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THE EFFECT OF COLOR ON THE LOCALIZATION OF THE SOURCES OF THE HUMAN VISUAL EVOKED RESPONSE

DISSERTATION

Presented in Partial Fulfillment of the Requirements for the Degree Doctor of Philosophy in the Graduate School of The Ohio State University

By
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The Ohio State University
1976

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FIELDS OF STUDY


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INTRODUCTION

A change in the light stimulating the eye can markedly influence electric currents in the brain. This phenomenon, first reported by Caton a century ago, is the physiological basis of the visual evoked response (VER). It was some 50 years later before Berger, using the electron tube, succeeded in recording human brain waves from the intact skull. He named this electric activity the electroencephalogram (EEG). Work on the human VER was still hampered by the predominance of the ongoing EEG. It was not until about 1960 that the electronic signal averager became available and allowed isolation of the VER. Soon there were a plethora of reports on the abundant parameters that correlated in some degree with some feature of the VER. Work aimed at the functional significance of the VER produced conflicting reports, only some of which have been resolved. Vaughan[1] reflects the growing attitude among VER researchers that first we must know in detail the "when and where" of the VER before it can become an analytical tool in the study of brain mechanisms.

Researchers at several laboratories including this one have attempted to find the sites of brain activity responsible for the various time components of the VER. In the
process of our localization study, we discovered a color sensitivity in the potential distribution over the surface of the head at the latency of the first major peak (ca. 80 ms). The purpose of this dissertation is to explore the effect of different colored stimuli on the source localization of this peak and thereby reveal a topographical distribution of color sensitivity in the VER.

Before considering the location of the source of the VER and its color sensitivity we need to agree on its general meaning. Creutzfeldt and Kuhnt [2] define evoked potentials in general as the bioelectric response of nervous tissue (field potentials) following adequate stimulation or electrical stimulation of sensory organs, afferent nerves, or other cerebral structures neuronally connected with the recorded area (p 595). However, the human VER is operationally defined as the scalp potential response that is synchronized with a repetitive visual stimulus. Considerable effort has been spent in clarifying the implied relations of these two definitions. The two main controversies involved here will be only briefly reviewed.

The first question is whether or not scalp potentials reflect cortical potentials. In a hemispherectomy studied by Cobb and Sears [3], artificial generators located in the midbrain had to be much larger than those typical of brain tissue in order to produce measureable scalp potentials.
Abraham and Ajmone-Marson [4] found that small cortical sources often did not produce measureable potentials at the scalp. These results were confirmed by Cooper et al. [5] whose comparison of scalp and cortex records showed only limited similarities. Heath and Galbraith [6] also found limited similarities, but Corletto et al. [7] and Rayport et al. [8] found satisfactory agreement. The important difference in the latter experiments was their use of relatively large cortical electrodes, 2 mm in diameter compared to 150 µ and 50 µ in the other studies. There is now general agreement that scalp electrodes record accurate but attenuated versions of potentials on the cortex immediately below them. However, small sources are attenuated heavily as are deep sources. These results are predicted by the concentric shell models of Vaughan [1] and Geisler and Gerstein [9].

The second controversy involves relating cortical neurons to cortical potentials. It centers not so much around proving a causal relation as determining what the mechanism of the relation is. First conjectures were that nerve action potentials were spatially and temporally summated to produce evoked potentials. Fox and O'Brien [10] found that the post-stimulus histogram of a single cortical cell's spikes was the same shape as the evoked potentials recorded from the same location after the cell died. Creutzfeldt [2] confirms this finding, but attributes the slow waves to
post-synaptic potentials. Admittedly there is a correlation between these two mechanisms. Towe's model [11] suggests that primary evoked potentials are spatial summations of slow post-synaptic potentials of numerous neurons. Glial cells are possible messengers but are not considered sources by Creutzfeldt [2]. Of course this work was on animals and extrapolation to humans should be marked by caution. Opportunities for collecting human data are rare and the circumstances not ideal. Although the electrogenic basis of the VER is still in dispute, most researchers believe the VER derives from cortical neurons. Lippold [12] is the single investigator suggesting a non-cortical source. His hypothesis is that longitudinal movements of the eyes modulate the standing potentials across the eyes and thereby produce fluctuating currents at the back of the head. There is no agreement yet as to how well his data support this hypothesis.
CHAPTER I
LITERATURE REVIEW

This chapter presents a review of the two topics this dissertation brings together: the location of human VER sources and the existence of color sensitive regions in the visual cortex.

Source Localization

Three general approaches to VER source localization have been developed so far. The first approach uses studies of the functional anatomy of the brain to specify possible VER sources. The second approach investigates the local electrophysiology of the possible anatomical sources. The last approach uses the theory of volume conductors to relate the topographical distribution of scalp potentials to inferred equivalent dipole sources.

a. Functional Anatomy

The historical development of the gross anatomy of the visual system has been reviewed by Holmes [13], Polyak [14], and others. It is now known that some 70-80% of optic tract fibers connect the retina, via the chiasm, to the lateral geniculate body. The rest of the optic fibers go to the
superior colliculus, pretectal nuclei, and the nucleus paralemniscalis. The optic radiation connects the geniculate to the striate cortex located near the occipital pole in and around the calcarine fissure.

Except for pupillary control, the visual function of the non-geniculate fibers in man is still unclear. Brindley et al. [15] compare the functional studies of the non-geniculate fibers in animals with their data on two humans who are considered cortically blind. When striate cortex is ablated, dogs and cats and tree shrews can still localize moving objects, but monkeys only occasionally track them. Only sudden changes in light level could be sensed by Brindley's patients. Thus the non-geniculate system is a highly unlikely VER source for constant luminance stimuli.

Holmes [13], Polyak [14], and Spalding [16] have made clinical studies of visual deficiencies due to war wounds of the occipital cortex and inferred the function and retinotopic distribution of the visual cortex. An exact visual field mapping on the striate cortex allows distinct orientations of active nervous tissue to be used in predicting VER topography. Holmes [13] produced a conjectural cortical map, the details of which suffered from insufficient data and no post-mortem confirmation. Spalding [16] was the first to locate the cortex associated with central vision. He placed the central 8-10° on the occipital pole facing posteriorly
and postero-medially. He also placed the horizontal meridian in the floor of the calcarine fissure and found that macular vision was only unilaterally represented. Work by Daniel and Whitteridge [17] and Rolls and Cowey [18] on monkeys indicates considerably larger areas of the striate cortex devoted to the central 1° or 2° of vision. This has led Jeffreys and Axford [19] to suggest that Spalding is in error and that the occipital pole maps only a couple degrees of the central field. Brindley and Lewin [20] have recorded the visual field locations of human phosphenes, and their data appears to support Jeffreys' contention. Marg et al. [21] have recorded the receptive fields of human cortical cells using microelectrodes, but they have not mapped the striate cortex yet. Brindley [22] has confirmed the classic studies which showed a high degree of variability in the conformation of human striate cortex. However, Brindley et al. [23] reject the notion of adjacent points of the visual field maintaining their relative relations when mapped to the cortex.

Mappings of the striate cortex for monkeys (and cats) have been thoroughly explored electrophysiologically, but their cortical architecture is largely different from humans. Chimpanzees have cortical folding patterns relatively close to man but have not been carefully studied. About one man in four has a large vertical fold in the calcarine fissure
much like the chimp according to Polyak [14]. All studies agree that the lateral visual fields are represented in the floor and roof of the calcarine fissure although the location of the horizontal meridian is contested. The general inversion of upper and lower fields to lower and upper cortex (relative to the calcarine) is undisputed as is the projection of left and right visual field to right and left hemispheres respectively, and the mapping from fovea to periphery onto posterior to anterior cortex.

Parastriate cortex [Brodmann 18 and 19] lies adjacent to the striate cortex on the occipital lobe and receives no fibers from the geniculate. Rather, parastriate connections come from adjacent striate and contralateral striate cortex via the corpus callosum. Callosal fibers are received almost entirely from that part of contralateral striate representing the vertical meridian of the visual field, especially near the fovea. Details of retinotopic mapping on the parastriate are not known, but it is reasonable to assume a representation similar to that of the monkey. Zeki [24,25] and others have shown that there is an orderly mapping of the upper field onto the lower prestriate cortex and the lower field onto the upper prestriate cortex of the monkey with an extension of the calcarine fissure marking the horizontal meridian. The clinical observations of Holmes [13], Polyak [14], and Penfield and Jasper [26] agree with the lesion
studies of Gross [27] and others in monkeys in their finding that the parastriate functions as a visual discriminator of three-dimensional objects and patterns.

Inferotemporal cortex receives large input from parastriate cortex and is also involved in visual discriminations, especially color and concurrency. Again the observations of clinical and cortical ablation studies in monkeys agree: "The deficit after foveal prestriate lesions appears to be more a sensory, perceptual, or attentional one. By contrast, inferotemporal lesions produce an impairment relatively more sensitive to associative factors." [27, p. 463]

b. Local Electrophysiology [2, unless otherwise indicated]

The analysis of local potential distributions is not only the most definitive approach to VER source localization, it is also the most difficult technically. Extensive single cell studies have been done in cat and monkey visual cortex as well as in the geniculate. However, these data remain difficult to interpret in terms of resultant scalp potentials. The powerful current source density mapping technique requires accurate and reproducible potentials from many locations or the derivatives it relies on become uselessly noisy. The ongoing activity of the brain contaminates evoked potential records severely unless potential readings are signal averaged. Time limitations have prevented investigators
from gathering sufficiently accurate data to analyze current distributions even in the case of electrically stimulated cat visual cortex. Anesthetics each add variability to cortical recordings and obscure sources. Probably the most fruitful approach would be to chronically implant electrodes around possible sources in a monkey's brain and average potential responses for various stimulus conditions. Although this is a very feasible method, it has attracted little interest [1].

