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Effects of lithium on auditory evoked potential and electroencephalogram spectral edges

Zak, Francis Anthony, Jr., Ph.D.

The University of Arizona, 1992
EFFECTS OF LITHIUM ON AUDITORY EVOKED POTENTIAL
AND ELECTROENCEPHALOGRAM SPECTRAL EDGES

by
Francis Anthony Zak, Jr.

A Dissertation Submitted to the Faculty of the
DEPARTMENT OF ELECTRICAL AND COMPUTER ENGINEERING
In Partial Fulfillment of the Requirements
For the Degree of
DOCTOR OF PHILOSOPHY
WITH A MAJOR IN ELECTRICAL ENGINEERING
In the Graduate College
THE UNIVERSITY OF ARIZONA

1992
As members of the Final Examination Committee, we certify that we have read the dissertation prepared by Francis A. Zak, Jr., entitled Effects of Lithium on Auditory Evoked Potential and Electroencephalogram Spectral Edges and recommend that it be accepted as fulfilling the dissertation requirement for the Degree of Doctor of Philosophy.

Final approval and acceptance of this dissertation is contingent upon the candidate's submission of the final copy of the dissertation to the Graduate College.

I hereby certify that I have read this dissertation prepared under my direction and recommend that it be accepted as fulfilling the dissertation requirement.

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ACKNOWLEDGEMENTS

The author would like to express gratitude to the following individuals and organizations: Dr. Kenneth C. Mylrea, Dr. Michael D. Karol, Dr. Michael D. Mayersohn, Dr. Edward M. Lonsdale, Dr. Glen C. Gerhard, Martie P. Fankhauser, Dr. Ahbijit C. Mahalanobis, and Hughes Aircraft Company.
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ABSTRACT

The effects of lithium on auditory evoked potential and electroencephalogram spectral edges are examined. The nature of the relationship between spectral edge and serum lithium concentration is investigated, with the goal of establishing a unique and functional relationship, thus enabling the spectral edge to be used as an index, or surrogate measurement, of serum lithium concentration.
1.0 INTRODUCTION

This experiment was an investigation of the effects of lithium on the frequency spectra (both magnitude and phase) of the electroencephalogram (EEG) and the auditory evoked potentials (AEPS). The goal of the experiment was to establish whether the frequency content of any of the spectra changes in response to lithium and, if so, if it changes in a consistent and predictable manner as the serum lithium concentration changes.

The spectral edge was used as the index of the spectral frequency content. The x% spectral edge is the frequency below which x% of the power in the spectrum lies. As the power in the spectrum shifts to higher frequencies, the spectral edge shifts upward and vice versa.

If a relationship could be established between the spectral edge and the serum lithium concentration, then a relationship might exist between spectral edge and the serum concentration of other drugs; if so, measurement of the spectral edge could potentially replace blood sampling and drug assays as an indicator of serum concentration for those drugs. Such a measurement would have several advantages: (1) it is noninvasive, thereby preventing the possibility of infection; (2) it is painless, a significant advantage for patients on long-term drug therapy who must have their blood drawn periodically for drug assays;
(3) drug assays indicate total drug concentration (unbound drug + bound drug) and the amount of unbound drug, which is the pharmacologically active component, changes under certain physiological conditions (such as decreased plasma protein binding for drugs that are protein-bound); and (4) for drugs which exert their effect on the central nervous system, EEG and AEP effects are direct effects of the drug, whereas blood levels are correlates of the drug effects.

The experiment was thus set up to measure the spectral edge as the serum lithium concentration was varied. Sixteen study subjects were recruited and the experiment was divided into two phases. In Phase 1, ten study subjects were orally dosed with lithium carbonate to three different steady-state levels. The EEG, AEP, and serum lithium levels were measured concomitantly at baseline (before lithium administration), during the attainment of the first steady-state, and at the second and third steady states. In Phase 2, eight study subjects were orally dosed to one steady-state level and the EEG, AEP, and serum lithium levels were measured concomitantly several times at baseline and several times at steady-state.

The EEG and AEP were recorded under resting conditions. The AEP stimulus was delivered monaurally through a pair of headphones and consisted of a sequence of clicks, alternating between a single-click and a double-click (pair
of single-clicks) with a total of 1000 single-clicks and
1000 double-clicks; the double-clicks enabled the
examination of evoked potential recovery.

The EEG and AEP were recorded from the Cz (vertex)
electrode with a mastoid reference and a forehead ground.
After amplification, filtering, and digitization by an 8-bit
analog-to-digital converter (ADC), the EEG and AEP were
stored on hard disk; the data acquisition and storage were
controlled by a Digital Equipment Corporation (DEC) MicroVAX
minicomputer.

The data analysis was performed in FORTRAN on a DEC
VAX 11/780 computer. A Fast Fourier Transform was performed
on the EEG and AEP data, followed by calculation of the
magnitude, phase, and power spectra. Spectral edges were
calculated and graphed as a function of time since initial
dose (or, equivalently, study day, since each study day was
a 24 hour increment on the time since the initial dose) and
as a function of serum lithium concentration.
2.1 EEG SIGNAL DESCRIPTION AND CLASSIFICATION

2.1.1 Overview

The electroencephalogram (EEG) is a signal consisting of the time variation of the cerebral cortex or scalp potential. This potential is commonly measured as a differential voltage between two electrodes on the scalp or cerebral cortex with reference to a third (indifferent) electrode and is the resultant field potential due to the firing of large numbers of cortical neurons. The following discussion will center on the EEG recorded from the scalp, as this type of recording was used in this experiment. The method of recording the EEG, the clinical uses of the EEG, the mechanism of EEG generation and relevant cerebral cortex physiology, and the statistical properties of the EEG will all be discussed in later sections.

The EEG is a signal of constantly-changing amplitude and frequency content. The amplitude and frequency content are a function of numerous subject variables, including vigilance, state of arousal, mental alertness, and physical condition.

The peak-to-peak amplitude of the EEG ranges from 10 to 100 uV, with 10 to 50 uV being the more common range for adults. The EEG amplitudes are typically measured as

\(^1\)References for this section are (8,9,12,13,35,51).
peak-to-peak values rather than as absolute values, since the former are less affected by variables such as the interelectrode distance.

The clinically-relevant EEG frequency range extends from 0.1 to 100 Hz. In the normal adult, the medium (8 to 13 Hz) and fast (14 to 30 Hz) frequencies predominate the EEG, while the slow (0.3 to 7 Hz) and very fast (> 30 Hz) frequencies are more sparse. The EEG frequency range is divided into several bands, namely the delta, theta, alpha, and beta bands; each of these bands will be discussed in more detail in the sections which follow.

EEG activity may be described as being any of the following: (1) paroxysmal or non-paroxysmal; (2) evoked or spontaneous; and (3) focal or diffuse. Paroxysmal activity is transient activity that occurs in short bursts for short periods of time, such as epileptic spikes; non-paroxysmal activity is more constant activity that lasts for longer periods of time, such as the alpha rhythm (see Section 2.1.2) when the eyes are closed. Evoked activity is activity that occurs in response to sensory stimulation, such as visual evoked potentials; spontaneous activity is activity that occurs without the need for sensory stimulation, such as the normal adult day time background activity. Focal activity is activity that is localized over a small area, such as activity at an epileptic locus;
diffuse activity is activity that is spread over a large area, such as the alpha rhythm. Based on (1) and (2), Dumermuth (1977) has classified EEG activity into the following three categories: (1) spontaneous non-paroxysmal; (2) spontaneous paroxysmal; and (3) evoked. Table 2.1.1-1 presents example activities from each of these categories.

In the time domain (e.g., as observed on an oscilloscope or strip-chart recorder), the EEG appears as a combination of waves of various amplitudes, frequencies (mostly less than 30 Hz), and durations; sometimes a particular train of rhythmic waves will appear for a short time and then disappear.

In the frequency domain (e.g., as observed on a signal or spectrum analyzer), the EEG appears as shown in the spectral plots of Figure 2.1.1-1. These plots show that most of the power is concentrated at frequencies below 30 Hz.

2.1.2 Alpha Rhythm

The alpha rhythm (AR), shown in Figure 2.1.2-1, is a medium-frequency EEG wave that occurs during wakefulness over the posterior head regions, with higher voltages over the occipital areas. The frequency range of the AR is 8 to 13 Hz. The frequency is slightly unstable, with the mean adult frequency being 10.2 +/- 0.9 Hz. During the first decade of life, the frequency progressively increases from 4 Hz at 4 months of age to 10 Hz at 10 years of age; in
CATEGORIES OF EEG ACTIVITIES

**Spontaneous non-paroxysmal activity**

Activities without significant temporal changes
- Normal spontaneous waxing activity
- Alpha variants
- Beta activity
- Continuous slow rhythm
- Polymorphous slow activity

Activities slowly changing with time
- Sleep activity
- Postictal background activity
- Fluctuating activity in coma
- Hyperventilation activity
- Seizure discharges

Activities of intermittent type
- Sigma activity in form of sleep spindles
- Mu-rhythm
- Intermittent slow rhythms
- Psychomotor variant pattern

**Spontaneous paroxysmal activity**

- Spikes, Sharp Waves
- Spike/wave-complexes
- Rhythmic 3/sec Spike and Wave formations
- Paroxysmal slow waves
- 14+6/sec positive spikes
- SSLE complexes
- K-complexes and Vertex potentials in sleep

**Evoked activity**

- Evoked transient potentials
- Photic driving (well suited for spectral analysis)
- Arousal activity
- Eye-closing effects
- Lambda waves

---

Table 2.1.1-1. Classification of EEG activities (from ref. 12).
Figure 2.1.1-1. Typical EEG spectrums (from ref. 12 and 30).
Figure 2.1.2-1. Major EEG rhythms (from ref. 51).
elderly individuals, the frequency decreases.

The AR amplitude is variable but mostly less than 50 uV in adults. The amplitude is constantly increasing and decreasing such that the AR appears on an EEG machine or an oscilloscope as trains of waves with a spindle shape containing a wide portion and a narrow portion. The waveform is usually rounded; sometimes the waveform exhibits the sharp configuration where the positive peaks are sharp and the negative peaks are rounded. The sharp configuration is usually caused by beta waves mixing with the alpha waves.

The AR is best seen with the eyes closed and under conditions of physical relaxation and relative mental inactivity. The AR is temporarily blocked by influx of light (eye opening), other afferent stimuli (auditory, tactile, and somatosensory), and mental activities (attention, especially visual, and mental effort); the degree of reactivity may be complete blockage, suppression, or attenuation with voltage reduction. Of these three sources of AR attenuation, the influx of light produces the greatest blocking effect. Immediately after the eyes are closed, the AR may exhibit the squeak effect, which is a momentary acceleration of the AR frequency. When higher alertness attenuates the AR, the AR is supplanted by desynchronized low-voltage fast activity.

At the earliest stage of drowsiness, alpha dropout
occurs: the trains of alpha waves gradually disappear and are replaced by a low-voltage pattern of mixed slow (mostly theta range) and fast frequencies; in infants and children, the alpha waves are replaced by various types of slow patterns.

2.1.3 Beta Rhythm

The beta rhythm (BR), also called fast activity and shown in Figure 2.1.2-1, consists of all EEG activity with frequencies greater than 13 Hz. Usually, BR frequencies do not exceed 35 Hz, although the frequencies may reach a maximum of 50 Hz during intense mental activity. The amplitude of the BR seldom exceeds 30 uV and may be locally enhanced over bone defects.

The BR waves are classified on the basis of their quantity or location. On the basis of quantity, EEG records of BR waves are classified as either F1 (a moderate increase of fast activity) or F2 (a marked increase of fast activity).

On the basis of location, BR waves are classified as either frontal, central, posterior, or diffuse. Frontal beta is fairly common and consists of brief trains of 20 to 25 Hz activity and larger-amplitude trains of 20 to 25 Hz activity occurring for variable periods. Frontal beta appears during intense mental activity or central nervous system activation and during tension.

Posterior beta is 14 to 19 Hz activity which is similar
to alpha rhythm in its reactivity: it has a blocking response to eye opening, is enhanced with eye closure, and disappears during intense mental activity (in contrast to frontal beta, which increases during intense mental activity).

Central beta is activity at approximately 20 Hz that is often mixed with and reactive like a rhythm related to motor cortex functions called the mu rhythm (MR): both the MR and central beta are blocked by motor activity, thinking about movement, or tactile stimulation. Central beta is absent in emotionally-stable people, normally occurring in people with aggressive and domineering personalities.

Barbituates, sedatives, and minor tranquilizers increase the quantity and amplitude of BR waves. Sleep-inducing medication augments frontal beta activity in the 25 to 30 Hz and 35 to 40 Hz ranges. The BR is found in almost every healthy adult, mainly over the frontal and central regions, and has to be particularly abundant in quantity and of rather high voltage to be termed abnormal.

2.1.4 Delta Rhythm

The delta rhythm (DR), shown in Figure 2.1.2-1, consists of all EEG waves with frequencies below 4 Hz. Like the theta rhythm to be discussed in the following section, the DR occurs more often in the normal waking EEGs of infants than in that of adults; the DR also occurs in deep sleep,
brain disease, stupor, and under general anesthesia.

The DR tends to be sporadic, sometimes occurring only once every 2 to 3 seconds when it does occur. In infants, bursts of DRs may have amplitudes from 50 to 100 uV. The DR does not require the reticular activating system (see Section 2.4.3) for its generation, as it has been demonstrated to occur even when the cortex is separated from the brainstem.

2.1.5 Theta Rhythm

The theta rhythm (TR), shown in Figure 2.1.2-1, consists of all EEG waves with frequencies between 4 Hz and 8 Hz. TR occurs mainly in young children and tends to decline with age: by the age of ten years, the TR is usually not very prominent, and by the age of twenty-five or thirty years, only a small amount of TR exists.

In young children, the TR is diffuse, while in older people, the TR tends to occur in the parietal and temporal regions. The TR amplitude is generally less than 50 uV in infants and less than 30 uV in young children, while in adults TR amplitudes greater than 20 uV are considered abnormal and caused by some pathology.

The TR is considered an emotional correlate of disappointment and frustration, as in younger children it tends to occur concomitantly with feelings of disappointment and frustration and at the conclusion or interruption of a
pleasurable stimulus. In adults, the probability of TR occurring is higher during drowsiness.
2.2 Setup for Recording the EEG

2.2.1 Overview

The clinical EEG is recorded with the subject awake, eyes closed, recumbent, and in a relaxed state. These conditions maximize the alpha rhythm and minimize noise interference due to muscle and electrode artifact.

Figure 2.2.1-1 shows a typical setup for recording the EEG. In this setup, an electrode pair from the patient connects to the input of a high-gain differential amplifier. The amplified EEG signal is band-pass-filtered by feeding it through a cascade of an adjustable low-pass filter and an adjustable high-pass filter. The filtered EEG signal may be further amplified as necessary before finally being applied to either a strip-chart recorder for visual display and a hard copy or to an analog-to-digital converter (ADC), which converts the analog EEG signal into a digitized signal for storage on computer storage media or further signal processing. If a strip-chart recorder is used, the analog EEG signal may also be applied to an analog tape recorder for permanent storage.

The following sections will briefly describe the electrode montages and locations, the amplifier, and the filters.

References for this section are (28,41,51).
Figure 2.2.1-1. Setup for recording the EEG.
2.2.2 Electrode Locations and Montages

Electrodes are mounted to the head in locations determined by the International Federation 10-20 System (see Figure 2.2.2-1). In this system, for which the full standard placement consists of 21 electrodes, the placement of electrodes is determined by measurements from specific anatomical landmarks; thus, the system provides repeatability of electrode placement, both over time from the same laboratory and between different laboratories.

Montage refers to the specific combination of electrodes examined (or recorded) at a particular instant of time. The International Federation System defines three types of montages: (1) bipolar; (2) reference, or monopolar; and (3) average.

The bipolar montage, shown in Figure 2.2.2-2, consists of pairs of closely-spaced electrodes examined either in a front-to-back sequence (AP, or longitudinal, bipolar montage, where AP stands for anterior to posterior) or side-to-side sequence (transverse, or coronal, bipolar montage).

The monopolar montage, shown in Figure 2.2.2-1, consists of one monopolar lead measured with respect to a distant reference electrode which is usually attached to one or both earlobes.

The average montage, shown in Figure 2.2.2-2, consists of one monopolar lead measured with respect to a system or
Figure 2.2.2-1. International Federation 10-20 system (from ref. 41).
Figure 2.2.2-2. Montages: longitudinal bipolar on left, transverse bipolar in center, and monopolar on right (from ref. 41).
reference electrode which is connected through equal high resistances to all of the rest of the electrodes.

In the bipolar montage, far-field activity common to both of the closely-spaced electrodes in the pair is cancelled, thus providing for sharp localization of the response. The bipolar montage also enhances areas of rapid change in polarity as well as rapid changes in voltage.

The reference montage is used for detecting voltage differences. In general, higher voltages are seen as the interelectrode distance increases; thus, voltages appear to be higher in the monopolar montage than in the bipolar montage.

The selection of a montage depends on the nature of the investigation. In general, for locating abnormalities, montages are used that have some electrodes inside the field of abnormal activity and some electrodes outside of the field of abnormal activity.

2.2.3 Amplifier

The EEG amplifier is an adjustable high-gain differential amplifier with high input impedance, a high common mode rejection ratio (CMRR), a frequency response from DC to at least 100 Hz, and input protection circuitry to minimize patient shock hazards.

The amplifier must amplify the EEG signal from an amplitude as low as 10 uV to an amplitude in the 1 V to 10 V range.
range (the standard is 2.8 V) for application to the recording device or the ADC; this voltage amplification corresponds to a gain in linear units of 100,000 to 1,000,000 or in logarithmic units of 100 dB to 120 dB. Since the EEG amplitudes can differ considerably from recording session to the next, an adjustable gain is provided on the amplifier.

The combination of the amplifier input impedance with the electrode impedance forms a voltage divider which results in signal attenuation. The amplifier input impedance must be high in order to minimize this attenuation.

The differential EEG signal is not the only signal present at the electrodes: present also are common-mode signals such as 60-Hz noise voltages that have capacitively-coupled into the patient's body from nearby electrical equipment and AC power mains wiring. These common-mode signals often have greater amplitude (typically on the order of millivolts) than the EEG and, if amplified, would obscure and distort the EEG. In order to amplify the differential EEG signal but not the common-mode interference signals, the amplifier must have a high CMRR which is the ratio of the amplifier's gain of differential signals to the amplifier's gain of common-mode signals. EEG amplifiers have CMRRs in linear units of $10^3$ to $10^5$ or in logarithmic units of 60 dB to 100 dB.
To prevent signal distortion, the amplifier must have a minimum bandwidth of 0.16 Hz to 100 Hz, which is the bandwidth of the EEG signal. An amplifier's bandwidth is the range of frequencies over which it provides flat gain (minimal variation of gain with frequency) and linear phase shift (linear variation of phase with frequency). A flat gain and linear phase shift are necessary to prevent distortion of the signal.

To prevent the patient from exposure to electrical shock hazards, the amplifier must employ input circuitry which isolates the electrode leads from the amplifier AC power ground. This isolation prevents potentially hazardous fault currents from flowing through the patient's body via the electrode leads to the amplifier AC power ground.

2.2.4 Filters

To reject extraneous noise outside the EEG passband (which for most clinical applications is 0.16 to 100 Hz) and thus improve the discrimination of the EEG signal against the background noise (e.g., muscle artifact), the EEG is bandpass filtered.

The bandpass filter is normally realized as a cascade of a lowpass filter (LPF) and a highpass filter (HPF), both of which have adjustable 3 dB points. Thus, the lower 3 dB point, the upper 3 dB point, and the bandwidth are all adjustable, enabling the filtering to be tailored to
meet the needs of a particular setting or application.

Both the LPF and the HPF are normally realized as first-order filters. The filters are chosen to be of such low order because higher-order filters typically produce excessive phase shifting at frequencies near the 3 dB points, thus introducing significant distortion.
2.3 Applications of the EEG

2.3.1 Clinical Applications

The EEG has been used in a wide variety of clinical applications. The EEG can be used to evaluate the state of the nervous system when it cannot be evaluated by clinical means (e.g., during coma); in addition, characteristic EEG changes have been associated with various abnormalities and adverse conditions (e.g., cerebral hypoxia) and chemical agents (e.g., anaesthetics).

Thus, the principal clinical applications of the EEG are as follows: (1) to monitor the state of the nervous system in comas, encephalopathies, and cardiorespiratory failure; (2) to detect and monitor seizure discharges in epilepsy for diagnosis, classification, and focus localization; (3) to follow the progress of systemic metabolic disorders, especially renal disorders; (4) to demonstrate signs of a cerebrovascular accident in cerebral ischemia, even after the clinical symptoms subside; (5) to control the depth of anaesthesia, analgesia, induced hypotension, and induced hypothermia; (6) to warn of impending anoxic brain damage during surgical operations where brain function is at risk (e.g., vascular surgery) or under hypotension; (7) to perform sleep staging (in

References for this section are (5,14,15,23).
combination with electromyography and monitoring of eye movements); (8) intrapartum fetal monitoring; and (9) identification of neonatal disorders.

2.3.2 Quantitative Pharmaco-EEG

Quantitative pharmaco-EEG (QPE) is a discipline which describes drug effects on the central nervous system (CNS) by using the EEG. QPE is particularly useful in the industrial development of a drug, where it can be used as follows: (1) to screen new drugs that are presumed to be active on the CNS; (2) to describe such pharmacodynamic profiles of the drug as dose-effect and time-effect relationships, thereby facilitating dosage definitions; and (3) to evaluate the CNS toxicity of drugs that are developed primarily for target organs other than the CNS.

A wide variety of drug classes have been examined, including psychotropics, analgesics, hypnotics, antiepileptics, and gerontopharmacological agents. Typical target EEG parameters (i.e., indices for assessing the drug effects) include the percentage of power in the various frequency bands and the peak frequencies in each band (usually the peak alpha frequency).

The effects of the psychotropics have been extensively characterized and will be presented as an example of QPE classification. The psychotropics can be divided into the following four classes based on their EEG effects (see
Table 2.3.2-1), a classification which correlates with their clinical therapeutic classification: (1) neuroleptics (e.g., chlorpromazine), which are psycho-sedatives used to treat schizophrenia, increase power in the 5.5 to 8.5 Hz and 12 to 18 Hz bands and decrease power in the 10.5 to 12 Hz band; (2) anxiolytics (e.g., diazepam), which reduce tension and anxiety and are used to treat anxiety neurosis, increase power in the 12 to 18 Hz band and decrease power in the 10.5 to 12 Hz band; (3) tricyclic antidepressants (e.g., imipramine), which elevate mood and are used to treat depressive neuroses and psychoses, increase power in the 21 to 30 Hz band; and (4) psychostimulants (e.g., dextroamphetamine), which activate drive and performance and are used to treat mental or motor retardation and narcolepsy, decrease power in the 1.5 to 5.5 Hz and 5.5 to 8.5 Hz bands. Note that the power referred to here is relative power, i.e., power in aspecific band relative to the total power, not absolute power; in fact, if absolute power is used, the classifications are no longer valid. In the assessment of drug pharmacodynamic characteristics, QPE is used to establish dose-effect (see Figure 2.3.2-1) and time-effect (see Figure 2.3.2-2) curves and drug activity in relation to bioavailability, including the relation between plasma levels and EEG effects (see Figure 2.3.2-3).
Table 2.3.2-1. Classification of psychotropic drugs based on EEG effects (from ref. 23).

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<th>5-8.5</th>
<th>8.5-10.5</th>
<th>10.5-12.2</th>
<th>12.5-18.0</th>
<th>21.0-30.0</th>
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<td>Haloperidol type</td>
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<td>Low sedation</td>
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<tr>
<td>Amphetamine type</td>
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<tr>
<td>Methylenephedrine type</td>
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</table>

*Table Legend: ↑ increase, ↓ decrease, ♦ no change, - not specific for this type of drug, characteristic alterations*
Figure 2.3.2-1. Dose-effect curve for mepindolol (from ref. 23).
Figure 2.3.2-2. Time-effect curve for Lormetazepam (from ref. 23).
Figure 2.3.2-3. Relation between plasma levels and EEG effects for Lorazepam (from ref. 23).
2.4 Electrogenesis of the EEG

2.4.1 Neuron Physiology and Nerve Impulse Transmission

The nervous system is composed of glial cells, which perform a structural supportive function, and neurons, which are cells that conduct nerve impulses.

Figure 2.4.1-1 shows a typical neuron and its connection to other neurons. The neuron consists of a soma (or cell body), one or more dendrites (usually several), and one or more axons (usually one). The soma contains ribosomes called Nissl bodies for respiration and a nucleus for directing the metabolic activity of the cell. The dendrites are short, branched segments; the axon is a long projection.

Nerve impulses propagate along the membranes of the dendrites, soma, and axon; although nerve impulses can travel in either direction along the dendrites and the axon, dendrites usually carry impulses toward the soma and the axon usually carries impulses away from the soma. Some axons have myelin sheaths spaced periodically along the length of the axon which function to increase the speed of conduction by enabling the impulse to jump across the gaps of neighboring sheaths; conduction which occurs in this manner is known as saltatory conduction.

At the terminal end of an axon is a structure called a

References for this section are (16, 26, 51).
Figure 2.4.1-1. Typical neuron (from ref. 16).
terminal bouton. This structure is used to interface with other neurons. Typically, the axon of one neuron connects to the dendrite of another neuron, but the axon may also connect to the soma of the other neuron.

The connection between axons and dendrites and between axons and somas is known as a synapse and is not a direct physical connection; instead, a space of about 500 Angstroms called the synaptic cleft separates the connecting structures.

Under equilibrium conditions, when a neuron is not propagating an impulse, a resting potential of approximately 70 mV exists across the membrane of the neuron, with the inside of the membrane negative with respect to the outside of the membrane. This potential is the result of an imbalance of sodium ions (Na\(^+\)) and potassium ions (K\(^+\)) across the membrane: at equilibrium (no impulse propagating), the sodium ion concentration just outside the membrane is greater than the potassium ion concentration just inside the membrane, the outside has more positive charges than the inside, and the inside of the membrane is thus negative relative to the outside of the membrane. This concentration difference is maintained by an active transport process (that is, a process which maintains a concentration difference against a concentration gradient by the expenditure of energy) called the sodium-potassium pump that
uses ATP (adenosine triphosphate) as the energy source.

A nerve impulse is a shift in the potential across the membrane from the resting potential of \(-70\) mV to a potential of approximately \(+30\) mV, a value called the action potential. This shift in potential is caused by a transient increase in the membrane permeability, causing sodium ions to rush in and potassium ions to rush out, with more sodium ions rushing in than potassium ions rushing out, and thus the inside of the membrane becoming positive with respect to the outside. The membrane permeability change is triggered by the presence of the action potential in the section of membrane just preceding the section in which the action potential is being generated.

A nerve impulse is transmitted across the synapse by chemical, rather than electrical, means. The membrane of the axon on the transmitting side of the synapse is called the pre-synaptic membrane and its potential, the pre-synaptic potential (PRSP); the membrane of the dendrite on the receiving side of the synapse is called the post-synaptic membrane and its potential, the post-synaptic potential (POSP). A nerve impulse arriving at the terminal bouton of the axon causes the release of chemicals called neurotansmitters into the synaptic cleft. The nervous system contains approximately eight different neurotansmitters, some examples being serotonin, acetycholine, and
5-hydroxytryptamine. The neurotransmitters diffuse across the synaptic cleft and bind with receptor sites on the post-synaptic membrane, causing receptors on the membrane to open, ionic current to flow into the post-synaptic neuron, and a POSP to be generated.

Once the POSP is generated, it travels to the soma in a graded manner, that is, the potential decreases with distance along the dendrite. The amplitude of the POSP at the soma is approximately 1 mV. The soma sums all of the inputs from all of the dendrites and from all of the axons connected to the soma; if the sum of all of the inputs within a short time period exceeds a certain threshold, which is usually tens of millivolts and is different for each different soma, then an action potential, or spike, is generated. The influence of a particular POSP on the summation at the soma may be either excitatory (depolarizes the membrane of the soma, increasing the likelihood of a spike generation) or inhibitory (hyperpolarizes the membrane of the soma, decreasing the likelihood of a spike generation).

Once the spike is generated at the soma, it travels down the axon toward the terminal bouton. The axon propagates action potentials in an all-or-none fashion: the potential propagates down the axon with no attenuation, in contrast to the graded manner in which the potential
propagates down the dendrites.

The total time it takes from the time an action potential is generated in the soma of one neuron to the time at which an action potential is generated in the next neuron is from 1 to 2 msec. After a spike is generated by a neuron, the neuron cannot generate another spike for a period of from 1 to 2 msec, a period of time known as the absolute refractory period.

The refractory period limits the maximum spike frequency to 500 to 1000 Hz. Neurons in sensory input pathways typically fire at this maximal rate; cortical neurons typically fire at a slower rate of 30 to 150 Hz.

2.4.2 Cerebral Cortex Anatomy

The cerebral cortex (CC) is the outermost layer of the brain, ranging from 1.5 to 4.0 mm thick. The CC, the functional part of the cerebrum and the center of human intellectual functioning, is arranged in six layers, as shown in Figure 2.4.2-1. These six layers are comprised mainly of pyramidal cells (PCs) and granule (or stellar) cells (GCs).

GCs have small cell bodies. The dendrites of a GC are radially arranged around its cell body and terminate near the GC. The axon of a GC, which commonly branches repeatedly, terminates near the GC on neighboring cell bodies and dendrites.
Figure 2.4.2-1. The six layers of the cortex (from ref. 51).
PCs are triangular, vary greatly in size, and can be large. A PC is oriented with its base down and its apex directed toward the cortical surface. A PC consists of: (1) a long apical dendrite that ascends from the cell body to the outermost cortex layer and branches terminally; (2) a network of dendrites at its base that is horizontally-oriented and terminates near the cell body; and (3) an axon that may ascend to the cortex, branch, and project to other areas of the cortex or reenter the cortex and either project to other subcortical structures such as the thalamus or send feedback branches on the parent cell.

2.4.3 Mechanism of EEG Electrogenesis

The EEG is the resultant potential due to the superposition of a large number and variety of volume-conductor fields (VCFs). A VCF is a field generated at some point in a medium that spreads throughout the extent (volume) of the medium due to the propagation characteristics of the medium for that field.

The VCFs which comprise the EEG originate in the PCs (see Figure 2.4.3-1) when a synaptic ending on the apical dendrite of a PC becomes active, usually as a result of a dendritic postsynaptic potential (DPSP), which may be either excitatory (negative potential) or inhibitory (positive potential). As a result of the DPSP, a potential difference is created between the synapse and the rest of the dendrites
Figure 2.4.3-1. Pyramidal cell becoming active.
(from ref. 51).
and the soma, causing a current flow between the synapse (which becomes a current source) and the soma and dendrites (which become current sinks) and a radially-oriented current dipole to form. Variations in the orientation and strength of this dipole constantly occur and, due to ohmic resistance in the volume conductor formed by the brain and its associated tissues, the cerebrospinal fluid, and the skull, produce wavelike potential fluctuations in this volume conductor. The resulting surface potential depends on the DPSP sign, orientation, and location relative to the measurement site (the recording electrodes).

The magnitude of the VCF produced by a single PC current dipole is extremely small. The much larger amplitudes of the EEG surface potentials are due to two phenomena: (1) synchronization; and (2) PC orientation.

Each individual wave of a surface EEG recording is actually the superposition of a large number of VCFs occurring simultaneously. The underlying process which brings groups of PCs into unified action is called synchronization. Synchronization is due to a rhythmic and pacemaker function provided by the reticular activating system, which determines the intensity and pattern of the EEG by controlling the overall excitation of the brain.

A group of neurons which fire simultaneously would produce little far-field activity (surface potentials) if
the neurons were arranged such that the vectorial sum of their dipoles cancelled in the far field. The orientation of the PCs in the cortex results in a net surface potential which is the summation of the VCFs produced by each of the PCs: the PCs are oriented vertically with the long apical dendrites of neighboring PCs running parallel to one another. Indeed, the GCs contribute little to surface potentials because of their orientation: radial arrangement of their dendrites around their cell bodies, producing fields of current flow between the dendrites and the soma that sum to zero when viewed from the relatively great distance to the surface. In addition, PC axon potentials contribute little to the surface potentials partly because of the orientation of the axons: the axons run in many directions relative to the surface and thus the fields produced by individual axons cancels at the surface (the other reason axon potentials contribute little to surface potentials is that the axons tend to fire asynchronously with regard to neighboring axons).
2.5 Statistical Properties of the EEG Signal

The EEG is a set of values (scalp or cortex potential) as a function of time and is therefore classified as a multivariate time series. The amplitude and frequency content - and hence the pattern - of the EEG are a function of numerous variables, including both internal (subject) variables - such as vigilance, state of arousal, concentration on a task, and the physical and chemical environment of the brain - and external (environmental) factors, such as the time of day (the sleep EEG differs markedly from the waking EEG) and the subject's setting, which influences the subject's state of arousal. In addition, the EEG is corrupted by varying levels of noise, including instrumental and brain noise (diffuse, non-synchronized activity). Because of these factors, the overall EEG pattern is fairly irregular, constantly changing, and unpredictable and hence the EEG is classified as a random signal.

In contrast to deterministic signals (such as the sine wave output of a function generator), random signals cannot be described by explicit mathematical equations; instead, random signals are described by statistical terms such as probability distributions and their moments (such as the

References for this section are (12,13,18,30).
mean and variance), frequency spectra, or correlation functions.

While the overall pattern of the EEG is irregular, certain periods of time can be defined in which the statistics of the EEG are more or less constant, that is, in which the EEG is stationary: in particular, normal background activity in the healthy subject in a relaxed, quiet state with eyes closed frequently exhibits stationary characteristics; the EEG under these conditions is frequently modeled as a stationary, normal (Gaussian), ergodic, and mixing random (or stochastic) process. Each of these terms will now be defined.

If the value of a random variable is measured a number of times, it will be found that certain values of the variable occur more often than others; the relationship between the probability of obtaining a certain value of the variable and the value of the variable is called the probability distribution. Several probability distributions exist; one of the most common is the normal or Gaussian distribution, shown in Figure 2.5-1. The probability distribution of the EEG signal is frequently modeled as a Gaussian distribution.

