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EVOKED CORTICAL RESPONSES TO ELECTRICAL STIMULATION OF THE ISCHEMIC RETINA

M. L. Wolbarsht, Ph.D. Department of Ophthalmology DUKE UNIVERSITY MEDICAL CENTER Durham, NC 27710

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INTRODUCTION

The objective of this program has been the early detection of the disturbances in retinal blood flow, such as ischemia, that are the precursors of blackout and unconsciousness. External electrical stimulation of the peripheral retina has been used to evoke cortical responses while still allowing normal visual function. The purpose of the present work has been to test techniques that might furnish early warning of loss of brain function or blackout resulting from high positive G forces that produce circulatory stasis in the head, particularly in the brain or eye. During the present period the electrical evoked central response (EER) technique was used at the limits of its detection capabilities and compared with similar techniques using visual stimulation. Investigations on cats were carried out to determine if a decrease in peripheral blood flow could be equated with loss of responsiveness to electrical stimulation to peripheral portions of the retina from external electrodes. The electrically evoked cortical responses (EER) were monitored by scalp electrodes in the region of the inion similar to the conventional method for recording the responses evoked by visual stimulation (VER). Theoretical analysis of this situation suggests that the EER approach is more favorable than the VER. The optical stimulation used in the VER preferentially evokes cortical responses from the central or macular portion of the retina. However, the electrical stimulation used in the EER may be delivered to stimulate the peripheral portion of the retina preferentially. In order for a cortical surface recorded electrically evoked response from the visual system to be useful as the criterion for the positive detection of the effects of high G forces, the loss of visual function should have a short latency.

Another consideration is that normal visual function should be impaired as little as possible during the tests of brain function prior to blackout. Here also the EER may have some advantages. The electrical responses used in the EER mainly stimulated the peripheral retina. Thus, any changes in the perception of visual space due to a combination of the electrical stimulation with the psychological optical image will be in the most peripheral portion of the retina. This corresponds to the peripheral environment and will be less noticeable, as it will degrade visual function only in the less important portions of the visual fields.

"G" tolerance by pilots is often exceeded in present day military jet aircraft. The heart is not powerful enough to force blood into the brain when the body is accelerated downward by aircraft maneuvers. The blood pools in the legs and abdomen, and freshly oxygenated blood cannot reach the eyes and brain. Visual sensitivity is first reduced in the periphery, then in the center. Even later, if the interruption of blood flow is maintained, total blackout and unconsciousness will follow in a rapid sequence.

VISUAL (OPTICAL) STIMULUS

The Naval Air Development Center at Warminster, PA, currently has a program on blackout detection, which was reviewed by Cohen in 1979, and more recently by Nelson and Hrebien (1982 a,b). In the normal eyes the internal pressure is between 8 and 20 mm Hg with the most usual value about 12 mm Hg. This intraocular pressure impedes blood flow to the retina relative to flow through the cortex, the equivalent of 1 G of downward acceleration. Thus, with downward acceleration the retina becomes ischemic sooner than the brain. This decreased blood flow with downward G will produce visual changes before the loss of CNS function, and, for this reason, tests of human tolerance to downward G forces generally use visual performance.

Brown & Watanabe (1965) have shown that total anoxia reduces cortical function first and then progresses to the lateral geniculate nucleus, finally reaching the retina. In the retina, photoreceptors are affected last. However, the effect of blood stagnation during downward acceleration first shows up by loss of function of the inner retina. Here, as the blood vessels are occluded, the

local vessel pressure falls below the normal intraocular pressure. This begins in the capillaries as the resistance to blood flow is higher in those smaller vessels. As the peripheral capillaries are somewhat smaller than the central ones, the peripheral vessels are more sensitive to blood pressure changes than the central ones. All this results in the loss of function in the peripheral retina first, (Ward, 1968). The restriction of peripheral vision is followed by progressive deterioration of central vision, and finally total blackout. The whole process is attributed to ischemia of the inner retina. The loss of retinal function seems to be an earlier stage of the development of unconsciousness due to cerebral hypoxia (Doolittle, 1924; Duane, 1954; Fraser, 1966; Leverett, Kirkland, Schermerhorn & Newsom, 1966; and Mercier and Duguet, 1947).

