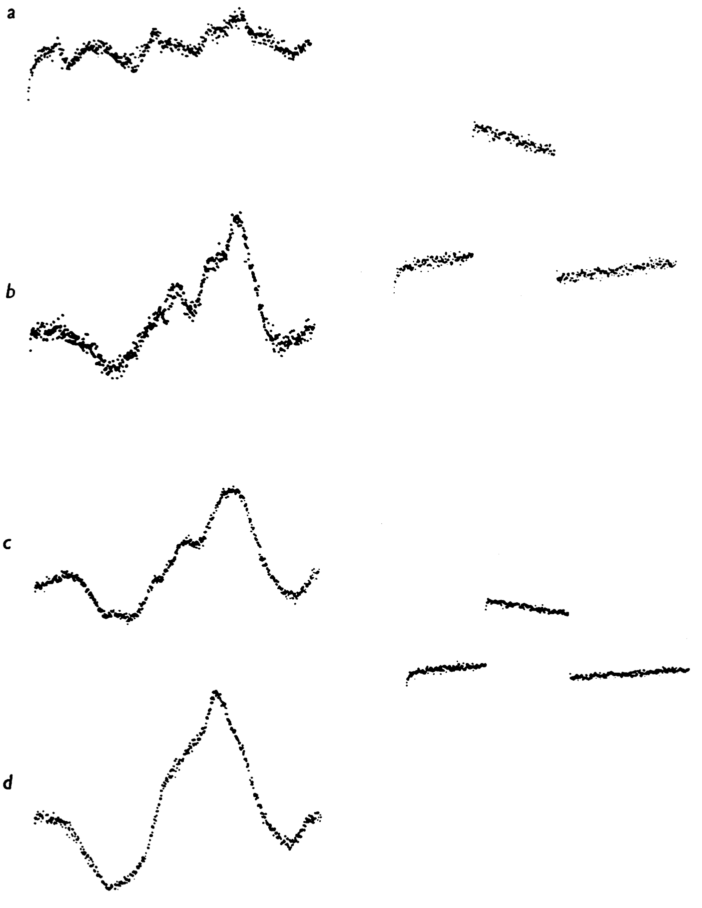
give detectable responses in the far periphery they would have been too large to resolve local differences in the responses of more central retina. In Text-fig. 9 the amplitude of the electroretinogram per square degree of stimulus is plotted as a function of distance from the fixation point.

The shapes of records *a* to *g* in Text-fig. 8 do not differ greatly. The only clear differences are that the peak of the *b*-wave comes a little later in the parafoveal record (*g*) than in more peripheral records, and that the amplitude of the *a*-wave is a larger fraction of that of the *b*-wave in the extreme periphery (*a*) and (*b*) and in the parafovea (*g*) than intermediately.



Text-fig. 10. Electroretinograms for a small field at various eccentricities. The field was 2° in diameter, and was flashed on for 7 msec every 70 msec at luminance 339 cd/m². A steady surround of 17·0 cd/m² extended to at least 60° in all directions. All records are sums of 2856 responses. (*a*) Field centred on fixation point. (*b*) Field centred 2° to nasal side of fixation point. (*c*) Field centred 4° to nasal side of fixation point. (*d*) Calibration 5·5 μV and 20 msec.

However, the foveal record, *h*, differs very clearly from the rest. Text-figure 10 compares this foveal record with those obtained with a stimulus of the same angular subtense displaced by 2° and 4° from the fixation point. At 4° eccentricity there is no detectable response. Besides indicating how special to it are the properties of the fovea, this is further evidence of the effectiveness of our precautions in preventing stimulation by stray light. Text-figure 11 compares the foveal record with those obtained with larger stimuli centred on the fixation point. Only when the field is small enough to be strictly foveal (record *a*) does the response differ conspicuously in its shape from the responses of peripheral retina. As



Text-fig. 11. Electroretinograms produced by centrally fixated stimuli. Stimuli of diameters (*a*) 2°, (*b*) 4° 30′, (*c*) 7° 22′, (*d*) 11° 34′ were flashed on for 7 msec every 70 msec at luminance 339 cd/m². A steady surround of 17·0 cd/m² extended to at least 60° in all directions. Records *b*, *c* and *d* are sums of 1428 responses, record *a* the sum of 2856 responses. Record *a* is displayed at half the vertical gain used for record *b* to compensate for its being the sum of twice as many responses. The upper calibration (5·5 μV and 20 msec) is thus applicable to both of them. Records *c* and *d* are displayed at the same gain as *a*, and the lower calibration (also 5·5 μV and 20 msec) is applicable to them.

might be expected from the progressive increase in the time between the beginning of the flash and the peak of the *b*-wave in the last three records of Text-fig. 8, the peak of the *b*-wave comes progressively a little earlier as the size of a centrally fixated stimulus increases.