For a random signal, a recording of the signal over a particular time period - that is, a sample function - is only one possible sample function out of the set of infinite
Figure 2.5-1. Gaussian (normal) distribution (from ref. 48).
sample functions (or the ensemble) that could have been simultaneously recorded over that same time period. An accurate calculation of the statistical parameters of the signal, such as the mean and variance, would require that the parameters be calculated as the average of each of the parameters computed from the individual sample functions of the ensemble. In practice, only one possible sample function can be recorded as, for example, in the recording of one five-second epoch of the EEG; in this case, the property of ergodicity is invoked, which allows ensemble averages to be replaced by averages over time. Thus, for example, the average amplitude in a selected frequency band in the EEG can be computed by averaging the average amplitudes computed from a selected number of successive five-second epochs.

The property of mixing implies that the observation interval is short enough that the interval is stationary: that is, the interval is not so long that the statistics of the process vary significantly over the interval. In the recording of the EEG, this requirement is satisfied by choosing the epoch length sufficiently small so that non-stationarity is avoided (see Section 8.1.6.7).
2.6 Description of the AEP Signal

2.6.1 Overview

Evoked potentials (EPs) are sequences of waves (potentials) produced by the brain in response to sensory stimuli. Based upon the distance of the recording electrodes from the structures in the brain which generate them, EPs can be divided into near-field potentials (NFPs) or far-field potentials (FFPs).

NFPs are recorded from electrodes located close to or on the structures which generate them. An example of an NFP is an EP measured by inserting a needle electrode into a specific nerve associated with the transmission of the nerve impulse from the sensory structure involved in the particular type of EP being studied.

FFPs are recorded from electrodes located a relatively great distance from the structures which generate them. An example of an FFP is an EP with generating structures in the brain stem that is recorded with scalp electrodes. The amplitude of FFPs is very small - typically less than 2 uV - and thus FFPs can only be measured with special averaging techniques. In a volume conductor such as the skull (see Section 2.4.3), the FFP amplitudes decrease in proportion to the square of the distance from the generators to the

References for this section are (7,38,40,46).
Auditory evoked potentials (AEPs) are EPs elicited by an acoustic stimulus. An AEP is usually recorded from scalp electrodes as a differential voltage between a vertex electrode and a mastoid electrode with reference to a forehead electrode (see Section 2.7.2). As recorded from the scalp, the AEP is a mixture of NFPs and FFPs.

The acoustic stimulus for the AEP (see Section 2.7.3) is usually a brief, high-intensity click delivered monaurally to the same ear behind which the mastoid electrode is mounted (ipsilateral recording; see Section 2.7.3). An AEP response may be classified as either an onset/transient response (OTR) or frequency-following response (FFR), depending upon whether the stimulus period is greater than (OTR) or less than or equal to (FFR) the time for the AEP response to subside.

In the time domain, which is the domain in which the AEP is observed in clinical practice, the AEP consists of a sequence of peaks extending from the onset of the acoustic stimulus up to approximately one second after the stimulus, with the amplitude of the peaks ranging from 0.1 uV for the earlier components to 10 uV for the later components. Figure 2.6.1-1 shows a representative AEP.

This one-second time period following the stimulus is divided into four intervals: early (0 to 10 msec), middle
Figure 2.6.1-1. Auditory evoked potentials (from ref. 40).
(10 to 50 msec), late (50 to 250 msec), and long (greater than 250 msec). Each of these classifications will now be discussed further.

### 2.6.2 Early Latency Components

The early AEPs, shown in Figure 2.6.2-1, consist of seven peaks numbered I through VII which occur in the first 10 msec following a click stimulus (some classification systems define the early AEP period from 2 to 12 msec). These AEPs, which are far-field potentials composed mainly of transient potentials, are produced by successive activation of the various nuclei and tracts in the neural pathway of the brainstem from the cochlea to the pons (see Section 2.9.4) and are thus typically called brainstem AEPs (BAEPs). The amplitude of the BAEPs is very small, varying from 0.01 to 2 μV, and thus the BAEP can only be measured by a special signal-processing technique called time-locked signal averaging (see Section 2.7.4). The absolute amplitude of the BAEPs is rarely measured, as it is too variable for clinical use; rather, relative amplitudes are used.

The polarity of each of the seven peaks is positive at the vertex electrode. The convention for display of the BAEPs (and all AEPs) is the same as in electroencephalography: negativity at the vertex electrode is plotted upwards. The time delay between particular peaks or from the onset of the stimulus to the occurrence of a
Figure 2.6.2-1. Early auditory evoked potentials (from ref. 40).
particular peak is called latency.

Wave V, which has an average amplitude of 0.61 uV and an average latency of 5.63 msec with a range of 5 to 9 msec, is the largest and most stable of the BAEP components. Wave I occurs 4 msec earlier than Wave V at 1/3 to 1/2 its amplitude. Wave II is usually quite small and not present in every individual. Wave III is quite prominent and occurs 2 msec later than wave I. Wave IV often occurs as a small component on the leading edge of wave V. Waves VI and VII are highly variable between subjects and frequently not observed; while labelled part of the BAEPs, they may contain contributions from structures located outside of the brainstem.

The intercomponent latencies are extremely consistent between subjects with normal hearing and therefore deviations in the latencies are used to define and localize brainstem abnormalities. Commonly used intercomponent latencies for this purpose are the I to III, III to V, and I to V latencies, which have latencies in normals of 2.6 msec, 2.2 msec, and 4.5 msec, respectively. Also utilized for this purpose is the V to I amplitude ratio, which is 2.51 in normals.

The BAEPs are relatively unaffected by the subject’s state of consciousness or drugs, especially sedatives, but are affected by stimulus factors (see Section 2.7.3); hence,
BAEPs are affected by exogenous (stimulus) factors, rather than endogenous (subject) factors.

2.6.3 Middle Latency Components

The middle-latency components (MLC), shown in Figure 2.6.1-1, are a sequence of negative-positive waves with latencies from 10 to 50 msec, consisting predominantly of the following four components: N, P, N (latency = 20 msec), P (latency = 30 msec), and N (latency = 40 msec). The amplitude of these components is typically 1 uV but ranges from 0.5 to 3 uV.

The MLC are typically recorded with bandpass filter settings of 25 to 200 Hz, 30 to 300 Hz, or 10 to 500 Hz; the N and P components have been postulated to be BAEP wave V components that are distorted by these relatively narrow bandwidths. The MLC are little affected by endogenous factors; in contrast to the BAEPs, the MLC are abolished by barbiturate-induced anesthesia.

The source of the MLC is unknown, but is probably in the primary auditory pathway in the auditory cortex. Sound-evoked muscle activity from reflex contractions in the periauricular, facial, and neck muscles occurs in the same time period as the MLC but has been shown not to be involved in the generation of the MLC. Because the source of the MLC is unknown and controversial, the clinical applications of the MLC are somewhat limited.
2.6.4 Late Latency and Long Latency Components

The sequence of negative-positive components with latencies from 50 to 250 msec are called the late latency components while those with latencies greater than 250 msec are called the long latency components. Sometimes all components with latencies greater than 50 msec are referred to as the long latency components, while to add further confusion, the components with latencies greater than 50 msec are referred to as late components in this experiment. In this section, the components with latencies greater than 50 msec are referred to as the late/long latency components (LLLC).

The LLLC consist primarily of the following components: N1 or N100 (latency = 100 msec), P200 or P2 (latency = 200 msec), N200 or N2 (latency = 280 msec), and P300 or P3 (latency = 300 msec); in addition to these components, which occur in response to a transient acoustic stimulus, a vertex-negative (i.e., negative polarity at the vertex electrode relative to the reference electrode), sustained DC potential shift called the sustained potential occurs sometimes in response to continuous acoustic stimulation.

The amplitude of the N100 and P200 components ranges from 1 to 10 uV and for the P300 component can be as high as 20 uV. The LLLC are typically recorded with a bandpass filter setting of 0.1 to 100 Hz; if the sustained potential
is to be recorded also, the lower 3 dB point of the bandpass filter must be set to DC.

The LLLC are affected by both exogenous factors (the stimulus rise and fall times, repetition rate, duration, intensity, and frequency) and endogenous factors (the subject's level of arousal and cognitive processes of attention and expectation). Changes in the subject's state of arousal produce changes in the morphology and amplitude of the components; changes in the subject's focus of attention cause the amplitude of N1 to change by as much as 50%; and changes in the subject's state of arousal or focus of attention cause drastic shifts in the latencies of the N2 and P3 components. The amplitude of the N2 component increases during sleep, with the amplitude changing as a function of the sleep level. The P3 component is elicited when a task-relevant stimulus is presented; the P3 latency changes in response to the task difficulty, while the P3 amplitude changes in response to the expectations of the stimulus. The amplitude of the sustained potential is enhanced as the subject's attention is increased.

The source of the LLLC is unknown, but the auditory cortex must be intact for the LLLC to occur. The LLLC are used primarily for evaluating cognitive functions.
2.7 Setup for Recording the Auditory Evoked Potentials¹

2.7.1 Overview

This section will briefly describe the setup for recording the AEP. Individual components will be discussed in the sections which follow.

Figure 2.7.1-1 shows a typical setup for recording the AEP. This setup, similar to the setup for recording the EEG but with the addition of components for producing the audio stimulus, consists of electrodes, an amplifier, filters, an ADC, an audio generator, headphones, and a computer. The computer initiates an audio stimulus by sending a trigger pulse to the audio generator, which in conjunction with the headphones produces the desired audio stimulus. This stimulus initiates an AEP from the subject. The AEP is transduced by electrodes, amplified by a high-gain differential amplifier, bandpass filtered, and fed to the input of an ADC.

Simultaneous with the delivery of the trigger pulse to the audio generator, the computer initiates data acquisition by sending a train of pulses to the ADC. Each pulse causes the ADC to digitize one data point. Each digitized data point from the ADC is read into the computer memory and then stored on magnetic storage media such as tapes or disks. The

¹References for this section are (7,33,38,40,46).
Figure 2.7.1-1. Setup for recording the AEP.
frequency of the pulses sent to the ADC is the digitizing frequency. The length of the train of pulses, which is the interval of data collection, comprises one epoch of data. Since the AEP amplitudes are so small, it is necessary to collect hundreds to thousands of epochs of data and average the epochs so that the AEPs can be discriminated from the background noise and EEG activity (see Section 2.7.4).

2.7.2 Electrode Locations and Montages

For recording the AEP, a monopolar, or reference, montage (see Section 2.2.2) is most commonly employed. The active electrode is connected to Cz (see Figure 2.2.2-1) and the reference electrode to an earlobe or linked earlobes, a mastoid process or linked mastoid processes, the neck, or the larynx. The ground electrode is normally attached to the forehead.

If the earlobe or mastoid electrode is attached to or behind the same ear to which the audio stimulus is delivered, the recording is called ipsilateral; if the electrode is attached to or behind the opposite ear, the recording is called contralateral.

Each of these electrode configurations yields a waveform of slightly different morphology. The ipsilateral mastoid configuration is most commonly employed. In comparison to the ipsilateral recording of the early AEP, contralateral recording shows: (1) smaller amplitudes of
waves I, III, and V; (2) larger amplitude of wave IV; (3) increased latency of waves II and V; and (4) components in the 2 to 4 msec region which are out of phase with those in the ipsilateral recording. The contralateral recording is sometimes used to help locate wave IV, as wave IV in the ipsilateral recording is smaller and sometimes indistinguishable.

In comparison to the vertex to mastoid recording of the early AEP, the vertex to earlobe recording produces a larger wave I amplitude while the vertex to neck recording produces a smaller wave I amplitude and larger wave V amplitude.

2.7.3 Stimulus

The usual stimulus for eliciting onset/transient AEP responses (the type of responses utilized in this experiment) is a click of negative polarity (i.e., a rarefaction click) and 100 msec duration. Since averaging is necessary to extract the resulting response from the background noise (see Section 2.7.4), the click is repeated, at an interval long enough to allow the response to subside before the next click is presented (otherwise, steady-state AEPs would be recorded) and with a sufficient number of repetitions to decrease the background noise to an acceptable level (see Section 2.7.4).

The morphology, latency, and amplitude of the brainstem AEP (BAEP) components are affected by the intensity,
frequency, and polarity of the click stimulus. As the stimulus intensity increases, the latency of the BAEP components decreases, as shown for wave V in Figure 2.7.3-1. The effect of stimulus intensity on the amplitude of the BAEP components has not been extensively studied, but in general, the amplitudes increase as the stimulus intensity increases, as shown in Figure 2.7.3-1 for wave V. As the stimulus frequency increases, the BAEP latencies increase as shown in Figure 2.7.3-2 for wave V and the amplitudes decrease as shown in Figure 2.7.3-2 for wave V also.

The polarity of the click stimulus affects the BAEP response. The polarity determines whether the resulting audio stimulus is a condensation stimulus or a rarefaction stimulus. For positive stimulus polarity, the headphone speaker diaphragm first displaces inward (toward the ear), then outward, forming a condensation stimulus; for negative stimulus polarity, the diaphragm first displaces outward, then inward, forming a rarefaction stimulus.

A rarefaction stimulus is normally used. In contrast to a condensation stimulus, a rarefaction stimulus produces shorter latencies for waves I, IV, and VI; larger amplitudes for waves I and IV; and a longer wave I to wave V interpeak latency. Waves III and V are not affected by the stimulus polarity.

A binaural stimulus (stimulus delivered simultaneously
Figure 2.7.3-1. Intensity effects (from ref. 38).
Figure 2.7.3-2. Frequency effects (from ref. 38).
to both ears) produces larger BAEP amplitudes than a monaural stimulus (stimulus delivered to one ear only), which is the stimulus normally employed in clinical practice.

2.7.4 Time-Locked Signal Averaging

The AEP signal is contaminated by various types of background activity, including the EEG, muscle and eye artifact, and instrument noise. The small-amplitude AEP (0.01 to 10 uV P-P) is normally indiscernible in this larger-amplitude background activity (the EEG amplitudes range from 10 to 50 uV P-P).

In order to extract the AEP from this much larger background activity, the technique of time-locked signal averaging (also called ensemble averaging) is employed. This method consists of averaging the measured responses to a number of stimulus presentations. With averaging, the amplitude of the AEP remains constant while the amplitude of the background activity decreases, since the background activity is random in relation to the stimulus.

The number of averages is determined by the amplitude of the AEP in relation to the amplitude of the background activity. The early AEPs, which have small amplitudes in comparison to the EEG, generally require 1000 to 2000 averages; the late AEPs, which have amplitudes comparable to the EEG, generally require 50 to 100 averages.

In this method, the AEP signal s(t) is modeled as a
deterministic signal with an invariable delay in relation to the stimulus, while the background activity \( n(t) \) is modeled as stationary noise (a random signal) with no correlation to the AEP. The measured signal \( r(t) \) is a random signal (due to the presence of the noise), modeled as the sum of the AEP signal \( s(t) \) and the noise signal \( n(t) \) (a statistically orthogonal decomposition):

\[
r(t) = s(t) + n(t). \tag{2.7.4-1}
\]

Averaging \( N \) epochs yields

\[
\frac{1}{N} \sum_{i=1}^{i=N} r(t) = \frac{1}{N} \sum_{i=1}^{i=N} s(t) + \frac{1}{N} \sum_{i=1}^{i=N} n(t), \tag{2.7.4-2}
\]

which can be written as

\[
\bar{r}(t) = \bar{s}(t) + \bar{n}(t). \tag{2.7.4-3}
\]

Since \( s(t) \) is assumed to be invariant, \( \bar{s}(t) = s(t) \). In addition, the mean and variance of \( n(t) \) are as follows:

mean of \( n(t) = E[n(t)] = 0 \) and

\[
\text{variance of } n(t) = \sigma_n^2, \tag{2.7.4-4}
\]

where \( \sigma \) is the variance of the EEG. After averaging, the variance is reduced by \( N \).

The signal-to-noise ratio (SNR) is defined as the ratio of signal power (which is equal to \( s(t) \)) to noise power (which is equal to the noise variance). Hence, the SNR before averaging (SNR \( b \)) and the SNR after averaging (SNR \( a \)) are given as
Thus, $\text{SNR}_b = N \times \text{SNR}_a$, that is, the improvement in SNR with averaging is proportional to the number of epochs averaged. Alternatively, $s(t)$ (which is a voltage) is enhanced with averaging by a factor of $\sqrt{N}$ over the noise, where $\sqrt{N}$ is the square root of $N$.

While background noise decreases by a factor of $\sqrt{N}$ with averaging, isolated large potentials (artifacts that usually occur only once over the averaging process, such as coughing artifacts) decrease by a factor of $N$ with averaging, and intermittent large potentials (artifacts that may occur several times over the averaging process, such as eye blink artifacts) decrease with averaging by a factor somewhere between $\sqrt{N}$ and $N$.

2.7.5 Artifact Rejection

During the AEP recording session, the background electrical activity discussed in Section 2.7.4 may be intermittently increased due to subject muscle contractions and motions such as head movement, face and scalp muscle contractions, eye opening and closing, coughing, swallowing,
etc. These motions and contractions induce high-amplitude transient noise voltages called artifacts into the electrodes; the artifact amplitudes are often greater than the highest EEG amplitudes (100 uV).

If the number of averages is not sufficiently high, the artifacts can cause distortion in the resulting averaged AEP. Indeed, if the artifact amplitude is sufficiently high, the ensuing high-gain amplification may cause the amplifier output, ADC output, or both amplifier and ADC outputs to saturate (swing to their maximum positive or negative outputs), resulting in additional distortion.

Two techniques are commonly utilized to prevent distortion of the AEP signal due to the presence of artifacts: (1) set the number of averages sufficiently high; and (2) employ an artifact rejection technique.

As shown in Section 2.7.4, averaging decreases the background noise by a factor of $\sqrt{N}$, where $N$ is the number of averages. In contrast to the $\sqrt{N}$ reduction of background noise, averaging decreases isolated large potentials by a factor of $N$, and intermittent large potentials by a factor somewhere between $\sqrt{N}$ and $N$.

The artifact rejection technique consists of checking the amplitude of each data point to see if the amplitude exceeds the saturated amplifier output or the saturated ADC output; if so, the entire epoch of data containing the bogus
data point is discarded. The entire epoch of data must be discarded rather than just the bogus data point or points because signal distortion results if the averaged AEP contains data points which are the resultant averages of different numbers of averages.

With the usual amplifier gains and ADC ranges employed in clinical practice, the artifact rejection limits typically correspond to rejecting scalp voltages with magnitudes greater than 40 μV P-P.

2.7.6 Amplifier

The AEP amplifier is an adjustable high-gain differential amplifier similar to the EEG amplifier and with similar requirements for high input impedance, high CMRR, and input protection circuitry. However, in order to amplify the 0.1 μV brainstem AEPs, which are 100-times lower in amplitude than the lowest-amplitude EEG components, to the same level as the amplified EEG, the AEP gain must be higher than the gain of the EEG amplifier. In addition, the AEP components have responses out to 3 kHz in contrast to the 100 Hz upper limit for EEG signals; hence, the AEP amplifier must have a much broader frequency response than the EEG amplifier.

2.7.7 Filters

Bandpass filters are used in the recording of AEPs. The purpose of the filters is the same as it is for EEG
recording: to attenuate noise outside the passband.
Different filter settings are used for each of the four AEP bands; these filter settings are given in Sections 2.6.2 through 2.6.4.

The filter types are similar to those of the EEG: first-order lowpass and highpass filters. As for the EEG, sharp filter rolloffs must be avoided in order to prevent the excessive phase-shifting and thus signal distortion that occurs near the cutoff frequencies.

The early AEP high-pass filter setting of 150 Hz is sometimes increased to 300 Hz to attenuate muscle artifact in the 100 Hz to 300 Hz range; this higher setting, however, alters the response morphology.
2.8 Clinical Applications of the AEP

The AEP offers the follows advantages in clinical applications: (1) it is noninvasive; (2) it is objective; and (3) because it does not require an overt behavioral response, it is useful on subjects unable or unwilling to describe their sensory experiences.

Some of the clinical applications of the AEP are as follows. Firstly, the AEP can be used to determine whether abnormalities such as lesions or tumors are present in the auditory pathway. The AEP, in fact, is a particularly sensitive indicator of the presence of acoustic tumors, and correlations have been found between the size and location of acoustic tumors and various AEP parameters.

Secondly, the AEP can be used to determine the site of any abnormalities, that is, whether the abnormalities are present in the cochlea, brainstem, or cortex.

Thirdly, the AEP can be used to detect other brainstem and cortical pathologies that affect the auditory system, such as lesions, tumors, vascular dysfunction, multiple sclerosis, and demyelination.

And lastly, the AEP can be used in lieu of standard audiometric tests to assess hearing and functional deafness. Because it does not require overt behavioral responses from

References for this section are (7,40,45,46).
the subject, the AEP is particularly useful in this application for infants, children, and uncooperative patients.
2.9 Electrogenesis of the AEP

2.9.1 General Characteristics of Sound

Sound is a longitudinal mechanical wave produced by vibrating matter, wherein the material particles transmitting the sound wave oscillate in the direction of the wave propagation. Sound can propagate in solids, liquids, or gases that are elastic.

In solids, the speed of sound is given as

\[ v = \sqrt{\frac{Y}{\rho}} \]  

(2.9.1-1)

where \( v \) is the sound velocity, \( Y \) is Young's modulus, and \( \rho \) is the density of the solid. Young's modulus is a parameter which expresses the stretching property of a solid.

In gases and liquids, the speed of sound is given as

\[ v = \sqrt{\frac{B}{\rho}} \]  

(2.9.1-2)

where \( B \) is the Bulk modulus of elasticity, which gives the change in volume of a body resulting from a change in pressure on the body.

Thus, the speed of sound in a material is a function of both the elastic properties of the material (\( Y \) or \( B \)) and the inertial properties of the material (\( \rho \)) as follows:

References for this section are (16,21,26,38).
The speed of sound is also a function of temperature, with the speed increasing as the temperature increases. In air at 0 deg C, the speed is 331.3 m/sec.

A sound wave may be considered a displacement wave or a pressure wave. As a displacement wave, a sound wave can be written as

\[ y(t) = y_m \cos(kx - \omega t), \]  

(2.9.1-5)

where \( y(t) \) is the wave displacement at time \( t \), \( y_m \) is the maximum wave displacement, \( \lambda \) is the wavelength, \( \omega \) is the angular frequency, and \( k = \frac{2\pi}{\lambda} \).

As a pressure wave, a sound wave can be written as

\[ p(t) = P \sin(kx - \omega t), \]  

(2.9.1-6)

where \( p(t) \) is the pressure at time \( t \) and \( P \) is the maximum pressure, given by

\[ P = kpv^2y_m. \]  

(2.9.1-7)

The displacement wave is 90 degrees out of phase with the pressure wave; thus, when the excess pressure of a sound wave at a point is at a maximum or minimum, the displacement from equilibrium at that point is zero, and vice versa. Condensations (or compressions) are high-pressure regions where the particles of matter are close together;
rarefactions are low-pressure regions where the particles of matter are sparse.

The intensity of a sound wave is the rate of its energy propagation through space or, more formally, the power transmitted across a unit area normal to the direction in which the wave is traveling. The power in a wave is given as

$$\text{power} = 2\pi^2 y_m^2 f^2 \rho v = 2\pi^2 p^2 f^2 \rho v,$$

(2.9.1-8)

where \( f \) is the frequency. Thus, the intensity of a sound wave is proportional to the square of the frequency and the square of the amplitude. The units of intensity will be discussed in Section 2.9.3.

On the basis of their frequencies, sound waves are classified as either infrasonic (less than 20 Hz), audible (between 20 Hz and 20 kHz), or ultrasonic (greater than 20 kHz). A vibrating system such as a guitar string or the air column in an organ pipe resonates at a certain frequency characteristic of the system and at integer multiples of the characteristic frequency. This characteristic frequency \( f_c \) is the lowest resonant frequency and is called the fundamental frequency. The integer multiples of the fundamental \( (n f, \text{ where } n \text{ is an integer}) \) are called harmonics and, together with the fundamental, form a harmonic series. The fundamental \( (n = 1) \) is the first harmonic; the first overtone \( (n = 2) \) is the second harmonic, and so on.
When two sound waves of different frequency travel in the same direction (for instance, when two guitar strings are plucked simultaneously), the waves interfere in time: at any point in space, the amplitude of the resultant wave at that point is the sum of the amplitudes of the individual waves at that point and the amplitude at that point is therefore not constant but varies with time, resulting in variations of loudness with maximums of amplitude called beats. The number of beats per second is equal to the difference of the frequencies of the individual waves.

Similarly to light waves, sound waves undergo a Doppler effect, which is an apparent shift in the observed frequency of sound waves emitted by a source depending on the relative velocity of the source and the observer. If the source or observer or both are moving toward each other, the pitch (frequency) increases; if the source or observer or both are moving away from each other, the pitch decreases. The Doppler-shifted frequency is given as

$$f_d = f \frac{v \pm v_o}{v \mp v_o},$$  \hspace{1cm} (2.9.1-9)$$

where $f_d$ is the Doppler-shifted frequency, $f$ is the frequency of sound emitted by the source, $v$ is the speed of sound in the medium, $v_o$ is the observer velocity, and $v_s$ is the source velocity. The upper signs in the numerator and denominator are for motion of the source or observer toward
2.9.2  Ear Physiology

Figure 2.9.2-1 is a diagram of the ear, which can be divided into three sections: the external ear, the middle ear, and the internal ear. The external ear consists of the external auditory meatus (or pinna) and the auditory canal. The middle ear consists of the tympanic membrane (or eardrum) and three movable bones: the malleus (or hammer), the incus (or anvil), and the stapes (or stirrup). The internal ear consists of the cochlea, the semicircular canals, and the origin of the vestibulocochlear nerve (the VIIIth nerve).

The pinna directs sound waves into the auditory canal, which then channels the waves to the tympanic membrane, a flexible membrane. Within the middle ear, the tympanic membrane connects to the malleus, the malleus connects to the incus, the incus connects to the stapes, and the stapes connects to the oval window, a flexible membrane in the cochlea. The sound waves impinging upon the tympanic membrane cause it to vibrate, and these vibrations are passed through the malleus, incus, and stapes to the oval window, causing it to vibrate.

The cochlea is a coiled structure, wider at its base than at its apex, which contains the following three tapered, parallel, fluid-filled canals: (1) the vestibular canal,
Figure 2.9.2-1. Human ear (from ref. 16).
which contains the fluid perilymph and has the oval window at its end; (2) the central canal, which contains the fluid endolymp and a structure called the Organ of Corti; and (3) the tympanic canal, which contains perilymph and a flexible membrane called the round window at its end.

The Organ of Corti runs the full length of the cochlea and consists of the basilar membrane, hair cells, fibers, and the tectorial membrane. The basilar membrane contains hair cells which connect to the auditory part of the VIIIth nerve. The tectorial membrane overhangs the basilar membrane and contains 24,000 fibers which progressively increase in length from the base to the apex of the cochlea.

The oval window vibrations cause pressure waves in the perilymph of the vestibular canal. These pressure waves cause waves in the basilar membrane of the Organ of Corti, causing the hair cells along the basilar membrane to touch the fibers of the overhanging tectorial membrane, the point along the cochlea where the contact is made depending upon the frequency of the wave. When the hair cells are touched, they generate nerve impulses, which are then transmitted via the VIIIth nerve to the auditory cortex in the temporal lobe of the cerebrum. Impulses from different hair cells stimulate slightly different areas in the auditory cortex.

The perilymph vibrations continue to the apex of the cochlea, where they reverse directions and travel along the
perilymph of the tympanic canal to the round window. The round window is not connected to any other structure, serving only to damp out the vibrations in the perilymph and thus prevent reflections of the vibrations which would result in interference and concomitant audio distortion.

The pitch (frequency) of a sound is determined by the position along the basilar membrane of the hair cells that are stimulated: high frequency sounds stimulate hair cells close to the base of the cochlea, while low frequency sounds stimulate hair cells close to the apex of the cochlea. The amplitude of a sound is determined by the strength of the vibrations striking the Organ of Corti, and is coded in the VIIIth nerve by the number of fibers carrying impulses: the louder the sound, the more the number of fibers carrying impulses. The quality of tone is determined by the overtones present, which stimulate secondary areas of the Organ of Corti.

The external and middle ear components serve to match the impedance of the outside air to the impedance of the perilymph in the vestibular canal, resulting in more efficient energy transfer.

2.9.3 Hearing

The intensity of sound waves is normally expressed as a relative amplitude in dB as either the intensity of the wave relative to the threshold intensity of human hearing or the
RMS pressure of the wave relative to the threshold pressure or some other parameter, to be discussed below. The threshold intensity, or the minimum audible intensity for the most sensitive of human ears, is $10^{-12}$ W/cm; the threshold pressure, or the RMS pressure at the threshold intensity, is 20 uPa (Pa being the Pascal unit of pressure, which is $1 N/m^2$). Thus, if relative intensities are used, the intensity of a sound wave in dB is given as

$$I_L = 10\log \frac{I}{I_0},$$

(2.9.3-1)

where $I_L$ is the intensity of the sound wave in dB, $I$ is the intensity of the sound wave in W/cm, and $I_0$ is the threshold intensity, equal to $10^{-12}$ W/cm.

Relative pressures are commonly used in audiometry. Several intensity units employing relative pressures are in use, including dB SPL, peak SPL, peak-equivalent SPL, SL, HL, peak-equivalent HL, and nHL. The units used depend upon whether the stimulus is sustained or brief and whether it is complex (such as a click) or a pure tone.

dB SPL is used to express the intensity of a sustained stimulus: it is the RMS pressure of a sound relative to the threshold pressure. peak SPL is used to express the intensity of a brief stimulus: it is the intensity of the sound at the peak of the pressure change relative to the threshold pressure. Peak-equivalent SPL is also used to
express the intensity of a brief stimulus: it is the SPL of a long-duration tone that has the same peak-to-peak amplitude as the brief stimulus being measured.

The sensitivity (the ability to hear sounds of the lowest intensity) of human hearing varies with frequency, with the ears being most sensitive in the frequency range of 2 kHz to 4 kHz. HL and peak-equivalent HL units take this frequency-dependent sensitivity into account by expressing the intensity of sustained pure tones (HL) or brief tonal stimuli (peak-equivalent HL) relative to normal thresholds at the particular sound frequency employed.

The threshold for hearing a brief stimulus varies with the duration of the stimulus. nHL units take this duration-dependent threshold into account by expressing the average threshold intensity in a group of normal young adults for the particular stimulus being measured.

SL units are useful in evaluating patients with a hearing loss, for they express the intensity relative to the particular threshold of the subject being tested.

Some common sound intensities are whisper (20 dB), normal conversation (60 dB), and pain threshold (120 dB). Figure 2.9.3-1 shows the frequency response characteristics of the human ear, demonstrating the frequency dependence of both the threshold intensity (bottom portion of graph) and the pain threshold (upper portion of graph).
Figure 2.9.3-1. Frequency response of human ear (from ref. 16).
When sound waves impinge upon the ear simultaneously, interference occurs; constructive interference results in beats, with the beat frequencies equal to the magnitudes of the differences between each pair of frequencies. The human ear can only detect beat frequencies less than 7 Hz.

The following general relationships hold between the subjective characteristics of a sound wave and its physical properties: (1) loudness (subjective) corresponds to intensity (physical); (2) pitch (subjective) corresponds to frequency (physical); and (3) quality (subjective) corresponds to the number and relative intensity of the overtones (physical).

2.9.4 Mechanism of AEP Electrogenesis

The AEPs represent the sequential firing of neurons and neural ganglia in the neural pathway from the cochlea to the brainstem (brainstem AEPs, or BAEPs) and then to the auditory association area in the cortex (middle AEPs) and then to higher cortical areas (long and late AEPs). The mechanism by which the firing of individual neurons and neural ganglia produces a potential at the scalp surface is volume conduction, which is discussed in Section 2.4.3. The remainder of this section will delineate the neural sources for some of the BAEP waves.

Figure 2.9.4-1 is a cross-section of the brainstem showing the relevant neural sources for the BAEPs. Wave I is
Figure 2.9.4-1. Cross-section of brainstem (from ref. 40).
generated by the auditory nerve fibers, possibly in the dendrites. Wave II is generated by activity in the cochlear nucleus and possibly by activity in the auditory nerve. Wave III is generated by overlapping contributions from the superior olivary complex, the trapezoid body, and the lateral lemniscii, with the amount of contribution from each of these structures unknown but possibly dependent upon the orientation of the recording electrodes. The Wave IV-V complex is probably generated in the axons and/or the nuclei of the lateral lemnisci.
2.10 Statistical Properties of the AEP Signal

As discussed in Section 2.7.4, the AEP is a signal that is assumed to recur identically with each presentation of the stimulus. Thus, if one sample function of the signal is known, all possible sample functions are known, and the AEP is therefore a deterministic signal, that is, its values can be predicted and can be described by explicit mathematical equations.

Deterministic signals can be classified as periodic, almost periodic, and transient. Periodic signals are repetitive and can be decomposed by Fourier analysis (see Section 8.1.1) into a set of harmonically-related sine waves; almost periodic signals can be decomposed by Fourier analysis into a combination of harmonically-related and non-harmonically-related sine waves; and transient signals are not repetitive and a Fourier analysis frequently yields a decomposition into sine waves of all frequencies.

The AEP under this classification system is a periodic signal. This periodic signal consists of repetitions of transient AEP responses (as classified by the field of audiology), with the period of repetition sufficiently long so that the transient AEP response completely subsides by the end of the repetition period (see Section 2.6.1).
3.0 PHARMACOKINETICS

3.1 Bioavailability and Chemical Form

For the majority of drugs to be pharmacologically active, they must be absorbed into the systemic circulation, where they can be delivered to the target organs or tissues on which they exert their intended effect (some exceptions being drugs applied topically and eye drops). The amount of drug that actually reaches the systemic circulation is affected by several factors, among them the drug formulation, the chemical form, and a possible first-pass effect.

For solid dosage forms, differences in synthesis procedures, manufacturing processes, and formulations of the same chemical entity (for example, a crystalline structure versus an amorphous structure) can result in a drug product with different dissolution and disintegration properties. These properties may, in turn, affect the amount of drug absorbed. For all dosage forms, the degree of absorption may be affected by such factors as pre-systemic metabolism, solubility, and chemical stability. The fraction of the drug which reaches the systemic circulation is symbolized by F. For injections, F is 1.

