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Investigation of averaged evoked brain potentials

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AN INVESTIGATION

OF

AVERAGED EVOKED BRAIN POTENTIALS

by

Merlin W. Montgomery

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ABSTRACT

The use of Fourier transformation to describe and compare averaged evoked brain potentials is investigated. One method of computation of the transform is presented with examples of its application. Some possible implications and uses are discussed.

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CHAPTER I

INTRODUCTION

Averaged evoked potentials (AEPs) are widely used in the investigation of brain electrical response following sensory stimulation. The technique of recording these responses is essentially the same as that employed in electroencephalography and may be considered a special case of EEG signal analysis.

Electroencephalography (EEG) is the technique of recording and interpreting the spontaneous voltage fluctuations of the brain. Its history (Magoun 1959) begins in 1875 with the publication of Richard Caton's article (Caton 1875) reporting brain voltage fluctuations recorded from rabbits. Nearly fifty years later, in 1924 (Magoun 1959), Hans Berger, a German psychiatrist, began recording the varying electrical potentials of the human brain through the intact skull. His early work was reported in 1929 (Berger 1929) and was confirmed by Adrian and Mathews at Cambridge in 1933 (Adrian et al 1934). The first human electroencephalograms (EEGs) recorded in the United States were probably done at Harvard in 1934 (Magoun 1959, Gibbs et al 1935).

The manner in which brain voltage fluctuations are produced is not fully understood. It is generally agreed that the measured potential represents the sum of the fluctuations of many millions of individual neurons. In addition, the voltage fluctuations of the individual cells are more or less synchronized depending upon the location and function of the cells and the overall activity of the brain (Magoun 1959).

It is felt that the electrical activity of the cell bodies and their receptor structures (dendrites) is largely responsible for the measurable voltage fluctuations. The nerve impulse (axonal action potential) of the cell's effector structure is almost certainly not associated with these fluctuations (Magoun 1959).

The brain's voltage variations can be detected indirectly on the scalp and directly on its surface and in its depths. They may occur slowly over a period of many seconds, minutes or hours (the so-called dc potentials) or as rapidly as hundreds of times per second (recordable from the cerebellum only). Their amplitudes generally range from 1 to 100 microvolts, but may reach a few hundred or even 1000 or more microvolts.

The frequencies and amplitude of the voltage fluctuations vary from area to area throughout the brain and from time to time in any area. Generally, homologous areas on the right and left sides of the brain have fluctuations which are synchronous and of similar amplitude.

By placing the electrodes (usually 12 or more) on the scalp, these minute voltage fluctuations can be readily recorded. For each tracing ("channel") two electrodes are connected to an R-C coupled, push-pull amplifier. The potential of one electrode with respect to the other as both vary in time can thus be amplified for display by various means. Ink-writing units and moving graph paper are the most widely used for clinical applications. The recorded EEG is therefore a voltage-time graph with voltage on the ordinate and time on the abscissa.

Most modern electroencephalographs have eight to sixteen channels, i.e., independent, identical sets of amplifiers and ink-writing units which record from eight to sixteen electrode pairs simultaneously on one strip of paper. The resulting graph is called a multi-channel electroencephalograph.

EEG signals have been found to change with both physiological and pathological changes in brain function. Because of the clinical importance of these changes, electroencephalography is available as a diagnostic aid in nearly all neurological and psychiatric hospitals, most medical schools and in many private hospitals and practices.

The clinical interpretation of EEGs is almost exclusively a process of pattern recognition by skilled electroencephalographers. These patterns may involve the whole record, a small part of it, or the subtle relationships between parts of the record. Patterns associated with normal changes (Gibbs and Gibbs Vol. 1 1950) such as occur during sleep-wakefulness cycle and with increasing age in childhood have been found. Also such pathological conditions as epilepsy, brain tumor, and brain damage may produce characteristic changes in the EEG record. (Gibbs and Gibbs, Vols. 2, 3 1952)

The problem of extracting this or other significant information from the spontaneous EEG by mathematical methods of signal analysis, is an important and challenging one. This thesis deals with a related problem.

Rather than the spontaneous voltage fluctuations of the brain, the responses associated with sensory stimulation are studied. Interestingly enough, Caton was recording responses to stimulation when he discovered the spontaneous activity technique (Caton 1875). However, the present technique of evoked response detection was pioneered by Dawson in 1942 (Dawson 1942, 1951).

Basically this approach considers the evoked response to be a minute signal masked by the "noise" of the brain's other electrical activity (Krauss 1963). When a large number of these responses containing uncorrelated "noise" are added together, the noise should tend to cancel out. The sum would then be proportional to the average evoked response. The result is called the average evoked potential (AEP).

In order to obtain the AEP two major modifications of conventional electroencephalography are necessary (Figure 1). First, some form of sensory stimulation is employed (e.g. a stroboscopic photic stimulator). Second, segments of the record following the stimulus presentations are summed (Figure 2, adapted from Ellingson, 1967).

Frequently a single pair of electrodes is used. Usually one electrode is placed over the area of the brain mediating the sensory modality stimulated, in this case the occipital or "visual" cortex. The other electrode is placed at a remote location, commonly an electrically neutral one such as an earlobe. The amplifying system is usually the same as that used for conventional electroencephalography.

Generally a conventional electroencephalograph is recorded throughout the entire series of stimulus presentations. This continuous record of the brain's electrical activity is necessary to verify the level of consciousness of the subject for correlation with the responses to the stimuli.

The stimulus trigger provides signals which can be used to mark the record and control the summing device. If the record is on magnetic tape it may be played into the summating instrument at a convenient time and rate. Following each stimulus, as indicated by the trigger signal, the summating instrument accepts the amplifier or tape recorder output for a period of time adequate to include the evoked response. As each succeeding response is accepted its values at each point in time are added to the values of its predecessors at corresponding points in time. Both analog and digital computing devices have been used for this purpose.

It is assumed that the ongoing brain activity or "noise" will produce voltage fluctations occurring randomly in time with respect to the stimulus and will tend to sum to zero. The evoked response is assumed to generate voltage fluctuations "time locked" to the stimulus which will sum to definite positive and negative values (Figure 2).

After an appropriate number of responses have been processed their sum is called the average evoked potential

(AEP) and may be displayed by ink-writing units, oscilloscopes, or X-Y plotters.

Differences in the AEPs have been reported for such normal physiologic conditions as attentiveness and sleep compared to relaxed wakefulness (Donchin et al 1967, Garcia-Austt 1963, Wilkinson et al 1966), increasing age in infancy (Ellingson 1967, Ferriss et al 1967), learning involving the stimulus (Begleiter et al 1967, John et al 1963), and time of presentation of the stimulus in relation to on going brain activity (Lansing 1957). Changes have also been reported for abnormal conditions such as induced hypothermia (Boakes et al 1967), developmental retardation (Barnet et al 1967), drug administration (Purpura et al 1958), and operatively removed occipital (visual) cortex (Corletto et al 1967).

The interpretation of EEGs and AEPs involves empirically demonstrated relationships. That is, recognizable patterns in the recorded brain voltage fluctuations (spontaneous or evoked) have been found to be associated with certain of the brain's functional states.

The AEP is usually described in terms of the time of occurrence ("latency") and amplitudes of its peaks of positive and negative fluctuation. There is probably additional significant information contained in the AEP which is not described by these measurements.

From an engineering point of view, the light stimulus may be regarded as an impulse function $\delta(t)$ and the AEP the empirically determined impulse response $y(t)$ of the system. Taking the Fourier transform of a waveform yields the sinusoidal waves (amplitude and phase) which if added together would reproduce the original waveform. If that waveform is the impulse response of a system, its Fourier transform is the system function $H(j\omega)$.