Visually evoked potentials have been recorded all along the visual pathway of cats and monkeys. However, little attempt has been made to find regions of maximal response or to correlate local potentials with scalp records. Furthermore, all the animal records show high frequency oscillatory activity in the evoked responses which does not appear at the scalp. Presumably this results from different nerve conduction velocities, but it does not appear in any of the human cortical records, even those deep in the calcarine fissure. Since few animal studies use any visual stimuli besides full field flash, the single largest contribution they make to VER localization is in identifying the times of maximal activity along the visual pathway. In the monkey optic tract activity peaks at a latency of 12-22 ms with the geniculate peaking a few milliseconds later. Striate recordings from various monkeys show large interspecies and
individual variations in form, oscillation content, and latency. In unanesthetized rhesus monkeys, response peaks in 40 to 60 ms. The prestriate cortex of the squirrel monkey is characterized by a positive potential lasting up to 150 ms with a peak latency some 8-15 ms later than that of the striate. Gross [27] reports that inferotemporal potentials in monkey are marked by an early negative deflection peaking around 40 ms followed by a long complex positive wave lasting up to 400 ms. Padmos et al. [28] recently compared the occipital scalp potentials of monkey and man for pattern stimuli and found contour specificity lacking in the monkey's VER. This suggests important functional differences between human and monkey visual cortex.

Depth recordings in human subjects are naturally sparse. The work on scalp-cortical potential comparisons has not included recordings from sufficient cortical locations to describe the sources. Wilson and Nashold [29] recently placed chronic depth electrodes in the midbrain of 13 patients undergoing therapeutic coagulation. The results confuse localization efforts in that they confirm visual responses in 18 parts of the midbrain. Some of these records are similar to the VER. Although there have been several somatosensory evoked potential studies from human cortex, there has been little equivalent work in the auditory and visual modalities. From sketchy reports, MacKay and Jeffreys [30]
conclude that evoked cortical potentials from flash stimuli are largest around the calcarine fissure and are marked by a positive wave at 50 ms followed by a negative wave at 90 ms on the lateral surface of the occipital pole. However, reverse polarity peaks are seen at the mesial surface with the secondary wave positive at 70 ms.

Lacking adequate corroborated data on local evoked potentials in both monkey and man, all results from other localization approaches will remain only suggestive. Opportunities for critical experiments, acute and chronic, with monkeys, especially chimpanzees, have been largely overlooked. As the use of implanted electrodes for locating epileptic foci becomes more routine, we can expect more detailed human data. In general the more cases in which vision research can make "in depth" electrode data valuable medically, the more often that such recordings will be ethically approved.

c. Topology and Volume Conduction

As the EEG developed into a clinical tool, more attention was paid to the spatio-temporal properties of the potential distribution over the scalp. Complex toposcopic display systems were developed to aid in the analysis of up to 400 channels of simultaneous potentials. Remond and his associates have long worked in EEG topology with the intent
of answering the "when and where" of brain wave sources. Walter [31] has explained principles of interpretation of topological EEG data and related the topology to hypothetical dipole sources. Offner [32] described EEG data in terms of instantaneous contour maps. Shaw and Roth [33] developed an analysis scheme for localizing EEG sources and distinguishing between stationary and moving sources. Frank [34] and others developed the equations relating surface potentials to a dipole source in a homogeneous conducting sphere, and Brazier [35] applied them to the EEG. Geisler and Gerstein [9] formulated the relation of scalp potentials to a dipole embedded in a conducting sphere covered by two shells of different conductivity. They measured auditory evoked potentials in the different layers of a monkey's head and compared their data to their model's predictions. Thus the VER became a popular topic growing out of a well-developed EEG background.

Early studies of the human VER all used simple flash stimuli and few electrode positions. Cigánek [36] reported significant scalp potentials at all electrode positions but was able to distinguish a sensory specific maximal response near the occipital lobe for early components. Later components seemed more centrally located and sensory non-specific. Kooi [37] and associates were able to confirm with their clinical studies that occipital responses during the first 100 ms result from the basic perceptual process of
vision. Schreinemacher and Henkes [38] showed waveform changes for stimulation of different retinal fields when they carefully adapted the rest of the retina to prevent stray light effects. Soon there was an accumulation of evidence that the topography of the VER depended on the visual field stimulated. Furthermore, striking changes in topography could be introduced by changing the stimulus from a blank flash to a patterned field [39]. These two findings form an experimental basis for inferring source locations.

Jeffreys and Axford [19] probably have developed the most detailed localization analysis. Their electrodes were placed transversely across the back of the head and longitudinally down the center of the head. The stimulus was a 14' checkerboard pattern filling the halves, quadrants and octants of a 6° field and presented tachistoscopically in exchange for an equal luminance blank field. Amplitudes were monopolarly derived against a right earlobe reference and measured against a baseline value. They identified two components (CI and CII) both of which reverse polarity with upper and lower field stimulation. Only CI shows a midline polarity reversal for left and right half fields. There are consistent differences between adjacent upper and lower quadrants and between adjacent vertical and horizontal octants for CI. The polarity and form of the longitudinal distributions of CI are different from that of CII. By
selecting only the central or outer parts of the pattern for the stimulus, differences were found in the relative contributions of these regions to the CI and CII responses. In localizing CI sources, Jeffreys and Axford refer to the homogeneous sphere dipole model. They suggest that the horizontal parts of the upper quadrants are represented in the floor of the contralateral calcarine fissure while the vertical part is represented on the lower contralateral mesial surface. Lower field quadrants are represented in corresponding upper calcarine and mesial cortex. They place CII sources in extrastriate cortex with upper quadrants originating on the contralateral lower surfaces of the occipital lobe and lower quadrants on the upper surfaces. Jeffreys is his own best subject for this scheme of visual field projections. Only those scheme predictions which were specifically included in his conclusions seem to hold up to intersubject variability. One subject out of the four reported showed systematic departure from the scheme's predictions. Recalling that Polyak [14] found one subject in four with a large vertical fold in the calcarine cortex, one might expect corresponding differences in potential topography.

In a similar study by Halliday and Michael [40], reversing checkboard octants were used to stimulate 11 subjects while potentials were recorded from 10 positions around the occipital pole. While confirming polarity
reversals for upper and lower half and quadrant fields, they
did not find that the horizontal octants of adjacent upper
and lower quadrants showed the strong polarity reversals
that Jeffreys and Axford found. Rather, it was the vertical
octants of these quadrants that showed strong polarity re­
versals, so they were implicated as sources of the quadrant
polarity reversals seen in both studies. This finding rules
out polarity reversals resulting from activation of the op­
posed surfaces of calcarine cortex. Halliday and Michael
suggest that the source of these potentials is extrastriate
cortex. If upper field sources were located on the under­
surface of the occipital lobe and lower field sources on the
upper convexity of this lobe, the location of Jeffreys CII
sources, then potentials from the latter region should be
larger because of the proximity of the recording electrodes.
This was not observed consistently. Their second hypothesis
for polarity reversal was that there are two sets of neurons
in the same regions of extrastriate cortex and that they are
active with opposite polarities. In a later paper Michael
and Halliday [41] test these hypotheses and conclude that
the ear reference explained the amplitude inconsistencies
and that indeed the sources were the lower and upper surfaces
of the occipital lobe.

The discrepancies between Jeffreys and Axford's work
and that of Halliday and Michael can be explained. In the
case of the former, two separate peaks were identified with hypothetical sources while in the latter, peak-to-peak measurements were employed. The apparent result is that Halliday and Michael used both of Jeffrey's components to locate one source in extrastriate cortex. If they had used baseline references for each peak, the similarity in their waveforms indicates they would have found the same results. Another explanation was recently forwarded by Estevez and Spekreijse [42] on the basis of stimulus differences. They previously had presented evidence that pattern reversals stimulate two independent responses: contrast increase and contrast decrease. Jeffreys and Axford's stimulus would include only the former, but Michael and Halliday's would be dominated by the latter. Estevez and Spekreijse show that CII is lacking for foveal pattern reversal stimuli and suggest a nonlinear interaction for foveal contrast increase and decrease mechanisms to explain the differences in the results. This type of confusion results from the numerous arbitrary choices that haunt and typify VER analyses.

Biersdorf and Nakamura [43,44,45] in a series of papers have studied the polarity reversal associated with left and right half and quarter field stimulation, first with blank fields and then with flashed checkerboards. The equipotential contour mapping technique they employ allows a more detailed reconstruction of the spatio-temporal distributions.
The maps show that strong contralateral localization appears only during the early part of the response, before about 100 ms. Pattern response maps show less tilt and more left-right symmetry than those from blank flashes. The pattern data are also in excellent agreement with that of Jeffreys' CI except for some upper and lower half field ambiguity which might be explained on the basis of flash-tachistoscope differences. Halliday and Michael [40] also report significant left-right amplitude and polarity differences.

Ristanovic [46] has further developed the cruciform geometry model of Jeffreys' CI generators. He points out that upper and lower calcarine cortex regions are not electrically or physically isolated from each other, so one expects these two source areas to cancel at the scalp when equally activated. However, not so for mesial surface sources separated by the highly insulating membrane, the falx cerebri. He presents an electrical analog model of the early activity of visual cortex. It features linear additivity of independent sources as shown by Jeffreys and Axford [19] to be approximately true for the summation of octants to equal a quadrant and quadrants to equal half fields. An additive relation for monocular and binocular stimulation was not found to generally hold for Jeffreys' CI and CII components. Ristanovic indicates that some subjects' records show almost complete additivity of monocular
potentials in binocular records, and he concludes that there is high intersubject variability in monocular-binocular additivity.