The process leading to visual blackout in unprotected and uncompensated human subjects during acceleration is unlikely to be simply a result of blood flow changes as described above. (Betz, 1972; Krutz, Rositano, and Mancini, 1975). Nevertheless, the sequence of changes in the blood flow in the eyes and brain during acceleration can be the basis for showing human resistance to downward acceleration may be enhanced. Resistance to downward acceleration can be increased by placing the subject's back toward the acceleration, replacing the head-to-toe accelerative forces by chest-to-spine ones. This position increases the tolerance to over 11 Gs. Blackout can be avoided when blood pooling in the lower extremities and the abdomen is inhibited, and the circulating blood volume is increased. The inflation of the bladders in a conventional G-suit does just this and provides about 1.5 or 2.0 Gs additional tolerance. The increased intra-thoracic pressure during exhalation against a closed or partially closed glottis (the L1 and M1 maneuvers) also diminishes blood pooling by about the same amount.

The use of these protective measures requires some method for evaluating G tolerance reserve with the following characteristics:

- 1. High reliability and reproducibility.
- 2. Physically and behaviorally non-invasive.
- 3. Objective and points.
- 4. Insensitivity to experimental artifacts.
- 5. Rapid on-line, real time discrimination.
- 6. The largest possible margin between the initial detection of a decrease in G tolerance and the boundary of unconsciousness.

Visual behavioral responses are not stable and often distract from adequate performance on other concurrent visual tasks. Only objective measures of the integrity of the visual system during retinal ischemia seem able to meet most, if not all, of the above criteria.

The NADC program (Cohen, 1979; Nelson and Hrebien, 1982 a,b,c) is based upon the work of Duane et al (1962), who demonstrated visually discriminable photic driving of the filtered EEG, which followed the frequency of this test light. Some subjects exposed to accelerative forces in the human centrifuge showed loss of peripheral light sensitivity and photic driving of the EEG, along with collapse of the retinal arterioles. Blackout occurred in the systolic phase collapse. Photic driving ceased before grayout or dimming of the peripheral visual field.

Visual evoked responses (VER) furnish an objective test now that real time digital computer processing methods allow the reliable detection of small amplitude bioelectrical signals. Since changes in visual function should provide a reliable indicator of G tolerance (Coburn, 1970; Gillingham and Krutz, 1974) and since both the visual evoked cortical responses (Cohn, 1969, Donchin and Lindsley, 1969; Richards, 1977) and electroretinograms (Tepas, Armington and Kropfl, 1962; Ward, 1968) have been shown to provide reliable indicators of visual functioning, it appears these techniques may furnish a simple, yet reliable, approach to the determination of human tolerance to acceleration. The recent work at NADC has borne this out (Nelson and Hrebien, 1982 a,b,c).

The electroretinogram (ERG) is generated by the retinal receptors (negative a-wave) and the neural activity of the inner layers of the retina (positive b-wave) according to Ward (1968). The appearance of the various components of the ERG gives a measure of retinal ischemia and thus, G tolerance. The ERG response to a high luminance stimulus is much easier to detect than the VER. However, the ERG almost disappears as stimulus luminance decreases, while the VER still remains quite detectable. In this way, the ERG may be a better indicator of retinal function than the VER. Ward (1968) has observed that the amplitude of the ERG b-wave was markedly diminished in anesthetized dogs exposed to downward acceleration, and disappeared completely when the acceleration was doubled. Also, the ERG is an area effect, and thus photometrically represents peripheral retinal responses. In this point, the ERG has an advantage over the VER. The value of the ERG for detection of detrimental G forces in humans is not presently known, however.