The chemical form of the drug is important, for the

References for this section are (19, 29, 52).
active drug moiety may only be a part of the total chemical form in which the drug is administered: e.g., in a dose of LiCl, only a fraction of the dose contains the active drug Li, the fraction being equal to the molecular weight of Li divided by the total molecular weight of LiCl. The factor which accounts for the chemical form is symbolized S. S is the fraction of the administered dose which is the active drug. For a drug in its parent form, S is 1.

The amount of drug which actually reaches the systemic circulation can thus be calculated as follows:

\[
\text{amount of drug reaching} = (S)(F)(\text{dose}) \quad (3.1-1)
\]

systemic circulation

The first-pass effect may also be important for drugs which are metabolized. Substances absorbed from the GI tract do not immediately enter the systemic circulation: they first pass to the liver through the portal circulation and may undergo significant metabolism before actually reaching the circulation. Thus, a portion of the active drug may be metabolized to an inactive form before it reaches the systemic circulation. This effect is called the first-pass effect and it reduces the bioavailability.

3.2 Volume of Distribution

The volume of distribution (Vd) is the total volume it would take a fluid having the same drug concentration as the plasma to contain the total amount of drug which is present
in the body. $V_d$ is defined as follows:

$$V_d = \frac{A_b}{C_p}, \quad (3.2-1)$$

where $A_b$ is the total amount of the drug in the body and $C_p$ is the plasma concentration of the drug.

$V_d$ according to the above equation would have units of volume, typically liters (L). It is common practice, however, to normalize $V_d$ to patient weight; thus, the units of $V_d$ are often reported as L / (kg of body weight).

$V_d$ may not in all cases correspond to a real volume. In fact, if the drug is present in tissues or fluids outside the plasma compartment, $V_d$ will be larger than the volume of the plasma compartment, which is typically 3 L.

$V_d$ is a function of properties of the drug which control the tendency for the drug to be in the tissues or in the plasma; these properties of the drug include its lipid vs. water solubilities and its plasma protein vs. tissue bindings. Factors which keep the drug in the plasma - such as low lipid solubility, high water solubility, increased plasma protein binding, and decreased tissue binding - reduce $V_d$; conversely, factors which keep the drug in the tissues - such as high lipid solubility, low water solubility, decreased plasma protein binding, and increased tissue binding - increase $V_d$. 
3.3 Clearance

Clearance (CL) is a parameter which accounts for drug loss from the body. If a drug is being removed from a volume \( V \) where its instantaneous concentration is \( C \) and its rate of removal is \( \frac{dx}{dt} \), where \( x \) is the amount of drug in the volume \( V \), then CL is defined as

\[
CL = \frac{dx/dt}{C}.
\]  

(3.3-1)

Thus, CL is the rate of removal of the drug per unit concentration.

Alternatively, if a volume \( V_b \) of plasma is completely cleared of a drug in a time interval \( \Delta t \), then CL is also given by

\[
CL = \frac{V_b}{\Delta t}.
\]  

(3.3-2)

Thus, CL represents the volume of plasma from which the drug is completely removed per unit time.

For the simplest of systems (the one compartment model), CL is given by

\[
CL = k \frac{V}{d},
\]  

(3.3-3)

where CL is the total body clearance, \( k \) is the elimination rate constant (\( \text{hr}^{-1} \)), and \( V \) is the volume of distribution (L/kg). From this equation, it can be seen that the units of CL are L/kg/hr, i.e., volume / patient weight / unit time.

Since at steady-state, the amount of drug eliminated
from the body over a given time interval equals the amount administered over that same interval, CL can be considered the proportionality constant that makes the average steady-state plasma level of a drug equal to its rate of administration:

\[ R = CL \frac{C_{ss}}{A}, \]  

(3.3-4)

where \( R \) is the rate of drug administration and \( C_{ss} \) is the average steady-state drug concentration. From this equation, it might appear that CL indicates the rate of drug removal; however, the rate of drug removal depends on both the plasma concentration of the drug and the clearance, a fact which can be seen by writing the equation for \( R \) for an oral dosing regimen:

\[ R_a = \frac{SF \text{ dose}}{\tau}, \]  

(3.3-5)

where \( \tau \) is the dosing interval. Setting Equations 3.3-4 and 3.3-5 equal yields

\[ CL = \frac{SF \text{ dose}}{C_{ss} \tau}. \]  

(3.3-6)

Drug clearance occurs principally by: (1) renal clearance (CL\(_r\)), which is excretion of unmetabolized drugs (usually water-soluble drugs) through the kidneys; and (2) metabolic clearance (CL\(_m\)), which is clearance by the metabolism of drugs, often principally in the liver (fat-soluble drugs are often metabolized to water-soluble drugs.
for excretion by the kidneys). These two routes of elimination and other routes (whose clearances are symbolized by CL) are assumed to be independent; thus, they sum to produce the total body clearance (CL):

\[
CL = CL_m + CL_r + CL_o
\]

(3.3-7)

\( CL \) may be proportional to body surface area (BSA), cardiac output, plasma protein binding (PPB), and organ blood flow. The relationship between CL and BSA is most often modeled as a linear relationship for drugs whose CL is a function of BSA.

If cardiac output decreases, then blood flow to the liver and kidneys decreases; since blood flow to either the liver or kidneys may limit the rate at which these organs can perform their clearance functions and total CL is a function of both renal and metabolic clearance, then CL decreases also. Hence, CL may be a function of cardiac output.

If PPB decreases for a drug that is highly protein bound, then the fraction of free drug in the plasma increases; however, the increased amount of free drug in the plasma is distributed to the tissues, resulting in a decreased average steady-state plasma concentration. From Equation 3.3-6, the calculated CL increases. The increase in the calculated CL is in general directly proportional to the change in \( \alpha \), the fraction of free drug. The parameter \( \alpha \) is
given by

\[ \alpha = \frac{C_{\text{free}}}{C_{\text{total}}} \]  

(3.3-8)

where \( C_{\text{free}} \) is the plasma concentration of unbound drug, and \( C_{\text{total}} \) is the plasma concentration of bound drug.

However, instead of being proportional to \( PPB \) (change in \( \alpha \)), CL may be proportional to blood flow to an organ which metabolizes or excretes the drug very efficiently. The parameter on which CL is dependent can be determined by comparing \( \alpha \) with a quantity called the extraction ratio (ER). The ER is the fraction of drug passing through an organ which is cleared after a single pass through the organ and is given by

\[ \text{ER} = \frac{\text{blood or plasma drug clearance}}{\text{blood or plasma flow to organ}} \]  

(3.3-10)

If ER is less than \( \alpha \), then CL is dependent upon \( PPB \) (change in \( \alpha \)); if ER is greater than \( \alpha \), then CL is dependent upon blood flow to that organ.

3.4 First-Order Kinetics

For many drugs (including lithium), the rate of drug elimination from the body at any instant of time is directly proportional to the amount of drug in the body at that time.
This relation can be expressed mathematically as

\[ \frac{dx(t)}{dt} = kx(t), \quad (3.4-1) \]

where \( x(t) \) is the amount of drug in the body at time \( t \) and \( k \) is a proportionality constant known as the elimination rate constant (to be discussed in Section 3.5).

Equation 3.4-1 is a first-order differential equation and is therefore said to describe first-order elimination kinetics. The solution of this equation is given as

\[ x(t) = x(0)e^{-kt}, \quad (3.4-2) \]

where \( x(0) \) is the amount of drug in the body at time \( t=0 \).

Figure 3.4-1 is a graph of \( x(t) \) versus time showing the exponential decay of \( x(t) \).

It is common practice to graph the logarithm of Equation 3.4-2 in order to obtain a straight-line decay for convenience in certain pharmacokinetic calculations; taking the natural logarithm of this equation yields

\[ \ln x(t) = \ln x(0) - kt. \quad (3.4-3) \]

Figure 3.4-1 presents a graph of Equation 3.4-3.

An expression similar to Equation 3.4-2 for plasma concentration \( C_p(t) \) instead of amount \( x(t) \) can be derived from the relation \( x(t) = C_p(t) V \) and is given as

\[ C_p(t) = C_p(0)e^{-kt}. \quad (3.4-4) \]
Figure 3.4-1. Decay of $x(t)$ and $\ln x(t)$ (from ref. 52).
3.5 Elimination Rate Constant

The constant $k$ in Equations 3.4-1 through 3.4-2 has units of inverse time and is known as the elimination rate constant. $k$ determines the rate of decay of the plasma concentration for drugs eliminated by first-order kinetics (see Figure 3.4-1 and Equation 3.4-1); in fact, $k$ is the slope of the $\ln C$ versus time plot:

$$
\frac{\ln \left( \frac{C_{p1}}{C_{p2}} \right)}{\Delta t} = k,
$$

(3.5-1)

where $C_{p1}$ and $C_{p2}$ are two different concentrations and $\Delta t$ is the difference in time between them.

Physiologically, $k$ represents the fraction of the total amount of drug in the body removed per unit of time and is defined in terms of the volume of distribution $V_d$ and the clearance $CL$ as

$$
k = \frac{CL}{V_d},
$$

(3.5-2)

3.6 Elimination Half-Life

The elimination half-life (EHL) is the time required for the total amount of drug in the body to decrease by one-half; it is also the time required for the plasma concentration to decrease by one-half. If $x$ is the initial amount of drug in the body, after one EHL, the amount in the body will be $\frac{1}{2} x$; after two EHLs, it will be $\frac{1}{2} \left( \frac{1}{2} x \right) = \frac{1}{4} x$;
after n EHLs, it will be $2^n$.

The EHL is useful for predicting the temporal variation of the plasma drug concentration and for estimating the time to reach steady-state (see Section 3.7) plasma drug levels for drugs that follow first-order elimination kinetics. The EHL is related to the elimination rate constant as follows:

$$t_{1/2} = \frac{\ln(2)}{k},$$  

(3.6-1)

where $t_{1/2}$ is the elimination half-life and $k$ is the elimination rate constant.

3.7 Steady State

Steady-state (SS) is a condition in which the amount of drug entering the body in a given time period equals the amount leaving the body (excreted) in the same time period; thus, at SS, the plasma drug concentration is constant (plateaus).

For drugs which follow first-order elimination kinetics (see Section 3.4), SS is considered to have been reached after five elimination half-lives, because after this amount of time, the plasma concentration has reached 99.3% of its final value, shown as follows:

$$C(t) = C_{ss} (1 - e^{-\frac{t}{t_{1/2}}})$$

and

$$C(t) = C_{ss} (1 - e^{-\frac{t}{5t_{1/2}}})$$  

(3.7-1)
\[ C(t = 5\tau) = C(t) \left(1 - e^{-\frac{\tau}{5\tau}}\right) = 0.993 C_{ss} \quad (3.7-2) \]

3.8 Two-Compartment Model with an Oral Dosing Regimen

In a two-compartment model (2CM), the body is considered to be composed of two compartments: a central compartment (CC) with volume \( V \) (for initial volume) and a peripheral compartment (PC) with volume \( V \) (for tissue volume). Three different 2CMs exist. Figure 3.8-1 is a block diagram of one of the most common 2CMs, in which elimination occurs out of the CC. In the other two 2CMs, elimination occurs either out of the PC or out of both. The following discussion will center on the 2CM presented in Figure 3.8-1.

The CC is rapidly equilibrating (often modeled as instantaneous) and consists of the blood and those organs with high blood flow; drugs enter into and are eliminated from the body through the CC. The PC requires a longer time for equilibration and often consists of the organs with low blood flow and the tissues. \( V_t \), the volume of the PC, is usually greater than \( V_i \), the volume of the CC. If the drug concentrations in the central and peripheral compartments are equal at steady-state, then \( V_d \), the volume of distribution (see Section 3.2), is given by

\[ V = V_i + V_t \quad (3.8-1) \]
Figure 3.8-1. Block diagram of two-compartment model (from ref. 52).
Figure 3.8-2 shows the plasma concentration time profile for a drug described by a 2CM after a single oral dose of the drug. This curve represents the time profile of the CC drug concentration (because the CC contains the plasma) and is characterized by an absorption phase and a biphasic decay phase consisting of a distribution phase and an elimination phase. Absorption, distribution, and elimination are characterized by rate constants as shown in Figure 3.8-3.

In the absorption phase, the drug is absorbed from the GI tract into the systemic circulation and the CC concentration increases. In the distribution phase, the drug passes from the CC into the PC, elimination occurs from the CC out of the body, and the CC concentration starts to decrease. In the elimination phase, the drug concentrations in the CC and PC are in equilibrium and the drug continues to be eliminated from the CC out of the body. The CC concentration declines at a slower rate than in the distribution phase. \( \theta \), the slope of the concentration versus time curve during the distribution phase, is usually much greater than \( B \), the slope of the concentration versus time curve during the elimination phase; hence, the elimination rate constant \( k \) is approximated by \( B \) and the half-life is determined from Equation 3.6-1 with \( k = B \).

The equation for the CC drug concentration as a
Figure 3.8-2. C(t) for single oral dose.
Figure 3.8-3. Definition of two-compartment model rate constants (from ref. 19).
function of time for oral dosing with first-order absorption is found by first writing the first-order differential equations describing the passage of drug into and out of the CC, taking the Laplace transform of the resulting first-order differential equation, simplifying the resulting algebraic equation, and then taking the inverse Laplace transform of the simplified equation, yielding the following triexponential equation:

$$C(t) = A e^{-kt} + B e^{-\lambda_1 t} + C e^{-\lambda_2 t}, \quad (3.8-2)$$

where $C(t)$ is the CC drug concentration,

$$A = \frac{k_a F x_0}{V_c} \frac{(E_2 - k_a)}{(\lambda_1 - k_a) (\lambda_2 - k_a)}, \quad (3.8-3)$$

$$B = \frac{k_a F x_0}{V_0} \frac{(E_2 - \lambda_1)}{(k_a - \lambda_1) (\lambda_2 - \lambda_1)}, \quad (3.8-4)$$

$$C = \frac{k_a F x_0}{V_0} \frac{(E_2 - \lambda_2)}{(k_a - \lambda_2) (\lambda_1 - \lambda_2)}, \quad (3.8-5)$$

$$E = k_{10} + k_{12}, \quad (3.8-6)$$

$$E = k_{21}, \quad (3.8-7)$$

$$\lambda = E + E - \lambda, \quad (3.8-8)$$

$$\lambda_2 = \frac{(E_1 + E_2) \pm \sqrt{(E_1 + E_2)^2 - 4k_{12}k_{21} - E_1 E_2}}{2}, \quad (3.8-9)$$
k is the absorption rate constant, $k_{12}$ is the rate constant for distribution from the CC to the PC, $k_{21}$ is the rate constant for distribution from the PC to the CC, and $k_{10}$ is the rate constant for elimination from the CC.

For a multiple oral dosing regimen with a dosing (time) interval of $\tau$, the plasma concentration depends on the relation of $\tau$ to $t_{1/2}$. For $\tau \gg t_{1/2}$, little drug, if any, is present in the plasma from the previous dose and thus the plasma concentration depends primarily on $V_d$, that is, no accumulation of drug in the body occurs.

For $\tau \ll t_{1/2}$, some drug from the previous dose is still present in the plasma and accumulation occurs (see Figure 3.8-4). The plasma concentration increases, but so does the rate of elimination, and thus the plasma concentration plateaus and a steady-state condition is reached. The plasma concentration depends primarily on $\text{Cl}$ and fluctuates between a minimum concentration $C_{ss(\text{min})}$ and a maximum concentration $C_{ss(\text{max})}$ over $\tau$ with an average concentration of $C_{ss(\text{ave})}$ (see Figure 3.8-5), which is given by

$$C_{ss(\text{ave})} = \frac{FD}{\beta V_d \tau}. \quad (3.8-10)$$

$V$ is a parameter relating the plasma concentration to the amount of drug in the body during the elimination phase and is given by
Figure 3.8-4. Accumulation.
Figure 3.8-5. Fluctuation over the dosing interval (from ref. 52).
where $AUC_\infty$ is the total area under the concentration versus time curve.
4.0 LITHIUM

4.1 Clinical Uses

Since the discovery of its antimanic effect in humans by Cade in 1949, lithium has been widely used in psychiatry in two principal applications: (1) as an antimanic for the short- and long-term treatment of mania, hypomania, and the manic phase of manic-depressive illness (a bipolar affective disorder); and (2) as a relapse-repressive prophylactic for the long-term treatment of both phases (mania and depression) of manic-depressive illness.

Because they have a faster onset than lithium (lithium typically takes several days), neuroleptic drugs are frequently administered for the initial control of an acute manic attack. However, lithium is superior to neuroleptics for long-term treatment of mania, since it normalizes the patient rather than exert a pharmacologic effect upon the patient as neuroleptics do.

As a prophylactic, lithium reduces the frequency, duration, and intensity of both the manic phase and the depressive phase of manic-depressive illness. While lithium is ineffective in the treatment of non-recurring depression, it is as effective an antidepressant as imipramine in the treatment of recurrent endogenous (i.e., chemically-related)

References for this section are (1,2,3,20,37,42).
depression and it enhances the action of both types of standard antidepressants (the tricyclics and the monoamine oxidase inhibitors).

4.2 Chemical Properties and Dosage Forms

Lithium is a member of the alkali metal group. In compounds, lithium exhibits only one oxidation state (+1) and has a low ionization energy. The diameter of the lithium atom is 1.55 Angstroms, while that of the lithium ion is 0.60 Angstroms.

Lithium is only available commercially in solid oral form. Solid oral forms are preferred over other forms (solutions, parenteral injections, and suppositories) for the following reasons: (1) oral absorption is essentially complete (see Section 4.6); (2) parenteral injections produce high and potentially toxic serum levels immediately following the injections; (3) the onset of lithium's therapeutic action is slow (typically several days; see Section 4.5) which precludes the use of lithium for acute conditions and therefore the fast absorption afforded by solutions and parenteral injections is not needed; and (3) lithium has a local irritating effect and therefore cannot be used in suppositories.

The oral forms available are either conventional or sustained-release tablets (SRTs). SRTs prolong the absorption time (see Section 4.6) and therefore reduce the
serum concentration peaks and troughs associated with an oral dosing regimen (see Figure 4.2-1). Because of the reduced serum concentration peaks and troughs and the prolonged absorption time, SRTs may be preferred over conventional tablets, especially when dosing is frequent. The reduced peaks and troughs reduce the likelihood that the serum concentration will rise above the therapeutic range (see Section 4.3) maximum where toxicity may result or fall below the therapeutic range minimum where no therapeutic effect exists. The prolonged absorption time provides three main advantages: (1) a slow rise in serum lithium concentration, thus preventing some of the side effects (see Section 4.3) associated with lithium therapy, the occurrence of which has been correlated with rapid rises in serum lithium concentration; (2) a lower concentration of lithium in the gastrointestinal (GI) tract, thus reducing the GI side effects caused by the local irritating effect of lithium; (3) a less frequent (but higher) dose can be given, thus benefitting those patients on long-term therapy who have trouble maintaining a frequent dosing regimen and sometimes forget to take a dose.

A number of lithium salts have been used, including the following: chloride, citrate, sulphate, monoglutamate, acetate, and carbonate. Of these salts, the carbonate has been the most popular, because the carbonate anion has the
Figure 4.2-1. Reduction of peaks and troughs with sustained-release tablets (from ref. 2).
lowest equivalent weight of the anions used, yielding a salt with the highest ratio of lithium ion (Li$^+$) per unit weight and thus the smallest capsule or tablet for a given amount of Li$^+$.

In the United States, lithium carbonate (chemical formula LiCO$_3$) is the only lithium salt marketed. Each tablet or capsule contains the standard unit dosage of 300 milligrams (mg) of LiCO$_3$. Since lithium is monovalent, 1 millequivalent (mEq) equals 1 millimole (mmol). 1 mmol of Li$^+$ is 6.9 mg of Li$^+$ and is contained in 1 mmol of LiCO$_3$, which is 37 mg of LiCO$_3$; thus, a 300-mg LiCO$_3$ tablet contains $300 / 37 = 8.1$ mEq of Li$^+$ (or $6.9 \times 8.1 = 56$ g of Li$^+$).

Approximately 10% to 15% of a dose administered in tablet form is lost in the stool, while the remaining 85% to 90% of the dose is recovered in the urine, the kidneys being the major route of lithium elimination (see Section 4.8); thus, the bioavailability of lithium tablets is on the order of 85% to 90%.

### 4.3 Therapeutic Range and Toxicity

Lithium has a narrow therapeutic range of serum concentration levels: below the lower limit, or threshold, of the range, lithium produces little, if any, effect; above the upper limit of the range, toxicity may develop.

The therapeutic range is generally considered to be
0.6 to 1.5 mEq/L, with the range 0.8 to 1.5 mEq/L being employed for short-term anti-manic therapy and the range 0.6 to 1.2 mEq/L being employed for long-term relapse-repressive therapy. A level of 1.2 mEq/L has been associated with a favorable effect in nearly all patients; this level is too high for an initial level, however, as side effects are associated with the use of lithium and the side effects produced by an initial level of 1.2 mEq/L are similar to some of the side effects produced at the higher toxic levels. Hence, a lower initial level of 0.8 to 1.0 mEq/L is employed, with a gradual increase to higher levels, if necessary.

The side effects associated with the use of lithium have been divided into three groups (Greene, 1975) as shown in Table 4.3-1. Group I side effects occur initially but usually subside. Group II side effects are persistent and, though harmless, may be annoying to the patient, in which case they may be alleviated by reducing the dosage. Group III side effects are serious; they are indicators of impending toxicity and require that the dosage be reduced or the treatment discontinued.

At serum levels of 1.5 to 2.0 mEq/L, toxicity develops. At the toxic stage, some cardiovascular impairment exists but the principal effect is on the central nervous system. In addition, a vicious cycle develops because once a critical serum level is reached, nephrotoxicity develops,
### Table 4.3-1. Side effects of lithium (from ref. 20).

<table>
<thead>
<tr>
<th>GROUP 1</th>
<th>GROUP 2</th>
<th>GROUP 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial, transient, harmless</td>
<td>Persistent, harmless</td>
<td>Prodromas of intoxication</td>
</tr>
<tr>
<td>Fine tremor of hands</td>
<td>Fine tremor of hands</td>
<td>Course tremor of hands</td>
</tr>
<tr>
<td>Polyuria</td>
<td>Polyuria</td>
<td>Vomiting</td>
</tr>
<tr>
<td>Polydipsia</td>
<td>Polydipsia</td>
<td>Diarrhea</td>
</tr>
<tr>
<td>Nausea</td>
<td>Weight gain</td>
<td>Dystarthria</td>
</tr>
<tr>
<td>Loose stools</td>
<td>Edema</td>
<td>Lethargy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vertigo</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tinnitus</td>
</tr>
</tbody>
</table>
the renal elimination of lithium is reduced, and the serum level rises even higher. After a few days, poisoning occurs and death may ensue as a result of a combination of effects but usually due to pulmonary complications such as pneumonia and respiratory failure.

No antidote exists for lithium poisoning. The only cure is cessation of lithium intake and supportive therapy. A few days after lithium intake cessates and the serum lithium levels are reducing, a transient increase in serum levels called the rebound phenomena occurs due to the mobilization of the extravascular stores of lithium.

4.4 Serum Level Monitoring and Assays

Successful lithium therapy involves the maintenance of the serum lithium concentration within narrow bounds (see Section 4.3). Because the serum lithium concentration determined during the post-absorptive phase at a standard interval after the last intake of lithium varies less than the serum lithium concentration determined during the absorptive phase, a standard interval has been set for the time of the blood samples for serum lithium determination. This interval had to be set greater than ten hours, because the absorption phase lasts from three to six hours for standard preparations and from eight to ten hours for sustained release preparations. This interval has been chosen to be twelve hours and is called the twelve-hour
standard serum lithium determination, abbreviated 12h-stSLi. All serum lithium concentrations in the recent pharmaceutical literature are assumed to have been determined at the 12h-stSLi. The serum lithium concentration assay is performed by either flame photometry or atomic absorption spectrophotometry, both of which are rapid and accurate.

4.5 Dosing

The dose required to maintain a specific serum lithium concentration varies greatly between individuals, ranging anywhere from 12 to 80 mEq/L/day of Li. The reason for this variation is the variation in renal lithium clearance (RLC) between individuals. At steady-state, the rate of lithium administration equals the rate of elimination. Since lithium is eliminated almost exclusively through the kidneys, the RLC determines the maintenance dosage, and since the RLC varies between individuals, the maintenance dose does also.

The use of a single daily dose is usually avoided, for two reasons: (1) a relation between therapeutic response and the 12h-stSLi has not been established for a single daily dose; and (2) the peak serum level reached may expose the patient's organs (especially the distal part of the nephron) to unacceptably high lithium concentrations.

The dosing regimen depends on whether the therapy is short-term (anti-manic) or long-term (prophylactic). For
short-term therapy, it is desirable to reach a therapeutic range of 0.8 to 1.6 mEq/L as rapidly as possible; however, a large initial dose cannot be given, because the resulting steep serum concentration rise has been correlated with side effects. Thus, the usual dosing regimen consists of starting with a 50 mEq/day priming dose of Li divided into three or four doses per day, then taking a 12h-stSLi after five days and adjusting the dosage accordingly. The manic episode usually subsides after six to ten days.

For long-term therapy, a range of 0.6 to 1.2 mEq/L is optimal. The patient is usually started on 10 to 15 mmol/day of Li divided into two doses per day. After one week, a 12h-stSLi is taken and the dosage is adjusted accordingly. Thereafter, a 12h-stSLi check is performed every third month.

4.6 Absorption

This discussion will center on absorption from the GI tract, since lithium is administered orally. The lithium ion is small and therefore well absorbed along the entire GI tract. The course and completeness of the absorption are determined by the disintegration and dissolution properties of the lithium tablet.

The disintegration and dissolution of conventional tablets are highly dependent upon the varying chemical environment in the GI lumen; as shown in Figure 4.6-1, a high peak concentration follows intake of the tablets. With
Figure 4.6-1. Absorption of tablets (from ref. 2).
sustained-release tablets, the absorption curve is more uniform and the high peak concentration following tablet intake is avoided (see Figure 4.6-1).

Lithium carbonate is absorbed almost completely from the GI tract within three to six hours for conventional tablets and within eight to ten hours for sustained-release tablets. For conventional tablets, peak serum levels are reached after approximately three hours.

4.7 Distribution

Compared to its fairly rapid absorption, lithium's distribution occurs at a somewhat lower rate. The distribution of a dose is essentially complete after six to ten hours and reaches equilibrium (steady-state) after approximately five days.

Lithium initially distributes into a central distribution space which comprises 24% to 38% of the body weight. The final distribution space, i.e., the apparent volume of distribution (Vd; see Section 4.7), comprises 50% to 100% of the body weight. Lithium's Vd varies markedly between individuals and varies with age: 120% of the body weight in young people and 90% of the body weight in the elderly (hence, geriatric patients need smaller doses than do young people).

Lithium does not bind to plasma proteins but distributes throughout the body water. As shown in Table 4.3-2, lithium
<table>
<thead>
<tr>
<th>Tissue</th>
<th>mmol/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain, grey matter</td>
<td>0.72</td>
</tr>
<tr>
<td>Brain, white matter</td>
<td>0.65</td>
</tr>
<tr>
<td>Cerebellum, grey matter</td>
<td>0.35</td>
</tr>
<tr>
<td>Brain stem (mesencephalon)</td>
<td>0.51</td>
</tr>
<tr>
<td>Liver</td>
<td>0.22</td>
</tr>
<tr>
<td>Spleen</td>
<td>0.21</td>
</tr>
<tr>
<td>Kidney</td>
<td>0.60</td>
</tr>
<tr>
<td>Lung</td>
<td>0.51</td>
</tr>
<tr>
<td>Pancreas</td>
<td>0.38</td>
</tr>
<tr>
<td>Muscle</td>
<td>0.39</td>
</tr>
<tr>
<td>Heart</td>
<td>0.42</td>
</tr>
<tr>
<td>Thyroid gland</td>
<td>0.83</td>
</tr>
<tr>
<td>Bone: iliac crest (compact)</td>
<td>0.77</td>
</tr>
<tr>
<td>Vertebral body (spongy)</td>
<td>0.59</td>
</tr>
</tbody>
</table>

Table 4.3-2. Tissue distribution of lithium (from ref. 2).
distributes unevenly throughout the body: at less than one-half the serum lithium concentration in the erythrocytes, cerebrospinal fluid, and liver; at the serum lithium concentration in the heart, lung, kidney, and muscle; and at greater than one-half the serum lithium concentration in the thyroid gland, bone, and brain.

4.8 Elimination

Lithium is not metabolized. Elimination occurs predominantly through excretion by the kidneys, with a small amount (approximately 10% to 15%) lost through sweat and feces. In the kidney, lithium passes freely through the glomerular membrane. The renal lithium clearance (RLC) varies from 8 to 40 mL/min, with an average of 25 mL/min in a healthy adult with a normal diet and normal renal function. Since the glomerular filtration rate (GFR) is 120 mL/min, the RLC is approximately 20% of the GFR; therefore, approximately 80% of the lithium filtered through the glomeruli is reabsorbed by the renal tubules. This absorption occurs predominantly in the proximal convoluted tubules (PCTs), where lithium is absorbed in the same ratio as water and sodium (due to their similar size and valence, lithium and sodium are handled similarly in the PCTs).

The RLC has a circadian rhythm, with higher values during the daytime. The RLC is reduced when the kidneys are impaired or under conditions of dehydration. In dehydration,
the sodium balance is negative, and the kidney attempts to save sodium by increasing reabsorption of sodium in the PCTs. Since lithium and sodium are handled similarly in the PCTs, the reabsorption of lithium is increased, and the RLC is reduced.

For a patient who has reached steady-state, elimination is governed by first-order kinetics (see Section 3.4) and can be described by a two-compartment model. The serum elimination half-life (SEHL) ranges from 14 to 33 hours in normal and healthy individuals, with an average of 24 hours. The SEHL has a circadian variation and also varies with age: the night-to-day ratio is 2.5, and the average SEHL in adolescents is 18 hours compared to an average SEHL of 36 hours in the elderly.

The body contains extravascular stores of lithium, particularly in muscle and bone, which are never mobilized during steady-state. If intake is totally stopped, a more complex model is necessary to describe the elimination kinetics due to the mobilization of these extravascular stores. These extravascular stores create a 'whole-body EHL' (Amdisen, 1977) which is greater than the SEHL and also cause a phenomenon known as the rebound effect during hemodialysis, where after an initially successful reduction in serum lithium levels a paradoxical rise in the levels occurs due to the mobilization of the extravascular stores.
5.0 REVIEW OF APPLICABLE RESEARCH TO DATE

5.1 Effects of Lithium on the EEG

A number of investigators have studied the effects of lithium on the EEG (14,15,24,25,27,32,39,50,53). Many of the studies which appeared in the 1960s and 1970s were based on visual analysis of the EEG records. A summary of the findings from these studies of lithium-induced EEG changes is as follows: (1) a decrease of alpha activity, with marked irregularity and disorganization; (2) an increase of slow activity with increased amplitudes; (3) a slight increase of fast beta activity; (4) a marked increase of epileptic potentials, with a frequent finding of high-amplitude slow and sharp waves and spike and wave complexes; and (5) an exaggeration of focal abnormalities. Property (4) correlates with lithium's known epileptogenic property, that is, its tendency to produce epileptiform spikes and waves in the EEG.

All of the studies to date have failed to establish a correlation between the degree of EEG changes and either the serum lithium level or the presence of a therapeutic effect. In none of these studies was the spectral edge used as an index of the EEG change.

However, Stanski et al. (44) have demonstrated a relationship between serum thiopental concentration and spectral edge and shown that the relationship can be
characterized by an inhibitory sigmoid $E_{\text{max}}$ pharmacodynamic model. The spectral edge is now routinely used in the operating room as an index of anesthetic depth.

5.2 Effects of Lithium on the AEP

In September of 1965, Gartside et al. (17) published results on a study of the modification of the somatosensory evoked response (SEP) by lithium. In this study, the authors found that lithium modifies the cortical recovery cycle in normal individuals. The recovery cycle is found by presenting to the subject a paired stimulus consisting of a conditioning stimulus followed by a test stimulus. The interstimulus interval (i.e., the time between the conditioning stimulus and the test stimulus) is varied; for each interval, a measurement is made of the amplitude of the first negative-to-positive wave following the conditioning stimulus and following the test stimulus. The ratio of the amplitude of the conditioning stimulus response to the test stimulus response is computed and plotted as a function of the interstimulus interval (ISI), resulting in the recovery cycle.

The response to the conditioning stimulus contains overlapping components from the response to the test stimulus; thus, the conditioning stimulus response must be removed from the test stimulus response. This removal is accomplished by presenting to the subject an alternating...
stimulus paradigm consisting of a single stimulus conditioning stimulus), then a double stimulus (conditioning stimulus followed by a test stimulus), then a single stimulus, then a double stimulus, etc. The response to the test stimulus is found by subtracting out the response to the single stimulus immediately preceding the double stimulus.

Normal individuals have a peak at an ISI of 20 to 25 msec where the ratio exceeds a value of one. Depressed patients do not have this peak and the ratio remains less than one until the ISI exceeds 500 msec; if clinical improvement occurs in the depression, the peak at 20 to 25 msec appears.

The authors measured pre-lithium (baseline), lithium, and post-lithium recovery functions. The pre-drug functions showed the recovery ratio was greater than or equal to one for an ISI of 15 to 25 msec. Under lithium, the ratios were less than one for this ISI. Two to four weeks after cessation of lithium, the ratio for this ISI returned to its pre-lithium lithium values.

Several researchers have examined the effects of lithium on AEPs in the time domain (22,43,47). Small et al. (43) have found small but significant changes in the amplitude and latency of wave V of the BAEPs under lithium. Straumanis et al. (47) have found amplitude increases of the
P30 and P50 middle-latency components in depressive patients during lithium treatment. Hegerl et al. (22) have found the following changes in some of the late-latency components: a pronounced increase of the P1 amplitude, a less pronounced but significant increase of the N1 amplitude, an increase of the P1 latency.

None of these experiments has correlated the AEP changes with serum lithium levels. In addition, no research to date has examined the effects of lithium on AEPs in the frequency domain or attempted to utilize the spectral edge as an index of these effects.
6.0 DESCRIPTION OF EXPERIMENT

6.1 Overview

The clinical portion of this project consisted of two different phases: Phase 1 and Phase 2. In Phase 1, subjects were dosed on lithium to three different steady-state levels while their serum lithium levels and brain waves were recorded. The goals of Phase 1 were to determine if:

1. lithium alters brain waves;
2. the amount of alteration (if any) can be related to the dose; and
3. tolerance to lithium develops and can be determined from the brain waves.