The analysis of later components of the VER for their source locations has not been highly developed. One might expect that the later peaks would correlate with psychological variables and have sources in associational cortex. Interpretations of the possible "meaning" of the later peaks varies widely, and there has been little success in elucidating parameters which might produce strong enough local potential gradients to infer possible sources. Lehtonen [47] has succeeded in isolating two possible sources for the 120-260 ms components. Varying interstimulus interval and contour shows statistically significant differences in the behavior of vertex and occipital potentials. Vaughan [48] found a primary maximum near the occiput and a secondary maximum near the vertex. Using a blank flash, Kooi [49] has recorded two prominent peaks over temporal cortex. The question whether these responses are sensory specific or not is still debated [50].

As previously mentioned most workers in VER localization are referring potential topology to hypothetical dipole sources. This approach is reliable only to the degree that the sources are of limited extent or "focal" and the model of the head is accurate. For small sources buried deep in
the head, an equivalent dipole is probably a good approximation. However, in this case the attenuation relative to sources nearer the scalp is so severe that sensing known midbrain sources is practically impossible [51,1]. This simplifies localization efforts somewhat but leaves large portions of cortex as possible sources. For flash stimuli in the monkey, local evoked potential records show striate, prestriate, and inferotemporal cortex all active at about the same time. The effect of pattern stimuli in man is to produce strong potential gradients near the occipital pole suggesting that inferotemporal activity is attenuated. This suggestion needs to be tested in monkey whose inferotemporal cortex seems to function like that of man. In both man and monkey, inferotemporal cortex is activated not only through the striate but also through the superior colliculus via the pulvinar. It is essential that stimuli be found and tested which minimize, separate, or otherwise control activation through these pathways so that limited cortical regions are stimulated at one time. Otherwise, the interpretation of potential maps is hampered by the possibility that strong gradients result from some fluke configuration of distributed sources and not from local cortical activity. In fact the VER can be a valuable tool for discovering the physiological function of regions of cortex by inferring which stimulus parameters affect which cortical areas. Confirmation by local electrophysiology would remain essential
although its interplay with mapping and stimulus variation could certainly be more general. For instance, local gross potentials could be used to specify stimulus parameters and predict potential map features.

The matter of an inverse solution of the equations for a dipole in a double-shelled sphere is not a trivial one. Most researchers visually fit their limited data to the known surface potential distributions for radial and tangential dipoles at various depths in the shell model. The inverse solution for the homogeneous sphere is a tractable problem although few reports fit data to dipoles this way. Schneider and Gerin [52] were able to use this model to locate epileptic foci. They present a method of quantitatively estimating the orientation and location of the dipole from features of the mapping. Kavanagh [51] has developed and used a computer program to fit contour maps to the shell model, but this required a substantial investment in programming plus some $50.00 per solution in computer time. Analyzing data for some 40 simultaneously recorded channels, he compares the dipole locations from the fits to the homogeneous model to those from the shell model for several different latencies. The fits are in about the same location for both models, but his stimulus was a centered blank flash to either eye or both. Hence it is not surprising that for both his subjects the dipoles are located between the hemispheres. For the
homogeneous sphere model, one subject's data did not produce a localizable dipole for the first 115 ms. The other subject localized well, but rather deep in the head with radical changes in dipole direction over time. Fitting the same data to the shell model brought the sources a little nearer the scalp but greatly increased the volume of standard deviation and prevented a convincing anatomical interpretation. Again the dipole's direction, but not the general location, changes in time. The program is not capable of deciding between one or two dipole sources and requires an approximate location for a starting point. Attempts to force a strong midbrain source as a solution by picking a deep starting point were all unsuccessful. Standard deviation volumes increase dramatically when two dipole sources are chosen from the interpretation of contour maps.

Henderson et al. [53] have also developed a computer program to find the inverse solution of the equations of a dipole source imbedded in a homogeneous sphere, the simpler model. However, the sixteen electrode positions they used were not recorded simultaneously but over four different runs. Jeffreys and Axford [19] have argued that simultaneous recording is essential due to baseline shifts. Their study was further limited by the use of a simple full-field flash and too few repetitions to find a standard deviation volume. The earliest peak they localized was at 128 ms and like
their later peaks, it was placed in the posterior region of the right hemisphere near the midline. Hence, without carefully chosen stimuli, the power of a computer-derived inverse fit to detailed contour maps is dissipated in inconclusive results.

Vaughan [1] criticizes his own early attempts to resolve VER components and similar work by Lehman and Fender [54]. In both cases, Gaussian distributions were fit to the various VER peaks. However, this choice is arbitrary like the instructions given the computer for deciding what constitutes a peak. As a result the computer "assumes the biases of the investigator and retains little of his flexibility." [1, p. 183] The principle component factor analysis technique advocated by Donchin always seeks out the largest source of variance, the background EEG, and is of little physiological value according to Vaughan. Vaughan's second effort is an improvement of the shell model. Instead of assuming a single small source, he approximates the geometry of distributed cortical sources with dipole sheets arranged as spherical segments (cap-shaped) or plane annular sectors bounded by arcs of two different radii. He can then closely fit almost any cortical geometry by summing the effects of a small number of dipole sheets, all of which are assumed to add linearly. An important product of Vaughan's dipole sheet calculations is that scalp potentials are very
sensitive to the orientation and extent of the sources. For equal angular extent, "cap" sources have roughly a ten-fold greater effect than annular sector sources, and a 20° increase in "cap" source angle can produce a ten-fold increase in the scalp potential maximum. Experimental observations of these effects were mentioned earlier [4,3,5]. Vaughan has not published the equations relating these dipole sheets to scalp potentials. However, he claims to have compared potential maps for many different stimulus conditions and sensory modalities to the potential distributions he calculates from the geometry of assumed active cortex. In every case he says the fit is good. Kooi et al. [55] take strong exception to the source localization of the auditory evoked response in Vaughan's one detailed report [56] that uses this technique. Vaughan[1] claims to have resolved the controversy by determining that Kooi's sternovertebral reference site was not inactive as it was supposed to be and that Vaughan's nose reference was indeed inactive.

The issue of an inactive reference site has long been controversial. There are three ways of recording scalp potentials: (a) bipolar, which gives gradient information, (b) monopolar-single reference, which relies on one site unchanged in potential, and (c) monopolar-average reference which allows each active site to contribute to the reference potential. For contour mapping this author feels that it is
best to start with monopolar recording, using bipolar to accurately place peak locations. Offner [32] was first to suggest an average reference approach; this could be a weighted average as in some ECG work. Kavanagh [51] has tested the validity of an equally weighted average reference from 41 electrodes. Of course the reference is correlated with the active electrode potentials, and in fact the average correlation with the active electrode potentials is above the 5% significance level at 0.526. Compared to a single reference, the average value at the 41 active electrodes located all over the scalp did not exceed ±2 μv for a typical active electrode swing from +4 to -7 μv.

The weighted-average and the single reference both require finding sites whose potential is relatively unchanged by the stimulus. Most investigators use relatively remote sites: the ear lobe, the chin, the nose, but there is no guarantee that physically remote means electrically inactive. Hence, data taken with different references are often compared to make reference artifacts less likely. Single-ended recording from a given ground and reference electrode combination can theoretically insure an inactive reference for the given stimulus, environmental conditions, and subject. However, common mode interference must be handled by either signal averaging at a sweep rate that is carefully chosen for non-synchrony with the line frequency or by providing
common mode isolation in coupling a battery-supplied amplifier to an averager. These approaches to an inactive reference have not received careful treatment in the literature.

Thus far we have only cited work with averaged transient VER's. Another type of VER work employs synchronous detection techniques to improve the signal-to-noise ratio and produce the so-called steady state VER. Using this technique, Milner et al. [57] have attempted to localize brain lesions from changes in pattern responses and relative changes in response over the stimulus frequency spectrum. Little other localization work has employed steady state measurements although steady state contour maps for various frequencies could be produced. It is not yet clear how transient and steady state sources are related, but in a field like VER localization every approach deserves consideration.

Functional anatomy studies have not yet clarified an important point: the retinotopic representation of the macular field on striate and extrastriate cortex. Local electrophysiology is our best source of knowledge about the relative activity of the possible cortical generators, and so far it has given us almost no definitive information, either in monkey or man. Topographic and volume conduction studies have begun to estimate likely source locations but there are conflicting interpretations.
Color Sensitivity

Single cell recordings from human visual cortex show no noticeable color effects on receptive fields [21]. However, these recordings are so limited in scope and number that there is no real reason to believe that the color sensitivity of human visual cortex is significantly different from that of monkey cortex. Although most early work in monkey cortex indicated that only a small proportion of the cells were color sensitive, more recent studies have shown that the major proportion of cortical cells are color selective in the foveal regions of areas 17, 18, and V4 [58, 59]. Furthermore, cells in the same cortical column show the same color preference. Gouras [60] also found that single cells with similar color opponent properties are segregated into patches in layer 4B of foveal striate cortex.

Gouras and Padmos [61] used a microelectrode to record graded responses or highly local evoked responses in foveal striate cortex of rhesus. They reported that the amount the various cone mechanisms contributed to the response varied from one region of foveal striate cortex to another. This is not surprising since layer 4B receives a major input from the lateral geniculate nucleus and should therefore be expected to contribute heavily to the early (60 ms) peak they measured.
Again the major problem with intercellular and micro-electrode recordings is that they are not clearly related to scalp potentials. Hence, they can only be suggestive of a distribution of color sensitivity in the VER. However, macroelectrode cortical records are similar to the VER. Massopust et al. [62] employed macroelectrodes and semi-macroelectrodes to record local evoked responses in squirrel monkey and found extended regions of visual cortex differentially sensitive to red or blue. A red sensitive region was located near the occipital pole surrounded by a blue sensitive region and a small blue sensitive region was located lateral to the pole; all of this on surface cortex. Calcarine cortex did not respond differentially to color except immediately beneath the color sensitive surface cortex. Peak latencies varied from 40 to 70 ms with red shorter than blue and calcarine shorter than surface responses. Both the micro and macroelectrode data support the notion of a color sensitive topography in the cortex. However, the color sensitive patches found using microelectrodes are in foveal projection areas of cortex while the corresponding regions determined by macroelectrodes are not in or near foveal cortex.