In this thesis one method and some implications of Fourier transformation of AEPs will be investigated.

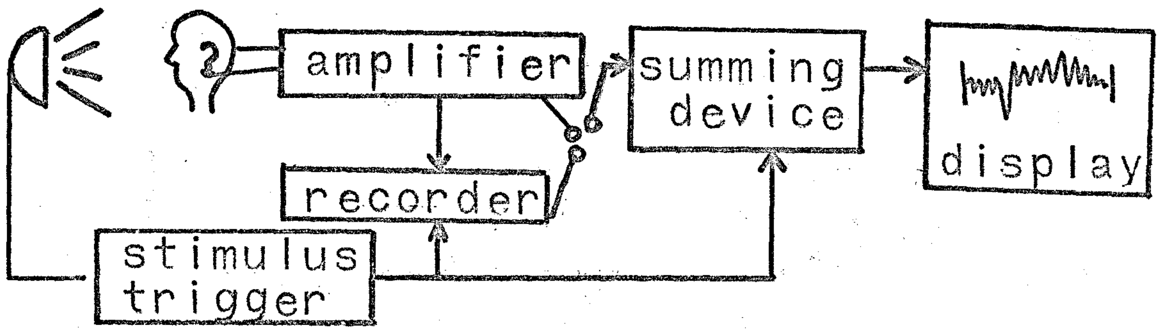
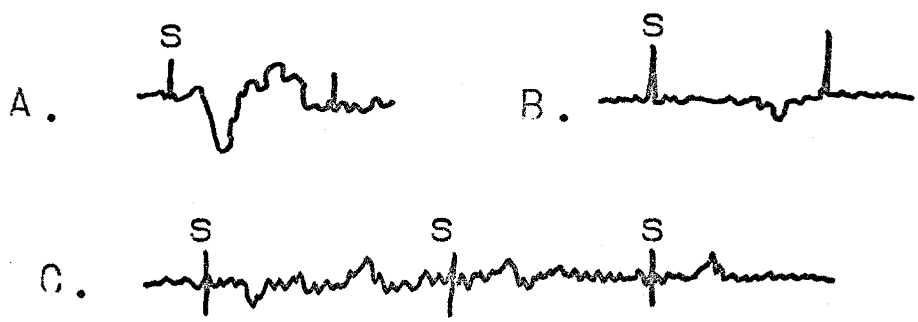

amplifier
summing device
display
recorder
stimulus trigger

Figure 1



A. the sum of 60 responses

B. the sum of 60 similar segments of record but without stimulus

C. segment of continuous ink-writer record with responses masked by ongoing brain activity

Note: the first spike in A and B is an artifact coinciding with presentation of the stimulus (s) the second spike occurs 500 msec later

Figure 2

CHAPTER II

MATHEMATICAL CONSIDERATIONS

Introduction

Discussion of AEPs in terms of mathematical models involves two interrelated problems. One of these problems is to describe how average evoked potentials are obtained; the other is to describe the AEPs themselves. For either problem the choice of an appropriate model is dependent upon assumptions made concerning brain electrical activity and response.

The brain's spontaneous electrical activity is generally represented by a Gaussian stochastic process. This model is sufficiently accurate for most present applications and is considerably easier to use than are other possibly more realistic models (Siebert 1959).

The evoked electrical activity may be considered as occurring independently of the spontaneous activity, or as an expression of some change in that activity.

The Deterministic Approach

The assumption usually made is that the brain's electrical response to one light flash is essentially the same as it is to any other, and the problem of recording this response is one of signal detection (Krauss 1963). Thus, following a light flash, the recordable electrical activity y(t) is considered to be the sum of the activity produced as a response to the flash and that generated by the ongoing brain activity. If the response activity is the signal s(t) and the ongoing activity is noise n(t) then: $y(t) = s(t) + n(t)$.

If n(t) has a Gaussian amplitude distribution which is uncorrelated with the stimulus and a number of outputs are summed, n(t) will tend to sum to zero. The signal to noise ration will be increased in proportion to the square root of the number of outputs summed. Also, the variance of y(t) is assumed to equal the variance of n(t).

This is the assumption underlying most evaluations of differences between AEPs recorded under different conditions (Donchin 1966, Ruhkin 1965). That is, to be significant the difference must be greater than could be expected on the basis of noise interference. There is reason to believe that the evoked electrical responses s(t) are not identical, even under similar conditions (Brazier 1964, Ellingson 1967).

To account for this variability, a "set" of possible responses can be assumed (Welch 1966). This set is subdivided into subsets of responses any one of which may occur under the circumstances appropriate to that subset.

Thus, in determining the variance of the summed responses, the variance of the evoked responses, as well as that of the noise must be considered.

This is a statistical approach in that the AEP is not considered to be an estimate of a single response, but an estimate of the average of a group of responses.

The Probabilistic Approach

Goldstein (Goldstein 1961) has suggested that probabilistic models are appropriate when the phenomenon studied is too complex and/or insufficiently understood for the application of other methods, or when the phenomenon is in fact, probabilistic. Both have been considered appropriate ways of thinking about brain electrical activity (Brazier 1963, Goldstein 1961).

If this activity is probabilistic, then the AEP is not an estimate of some response or group of responses obscurred by noise. Rather, it is an estimate of the brain's altered on going activity. When no stimulus is presented, the electrical activity of the brain as estimated by its average tends to be zero. Averages of the brain's electrical activity following stimuli tend not to equal zero.

The applications of probabilistic models, i.e. the Stochastic process model to EEGs (Brazier 1963, Siebert 1959) and AEPs (Goldstein in Commun. Biophysics Gp. 1959) has been discussed elsewhere.

Basically, a stochastic process is a collection of time functions. A multi-channel EEG could be one example. Perhaps a better one is the collection of the brain's voltage fluctuations, whether recorded or not.

If the stochastic process is stationary, i.e. certain (specified) of its statistics do not vary with time, and if it is ergodic for the mean, i.e. the averages of all its member functions are nearly identical, then a sample average of one member function can be considered a good indication of the mean of the process.

For application to AEPs Goldstein (Commun. Biophysics Gp. 1959) has suggested a "periodically time-varying" stochastic process, i.e. one with periodically varying statistical characteristics. Thus, the mean (or other statistics) of the process at one point in its period can be estimated by the mean of values from one of its member functions, if these values are obtained by periodically sampling that function at the appropriate point in its period.

This model would be appropriate for those experiments in which periodic stimuli are employed. In order to deal with AEPs obtained from responses to aperiodic stimuli, the model would have to be generalized. This generalization would require considerations of a stationary or periodically varying random process whose statistics vary in some regular way following an impulse input. The way in which the process's statistics vary would depend on whether the stimuli occurred periodically or randomly and upon the time in the process cycle at which they occurred.

Fourier Transformation

Regardless of what assumptions are made about brain electrical activity, the AEP is an established empirical phenomenon. Certain characteristics of AEPs, such as the "latencies" of their "peaks" are remarkably reproducible regardless of investigator or averaging process, and have been shown to vary according to experimental subject and conditions. As AEPs become more widely employed in investigation of the sensory systems, comparisons of AEPs by amplitude and latencies of their peaks will become less satisfactory.

One way of describing an apparently irregular wave form such as the AEP is in terms of the sinusoidal wave components necessary to simulate it. For biological systems it is especially important to remember that such sinusoidal components probably were not responsible for the original wave. Nevertheless, determining the amplitudes and phase (lag) of the components of AEPs would provide an objective means of comparison. The Fourier transform provides this information. Its defining equation:

$$H(j\omega) = \int_{-\infty}^{\infty} h(t) e^{-j\omega t} \, dt$$

may be thought of as a special case of the Laplace transform:

$$H(s) = \int_{0}^{\infty} h(t) e^{-st} \, dt$$

where

$$s = (\sigma + j\omega)$$

The convergence term, σ, is equal to zero and the lower limit of the integral is zero because the AEP does not exist before the stimulus occurs and essentially zero one second later.