The highest serum lithium levels attained during Phase 1 were at the lower end of the therapeutic range (0.6 mEq/L) instead of at the desired midpoint of the range (0.9 mEq/L). In addition, the precision of the lithium assays, which were performed by a commercial laboratory, was insufficient for distinguishing different low concentrations (< 0.1 mEq/L). Therefore, Phase 2 was undertaken. In Phase 2, subjects were dosed on lithium to one steady-state level while their serum lithium levels and brain waves were recorded. The subjects were given a higher dose (1,200 mg/day) than the highest dose given during Phase 1 (900 mg/day); several baseline (before lithium) brain waves were recorded; and several steady-state brain waves were recorded. The goals of Phase 2 were goals (1) and (3) of Phase 1. Following is a detailed description of the data.
acquisition hardware and software and the protocols and procedures for Phase 1 and Phase 2.
6.2 Hardware Configuration

6.2.1 Introduction

This section will describe the hardware configuration for acquiring and recording the EEG and the AEP. More detailed descriptions of some of the system components will be presented later; in particular, the electrodes, audio click generator, and impedance meter will be discussed further in Sections 7.1 through 7.3.

6.2.2 Overview

Figure 6.2.2-1 is a diagram of the experimental setup. Three electrodes attached to the subject's scalp picked up the brain wave signal (BWS), which was either an EEG or an AEP. The electrodes connected via a shielded cable to the input of a bioelectric amplifier (BA). The BWS was amplified and filtered by the BA and then fed to an analog-to-digital converter (ADC), which was a peripheral component of a micro-computer. The ADC output was fed to one of the digital input ports of the computer, which controlled both the acquisition of data from the ADC and the production of the AEP auditory stimulus.

The AEP auditory stimulus was produced by the click circuit (CC; see Section 7.2), a custom-designed circuit which produced a train of alternating single- and double-click pulses synchronized to the computer system clock. These pulses were fed to one earpiece of a pair of
Figure 6.2.2-1. Experimental setup.
headphones mounted on the study subject's head.

6.2.3 Electrodes

Three silver-plated recessed-cup electrodes were utilized, each of which consisted of a thin, high-flexibility, two-feet-long wire bonded to the electrode at one end and a small pin connector at the other end.

The EEG and the AEP were recorded with the same electrode montage: one electrode was mounted on the vertex, one on the mastoid, and one on the forehead; the procedure for mounting the electrodes is described in Section 6.6. After the electrodes were mounted, the integrity of their connections to the skin was assessed utilizing an impedance meter (see Section 6.2.9 for a description of the procedure and the meter).

A shielded cable with a square, quick-disconnect connector for connection to the BA and alligator clips for connection to the electrode assembly pin connectors connected the electrodes to the BA input. The electrode connections to the BA input were as follows: vertex (Cz) electrode to BA positive input; mastoid electrode to BA negative input; and forehead electrode to BA ground, or reference, input.

The electrode connections to the BA were such that the differential voltage between the vertex (positive electrode) and the mastoid (negative electrode) with reference to the
forehead (ground or reference electrode) was amplified. Thus, according to the International 10-20 System (see Section 2.2.2), this montage was a reference (monopolar) montage.

In order to reduce their susceptibility to noise and motion artifact (see Section 7.1.5), the electrodes were chlorided: once at the beginning of Phase 1 and once at the beginning of Phase 2. Appendix A outlines the electrode chloriding procedure.

6.2.4 Amplifier

The BA was a Hewlett-Packard 8811A Bioelectric Amplifier which was connected into the recording system as follows: (1) the input was from the patient electrode cable; and (2) the output was connected to a coaxial tee, one side of which was fed via a coaxial cable to the input of an oscilloscope used for monitoring purposes, the other side of which was connected via a coaxial cable to the ADC channel 0 input on an external interface box mounted on the computer.

The BA was used for two main purposes: (1) to bandpass filter the BWS; and (2) to amplify the BWS. The bandpass filters in the BA had simple first-order lowpass and highpass rolloffs, with separate front-panel controls for the lower and upper corner frequency settings. The filters were used: (1) for noise reduction, to attenuate noise
outside of the BWS passband; and (2) as anti-aliasing filters, to band-limit the BWS for prevention of aliasing. The filter settings for each of the three BWS recordings were .15 to 100 Hz (EEG), 150 to 3000 Hz (early AEP), and 0.5 to 1000 Hz (mid/late AEP).

The BA amplifier function was used to amplify the BWS to as high of a peak-to-peak amplitude as possible that would not saturate either the amplifier output or the ADC. Since the maximum amplifier output swing was +/- 15 V and the maximum ADC input voltage range was +/- 10V, the amplified output had to be kept below +/- 10V. The maximum peak-to-peak amplitude was necessary in order to get maximum ADC resolution.

In order to achieve this output amplitude level, the BA had to be be set for its maximum voltage gain of 10, or 20 dB. This gain was adequate for the EEG and the mid/late AEP, but was not quite adequate for the early AEP, which required an additional gain of 2 from an amplifier which was part of the ADC card.

The BA had a front-panel offset voltage adjust control which was used to nullify the offset voltage due to the BA input stage. Before the electrodes were attached to the subject, all three of the electrodes were shorted together and the offset control was used to adjust the amplifier output level (as monitored on the oscilloscope) to OV. The
amplified offset voltage must be as close to 0V as possible in order to prevent the possible that a large BWS input signal may cause the amplifier output or the ADC input to saturate.

6.2.5 Analog to Digital Converter

The ADC was a Data Translation analog-to-digital converter card with four channels and a programmable gain for each channel of one, two, four, or eight. The ADC card plugged into an internal card cage inside the computer (see Section 6.2.8 for a description of the computer); interface to the ADC was through an external interface box mounted on the outside of the computer. The interface box contained four BNC female connectors for the four ADC channel inputs; a ribbon cable connected the BNC connectors to the ADC card inputs inside the computer. This cable was found to be a source of 60-Hz noise pickup and had to be shielded by wrapping it with a piece of aluminum foil and grounding the foil.

The ADC had twelve bits of resolution and an input voltage range of -10V to +10V with a corresponding digital output range of -2048 to +2048. Thus, the ADC output resolution was a voltage of

$$\frac{10 - (-10)}{2048 - (-2048)} = 4.88 \text{ mV.}$$  \hspace{1cm} (6.2.5-1)

The level of the EEG and the mid/late AEP after
amplification by the BA was approximately \(\pm 4\)V peak; the level of the early AEP was approximately \(\pm 2\)V peak. For the EEG and the mid/late AEP, no additional ADC gain was utilized in order to prevent saturation of the ADC due to artifacts (see Section 2.7.5) and the resulting corruption of the EEG data and loss of the mid/late AEP data through the artifact rejection algorithm utilized in the analysis program HAC_WINDOW (see Section 8.2). For the early AEP, an additional ADC gain of two was utilized in order to bring the early AEP level to the same level as the EEG and the mid/late AEP and thus to increase the resolution.

Through FORTRAN calls to Data Translation subroutines, the user selected the start protocol (start on an external trigger or start on a subroutine call), the acquisition protocol (single word, single buffer, or multibuffer), the digitizing frequency, and the gain. The computer provided the timing and synchronization signals for the ADC card, thus making coordination of the ADC acquisition process transparent to the user.

In order to synchronize the start of data acquisition with the start of audio click production, the external trigger start protocol was utilized. The external trigger was provided by a Data Translation digital-to-analog converter (DAC) card, an eight-channel DAC with programmable channel voltages from \(-10\)V to \(+10\)V. The DAC card plugged
into the internal card cage in the computer; the eight DAC channels were connected via a ribbon cable to BNC connectors on the external interface box on the computer.

Channel 0 of the DAC was used as the start trigger line. A BNC tee was connected to the DAC channel 0 connector on the external interface box. One side of the tee was connected via a coaxial cable to the ADC external trigger input on the same interface box; the other side of the tee was connected via a coaxial cable to the trigger input on the audio click generator unit. The channel 0 voltage level was set by a FORTRAN call to a Data Translation subroutine with the desired voltage level as a pass parameter: with channel 0 at 0V, both the ADC and the CC were held in a reset state, wherein the ADC would not acquire data and the CC would not produce audio clicks; when channel 0 was programmed to 0V, the ADC was triggered to start acquiring data and the CC was triggered to start producing audio clicks.

The ADC acquisition protocol was set by FORTRAN calls to specific subroutines for each of the three protocols, with pass parameters specifying the number of words in the buffer (for single buffer and multibuffer transfers) and the number of buffers (for multibuffer transfers). The following protocols were utilized: (1) the EEG protocol was a single buffer acquisition of length 4096 words; (2) the early AEP
protocol was a multibuffer acquisition with 500 buffers, each of length 8192 words; and (3) the mid/late AEP protocol was a multibuffer acquisition with 200 buffers, each of length 8192 words.

The ADC digitizing frequency was set by an integer pass parameter in the FORTRAN call to the Data Translation ADC subroutine, with the pass parameter specifying a factor to divide into 1 MHz to get the digitizing frequency as follows:

\[ \text{digitizing frequency} = \frac{1\text{MHz}}{I}, \]  \hspace{1cm} (6.2.5-2)

where \( I \) is the integer pass parameter with a minimum value of 20. Thus, the maximum digitizing frequency was 50 kHz. The digitizing frequencies for each of the three BWS types in this experiment were as follows: (1) 1 kHz \(( I = 1000)\) for the EEG; (2) 23.25581395 kHz \(( I = 43)\) for the early AEP; and (3) 32.25806452 kHz \(( I = 31)\) for the mid/late AEP.

6.2.6 Click Circuit

The click circuit (CC) was a circuit that was custom designed and constructed by the author for producing headphone audio drive pulses (clicks) that were synchronized to the computer clock. This circuit was mounted in a small enclosed aluminum chassis and was powered from two external, 120 VAC input power supplies: one supply provided +5 VDC, the other provided +/- 12 VDC.
The CC had the following input connections: (1) a 5-pin circular connector brought in the three DC voltages from the two external power supplies; (2) a coaxial cable carried the computer clock output from the external interface box to a BNC jack on the CC; and (3) three coaxial cables carried the DAC channels 0 through 2 outputs from the external interface box on the computer to BNC jacks on the CC.

The computer clock was utilized as the reference signal from which the pulse periods in the CC were derived, thereby providing synchronization between the data acquisition, which was synchronized to the computer clock, and the audio click production. DAC channel 0, as discussed previously in Section 6.2.5, was the start trigger. DAC channel 1 selected the mode: 0V = early (pulse period = 88.06 msec) or +5V = late (pulse period = 507.9 msec). DAC channel 2 selected the pulse morphology: -5V = single pulses, 0V = double pulses, and +5V = alternating pulses. The audio output from the circuit was sent to a front-panel phone jack. 6.2.7 Headphones

A pair of TDH-49 headphones was used to produce the AEP audio stimulus. These headphones are one of the standard headphones used in the audiology field for audio stimulus production.

Only the one earphone was used for audio stimulation; this earphone was mounted on the left ear, the same ear
behind which the mastoid electrode was mounted (ipsilateral recording). A shielded cable connected this headphone to a front-panel phone jack on the click circuit. The headphones were not shielded, that is, did not contain mu metal to absorb the magnetic field generated by the speaker coil during click production; therefore, the electrode wires were routed as far away as possible from the active earphone in order to reduce coupling of the click artifact into the electrode wires and resulting distortion of the data. The headphones were driven by the click circuit to produce an 80 db SPL condensation click.

6.2.8 Computer

The computer used for data acquisition was a Digital Equipment Corporation MicroVAX minicomputer which was located in the College of Pharmacy and had a VAX/VMS operating system, FORTRAN programming language, and a Data Translation software package for controlling the peripheral devices (ADC and DAC). Data analysis was subsequently performed on VAX 11/780 computers at both the University of Arizona and Hughes Aircraft Company in Tucson. In the remainder of this section, 'computer' refers to the MicroVAX.

The computer was located in the laboratory in which the BWS were recorded. For permanent storage, the computer had an external dual hard disk drive and an internal streaming tape drive for TK50 tapes. The storage capacity of each of
the hard disks was 70 Megabytes and of the TK50 tape was 96
Megabytes. Two Rainbow graphics terminals provided operator
interface to the computer, one on each side of the study
subject: one terminal was used to run the acquisition
program, the other to perform backups of the data as it was
collected. Also connected to the computer were a Tektronix
graphics terminal and a Printronix printer. The Tektronix
terminal was used to display the brain wave data immediately
after it had been acquired, in order to verify the integrity
of the recording system; the printer was used to obtain hard
copies of programs and data.

6.2.9 Impedance Meter

The impedance meter (IM) was a custom-built unit used
to assess the integrity of the electrode connections to the
subject. The IM, which was powered by a 9V transistor
battery, was constructed by the author from the design of a
similar unit in use by the University of Arizona College of
Medicine Speech and Hearing Clinic. Both a technical
description and a schematic of the meter are given in
Section 7.3.

On its front panel, the IM had a power switch, two
electrode input jacks, and an analog meter calibrated to
display electrode impedance. After the electrodes were
attached to the subject, the impedance between each
different pair of electrodes — that is, vertex to mastoid,
vertex to forehead, and mastoid to forehead - was measured by plugging the pair of electrodes to be measured into the IM front-panel jacks, activating the power switch, and reading the impedance indicated by the meter.

The acceptable impedance level for an electrode pair was an impedance of less than 5 kilohms. If the impedance of a pair was greater than or equal to 5 kilohms, at least one of the electrodes in the pair was considered to have needed remounting. In order to help locate the bad electrode, the readings from all three electrode pairs were compared. If the readings from two of the pairs that contained a common electrode were high, the electrode common to the pairs was the electrode in need of remounting. For example, if the vertex to mastoid and the mastoid to forehead readings were high but the vertex to forehead was not, the mastoid electrode was causing the high reading and needed remounting.
6.3 Data Acquisition Software

The FORTRAN program THIS_IS_IT, written by the author, was used to acquire the brain wave data, store it on disk, and display it. A copy of the program is given in Appendix B. Table 6.3-1 summarizes the important acquisition parameters.

The program can be used in three different modes: (1) to acquire and display all three filetypes (EEG, early AEP, and mid/late AEP); (2) to acquire and display one filetype; or (3) to display one filetype. The user is prompted to choose the mode at the beginning of the program. This section will outline the operation of the program in the three-file acquisition and display mode, because this mode was the principal one utilized in the experiment.

In addition to the mode, the user is prompted at the beginning of the program to enter the following parameters: (1) the ADC programmable gain (1, 2, 4, or 8); and (2) the subject's initials. For the first two subjects in Phase 1, a gain of one was utilized; for all of the remaining subjects in Phase 1 and Phase 2, a gain of two was utilized.

The acquisition portion of the program consists of three loops, one each for the EEG, early AEP, and mid/late AEP. At the start of each of the loops, the user is prompted to set the bioelectric front-panel filter controls to the correct settings, which are 0.15 to 100 Hz for the EEG, 150 to 3000 Hz for the early AEP, and 0.5 to 1000 Hz for the
<table>
<thead>
<tr>
<th>Parameter</th>
<th>EEG</th>
<th>early AEP</th>
<th>mid/late</th>
</tr>
</thead>
<tbody>
<tr>
<td>stimulus freq. (Hz)</td>
<td>N/A</td>
<td>11.35</td>
<td>1.968</td>
</tr>
<tr>
<td>click pulse width (usec)</td>
<td>N/A</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>intrapulse period (msec)</td>
<td>N/A</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>stimulus ampl. (dB SPL)</td>
<td>N/A</td>
<td>80</td>
<td>80</td>
</tr>
<tr>
<td>sampling freq. (kHz)</td>
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<td>23.25</td>
<td>2.016</td>
</tr>
<tr>
<td>number of sample points per epoch</td>
<td>4096</td>
<td>256</td>
<td>1024</td>
</tr>
<tr>
<td>epoch length (msec)</td>
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<td>11.01</td>
<td>507.9</td>
</tr>
<tr>
<td>number of epochs</td>
<td>1</td>
<td>1000 SC</td>
<td>1000 SC</td>
</tr>
<tr>
<td></td>
<td></td>
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<tr>
<td>buffer length (words)</td>
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<td>4096</td>
<td>1024</td>
</tr>
<tr>
<td>number of buffers</td>
<td>1</td>
<td>128</td>
<td>100</td>
</tr>
<tr>
<td>total number of words</td>
<td>4096</td>
<td>524,288</td>
<td>102,400</td>
</tr>
<tr>
<td>disk file size (blocks)</td>
<td>17</td>
<td>2000</td>
<td>400</td>
</tr>
</tbody>
</table>

Table 6.3-1. Stimulus, acquisition, and storage parameters. SC is single-click; DC is double-click.
mid/late AEP.

On the first loop, the EEG signal is acquired by a call to the subroutine EEG. This subroutine sets the ADC digitizing frequency to 1 kHz, starts the data acquisition by starting the ADC digitizing clock, and, using the Data Translation (DT) single-buffer subroutine DSBR, acquires a single 4096-word (1 msec per word) buffer of EEG data. Once the buffer is filled, it is written to a hard disk file with the name AAA_BBBBB_CCCC_eeg_xD.data, where AAA is the subject's initials, BBBBB is the date (e.g., 13SEP89), CCCC is the time based on a 24 hour clock (e.g., thirty minutes after 7:00 AM is 0730), and D is the gain (1 for the EEG and mid/late AEP; 2 for the early AEP except for the first two Phase 1 subjects, for whom the gain was 1). When the file write completes, the ADC clock is stopped, and control returns to the main program.

The remaining two acquisition loops acquire the AEP signals, first the mid/late AEP, then the early AEP. At the start of each of these loops, the ADC digitizing frequency is set (mid/late AEP: 32.258 kHz; early AEP: 23.255 kHz). Next, a hard disk file is opened. For the mid/late AEP, the filename is AAA_BBBBB_CCCC_lat_alt_xD.data, with AAA, BBBBB, CCCC, and D as for the EEG filename; the early filename is identical except that 'lat' is replaced by 'ely'.

A call is made to the DT multibuffer read subroutine
DTMBR which prepares the ADC and the computer for multibuffer data acquisition, and then the four channels of the DAC are simultaneously programmed as follows: (1) channel 0, which is the click circuit reset line, is set to 0 V, enabling the click circuit to start producing audio clicks; (2) channel 1, which controls the period between the audio clicks, is set to either +5 V (mid/late AEP) or 0 V (early AEP); (3) channel 2, which controls the click morphology (single, double, or alternating), is set to 0 V, which sets the alternating mode; and (4) channel 3, which is connected to the ADC external trigger input, is set to 0 V, which starts the ADC digitizing clock and thus data acquisition.

A sequence of calls is then made to various DT subroutines to acquire sequential buffers of data and simultaneously (in real time) write them to disk. For the mid/late AEP, a total of 200 buffers of length 8192 words (31 usec per word) are acquired; for the early AEP, a total of 500 buffers of length 8192 words (43 usec per word) are acquired. For the mid/late AEP, the epoch length (interval between click production) is 16,384 words, or 16,384 * 31 usec = 507.9 msec, which corresponds to a click frequency of 1.97 Hz; for the early AEP, the epoch length is 2048 words, or 2048 * 43 usec = 88.06 msec, which corresponds to a click frequency of 11.35 Hz. When the final
acquired buffer has been written to disk, the click circuit is put in the reset state to stop click production. This step is the last one in the AEP loop; if the mid/late AEP has just been acquired, the loop is repeated for the early AEP.

At this point, data acquisition is complete. Two of the three signals that have just been acquired are output to the Tektronix graphics terminal so that the user can verify the integrity of the data acquisition and processing by checking for corrupt data points. First, the subroutine READ_EEG is called. This subroutine calls the DT single-buffer read subroutine MSSBR to read the 4096-word EEG hard-disk data file into an array. The array is then passed to the subroutine OSCOPE, which automatically scales the data and, utilizing a Tektronix software driver, plots a graph of ADC output (which has a range of -2048 to +2048) versus data point (which has a range of 1 to 4096) on the Tektronix terminal.

Next, the subroutine CHOP_IT is called. This subroutine trims the early AEP file storage requirements from 16,000 disc blocks to 2000 disc blocks by retaining only the first 256 words of the 2048-word early AEP epoch. The first 256 words represent the first $256 \times 43$ usec = 11 msec of data, which is more than necessary to cover the usually defined early upper range of 10 msec. The remaining $2048 - 256 =
1792 words were only present to get the correct stimulus frequency, since the click circuit sets the stimulus frequency by counting computer clock pulses.

The subroutine CHOP_IT starts by reading 32,768 words of data from the early AEP file stored on hard disk into an array IDTBUF. Then, the first 256 words of each consecutive 2048-word block of IDTBUF are stored consecutively in the 4096-word array IDATA until a total of sixteen 256-word blocks of data (a total of 4096 words) have been stored in IDATA. Then, IDATA is written to a hard disk file with the same filename as the early AEP data file except that the extension is '.CHOP' instead of '.DATA'.

The next 32,768-word block of data is read, and the process outlined in the above paragraph is repeated until a total of 128 32,768-word blocks (a total of 4.194304 megawords) have been read and 128 4096-word blocks (524,288 words) have been stored in the chopped file. The early AEP disk file size is thus cut by a factor of eight (32,7678 / 4096).

After the subroutine CHOP_IT completes, the subroutine READ_CHOP is called to read the data back in from the chopped early AEP data hard disk file and display the early single-click AEP response on the Tektronix monitor for verification of correct signal acquisition and storage.

The subroutine READ_CHOP starts by reading 4096 words
of data from the hard disk early AEP chopped data file into the array IDTBUF. Then, for artifact rejection, the magnitude of every data point (word) of the first 256-word block is compared against the ADC saturation limits of -2048 to +2048; if all 256 data points are within the range of -2047 to +2047, the 256-word block of data is sent to the subroutine MEANCU for accumulation. In the accumulation mode, MEANCU computes a running sum of each 256-word block of data sent to it and keeps track of the number of summations performed. If any of the 256 points are outside of the range of -2047 to +2047, the 256-word block of data is not sent to MEANCU.

The above procedure is repeated for every other 256-word block of data stored in the chopped file (that is, all the single-click blocks) until all eight 256-word single-click blocks in the 4096-word array IDTBUF have been read. Then, another 4096-block of data is read into IDTBUF and the process is repeated until all 128 4096-word blocks of data (524,288 total words) in the chopped file have been read.

The subroutine MEANCU is then called in the average mode, in which it computes and returns a 256-word array which is equal to the average of all of the 256-word blocks of accumulated data and also returns the number of blocks averaged.

Finally, the subroutine READ_CHOP completes by calling
the subroutine OSCOPE to display the averaged 256-word array and the number of epochs (256-word blocks) averaged. At this point, the program THIS_IS_IT completes.

After the hard disk was nearly full (the disk capacity was 70 Mbytes, and it took approximately four study days worth of data to nearly fill it), the hard disk files were copied to a TK50 cartridge tape using the TK50 internal drive in the uVAX computer. When the experiment was completed, the TK50 tapes were then taken to the University of Arizona Computer Center, where they were copied to reel-to-reel tapes. The reel-to-reel tapes were then taken and copied to hard disks on a VAX 11/780 mainframe at Hughes Aircraft Company, where the data analysis was performed.

When both of the experimental phases had been completed, it was decided to reduce the mid/late AEP data file sizes from 6400 disk blocks to 400 disk blocks in order to reduce the disk storage space requirements. The file sizes were reduced by decimating the digitizing frequency by sixteen. For this purpose, the program LATE_CHOP (see Appendix C) was used. This program starts by reading a 16,384-word block of data from the late AEP hard disk data file into an array IDTBUF. Starting at the first data point, every sixteenth data point of IDTBUF is written to a new hard disk data file with the same name as the original data file except that the extension is '.CHOP' instead of '.DATA'. After 1024 words
(16,384 / 16) have been written to this chopped file, another 16,384-word block of data is read and the process is repeated until a total of 100 16,384-word blocks of data (1.6384 megawords of data) have been read and a corresponding total of 100 1024-word blocks of data (102,400 words of data) have been stored in the chopped file. The chopped late AEP data file is thus one-sixteenth the size of the original late AEP data file.
6.4 Blood Sampling and Lithium Assays

The blood draws were performed in the morning when the subject arrived in the laboratory for the brain wave recordings, twelve hours after the last dose (taken the previous evening) in order to comply with the 12h-stSLi.

A registered nurse performed the blood draws, which were performed just prior to the brain wave recordings. Two 1 mL tubes of plasma were drawn from the patient and then centrifuged for half an hour to separate the plasma from the coagulate (the coagulate is heavier than the serum and settles to the bottom of the tube). After centrifugation, the serum from each of the tubes was extracted and placed in a separate tube. One of the tubes was placed in a freezer for long-term storage; the other tube was sent to National Health Laboratories in Phoenix for a lithium assay.
6.5 Procedure for Recording the Brain Waves

The brain waves, i.e., the EEG and the AEP, were recorded using the equipment outlined in Section 6.2. Figure 6.2.2-1 shows the experimental setup for recording the brain waves.

AC power was applied to the amplifier for at least five minutes before the morning's first brain wave recordings so that the amplifier would be in thermal equilibrium before the recordings began. Upon arrival in the laboratory, the subject was seated in a location in the laboratory in which 60-Hz interference from neighboring AC power outlets and devices was minimal. To further reduce 60-Hz interference, all equipment in the laboratory except that needed for the recordings was turned off, including the overhead fluorescent lights. Indeed, the lights had been found to be a source of large 60-Hz noise spikes which at times coupled into the brain wave signals with sufficient amplitude to obscure the desired signal.

Three silver-plated-metal recessed-cup electrodes were used. These electrodes consist of a concave silver-plated metal cup attached to a two-foot length of high-flexibility wire which is terminated in a subminiature plug-tip connector. The cup was filled with a silver chloride (AgCl) electrolyte paste and then pressed firmly down on the skin until paste oozes through the small hole at the top of the
cup. By providing a thick layer of electrolyte paste between the electrode and the skin and thus reducing the amount of electrode surface area in direct contact with the skin, the recessed-cup electrode reduces motion artifact, which is electrical noise generated by relative movement between the electrode and the skin that occurs when the subject moves or contracts muscles in the area of the electrode.

The three electrodes were chlorided once before the beginning of Phase 1 using the procedure outlined in Appendix A. Chloriding is the process of electrolytically depositing a layer of AgCl on the outer surface of the electrode and provides two main benefits: (1) up to a certain thickness of the chloride layer, it reduces electrode impedance, thus reducing signal attenuation; and (2) it reduces electrical noise.

The electrode montage was the same for the EEG recording and the AEP recording: one electrode was mounted on the vertex (Cz); one on the mastoid (flat bony protrusion behind the pinna); and one on the forehead. The electrodes were attached to the subject using the following procedure: (1) Rub the mounting area briskly with a moist paper towel. This step cleans and removes some of the outer dead layers of skin in order to reduce the skin impedance. The lower the skin impedance, the greater the signal strength.
(2) Dip a cotton swab in Omni-Prep skin preparation paste or equivalent and rub the mounting area briskly with the swab. This paste is a conductive abrasive adhesive which further reduces the skin impedance, helps hold the electrode in place, and is electrically conductive.

(3) Squeeze a small glob of Teca electrode adhesive paste or equivalent into the electrode cup and then press the electrode down firmly on the mounting area until paste starts oozing from the hole at the top of the electrode. The paste is the AgCl electrolyte essential to the proper function of the electrode as an ion current to electron current transducer.

(4) Mount the vertex and forehead electrodes such that the leads are pointing toward the subject’s right shoulder; mount the mastoid electrode such that the lead is pointing down. Positioning the leads in this manner maximizes their distance from the left earphone and thus prevents magnetic coupling of the AEP click(s) into the leads and ultimately the brain wave recordings.

(5) On the vertex electrode, place a cotton ball on top of the electrode and press it down firmly. The cotton ball pulls the electrode down firmly in place on top of the scalp. On the mastoid and forehead electrodes, press a 2-inch strip of medical adhesive tape over the electrodes and the skin to hold the electrodes in place.
(6) Connect the forehead electrode connector to the black connector on the electrode impedance meter. Connect the mastoid electrode connector to the red connector on the meter. Turn the meter on and note the impedance reading. In a similar manner, measure the impedance of the following electrode pairs: (1) forehead to vertex; and (2) mastoid to vertex. The impedance of any of the three electrode pairs shall be five kilohms or less; if the impedance is greater than this value, the electrode or electrodes causing the high impedance must be remounted. If a particular electrode is causing high impedance, it will frequently cause the impedance of two of the three electrode pairs to be high and will be the common electrode in the two pairs. To remount the electrode, remove the electrode and wipe the electrolyte from the mounting area with a wet paper towel. Repeat all of the above steps.

(6) For strain relief, tape the electrode leads to the subject's shoulder: the mastoid lead to the left shoulder, and the vertex and forehead leads to the right shoulder.

(7) On the HP 8811A Bioelectric Amplifier, verify that the RANGE switch is set to .2 mV/10 DIV, the gain control is set to maximum, the front toggle switch is set to USE, and the function select switch is set to EEG RANGE
mV/100 DIV. Prepare to take an EEG reading by setting the lower cutoff frequency to 0.15 Hz and the upper cutoff frequency to 100 Hz.

(8) The DC offset at the amplifier output must first be nulled out. Short together all three alligator clips at the end of the amplifier input cable. On the oscilloscope (scope), set the timebase to 5 msec/div, the vertical sensitivity to 2 V/div, the trigger to auto, and the coupling to ground. Adjust the vertical position control until the trace is centered on the screen. The position of the trace on the screen at this point is the ground reference. Then set the coupling to DC and null the DC offset in the signal by first setting the sensitivity to 100 mV/div and then adjusting the position control on the amplifier until the EEG peak-to-peak excursions are centered about the ground reference. Reset the sensitivity to 2 V/div.

(9) Connect the subminiature probe tips on the ends of the electrode leads to the alligator clips on the end of the amplifier input cable as follows: vertex lead to positive input, mastoid lead to negative input, and forehead lead to chassis ground.

(10) Turn-off the overhead fluorescent lights and then check the scope display for excessive noise and 60-Hz noise spikes. If excessive noise is present, disconnect the
electrodes from the amplifier, remove the electrodes from the subject, and remount the electrodes to the subject by performing all of the above steps.

(11) Mount the TDH-49 headphones on the subject. Make certain that the active phone is placed over the subject's left ear (the ear behind which the mastoid electrode is mounted) so that the AEP recording will be ipsilateral.

(12) Run the acquisition program THIS_IS_IT. The following prompt will appear on the computer monitor:

ENTER: T FOR THREE-FILE ACQUISITION AND READ
(ACQUIRE EEG/EARLY/LATE THEN
DISPLAY EEG/EARLY/LATE)
OR
A FOR SINGLE-FILE ACQUISITION & READ
OR
R FOR SINGLE-FILE READ

Enter T. A T will enable the acquisition of an EEG, mid/late AEP, and early AEP.

(13) The following prompt will appear on the monitor:

ENTER EARLY AEP GAIN (1, 2, 4, OR 8)

Enter 2. A 2 will amplify the voltage at the ADC by two for the early AEP. This additional multiplication is necessary to get adequate vertical resolution for the early AEP, the amplitudes of which are typically ten to 100 times smaller than the EEG and late AEP amplitudes.

(14) The monitor bell will ring and the following prompt will appear on the monitor:
EEG FILTER SETTINGS: 0.15Hz TO 100 Hz
PRESS RETURN TO START DATA ACQUISITION
On the amplifier, set the lower cutoff frequency to 0.15 Hz and the upper cutoff frequency to 100 Hz. Inform the subject that the readings are going to begin, instruct him to close his eyes, and then press RETURN.

(15) After approximately four seconds, the monitor bell will ring and the following prompt will appear on the monitor:

LATE FILTER SETTINGS: 0.5 Hz TO 1 kHz
On the amplifier, set the lower cutoff frequency to 0.5 Hz and the upper cutoff frequency to 1 kHz, then press RETURN.

(16) After approximately one minute, the monitor bell will ring and the following prompt will appear on the monitor:

EARLY FILTER SETTINGS: 150 Hz TO 3 kHz
On the amplifier, set the lower cutoff frequency to 150 Hz and the upper cutoff frequency to 3 kHz, then press RETURN.

(17) After approximately three minutes, the monitor bell will ring and the following message will appear on the monitor:

DATA ACQUISITION COMPLETE
At this point, the acquisition program has written the EEG file and the early and late AEP files to the hard disk and will now perform the following steps: (1) read the EEG file back in from the disk and output it to either a monitor or a printer; (2) read the early AEP file back in from the disk; (3) chop the early AEP file, that is, remove the data from 10 msec to 88 msec after the click that was included only to get the proper click period; (4) write the chopped early AEP file to the disk; (5) read the chopped early AEP file back in from the disk and output both the single-click and double-click responses to either a monitor or a printer. The purpose of observing the responses at this point is to verify that the electrodes did not come loose during the acquisition or that excessive noise was not being introduced and distorting the data. When the EEG file has been read back in from the disk, the following prompt will appear on the monitor:

Where would you like the plot?, (Txa6, etc.)

Enter the computer port to which the destination device (monitor, printer, etc.) is connected.

(18) The following prompt will appear on the monitor:

DEVICE DRIVER NUMBER?
TEKTRONIX = 0
REGIS (DEC) = 2
HOUSTON INSTRUMENTS = 6
PRINTRONIX = 7
Enter the appropriate number for the desired destination device.

(19) The EEG plot of ADC value vs. data point (time) will now be sent to the destination device and the following prompt will appear on the monitor:

PRESS RETURN FOR NEXT PLOT

The range of the ADC values is -2048 to +2048. If the EEG plot is fairly well centered around zero, none of the ADC values are at -2048 or +2048, and resembles a typical EEG plot with no excessive noise spikes or oscillations, press RETURN to start the AEP plot. If any of the above conditions exist, the source of the problem must be identified and the appropriate acquisition steps above repeated to obtain a clean plot.
6.6 Phase 1

The objective of this phase was to determine the following: (1) if lithium alters the EEG and AEP frequency spectrums; (2) if so, the nature of the concentration-effect relationship, if any, between the plasma lithium levels and the parameters in the spectrum that get altered; and (3) if tolerance develops in the alterations.