There have been numerous studies of color effects in the VER, but many of them have produced conflicting conclusions. Early work by Clynes and Kohn [63] and Shipley
et al. [64] suggested the presence of wavelength-specific components in the VER, especially the later components. Further studies produced ambiguous results [65] which probably are reconciled by differences in the stimulus conditions [66]. In several papers Regan and others have shown that the different color mechanisms are segregated at least at the level of pattern sensitive cortical neurons when tested by steady state VER techniques [67]. Kinney and MacKay [66] have isolated latency differences between hue-changing stimuli and luminance-changing stimuli while Regan finds corresponding phase shift differences for different colors in steady state VER's [68]. The picture emerging from the VER data suggests that at least some color features are present when the stimuli and controls are designed to properly test for them.

Clynes [63,69] and his coworkers have used an 8-electrode rosette placed on left occipital scalp to record the bipolar VER from opposing electrodes. Using a correlational analysis they conclude that the topographical distributions of the VER waveforms differed for the different colors and that the individual components of these waveforms also had different topographies. Although they suggested that more electrode rosettes would further clarify these results, no one has attempted to refute or confirm their findings. Perhaps this is because their
conclusions rather overextend their experimental technique. Regan has remarked at the lack of further work on the possibility of a topographical distribution of color sensitivity in the human VER [50]. We have discovered differences in the equipotential contour maps of the first positive contralateral peak when using red verses white flashed checks in half field stimulation. This finding, taken in the context of Massopust et al. [62], Clynes and Kohn [63,69], and the several single cell groups, is the motivation for this dissertation.
CHAPTER II

METHOD AND APPARATUS

Basic Method Considerations

The most complete information that can be obtained from the human VER for any given time and set of stimulus conditions is the spatio-temporal distribution of signal averaged potentials over the surface of the whole head. This distribution depends on specifying a reference potential which is unchanged during the data collection process or at least does not change significantly at frequencies included in the VER band. The actual potential distribution can only be approximately measured because of the limited number of sample locations practically possible and because of perturbation from the sampling process. In general, the complete set of data for one measurement will not be the same for another measurement nor for another subject. The amplitude of the response and its reference base line are not exactly the same from run to run, but the shape of the distribution is more stable. These problems are discussed in more detail by Kavanaugh [51] and by Jeffreys and Axford [19].

While many researchers have employed statistical
methods to quantify the variation in the response, this approach can become unwieldy when many sample locations are required. Several compromises have necessarily been employed in the research for this dissertation. The maximum number of electrode positions used to sense the potential distribution was 28. This number was selected because it allowed sufficiently close electrode spacing and adequate scalp coverage at a reasonable financial investment for simultaneous recording capability. Not only does simultaneous recording of all channels reduce subject time allowing him to be more alert, but equally important it eliminates the need to compensate for run-to-run amplitude and base line fluctuations in assembling a potential distribution. The reference electrode was placed over the bridge and tip of the nose because this site is bilaterally symmetric and relatively remote physically and electrically from the active occipital cortex. Also this position allows a relatively large electrode as does the ground positioned on the cheek. Large electrodes have lower source impedance and therefore less noise. Subjects were selected for average-to-large response amplitude, low ongoing alpha levels, and good reproducability.

Even so, the base line region of the response was often contaminated by an anomalous early response probably due to synchronization of the after discharge with the flash [73].
The problem was alleviated by varying stimulus frequency randomly and by using an adapting surround. Still, clearly contaminated data had to occasionally be rejected.

Most of the conflicts in the VER literature are probably due to differences in the stimulus conditions. Full field blank flashes have gradually been replaced by partial macular field equal luminance checkerboard stimuli presented within a large adapting surround. The appearance of edge information or contour without overall luminance changes allows isolation of contour and luminance responses. One of the goals for this work was to determine what stimulus features might be associated with a topography of color sensitivity. To this end a general purpose oscilloscopic pattern generator was developed. Also an adaptation hemisphere was constructed so that its brightness and color could be controlled over a wide range. This equipment was supplemented by a xenon flash and checkerboard pattern so that many types of stimulus combinations were possible.

Design of Apparatus

a. Preamplifier System

The careful design of low-noise biological amplifiers is complicated by multichannel problems. The circuit designer's task is substantially simplified if he chooses to use operational amplifiers. Besides combining small
size, low cost, and high reliability with simple circuit configurations, the integrated circuit operational amplifier (IC op amp) can closely approach the performance of the best discrete designs. This section describes the design of a high performance integrated circuit biological amplifier and its use in a 24-channel head-mounted preamplifier for recording human evoked potentials.

Although the specific application should dictate amplifier specifications, the various biological applications share many requirements. Noise performance is crucial in our work because skin electrodes couple brain waves of only a few microvolts to the amplifier. Comparison of IC op amp noise specifications over our bandwidth (0.2 - 400 Hz) and source resistance range (10 - 100 kΩ, 20 kΩ typical) proved bipolar input devices still superior to FET-input devices [71,72]. The recently introduced mono op-10 CY (Precision Monolithics, Inc.) was chosen because it is a high performance dual instrumentation IC op amp which retains the excellent noise performance of the 725 without the intermodulation of high frequency noise into the band of interest which has been previously reported [73]. This feature, along with dual packaging and internal frequency compensation, reduces parts count and saves space.

Amplifier configuration was determined by the need for high common mode rejection ratio (CMRR), high differential
and common mode input impedances \((Z_{in\, \text{Diff}}, Z_{in\, \text{CM}})\), small size, and high gain (≈ 1000) in the presence of dc skin potentials and unbalanced source resistances. We confirm reports [74] that dc skin potential differences on the head reach 100 mV. Furthermore, unless electrode temperature and ionic environment are especially well controlled and bias currents low, conventional silver/silver chloride electrode bias potentials drift about 60 µV/min [75]. This drift requires that the amplifier be either ac coupled at some level or somehow rezeroed periodically. We compromised very low frequencies for low drift artifact by choosing ac coupling with a time constant of one second. Very stable pellet electrodes [76] or electrolyte bridging tubes [75] may make dc recording meaningful and bandwidth a choice of the experimenter. If capacitive coupling is employed before the common mode signal is rejected, CMRR will be limited at line frequencies and below unless precision coupling capacitors and resistors are selected. The possibility of a 90 kΩ source resistance imbalance calls for exceptionally high \(Z_{in\, \text{CM}}\) to prevent a severe reduction in CMRR [77]. Skin potentials may saturate op amps supplied at ±15 V if dc gain is much over 100. A simple but not widely known circuit that meets the requirements is shown in Fig. 1. Input stage analysis is simplified by hypothetically grounding one input because the other input is then amplified by the familiar
Figure 1. Schematic diagram of individual (single channel) biological amplifier.
inverting and noninverting op amp configurations. Let $e_2 = 0$; then side A output is $1.01e_1$, and side B output is $-101e_1$. Let $e_1 = 0$; then side A output is a virtual ground, and side B output is $101e_2$. With both inputs active, side B output is $101(e_2-e_1)$ thus rejecting common mode signals \([7^8]\). With its fully protected inputs the mono Op-10 C is not damaged by floating an input, and no path is provided to ground except through the source. The second stage is in a noninverting ac amplifier configuration producing a signal gain of 11 and a dc gain of 1. In our application four amplifiers feed an analog multiplexer whose output is more accurately recorded if the output offset of each amplifier is eliminated. So each amplifier is connected to a filter which blocks offset, offset drift, and the amplified dc signal, and rolls off response above 400 Hz. Second stage configuration was chosen primarily for printed circuit board layout considerations.

Noise of the amplifier of Fig. 1 was measured in a double-shielded cage over bandwidths sharply defined by a 24 dB/octave active filter with standard peaking (Krohnite 330N). Filtered noise was dc coupled to a true rms digital voltmeter (Fluke 8200A) whose BCD output was digitally averaged over 100 consecutive readouts (sample time of 25 sec). Noise performance typical of the 27 devices tested is shown in Fig. 2. Low frequency noise (0.1-10 Hz) is virtually
nonexistent since no device exceeded 500 nV p-p at the shorted inputs in a 30-second sample. Excellent control over noise parameters is indicated by the manufacturer's 90% guaranteed maximum specifications and confirmed by our tests.

Although complicated by noise and bias currents, attempted input resistance measurements did set a lower limit of 1 GΩ for both differential and common mode input resistance. Values of 80 GΩ differential and 100 GΩ common mode input resistance are quoted typical for this type circuit [71], but the 8 pF input capacitance limits Z_{in CM} above a few tenths hertz unless input guarding techniques are employed [77]. Without guarding, Z_{in CM} is 300 MΩ at 60 Hz thereby dropping CMRR for unbalanced sources of 10 kΩ and 100 kΩ from 118 dB at 0.2 Hz to 70 dB at 60 Hz. Other quoted typical values include a power supply rejection ratio of 81 dB at 60 Hz, 75 dB at 120 Hz, and a gain nonlinearity of <0.01% [79]. Measured performance is shown in Table 1.