The ERG and the VER both depend upon potentially annoying visual stimulation. However, the recent work at NADC (Nelson and Hrebien, 1982 a,b,c) shows that the VER may detect reliably without marked visual annoyance from the stimulus. On the other hand, the VER preferentially represents the central retinal responses. Thus, it may be that an alternative electrical response which combines the minimal visual distraction of the VER with the high sensitivity to peripheral retinal integrity of the ERG, such as the electrical stimulated cortical response (EER), could be a suitable measure of visual system function in an acceleration field to be used operationally as an early warning of blackout. The present program was designed to evaluate the ultimate sensitivity of the EER as an early warning for blackout during positive G.

ELECTRICAL STIMULUS TECHNIQUES

The scientific background for electrical stimulation of the retina from external sources has been cited in an earlier report (Wolbarsht, 1982) and need only be summarized here. Previous investigations have been devoted to the perceptual responses of electrical stimulation of the eye, and to the perceptual assessment of electrical stimuli presented in conjunction with flashes of light in various patterns within visual space (Motokawa, 1949). Simple electrical stimulation of the retina is equivalent to a diffusely presented light in the peripheral portion of the retina and threshold of this electrical response in the retina is greatly lowered by the ambient illumination. Also, the electrical excitability of the retina varies with a fixed time course after illumination (Motokawa, 1949). This indicates that both the frequency of electrical stimulation and the frequency content of any illumination must be considered in analyzing the cortical reponse to electrical stimulation of the retina.

The electrical excitability of the retina has been used as an indicator of oxygen deficiency (Motokawa & Iwama, 1949) while the inspired 02 partial pressure was changed. The tests were conducted on dark-adapted subjects in order to get maximum sensitivity, but the data is ambiguous

as there was a difference between the threshold levels with ascending and descending 02 levels, as compared with a normally oxygenated subject. Also, the minimum oxygen saturation of the blood was still well above that at which additional oxygen is normally administered. The responses to visual stimulation were very similar to those elicited by electrical stimulation, although electrical stimulation seemed to be more sensitive.

Dawson and Radtke (1977) used flickering light in conjunction with pulsating retinal electrical stimulation to the retina indwelling electrodes. However, changes in the retina threshold did not allow positive identification of the optically activated region of the retina.

PRESENT PROGRAM METHODS

The cat was selected for this experimental program on the basis of similarity to monkey and human systems, easy availability, and low cost. The animal was mounted in the optical stimulator with the eye immobilized. Refractive errors were corrected by a corneal contact lens. A catheter was inserted through the pars plana for direct manometric control of the intraocular pressure.

The animal handling techniques, including anesthesia have been described previously in detail (Wolbarsht, 1982). A summary of the methods used follows: All experiments were begun under I.V. administered phenobarbitol chloride anesthesia followed by a general anesthesia – 70% nitrous oxide and 30% oxygen at a level sufficient to suppress any reflex responses to corneal stimulation or intratoe web pressure. The animal was intubated and was respired artificially. The expired pC02 was monitored continuously and kept at 4.7%.

Normal body temperature was maintained by a heating pad. The life-support system was adequate to maintain satisfactory physiological condition for up to 48 hours, although the experimental sessions were never more than 8 hours long. A local anesthetic was applied to all incision points.

Gallamine triethoxide was used to assist in maintaining the high degree of immobility required to assure that both the electrical and visual stimulations were the same at all times during the experiment. Both gallamine triethoxide and nitrous oxide have little effect on the retinal and other central nervous system responses of cats and monkeys (Brown et. al., 1927, Enroth-Cugell and Pinto, 1970, Enroth-Cugell and Robson, 1966, Van Norren and Padmos, 1977, Venes, et. al., 1927). Obviously, it is important to minimize CNS effects from the anesthetic when studying the activity of the visual system, especially when using the evoked cortical responses. The iris was dilated and accommodation relaxed with several doses of Duke mix (10% phenylephrine; 0.5% mydriacyl, 1:1) applied every hour.