Using Euler's identity:

$$e^{-j\omega t} = \cos \omega t - j \sin \omega t$$

The equation may be rewritten:

$$H(j\omega) = \int_{-\infty}^{\infty} h(t) e^{-j\omega t}\, dt$$

$$= \int_{-\infty}^{\infty} h(t) \cos \omega t\, dt - j \int_{-\infty}^{\infty} h(t) \sin \omega t\, dt$$

In order to use sampled or discrete data the integrals are written as sums.

$$H(j\omega_m) = \sum_{n=-\infty}^{\infty} h(t_n) \cos \omega_m t_n\, dt - j \sum_{n=-\infty}^{\infty} h(t_n) \sin \omega_m t_n\, dt$$

Then letting

$$X_{(\omega_m)} = \sum_{n=-\infty}^{\infty} h(t_n) \cos \omega_m t_n\, dt$$

and

$$Y_{(\omega_m)} = \sum_{n=-\infty}^{\infty} h(t_n) \sin \omega_m t_n\, dt$$

the equation becomes

$$H(j\omega_m) = X(\omega_m) - jY(\omega_m)$$

The magnitude and phase of $H(j\omega)$ can then be determined and displayed as functions of ω.

$$|H(j\omega_m)| = \sqrt{X^2_{(\omega_m)} + Y^2_{(\omega_m)}}$$

$$\angle H(j\omega_m) = \tan^{-1} -Y(\omega_m) / X(\omega_m)$$

Interpretation of this information is based to some extent on the assumptions made concerning the AEP. In any case AEPs may be quantitatively compared on the basis of the sinusoids required to simulate them.

If the AEP is assumed to be the impulse response of the system extracted from noise, then its transform has additional meaning.

The system equation or transfer function is defined:

$$H(j\omega) = \frac{Y(j\omega)}{X(j\omega)}$$

where $Y(j\omega)$ is the output (AEP) and $X(j\omega)$ is the input (light flash) the photic stimulator produces a flash of light, $x(t)$ which may be regarded as an impulse. Since the Fourier transform of an impulse function is unity, the equation becomes:

$$H(j\omega) = Y(j\omega)$$

This implies that the system is completely characterized by the Fourier transform of its output when its input is an impulse. For that to be strictly true the system must be linear and $Y(j\omega)$ would have to be independent of the amplitude of the impulse. AEPs do, however, vary with the intensity of the light flash, but this does not exclude the possibility that there are ranges of stimulus amplitudes over which the system responds linearly.

Whether or not this transform will be useful in building mathematical models of the system, any such models must account for at least this level of complexity.

CHAPTER III

TECHNICAL CONSIDERATIONS

General

The data used in this project were obtained from recordings of evoked brain electrical activity of infants (Ellingson 1967) using visual stimulation (Figure 3) provided by a Grass model PS-1 Photo Stimulator which was triggered manually in a random manner. Coincident with each stimulus a marker artifact impulse was placed in the record to specify the start of each response.

A Grass model 78 electroencephalograph continuously amplified and recorded the brain's electrical activity and the marker impulses. The amplifier outputs were also recorded on 1/4" 8 channel magnetic tape with one channel recording the marker artifacts. Frequencies greater than 100 Hz were filtered out for recording on magnetic tape.

At a later time, the tape recorded signals were played into the Enhancetron 800 (Nuclear Data Inc., Palatine, Illinois) which summed fifty responses (one second segments of the activity following the marker artifacts). These sums were each displayed by an X-Y plotter and their graphs used as the AEPs for the project.

Two infants and one adult were used as subjects. One AEP was obtained for each subject using an amplifier with its lower bandwidth adjustment (time constant) set at 0.1. In addition the responses of one of the infants were simultaneously recorded using amplifiers with time constant of 0.6 and 0.01.

Each one second graphical AEP was manually converted to 50 digital values taken at equal increments in time. Using these digital data and an IBM 1800 series Data Acquisition and Control System, the magnitude and phase of the Fourier transform of each AEP were computed and displayed.

The Summing Operation

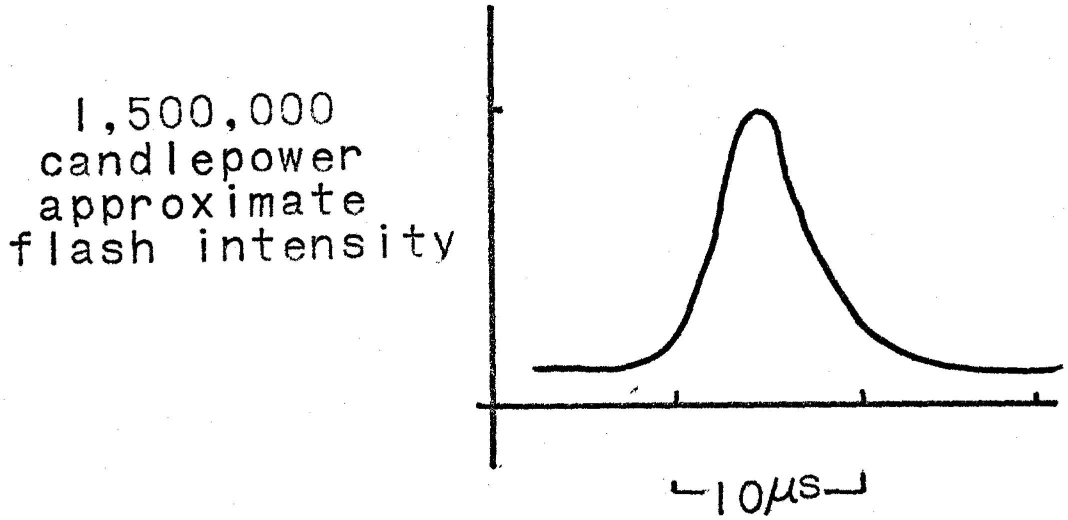
The Enhancetron samples the taped responses for a specified time period (in this case one second) following each artifact impulse and each sampled voltage is compared to 256 internal reference voltages. For each of 512 samples taken there is a corresponding memory unit. One count is added to the "i^{th}" memory unit for each reference level below the "i^{th}" sample voltage and one count is subtracted from that memory unit for each reference level above the sampled voltage. The count remaining in that memory unit represents the value of the sampled voltage in relation to the 256 internal reference voltages. The 512 memory units then represent the relative values of the 512 samples of the response. After each successive response is sampled and its values compared to the reference levels, counts are added and subtracted from each memory unit for each sample voltage. The counts remaining in the memory units represent the relative algebraic sums of the voltages sampled from the responses at corresponding time increments.

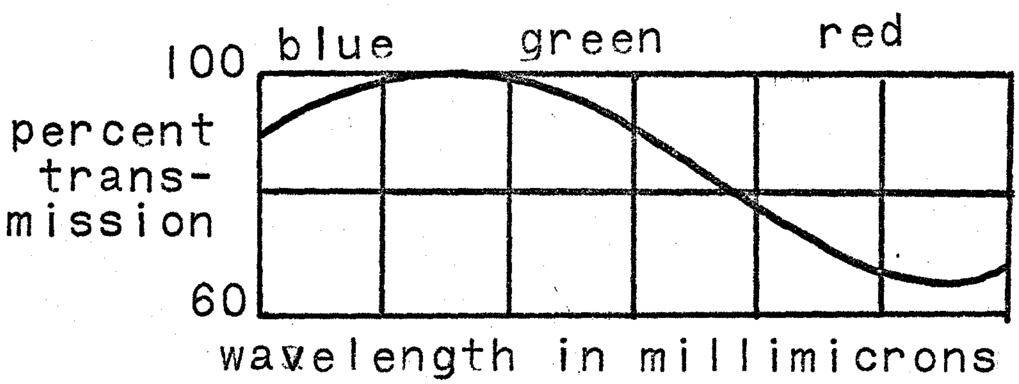
Computation of the Fourier Transform

The choice of values for ω presented some problems. Significant variations in both $|H/\omega|$ and $\angle H j\omega$ were found at increments of .25π radians or 1/8 Hz. Computing the integrals using all 512 data points and a large range of frequencies would have been impractically time consuming and costly. For this reason only 50 sample values were used and the integral computed to $\omega_m = 30$ Hz.