Ten study subjects (STS) were recruited by advertisements in the University of Arizona (UA) campus newspaper and bulletin-board flyers (see Appendix D) in the UA medical and pharmacy schools. To qualify for the study, the STS were required to pass a physical examination which included blood and urine tests. The examination was administered by a medical school intern.

Prior to the examination, the STS were given two forms to read: one form (see Appendix D) explained the study design, rules, and possible lithium side effects; the other form (see Appendix D) was a consent form. At the examination, the physician further explained the study design and rules and the possible lithium side effects. If the STS wished to continue with the study, the physician witnessed the signature of the STS on the consent form, which stated that the STS agreed to abide by the study rules and understood the possible side effects and risks associated with the use of lithium.
One of the conditions for participating in the study was that the STS was to abstain from nicotine, caffeine, alcohol, prescribed and over-the-counter medications, and illegal drugs commencing one week prior to the study and continuing for the duration of the study. The purpose of this requirement was to eliminate the mixing of any brain wave effects caused by these substances with those (potentially) caused by lithium and therefore to avoid errors associated with attributing the effects caused by these other substances to lithium.

The pay scale was designed to encourage successful completion of the study. The STS was required to have a total of eight BWRs and BDs. If the STS dropped out of the study before the eighth BWR and BD, the STS was paid $10/time for each of the times the STS had a BWR and BD. The STS was paid $100 total for having all eight BWRs and BDs.

The STS reported to the lab for a baseline brain-wave recording (BWR) and blood draw (BD) on Day 0, which fell on a Thursday or Friday of the week immediately preceding the week of the start of lithium dosing. One week prior to Day 0, the STS had started the drug and medication abstinence discussed previously. The procedure for the BWR is described in Section 6.5 and for the BD in Section 6.4.

On Sunday night of the week following the week of Day 0, the STS took the first dose of lithium. The dosing
schedule for this week consisted of taking one 300-mg Lithonate tablet (a sustained-release lithium preparation) by mouth once a day in the evening for five evenings at the same time every evening. The STS reported to the lab the following morning for a BD and a BWR twelve hours after the evening dose was taken, thus complying with the time interval necessary for the 12h-stSLi.

The STS continued this schedule for five consecutive days, taking an evening dose and then having a BWR and BD the following morning. On Friday, when the STS had theoretically reached their first SS lithium level (five half-lives), they switched to a new dosing schedule, designed to bring them to a SS lithium level of twice the first SS level. Immediately after their Friday morning BWR and BD, the STS took a 300-mg Lithonate tablet and then followed this dose twelve hours later with another 300-mg tablet. They continued taking two tablets a day spaced twelve hours apart for five days. No BWRs or BLs were taken until the fifth day.

On Day 10, five days after they switched to the second dosing schedule, which was Wednesday of the following week and theoretically the point at which they had reached a second SS lithium level, the STS reported to the lab for a morning BWR and BL and then switched to the third, and final, dosing schedule. For this schedule, they took one
300-mg tablet three times a day: one in the morning, one at noon, and one in the evening. This schedule was designed to bring them to a SS lithium level of approximately three times the first SS level. The STS continued on this third dosing schedule for five days, during which time no BWRs or BLs were taken.

On Day 15, five days after they switched to the third dosing schedule, which was Monday of the following week and theoretically the point at which they had reached a third SS lithium level, the STS reported to the lab in the morning for a final BWR and BL.
6.7 Phase 2

Problems were encountered with both the lithium assays and the lithium serum levels in Phase 1. The problem with the assays was that the commercial laboratory which performed them recorded the serum levels to only the nearest tenth of a mEq/L. This level of resolution caused problems, especially during Days 1 through 5, where the serum levels for a particular subject were low because of the low dose and increased more slowly as the first SS (Day 5) was approached, but would frequently be reported the same for consecutive days because of the lack of resolution needed to distinguish the small incremental changes that were actually occurring.

The problem with the serum levels was that many of them did not reach the minimum therapeutic level of 0.6-mEq/L, even at the third SS. Since lithium has been shown to be therapeutically ineffective below this level, its anticipated effect on the brain waves would be minimal. A preliminary analysis of the Phase 1 data had, in fact, shown no consistent relation between the spectral edge and the serum lithium concentration.

Therefore, Phase 2 was undertaken. The main objective of Phase 2 was to determine if lithium alters the EEG and AEP frequency spectrums. In Phase 2, the STS were dosed to only one SS level and the dosage was increased to
1,200 mg/day to insure that the SS levels were in the therapeutic range. Arrangements were made with the assay laboratory to obtain another significant figure to increase the resolution of the serum levels.

Eight STS were recruited in the same manner as for Phase 1 and followed the same procedure for the physical examination and consent form as for Phase 1. The rules for drug abstinence were the same as for Phase 1.

The pay scale was again designed to encourage successful completion of the study. The STS was required to have a total of eleven BWRs and BDs. If the STS dropped out of the study before the eleventh BWR and BD, the STS was paid $10/time for each of the times the STS had a BWR and BD. The STS was paid $150 total for having all eleven BWRs and BDs.

The STS reported to the lab for the first baseline brain-wave recording (BWR) and blood draw (BD) on Day 0, which fell on a Wednesday of the week immediately preceding the week of the start of lithium dosing. One week prior to Day 0, the STS had started the drug and medication abstinence discussed previously. The procedure for the BWR is described in Section 6.5 and for the BD in Section 6.4.

In contrast to the single baseline BWR performed in Phase 1, five baseline BWRs were performed in Phase 2, the purpose being to assess the spectral edge (SE) pre-drug variance for comparison with the SE drug variance. These
five baseline BWRs were performed on five different days: Day 0 (Wednesday), Day 1 (Thursday), and Day 2 (Friday) of the first week; and Day 5 (Monday) and Day 6 (Tuesday) of the second week.

On the morning of Day 7 (Wednesday), the STS took the first dose of lithium. The dosing schedule for Phase 2 consisted of taking two two 300-mg Lithonate tablets by mouth twice a day in the morning and the evening. In order to comply with the 12h-stSLi, the evening dose time was set to insure that the next morning’s BD (on the days that it was taken) occurred twelve hours later.

On the morning of Day 9 (Friday), a BD and a BWR were taken. The BD at this point was used to calculate what the SS lithium level would be, so that the dosage could be adjusted if necessary to bring the level within the therapeutic range. Concern had existed that the higher dosages used in Phase 2 could bring the levels close to the toxic range (1.5 mEq/L and higher).

The following week, a BD and a BWR were taken every morning from Day 12 (Monday) to Day 16 (Friday). Phase 2 was complete after the BD and BWR on Day 16.
7.0 DESCRIPTION OF APPARATUS
7.1 Electrodes

7.1.1 Introduction

Scalp electrodes are not in direct contact with scalp tissue; instead, indirect contact is made to scalp tissue through an electrolyte bridge formed by the electrode jelly between the electrode and the skin. The electrode in contact with the electrode jelly forms a metal-electrolyte half-cell, the properties of which are discussed in the following sections.

7.1.2 Half-Cells

When a metal electrode consisting of metal atoms M is immersed in an electrolyte solution containing anions A and cations of the metal M (see Figure 7.1.2-1), each of the metal atoms at the electrode/electrolyte interface is oxidized to form a cation and a free electron, the cation being discharged into the electrolyte and the electron remaining in the electrode; each of the electrolyte anions at the interface is oxidized to a neutral atom, releasing one or more electrons to the electrode. This process is represented by the following equations:

References for this section are (10,11,28,41,51).
Figure 7.1.2-1. Ions at the metal-electrolyte interface (from ref. 10).
A thermodynamic equilibrium is established, in which the rate at which metal atoms lose electrons and pass into solution is exactly balanced by the rate at which metal ions in solution deposit on the electrode as metal atoms.

Before the electrode was immersed in the electrolyte, the electrolyte contained an equal number of anions and cations, thus maintaining neutrality of charge. Once thermodynamic equilibrium is established, however, the cation concentration in the immediate vicinity of the interface changes, affecting the anion concentration here also, and a region known as the space-charge region (SCR) is formed, wherein neutrality of charge is not maintained. The SCR (see Figure 7.1.2-1) consists of two regions of opposite charge, forming an electrical double layer: a compact layer of one type of charge at the metal surface and a more diffuse layer of opposite charge extending much further from the interface.

Since neutrality of charge is not maintained in the SCR, an equilibrium potential difference known as the half-cell potential (HCP) is established between the metal and the electrolyte. The HCP is a function of several factors, the more important being the electrode material, electrolyte
ion concentrations, and temperature.

Since the measurement of potential requires two measurement points, the HCP cannot be measured without a second electrode immersed in the electrolyte. If two electrodes are present, the actual potential measured is the difference between the half-cell potentials of the two electrodes. To solve this problem and thus enable measurement of individual HCPs, a certain electrode is arbitrarily assigned a HCP of zero at standard conditions and the HCP of all other electrodes is measured with respect to this electrode at these standard conditions. This reference electrode is the hydrogen electrode and the standard conditions are 25 deg C, ionic activity = 1, and partial pressure = 1 (for gases); the HCPs when measured in this manner are called standard half-cell potentials (SCHPs). (Note: the ionic activity is defined as the availability of an ionic species in solution to enter into reaction.) Table 7.1.2-2 shows representative SCHPs for some common electrodes.

When conditions differ from the standard conditions, the HCPs differ from the SCHPs and the HCPs are then calculated from the Nernst equation: for the reaction

\[ \alpha A + \beta B \leftrightarrow \gamma C + \delta D + ze^- \]

(7.1.2-3)

the Nernst equation is
<table>
<thead>
<tr>
<th>Cell</th>
<th>Electrode reaction</th>
<th>Potential, V</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metal-ion potentials:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Al(^{3+}):Al</td>
<td>(\text{Al} = \text{Al}^{3+} - 3\text{e}^-)</td>
<td>-1.66</td>
</tr>
<tr>
<td>Zn(^{2+}):Zn</td>
<td>(\text{Zn} = \text{Zn}^{2+} - 2\text{e}^-)</td>
<td>-0.763</td>
</tr>
<tr>
<td>Fe(^{3+}):Fe</td>
<td>(\text{Fe} = \text{Fe}^{3+} - 2\text{e}^-)</td>
<td>-0.440</td>
</tr>
<tr>
<td>Ni(^{2+}):Ni</td>
<td>(\text{Ni} = \text{Ni}^{2+} - 2\text{e}^-)</td>
<td>-0.250</td>
</tr>
<tr>
<td>Pb(^{2+}):Pb</td>
<td>(\text{Pb} = \text{Pb}^{2+} - 2\text{e}^-)</td>
<td>-0.126</td>
</tr>
<tr>
<td>Ag(^+:AgCl)</td>
<td>(\text{Ag} - \text{Cl}^- = \text{AgCl} - \text{e}^-)</td>
<td>-0.2224</td>
</tr>
<tr>
<td>Hg(^{2+}):Hg(_2)Cl(_2)</td>
<td>(2\text{Hg} - 2\text{Cl}^- = \text{Hg}_2\text{Cl}_2 - 2\text{e}^-)</td>
<td>-0.2681</td>
</tr>
<tr>
<td>Cu(^{2+}):Cu</td>
<td>(\text{Cu} = \text{Cu}^{2+} + 2\text{e}^-)</td>
<td>-0.349</td>
</tr>
<tr>
<td>Cu(^+:Cu)</td>
<td>(\text{Cu} = \text{Cu}^+ + \text{e}^-)</td>
<td>-0.521</td>
</tr>
<tr>
<td>Hg(^+:Hg)</td>
<td>(2\text{Hg} = \text{Hg}^0 - 2\text{e}^-)</td>
<td>-0.797</td>
</tr>
<tr>
<td>Ag(^+:Ag)</td>
<td>(\text{Ag} = \text{Ag}^+ + \text{e}^-)</td>
<td>-0.799</td>
</tr>
<tr>
<td>Au(^{3+}):Au</td>
<td>(\text{Au} = \text{Au}^{3+} - 3\text{e}^-)</td>
<td>-1.50</td>
</tr>
<tr>
<td>Au(^+:Au)</td>
<td>(\text{Au} = \text{Au}^+ + \text{e}^-)</td>
<td>-1.68</td>
</tr>
<tr>
<td>Redox potentials:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cr(^{3+}):Cr</td>
<td>(\text{Cr}^{3+} = \text{Cr}^3+ + \text{e}^-)</td>
<td>-0.40</td>
</tr>
<tr>
<td>H(^+):H(_2)</td>
<td>(\text{H}_2 = 2\text{H}^+ + 2\text{e}^-)</td>
<td>0.0000 (std.)</td>
</tr>
<tr>
<td>Cu(^{2+}):Cu</td>
<td>(\text{Cu}^+ = \text{Cu}^{2+} + \text{e}^-)</td>
<td>-0.153</td>
</tr>
<tr>
<td>Fe(^{3+}):Fe(^{2+})</td>
<td>(\text{Fe}^{3+} = \text{Fe}^{2+} + \text{e}^-)</td>
<td>-0.7701</td>
</tr>
<tr>
<td>Cl(^-):Cl(_2)</td>
<td>(2\text{Cl}^- = \text{Cl}_2 - 2\text{e}^-)</td>
<td>-1.3513</td>
</tr>
</tbody>
</table>

Table 7.1.2-2. Standard half-cell potentials (from ref. 10).
where \( E \) is the HCP, \( E \) is the SHCP, \( R \) is the universal gas constant, \( T \) is the temperature, \( F \) is Faraday’s constant, and \( a \) is the ionic activity. The ionic activity is given as

\[
a = \delta C,
\]

where \( C \) is the concentration and \( \delta \) is the activity coefficient, which is 1 for an infinitely-dilute solution.

**7.1.3 Overvoltage**

As current passes thru an electrode, the equilibrium HCP \( E(0) \) is altered, resulting in a new potential \( E(i) \), the magnitude of which depends on the current density. This change in potential is defined as the overvoltage (OV) \( n \):

\[
n = E(i) - E(0).
\]

The OV can be positive or negative, the polarity being determined by the direction of the current flow.

When the current is small enough to prevent the equilibrium reaction rates from being significantly disturbed, the HCP is close to its equilibrium value, \( n \) is close to zero, and the electrode is operating reversibly. If \( n \) is nonzero, the electrode is polarized and is operating irreversibly.

OV is caused by five independent physical mechanisms. Because these mechanisms are independent, the OV components
due to each of them add to produce the total OV:

$$n = n_t + n_d + n_{rct} + n_{c} + n_{res}$$  \hspace{1cm} (7.1.3-2)

where $n_t$ is the OV component due to the charge transfer process, $n_d$ is the OV component due to diffusion, $n_{rct}$ is the OV component due to chemical reaction at the electrode, $n_c$ is the OV component due to crystallization, and $n_{res}$ is the OV component due to resistance polarization.

For small electrode current densities, i.e., at conditions close to equilibrium, $n_t$ is usually the dominant component of $n$, while at higher electrode current densities, $n_d$ is usually the dominant component of $n$. Each of the five OV components will now be discussed briefly in the following sections.

### 7.1.3.1 Charge Transfer Overvoltage Component

The OV component $n_t$ is due to the ionic flow change across the SCR which occurs to support the current change through the electrode. At equilibrium, the rate at which ions pass from the electrode into solution (the dissolution current density $J^+$) equals the rate at which ions are deposited onto the electrode (the deposition current density $J^-$). As the current through the electrode changes, the ionic flow rate across the SCR changes to satisfy the electrode current demands. The ionic flow rate change occurs as a result of a change in the electrostatic potential (ESP)
across the compact double layer of charge in the SCR. The ESP change, in turn, occurs through changes in the activation energies for dissolution and deposition (see Figure 7.1.3.1-1): depending on the current direction, the activation energy for dissolution will either increase or decrease and that for deposition will do the opposite in order to adjust the ionic flow rate to accommodate the electrode current change.

Thus, \( n \) is equal to the change in ESP across the SCR \( t \) and is related to the electrode current density \( J \) by

\[
\frac{J}{J_0} = e^{\frac{znF}{RT}} - e^{\frac{-(1-a)znF}{RT}},
\]

(7.1.3.1-1)

where \( J_0 (= J^+) \) is the exchange current density and \( \alpha \) is the transfer coefficient, which is the fraction of \( n \) that decreases the dissolution activation energy \( (0 \leq \alpha \leq 1) \).

### 7.1.3.2 Diffusion Overvoltage Component

The OV component \( d \) is due to the change in ionic activity in the immediate vicinity of the electrode caused by a diffusion gradient generated as a result of current flow through the electrode. As current flows through the electrode, ions are either deposited on or released from the electrode, depending upon the polarity of the electrode and the polarity of the ions: for instance, positive ions are deposited on a negative electrode and released from a positive electrode. The ions thus accumulate or deplete at
Figure 7.1.3.1-1. Activation energies (from ref. 10).
the electrode, causing the concentration of ions at the electrode to be different from the concentration of the ions in the bulk of the solution and thereby establishing a diffusion current gradient. The local ionic concentration change at the electrode changes the ionic activity at the electrode and thereby the HCP.

The magnitude of $n$ can be calculated from the following equation:

$$|\eta_t| = -\frac{RT}{T} \ln \left(1 - \frac{J}{J_s}\right),$$  \hfill (7.1.3.2-1)

where $J$ is the current density and $J_s$ is the saturation density, which is constant for a particular electrode.

7.1.3.3 Chemical Reaction Overvoltage Component

The OV component $n_{\text{rct}}$ is due to a rate-limiting reaction that depends in some manner on the electrode current density; for example, a rate-limiting reaction that makes metal ions available for deposition. If the concentration of reactants is constant, the concentration of products depends on the cell current; thus, as the cell current varies, the amount of reaction products varies and the metal ion concentration adjacent to the electrode surface varies, causing a change in the overvoltage.

7.1.3.4 Crystallization Overvoltage Component

The OV component $n_{\text{c}}$ is due to a rate-limiting mechanism whereby metal ions deposited on the electrode surface are
incorporated into the electrode crystal lattice. This process involves an activation energy and therefore any change in the crystallization rate due to a change in the current (which changes the rate at which metal ions are deposited on the electrode surface) changes the HCP. The component \( n \) is normally very small and difficult to measure.

7.1.3.5 Resistance Polarization Overvoltage Component

The OV component \( n \) is due to the ohmic resistance of the electrolyte, the concentration gradient in the diffusion layer, and surface films on the electrode surface. The electrolyte ohmic resistance obeys Ohm's law. The conductivity of the diffusion layer is nonuniform and varies with the current flowing through the layer; thus, as current flow through the layer changes, a non-linear potential difference is created across the layer. The surface films can cause both diffusion and ohmic potentials.

7.1.4 Circuit Models

7.1.4.1 Electrode-Electrolyte Interface

Figure 7.1.4.1-1 presents a circuit model for the electrode-electrolyte interface. This model, which predicts the non-linear current-voltage characteristic of the electrode, accounts for the half-cell potential, charge-transfer OV, diffusion OV, and resistance polarization.
Figure 7.1.4.1-1. Electrode-electrolyte interface model (from ref. 10).
The half-cell potential $E_{hc}$ is modeled by a DC voltage source with a voltage of $E$. The charge-transfer overvoltage is modeled by the components $C$ and $R$. $R$ is the charge transfer incremental resistance defined as

$$R_t = \frac{RT}{2F I_0} \quad \text{(small-signals)} \quad (7.1.4.1-1)$$

$$R_t = \frac{RT}{\alpha zF I} \quad \text{(large-signals)}, \quad (7.1.4.1-2)$$

where $I$ is the steady-state electrode current and

$$I = \text{area} \times J. \quad (7.1.4.1-3)$$

Small-signal conditions exist when the current is such that

$$\eta < \frac{RT}{\alpha zF} \quad . \quad (7.1.4.1-4)$$

$C$ is the double-layer incremental capacitance. Both $C$ and $R$ are frequency-independent but depend non-linearly on the steady-state electrode current.

The diffusion overvoltage is modeled by the components $R$ and $C$, which are frequency-dependent and together constitute the Warburg impedance $Z$. At steady-state and all frequencies but very low frequencies, the Warburg impedance components are given by

$$R_D = \frac{RT}{2F^2} \sqrt{\frac{2}{\omega} \frac{1}{C_0} \sqrt{D}} \quad \text{and} \quad (7.1.4.1-5)$$
\[ C_d^p = \frac{Z^2}{RT} \cdot \frac{1}{\sqrt{2\omega}} C_v \sqrt{D}. \]  

(7.1.4.1-6)

The reaction and crystallization overvoltages would be modeled by RC elements in series with \( Z \) but are not included in the model because of the complex dependence of their element values on frequency. The resistance polarization overvoltage is modeled by the resistor \( R \).

At low frequencies, the model reduces to the circuit shown in Figure 7.1.4.1-2, where the electrode impedance consists of the sum of \( R \) and \( Z \). At high frequencies, the model reduces to the circuit shown in Figure 7.1.4.1-2, where the electrode impedance consists of the sum of \( R \) and \( Z \). Figure 7.1.4.1-3 shows typical element values at a frequency of 1 kHz.

Figure 7.1.4.1-4 shows the electrode impedance of Ag-AgCl electrodes as a function of frequency. The impedance decreases with frequency. Electrolytically depositing a layer of AgCl on the electrode reduces the low-frequency impedance.

7.1.4.2 Skin-Electrolyte Interface

The skin-electrolyte interface can be modeled by the circuit shown in Figure 7.1.4.2-1. The electrolyte is modeled by the resistance \( R \) as in the electrode-electrolyte model. The skin-electrolyte junction generates a half-cell
Figure 7.1.4.1-2. Model simplifications (from ref. 10).
Figure 7.1.4.1-3. Element values at 1 kHz (from ref. 10).
Figure 7.1.4.1-4. Impedance frequency dependence (from ref. 10).
Figure 7.1.4.2-1. Skin-electrolyte interface (from ref. 51).
potential $E$ which is modeled by the DC voltage source with voltage $E$. The epidermis is modeled by the parallel combination of the resistor $R$ and the capacitor $C$. The e dermis is modeled by the resistor $R$. u

The effect of the sweat glands and ducts is accounted for by the capacitor $C$, the resistor $R$, and the DC voltage source $E$, which models the half-cell potential $p$ generated across the skin during the production of sweat; these components are paralleled with the epidermis and dermis components.

7.1.5 Deleterious Effects

Electrodes can degrade the performance of the EEG or AEP recording system through three main factors: (1) DC offset voltage; (2) impedance; and (3) motion artifact. Each of these factors in regard to how it may impair the recording system performance will now be briefly discussed.

7.1.5.1 Offset Voltage

The equilibrium half-cell potentials at the electrode-electrolyte junction and the skin-electrolyte junction result in a DC offset voltage at the amplifier input terminals which may be large compared to the EEG or the AEP and which can’t be eliminated; the offset voltage is a function of the electrolyte composition and the skin condition.

The offset voltage causes two problems: (1) for DC
recording, the offset voltage is amplified by the amplifier's large gain and may cause the amplifier output to saturate; and (2) the offset voltage changes if the electrode moves in relation to the scalp, causing motion artifact (see Section 7.1.5).

The offset voltage can be reduced, but not eliminated, by using Ag-AgCl electrodes, which produce a small and stable half-cell potential.

### 7.1.5.2 Impedance

As discussed in Section 2.2.3, the combination of the electrode impedance with the amplifier input impedance forms a voltage divider which results in signal attenuation. In order that this attenuation be minimized, the electrode impedance should be as small as possible and the amplifier input impedance should be as large as possible.

Section 2.2.3 also discussed that impedance imbalance between the electrodes in an electrode pair results in a differential noise signal (from 60-Hz power line interference or other common-mode signals) at the amplifier input which is amplified along with the EEG or AEP signal. In order that this noise signal be minimized, the difference between the electrode's impedances should be as small as possible.

The electrode impedance is a function of the skin-electrolyte junction resistance and varies from kilohms to
hundreds of kilohms depending on the condition and preparation of the skin, the electrode jelly concentration, and the time since the jelly application (28). The skin-electrolyte resistance is reduced by using an electrode jelly with a high NaCl concentration and by removing as much of the stratum corneum (skin horny layer) as possible by either rubbing the skin with an alcohol-soaked pad or scraping it with sandpaper (removing the stratum corneum shorts out the components $E$, $C$, and $R$ in the model of the skin-electrolyte junction shown in Figure 7.1.4.2-1).

7.1.5.3 Motion Artifact

When an electrode moves in relation to the skin, low-frequency noise voltages called motion artifacts (see Figure 7.1.5.3-1) are generated; these motion artifacts are due to two main factors: (1) at the electrode-electrolyte interface, the electrical double layer is disturbed, momentarily causing a charge redistribution and thus a change in the half-cell potential; and (2) motion occurs at the skin-electrolyte junction, causing the resistance and the potential generated at this junction to change.

Motion artifact due to disturbance of the electrical double layer can be reduced by using recessed-cup electrodes, which minimize motion at the electrode-electrolyte junction. Motion artifact due to motion at the skin-electrolyte junction can be reduced by removing the
Figure 7.1.5.3-1. Motion artifact (from ref. 51).
horny layer of the skin as discussed in Section 7.1.4.2 to lower the skin resistance. Motion artifact due to movement at both of these junctions can be minimized by using electrodes with light-weight and flexible leads and by securing the leads to the patient, both of which reduce the mechanical load and the motion at the junctions.

7.1.6 Silver/Silver Chloride Electrodes

The Ag-AgCl electrode material consists of either pure Ag or Pt with a deposit of Ag; the latter provides better stability and reproducibility. A porous layer of AgCl is electrolytically-deposited on the surface. This AgCl layer, which is sparingly-soluble, is essential to the proper functioning of the electrode: it maintains the proper Ag ion activity in the electrolyte at the electrode surface and it also reduces motion artifact (see Section 7.1.5).

The Ag-AgCl electrode is a member of the class of electrodes called electrodes of the second kind, which are electrodes consisting of a metal in an electrolyte that forms a compound on the metal surface consisting of the metal ions and the electrolyte anions (10). When the Ag-AgCl electrode is acting as an anode, Cl ions and Ag ions combine to form AgCl on the electrode surface; when the electrode is acting as a cathode, the Cl ions pass into solution from the AgCl layer and thereby deplete it.

The impedance of Ag-AgCl electrodes is a function of
the AgCl layer thickness, the electrode surface area, and the signal frequency. The impedance initially decreases as the AgCl thickness increases, then increases as the thickness increases further. The initial decrease is due to the modification of the charge transport process caused by the initial thickness increase, while the final increase is caused by the high resistivity of AgCl, which is on the order of $10^5$ ohm-cm. The impedance is inversely proportional to the surface area and to the signal frequency (see Figure 7.1.4.1-4).

The Ag-AgCl electrode provides three main advantages over other electrodes which contribute to its popularity in biomedical applications; these advantages are: (1) excellent electrical stability; (2) reduced motion artifact (virtually artifact-free if used in a recessed-cup configuration); and (3) small drift rate and offset potential between pairs of electrodes, providing an advantage in low-frequency recording applications.
7.2 Audio Click Generator

7.2.1 Introduction

This section will describe the design and operation of the audio click generator, a device designed and constructed by the author for producing the audio clicks for the AEP recordings.

The functions of this device are to: (1) produce a periodic pulse train synchronized to the computer clock, with a pulse width of 100 usec and a pulse amplitude sufficient to drive a set of TDH-49 headphones to 80 dB sound pressure level (SPL); (2) provide a programmable pulse period of 88 msec for the early AEP or 507.9 msec for the late AEP; (3) provide a programmable waveform morphology of either single, double, or alternating pulses; and (4) provide a programmable start/reset line which when set to reset prevents the circuit from producing pulses and when set to start enables the production of pulses.

The click generator is composed of three circuits: a reset and interface circuit (RIC), a counting circuit (CC), and an output drive and pulse combining circuit (ODPCC). Each of these circuits will now be discussed in detail.

7.2.2 Reset and Interface Circuit

This circuit, shown in Figure 7.2.2-1, performs the following functions: (1) provides an internally-generated transistor-transistor logic (TTL) clock signal or the
Figure 7.2.2-1(a). Reset and interface circuit.
Figure 7.2.2-1(b). Reset and interface circuit (continued).
buffered TTL computer clock signal, selectable by a front-panel switch, to the counting circuit; and (2) converts the +/- 10V-range DAC control signals to TTL control signals which control reset, start, and waveform characteristics (pulse period, single pulse, double pulses, and alternating pulses).

U20A buffers the computer clock signal and feeds it to S0, a front-panel single-pole double-throw (SPDT) switch which selects the internal or the computer clock. S0 is also fed by the output of U3, an LM555 timer configured as an astable multivibrator (free-running clock). U3 is the internal clock set by R8, R9, and C7 to have the following timing characteristics:

\[
\text{frequency} = \frac{1}{0.693(R8+2R9)C7} = 1 \text{ kHz and (7.2.2-1)}
\]

\[
\text{duty cycle} = \frac{1}{R8+2R9}. \quad (7.2.2-2)
\]

The selected clock is then fed from S0 to the counting circuit.

Three of the four available DAC channels are used as control lines for the various programmable functions as follows:

(1) Channel 0 = 0V output pulses

= +5V reset (no pulse output)
(2) Channel 1 = 0V  early pulse period 
  = +5V  late pulse period 
(3) Channel 2 = -5V  single pulses 
  = 0V  double pulses 
  = +5V  alternating pulses 

DAC Channel 0 connects to the positive input of U4, an 
LM361 voltage comparator, through the R10 and R11 voltage 
divider, which halves the Channel 0 voltage in order to 
protect the U4 input (8V maximum input) if Channel 0 is set 
to its maximum value of 10V. The negative input of U4 is 
fixed at +0.7V by the forward-biased diode CR1. U4 has 
complementary TTL outputs which have been labelled RESET_0 
and PRESET_0. 

RESET_0 connects to the negative-edge trigger input of 
U14B, a 9602 connected as a monostable multivibrator (one­ 
shot), and is also buffered by U18C to become RESET_1, which 
connects to the reset inputs of 74193 binary counters in 
both the CC and the ODPCC. 

PRESET is buffered by U12C to become PRESET_1, which 
connects to AND gates in the CC and ODPCC, and is also 
buffered by U12D to become PRESET_2, which connects to one­ 
shots in the ODPCC. 

These reset and preset lines coordinate the circuit 
initialization as follows. In the reset state, when DAC 
Channel 0 is high (+5V), the positive input of U4 (half of
the DAC Channel 0 voltage, i.e., +2.5V) is more positive
than the negative input of U4 (+0.7V), forcing RESET_0 high
and PRESET_0, PRESET_1, and PRESET_2 low. The following
conditions are then present:

1. U6 and U7 in the CC are prevented from counting, since
   their master reset pins, which are connected to RESET,
   are high.

2. The outputs of U12A and U12B in the CC are held low
   since PRESET_1 is low, thereby preventing any pulses
   from U9 and U11 from passing to the ODPCC.

3. In the ODPCC, the following 9602 one-shots are held in
   the reset state by PRESET_2 being low and thereby
   prevented from producing pulses: U14A, which outputs
   the first pulse for the double-click mode (and the single pulse for the single-click mode); U16A, which
   controls the delay period between the first and the second pulses in the alternating-click mode; and
   U16B, which produces the second pulse for the double-
   click mode.

4. In the ODPCC, the output of U18B is held low by
   PRESET_1 - one of U18B’s inputs - being low, thus
   preventing any pulses from passing to U19, the output
   drive amplifier.

When DAC Channel 0 changes from +5V to 0V, changing the circuit mode from reset to click production, the positive
input of U4 is more negative than the negative input of U4, forcing RESET_0 low and PRESET_0, PRESET_1, and PRESET_2 high. The following conditions then occur:

1. Since RESET is low, U6 and U7 in the CC are no longer held in the reset state and hence count the computer clock pulses.

2. Since PRESET_1 is high, U12A and U12B pass pulses from U9 or U11 to the ODPCC.

3. Since PRESET_2 is high, U14A, U16A, and U16B in the ODPCC are no longer held in the reset state and produce pulses in response to trigger pulses from the CC.

4. Since PRESET_1 is high, U18B in the ODPCC passes pulses from U14A, U16A, and U16B to U19.

5. When RESET goes low, U14B, a 9602 one-shot, produces a 10-nsec pulse (set by R39 and C19). This pulse is sent to one of the inputs of U13D, an OR gate in the CC, and, while in the high state, prevents pulses from passing from the CC to the ODPCC. The purpose of this pulse is to (1) provide a delay time to allow all of the ICs in the circuit to clear from the reset state and reach the operational state; and (2) to prevent pulses from being produced by the circuit until all of the ICs are in the operational state.

DAC Channel 1 connects to the positive input of U5, an
LM311 voltage comparator; the negative input of U5 is fixed at +0.7V by the forward-biased diode CR2. The output of U5, which is open-collector, is pulled-up to +5V by R40 and connects to U15B and U20C in the CC. U15B, U20B, U20C, and U13A in the CC are configured as an ‘electronic’ single-pole, double-throw switch: the output of U13A is either the signal at U20B pin 4 (the pulses for the early mode from U9) or the signal at U20C pin 4 (the pulses for the late mode from U11), depending upon the state of U15B’s input. When DAC Channel 0 is set to 0V, the output of U5 is at 0V, and the early-mode pulses (U20B pin 4) pass to U13 pin 3; when DAC Channel 0 is set to +5V, the output of U5 is at +5V, and the late-mode pulses (U20C pin 4) pass to U13 pin 3.

DAC Channel 2 connects to the following inputs of three LM311 voltage comparators: the positive input of U0; the negative input of U1; and the positive input of U2. The negative input of U0 is fixed at +2.5V by the voltage divider formed by R0 and R1. The output of U0 is pulled-up to +5V by R2 and connects to one of the inputs of U18A, a triple-input AND gate in the ODPCC which controls the transmission of the alternating second pulse to the output drive amplifier for the alternating-click mode. When DAC Channel 2 is at 0V (double-click mode) or -5V (single-click mode), the output of U0 is 0V and the alternating second pulse cannot pass to the output drive amplifier; when DAC
Channel 2 is at +5V (alternating-click mode), the output of U0 is +5V and the alternating second pulse can pass to the output drive amplifier.