We have examined the cortical responses to visual and external electrical stimulation of the retina, and all of these responses were recorded with normal and elevated intraocular pressures. The overall objective of this program was to determine how great a sensitivity could be achieved by the use of scalp electrodes in the region of the inion to measure cortical potentials evoked by external electrical stimulation of the eye in a test for the occurrence of peripheral retinal ischemia. In most experiments, the retinal ischemia was induced by an increased intraocular pressure controlled manometrically. During the experiment the heart rate was continuously monitored, and at no time were heart rate changes detected which would be associated with pain perception.

The two channel basic optical stimulator has been described in detail in previous reports and other publications (Wolbarsht, 1978; Wolbarsht and Ringo, 1980; Crocker et al, 1980; and Wagner

et al, 1960). A Grass photoflash stimulator (Model PS-22A) was also used to give a large field visual stimulus.

The electrical stimulus was delivered to the eye through paired electrodes mounted at the inner and outer canthus or through cheek and brow. The electrical stimulus was generated by standard means and amplified as discussed previously (Wolbarsht, 1982). Conventional EKG electrodes were used for both recording and stimulation on the shaved but intact scalp above the inion, and on the shaved brow and lower lid and at the inner and outer canthus. The responses were viewed in single sweep form, or processed with a signal averager. All leads were capacity coupled.

The visual evoked potentials (VER) were obtained by stimulating the eye with either 300 ms or 10 ms pulses of light at a repetition rate of 1 per second through the 2 channel Maxwellian view optical system.

The intraocular pressure changes were obtained by lengthening or shortening the height of a column of saline connected to the vitreous cavity through a needle piercing the pars plana.

RESULTS

For comparison purposes, electrical evoked responses were also made from corneal stimulus electrodes. EERs were recorded using a stimulus electrode implanted into plastic corneal lens, as this gives the largest cortical response, and the inion recording electrode could be located optimally on the basis of this response.

As noted previously (Wolbarsht, 1982), the normal intraocular pressure in a cat is from 12 to 18 mm mercury (16 to 24 cm water). Raising the intraocular pressure to 118 mm Hg (155 cm of water) eliminated both the visual evoked response and the electrical evoked response. This effect was reversed when the intraocular pressure was lowered to the normal level as long as the elevated pressure phase was not maintained for more than five minutes. The use of stimulus isolation techniques did not eliminate the stimulus artifact, but usually it was at a minimum when negative with respect to the response. Often both polarities of the stimulus pulse had to be tried in order to obtain the maximum signal-to-noise ratio for the response. Previous work (Wolbarsht, 1982) on electrically evoked responses (EER) from stimulus electrodes at the inner and outer canthus showed a higher threshold than for an electrode in a corneal contact lens, 1.25 volts versus 0.950 volts. However, the canthal electrode placement was better for stimulation of the peripheral retina. As the responses for cheek and brow electrodes are more difficult to obtain consistently, this electrode placement was used only occasionally, for comparison purposes, in the present series of experiments. EKG electrodes covered with well-moistened electrode paste with an impermeable covering (Saran Wrap) to eliminate evaporation gave the best and most consistent results.

The purpose of the experiments in this study was to develop techniques for the most efficient and consistent recording of cortical responses to visual stimulation, with a minimum number of stimulus pulses. Both single pulse responses and low number (4 to 16) averaged single pulse responses were investigated.

Once an optimal electrode location was established, electrical stimulation was initiated to compare different detection techniques during normal intraocular pressure with the loss of detection of the responses as the pressure was raised.

The EER to a single electrical stimulus pulse can usually be seen and identified, but the presence of a great deal of both low and high frequency noise has made it difficult to use electronic detection techniques. The averaged responses to 4 to 16 stimulus pulses are sufficiently noise free for a conventional window discriminator to operate. Single response detection is more difficult.

Nelson and Hrebien (1982 a,b,c) have described an elegant Fourier transformation technique for noise suppression in a study of steady state optical stimulus situation, but their method is, unfortunately, not easily adaptable to detection of a single transient response.