It should be noted that for each AEP there are 512 sample values available from the Enhancetron compared to the 50 used here, and that the range of frequencies used extends beyond that considered to be accurate, i.e. $\leq 1/2$ the sampling frequency.

Numerical computation of the transform based on the equations given above while time consuming, is not complicated, and techniques for displaying the results will vary with the facilities available. For these reasons the programs written for the project are not included in this thesis.





Approximate spectual energy distribution of the lamp with no filter.

Figure 3

CHAPTER IV

RESULTS

The Fourier transforms of five AEPs were computed as described in Chapter III. AEP no. 1 is from a 3 day old infant (amplifier time constant 0.1). A 12 hour old infant was the subject for AEP no. 2 (time constant 0.1), no. 3 (time constant 0.6) and no. 4 (time constant 0.01). These AEPs of subjects classed as neonatal infants are compared with an AEP from an adult, no. 5.

The results are presented graphically. One AEP is shown as it was plotted from the Enhancetron and also from the 50 digital data points used in the Fourier transformation (Figure 4). Similar fidelity was obtained for the other AEPs. Plotting negatively upward is in keeping with EEG convention. Zero values for each AEP were located by sight since only the voltage fluctuations of the occipital lead with respect to the earlobe lead were recorded and the fluctuations of either with respect to ground are not known. The Figures 6 through 10 give the magnitude and phase of the Fourier transforms of the AEPs. These magnitudes are plotted with the highest value of each curve normalized to unity. The actual highest value is noted, but comparisons between AEPs on this basis are not justified because the original AEPs are not comparable in amplitude scaling.

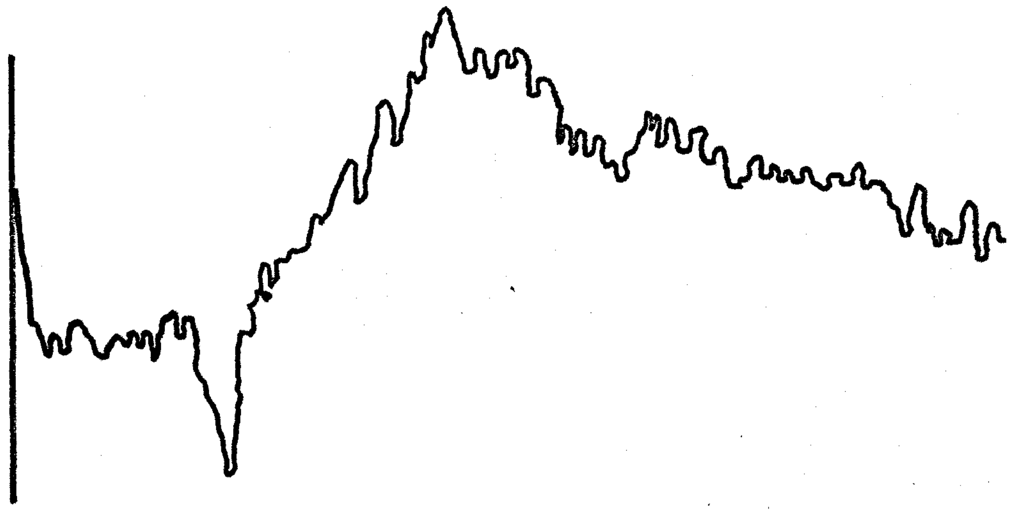
Figure 5 is offered as an aid in interpreting the phase plots, and shows the changing "position" of a sinusoid for various phase angles. Some artifact may be present in the phase plots because the phase change was assumed to be continuous and where consecutive values skipped quadrants the direction of continuity plotted is judgmental.

While this will not interfere with the very limited conclusions to be drawn from the results of this investigative project, it may be important in future work.

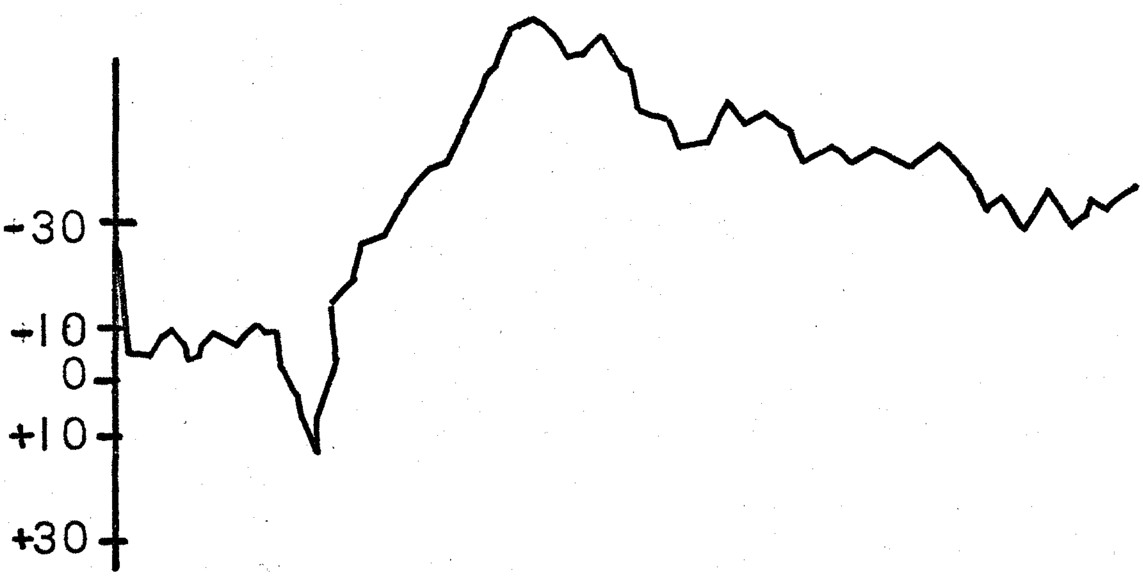
In general, the low frequency components predominate and the higher the frequency the greater the phase lag. The Fourier transforms of the infant AEPs computed from the same responses amplified by different amplifiers are noticeably different.

The Fourier transform of the adult AEP has less predominant low frequencies and a slower and more regular phase lag for increasing frequencies.

Perhaps the change of phase with frequency $\frac{\delta\theta}{\delta\omega}$ of their Fourier transforms will be a useful means of describing AEPs.