U1 and U2 form a window comparator, which has the following transfer function:

\[
V_{out} = +5V \text{ for } V < V_{in} < V_{out} = 0 = \text{ in } = 1
\]

\[
V_{out} = 0V \text{ for } V < V_{in} \text{ or } V_{in} > V
\]

In this case, the input signal is DAC Channel 2, which is applied to the negative input of U1 and the positive input of U2. The positive input of U1 is fixed at +1V by the voltage divider formed by R3 and R4; the negative input of U2 is fixed at -1V by the voltage divider formed by R5 and R6. The outputs of U1 and U2 are tied together, pulled-up to +5V by R33, and fed to one of the inputs of U20D, a two-input AND gate in the ODPCC which controls the transmission of the second pulse at its other input to the output drive amplifier. When DAC Channel 2 is at 0V (double-click mode), the outputs of U1 and U2 are off (open) = +5V and the second pulse can pass to the output drive amplifier. When DAC Channel 2 is at -5V (single-click mode), U1’s output is open and U2’s output is low, preventing the second pulse from passing to the output drive amplifier.

7.2.3 Counting Circuit

This circuit, shown in Figure 7.2.3-1, consists of:
Figure 7.2.3-1. Counting circuit.
(1) 74193 binary counters which count the input computer clock pulses, divide the clock frequency, and produce two separate pulse trains, one with the frequency needed for the early epoch (11.35 Hz) and the other with the frequency needed for the mid/late epochs (1.97 Hz); and (2) logic to select under computer control (via DAC Channel 1) which of the pulse trains is sent to the ODPCC.

A 74193 IC can be configured as a count-down or a count-up timer; all of the 74193s in the CC are configured as count-up timers. In the count-up mode, the 74193 counts the pulses at the CPu input (pin 5) and provides four outputs (Q0 through Q3, with Q0 representing the least-significant bit and Q3 the most-significant bit) which represent the binary value of the number of pulses received at the CPu input. The maximum count is sixteen pulses; on the sixteenth pulse, the 74193 outputs a negative-going pulse at the TCu output and starts counting again. The count starts either from zero or from the binary value set by the preload lines (P0 through P3, with P0 representing the least-significant bit and P3 the most-significant bit).

The operation of the CC is as follows. After RESET_1 transitions from high to low, all 74193s are enabled and U6 begins counting the computer clock pulses. On the sixteenth pulse, U6 outputs a pulse at its TCu output and starts counting again. U7 counts the TCu pulses from U6 and outputs
a pulse at its TCu output for every sixteen TCu pulses from U6. Thus, a TCu pulse is output by U7 for every $16 \times 16 = 256$ computer clock pulses and the subcircuit U6-U7 functions as a divide-by-256 counter.

The output of U7 feeds the subcircuits U8-U9 and U10-U11, each of which is configured as a divide-by-N counter, where N is a value determined by the settings of DIP rocker switches S1 for U8-U9 and S2 for U10-U11. U8-U9 divides pulses for the early mode; U10-U11 divides pulses for the mid/late mode. By setting the division factor N, S1 and S2 control the audio click frequency, because the TCu outputs from U9 and U11 trigger one-shots in the ODPCC which generate an output audio click pulse (or double pulse) for each TCu output generated by U9 or U11.

S1 and S2 set N by setting the preload counts on U8 through U11. As discussed previously, the preload count is the initial value of the count output on a 74193, which can be any integer value between zero and fifteen and is set by applying a TTL low to the PL input. When the count output exceeds the maximum of fifteen, the 74193 starts counting again from either zero or, if the TCu output is fed back to the PL input, from the preload count. U12A feeds back the TCu output from U9 to the PL inputs on U8 and U9 and U12B feeds back the TCu output from U11 to the TCu inputs on U10.
The TCu outputs from U9 and U11 are multiplexed to U14A and U17 in the ODPCC through the programmable single-pole, double-throw relay formed by U15B, U20B, U20C, and U13A. The purpose of this relay is to select the audio frequency - early (11.35 Hz) or mid/late (1.97 Hz) - by controlling which of the TCu outputs from U9 (early) or U11 (mid/late) pass to the ODPCC. When DAC Channel 0 is at 0V, U5-7 is low, U20B-5 is high and U20C-9 is low; thus, U9's TCu output can pass through U20B to the ODPCC while U11's TCu output cannot pass through U20C and therefore cannot pass to the ODPCC. The situation is reversed when DAC Channel 0 is at +5V.

### 7.2.4 Output Drive and Pulse Combining Circuit

This circuit, shown in Figure 7.2.4-1, performs the following functions: (1) produces pulses for the single-, double-, and alternating-click modes in response to the TCu trigger signals from the CC; (2) produces a trigger signal synchronous with the leading edge of the click so that the output from the circuit can be viewed on an oscilloscope; and (3) provides either a fixed (80-dB) or variable (via rheostat R36) output amplitude.

The operation of the circuit is as follows. The TCu output from U9 (early) or U11 (mid/late) in the CC triggers
Figure 7.2.4-1. Output drive and pulse combining circuit.
U14A, a 9602 one-shot, to produce a 100-usec pulse and U17, a 74193 counter, to advance one count. This 100-usec pulse is the single-click pulse and the first pulse in the set of two pulses in the double- and alternating-click modes.

A 9602 has two outputs available: positive-going (Q) and negative-going (Q). The Q output from U14A is inverted and buffered by U15A and fed to a BNC jack on the chassis for use as an oscilloscope external trigger signal.

The Q output from U14A feeds to the trigger input of U16A, a one-shot, and one of the two inputs of U13C, a two-input OR gate. U16A, which controls the time interval between the first and the second pulse in the set of two pulses produced in the double- and alternating-click modes, triggers on the negative-going edge of the 100-usec pulse and produces a pulse with a width of \((1 \text{ msec} - 100 \text{ usec}) = 900 \text{ usec}\).

The Q output from U16A feeds to the trigger input of U16B, a one-shot. U16B triggers on the negative-going edge of the time-delay pulse from U16A and produces a 100-usec pulse which is the second pulse in the set of two pulses produced in the double- and alternating-click modes. The Q output from U16B feeds to one of the inputs of U18A, a three-input AND gate, and U20D, a two-input AND gate.

U17, U18A, U18B, U13B, U13C, and U20D are used to control which of the pulses from U16A and U16B are sent to
the output drive amplifier (U19). In the single-click mode, DAC Channel 2 is set to -5V, which forces U0-7 and U1-7 low. Since U0-7 is low, U18A-12 is low; since U1-7 is low, U20D-11 is low; and since both of the inputs to U13B are low, the output of U13B is low and hence U13C-8, which connects to the output drive amplifier, follows the state of U13C-9. Since U13C-9 is the single-click pulse from U14A, the single-click pulse is fed to the output drive amplifier.

In the double-click mode, DAC Channel 2 is set to 0V, which forces U0-7 low and U1-7 high. Since U0-7 is low, U13B-5 is low and the output of U13B follows the state of U13B-4, which is the second pulse. Thus, the second pulse is fed to U13C-10. The signal at U13C-9 is the first pulse. Since the second pulse is not on when the first pulse is and vice versa, U13C combines the two pulses to produce the double pulse which then feeds to the output drive amplifier.

In the alternating-click mode, DAC Channel 2 is set to 5V, which forces U0-7 high and U1-7 low. Since U1-7 is low, the second pulse cannot pass through U20D-12 to U13B-4, which is forced low. However, the second pulse is also fed to pin 13 of U18A, a three-input AND gate. Since U0-7 is high, the second pulse can pass to U13B-5 when U18A-1 is high. U18A-1 is the Q0 output of U17, a 74193 counter which counts the TCu outputs from the CC. Q0 changes state on each succeeding TCu output. Thus, when Q0 is low, the second
pulse cannot pass through U18A but the single pulse passes through U13C as described previously for the single-click mode. On the next TCu output from the CC, Q0 is high, the second pulse passes through U13B to U13C-10, and the double pulse passes through U13C as described previously for the double-click mode. Thus, the circuit output alternates on each succeeding TCu pulse between a single-click and a double-click.

U18B functions as a gate to prevent pulses from passing to the output drive amplifier during the reset state, as described earlier. U21A, a low-power Schottky open-collector buffer gate, and the components R34 and CR3 function to 'square-up' the pulse, i.e., decrease the transition (rise and fall) times. When U21A-1 goes low, the output of U21A (U21A-2) is pulled down to a TTL low, the voltage of which is determined by the output characteristics of U21A. When U21A-1 goes high, U21A-2 goes to a high-impedance state (open) and R34 provides the current to bias CR3, a zener diode, to its zener voltage. Because the Low-Power Schottky TTL Logic Family provides faster transition times than the Standard TTL Family, U21A decreases the pulse transition times from U18B. The output of U21A could have been pulled-up to +5V through R34 without the need for CR3, but the addition of CR3 decreases the rise time by changing the effective time constant of the output circuit.
The level of the signal sent to U19, the output drive amplifier, is controlled by the division ratio set by the combination of R35 and either R36 or R37 and R38, depending upon the setting of the front-panel switch S3. If S3 is set to "ADJUST", R36, a front-panel potentiometer connected as a rheostat, controls the signal level; if S3 is set to "CALIBRATED 80 dB", R37 and R38 control the signal level. R37, a large resistance value, and R38, a smaller resistance value, were chosen such that the audio level produced by a pair of TDH-49 headphones connected to the audio output jack was 80-dB SPL (sound pressure level; see Section 2.9.3), as calibrated at the University of Arizona Speech and Hearing Clinic. This 80-dB SPL was used for the stimulus level in the experiments.

U19, an LH0033 buffer amplifier with a voltage gain of one, provides the large current needed for driving the low-impedance headphones. This amplifier has the frequency response necessary for passing the spectrum of the click (which extends beyond 10 kHz) without distortion.
7.3 Impedance Meter

The impedance meter measures the magnitude of the impedance in the pathway of an electrode pair. This impedance includes the impedance of two electrode/electrolyte junctions, two skin/electrolyte junctions, and the volume conductor formed by the skull, cerebrospinal fluid, brain, and associated tissues. If the impedance magnitude is less than 5 kilohms, the electrode connections to the skin are considered to be good.

Figure 7.3-1 shows a schematic of the circuit, which consists of an astable multivibrator (oscillator), filters, a divider network, an amplifier, a full-wave rectifier, and an analog panel meter. The electrode pair is connected into the circuit such that one of the electrodes connects to node 5 and the other electrode connects to ground; thus, the electrode pair forms an equivalent resistance from node 5 to ground.

The oscillator section produces a 1-kHz, TTL square wave which is filtered and then fed to a parallel resistance network consisting of two branches.

One branch of the network is the electrode impedance; the other branch is a string of three series resistances: R5, R6, and R7, with R6 being a potentiometer. The tap of R6 feeds an op-amp inverting amplifier circuit and then an active full-wave bridge rectifier circuit, with the analog
Figure 7.3-1. Impedance meter schematic.
meter connected across two legs of the diode rectifier bridge.

The oscillator output signal produces an AC voltage at node 7 and is then amplified and rectified, resulting in a current which drives the panel meter. As the electrode impedance changes, the voltage at node 7 changes, causing the meter current and thus the meter deflection to change; the amount of deflection change is proportional to the amount of impedance change.

The faceplate of the meter has a scale readout in kilohms. The meter, which is actually a microammeter with a full-scale current of 100 μA, is calibrated by connecting a resistance R to the electrode input jacks and adjusting R6 until the meter indicates an impedance of R.
8.0 ANALYSIS

8.1 Signal Processing Concepts

8.1.1 The Fourier Series

The Fourier Series (FS) is used to approximate a deterministic, periodic signal as a sum of cosine and sine terms at discrete frequencies.

As originally shown by Fourier in 1822, any deterministic, periodic signal $f(t)$ with period $T$ and repetition frequency $f = \frac{1}{T}$ can be created by summing a constant and a series of sine waves with specific amplitudes $(A)$ and phases $(\phi)$ and frequencies that are integer multiples of $f$:

$$f(t) = A_0 + \sum_{n=1}^{\infty} A_n \sin(n\omega_0 t + \phi_n), \quad (8.1.1-1)$$

where $\omega = \frac{2\pi f}{T}$. $A_0$ is the DC or steady component of $f(t)$ and is equal to the mean value of $f(t)$. The terms in the summation are called harmonics: the term for $n=1$, which is the repetition frequency, is the first harmonic and is also called the fundamental; the second harmonic is the term for $n=2$; the third harmonic is the term for $n=3$, etc.

An alternative expression for $f(t)$ eliminates the phase

References for this section are (6,12,13,30,31,36,48,49).
angles by resolving each of the harmonics into a cosine term (called the in-phase, or I, component) and a sine term (called the quadrature, or Q, component), as follows:

\[ A \sin(n\omega t + \phi) = a_n \cos(n\omega t) + b_n \sin(n\omega t). \]  

(8.1.1-2)

Thus, Equation 8.1.1-1 becomes

\[ f(t) = a_0 + \sum_{n=1}^{\infty} (a_n \cos(n\omega t) + b_n \sin(n\omega t)). \]  

(8.1.1-3)

The coefficients \( a_0 \), \( a_n \), and \( b_n \), which are called Fourier spectral coefficients, are given by

\[ a_0 = \frac{1}{T} \int_{-T}^{T} f(t) \, dt, \]  

(8.1.1-4)

\[ a_n = \frac{2}{T} \int_{-T}^{T} f(t) \cos(n\omega t) \, dt, \]  

(8.1.1-5)

\[ b_n = \frac{2}{T} \int_{-T}^{T} f(t) \sin(n\omega t) \, dt. \]  

(8.1.1-6)

Equations 8.1.1-2 and 8.1.1-3 are called the trigonometric Fourier series representation of \( f(t) \):

Equation 8.1.1-2 utilizes polar coordinates whereas Equation 8.1.1-3 utilizes rectangular coordinates. At this point, it should be noted that the trigonometric Fourier series representation is valid only for real-valued \( f(t) \); complex-valued \( f(t) \) can be represented by the exponential Fourier series, which describes \( f(t) \) as a summation of
complex exponentials. However, since the EEG and AEP are real-valued, subsequent discussions will assume a real-valued f(t).

Each of the harmonics has a magnitude \( c_n \) and a phase \( \phi_n \), given by

\[
c_n = \sqrt{a_n^2 + b_n^2} \quad \text{and} \quad \phi_n = \tan^{-1}\left(-\frac{b_n}{a_n}\right).
\]

A discrete signal may be represented by the Finite Fourier series (FFS). Consider a discrete signal \( f_r \) which has been derived from a continuous signal \( f(t) \) by sampling \( f(t) \) with a sampling interval of \( dt \) and an observation interval of \( T \). \( f_r \) thus consists of \( N = \frac{T}{dt} \) sample values and the FFS representation of \( f_r \) is

\[
f_r = \frac{A_0}{2} + \sum_{k=1}^{n-1} \left[ A_k \cos(x) + B_k \sin(x) \right] + A_n \cos\left(\frac{2\pi nr}{N}\right), \quad (8.1.1)\]

where \( x = \frac{(2\pi kr)}{N} \), \( r = 0, 1, \ldots, n \); \( k = 0, 1, \ldots, n \); and \( N = 2n \). The FFS coefficients are given by

\[
A_k = \frac{1}{N} \sum_{r=-n}^{n-1} X_r \cos\left(\frac{2\pi kr}{N}\right), \quad k = 1, 2, \ldots, n, \quad (8.1.1-10)
\]
$$B_k = \frac{1}{N} \sum_{r=0}^{n-1} X_r \sin(\frac{2\pi kr}{N}), \quad k=1,2,\ldots,(n-1), \quad \text{and} \quad (8.1.1-11)$$

$$A_o = \text{average value of } f_x = \frac{2}{N} \sum_{r=0}^{n-1} X_r. \quad (8.1.1-12)$$

A Fourier spectrum is a plot of either the magnitude $c_n$ (magnitude spectrum) or the phase $\phi_n$ (phase spectrum) as a function of the angular frequency $\omega$. For deterministic, periodic signals the Fourier spectrum consists of frequency components located at discrete multiples of the basic repetition frequency; it is therefore called a discrete spectrum or a line spectrum. At each of the discrete frequencies, a vertical line is drawn with a height proportional to the value of the magnitude or phase at that frequency.

For a random stationary signal, only a portion of the infinite-duration signal can be observed. This observed portion, i.e., the observation interval $P$, introduces a periodicity, because the Fourier series representation of the signal would take $P$ as the fundamental period of the signal. Thus, due to the periodicity introduced by the finite observation interval, the Fourier spectrum of a random stationary signal consists of discrete spectral lines located at the fundamental frequency $1/P$ and its harmonics. The frequency content of the signal can therefore be
extracted from a Fourier series analysis, but since the signal is not deterministic and therefore cannot be explicitly expressed by a mathematical function, the Fourier series coefficients cannot be evaluated directly; the usual way around this problem is to analyze the frequency content by computing the discrete Fourier transform, which will be discussed in Section 8.1.3.

8.1.2 The Continuous Fourier Transform

Whereas the frequency content of periodic signals can be determined by a Fourier series analysis, the frequency content of aperiodic signals is determined by a Fourier transform (FT) analysis.

The FT is a mathematical operation which is widely used in engineering to transform the time domain representation of a signal \( f(t) \) into its frequency domain representation \( F(\omega) \) and is defined as

\[
F(\omega) = \int_{-\infty}^{\infty} f(t) e^{-j\omega t} dt. \tag{8.1.2-1}
\]

The function \( F(\omega) \), called the spectral density function of the signal \( f(t) \), represents the function \( f(t) \) as a sum of continuous sinusoidal frequency components. Thus, the spectrum of an aperiodic deterministic signal is a continuous spectrum, in contrast to the spectrum of a periodic deterministic signal, which is a discrete spectrum. Figure 8.1.2-1 illustrates the Fourier transforms of
Figure 8.1.2-1. Single pulse (from ref. 48).
periodic and aperiodic signals: Figure 8.1.2-1(d) is the
discrete spectrum produced by Fourier transforming the
periodic pulse train shown in Figure 8.1.5-1(c), and
Figure 8.1.2-1(b) is the continuous spectrum produced by
Fourier transforming the aperiodic pulse shown in
Figure 8.1.2-1(a).

The relationship between the continuous Fourier
transform $F(w)$ and the complex exponential Fourier series
coefficients $F$ is

\[ F = F(w) \bigg|_{\omega = n\omega_0}, \quad (8.1.2-2) \]

where $\omega_0$ is the fundamental frequency.

8.1.3 The Discrete Fourier Transform

The discrete Fourier transform (DFT) is a numerical
approximation to the FT for sampled signals, for which it is
used to compute the the discrete Fourier coefficients. While
the FT represents a continuous signal as a continuous sum of
exponential functions over the entire real line, the DFT
represents a sampled signal as a finite sum of exponential
functions. The defining equation of the DFT is

\[ X_n = \frac{1}{N} \sum_{k=0}^{N-1} x_k e^{-j \frac{2\pi nk}{N}}, \quad (8.1.3-1) \]

where $X$ is the output complex spectral coefficient at
$n$.
frequency \( n \); \( n \) is the discrete frequency index, with values of 0, 1, ..., \( N-1 \); \( N \) is the number of data points; \( k \) is the discrete time index; and \( x \) is the input time sequence \( x_k \) amplitude at time \( k \).

Equation 8.1.3-1 defines an \( N \)-point DFT. An \( N \)-point DFT \( X \) computes \( N \) frequency coefficients: a DC term \( X_0 \), positive frequency coefficients \( \{X_1, X_2, \ldots, X_{N/2}\} \), and negative frequency coefficients \( \{-X_{N/2+1}, X_{N/2+2}, \ldots, X_{N-1}\} \). The coefficient \( X_{N/2} \) is called the Nyquist frequency coefficient; its frequency, called the Nyquist folding frequency or simply Nyquist frequency, is the maximum signal frequency which may be recognized by sampling and is equal to half the sampling frequency (see Section 8.1.6.3).

Figure 8.1.3-1 shows an example amplitude spectrum produced by an eight-point DFT. Several important properties of the DFT spectrum are as follows. First, the negative frequency coefficients are the complex conjugates of the positive frequency coefficients:

\[
X(-n + 1) = X^*(-n - 1). \quad (8.1.3-2)
\]

Because of this property, the following two properties are true. Firstly, the magnitude spectrum has even symmetry \( \{X_n\} \) about the point \(- \frac{N}{2}\), that is,
Figure 8.1.3-1. Example eight-point DFT amplitude spectrum (from ref. 6).
Secondly, the phase spectrum has odd symmetry about the point \( N \), that is,

\[
\frac{1}{2} N < X(-1) = -\left(\frac{1}{2} N \right).
\]

A second important property of the DFT spectrum is that the spectrum is periodic with a period of \( N \), that is,

\[
X(N + 1) = X(1). \quad (8.1.3-5)
\]

This periodicity arises because the DFT operation implicitly forces the observation interval \( P = NT \) to be the signal's repetition period (see Figure 8.1.3-2) and thus imposes a periodicity on the signal which results in a periodic spectrum (see Figure 8.1.3-3).

The frequency resolution of the DFT analysis, that is, the frequency spacing between the Fourier coefficients, is given by

\[
\Delta f = \frac{1}{P}, \quad (8.1.3-6)
\]

where \( \Delta f \) is the frequency resolution (Hz) and \( P = NT \) is the record length (seconds).

If \( F(\omega) \) is the continuous Fourier transform of a truncated time signal with an observation interval of \( T \) and \( F \) is the discrete Fourier transform of the same signal, then the relation between the continuous Fourier transform and
Figure 8.1.3-2. Imposition of periodicity by DFT (from ref. 6).
Figure 8.1.3-3. Periodicity of the DFT spectrum (from ref. 6).
the discrete Fourier transform is given as

\[ F(\omega) \bigg|_{\omega = n\Omega} = T F(n\Omega), \quad (8.1.3-7) \]

where \( \Omega = \frac{2\pi}{NT} \).

In summary, then, an \( N \)-point DFT performed on an \( N \)-point discrete data sequence produces \( \frac{N}{2} + 1 \) useful frequency coefficients: a DC term \( X_0 \) and \( \frac{N}{2} \) positive frequency coefficients \( X_k \), \( k = 1, 2, \ldots, \frac{N}{2} \), which are located at \( k \) discrete frequencies of \( \Omega \).

8.1.4 The Fast Fourier Transform

The Fast Fourier Transform (FFT) is an algorithm for efficient computation of the DFT. This algorithm, first published in 1965 by Cooley and Tukey, reduces the number of arithmetic operations required for computation of the DFT and thus reduces the DFT computation time. Indeed, the time savings afforded by the FFT first made possible real-time spectral analysis in the clinical laboratory via the mini- or micro-computer. At the end of this section after the basic mechanics of the FFT algorithm have been discussed, the number of arithmetic operations required for direct calculation of the DFT will be compared to the number of operations required for calculation of the DFT via the FFT.
Various versions of FFT algorithms exist; the two main classes of algorithms are the decimation-in-time (DIT) and decimation-in-frequency algorithms. The algorithm used in this experiment was a radix-2 DIT algorithm and is therefore the algorithm which will be discussed in this section.

In the radix-2 DIT algorithm, the term 'radix-2' denotes that \( N \), the total number of data points, is a power of 2, i.e., \( N = 2^r \), where \( r \) is an integer. This algorithm is based on the principle that any \( N \)-point DFT, where \( N \) is a power of 2, can be decomposed into a sum of two \( \frac{N}{2} \)-point DFTs, each of which can be decomposed into a sum of two \( \frac{N}{4} \)-point DFTs, and so on. This process of decomposition continues until the original \( N \)-point DFT is finally broken down into the sum of 2-point DFTs.

The decomposition process will now be discussed. Let \( x(n) \) be the input sequence of length \( N \) sample points. \( X(k) \), the DFT of \( x(n) \), is defined as

\[
X_k = \frac{1}{N} \sum_{n=0}^{N-1} x(n) W_n^k, \tag{8.1.4-1}
\]

where \( k \) is the discrete frequency index, with values of 0, 1, \( \ldots \), \( N-1 \), and \( W \) is the weighting factor, given by

\[
W_n = e^{-j\frac{2\pi}{N}}. \tag{8.1.4-2}
\]

Now define the following subsequences:
$$x(n) = x(2n)$$

1

= sequence of even terms of $x(n)$ and (8.1.4-3)

$$x(n) = x(2n+1)$$

2

= sequence of odd terms of $x(n)$, (8.1.4-4)

where $n = 0, 1, ..., \frac{N}{2} - 1$.

Note that $x(n)$ can be written as the sum of $x(2n)$ and $x(n)$:

1

$$x(n) = x(n) + x(n), \text{ for } n = 0, 1, ..., \frac{N}{2} - 1. \quad (8.1.4-5)$$

2

Thus, $X(k)$ can be written as

$$X(k) = \frac{1}{N} \sum_{n=0}^{\frac{N}{2}-1} x(2n) W_N^{2nk} + \frac{1}{N} \sum_{n=0}^{\frac{N}{2}-1} x(2n+1) W_N^{(2n+1)k} \quad (8.1.4-6)$$

$$= \frac{1}{N} \sum_{n=0}^{\frac{N}{2}-1} x(2n) W_N^{2nk} + W_N^k \frac{1}{N} \sum_{n=0}^{\frac{N}{2}-1} x(2n+1) W_N^{nk}. \quad (8.1.4-7)$$

Since $W_N^N = W_N^{N/2}$,

$$X(k) = \frac{1}{N} \sum_{n=0}^{\frac{N}{2}-1} x(n) W_N^{nk} + W_N^k \frac{1}{N} \sum_{n=0}^{\frac{N}{2}-1} x(2n+1) W_N^{nk} \quad (8.1.4-8)$$

$$= \frac{1}{N} \sum_{n=0}^{\frac{N}{2}-1} x(n) W_N^{nk} + W_N^k \frac{1}{N} \sum_{n=0}^{\frac{N}{2}-1} x(2n+1) W_N^{nk} \quad (8.1.4-9)$$

$$= X(k) + W_N^k X(k), \quad (8.1.4-10)$$
where \( X(k) \) is the \((-\)\)-point DFT of even samples of \( x(n) \) and 
\[
X(k) = \sum_{n=0}^{N/2} x(2n) e^{-j2\pi nk/N},
\]
\( k = 0, 1, \ldots, N/2 - 1 \) for even samples of \( x(n) \).

\[ X(k) \]
\( k = 0, 1, \ldots, N/2 - 1 \)

Thus, the original \( N \)-point DFT has been decomposed into
\[ X(k) \]
\( k = 0, 1, \ldots, N/2 - 1 \)

the sum of two \((-\)\)-point DFTs. Each of these \((-\)\)-point DFTs
\[ X(k) \]
\( k = 0, 1, \ldots, N/2 - 1 \)
can in turn be decomposed into the sum of two \((-\)\)-point DFTs, and so on, until only two-point DFTs remain.

Equation 8.1.4-10 can be simplified to reduce the number
\[ X(k) \]
\( k = 0, 1, \ldots, N/2 - 1 \)
of DFTs required for the computation of \( X(k) \), where \( k \) ranges
\[ X(k) \]
\( k = 0, 1, \ldots, N/2 - 1 \)
from 0 to \( N - 1 \). Since \( W = -W^N \),
\[ X(k) = X(k) + W \sum_{n=0}^{N/2} x(2n) e^{-j2\pi nk/N}, \]
\( k = 0, 1, \ldots, N/2 - 1 \) and
\[ X(k + N/2) = X(k) - W \sum_{n=0}^{N/2} x(2n) e^{-j2\pi nk/N}, \]
\( k = 0, 1, \ldots, N/2 - 1 \).

Thus, the number of DFTs is reduced from \( N \) to \( N/2 \).

Equations 8.1.4-11 and 8.1.4-12 are known as the butterfliy computation and can be represented by the signal flow graph of Figure 8.1.4-1. The factor \( W \) is called the \( N \) twiddle factor. The two input nodes of the butterfly are
Figure 8.1.4-1. Butterfly signal flow graph (from ref. 49).
called the primary node and the dual node: the dual node is the node that gets multiplied by the twiddle factor. The butterfly computation is the core computation of the FFT: the entire FFT is performed by computing butterflies and combining them in patterns determined by the particular FFT algorithm.

Thus, the general FFT procedure for computation of an N-point DFT is as follows: (1) perform two-point DFTs via butterfly computations on the input sequence; (2) perform four-point DFTs via butterfly computations on the outputs of the two-point DFTs; and (3) continue this process until N-point DFT coefficients result.

Figure 8.1.4-2 shows a signal flow graph for an FFT computation of an eight-point DFT. As can be seen in Figure 8.1.4-2, the output sequence is sequentially ordered, while the input sequence is not. Each sequential set of butterfly computations is called a stage; each stage has \( \frac{N}{2} \) butterflies. Within a stage, a set of butterflies which share previous stage butterflies as input sources is called a group. Thus, in Figure 8.1.4-2, Stage 1 has four groups of one butterfly each, Stage 2 has two groups of two butterflies each, and Stage 3 has one group of four butterflies. The spacing between butterfly input nodes is called the dual node spacing; both the dual node spacing and the twiddle factor exponent depend on the group and stage of
Figure 8.1.4-2. FFT computation of eight-point DFT (from ref. 49).
The FFT algorithm contains two main sections: a bit-reversing section and a butterfly computation section. The bit reversing section rearranges the input sequence in memory into the bit-reversed order required for the input stage. The butterfly computation section proceeds stage by stage to calculate the butterflies, starting at the input stage and working toward the output stage. At each stage, the points from memory to participate in the butterfly calculations are selected, the weighting factors for that stage are calculated, and, for each weighting factor in that stage, all of the butterflies in that stage that use that particular weighting factor are calculated.

The leftmost (input) stage is stage 1; the rightmost stage is \( \log N \). At the \( L \)th stage, the increment between \( \frac{N}{2^L} \) weighting factor exponents is \( \frac{N}{2^{L-1}} \) and the butterfly widths are \( 2^{L-1} \), which is also the memory address separation of the points which participate in the butterfly calculation. Each \( \frac{N}{2} \) stage requires \( \frac{N}{2} \) butterfly calculations.

The number of complex multiplications is used as a figure of merit to determine the computational savings afforded by the FFT over the DFT. The number of complex multiplies needed to compute the DFT via Equation 8.1.3-1 is \( \frac{N}{2} \); the number needed to compute the FFT is equal to the
total number of butterfly calculations required times the number of multiplications per butterfly, which is one. The total number of butterflies is equal to the number of stages \( N \) (log \( N \)) times the number of butterflies per stage \( \frac{N}{2} \); hence, the total number of complex multiplications required in the FFT is \( \frac{N}{2} \log N \). As shown in Table 8.1.4-1 for different values of \( N \), the difference in the number of complex multiplications (and hence the difference in computation time) becomes increasingly significant as \( N \) increases.

8.1.5 Sampling

Sampling is the conversion of an analog signal to a discrete signal and is performed by an analog-to-digital converter (ADC). An ADC takes an analog signal input \( f(t) \) and produces at its output a sampled signal \( f_s(t) \) consisting of a set of uniformly-spaced discrete samples in time, usually in digital representation.

The process of analog-to-digital conversion can be represented mathematically as the multiplication of the input signal \( f(t) \) by the periodic gate function \( f_s(t) \):

\[
f_s(t) = f(t) \ p_T(t).
\]

(8.1.5-1)

The periodic gate function \( p_T(t) \), shown in Figure 8.1.5-1, consists of periodically-repeating square pulses with period \( T \), pulse width \( \tau \), and amplitude 1. Ideally,
<table>
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</table>

Table 8.1.4-1. FFT versus DFT computational savings (from ref. 49).
Figure 8.1.5-1. Periodic gate function (from ref. 48).
p (t) would have \( r = 0 \) (in which case it would be a periodic \( T \) impulse function instead of a periodic gate function); however, in practice, the sampling window \( r \) can only be made finite in width and thus \( p (t) \) is modeled as a gate function rather than an impulse function.

The spectrum of the sampled signal is found as follows. First, since \( p (t) \) is periodic, it is written as a Fourier series:

\[
P_T(t) = \sum_{n=-\infty}^{\infty} P_n e^{j\omega_0 t}.
\]  

Thus,

\[
f_s(t) = f(t) \sum_{n=-\infty}^{\infty} P_n e^{j\omega_0 t}.
\]  

Next, the Fourier transform of the above equation is taken and, after some manipulation, the result is

\[
F_s(\omega) = P_0 F(\omega) + \sum_{n=-\infty}^{\infty} P_n F(\omega - n\omega_0), \quad n \neq 0.
\]  

Thus, the spectrum of a sampled signal consists of the spectrum of the input signal repeated at multiples of the sampling frequency (see Figure 8.1.5-1).

8.1.6 Spectral Analysis

8.1.6.1 Power Spectral Density

The power spectral density (PSD) function \( S(f) \), also called the auto spectral density function, describes the distribution of the time-averaged power in a signal \( f(t) \)
over frequency.

The time-averaged power $P$ in a signal $f(t)$ is given as

$$ P = \lim_{T \to \infty} \frac{1}{T} \int_{-\frac{T}{2}}^{\frac{T}{2}} |f(t)|^2 dt. \quad (8.1.6.1-1) $$

The PSD function $Sf(\omega)$ is defined such that its integral yields the time-averaged power $P$ in $f(t)$:

$$ P = \frac{1}{2\pi} \int_{-\infty}^{\infty} S_f(\omega) d\omega. \quad (8.1.6.1-2) $$

Several formulations exist for the mathematical definition of $Sf(\omega)$. Currently, the most popular method of defining $Sf(\omega)$ is the Fourier transform method, due to the development of the fast Fourier transform (see Section 8.1.4) and the minicomputer, which have together made possible the fast computation of the discrete Fourier transform (see Section 8.1.3) in both the clinical and research laboratories.

For a signal $f(t)$ having a Fourier transform $F_T(\omega)$ over the interval $(-\frac{T}{2}, \frac{T}{2})$, the Fourier transform method of defining $Sf(\omega)$ is

$$ Sf(\omega) = \lim_{T \to \infty} \frac{|F_T(\omega)|^2}{T}, \quad (8.1.6.1-3) $$

where $T$ is the observation interval and $|F_T(\omega)|$ is the magnitude of $F_T(\omega) = a_T(\omega) + jb_T(\omega)$ and is given as
The power spectrum, or simply spectrum, of a signal is a plot of $S(w)$ versus frequency. From Equation 8.1.6.1-3, the power spectrum contains magnitude information only; all phase information is lost.