Compared with other configurations, the circuit of Fig. 1 features high performance and simplicity at the nominal expense of increased dependence on resistance match for high CMRR [78]. It can be easily modified by choice of feedback ratio and second stage coupling to provide more bandwidth, more gain, less offset. In fact, deleting the
# Table 1

**Measured Performance of the Individual Amplifier and 24 Channel Preamplifier**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Individual Amp (Figure 1)</th>
<th>24 Amp System Unipolar Mode</th>
<th>24 Amp System Bipolar Mode</th>
</tr>
</thead>
<tbody>
<tr>
<td>Input Bias Current</td>
<td>±2 nA, typical</td>
<td>±2 nA, active inputs</td>
<td>±3.5 nA, typical</td>
</tr>
<tr>
<td></td>
<td>either input</td>
<td>40 nA, reference input</td>
<td>any input</td>
</tr>
<tr>
<td>Input Resistance</td>
<td>&gt;1 GΩ, active input</td>
<td>&gt;10 MΩ, reference input</td>
<td>&gt;1 GΩ</td>
</tr>
<tr>
<td></td>
<td>either input</td>
<td></td>
<td>any input</td>
</tr>
<tr>
<td>CMRR @ 60 Hz @ source resistance imbalance</td>
<td>&gt;90 dB @ 10 kΩ</td>
<td>&gt;80 dB @ 10 kΩ (with $R_{\text{ref}} = 1 \text{kΩ}$), &gt;60 dB @ 90 kΩ (with $R_{\text{ref}} = 10 \text{kΩ}$)</td>
<td>89 dB, typical @ 10 kΩ, 63 dB, typical @ 90 kΩ</td>
</tr>
<tr>
<td></td>
<td>&gt;70 dB @ 90 kΩ</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frequency Response, small signal, 0.16 Hz —</td>
<td>4-8 kHz, 6 kHz typical</td>
<td>3-7 kHz, 5 kHz typical</td>
<td>3-7 kHz, 5 kHz typical</td>
</tr>
<tr>
<td></td>
<td>typical, varies with device</td>
<td>signal source at active input, see text</td>
<td>typical, varies with device</td>
</tr>
<tr>
<td>Noise</td>
<td>See Fig. 2</td>
<td>See Fig. 3</td>
<td>See Fig. 3</td>
</tr>
<tr>
<td>Common Mode Voltage Range</td>
<td>±13 volts minimum</td>
<td>±13 volts minimum</td>
<td>±13 volts minimum</td>
</tr>
<tr>
<td>Gain</td>
<td>1111, ±0.5%</td>
<td>1111, ±0.5%</td>
<td>1111, ±0.5%</td>
</tr>
<tr>
<td>Output Resistance</td>
<td>&lt;1Ω for $\Delta I_{\text{out}} = 5 \text{mA}$ @ $V_{\text{out}} = 10 \text{volts}$</td>
<td>&lt;1Ω for $\Delta I_{\text{out}} = 5 \text{mA}$ @ $V_{\text{out}} = 10 \text{volts}$</td>
<td>&lt;1Ω for $\Delta I_{\text{out}} = 5 \text{mA}$ @ $V_{\text{out}} = 10 \text{volts}$</td>
</tr>
<tr>
<td>Power Supply Current @ ±15 V</td>
<td>±7.5 mA</td>
<td>±180 mA</td>
<td>±180 mA</td>
</tr>
</tbody>
</table>
capacitor and trimming the offset make the circuit an excellent dc amplifier with offset drifts of 0.3 \( \mu \text{V/°C} \) and 12 \( \text{pA/°C} \) (mono Op-10A) \[^{79}\]. A single variable resistor, preferably reciprocal taper, can be added to the first stage to vary gain without affecting CMRR \[^{78}\].

The decision to use a head-mount for our 24-channel preamplifier was based on several considerations. Many commercial preamplifiers use guarding and/or remote probe impedance matching to control interference pick-up and capacitive loading of shielded cables, but the short input leads made possible by a head-mount can obviate these complications. Furthermore, some kind of head-mount is usually needed for electrode support and strain relief. Such arrangements typically result in multiple low-level connections which increase chances of wrong or intermittent connections. Finally, the low parts count of the circuit of Fig. 1 and the nominal extra cost of miniature precision components make a head-mounted system attractive.

The performance of an individual amplifier may deteriorate when other amplifiers share the same source resistance with it. For unipolar (monopolar) recording in our system, the 24 noninverting inputs are connected to one reference electrode and each inverting input to its own active electrode. For bipolar operation both the inverting input of one amplifier and the noninverting input of the
next amplifier are connected to one electrode. In either case all source paths are completed through one grounding electrode. In the unipolar mode the source between the reference and ground electrodes is loaded by an approximate input capacitance of $24 \times 8 \text{ pF} = 192 \text{ pF}$, which reduces $Z_{in \ CM}$ and can drop CMRR at 60 Hz to 40 dB for a 90 kΩ source imbalance. Furthermore, 24 input bias currents as well as their associated noise currents are drawn through the resistance associated with the reference electrode as are 48 drawn through that of the grounding electrodes. Worst case dc analysis allows all bias currents to be maximum in the same direction, ground electrode resistance to approach 100 kΩ, and dc skin potential to add a full 100 mV input offset. The maximum mono Op-10 CY bias current of 7 nA would then result in a first stage dc output of 13.6 V which is outside the linear range of the op amp when it is ±15 V supplied. The noise currents add in rms fashion and become the predominant noise source in a 400 Hz band for reference-to-ground resistances above approximately 20 kΩ. Finally, signal at the reference electrode is amplified by 1111 and appears at all 24 outputs. With high gain and a compact layout, the distributed capacitance from the 24 outputs to the common connection of the 24 noninverting inputs proved sufficient to produce oscillation. All of the above effects depend directly on the source resistance in the reference-
to-ground path ($R_{ref}$). In most cases large ground and reference electrodes and/or fine abrasive electrode pastes can be used to hold $R_{ref}$ below 10 kΩ. When this was done, our circuit was still unstable. Lowering bandwidth only demonstrated that the amplifiers would oscillate well into the band of interest. In an attempt to cancel the effective output-to-input capacitance, the output of the first channel was inverted and fed back to the reference electrode input via a miniature adjustable capacitor (5-40 pF). This technique worked, but not perfectly. While no single feedback capacitor setting was found which would maintain stability over a variation of $R_{ref}$ from 0-100 kΩ, the capacitor is easily set for stability over the 0-10 kΩ range of $R_{ref}$, as well as for variations of ±50% about values up to 100 kΩ. Bandwidth for sources up to 100 kΩ at the active inputs is essentially unaffected by capacitor setting, but reference input frequency response with $R_{ref} = 10$ kΩ can drop to 650 Hz or show peaking out to 5 kHz, dependent on capacitor setting. For $R_{ref}$ below 10 kΩ, CMRR and noise are both only slightly affected by capacitor setting. In the bipolar mode, only two amplifier inputs share the same source resistance, so performance is degraded little. Input capacitance is approximately doubled and affects $Z_{in CM}$ and CMRR, while noise current is increased by $\sqrt{2}$. Of course, the feedback capacitor must be adjusted down or removed, or else
Figure 3. Rms noise of a typical device (#8) as a function of bandwidth (0.2 Hz to frequency indicated on abscissa).
all channels will oscillate. In practice the feedback capacitor requires adjustment only once for each subject for each mode. Measured performance of the multichannel system is summarized in Table 1. The curves of Fig. 3 demonstrate the effect of added noise currents. For each source resistance, noise is seen to increase only slightly from individual, to bipolar, to unmatched unipolar ($R_{\text{ref}} = 2k\Omega$) mode but significantly increases for the matched unipolar mode.

Six channels were laid out on each of 4 single-sided printed circuit boards, 2 on either side of the head, with input jacks near the upper edge and outputs at the back. For convenience, each board was equipped with high reliability switches which select unipolar, bipolar, or calibrate modes. Subject protection is provided by fusing each input with 2 mA microfuses which each add about 2 kΩ to the source resistance. Resistors are 1/10 watt metal film with ratios matched to better than ±0.5% (guaranteeing a low frequency CMRR of at least 80 dB). Coupling capacitors are nonpolar tantalum etched foil. The plastic head band was converted from an indirect ophthalmoscope mount and adjusts to fit all head sizes and shapes comfortably. Figure 4 shows a subject wearing the completed system. Total weight is 700 g; parts cost about $30.00 per channel.
Figure 4. Subject wearing completed 24-channel preamplifier with all electrodes and cables attached.
b. Multiplexer System

In biomedical research it is often necessary to record many channels of analog information simultaneously. The FM instrumentation tape recorder is generally used for this purpose at considerable cost per channel. One approach toward reducing the per channel cost is time-division multiplexing which makes more effective use of often wasted recorder bandwidth [80]. This approach has the further advantage of requiring fewer amplifiers when multiplexing is done at low signal levels because it compresses several channels into one. Low-level multiplexing is now inexpensive due to the introduction of the CMOS analog switch in integrated form [81]. The following discussion describes the design and application of a 24-channel time-domain multiplexing and control system which employs a digital signal-averaging computer (Fabri-Tek 1052) and a seven track FM instrumentation tape recorder (Ampex FR-1300).

Signal averagers can improve signal-to-noise ratio only for recurrent signals synchronized to a repetitive trigger pulse. In our VER work the trigger pulse is produced by the visual stimulator. The trigger initiates a sequence of 256 samples of each VER signal where the samples are spaced at fixed time intervals. For each sample, our averager integrates the signal for 45 µs, performs an A/D conversion of the integrated sample, and stores the value in a register.
assigned to that time slot. Each time the stimulus is repeated, new sample values are added to the previous values stored in the registers. These synchronized responses sum linearly with the number of repetitions (n), but the random noise increases by only \( \sqrt{n} \), producing a signal-to-noise improvement equal to \( n/\sqrt{n} = \sqrt{n} \). In our four-channel averager the channels are sampled in a 1-2-3-4 sequence, so each channel fills its own 256 registers over the same time interval.