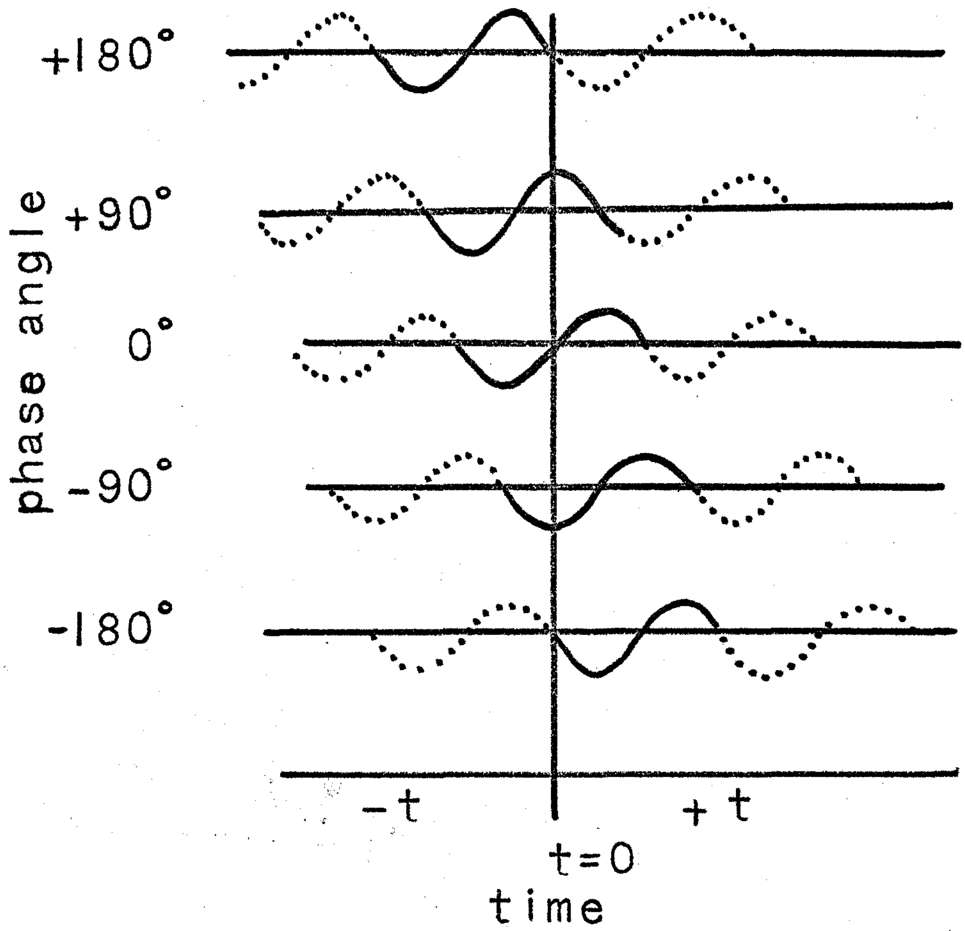


AEP No. 2 plotted
from Enhancetron



AEP No. 2 plotted from 50 points

Figure 4



The relative position in time of a sinusoid shown for different phase angles

Figure 5

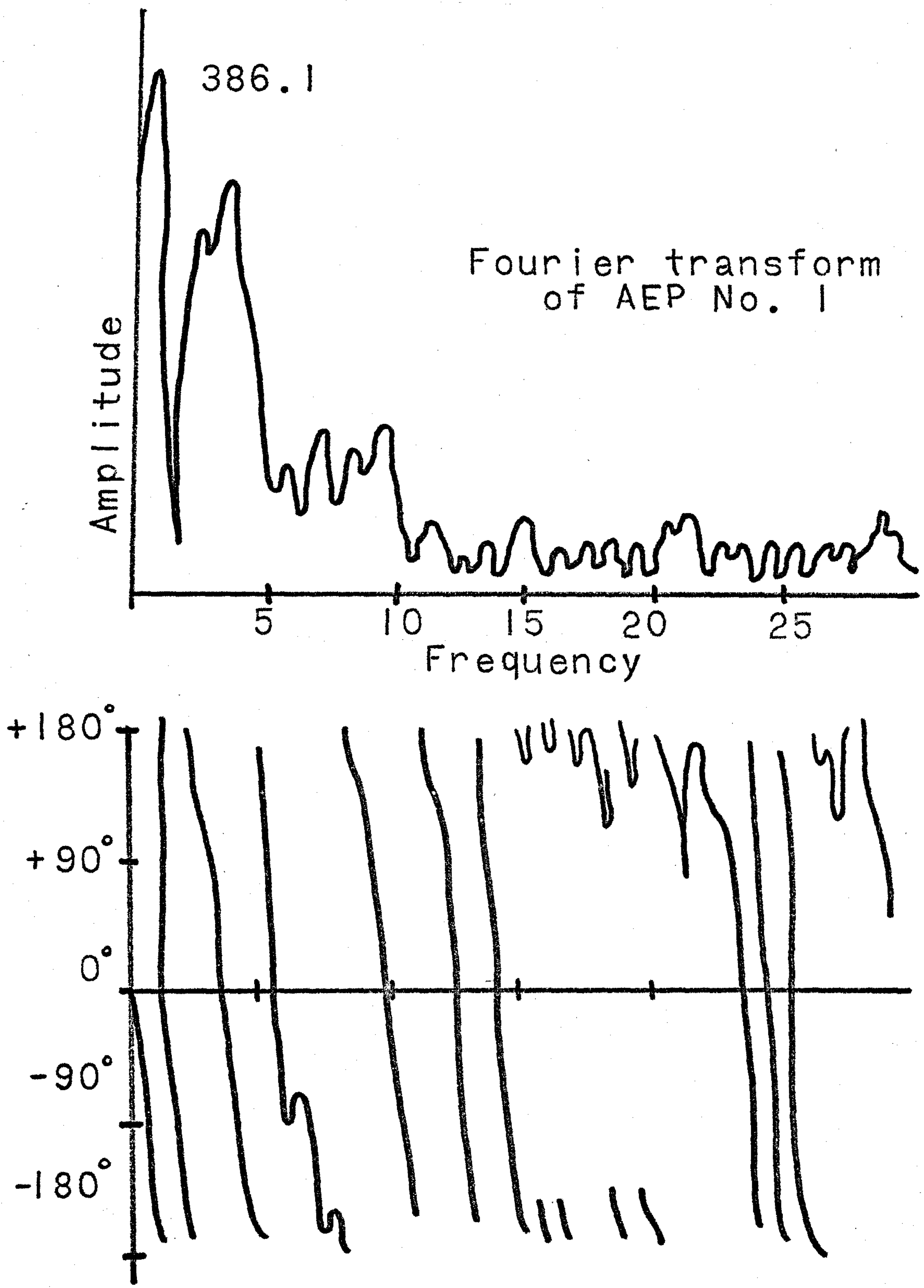

386.1
Fourier transform
of AEP No. 1
Amplitude
5
10
15
20
25
Frequency
+180°
+90°
0°
-90°
-180°

Figure 6

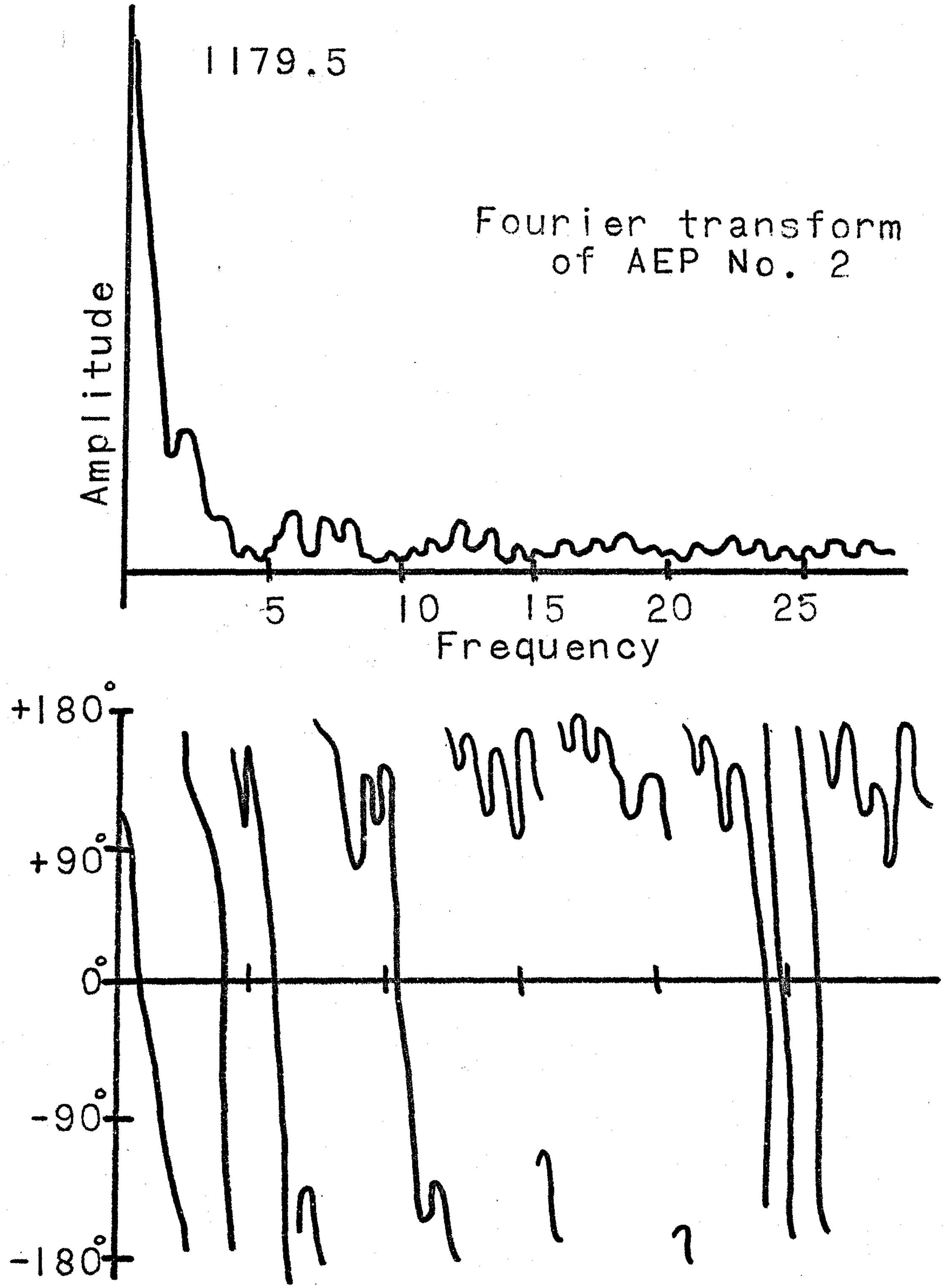

1179.5
Fourier transform of AEP No. 2
Amplitude
5
10
15
20
25
Frequency
+180°
+90°
0°
-90°
-180°

Figure 7

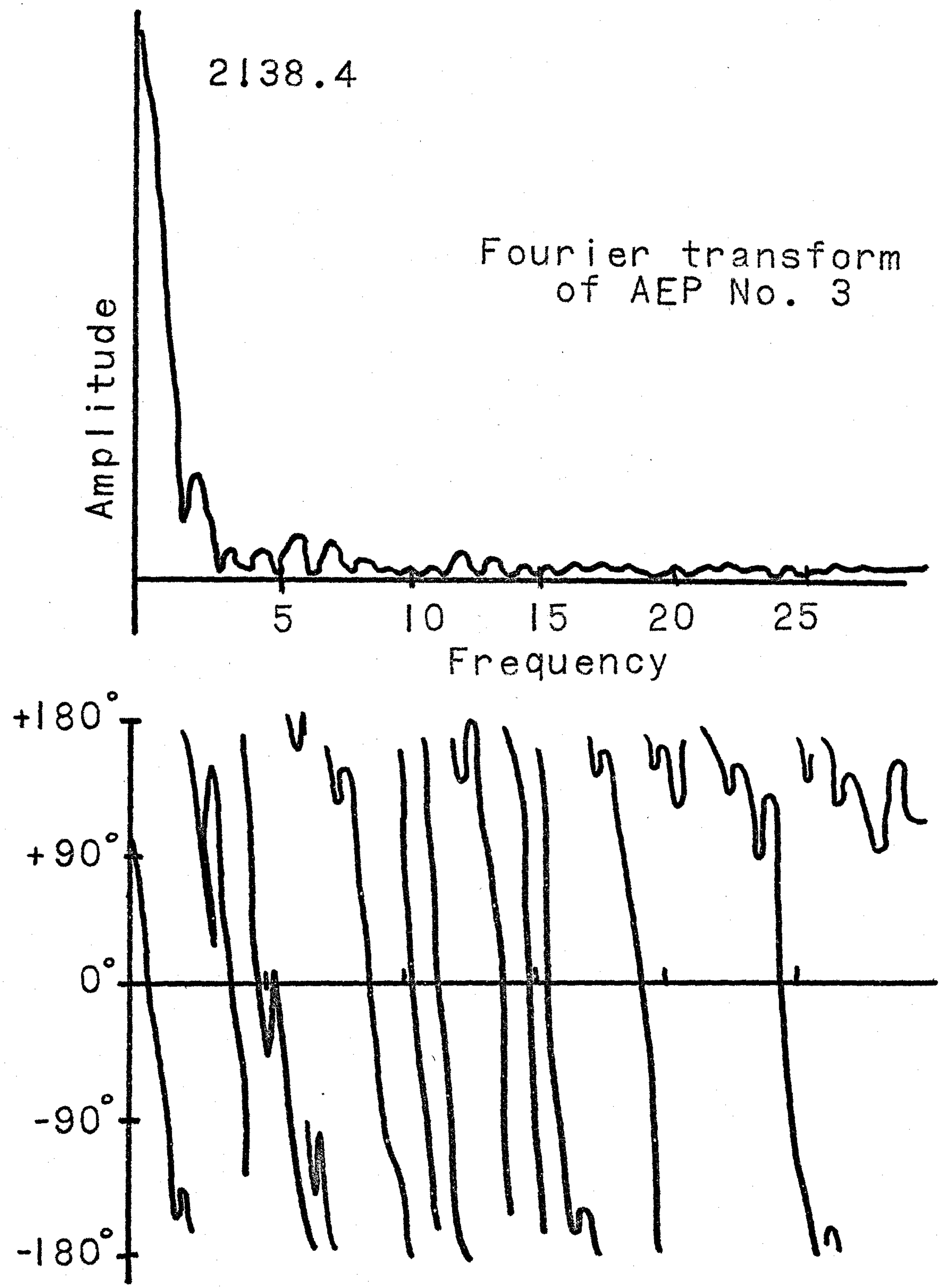

2138.4
Fourier transform
of AEP No. 3
Amplitude
5
10
15
20
25
Frequency
+180°
+90°
0°
-90°
-180°

Figure 8

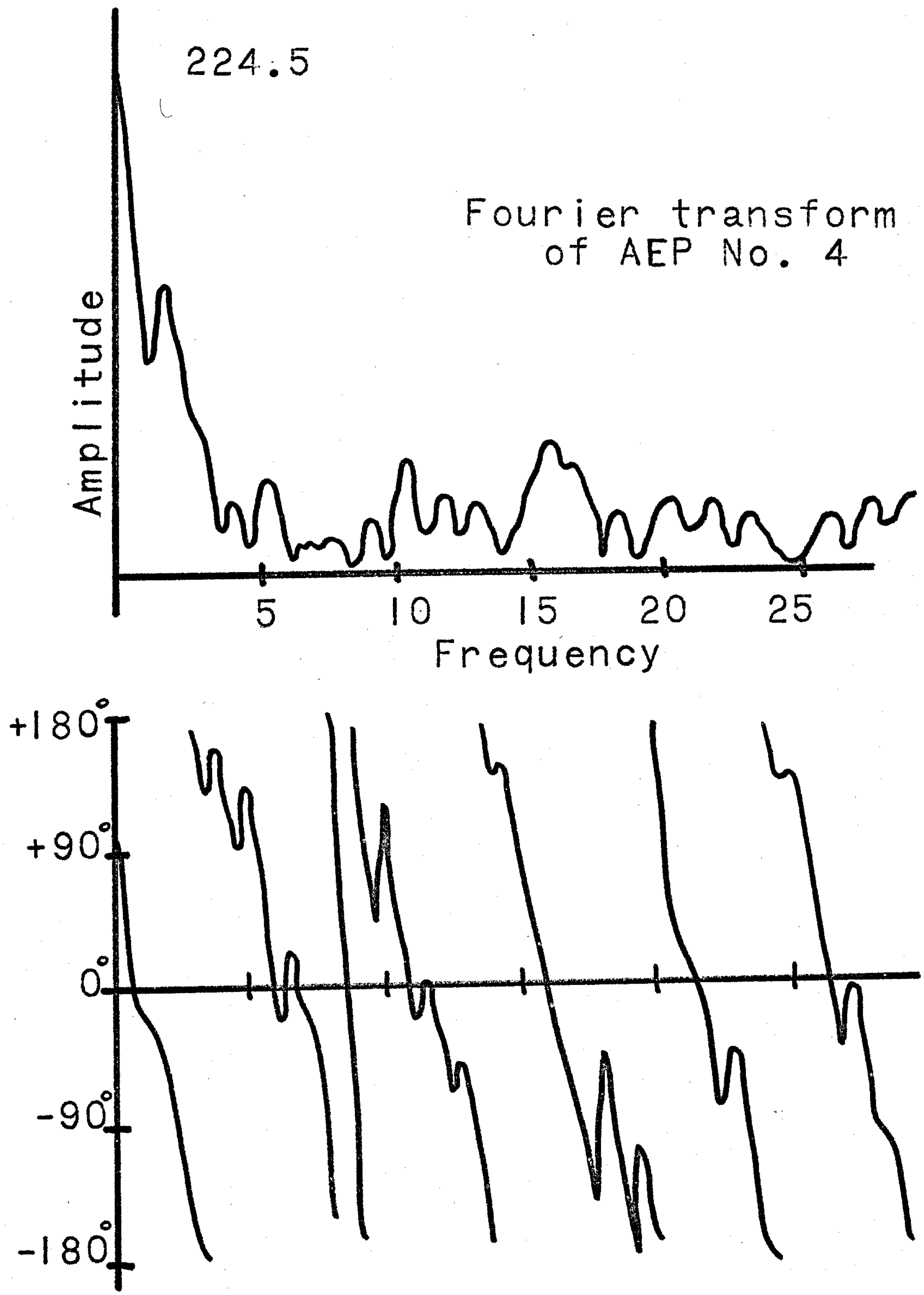