For a digitized signal, the observation interval $T$ becomes the observation interval $P = NT$, where $N$ is the number of data points; the DFT $F_N(w)$ replaces the continuous Fourier transform $F(w)$, where $F_N(w)$ is the DFT of $f(kT/N)$ for $k = 0, 1, \ldots, N - 1$; and Equation 8.1.6.1-3 becomes

$$S_N(\omega_n) = \lim_{P \to \infty} \frac{|F_N(\omega_n)|^2}{P}. \quad (8.1.6.1-5)$$

### 8.1.6.2 The Periodogram

To compute the PSD from Equation 8.1.6.1-5 requires an infinite observation interval $P$. In practice, only a finite observation interval can be used and thus only an estimate $\hat{S}_N(\omega_n)$ of the actual PSD $S(\omega)$ can be computed. With a finite observation interval, Equation 8.1.6.1-5 becomes

$$\hat{S}_N(\omega_n) = \text{estimate of } S_N(\omega_n) = \frac{|F_N(\omega_n)|^2}{P}. \quad (8.1.6.2-)$$

Equation 8.1.6.2-1 defines the periodogram. The periodogram is used to compute an estimate of the PSD for both deterministic and random signals; however, the periodogram estimate is biased (see Section 8.1.6.4) due to
leakage and is inconsistent (see Section 8.1.6.5). Other possible problems with spectral analysis techniques are aliasing (see Section 8.1.6.3) and instationarity of the data (see Section 2.5).

8.1.6.3 Aliasing

As discussed in Section 8.1.5, the spectrum of a sampled signal $F(f)$ consists of the spectrum of the original signal $F(f)$ repeated at multiples of the sampling frequency $f$, where the spectrum replicas at each sampling frequency multiple are weighted in amplitude by the coefficients of the sampling waveform Fourier series (see Figure 8.1.5-1).

Now assume the signal $F(f)$ is band-limited such that the frequency $B$ is the highest frequency present in $F(f)$ and consider the effect of increasing $B$ while keeping $f$ constant. At $B = f / 2$, the spectrums of adjacent spectral replicas are just about to overlap. When $B > f / 2$, the spectrums of adjacent spectral replicas overlap (see Figure 8.1.6.3-1); thus, high frequencies in one spectral replica overlap into the adjacent spectral replica such that they appear to be (or are aliased as) lower frequencies; this phenomenon is known as aliasing and results in signal distortion.

The frequency $f / 2$ is called the Nyquist folding frequency: it is the maximum frequency which may be
Figure 8.1.6.3-1. Aliasing (from ref. 48).
recognized by equidistant sampling. No procedures exist to compensate for aliasing after sampling; therefore, signals with frequency greater than the Nyquist frequency must be removed from the data prior to digitizing, either by filtering the data with analog low-pass filters (anti-aliasing filters) before the data is input to the ADC, or by choosing the sampling frequency such that the Nyquist frequency is greater than the highest frequency actually present in the data (oversampling). If the data is filtered, signals with frequencies greater than the Nyquist frequency must have their amplitudes in volts attenuated by a factor of at least twenty in order to avoid distortion due to aliasing.

8.1.6.4 Bias, Leakage, and Windowing

If \( x \) is an estimate of a parameter \( c \) (for example, \( x \) could be the periodogram estimate of the PSD \( c \) at a particular frequency), then the bias of the estimate \( x \) is defined as

\[
\text{bias} = E(x) - c ,
\]

where \( E(x) \) is the expected value of \( x \).

A desirable characteristic for the estimator \( x \) is that \( x \) be an unbiased estimator: that is, \( E(x) = c \), or the ensemble mean of the parameter estimate equals the parameter. The less bias the estimate has, the closer the estimate of the parameter is to the true value of the parameter.
The periodogram estimate is asymptotically unbiased, which means that it is only unbiased for an infinitely-large sample size $N$: if $N$ is not infinitely large, the periodogram estimate is biased.

The periodogram bias arises because of the restricted observation interval $P = NT$. When a time series $f(t)$ is sampled, the sampling of $f(t)$, which is assumed to be a series of infinite duration, must of necessity be restricted to a finite observation interval. The effect of truncating the observation of $f(t)$ to the finite observation interval $P$ is the same as though $f(t)$ were multiplied by the rectangular gate function $g(t)$ (see Figure 8.1.6.4-1), producing a truncated function $f(t)$:

$$f(t) = f(t)g(t), \quad (8.1.6.4-2)$$

where $g(t) = 1$ for $|t| <= \frac{NT}{2}$ and $g(t) = 0$ for $|t| > \frac{NT}{2}$. The gate function $g(t)$ is also called a window function due to the effect it produces of looking at the infinite-duration time series $f(t)$ through a window (the finite observation interval $P$).

$F(\omega)$, the Fourier transform of $f(t)$, becomes

$$\hat{f}(\omega) = \int_{-\infty}^{\infty} f(t)g(t)e^{-j\omega t} dt = F(\omega) \otimes G(\omega). \quad (8.1.6.4-3)$$

Thus, the effect of the window in the frequency domain is
Figure 8.1.6.4-1. Mainlobe window (from ref. 12).
that \( F(w) \), the Fourier transform of \( f(t) \), is convolved with \( G(w) \), the Fourier transform of \( g(t) \), called the spectral window.

Ideally, in order that \( F(w) \) give a correct measure of \( F(w) \), \( G(w) \) should be an impulse function. However, as shown in Figure 8.1.6.4-1, \( G(w) \) is actually a \( \sin x / x \) function, given as

\[
G(\omega) = T \frac{\sin(\frac{\omega T}{2})}{\left(\frac{\omega T}{2}\right)}. \tag{8.1.6.4-4}
\]

Due to the \( \sin x / x \) function, the sidelobes of \( G(w) \) decay slowly: the sidelobes decay proportionately to \( 1 / kr \), where \( \omega = k \, d\omega \) and \( \omega = 2\pi / T \). The first sidelobe is 13 dB below the main sidelobe; thus, if a frequency component at the main lobe frequency and a frequency component at the first sidelobe frequency differ by 13 dB or more, they will be inseparable (because they fit in the envelope of \( G(w) \)).

This slow sidelobe decay of \( G(w) \) causes power present in the main lobe to leak into adjacent frequency bands, inducing correlation between the Fourier coefficients of neighboring frequency bands and thus distorting the frequency domain representation of \( F(\omega) \); this effect is called leakage and results in bias (see Section 8.1.6.4).

Leakage can be reduced by smoothing, also called rounding off, which can be accomplished by either:
(1) modifying the time-domain rectangular gate window; or
(2) modifying the frequency-domain spectral window, which is
the filter shape of the main lobe (see Figure 8.1.6.4-1).

The time-domain window modification procedure consists of multiplying the time series data over the interval 0 to P
by a window function. A window function has a value of one
over most of the interval from 0 to P, but instead of
transitioning sharply to zero at the endpoints t=0 and t=P
as the rectangular gate function does, it slopes gradually.
Numerous window functions exist, all differing in the manner
in which the slope tapers from 0 to 1 at the interval
endpoints.

By tapering gradually at the interval endpoints, the
window function obviates the sharp discontinuities of the
rectangular gate function which, by the Gibbs phenomenon,
cause the sin x / x side lobe pattern which results in
leakage. The window function thus reduces leakage by
reducing the side lobe levels.

The spectral window modification procedure consists of
convolving the Fourier-transformed data with a suitably
chosen spectral window and will be discussed further in
Section 8.1.6.6. Note that multiplication in the time domain
is equivalent to convolution in the frequency domain and
thus the two window modification procedures are equivalent.

A tradeoff exists between frequency resolution and bias.
A window effectively broadens the main lobe filter width, thus reducing frequency resolution. Concomitantly, the window reduces side lobe levels, which reduces leakage. Hence, in order that the bias be reduced, some frequency resolution is sacrificed.

8.1.6.5 Consistency

Consistency is a property related to the asymptotic (i.e., large sample size) behavior of an estimate: an estimate is consistent if its variance decreases to zero as the sample size becomes infinitely large.

The amount of uncertainty in an inconsistent estimate is described by a parameter called the standard error, which is equal to the standard deviation of the estimate divided by the mean of the estimate. Calculation of the standard error requires a knowledge of the estimate probability distribution: for PSD estimates, the distribution is a $\chi^2_k$ distribution, where $k$ is the number of degrees of freedom, and the standard error is given by

$$\text{standard error} = \sigma = \frac{\sigma^2}{u_k} = \sqrt{-} \quad (8.1.6.5-1)$$

where $\sigma$ is the estimate standard deviation, $u$ is the estimate mean, and $k$ is the number of degrees of freedom.

If the number of samples is greater than or equal to thirty, the $\chi^2_k$ distribution tends toward a Gaussian $\mathcal{N}$ distribution, for which $k$ is given by...
\[ k = 2BP, \quad (8.1.6.5-2) \]

where \( B \) is the resolution bandwidth and \( P = NT \) is the record length.

The resolution bandwidth \( B \) is the minimum discernible frequency difference between spectral components: components closer together than \( B \) in frequency cannot be distinguished. Statistically, \( B \) is the minimum frequency span between spectral components that makes the components orthogonal (statistically independent). For a DFT analysis, \( B \) is a function of the rectangular gate window bandwidth (which is \( \frac{2}{P} \); see Section 8.1.6.4) and the number of Fourier components \( P \) averaged (in the process called frequency band averaging, to be discussed below): without averaging, \( B \) is equal to one-half the gate window bandwidth, or \( \frac{1}{P} \); with averaging, \( B \) increases in proportion to the number of Fourier components averaged. Thus, \( B \) is given as

\[ B = \frac{m}{P}, \quad (8.1.6.5-3) \]

where \( m \) is the number of Fourier components averaged.

For a Gaussian process, then, the standard error is

\[ \text{standard error} = \sqrt{\frac{2}{k}} = \sqrt{\frac{2}{2BP}} = \sqrt{\frac{1}{m}}. \quad (8.1.6.5-4) \]

If no averaging is performed (\( m = 1 \)), the standard error is 100% and the estimate is inconsistent (unreliable).
In order to improve the consistency of the estimates (reduce the standard error), the degrees of freedom must be increased, which can be accomplished by: (1) increasing the effective record length $P$ by a process called ensemble averaging (EA); (2) increasing the effective resolution bandwidth $B$ by a process called frequency band averaging (FBA); or (3) a combination of EA and FBA. Both the EA and FBA processes are also referred to as smoothing.

EA (smoothing over ensembles) consists of taking $m$ epochs of data, each with a record length of $P = NT$, computing the power spectrum of each epoch, and then averaging the spectrums to yield the smoothed spectrum. The formula for EA is

$$\hat{S}(k) = \frac{1}{m} \sum_{l=1}^{m} S_l(k), \quad (8.1.6.5-5)$$

where $\hat{S}(k)$ is the smoothed PSD spectral estimate, $m$ is the number of epochs, $S_l(k)$ is the PSD estimate from the $l$th spectrum, and $k$ is the discrete frequency index, with values of $0, 1, \ldots, (N-1)$. The resulting smoothed spectrum in EA has $2m$ degrees of freedom. The process on which EA is performed is assumed to be stationary, since the statistics of the epochs are being averaged together.

FBA (smoothing over frequency) consists of taking $l$ neighboring spectral estimates and averaging them together
to yield one spectral estimate which is the average of the \( l \) estimates and lies at the midpoint of the frequency interval spanned by the \( l \) estimates. A simplified formula for FBA is

\[
\hat{S}(i) = \frac{1}{l} (S(k) + S(k+1) + \ldots + S(k+l-1)), \quad (8.1.6.5-6)
\]

where \( S(i) \) is the smoothed PSD spectral estimate, \( l \) is the number of raw (unsmoothed) spectral estimates to be averaged, \( S(k) \) is the raw PSD estimate, \( k \) is the discrete frequency index of the raw PSD spectrum, and \( i \) is the discrete frequency index of the smoothed estimate, defined as the midpoint of the range from \( k \) to \( (k+l-1) \). The FBA formula is a simple moving arithmetic average, equivalent to low-pass-filtering the periodogram, and changes the effective main lobe filter shape to trapezoidal. This formula can be generalized to the following formula, which consists of convolving the raw spectral estimates with a spectral window:

\[
\hat{S}(i) = \frac{1}{m} \sum_{i=-m}^{m} a(i) S(k-i), \quad k=0,1, \ldots, \frac{N}{2}, \quad (8.1.6.5-7)
\]

where \( a(i) \) is the \( i \)th spectral window weight. An example of a spectral window is the Hanning window, for which \( m = 1 \),

\[
a(0) = \frac{1}{2}, \quad a(-1) = a(1) = \frac{1}{4}.
\]

In FBA, each of the resulting smoothed estimates is a \( \chi \) variable with approximately 2\( l \) degrees of freedom. The
penalty for using FBA is a decrease in frequency resolution.

EA is the averaging of complete sets of spectra, each computed from a different segment of the time sequence. The time sequence is divided into m segments which each consist of N points. N is chosen from the resolution requirements:

\[ P = \frac{N}{T} \text{ s s} \]

Hence,

\[ N_s = \frac{1}{bT}. \quad (8.1.6.5-9) \]

The smoothed estimate \( \hat{S}(k) \) is computed as

\[ \hat{S}_x(k) = \frac{1}{m} \sum_{l=1}^{m} \overline{S}_1(k), \quad k=0,1,\ldots, \frac{N_s}{2} - 1, \quad (8.1.6.5-10) \]

where \( S_1(k) \) is the kth spectral component of the spectrum computed from time segment l. The result of EA is a spectrum consisting of \( \frac{N}{2} \) components at frequencies of

\[ 0, b, 2b, \ldots, (\frac{N}{2})b. \]

The random process for which the EA PSD estimate is computed is assumed to be stationary, since the statistics of each of the segments are being averaged. The resulting smoothed PSD estimate has \( n = 2m \) DOF.
8.1.6.6 Computational Procedure

This section will summarize the procedure to be followed for the computation of magnitude, phase, and power spectra of a discrete-time signal \( f(k) \). \( f(k) \) is assumed to be a digitized signal consisting of \( N \) samples for \( k=0 \) to \( N-1 \). \( T \) is the sampling interval (in seconds) and \( P = NT \) is the observation interval (in seconds).

Step 1

Remove any DC offset from \( f(k) \) by centering \( f(k) \) around zero. Thus, compute the mean of \( f(k) \) over \( P \) and subtract the mean from each of the \( N \) samples of \( f(k) \).

Step 2

In order to reduce leakage, taper \( f(k) \) by multiplying \( f(k) \) by a suitably-chosen window \( w(k) \) (see Section 8.1.6.4), yielding the tapered function \( a(k) \).

Step 3

Compute the DFT of \( a(k) \), which yields a DC term and \( N/2 \) complex positive-frequency coefficients \( b(k) = r(k) + ji(k) \), where \( r(k) \) is the real part of \( b(k) \) and \( i(k) \) is the imaginary part of \( b(k) \). The coefficients are located at discrete frequency indices from \( k = 0 \) (DC term) to \( k = N/2 \) (Nyquist frequency term), which correspond to discrete frequencies of \( k / P \).
Step 4

Calculate the following "raw" spectrums:

a. power spectrum (periodogram):

\[ P(k) = b(k) + i(k). \]  
(8.1.6.6-1)

b. magnitude spectrum:

\[ M(k) = \sqrt{P(k)}. \]  
(8.1.6.6-2)

c. phase spectrum:

\[ \phi(k) = -\tan^{-1} \frac{i(k)}{b(k)}. \]  
(8.1.6.6-3)

Step 5 (for random data)

To improve the consistency of the estimates, perform either: (1) frequency band averaging, by convolving the spectral estimates with a spectral window (Equation 8.1.6.5-7); or (2) ensemble averaging, by repeating Steps 1 through 4 for each epoch and then averaging the spectral estimates at each frequency from each epoch's spectrum (Equation 8.1.6.5-5).

Step 6

Multiply \( M(k) \) by \( G \) and \( P(k) \) by \( G' \), where \( G \) is the voltage gain of the system from the electrodes to the output of the ADC.

8.1.6.7 EEG Spectral Analysis

Spectral analysis of the EEG, which is a random signal,
follows the procedure for spectral analysis given in Section 8.1.6.6 with the inclusion of Step 5 for random data. A critical parameter in EEG spectral analysis is $P$, the time length of each of the epochs used in ensemble averaging. The choice of the epoch length is a tradeoff between two factors: stationarity and frequency resolution. If the epoch length is too long, the statistics of the EEG will vary too much over the epoch, and the epoch will therefore be non-stationary. In fact, the actual length of time over which the epoch is stationary is determined by the subject's behavioral state. With subjects under controlled and equivalent behavioral conditions, various studies have shown that the length of time over which the epoch is stationary varies between five and sixty seconds.

On the other hand, the frequency resolution, which is equal to $\frac{1}{P}$, will be inadequate - that is, not small enough - if the epoch length is too small. Thus, the epoch length should be short for stationarity but long for frequency resolution. In clinical practice, it is common to use epoch lengths of five or ten seconds.

If ensemble averaging and frequency band averaging are not employed, each spectral estimate has a Chi-square distribution with only two degrees of freedom (DOF). This low number of DOF results in a high standard error (see Section 8.1.6.5). To get acceptable spectral estimates, at
least 60 DOF are needed. If only ensemble averaging is used, an ensemble of 30 epochs results in 60 DOF. In practice, it is common to use a combination of ensemble averaging and a spectral window (frequency band averaging), although a spectral window results in a decreased frequency resolution.

A typical clinical EEG has the following parameters (Lopes da Silva, 1982): (1) N (number of points) = 1024; (2) \( P = \) epoch length = 10 seconds; (3) number of epochs used in ensemble averaging = 10; (4) an elliptic spectral window five sample points wide for frequency band averaging; (5) an equivalent resolution bandwidth of 0.5 Hz; and (6) 93 DOF per spectral estimate.

### 8.1.6.8 AEP Spectral Analysis

Spectral analysis of the AEP, which is modeled as a deterministic signal, follows the procedure for spectral analysis given in Section 8.1.6.6 with the exclusion of Step 5 for random data.

An important note about AEP spectral analysis via the DFT is that the maximum observation interval \( P \) is equal to the interstimulus interval and thus the maximum frequency resolution is equal to the stimulus frequency. Thus, the stimulus frequency is chosen based on not only the considerations given in Section 2.7.3 (for instance, its effects on the resulting AEP peak latencies and amplitudes), but also the desired DFT frequency resolution.
8.2 Analysis Software

The program HAC_WINDO W, written by the author, was used to analyze the brain wave data. The main purpose of this program, which was written in FORTRAN software and run on a VAX 11/780 mainframe VAX/VMS operating system, was to perform Fast Fourier Transforms (FFTs) on the brain wave data files, calculate magnitude, phase, and power spectra from the FFTs, and calculate spectral edges of each of the spectra.

The program was written to output data in a format suitable for use with DECGRAPH, a business graphics package. For this purpose, the program outputs x-axis and y-axis data into graphics load files, which are files with a .GRL extension. The format for the graphs is contained in a separate file called a graph description file, which has a .GRG extension. This file is created by running DECGRAPH interactively (from a terminal), selecting the desired graph format, and storing the format in the graph description file.

The graphs are created by running DECGRAPH either interactively or noninteractively (from a batch job). DECGRAPH uses the graphics load files and the graph description files to create graphs in sixel format; the sixel graphs have a .GRS extension. A DEC command procedure called GRAPH SIXEL.COM was used to tailor the sixel graphs for printing on a DEC LN03 laser printer.
The program HAC_WINDOW starts by requesting keyboard input from the user. The user selects: (1) whether a frequency domain analysis will be performed; (2) whether an autocorrelation analysis will be performed; (3) the desired spectral edge; (4) Phase 1 or Phase 2; (5) the analysis mode: all subjects in one phase, one subject, or one file; (6) the Phase 1 study days analyzed: all eight, or four (the baseline and the three steady-states); (7) the filetype: EEG, early AEP, or mid/late AEP; (8) whether the input time series will be graphed; and (9) whether the magnitude, phase, and power spectra will be plotted. The following discussion will assume that the all-subject analysis mode is selected, as this mode was used almost exclusively for the analyses.

The program contains the following three nested DO loops, given in the order in which they occur in the program: (1) a 'click loop' which, for the AEP, loops once for each AEP click type (single or double) and, for the EEG, loops only once; (2) a 'subject loop', which loops once for each of the study subjects in the selected phase; and (3) a 'day loop', which loops once for each of the study days in a particular phase.

The function of the click loop is to make the program execute twice (except for keyboard input) if an AEP is being analyzed. Thus, the program really starts at the subject
loop. At the beginning of this loop, some of the output files for the analysis results are opened. Table 8.2-1 delineates the output files created and the contents of each of the files.

The day loop then starts. At the beginning of this loop, the subject’s brain wave data file for the loop study day is read from the hard disk. For the EEG, the subroutine READ_EEG is called; this subroutine decimates the sampling frequency by four by reading the first point of the data (which is a single 4096-point epoch) and every fourth data point thereafter into a 1024-point array AMEAN; thus, the data length is cut by four, reducing the processing requirements.

For the AEP, time-locked signal averaging with artifact rejection is performed on the data (which consists of interlaced single- and double-click epochs of length 256 points for the early AEP and 1024 points for the mid/late AEP) as the data is read in. The signal averaging and artifact rejection are performed as follows:

1. Read a block (early: 4096 points; mid/late: 1024 points) of data into the temporary storage array IDTBUF. For the mid/late AEP, the block read depends on the click loop count (one for single-click; two for double-click). The single-click block is the first stored block and subsequent single-click blocks are located every other block thereafter;
<table>
<thead>
<tr>
<th>FILENAME</th>
<th>CONTENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>xxx_PHa_DAYb_c_TIME.GRL</td>
<td>BRAIN WAVE (TIME) DATA</td>
</tr>
<tr>
<td>xxx_PHa_DAYb_c_d.GRL</td>
<td>SPECTRAL DATA</td>
</tr>
<tr>
<td>xxx_c_d_yy_NORM.GRL</td>
<td>SPECTRAL EDGE VS. STUDY DAY DATA</td>
</tr>
<tr>
<td>xxx_c_d_yy_VS_CONC_NORM.GRL</td>
<td>SPECTRAL EDGE VS. CONCENTRATION DATA</td>
</tr>
<tr>
<td>xxx_c_d_yy_AVER.GRL</td>
<td>SPECTRAL EDGES OF AVERAGE BASELINE AND DRUG SPECTRUMS (PHASE 2)</td>
</tr>
<tr>
<td>xxx_c_d_yy_MEAN_SE.GRL</td>
<td>MEANS AND VARIANCES OF BASELINE SPECTRAL EDGES AND DRUG SPECTRAL EDGES (PHASE 2)</td>
</tr>
</tbody>
</table>

**LEGEND**

xxx = SUBJECT'S INITIALS

a = 1 OR 2

b = 0 - 5, 10, 15 (PHASE 1)

= 0 - 2, 5, 6, 9, 12 - 16 (PHASE 2)

c = EEG, ELY_SGL, ELY_DBG, LAT_SGL, OR LAT_DBG

d = MAG, PHA, OR POW

yy = SPECTRAL EDGE PERCENTAGE

Table 8.2-1. Output files created by HAC_WINDOW.
the double-click blocks are interlaced between the single-click blocks.

2. Check a segment (early: 256 points; mid/late: 1024 points) of IDTBUF (that is, an epoch of data) to see if any data points are at the ADC saturation voltages of +/- 10 V; if so, skip the next step (reject the entire epoch of data).

3. Set the temporary storage array DATA equal to the epoch of data and then call the subroutine MEANCU in the accumulate mode. In this mode, MEANCU adds the array DATA to the previous array DATA and keeps track of N, the number of arrays accumulated. Thus, MEANCU computes a running sum of DATA, that is

\[
DATA(k) = \sum_{n=1}^{N} DATA(k), \quad k=1,2,\ldots,N_{pts}, \quad (8.2-1)
\]

where Npts is the number of points in the epoch (256 for the early AEP and 1024 for the mid/late AEP).

4. For the early AEP, repeat steps 2 and 3 until all of the appropriate epochs of data (single-click or double-click) in the 4096-point block have been either accumulated or rejected (the number of epochs is thus 4096/256/\(=\) = 8).

5. Repeat steps 1 through 4 until all of the blocks (early: 500; mid/late: 200) from the subject’s brain wave data file on the disk have been read in.

6. Call the subroutine MEANCU in the calculate average mode. In this mode, MEANCU calculates the average array
AMEAN from the accumulated array DATA and the number N of accumulations as follows:

\[ \text{AMEAN}(k) = \frac{1}{N} \sum_{i=1}^{N} \text{DATA}(i), \quad k = 1, 2, \ldots, \text{Npts.} \quad (8.2-2) \]

The array AMEAN now contains the digitized, time-domain brain wave signal, with 1024 points for the EEG and mid/late AEP, and 256 points for the early AEP. However, it was found that the first 0.6 to 0.8 msec of the early single-click AEP and the first 1.1 to 1.3 msec of the early double-click AEP were contaminated by a click artifact from the headphones. Thus, the first 25 points (1.075 msec of the early single-click AEP and the first 35 points (1.505 msec) of the early double-click AEP were discarded in order to prevent distortion of the analysis. The corrupt data points were discarded by analyzing only a 128-point (5.504 msec) subsegment of the 256-point segment, the starting point for the subsegment being at point 25 (1.075 msec) for the early single-click AEP and at point 35 (1.505 msec) for the early double-click AEP. Thus, the time span for the early single-click AEP is 1.075 msec to 1.075 + 5.504 = 6.579 msec and for the early double-click AEP is 1.505 to 1.505 + 5.504 = 7.009 msec, both of which were adequate to span the first five brainstem AEP waves (waves I through V). The subsegment length of 128 points was chosen because the FFT requires a power-of-two time series length. An alternative approach to
a smaller subsegment for avoiding distortion would have been to define a new 256-point segment consisting of the artifact-free data points and padded with zeroes at the end to get the 256-point length.

As preparation for the DFT, DC offset is removed from AMEAN by first calculating the average value of AMEAN and then subtracting this value from each constituent data point of AMEAN, as follows:

$$\bar{x} = \text{average of AMEAN} = \frac{1}{N} \sum_{k=L}^{H} AMEAN(k). \quad (8.2-3)$$

$$AMEAN(k) = AMEAN(k) - \bar{x}, \quad k = L, L+1, \ldots, U, \quad (8.2-4)$$

where $N$ is the number of data points (1024 for the EEG and mid/late AEP and 128 for the early AEP), $L$ is the data point lower index (1 for the EEG and mid/late AEP, 25 for the early single-click AEP, and 35 for the early double-click AEP), and $H$ is the data point upper index (1024 for the EEG and mid/late AEP, 152 for the early single-click AEP, and 162 for the early double-click AEP).

Next, to reduce leakage in the spectral estimates, the time series $AMEAN(k)$ is windowed. The windowing procedure consists of multiplying the time series $AMEAN(k)$ by the window function $W(k)$ to produce the windowed time series $A(k)$. $W(k)$ was chosen to be a Blackman-Harris window because this window provides extremely low sidelobe levels. The
windowing procedure is as follows:

\[ A(k) = W(k) * \text{AMEAN}(k + L - 1), \quad k = 1, 2, \ldots, N(8.2-5) \]

where \( N \) is the number of data points (given previously in Equation 8.2-4) and

\[ W(k) = A0 - A1\cos\left(\frac{2\pi k}{N}\right) - A2\cos\left(\frac{4\pi k}{N}\right) - A3\cos\left(\frac{6\pi k}{N}\right), \quad (8.2-6) \]

where \( A0 \) is 0.35875, \( A1 \) is 0.48829, \( A2 \) is 0.14128, and \( A3 \) is 0.01168, and \( L \) is the data point lower index with values as in Equation 8.2-4.

The array \( A \) (the windowed time series) is now submitted to the subroutine FFT1, which performs an \( N \)-point DFT on \( A \) using a radix-2 decimation-in-time FFT algorithm. The subroutine replaces the \( N \)-point time series in \( A \) with the \( N \)-point DFT of \( A \), with \( \frac{N}{2} \) positive frequency coefficients and \( \frac{N}{2} - 1 \) negative frequency coefficients. The coefficients of \( A(k) \) are all complex, that is, \( A(k) = A_r(k) + j A_i(k) \), with \( A_r(k) \) being the real part of \( A(k) \) and \( A_i(k) \) being the imaginary part of \( A(k) \). The FFT algorithm does not divide by \( N \) (see Equation 8.1.3-1) and the discrete time index starts at one, not zero; thus, the DFT operation performed by the FFT algorithm can be written as

\[ B(k) = A(k), \quad k = 1, 2, \ldots, N \]

\[ A(k) = \sum_{n=1}^{n=N} B(k) W_n^{nk}, \quad k=1,2,\ldots,N, \quad (8.2-7) \]
where \( W_N = e^{-j\frac{2\pi}{N}} \). \(^{(8.2-8)}\)

The array \( A(k) \) thus contains the complex frequency coefficients of the DFT of the input time series. The magnitude, phase, and power spectra are now computed and stored in the arrays \( FM(k) \), \( FI(k) \), and \( FPOW(k) \), respectively, as follows. For the magnitude spectrum

\[
FM(k) = \sqrt{A_r^2(k) + A_i^2(k)}.
\]  
\(^{(8.2-9)}\)

For the phase spectrum,

\[
FP(k) = \tan^{-1} \frac{A_i(k)}{A_r(k)}.
\]  
\(^{(8.2-10)}\)

For the power spectrum,

\[
FPOW(k) = 20 \log(FM(k) + 2049).
\]  
\(^{(8.2-11)}\)

Each of the spectra is saved in a graphics load file with a filename as shown in Table 8.2-1.

In preparation for the spectral edge analysis, spectral coefficients outside the passband of interest are set to zero in order to prevent them from affecting the analysis. Hence, \( FM(k) \), \( FI(k) \), and \( FPOW(k) \) are set to zero for the following values of \( k \): (1) for the EEG, \( k = 1 \) (DC) and \( k > 410 \) (100 Hz); (2) for the early AEP, \( k = 1 \) (DC) and \( k > 17 \) (3.09 kHz); and (3) for the mid/late AEP, \( k = 1 \) (DC) and \( k > 508 \) (1 kHz).

Now, spectral edges for each of the three types of
spectra are calculated by calling the subroutine NUMINT with the pass parameters Npts and the array F(k) = FM(k), FP(k), or FPOW(k), as appropriate. NUMINT calculates the spectral edge of the spectrum F(k) over the discrete frequency range of k = 0 to k = Npts. Npts was set to \( \frac{N}{2} \), where N is the number of points in F(k), as defined previously (the points in F(k) from k = \( \frac{N}{2} + 1 \) to k = N are negative frequency components and are therefore ignored).

NUMINT first calculates the total area of F(k) from k = 0 to k = Npts by adding the areas of the trapezoids between neighboring points of F(k), as shown in Figure 8.2-1. For the trapezoid between the points x = k to x = k + 1, the area of the trapezoid is

\[
\text{trapezoid area} = \frac{1}{2} \left[ F(k) + F(k+1) \right]. \quad (8.2-12)
\]

Starting at the first trapezoid from k = 1 to k = 2, the areas of succeeding trapezoids are added until the total area exceeds A_{se}, with A_{se} defined as

\[
A_{se} = \text{spectral edge area} = \frac{x}{100} A_{tot}, \quad (8.2-13)
\]

where x is the desired spectral edge percent and \( A_{tot} \) is the total area of F(k).

The area of the trapezoid from k = c to k = c + 1 that caused the running sum area \( A_{temp} \) to exceed \( A_{se} \) is
Figure 8.2-1. Spectral edge area computation.

\[ A_1 = \frac{1}{2} \left[ f(a) + f(b) \right] \]
subtracted from $A_{\text{temp}}$. The trapezoid from $k = c$ to $k = c + 1$ is divided into 10,000 trapezoids, and the areas of the trapezoids are added to $A_{\text{temp}}$ until $A_{\text{temp}}$ exceeds $A$; the left $x$-coordinate of the trapezoid which causes this overrun is taken as the spectral edge.

The spectral edges from each of the spectra are written to graphics load files with filenames as shown in Table 8.2-1. The program creates files that contain spectral edge vs. study day and spectral edge vs. lithium concentration.

The day loop is repeated until the spectral edges for each of the study days for the current subject have been calculated. After the day loop is complete, various analyses are performed on the spectral edge data, as outlined in Sections 8.3.1 through 8.3.4. The subject loop is then repeated until the spectral edges from all of the subjects in the selected phase have been calculated, and then, if an AEP file is being analyzed, the click loop is repeated for the double-click data.
8.3 Frequency Domain Analysis

8.3.1 Visual Analysis of Spectra

The program HAC_WINDOW (see Section 8.2) was used to generate magnitude, phase, and power spectra for each of the study subjects' brain wave files (EEG, single-click early and mid/late AEP, and double-click early and mid/late AEP) on each of the study days. The frequency ranges for the spectra were as follows: (1) EEG: 0.244 to 99.85 Hz; (2) early AEP: 181.68 to 3088.66 Hz; and (3) mid/late AEP: 1.97 to 994.2 Hz. Table 8.2-1 summarizes the files that were created; the mathematics used in the generation of the spectra is discussed in Section 8.2. Representative graphs from Study Day 15 of Phase 1 are shown in the figures delineated in Table 8.3.1-1, listed by the mode.