DISCUSSION

Criteria for deciding when the effects of stray light have been eliminated

We have four tests to decide when a background suffices to prevent electroretinographic responses to stray light falling outside the geometrical image of the stimulus:

1. Examination of the effects of various strengths of background on the response to a constant stimulus (Text-figs. 1 and 2).
2. Comparison of the effects of an in-phase and an out-of-phase grating background on the response to a grating stimulus (Text-fig. 6*c* and *d*).
3. Comparison of the responses to similar stimuli falling on the blind spot and on retina (Text-fig. 7).
4. Comparison of the responses to similar stimuli falling on the fovea and a few degrees from it (Text-fig. 10).

The first of these tests is chiefly of value in showing what backgrounds certainly do not suffice. The large late peak in the first three records of Text-fig. 1 cannot reasonably be explained on any hypothesis except that of stray light, for it is very greatly depressed by an intensity of steady illumination outside the geometrical image of the stimulus which, when put within the geometrical image, has no effect. The experiment of Text-fig. 1 thus shows that for a large and long stimulus a background fifty times dimmer than the stimulus (2·57 cd/m^2 against 129 cd/m^2) certainly does not suffice, and one fifteen times dimmer (8·5 cd/m^2 against 129 cd/m^2) probably does. If Weber's law holds as well for man's electroretinogram as it does for the frog's (Brindley, 1956), the fraction needed should be nearly independent of the absolute value of the luminance. Slightly stronger backgrounds would probably be necessary for smaller stimuli, because reduction in area of the stimulus should decrease the direct signal more than the stray-light signal. Weaker backgrounds would probably suffice for briefer stimuli, because the electroretinographic Weber fraction presumably resembles the sensory Weber fraction in decreasing with the duration of the stimulus when this is below a few hundredths of a second.

The second test (Text-fig. 6) shows clearly that steady illumination at 2/11 of the actual stimulus luminance (19·1 cd/m^2 against 107 cd/m^2), i.e. 1/11 of the mean luminance that the stimulus contributes to the central 30° square, abolishes at least most of the response to stray light falling outside the central square; for if any substantial fraction of the observed responses were due to such stray light, the effects of in-phase and out-of-phase gratings could not differ as they do.

The third test shows that the background luminance that we chose for demonstrating the blind spot (here only 1/20 of the stimulus; but these stimuli were only 7 msec in duration, and reduction in duration is certainly to some extent equivalent to reduction in luminance) leaves little that can be attributed to stray light. There is indeed a small response, but part of this must be due to encroachment of the geometrical image of the stimulus on to retina at the margins of the disk, and part may perhaps come from muscular or electroencephalographic artifacts; the residue that is due to stray light can hardly exceed 1/6 of the amplitude of Text-fig. 7*a*.

The fourth test, again with a background luminance 1/20 of that of the stimulus, closely resembles the third. Here too, if there is in the slight and perhaps insignificant response obtained when the stimulus was placed 4° from the fovea (Text-fig. 10*c*), any part due to stray light, it can hardly exceed 1/6 of the amplitude of the foveal response (Text-fig. 10*a*).

Comparison with the conditions used by Armington et al. (1961)

In their photopic experiments these authors used 18 flashes per second, each of luminance (23,000 foot-lamberts multiplied by the transmission fraction of Corning filter 2434), i.e. probably about 28,000 cd/m^2. These stimuli were placed on a background of 0·2 foot-lamberts, i.e. 0·7 cd/m^2 or probably about 1/40,000 of the flash luminance. Our experiments suggest that such a background would be too weak by several orders of magnitude to eliminate the effects of stray light. In the scotopic experiments of Armington and his collaborators the luminance of the background seems to have been an even smaller fraction of that of the flash.

The special features of the foveal electroretinogram

Foveal and extrafoveal cones differ in structure, and the corresponding bipolar cells differ in structure, organization and orientation. It is thus not surprising that the foveal electroretinogram is different from the extrafoveal. The difference is not to be attributed solely to the fact that the fovea contains no rods, for at 14·3 flashes/sec it is very probable that all our responses, extrafoveal as well as foveal, depended solely on cones.

Additivity

The exact additivity that we have demonstrated on a large and on a moderate scale was what we expected to find by analogy with the frog (Brindley, 1956, 1957), and we regard it mainly as confirmatory evidence that we succeeded in reducing the stray-light component of our records to a negligible fraction of the whole. The rough additivity on a small scale shown by the grating experiment was not to be predicted from any previously known fact, and is a little surprising. It would be interesting, but technically difficult, to examine whether additivity holds on an even smaller scale.