224.5
Fourier transform
of AEP No. 4
Amplitude
5
10
15
20
25
Frequency
+180°
+90°
0°
-90°
-180°

Figure 9

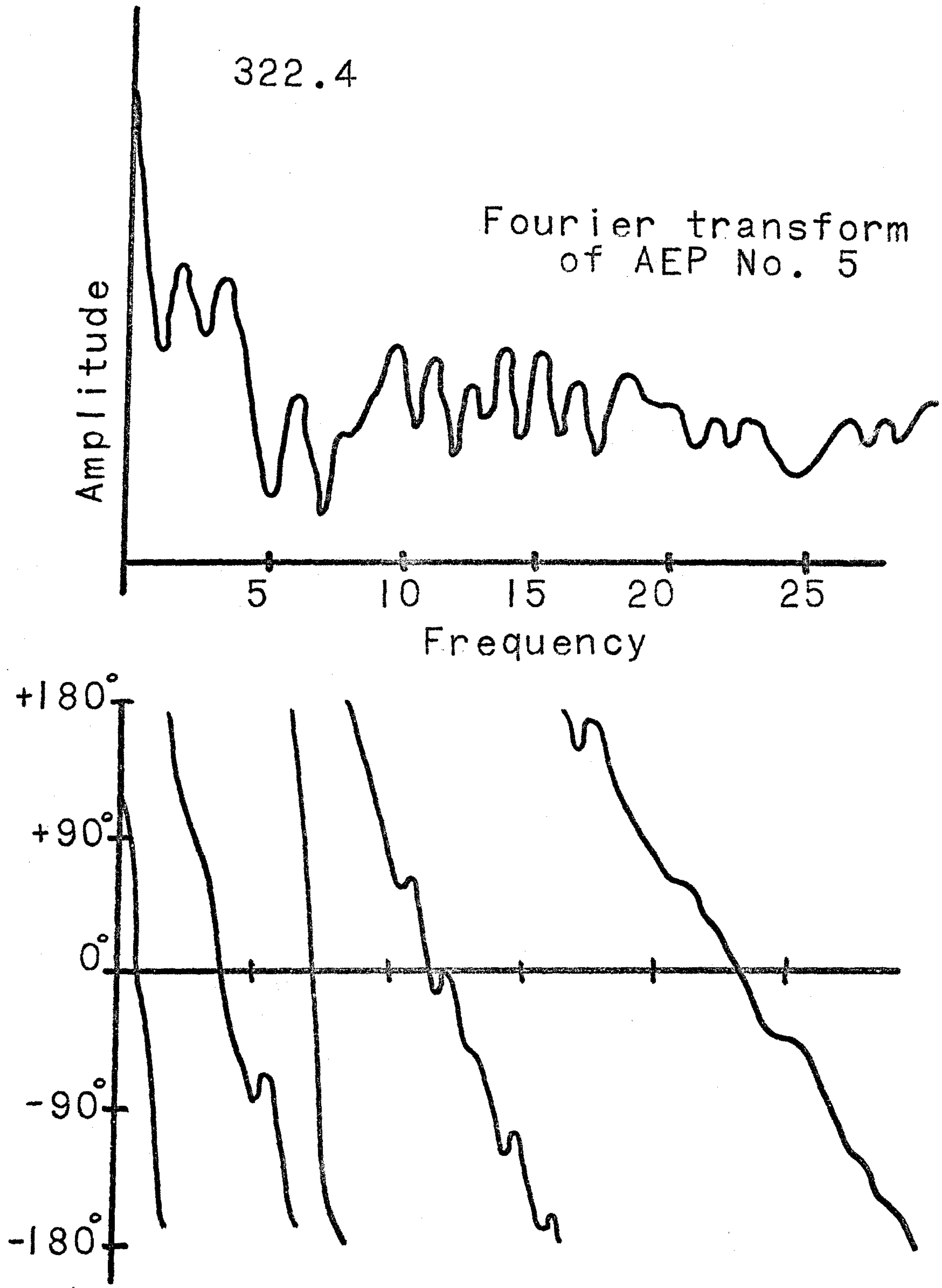

322.4
Fourier transform
of AEP No. 5
Amplitude
5
10
15
20
25
Frequency
+180°
+90°
0°
-90°
-180°

Figure 10

CHAPTER V

CONCLUSION

The feasibility of the computation of the Fourier transforms of AEPs by digital computer has been demonstrated. The transforms of the four neonatal AEPs are more like each other than any one of them is like the transform of the adult AEP.

The usefulness of the Fourier transform to compare and contrast AEPs clinically and in neurophysiological research depends on the extent to which the differences in magnitude and phase of the transforms can be quantified. A large series of transforms would be required to determine which comparisons, if any, would be significant. As performed for this project, computation and plotting of each transform required more than 10 minutes of computer time. The number of sample values probably should not be reduced below 50, but the number of values of ω considered could be substantially reduced (from 240) if the significant frequency components were known. Another method of computation reportedly 100 times faster than the direct approach could also be used (Brigham 1967). This recent publication was not available at the time this project was undertaken.