At present, two detection methods are being evaluated. The first consists of a tuned delay line. The circuit uses a combined inductive-capacitative filter tuned to the expected shape of the response. Both the stimulus artifact and the background noise are largely suppressed allowing subsequent amplitude discrimination as the basis for recognition or threshold evaluation. The theory and details of the circuit used are given in the appendix. Even if single pulse response detection is not possible with this technique, subsequent averaging will be enhanced, and 2 to 4 repetitions may give sufficient reliability for field use.

The second method uses an electronic comparison method in which the signal is digitized and compared with a template (averaged) response and points of correspondence are noted. Identification is based on a statistical evaluation of the number of points of exact (or near) correspondence. Available computer facilities do not allow the use of this technique in a real time, on line situation, but analysis of recorded data is possible and preliminary results are encouraging.

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APPENDIX A

TUNED DELAY LINE FILTER AND ASSOCIATED CIRCUITRY

Classical signal detection and estimation theory (Van Trees 1968) yields the well known result that a matched filter provides optimal detection of an exactly known waveform in the presence of band limited additive Gaussian white noise. The matched filter is optimal in the sense that its output, at a specified time interval after a given input, is a monotonic increasing function of the ratio of the probability that the desired signal was present in the noise to the probability that noise alone was present. This ratio is called the likehood ratio.

When the output of the matched filter is applied to an amplitude discriminator, the most probably occurrence of a signal, such as a nerve impulse in noise can be detected. Furthermore, the output of the matched filter is proportional to both the minimum mean squared error estimate and the conditional maximum likelihood estimate of the amplitude of the signal when present. The output can also be shown to provide the maximum attainable signal to noise ratio (Whalen, 1971). Thus, the output of the matched filter is a reasonable signal to apply to an amplitude or window discriminator to separate neural responses on the basis of amplitude. The characteristics of the matched filter are very simply defined as that filter whose impulse response is the time domain reflection of the known signal waveform.

Two assumptions have been made in the previous discussion. First, that the noise present is band limited, additive, Gaussian white noise. No exhaustive analysis of the properties of the biological noise has been made, but in the absence of conflicting evidence, these properties can be assumed to fit approximately in the 1 Hz to 5 KHz range of interest. If the noise in a given experimental situation is known to be non-white, a variation of the matched filter will provide the same advantages obtained by its use in the white noise case (Whalen, 1971). The second assumption is that all of the responses of interest in a given recording situation have nearly identical waveforms and differ only in amplitude. This is true for nerve impulses or evoked cortical responses made under similar recording conditions. By setting the matched filter to an average response, very little performance is lost. However, in some situations there may be several different waveforms of interest. This would require additional stages in the filter and several outputs, one for each waveform.

The matched filter for a continuous signal would be an analogue filter. However, a digital approximation (or "digital filter") is a particularly appropriate device for implementation of the matched filter, and in its simplest form, the output of the digital filter is a linear combination of samples at discrete time intervals of the input signal. This is accomplished by digitizing the signal and storing it in a computer. As the name implies, the digital filter is most commonly used with digital data in a computer. However, the analogue implementation of it in which the input signal is applied to a tapped delay line and summing amplifiers offers several advantages over conventional filters as its impulse response, and thus its phase as well as frequency characteristics are directly dependent upon the choice of the weighting coefficients. This makes the delay line filter sufficiently flexible to deal with a variety of signal and noise situation.

The well-known Shannon sampling theorem proves that a finite bandwidth imput signal, sampled at twice or more its highest frequency component, can be represented in terms of its samples with no loss of information. Therefore, a digital filter whose weighting sequence is the sampled time domain reflection of the known input signal will perform exactly as a matched analogue filter.

It can be shown that the output of the matched filter is also the conditional maximum likelihood estimator and the minimum mean squared error estimate of the amplitude of a known signal. Thus, the proper matched filter can approach the theoretical limit for amplitude estimation of a signal in noise.