The practicability of clinical electroretinographic perimetry

The ability to record, as we have done, a local response produced by a 2° stimulus on the fovea, a $4\frac{1}{2}$° stimulus 9° from the fovea, or an $11\frac{1}{2}$° stimulus in the far periphery of the visual field, and to do any of these in 100 sec of recording time, is already of interest in making possible the electroretinographic investigation of local retinal disorders, and not only, as hitherto, of disorders that affect the whole retina. The equipment needed, that of our second technique (Pl. 1*d*), is not complex, though some of it is expensive.

For such use, the frequency of stimulation that we used, 14·3 flashes/sec, is probably near the optimum, since higher frequencies give much smaller responses, and lower frequencies increase the time required for a given number of stimuli without making each response much larger. For an on-off ratio of 1:10 a background whose luminance is 1/20 of that of the flash (i.e. $\frac{1}{2}$ of the *mean* luminance) is probably not far from the optimum, but a fairly wide range of backgrounds is likely to be acceptable; whatever choice is made must be justified by showing that it distinguishes blind spot from retina and fovea from near extrafovea.

We think that with any co-operative subject it will be fairly easy to equal the spatial resolving power that we achieved, but difficult to improve on it greatly. A recording electrode that is optically better than ours can bring no more than a small advantage. Increase in the luminance of both stimulus and background, the proper ratio being preserved, will increase the amplitude of the responses, but only by a little. The Enhancetron, like all digital summing devices, is limited in the speed at which it can gain information, and when the duration of each of the 512 segments into which it divides each record is as short as 125 μsec (as it has to be at 14·3 flashes/sec), it can accumulate only two binary digits per time-segment per response, so that if the input has a fairly high signal-to-noise ratio some information will be wasted; but in electroretinographic perimetry with small stimuli the signal-to-noise ratio of a single record is so low that this waste is small, and it seems unlikely that substitution of an ideal computer for the Enhancetron could as much as double the rate of gain of information. Another technique that might be tried for improving the detection of very small signals is increased in the recording time; but recording times longer than 100 sec are tiresome for the subject, and though the final signal-to-noise ratio should in theory rise in proportion to the square root of the recording time, in practice it usually rises less because no subject can remain very still for very long.

SUMMARY

1. A technique has been developed for recording the electroretinogram of any small region of the human retina. Responses to stray light are suppressed by steady illumination of the whole retina outside the geometrical image of the stimulus.

2. The technique is easily capable of detecting the blind spot, and of examining the electrical response to a stimulus of 2° diameter centred on the fixation point.

3. For stimuli larger than several square degrees, the electroretinogram shows exact spatial additivity. On a finer scale it is at least roughly additive.

4. The foveal electroretinogram differs in shape from the extrafoveal. The electroretinograms of different regions of the extrafoveal retina differ greatly one from another in their amplitude per unit area of retina, but little if at all in their shape.

This work was supported in part by grant NB 03154 from the National Institutes of Health, U.S. Public Health Service and by contract Nonr 222 (82) between the Office of Naval Research and the University of California.

REFERENCES

ARMINGTON, J. C., TEPAS, D. I., KROPFL, W. J. & HENGST, W. H. (1961). Summation of retinal potentials. *J. opt. Soc. Amer.* **51**, 877–886.

ASHER, H. (1951). The electroretinogram of the blind spot. *J. Physiol.* **112**, 40*P*.

BOYNTON, R. M. & RIGGS, L. A. (1951). The effect of stimulus area and intensity on the human retinal response. *J. exp. Psychol.* **42**, 217–226.

BRINDLEY, G. S. (1956). The effect on the frog's electroretinogram of varying the amount of retina illuminated. *J. Physiol.* **134**, 353–359.

BRINDLEY, G. S. (1957). Additivity in the electroretinogram. *J. Physiol.* **137**, 51–52*P*.

CONE, R. A. & PLATT, J. R. (1964). Rat electroretinogram: evidence for separate processes governing b-wave latency and amplitude. *Science*, **144**, 1016–1019.

COOPER, S., CREED, R. S. & GRANIT, R. (1933). A note on the retinal action potential of the human eye. *J. Physiol.* **79**, 185–190.