One limitation of the AEP itself is that in averaging, relevant as well as irrelevant variation in the individual responses is obscured, and processes which depend on space-time distortion such as planning and imagnination would not be expected to reveal themselves in activity "time locked" to stimulus.

Still on the level of perception, the time invariance of the visual system is literally of vital importance. AEPs may reasonably be expected to reveal significant information about the development and function of visual perception (the auditory and somesthetic systems are also currently being investigated). It has been suggested that the AEP is an expression of the differing "arrival times" of sensory information taking different routes from the sensory organ to the cortex. In that case models based on the frequency response characteristics of a model system would have little anatomical meaning. In any case, models of the sensory systems must at least account for the level of complexity implied by the transforms of the AEPs of those systems.

Because of the time required to calculate each AEP, "on line" computation of the transforms would be practical only on a time sharing basis. Perhaps a special purpose analogue or digital computer coupled to the Enhancetron would provide the most economical and flexible means of computing the transforms.

Progress must be made in two areas before Fourier transformation of AEPs can be said to be useful and practical. Large series of AEPs must be transformed and norms established for the amplitudes and phase angles of their frequency components. The cost and time of computing the transforms must be reduced. The results of this project indicate that such progress is possible and that the Fourier transform may well provide a more comprehensive and quantitative means of comparing AEPs than is currently available.

BIBLIOGRAPHY

Adrian, E. D. and Matthews, B. H. C. The Berger rhythm; potential changes from the occipital lobes in man. Brain, 1934, 57: 355-385.

Barnet, A. B. and Lodge, A. Click Evoked EEG Responses in Normal and Developmentally Retarded Infants. Nature, April 15, 1967, Vol. 214, No. 5085: 252-255.

Begleites, H., Melton, M. G., and Kissin, B. Evoked Cortical Responses to Affective Visual Stimulus. Psychophysiology, 1967, Vol. 3, No. 4: 336-394.

Berger, Hans. Uber das Elektrenkephalogramm des Menschen. Arch Psychiat. 1929, 87: 527.

Brigham, E. O., and Morrow, R. E. The fast Fourier transform. IEEE Spectrum, Dec. 1967, Vol. 4, No. 12: 63-70.

Boakes, R. J., Kerkat, G. A., and Munday, K. A. Effect of Hypothermia on Cortical Evoked Potential. Life Sciences, 1967, 6: 457-459.

Brazier, M. A. B. Some Uses of Computers in Experimental Neurology, 1960, 2: 123-143.

Brazier, M. A. B. Information Carrying Characteristics of Brain Responses. Electroenceph. Clin. Neurophysiol., 1963, Suppl. 24: 55-67.

Brazier, M. A. B. Evoked Responses Recorded from the Depths of the Human Brain. Anals of N. Y. Acad. Sci., 1964, 112: 33-59.

Caton, R. The electric currents of the brain. Brit. M. J., 1875, 2: 278.

Communications Biophysics Group of Research Laboratory of Electronics and Siebert, W. M. Processing neuroelectric data. Techn. Rep. 351, Mass. Inst. Technol., 1959, 121.

Corletto, F., Gentilomo, A., Rosadini, G., Rossi, G. F., and Zattoni, J. Visual evoked potentials as recorded from the scalp and from the visual cortex before and after surgical removal of the occipital pole in man. Electroenceph. Clin. Neurophysiol., 1967, 22: 378-380.

Dawson, G. D. The automatic analysis of ultra low frequency transients. Electronic Eng., 1942, 15: 34-35.

Dawson, G. D. A summation technique for detecting small signals in a large irregular background. J. Physiol. (Lond.), 1951, 115: 2P.

Donchin, E. A Multivariate Approach to the Analysis of Averaged Evoked Potentials. IEEE Trans. on Bio-Medical Engineer., July, 1966, Vol. BME-13, No. 3: 131-139.

Donchin, E., and Cohen, I. Averaged evoked potentials and intramodality selective attention. Electroenceph. Clin. Neurophysiol., 1967, 22: 537-546.

Ellingson, R. J. Electroencephalograms of Normal, Full-term Newborns Immediately after Birth with Observations on Arousal and Visual Evoked Responses. EEG Clin. Neurophysiol., 1958, 10: 31-50.

Ellingson, R. J. Cortical electrical responses to visual stimulation in the human infant. EEG Clin. Neurophysiol., 1960, 12: 663-677.

Ellingson, R. J. Methods of recording cortical evoked responses in the human infant. Regional Development of the Brain in Early Life. Blackwell Scientific Publications: Oxford and Edenburgh, 1967, 413-435.

Ferriss, G. S., Davis, G. D., Dorsen, M. McF. and Hackett, E. R. Changes in latency and form of the photically induced average evoked response in human infants. EEG Clin. Neurophysiol., 1967, 22: 305-312.

Garcia-Austt, E. Influence of the states of Awareness Upon Sensory Evoked Potentials. EEG Clin. Neurophysiol., 1963 Suppl., 24: 76-89.

Garry, H. Applications of Continuous Averaging in Medicine. J. Med. Electron., 1961, Sept.-Nov., 21-23.

Gastaut, H. Correlation Between the electroencephalographic and the Psychometric variables (MMPI, Rosenweig intelligence tests). EEG Clin. Neurophysiol., 1960, 12: 226-227.

Gibbs, F. A., Davis, H., and Lennox, W. C. The EEG in epilepsy and in conditions of impaired consciousness. A.M.A. Arch. Neurol. & Psychiat., 1935, 34: 1133.

Gibbs, F. A., and Gibbs, E. L. Atlas of electroencephalography, Addison-Wesley Press, Cambridge, Mass., 1950-1952.

Goldstein, M. H., Jr. Averaging Techniques Applies to Evoked Responses. EEG Clin. Neurophysiol., 1961 Suppl., 20: 59-63.

John, E. R., Ruchkin, D. S., and Villegas, J. Signal Analysis of Evoked Potentials Recorded from Cats during Conditioning. Science, Aug., 1963, 141.

Krauss, J. B. Computerized Average Response and Autocorrelation Methods as related to Signal Detection Noise. Paper presented at the 1963 Rochester Conference on Data Acquisition and Processing in Biology and Medicine.

Lansing, R. W. Relation of brain and tremor rhythms to visual reaction time. EEG Clin. Neurophysiol., Aug., 1957, 9(3): 497-504.

Magoun, H. W. ed., Neurophysiology (Handbook of Physiology, Section 1). Washington, D.C. Amer. Physiological Society, 1959.

Purpura, D. P., Girado, M., Smith, T. G., Jr., and Gomez, J. A. Effects of systemically administered ω-amino and guanidino acids on spontaneous and evoked cortical activity in regions of blood-brain barrier destruction. Electroenceph. Clin. Neurophysiol., 1958, 10: 677-685.

Ruchin, D. S. An Analysis of Average Response Computations Based Upon Aperiodic Stimuli. IEEE Trans. on Bio-Medical Engineer., April, 1965, BME-12: 87-94.

Walter, D. O., and Adley, W. R. Analysis of Brain-Wave Generators as Multiple Statistical Time Series. IEEE Trans. on BioMedical Engineer., Jan., 1965, Vol. BME-12: 8-13.

Welch, A. J. Random Process Model for Neuroelectric Activity. The Bulletin of the Tulane University Medical Faculty, Nov., 1966, 25: 277-288.

Wilkinson, R. T., Morlock, H. C., and William, H. L. Evoked Cortical response during vigilance. Psychon. Sci., 1956, Vol. 4(6).