Our approach toward a 24-channel multiplexing system is to record six, four-channel multiplexer outputs on six tracks of the tape recorder with the remaining track used for recording multiplexer clock pulses. On playback the recorded clock pulses synchronize the four-channel signal averager's sampling of one track's multiplexed data so that four channels of data are directly demultiplexed and signal averaged simultaneously.

The Sample Theorem [82] states that if a signal's highest frequency is \( W \) Hz, then the signal is completely determined by giving its values at times spaced \( \frac{1}{2W} \) seconds apart. Therefore our 0.2-400 Hz signal band is passed by sampling every 1.25 ms. The 256 registers for that channel are thereby filled in 320 ms which is an appropriate response period for analysis of the VER. In our four-channel averager, samples must be taken four times as fast, that is, every 312.5 \( \mu \)s so that each channel is sampled at an 800 Hz
rate. The required 3.2 kHz clocking pulses are derived by counting down the averager's 640 kHz crystal clock and by resetting the counters with the stimulus-derived trigger pulse.

In Fig. 5 a block diagram of the system is shown. The preamplifiers raise the brain wave signals to the millivolt level where each signal is filtered and connected to one of the four inputs of one of the six quad bilateral switches (CD4016AE). Control voltages derived from the 3.2 kHz clock pulses sequentially connect one of the four inputs of each switch to the common output of that switch, thereby multiplexing the signal. The six dc amplifiers raise the six multiplexed signals to the nominal 1 volt level for recording on tracks 2 to 7 of the tape recorder. The dc components of the multiplexed signals must be preserved or severe crosstalk between channels could result. It takes exactly 1024 of the 3.2 kHz clock pulses to sequence through all the registers in the 320 ms after each stimulus. It is just these pulses which are gated to track 1 of the recorder.

A real-time display of the 24 brain-wave signals was devised to monitor signal quality and thereby prevent problems, such as poor electrode contact or equipment malfunctions, from producing a useless record. Two more CD4016AE switches are used to sequentially select two of the six multiplexed signals which are fed to the inverting inputs
Figure 5. Block diagram of multiplexing system.
of an available dual-beam differential input oscilloscope. The noninverting inputs are connected to a four-level staircase voltage, each step of which is synchronous with the 3.2 kHz clock pulses. The result is a chopped type display of eight channels per sweep; thus 3 sequential sweeps are needed to view all 24 channels.

A tape speed of 15 in/s was selected as the slowest speed which would allow a faithful reproduction of the data. In our recorder this speed corresponds to a nominal 5 kHz bandwidth in FM operation. Of course, this rounds the edges of our fast rise time signals, but it also produces ringing on the output LC filters of the tape recorder's reproduce modules. The amplitude of the ringing is a function of the difference between adjacent sample levels, and it takes two sample periods before it is completely damped. Therefore, the ringing causes crosstalk. Only one track is demultiplexed at a time; so, to prevent crosstalk, its LC filter is by-passed and replaced by an active filter whose parameters are carefully adjusted to produce a flat region toward the end of each data sample. This flat region is an accurate reproduction of the data sample. The output of the active filter is connected to all four inputs of the signal averager. The reproduced clock pulses are fed to a voltage comparator which carefully locates their leading edges in playback time. The voltage comparator resets a counter
which delays the start of the signal averager's 45 μs integrating sample time until the flat region at the end of the data sample is reached. The first pulse of each set of 1024 clock pulses starts the averager and enters the first sample on the tape into register 1 of channel 1. The next clock pulse enters the next sample into register 1 of channel 2. So data is entered into the averager's four sets of registers in a 1-2-3-4 sequence of channels. The data on one track is thus demultiplexed into four averaged signals. This process is repeated for each of the six data tracks to recover all 24 signals in averaged form.

Overall system performance has been reliable and accurate. In Fig. 6(A) there is no noticeable crosstalk between worst case channels: a square wave followed by a grounded channel. The capability for normal operation of the signal averager was retained; Figs. 6(B) and 6(C) allow comparison of normal signal averaging with that of the multiplexing system. Gains were not yet matched here but the waveshapes appear identical. The one problem encountered in a year of operation has been linked to stretch-damaged tape causing loss of clocking pulses which mixes the data of adjacent channels. After the recorder's brakes were properly adjusted, no more tape was damaged. For the operator of the equipment, the substantially increased channel capacity increased the complexity of his job only slightly.
Figure 6. System performance: (A) crosstalk from one channel with negative pulse signal (far left) to three grounded channels is not noticeable; comparison of non-multiplexed (B) and multiplexed (C) signal averaging shows no apparent differences except gain. For clarity, the dc levels of the four channels shown have been offset.
c. Pattern Generator

In vision research, control of the stimulus is essential. Optical systems have traditionally been used to produce the wide variety of stimuli required. As the special sensitivity of the visual system to the luminance step or "edge" became evident, researchers began to use patterned or contoured stimuli. In many cases it is easier to produce patterns with electronic circuits and displays than with optical systems. For our work on the human VER, an electronic pattern generator was developed to produce most of the various stimuli used in different laboratories. Hopefully then some of the discrepancies in the literature could be isolated to the different stimuli used.

Setting design goals for a general purpose oscilloscopic pattern generator involved several compromises. Many visual phenomena are affected by the brightness level to which the eye is adapted, and some phenomena are observed only with bright stimuli. Furthermore, it is a relatively simple matter to attenuate a bright display. For these reasons and because of our specific interest in the macular electroretinogram (ERG), high brightness (>3500 cd/m²) was a prime specification of the display. Cathode ray tubes (CRT) of the projection television type use high accelerating voltages and magnetic deflection systems to achieve high brightness. It is the current in the deflection yoke that
creates the magnetic field to deflect the electron beam, and this current cannot be changed instantaneously due to the inductance of the yoke. For a raster type display, the CRT beam is moved much faster in one axis than in the other. A low inductance yoke can improve the bandwidth of the deflection system in one axis at the expense of higher inductance and lower bandwidth in the deflection system of the other axis. Another parameter controlling the rate of change of yoke current is the applied voltage which cannot practically be increased indefinitely. The bandwidth required for a uniformly bright raster is determined by the size of the spot that the CRT beam makes on the phosphor. Spot size also sets the resolution or sharpness of the display. If the display is to change its pattern quickly, then a high speed phosphor is required. The image on the display should not only appear fused, but it must be refreshed fast enough so that all of the visual system's parameters to be studied will be stable. For example, the ERG is still responding to flickered stimuli at frequencies up to 110 flashes per second or more [83]. The image refresh rate, the spot size, and the raster sweep frequency are all interrelated in an optimal compromise. Setting two of these parameters will determine the optimal value of the third parameter. If the image is to be of high quality, the deflection system must be linear,
dc coupled, and free of jitter. The CRT face plate should be flat and of optical quality, and the phosphor should be white so various colors can be produced.

After consulting various display manufacturers, the Kratos model HM395 graphics CRT monitor was chosen as the best performance compromise at an acceptable cost. It uses a Thomas CRT model 5M216P45M whose P-45 phosphor is white with CIE coordinates of x=0.269 and y=0.311; persistence is medium with equal rise and decay times of 3.3 ms to 98% of final value. Display specifications are shown in Table 2.

Much of the flexibility that an electronic pattern generator can offer is lost if the Z axis input is not linear over its full dynamic range. In general, Z axis inputs control the cathode-to-grid voltage which is not linearly related to CRT beam current or brightness. What is required is a circuit which compensates for this nonlinearity. To this end the relationship between cathode-to-grid voltage and brightness was measured and plotted. The curve was then closely fit by a function with logarithmic, linear, and constant terms. A linearizer circuit was built to match this function. By synchronizing the X and Y sweep circuits with the Z axis input, it is possible to display a spatial luminance grating of any repetitive waveform that can be manufactured in electrical form.
### TABLE 2
**KRATOS CRT GRAPHICS DISPLAY SPECIFICATIONS**

<table>
<thead>
<tr>
<th><strong>GENERAL</strong></th>
<th></th>
</tr>
</thead>
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<tr>
<td><strong>CRT</strong></td>
<td>5&quot; round flat face</td>
</tr>
<tr>
<td><strong>Anode</strong></td>
<td>20KV</td>
</tr>
<tr>
<td><strong>Spot Size</strong></td>
<td>.010&quot; nom. .013&quot; max. (Max. change of 2:1 from 10 to 1000 FL)</td>
</tr>
<tr>
<td><strong>Large Step Settling</strong></td>
<td>5 microseconds Y axis</td>
</tr>
<tr>
<td><strong>Time to .25%</strong></td>
<td>500 microseconds X axis</td>
</tr>
<tr>
<td><strong>Spot Motion and Jitter</strong></td>
<td>.05%</td>
</tr>
<tr>
<td><strong>Linearity</strong></td>
<td>±1%</td>
</tr>
<tr>
<td><strong>Brightness</strong></td>
<td>1000 FL (4&quot; x 4&quot; 400 Line Raster 100 Hz frame rate)</td>
</tr>
<tr>
<td><strong>Deflection</strong></td>
<td>Magnetic</td>
</tr>
<tr>
<td><strong>Focus</strong></td>
<td>Electrostatic</td>
</tr>
<tr>
<td><strong>Phosphor</strong></td>
<td>P45</td>
</tr>
<tr>
<td><strong>Drift</strong></td>
<td>.5%</td>
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</tbody>
</table>