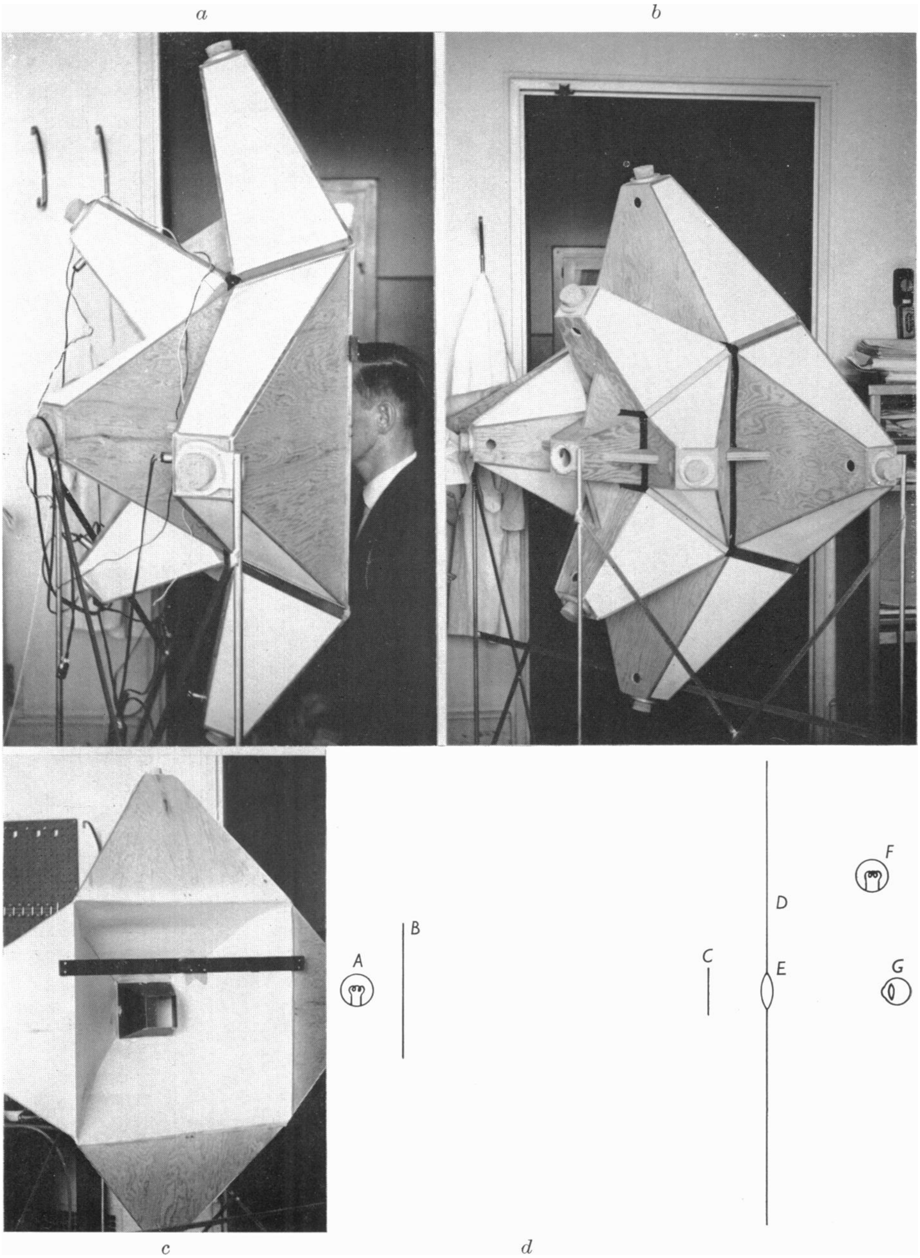
CRAMPTON, G. H. & ARMINGTON, J. C. (1955). Area-intensity relation and retinal location in the human electroretinogram. *Amer. J. Physiol.* **181**, 47–53.

FRY, G. A. & BARTLEY, S. H. (1935). The relation of stray light in the eye to the retinal action potential. *Amer. J. Physiol.* **111**, 335–340.

MONNIER, M. & BOEHM, F. (1947). Beiträge zum Elektroretinogramm des Menschen. I. Perimetrische Elektroretinographie. *Helv. Physiol. Acta*, **5**, 205–244.

RUSHTON, W. A. H. & WESTHEIMER, G. (1962). The effect upon the rod threshold of bleaching neighbouring rods. *J. Physiol.* **164**, 318–329.

WESTHEIMER, G. (1963). Optical and motor factors in the formation of the retinal image. *J. opt. Soc. Amer.* **53**, 86–93.


a
b
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EXPLANATION OF PLATE

a, *b* and *c*. The electroretinographic perimeter used in the experiments of Text-figs. 1–4 and 6. *d*. Diagram of the apparatus used in the experiments of Text-figs. 5, 7, 8, 10 and 11 *A* and *F*, lamps; *B*, rotating sectored disk; *C*, holder for neutral filters; *D*, screen of white cardboard; *E*, lens of focal length 25 cm and diameter 7·5 cm; *G*, subject's eye.