The overall signal processing system as originally designed for nerve impulses is diagrammed in Figure A-1. It consists of a tapped delay line matched filter, a baseline restorer, and a window discriminator (3 ms total delay). A new system is now being constructed for cortical responses with a longer delay (30ms).

Although matched filters have frequently been implemented on a digital computer, an analogue design is shown schematically in Figure A-2. This is derived from one described by Marks (1965) and Glaser(1971). The detailed circuitry is shown in Figure A-3 and consists of a tapped delay line of 3 ms total length with adjustments spaced every 0.1 ms. The delay line is of conventional lumped parameter design. It was inexpensively (parts less than \$100) constructed using surplus telephone torroidal inductors with standard 10% tolerance capacitors connected in parallel and parts selected to match within 1%. The signals present at each tap are combined into a weighted sum by two operational amplifiers. The variable weighting constants are adjustable from -1 to +1 by means of potentiometers. The filter is capable of matching any waveforms of less than 3 ms total duration with a bandwidth less than 5 KHz. The same delay line may be used to sort responses of several different shapes by adding summing amplifiers, weighting potentiometers and output stages for each shape. These additional units are connected to the delay line at the same points as those from the first unit. Each unit is then individually adjusted to its particular waveform. Adjustment is facilitated by a switch which changes the input to the opposite end of the delay line thus providing a "time domain reflection." A rectangular pulse of the desired duration (0.1 ms for the circuits shown) is applied to the filter and the weighting potentiometers are adjusted to obtain a replica of the impulse waveform at the output of the filter. With the input switched back to the beginning of the delay line, the filter will now have the desired impulse response. If a sample response from the actual preparation is displayed on a storage oscilloscope, it is possible to adjust the filter accurately during the course of an experiment.

During initial tests of the matched filter, the delay line termination resistors R1 and R2 should be adjusted to minimize reflections on the line. A convenient alignment scheme as used for nerve impulses is as follows.

A 2 volt rectangular pulse of 0.5 ms duration with a 20 ms repetition period is applied to the input of the filter. The waveform at point A is observed with the function switch set in the "adjust" position. R2 is adjusted for minimum reflection. The switch is placed in the "operate" position. The waveform is monitored at point B while R1 is adjusted for minimum reflection. The reflection should be a rectangular pulse of the same width as the input pulse and follow it by twice the delay (6 ms). The polarity will change from the same as the input pulse to its opposite as the termination resistor is varied. The tuning is optimal when the resistor is set for zero reflection. In pilot experiments, the time constants of the various nerve impulses used for testing were sufficiently similar that a single output tap matched all of them. In situations where several time constants are present, then additional output taps with tuning adjustments can be added.

The advantages of the analogue implementation of the matched filter are several. It operates on-line in real time. It is readily adjusted and readjusted during the course of an experiment by simple visual comparison. The digital implementation of the equivalent filter would require a high resolution analog to digital converter and a processor capable of performing 300,000 multiplication and 300,000 additions each second, which may be somewhat difficult to program on a typical laboratory computer.





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VARIABLE GAIN D.C. AMPLIFIER AND INVERTER

The variable gain amplifier allows the signal level to be adjusted to compensate for variations in overall signal level often experienced in electrophysiological recordings. It also allows for inversion of the signal to allow negative-going spikes to be properly handled by the baseline restorer and window discriminator. Adjustment of the gain before the window discriminator minimizes the need for readjustment of discriminator thresholds during an experiment. The gain adjustment could be made automatic in future models, causing the largest amplitude responses to maintain a constant amplitude.

THE BASELINE RESTORER

The baseline restorer ensures that each spike output of the matched filter is referenced to a common baseline before being presented to the window discriminator. Baseline drift in the signal is caused by several factors. DC drift in the preamplifier and electrodes is significant with the high gains used in extracellular recording. Even if AC (capacitive) coupling is used to remove this DC component, an additional baseline drift is introduced by the coupling of a signal whose average value is not zero (such as monopolar spike). The baseline restorer also removes miscellaneous low frequency noise. Plumb and Poppele (1964) and Gere and Miller (1967) have discussed the characteristics that are desired in such a circuit in more detail.