<table>
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<tr>
<th><strong>DEFLECTION AMPLIFIERS — X AND Y AXIS</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Input</strong></td>
<td>DC coupled single ended 1K ohm ground may be isolated</td>
</tr>
<tr>
<td><strong>Sensitivity</strong></td>
<td>±5 volts full screen – X axis</td>
</tr>
<tr>
<td><strong>Large Signal Sine Wave Response</strong></td>
<td>0 to +5 V dc full screen – Y axis</td>
</tr>
<tr>
<td><strong>100 KHz</strong></td>
<td>Y axis</td>
</tr>
<tr>
<td><strong>1 KHz</strong></td>
<td>X axis</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th><strong>Z AXIS AMPLIFIER</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Unblanking input</strong></td>
<td>+3 volts unblanks; 0.4 volts or less blanks for the full range of intensity level control. 10 MHz bandwidth.</td>
</tr>
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</table>
The checkerboard is another pattern often used as a visual stimulus. In Fig. 7 a block diagram of a pattern generator is shown. The circuits in this generator are designed to provide the X, Y, and Z inputs to the linearized Kratos display for producing a checkerboard pattern as well as the various grating patterns. The generator was designed and built by J. R. Brown with minor circuit modifications by the author. The X and Y sweep ramps are synchronized with unblanking pulses derived by counting down from the 5 MHz clock. To be well above electrophysiological fusion frequencies, an X sweep rate of 160 Hz was chosen. This allows 500 Y axis sweeps or "lines" over a four inch square from an 80 kHz Y sweep rate. Some high frequency tweaking was required to keep the Y axis ramp linear at the output of the display's deflection amplifier due to the limited bandwidth of the amplifier. Individual lines could not be resolved even at low brightness. The number of checks on an edge can be varied in two-fold steps from 2 to 32. There are ten brightness and ten contrast settings for checks and gratings. Both types of patterns can be reversed, black for white, in counterphase at frequencies up to 80 Hz. Also a pattern can be exchanged in the same way for a uniform field of equal average luminance. This pattern switching is synchronized to X and Y sweeps so
Figure 7. Block diagram of pattern generator.
that switching occurs only after an integral number of X sweeps. Trigger outputs were later provided to synchronize other equipment (signal averager) with the pattern switching.

An optical problem degraded the contrast at the check boarders and limited the brightness linearity. Measurements of brightness at various viewing angles proved that the phosphor surface is nearly Lambertian. Light from bright regions is reflected at the glass-air boundary of the face of the CRT, falls on dark regions, and illuminates them. To control this effect, a glass disc, two inches thick and five inches in diameter, was optically coupled to the CRT face with immersion oil. The front surface of the disc was multilayer coated for high transmission. The indices of refraction of the glass disc and the immersion oil, are the same as that of the glass bulb of the CRT. The thickness of the glass disc brings the glass-air boundary forward, further from the phosphor. This limits the angle of incident light which can be reflected back to the phosphor. This technique significantly improved the contrast of the checks and allowed a 2.5 log unit difference in brightness between white and black checks.

Actual maximum brightness of the display was measured at 8000 cd/m². To test the linearity of the Z axis, a two-cycle sine wave with full contrast and maximum brightness
was displayed. A photometer with a 0.006 inch test spot was scanned across a half cycle of the display with readings taken every 0.02 inches. Data are shown in Table 3: X is displacements in hundredths of inches, Y(OBS) are photometer readings, Y(CALC) are values calculated from the best sine wave fit to the observed data, OBS-CALC are the values of the differences. This table shows that linearity is about ±5%. 
**TABLE 3**

**SINE WAVE LINEARITY TEST**

<table>
<thead>
<tr>
<th>X</th>
<th>Y(OBS)</th>
<th>Y(CALC)</th>
<th>OBS-CALC</th>
</tr>
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<tbody>
<tr>
<td>0.0</td>
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<td>-1.08E-01</td>
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</table>

*See text for details.*
d. Adaptation Field

Most visual phenomena are affected by retinal adaptation level. Color effects have notoriously been confounded by luminance effects. Stray light from flashed stimuli can illuminate portions of the retina not intended for stimulation. All these possibilities can be controlled by use of an adaptation field. For this reason two hemispherical adaptation fields were employed; one for low brightness (-200 cd/m\(^2\)) and one for high brightness (-2000 cd/m\(^2\)).

The low brightness hemisphere has a 50 cm radius and is painted white. With chin rest support, the observer's eye is located at the radial center of the hemisphere and looks toward a 12.5 cm hole cut in the back of the hemisphere for presenting stimuli. Six microscope illuminator bulbs are partially enclosed and symmetrically located so that their beams light the hemisphere evenly. Power for the bulbs is brought into the double-shielded test room from a current regulated dc supply.

The high brightness hemisphere is similar but smaller with a 25 cm radius. It is designed to allow colored adaptation fields. The observer's eye is still located 50 cm from a 12.5 cm hole, so the adaptation field size is reduced from 180\(^\circ\) to 90\(^\circ\). Three 150W quartz-halogen bulbs are located between the hemisphere and the observer with
their beams masked from direct view. A dichroic reflector
directs each beam through three heat filters and a visible-
bandpass interference filter. Without this filtering, the
hemisphere was uncomfortable to view, and glass color fil-
ters placed in the beam would break from thermal stress.
After optional color filtering, the three beams are dif-
fused by ground glass so that they fill the hemisphere
evenly. Again, the lamps are dc powered and current con-
trolled. Normal operation color temperature for the
quartz-halogen bulbs is 3400°K, but the heat filters push
the color temperature up.

Experiment Design and Procedure

Because of the intersubject variability that the VER
often shows, confirmation of the original color difference
findings was to be the first experiment. This would be at
low brightness and include added controls for stray light.
Still there may be possible rod contributions and stray
light effects, so we decided to raise the adaptation above
rod saturation and then raise the stimulus brightness in
small steps from below threshold to maximum. This was to
be done with three different subjects and four different
colors to establish a spectral sensitivity for the dif-
f erent inferred source locations. Finally, blank flashes
and appearing checkerboards (checks exchanged for an equal
average luminance uniform field) would be used to determine
if the effect was associated with luminance change or with pattern change. Results would be interpreted in terms of equivalent dipoles and suspected VER source locations.

To avoid the possibility of abnormal VER potential distributions, only right-handed, nonastigmatic dark-haired, healthy subjects were selected. All three subjects tested 20/20 or better on the Snellen chart and passed the recently developed D and H Color Rule test for color normalcy.

Electrodes were the standard silver/silver chloride EEG type of 9 mm diameter. They were located on the scalp according to the International 10-20 EEG system with additions. Figure 8 shows an orthographic projection of the back of the head with electrode positions identified. The occipital protuberance or inion is labeled IN; OZ is located above IN by 10% of the midline distance from inion to nasion (nose bridge), OP is at 20%, PZ is at 30%, and CZ is at 50%. To the left of OZ at 15% of the horizontal distance to the nasion is TO5; at 30% is T5, at 50% is T3. Similarly, TO6, T6, and T4 are located to the right of OZ. Below TO5 at inion level is LI, and RI is below TO6. Halfway between T3 and CZ is C3; halfway between T5 and PZ is P3. On the right side, C4 and T4 are similarly located. Electrode sites were rubbed briskly with Redux Paste (Hewlett Packard), and electrodes were attached with
Figure 8. Orthographic projection of back of head showing electrode positions.
electrode cream (Grass type EC-2). This procedure always kept electrode impedances below 10 kΩ. Large silver/silver chloride electrodes were attached to the nose for a reference voltage and to the cheek for ground.

Light from a xenon flash lamp and reflector (Grass photic stimulator) was diffused with ground glass and filled the hole in either adaptation field. The left or right half of this hole was masked with white cardboard which had a black dot for a fixation mark on its edge. The dot was located at the center of the hole, so when the subject fixated it, the flash was presented in a lateral half field with a radius of 7.5° visual angle. Between the diffuser and the mask, a checkerboard pattern with 15' checks and a color filter could be inserted. A 6° square mask with fixation marks at left and right center positions was used in conjunction with the electronic pattern generator. Check size was set at 12' with 32 checks on a side. The flashtube was enclosed in a sound-deadening box, and with the shielded room's ventilating fan going, the click from the flash was inaudible. The spectral content of the flash and the transmission spectra of the color filters are shown in Fig. 9 as supplied by the manufacturer. The flashtube's spectrum is clearly only approximated by the curve shown (A) since the line radiation which is always present is not shown. Furthermore,
Figure 9. Spectra supplied by manufacturer for xenon flash and color filters.
the spectrum must change with flash intensity settings because the spectrum depends on current density, and this must change to provide more energy in the same flash duration. The filters used in this experiment are those of curves 1, 3, 4, and 5 which are named red, yellow, green, and blue respectively. In preliminary experiments, the filter of curve 2 produced the same results as that of curve 1, so it was not used. In Fig. 10 the spectral output of the P-45 phosphor is shown.

For most of these experiments, 16 electrode positions proved adequate to show the effect. Unused preamplifier channels were shorted at their inputs. Four channels were signal averaged "on line", and then hard-copied on an X-Y recorder. The remaining channels were multiplexed and stored on tape. Sessions ran about 1½ hours but data was collected for only 30 minutes of that time. Various flash stimulation frequencies were used initially, but later the interstimulus interval was randomly varied between 320 and 440 ms to desynchronize any after discharge. The period for appearing checks was 747 ms with the checks present 50% of that time. This long period allowed separation of the responses from check appearance and disappearance. Most of the time one eye was covered, but the other was occasionally used as was binocular stimulation. For all the recording, 256 responses were signal averaged.
Figure 10. Output power spectrum of P-45 phosphor.
Each condition was repeated two or three times dependent on the reproducability of the subject's response.
CHAPTER III
RESULTS

The data presented in this chapter are necessarily condensed from the raw records of over 300 runs (signal averaged responses) for each of 16 channels. There were 36 different stimulus conditions, 3 subjects, and on the average 3 repetitions for each combination. About 100 contour maps were plotted, but in most cases only typical maps or graphs derived from maps will be shown here. However, each map and graph is an average of two or more runs, and an attempt is made to mention any obvious differences between the condensed data and the raw records.

To aid in later interpretation of the data, the dipole concept will be introduced early and used throughout in describing the results.

Low Adaptation Level, Red vs. White Data
a. Flashed Checks

At the top of Fig. 11, typical VER's to red flashed checks in left or right half fields are shown. The ordinate is in microvolts and the abscissa is in milliseconds as is the case for all the VER's shown in this chapter.
Figure 11. VER's and contour maps for red flashed checks.
The dashed line response (marked R) is from the right occipital region at TO₆, the solid line response is on the left (marked L) at TO₅. These VER's are very similar to those previously reported for other subjects under similar conditions [44,45]. In this previous work it has been the first positive contralateral peak which was best localized. For the contour maps at the bottom of Fig. 11 as well as for all the other data in this chapter, it is the amplitude of the response at all electrodes at the latency of this first positive contralateral peak (generally around 80 ms) which has been plotted by measuring from a base line value at the beginning of the peak (generally around 60 ms). Each contour in the maps represents 1 μV; the dashed line is the zero voltage contour. Potentials at each electrode are indicated; values are in microvolts x 10. Actual latencies of the measurements for the maps are indicated. These conventions hold for all maps presented in this chapter. There is a clear polarity reversal in the map, as well as in the raw data, going across the back of the head. This reversal is near the midline with positive potentials on the side of the head contralateral to the field of stimulation maximal at the TO₅ or TO₆ position with a symmetrical negative maximum on the ipsilateral side.

The first indication of a color difference appeared
when the stimulus color was changed to white. To compensate for the brightness reduction of the red filter, which was estimated at a reduction of 80% from a heterochromatic match, the flash intensity was reduced four-fold and the brightness of the adaptation field was raised from 170 cd/m$^2$ to 340 cd/m$^2$. Fig. 12 shows the response of the same subject, subject M, to white flashed checks. Here the peak latency was greater, but from the VER's it is evident that a similarly shaped map would be found at slightly smaller latencies too. The contour maps show polarity reversals located far from the midline, and the VER's have similar shapes on either side of the midline.

These results can be compared to the predictions of a model of the head as a homogeneous sphere with a single equivalent dipole source imbedded in it. Figure 13 shows the potential distribution this model predicts along the row of electrodes across the back of the head. At the top is a plot for a dipole source oriented tangential to the surface of the scalp. Note the polarity reversal near midline and the difference in the slope near the midline compared to near the ears. At the bottom is a plot of a dipole oriented along a radius of the spherical model. Here the polarity reversals appear near the ears, and the slopes on either side of maximum are equal. The dipole in this figure is situated at half the distance from occipital scalp to the center of the spherical head. This is rather deep in the
Figure 12. VER's and contour maps for white flashed checks.
Figure 13. Potential distributions from tangential (upper) and radial (lower) dipoles.
head but the shell model of the head produces very similar potential distributions for a dipole located only one-fourth the length of the head's radius from occipital scalp [51].

The red-white difference was tested in another subject, subject A, whose measurement latencies were 68-84 ms. Figure 14 shows a graph of the potentials across the back of the head for the two subjects for red and white flashed checks. For red, polarity reversals are near the midline, and the distributions appear tangential. For white, polarity reversals are nearer the ears, and the distributions appear more radial in nature.

b. Blank Flash

Test conditions for the blank flash were the same as for flashed checks except the checks were removed so the flash brightnesses were double those used before. Figure 15 shows the red flashed-blanks response that typified both subjects A and M. Peak latency was shortened by 6 ms, but the map is little changed from that for checks; it resembles the distribution of a tangential dipole.

The VER's for white flashed-blanks were severely contaminated by an anomalous early response probably due to synchronization of the after discharge with the flash. Typical responses are shown in Fig. 16. Randomizing the flash frequency did not alleviate the problem. This effect reportedly occurs when an adaptation field is used to prevent stray light influence [38]. The blank flash study
Figure 14. Potential distributions for red and white flashed checks.
Figure 15. VER's for red blank flashes.
Figure 16. VER's for white blank flashes.
was not pursued further.

**High Adaptation Level, Color-Filter Data**

To clarify the color dependence of the red-white effect, the brightness of the adaptation field was raised to 2000 cd/m², and four different-colored flash stimuli and two different-colored appearing check stimuli were employed.

a. Colored Flashed Checks

For each color a series of flash intensities was employed coming up from below threshold to about a log unit above. There were no significant changes in the patterns of the contour maps over the flash intensity ranges tested. Figure 17 shows a graph of the responses across the back of the head of subject M to different colored flashes. These data and that of the next two figures were taken at a flash intensity twice that of threshold which is just enough to give clear responses while minimizing the possibility of stray light. In Fig. 17 there may be some degradation in the tangential character of the red response as compared to the data taken with adaptation at about a log unit lower brightness. However, there is a clear difference in the responses to yellow flashes which resemble a radial dipole located near the midline. The other colors appear more tangential in character than radial, perhaps best resembling a slightly tipped tangential dipole. In Figure 18
Figure 17. Potential distributions of subject M for various colors.
are the responses of subject A to the different colored flashes. Here the red response resembles a radial dipole localized near the surface of contralateral cortex. The blue and green responses show a gradual pattern change from that of the red response toward that of the yellow which is a more centered broad radial distribution, distinctly different from the other colors. The third subject was the only female, and her responses are shown in Fig. 19. Here the polarity reversals are located slightly off the midline on the contralateral side, and there are no obvious differences in the responses for different colored flashes.

A few exploratory runs were conducted on subjects M and A using colored adaptation fields. The rather sketchy data collected showed no change in the color effect when red or blue was substituted for white adaptation.

b. Appearing Checks

For these runs the brightness of the adaptation field was adjusted to about that of the stimuli. For white checks this was about 2000 cd/m²; for red checks it was about 1000 cd/m². The contour maps for subject M are shown in Fig. 20. There is rather little difference in the potential distributions for these two colors. In Fig. 21 responses for red and white stimulation of subject A is shown. Again the color differences are negligible.
Figure 18. Potential distributions of subject A for various colors.
Figure 19. Potential distributions of subject L for various colors.
Figure 20. Subject M's contour maps for red and white appearing checks.
Figure 21. Subject A's contour maps for red and white appearing checks.
Red appearing checks on a red adaptation field also showed no change in the contour maps. Also a few runs at low brightness (~200 cd/m²) showed no difference in red and white distributions. Other colors were not used for stimuli because there was no red-white difference.
CHAPTER IV
DISCUSSION

These data suggest that there is a topographical distribution of color sensitivity in the human visual cortex at least in some subjects, and that yellow sensitive areas are somehow separated from other color sensitive regions.

The data of Fig. 17 and Fig. 18 show a gradual increase in potential near the midline as the stimulus color approaches yellow. Perhaps this indicates a surface-positive yellow-sensitive region located on surface cortex near the occipital pole. If this were the case, the responses shown in these figures could result from linear summation of surface-negative activity in mesial cortex and surface-positive activity near the pole. Single cell records show ample instances of yellow sensitive cells in foveal striate cortex of monkey, and some of these cells are rather narrow band in spectral sensitivity. Certainly there must be other explanations for the data presented here, but thus far there are no strong indications of what they might be.

The fact that one of three subjects showed no color effect is disturbing. It may be an indication that some
people's cortex does not code for color, at least not in the same way. There is no further evidence here that the color effect is related to sex. Admittedly the number of subjects tested is small. It should now be possible to use a limited number of stimulus conditions to test numerous subjects for the color effect.

From the appearing check data it seems that the color effect is not present for pure pattern stimuli. Because of the poor quality of the white blank flash data, it is not possible to decide whether the effect is only sensitive to luminance changes or if luminance and pattern changes are both required. However, it is quite possible that the reason no color effect was seen for appearing checks was that the P-45 phosphor does not produce enough light in the yellow band; see Fig. 10.

Regan has noted the possibility that the VER does not have the same spectral sensitivity as the psychophysical tests show for the standard photopic observer [50]. However, Siegfried has used peak-to-trough amplitudes to compare color responses to a standard white and thereby reduce the amplitude variability of the VER [84]. The spectral sensitivity he derives is very similar to the psychophysical data. Although a relatively small luminance range by vision standards was employed in these experiments, it would seem that the range was sufficient for
a luminance effect control. Generally, the thresholds determined with the various color filters were in keeping with a heterochromatic brightness measure of their relative transmission.

The possibility of stray light contaminating the results is considered remote. There is no reason to expect that stray yellow light is much more effective than the other colors. Furthermore, data taken so close to threshold could hardly be contaminated by significant stray light hitting light adapted portions of the retina.

This study was primarily designed to demonstrate that color effects alone can change the potential distribution of the VER. Secondarily it was intended to suggest the topographical distribution of color sensitivity. As argued earlier, local cortical VER recording is probably the most direct way of proving the location of scalp recorded sources.

Several technical improvements in experiment design might sharpen the picture of the different color sensitive source locations. Certainly narrow band filters, more partial visual fields, and a continuous band appearing-check generator would be helpful. There may also be color sensitive topographies for other VER peaks and for other stimuli, e.g., reversing checks or disappearing checks.

At the present time the "meaning" of the VER is not
well understood. This study was an attempt to find out more about where it comes from and hopefully how it is produced. When more is known about the color components of the VER, it may be possible to develop a chromatic channel theory for the cortex.


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