The baseline restorer is essentially a diode clamping circuit which sets the most negative part of the waveform to a fixed zero value (Figure A-4). The circuit is designed for fast attack, since the preceding matched filter has removed any high frequency noise. The delay time is set by the time constant of R1 and C1, and should be several times longer than the response duration.

THE WINDOW DISCRIMINATOR

A single section of the window discriminator circuit employed is shown in Figure A-5. Although similar to other such circuits which have been described (Yamaura and Chichibui, 1967; Dyer and Beechey, 1971; Martin, 1969; Daigle, Morgan and Budak, 1973), the present circuit contains several notable differences. First, the input and reference are of opposite polarities and are summed at the inverting input of the computer. The diodes prevent excessive excursions from zero at this input. This increases the input signal range of the comparator by eliminating common mode voltage restrictions which occur when the reference voltage is applied to the non-inverting input. The circuit is DC coupled and will operate with very slowly changing voltage levels. The high frequency limit is approximately 1 MHz when a suitably short output pulse is set by the value of C1. With the values shown, the output is a 0.5 ms pulse. Another notable feature is the application of a small amount of positive feedback, or hysteresis. This increases the reliability of the discriminator for slowly changing signals and for fast signals. It prevents the output of the discriminator from taking on intermediate values which would cause ambiguous operation of the digital logic. This hysteresis does not, as claimed by Martin (1969), place a restriction on the minimum window width which can be set. It does, however, require that the input signal fall below the lower theshold by at least 100 mV before an output is registered. This presents no problems with the pulse type of input present at the window discriminator and adds a degree of noise immunity. A Z-axis intensification circuit such as has been previously described by other (Martin 1969) is included to indicate the position in the oscilloscope display of the various threshold levels in the window discriminator with reference to the input signal.



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Figure A-5. Single Section of Window Discriminator Circuit

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FIGURE LEGENDS

- Figure A-1. Block diagram for signal processing system. The DC coupled pre-amp and AC high gain amplifier are standard units. The DC coupled pre-amplifier is a negative capacitance feedback type in order to preserve high frequency components in the signal. The AC coupled high gain amplifier is used to amplify the low level output of the preamp to a level suitable for the matched filter. It uses minimal filtering. It is AC coupled to remove DC potentials such as liquid junction potentials, etc. The matched filter, variable gain amplifier, base line restorer, window discriminators and counters are described in the text. The counters are conventional types as may be required by the experimental design. The oscilloscope requires a suitable Z-axis input and a sufficient number of traces to display the requisite information. The present system is fourchannel.
- Figure A-2. Block diagram of matched filter. The output taps on the delay line are shown with variable weighting coefficient potentiometers and summing amplifiers. The parts enclosed in the dotted box are duplicated for multiple outputs for different spike shapes. The weighting potentiometers for the various outputs are then adjusted independently to their respective spikes.
- Figure A-3. Delay line matched filter. The design characteristics and adjustment are described in the text. In order to get the proper delay characteristics the section indicated in the dashed enclosure is repeated 27 times. Note that only a single output is shown. This assumes that all the responses to be sorted have approximately the same time constants. If more than one type is taken, additional summing amplifiers and weighting potentiometers may be added to provide outputs matched to each type.
- Figure A-4. Base line restorer. The operation and design of the circuit are described in the text. This circuit assures that all responses start from a common DC level. R1 and C1 determine the time constant of the restorer. Further details are given in the text.
- Figure A-5. Single section of window discriminator circuit. The circuit design is described in the text. C1 is set to give the output pulse proper width for succeeding circuit, such as an oscilloscope or counter. The Z-axis circuitry, not shown, is shared by all discriminators. The design will vary depending on the requirements of the particular oscilloscope.

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