Both the Phase 1 and Phase 2 graphs were visually searched for changes in the distribution of magnitude, phase, and power across the study days and also were compared with typical EEG and AEP graphs from the literature (see Figure 2.1.1-1 for the EEG). The purpose of this manual visual assessment was to supplement the more accurate automated spectral edge analysis of the spectra (see Section 8.3.2) to see if any additional information could be gained that was not gained through the automated analysis as a result of an error or a limitation in the automated analysis. In addition, the visual assessment was used to
<table>
<thead>
<tr>
<th>Spectrum</th>
<th>Figure</th>
</tr>
</thead>
<tbody>
<tr>
<td>EEG magnitude</td>
<td>8.3.1-1</td>
</tr>
<tr>
<td>EEG phase</td>
<td>8.3.1-2</td>
</tr>
<tr>
<td>EEG power</td>
<td>8.3.1-3</td>
</tr>
<tr>
<td>early single-click AEP magnitude</td>
<td>8.3.1-4</td>
</tr>
<tr>
<td>early single-click AEP phase</td>
<td>8.3.1-5</td>
</tr>
<tr>
<td>early single-click AEP power</td>
<td>8.3.1-6</td>
</tr>
<tr>
<td>early double-click AEP magnitude</td>
<td>8.3.1-7</td>
</tr>
<tr>
<td>early double-click AEP phase</td>
<td>8.3.1-8</td>
</tr>
<tr>
<td>early double-click AEP power</td>
<td>8.3.1-9</td>
</tr>
<tr>
<td>mid/late single-click AEP magnitude</td>
<td>8.3.1-10</td>
</tr>
<tr>
<td>mid/late single-click AEP phase</td>
<td>8.3.1-11</td>
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<tr>
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<td>8.3.1-12</td>
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<td>8.3.1-14</td>
</tr>
<tr>
<td>mid/late double-click AEP power</td>
<td>8.3.1-15</td>
</tr>
</tbody>
</table>

Table 8.3.1-1. Figure numbers for visual analysis of spectra.
Figure 8.3.1-1. Example EEG magnitude spectrum.
Figure 8.3.1-2. Example EEG phase spectrum.
Figure 8.3.1-3. Example EEG power spectrum.
Figure 8.3.1-4. Example early single-click AEP magnitude spectrum.
Figure 8.3.1-5. Example early single-click AEP phase spectrum.
Figure 8.3.1-6. Example early single-click AEP power spectrum.
Figure 8.3.1-7. Example early double-click AEP magnitude spectrum.
Figure 8.3.1-8. Example early double-click AEP phase spectrum.
Figure 8.3.1-9. Example early double-click AEP power spectrum.
Figure 8.3.1-10. Example mid/late single-click AEP magnitude spectrum.
Figure 8.3.1-11. Example mid/late single-click AEP phase spectrum.
Figure 8.3.1-12. Example mid/late single-click AEP power spectrum.
Figure 8.3.1-13. Example mid/late double-click AEP magnitude spectrum.
Figure 8.3.1-14. Example mid/late double-click AEP phase spectrum.
Figure 8.3.1-15. Example mid/late double-click AEP power spectrum.
compare the spectra with typical spectra as published in the literature in order to verify that: (1) the correct waveforms had been obtained after data acquisition and processing, thus assuring the correctness of the acquisition and processing; and (2) no noise or other interfering signals had mixed with and possibly obscured the brain wave signals, thus verifying the integrity of the experimental setup.

For Phase 1, the graphs were searched for changes in the distribution of magnitude, phase, and power as a function of the study day for, since each study day represented a different serum lithium concentration, such a trend would indicate a possible relation between serum lithium concentration and a spectral parameter.

For Phase 2, the graphs were searched as follows: (1) the consistency in the distribution of magnitude, phase, and power across the baseline spectra (the pre-drug spectra of Days 0 through 2, 5, 6) was compared to the consistency distribution of magnitude, phase, and power across the drug spectra (the spectra of Days 9 and 12 through 16) in order to determine if lithium changes the normal day-to-day variance in the spectra; and (2) the average baseline spectrum, computed by averaging the spectra of Days 0 through 2, 5, and 6, was compared to the average drug spectrum, computed by averaging the spectra of Days 9 and
12 through 16, in order to determine if lithium produces any gross effects on the spectra that can be observed visually, without the aid of computer analysis and, if so, if these effects are identical in everyone.

The results for both the Phase 1 and Phase 2 graphs were identical: (1) the spectra matched the spectra obtained from the literature; and (2) no consistent effect of lithium on any of the magnitude, phase, and power spectra could be found in or across any of the study subjects. At this stage of the total analysis, the conclusion was not that an effect did not exist, but that the effect, if it did exist, could not be identified without the aid of computer analysis, with which the analysis of the following sections was performed.

8.3.2 Spectral Edge Analysis

The program HAC_WINDOW (see Section 8.2) was used to calculate spectral edges of the magnitude, phase, and power spectra for each each of the study subjects' brain wave files (EEG, single-click early mid/late AEP, and double-click early and mid/late AEP) on each of the study days. The frequency ranges for the spectra were as delineated in Section 8.3.1; the spectral edge values were 1%, 5% through 95% in 5% increments, and 99%. The mathematics used in the calculation of the spectral edges is discussed in Section 8.2.

The spectral edges for each study subject were plotted
in two different formats: (1) as a function of study day (or, equivalently, time); and (2) as a function of serum lithium concentration (in mEq/L). Table 8.2-1 summarizes the files that were created. Representative graphs for the 95% spectral edges are shown in Figures 8.3.2-1 through 8.3.2-15 (for time as the abscissa) and Figures 8.3.2-16 through 8.3.2-30 (for serum lithium concentration as the abscissa).

Each of these graphs was visually searched for trends as follows. First, the graphs were divided into either Phase 1 or Phase 2 graphs, because the protocol for the two phases was different. Then, for each of the phases, the following procedure was utilized:

1. Choose a specific phase.
2. For a specific filetype (e.g., XXX_EEG_MAG_YY_NORM), a specific spectral edge, and a specific study subject, note the pattern of the variation of the dependent variable (spectral edge) as a function of the independent variable (either study day or serum lithium concentration).
3. Note and compare the patterns of the other study subjects for the same filetype and spectral edge.
4. Repeat steps 2 and 3 for the remaining spectral edges for this specific filetype.
5. Repeat steps 2 through 4 for the remaining filetypes in this phase.
Figure 8.3.2-1. Example EEG magnitude spectral edge vs. study day plot.
Figure 8.3.2-2. Example EEG phase spectral edge vs. study day plot.
Figure 8.3.2-3. Example EEG power spectral edge vs. study day plot.
Figure 8.3.2-4. Example early single-click AEP magnitude spectral edge vs. study day plot.
Figure 8.3.2-5. Example early single-click AEP phase spectral edge vs. study day plot.
Figure 8.3.2-6. Example early single-click AEP power spectral edge vs. study day plot.
Figure 8.3.2-7. Example early double-click AEP magnitude spectral edge vs. study day plot.
Figure 8.3.2-8. Example early double-click AEP phase spectral edge vs. study day plot.
Figure 8.3.2-9. Example early double-click AEP power spectral edge vs. study day plot.
Figure 8.3.2-10. Example mid/late single-click AEP magnitude spectral edge vs. study day plot.
Figure 8.3.2-11. Example mid/late single-click AEP phase spectral edge vs. study day plot.
Figure 8.3.1-12. Example mid/late single-click AEP power spectrum.
Figure 8.3.2-13. Example mid/late double-click AEP magnitude spectral edge vs. study day plot.
Figure 8.3.2-14. Example mid/late double-click AFP phase spectral edge vs. study day plot.
Figure 8.3.2-15. Example mid/late double-click AEP power spectral edge vs. study day plot.
Figure 8.3.2-16. Example EEG magnitude spectral edge vs. concentration plot.
Figure 8.3.2-17. Example EEG phase spectral edge vs. concentration plot.
Figure 8.3.2-18. Example EEG power spectral edge vs. concentration plot.
Figure 8.3.2-19. Example early single-click AEP magnitude spectral edge vs. concentration plot.
RFF_ELY_SGL_PHA_99_VS_CONC_NORM

\[ a = 3236.45 \text{ Hz} \]

Figure 8.3.2-20. Example early single-click AEP phase spectral edge vs. concentration plot.
Figure 8.3.2-21. Example early single-click AEP power spectral edge vs. concentration plot.
Figure 8.3.2-22. Example early double-click AEP magnitude spectral edge vs. concentration plot.
Figure 8.3.2-23. Example early double-click AEP phase spectral edge vs. concentration plot.
Figure 8.3.2-24. Example early double-click AEP power spectral edge vs. concentration plot.
Figure 8.3.2-25. Example mid/late single-click AEP magnitude spectral edge vs. concentration plot.
Figure 8.3.2-26. Example mid/late single-click AEP phase spectral edge vs. concentration plot.
Figure 8.3.2-27. Example mid/late single-click AEP power spectral edge vs. concentration plot.
Figure 8.3.2-28. Example mid/late double-click AEP magnitude spectral edge vs. concentration plot.
Figure 8.3.2-29. Example mid/late double-click AEP phase spectral edge vs. concentration plot.
Figure 8.3.2-30. Example mid/late double-click AEP power spectral edge vs. concentration plot.
6. Repeat steps 2 through 5 for the other phase.

The result of this analysis was identical to the result of the visual analysis: no consistent trends could be found in any of the series of graphs. In some subjects, portions of the curves showed consistent changes in the spectral edge with either time or serum lithium concentration; for example, the spectral edge of several successive points might change linearly or quasi-linearly with time or concentration, or an overall trend in the whole graph such as a tendency for the spectral edge to decrease with time or concentration could be noted. However, none of the curves showed any consistent functional dependence (e.g., linear) of spectral edge on either time or concentration across all of the data points in a particular graph, and even if an overall trend could be observed in one particular subject, the same overall trend could not be found in all of the other study subjects for that series of graphs.

8.3.3 Phase 2 Mean Spectral Edge Analysis

For the Phase 2 spectral edges calculated in Section 8.3.2 (EEG, single- and double-click early and mid/late AEP modes; magnitude, phase, and power spectra), the mean of the baseline spectral edges (Study Days 0, 1, 2, 5, and 6) and the mean of the drug spectral edges (Study Days 12 through 16) were computed for the 1%, 50%, and 99% spectral edges. Study Day 9 was excluded from the drug study
days because steady-state had not yet been reached on this day.

For each spectral edge in each filetype, a paired t-test was used to compare the baseline spectral edge means against the drug spectral edge means at the 0.05 level of significance. At this level of significance, the value of t must be greater than 1.895 for the drug effect to be considered significant. Appendix F presents the program T_TEST, which was used to perform the paired t-test computations.

Tables 8.3.3-1 through 8.3.3-3 present the results of the t-test computations for the EEG, early AEP, and mid/late AEP, respectively. As can be seen from these tables, a total of seven filetypes (EEG magnitude 50% and 99%, early AEP double-click magnitude 50%, mid/late AEP single-click magnitude 50% and 99%, and mid/late AEP double-click magnitude 1% and 50%) showed significant drug effects.

For the seven filetypes with significant drug effects, bar charts were drawn to show the relation between the baseline spectral edge and the drug spectral edge for each study subject; these charts are presented in Figures 8.3.3-1 through 8.3.3-7. As can be seen from these figures, the overall trend is for the drug spectral edge to decrease. An attempt was made to correlate the magnitude of the decrease with the serum lithium concentration by plotting the
<table>
<thead>
<tr>
<th>file</th>
<th>mean SE</th>
<th>t value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAG 01</td>
<td>1.23</td>
<td></td>
</tr>
<tr>
<td>50</td>
<td>2.43</td>
<td></td>
</tr>
<tr>
<td>59</td>
<td>4.22</td>
<td></td>
</tr>
<tr>
<td>PHA 01</td>
<td>0.35</td>
<td></td>
</tr>
<tr>
<td>50</td>
<td>0.14</td>
<td></td>
</tr>
<tr>
<td>99</td>
<td>0.89</td>
<td></td>
</tr>
</tbody>
</table>

Table 8.3.3-1. Results of t-test analysis on the EEG files. MAG is magnitude, PHA is phase, and SE is spectral edge.
<table>
<thead>
<tr>
<th>file</th>
<th>mean</th>
<th>SE</th>
<th>t value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SGL MAG 01</td>
<td>1.68</td>
<td>0.61</td>
<td>0.43</td>
</tr>
<tr>
<td>50</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>99</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DBL MAG 01</td>
<td>1.46</td>
<td>1.94</td>
<td>0.19</td>
</tr>
<tr>
<td>50</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>99</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SGL PHA 01</td>
<td>0.39</td>
<td>0.24</td>
<td>1.45</td>
</tr>
<tr>
<td>50</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>99</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DBL PHA 01</td>
<td>0.01</td>
<td>0.05</td>
<td>0.67</td>
</tr>
<tr>
<td>50</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>99</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 8.3.3-2. Results of t-test analysis on the early AEP files. SGL is single-click, DBL is double-click, MAG is magnitude, PHA is phase, and SE is spectral edge.
<table>
<thead>
<tr>
<th>file</th>
<th>mean</th>
<th>SE</th>
<th>t value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SGL MAG 01</td>
<td>0.56</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50</td>
<td>3.98</td>
<td></td>
<td></td>
</tr>
<tr>
<td>99</td>
<td>1.90</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DBL MAG 01</td>
<td>2.82</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50</td>
<td>3.91</td>
<td></td>
<td></td>
</tr>
<tr>
<td>99</td>
<td>0.46</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SGL PHA 01</td>
<td>0.93</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50</td>
<td>0.22</td>
<td></td>
<td></td>
</tr>
<tr>
<td>99</td>
<td>0.05</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DBL PHA 01</td>
<td>0.27</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50</td>
<td>1.72</td>
<td></td>
<td></td>
</tr>
<tr>
<td>99</td>
<td>0.15</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 8.3.3-3. Results of t-test analysis on the mid/late AEP files. SGL is single-click, DBL is double-click, MAG is magnitude, PHA is phase, and SE is spectral edge.
Figure 8.3.3-1. Relative spectral edges for the EEG_MAG_50 files.
Figure 8.3.3-2. Relative spectral edges for the EEG_MAG_99 files.
Figure 8.3.3-3. Relative spectral edges for the ELY_DB'L_MAG_50 files.
Figure 8.3.3-4. Relative spectral edges for the LAT_SGL_MAG_50 files.
Figure 8.3.3-5. Relative spectral edges for the LAT_SGL_MAG_99 files.
Figure 8.3.3-6. Relative spectral edges for the LAT_DBL_MAG_01 files.
Figure 8.3.3-7. Relative spectral edges for the LAT_DBL_MAG_50 files.
Figure 8.3.3-8. Spectral edge shift vs. concentration for the LAT_SGL_MAG_99 files.
spectral edge shift (baseline spectral edge - drug spectral edge) versus the average steady-state serum lithium concentration, as shown in the example graph of Figure 8.3.3-8 for the mid/late AEP single magnitude 99% file. No consistent relations were found between the spectral edge shift and the serum lithium concentration.
9.0 RESULTS AND CONCLUSIONS

The effects of lithium on the EEG and AEP magnitude, phase, and power spectrums have been examined, with the spectral edge used as an index of the net effect on the spectrums. An attempt has been made to correlate EEG and AEP spectral edges with time since initial dose and serum lithium concentration.

The following results have been obtained. Firstly, lithium produces statistically-significant decreases in selected magnitude spectral edges of the EEG, BAEPs, and mid/late AEPS; in particular, decreases were found in the following magnitude spectral edges: EEG 50% and 99%, BAEP double-click 50%, mid/late single-click 50% and 99%, and mid/late double-click 1% and 50%. No effects on any of the phase spectral edges were found.

Secondly, no correlations of these effects with either serum lithium concentration or time since initial dose were found, either through a visual search for patterns from plots of spectral edge versus concentration or study day, or through a visual search for patterns in plots of the frequency shift between the mean baseline and drug spectral edges as a function of the average steady-state serum lithium concentration.

Some of the factors which must be considered in the interpretation of the results are as follows. Firstly, due
to an insufficient number of epochs for ensemble averaging and the lack of the use of frequency band averaging, the EEG spectral estimates obtained in this analysis do not have a sufficient number of degrees of freedom for high confidence limits. In addition, because the number of epochs was low, the total observation period (equal to the observation interval times the number of epochs) was well below the typical period used in clinical practice (twenty seconds in this analysis versus three to five minutes in clinical practice).

Secondly, in regard to the mid/late AEPS, an optimum paradigm for eliciting the late and long potentials was not employed, the optimum paradigm being the presentation of an expectancy stimulus preceding the click stimulus. In addition, the middle, late, and long AEPS obtained in this experiment were corrupted by various levels of noise, and thus more averages were needed.

Thirdly, in regard to the double-click AEP, the data obtained was for only one value of the intrastimulus interval (the time period between the conditioning stimulus and the test stimulus) whereas this interval was varied in previous studies utilizing somatosensory evoked potentials.

Fourthly, in regard to the early AEP, the DFT frequency resolution of 181 Hz may not have been adequate for detection of small changes in the spectral distributions.
Fifthly, in regard to all of the Phase 1 data, most of the serum lithium concentrations were not high enough to fall in the therapeutic range and, in addition, only one baseline brain-wave recording was made.

Sixthly, lithium has been shown to produce epileptiform spikes in the EEG. Spikes are sometimes difficult to detect, especially through automated analysis, and would affect the spectral edge calculations.

And finally, many quantitative pharmaco-EEG investigations pre-screen the subjects for abnormal brain wave patterns, something which was not done in this experiment.

In conclusion, then, lithium does not affect either AEP or EEG phase spectral edges, but does produce statistically-significant decreases in both AEP and EEG magnitude spectral edges. The magnitude of the decrease is not correlated with the serum lithium concentration. Hence, neither the magnitude or the phase spectral edge can be used as an index of serum lithium concentration.
APPENDIX A

ELECTRODE CHLORIDING PROCEDURE (11)
2.3 CHLORIDING OF SILVER ELECTRODES

In Europe the electrodes most commonly used are made of pure silver coated with a layer of silver chloride which improves the recording characteristics (Section 2.5). An electrolytic method is used to coat the electrodes. They are placed in saline and made electropositive (anode), thus attracting negative chlorine ions that react with the silver to produce silver chloride. The chemical changes are shown by the following equations:

\[ \text{NaCl} \rightarrow \text{Na}^+ + \text{Cl}^- \]
\[ \text{Cl}^- + \text{Ag}^+ \rightarrow \text{AgCl} \]

The positively charged sodium ions react at the cathode surface to produce hydrogen:

\[ 2\text{Na}^+ + 2\text{H}_2\text{O} + 2 \text{electrons} \rightarrow 2\text{NaOH} + \text{H}_2 \]

Before chloriding, the metal should be cleaned by an electrolytic method in which the silver electrodes are placed in saline and made electronegative by about 9 V with respect to another electrode. Alternatively, they may be cleaned with an abrasive such as emery paper, but not with steel wool. The electrodes are then placed in a glass dish containing 3-5% sodium chloride in water (2-5 g/100 ml) and each connected to the positive terminal of a 1.5-V battery. The negative terminal is connected to another electrode immersed in the saline. After a few seconds the electrodes connected to the positive terminal will be covered with a dark coating of silver chloride. The currents, which will be about 2.5 mA/cm² of electrode surface, should be allowed to flow for about 1 min.

Guedes, Baker and Moore (1969) and Guedes (1972) have examined in great detail the effect of the chloride deposit on the impedance of silver electrodes. They showed that the impedance was different for different layers of chloride but it is doubtful whether the thickness makes a significant difference in EEG practice. Unfortunately, the measurements taken by these authors were all at frequencies greater than 10 Hz.

Pad electrodes are chlorided with the gauze cover in place; this protects the chloride layer from damage. This type needs rechloriding only at infrequent intervals, unless large electrode potentials develop as shown by long blocking times when switching montages (Section 4.7.3). A storage dish for these electrodes has been described, in which all electrodes are shorted together and maintained at a small positive potential by a carbon electrode (Cooper, 1956). This type of device for both pad and disc electrodes is commercially available. The silver chloride on disc electrodes can be damaged by handling and it should be renewed when patches of silver metal can be seen.

When chlorided silver electrodes are required for d.c. recording their preparation requires greater care (Section 2.8). Only pure silver should be used and saline should be made from analar grade sodium chloride and distilled water. The electrode surface must not be handled and the electrodes must be kept immersed in water or saline when not in use. For the greatest stability more complex procedures have to be used (Janz and Taniguchi, 1953; Taniguchi and Janz, 1957).
APPENDIX B

THIS_IS_IT
PROGRAM THIS IS IT! Multibuffer input, mass storage output, early and mid/late files

NOTE: FZM-FRANK ZAK MODIFICATION

ONLY THE MOST IMPORTANT FZMs ARE NOTED

MAIN PROGRAM IS SCAN0

FRANK A. ZAK, 13 OCT 88

Implicit Integer*4 (A-Z)

Include 'SYS$LIBRARY: VMSLIB.FOR'

Integer*2 IDC0(DC0LEN), IDCBO(DC0LEN), IDCBI(DC0LEN)

Integer*2 IDC0B(BC0LEN, 4)

Integer*2 MSC0(MSC0LEN)

Parameter IBFILM = 32768 IFZM

Integer*2 IDTBUF(IBFILM)

Common/IDTBUF/IDTBUF

Character*1 CP0RC, CTY0PE, CDUMM0, CGAIN0

Character*4 CP0RC0M, CTY0P0E, CGAIN, CGAIN1

Character*8 C0ME, C0RT0ME

Character*28 FILENAME0, FILENAME1

Character*32 FILENAME, FILENAME2, FILENAME3

Character*4 ADNAME, CKNAME, DANAME

Data ADNAME, CKNAME, DANAME '/AA00', 'AA00', 'AA00' /

Integer*2 RREL

DATA IRS0B /3/  

I VMSLIB status code no next buffer

Data AUTO /0/ 

Call CHECK PRIORITY len sure real time priority

Call DTDEVT IDCB, ADNAME 

If (IDCB(1).eq. 1) Go to 1

Call ERROR MESSAGE(IDCB)

Go to 1000 

1 Call DTDEVT(IDC0BO, CKNAME)

If (IDCB0(1).eq. 1) Go to 2

Call ERROR MESSAGE(IDC0BO)

Go to 1000 

2 Call DTDEVT(IDC0BI, DANAME)

If (IDCBI(1).eq. 1) Go to 3

Call ERROR MESSAGE(IDC0BI)

Go to 1000 

3 CALL DTADGN(IDC0BI, IGAIN)

If (IDCB1(1).eq. 1) GO TO 6

CALL ERROR MESSAGE(IDC0B1)

GO TO 1000 

6 CALL DT1CH(IDC0B, 0, 3)

If (IDCB(1).EQ. -1) GO TO 1000

CGAIN = ' X1'

IGAIN = 0

CALL DTADGN(IDC0B, IGAIN)

If (IDCB(1).EQ. 889) GO TO 889

CALL ERROR MESSAGE(IDC0B)

GO TO 1001 

889 WRITE(6, ('A')) ' ENTER: T FOR THREE-FILE ACQUISITION AND READ'

WRITE(6, ('A')) ' (ACQUIRE EEG/EARLY/LATE THEN'

WRITE(6, ('A')) ' DISPLAY EEG/EARLY/LATE)'

WRITE(6, ('A')) ' OR'

WRITE(6, ('A')) ' A FOR SINGLE-FILE ACQUISITION & READ'

WRITE(6, ('A')) ' OR'

WRITE(6, ('A')) ' R FOR SINGLE-FILE READ'

READ(5, 724) CDUMM0

724 FORMAT(A1) 

IF (CDUMM0.NE. 'T') GO TO 811

WRITE(6, ('A')) ' ENTER EARLY AEP GAIN (1, 2, 4, OR 8)'

READ(5, 888) CGAIN0

888 FORMAT(A1)

IF (CGAIN0.EQ. '1') IGAIN = 0

IF (CGAIN0.EQ. '2') IGAIN = 1

IF (CGAIN0.EQ. '4') IGAIN = 2

IF (CGAIN0.EQ. '8') IGAIN = 3

CGAIN(1:3) = 'X'//CGAIN0

AUTO = 1

CDUMM0 = 'G'

GO TO 79

811 IF (CDUMM0.EQ. 'A') GO TO 725

WRITE(6, ('A')) ' ENTER COMPLETE FILE NAME'

WRITE(6, ('A')) ' NOTE: EARLY FILE MUST BE CHOPPED'
READ(5,726) FILENAME
FORMAT(A29)
IF (FILENAME(18:20).NE.'EEG') GO TO 732
FILENAME=FILENAME(1:25)
GO TO 731
731 CPROC=FILENAME(22:22)
GO TO 723
725 WRITE(6,'(A)') ' ENTER G FOR EEG OR P FOR EVOKED POTENTIAL'
READ(5,728) CDUMMY
728 FORMAT(A1)
IF (CDUMMY.EQ.'G') GO TO 79
WRITE(6,'(A)') ' ENTER E FOR EARLY OR L FOR LATE'
READ(5,7) CTYPE0
7
FORMAT(A1)
816 IF (CTYPE0.EQ.'L') GO TO 10
IF (CTYPE0.NE.'E') GO TO 1001
CTYPE='ELY'
IDIV=43
DAC1=2048
IBLOCK=125
CGAIN(1:3)=CGAIN0(1:3)
IF (AUTO.GT.0) GO TO 777
WRITE(6,'(A)') ' ENTER EARLY AEP GAIN (1, 2, 4, OR 8)'
READ(5,778) CGAIN0
778 FORMAT(A1)
IF (CGAIN0.EQ.'1') IGAIN=0
IF (CGAIN0.EQ.'2') IGAIN=1
IF (CGAIN0.EQ.'4') IGAIN=2
IF (CGAIN0.EQ.'8') IGAIN=3
CGAIN(1:3)=X/C/GAIN0
CGAIN(1:3)=X/C/GAIN0
CALL DTADGN(IDCB,IGAIN)
IF (IDCB(1).EQ.1) GO TO 817
CALL ERROR MESSAGE(IDCB)
GO TO 1000
CTYPE='LAT'
IDIV .. 31
DAC1 .. 3072
IBLOCK .. 50
CGAIN(1:3)=X1
CALL DTCLK(IDCB0,0,1,IDIV)
IF (IDCB0(1).EQ.1) Go to 817
CALL ERROR MESSAGE(IDCB0)
GO TO 1000
IF (AUTO.GT.0) GO TO 818
77

WRITE(6,'(A)') ' ENTER CLICK TYPE: S FOR SINGLE, D FOR DOUBLE, A
* FOR ALTERNATING'
READ(5,77) CFPROC
77 FORMAT(A1)
818 IF (CFPROC.EQ.'A') GO TO 74
IF (CFPROC.EQ.'D') GOTO 78
IF (CFPROC.NE.'S') GO TO 1001
DAC2=1024
CPROCNAM=' SGL'
GO TO 79
74 DAC2=3072
CPROCNAM=' ALT'
GO TO 79
78 DAC2=2048
CPROCNAM=' DBL'
GO TO 79
79 IF (AUTO.GT.1) GO TO 819
WRITE(6,'(A)') ' ENTER INITIALS OF SUBJECT'
READ(S,75) CNAME
75 FORMAT(A3)
819 IF (CDUMMY.EQ.'G')
* CALL BELL(' EEG FILTER SETTINGS: 0.15Hz TO 100 Hz')
IF ((CDUMMY.EQ.'P').AND.(CTYPE0.EQ.'E'))
* CALL BELL(' EARLY FILTER SETTINGS: 150 Hz TO 3 kHz')
IF ((CDUMMY.EQ.'P').AND.(CTYPE0.EQ.'L'))
* CALL BELL(' LATE FILTER SETTINGS: 0.5 Hz TO 1 kHz')
WRITE(6,'(A)') ' PRESS RETURN TO START DATA ACQUISITION'
READ(5,727) CDUMMY0
727 FORMAT(A1)
CALL TIME(CTIME)
CALL DATE(CDATE)
IF(CDATE(1:1),EQ,'') CDATE(1:1)= '0'
CHEAEDR=NAME// '0'
CDATE(1:2)//CDATE(4:6)//CDATE(8:9)/
*" "/CTIME(1:2)/CTIME(4:5)/'
IF("CDUMI",EQ,'') GO TO 729
CGAINI(1:3)= '1'
FILENAME=CHEAEDR// 'Eoo'//CGAINI//'.DATA'
WRITE(6,730) FILENAME
730 FORMAT(/X,'FILENAME: ',A28)
731 CALL EEG(FILENAME)
729 FILENAME=CHEAEDR//CTYPE//CPROCTYPE//CGAINI//'.DATA'
WRITE (6,736) FILENAME
76 FORMAT(/X,'FILE NAME: ',A32)
8 NBIFSIZ=4  P
IBFSIZ=8192  P
IBFTOT=IBLOÓCK*NBIFSIZ
NRECS=IBFTOT  P

CC
Call DTMDBB( IDCB,IBCB,NBIFSIZ )
If (IDCB(1),.eq. 1) Go to 5
Call ERROR MESSAGE( IDCB )
Go to 1000

CC
Call MSINIT( IDCB,HSCB )
If (IER1( IDCB,'MSINIT' )) Go to 1000

CC
IDISC=((23768)*(IBFTOT/NBIFSIZ))/256+1
Call MSALOC( IDCB,-IDISC,-1 )  P
If (IER1( IDCB,'MSALLOC' )) Go to 1000

CC
Call MSOPNU( IDCB,FILENAME)
If (IER1( IDCB,'MSOPNU' )) Go to 1000

CC
Call MSRWHN( IDCB )

CC
Do 70 J=1,NBIFSIZ
I = J
Call DTMDBD( IDCB,I,IDTBUF(((I-1)*IBFSIZ)+1),IBFSIZ,I )
If (IER1( IDCB,'DTMBD' )) Go to 1000
Continue
70

CC
Do 80 J=1,NBIFSIZ
I = J
Call DTMDBB( IDCB,I )
If (IER1( IDCB,'DTMBB' )) Go to 1000
Continue
80

CC
IR = 1  P;read buffer
IW = 1  P;write buffer
RREL = NBIFSIZ  P;buffers released for read
RREL=0  P
IREAD = 0  P;buffers read successfully
IQUIS = 0  P;buffers queued for write
IWRT = 0  P;buffers written successfully
MBBAD = 0  P;write buffers completed in error

CC
Write( 6,95 )
Format(/X,'ACQUIRING EVOKED POTENTIAL DATA')

CC
95 96
Call DTMDBR( IDCB )
If (IER1( IDCB,'DTMBR' )) Go to 610
CALL DATA(IDCBI,1024,DAC2,DAC1,2048)
IF(IDCBI(1).EQ.1) GO TO 120
CALL ERROR_MESSAGE(IDC) 
GO TO 1000

100 CALL DTMBWN( IDC,IR,IW )
Go to (120,140,610), IDC(2)

120 CALL DTMBWN( IDC,IR )
WRITE (6,121) IR,IREAD,IDC(1)
C
C
FORMAT(/X,'IR= ',I1,' IREAD= ',I2,' IDCB= ',I1,' AT STEP 120')

C If (IDCB(1).EQ.ISNNB) Go to 520 lstop if no next buffer
C If (IREAD.EQ.(IBFTOT-1)) Go to 520 lstop if no next buffer
C
C IREAD = IREAD + 1
Call MSMBW( IDC,IR )
C If (IERR1(IDC,'MSMBW'))Go to 540
IQUEW = IQUEW + 1

C IR = JMOD( IR,NBUFS ) + 1
If (IR .eq. IW) Go to 140
Go to 100

140 Call MSMBWB( IDC,IR )
C If (IERR1(IDC,'MSMBWB'))Go to 540
IVER = IVER + 1
C If (RREL .ge. NRECS) Go to 500 lexit loop when complete

C Call DTMBR( IDC,IR )
C If (IERR1(IDC,'DTMBR')) Go to 1000
WRITE(6,141) IW,RREL
C
C FORMAT(/X,'BUFFER (*',I6,' RELEASED AT STEP 140')
C
C IW = JMOD( IW,NBUFS ) + 1
If (IR .eq. IW) Go to 120
Go to 100

500 CALL DTMBRB( IDC,IR )
C If (IERR1(IDC,'DTMBRB')) Go to 1000
WRITE(6,501) IW
C
C FORMAT(/X,'BUFFER (*',I6,' RELEASED AT STEP 500')
C
C IW = JMOD( IW,NBUFS ) + 1

C 510 CALL DTMBWB( IDC,IR )
C WRITE (6,511) IR
C
C FORMAT(/X,'BUFFER (*',I6,' READ AT STEP 510')
C
C If (IDCB(1).EQ.ISNNB) Go to 520
C If (IREAD.EQ.(IBFTOT-1)) Go to 540
C If (IREAD .eq. RREL) Go to 530
C IREAD = IREAD + 1

C Call MSMBW( IDC,IR )
C If (IERR1(IDC,'MSMBW')) Go to 540
IQUEW = IQUEW + 1

C IR = JMOD( IR,NBUFS ) + 1
Go to 510

520 Go TO 530
C
C If (IREAD .lt. (NRECS-1)) Call IERR1(IDC,'DTMBWB')
C
C 530 IREAD = IREAD + 1
Call MSMBW(IDCB, IR)

If (IERR1(IDCB,'MSMBW')) Go to 540

IQUEW = IQUEW + 1

IR = JMOD(IR,NBUFS) + 1

WRITE(6,541) IWRIT, IQUEW

540 FORMAT/X,'IWRIT= ',I2,' IQUEW= ',I2,' AT STEP 550'

If (IWRIT .ge. IQUEW) Go to 610

If (IWRIT .ge. IQUEW) Go to 610

Call MSMBWB(IDCB, IW)

If (IERR1(IDCB,'MSMBWB')) Go to 600

IWRIT = IWRIT + 1

CALL DTMBRB(IDCB, IW) IFZM

If (IERR1(IDCB,'DTMBRB')) Go to 1000

WRITE(6,551) IW

550 FORMAT/X,'BUFFER # ',I6,' RELEASED AT STEP 550'

If (IWRIT .ge. IQUEW) Go to 610

IWRIT = IWRIT + 1

CALL DTMBRB(IDCB, IWI IrZM

If (IERR1(IDCB,'DTMBRB')) Go to 1000

WRITE(6,551)

551 FORMAT/X,'BUrrER *',16,' RELEASED AT STEP 550'

IW = JMOD(IW,NBUFS) + 1

RREL=RREL+1

Go to 550

560 MWBAD = 1

!unsuccessful media write

610 MTOT = IWRIT + MWBAD

630 If (MTOT .ge. IQUEW) Go to 631

Call MSMBWB(IDCB, IW)

If (IERR1(IDCB,'MSMBWB')) Go to 600

IWRIT = IWRIT + 1

CALL DTMBRB(IDCB, IW) IFZM

If (IERR1(IDCB,'DTMBRB')) Go to 1000

WRITE(6,635) IW

635 FORMAT/X,'BUFFER # ',I6,' RELEASED AT STEP 630'

If (MTOT .ge. IQUEW) Go to 631

IW = JMOD(IW,NBUFS) + 1

INCW = INCW + 1

Go to 630

If (INCW .ge. NBUFS) Go to 631

Call DTMBOF(IDCB)

Call IERR1(IDCB,'DTMBOF')

640 Call DTMBDD(IDCB)

If (IERR1(IDCB,'DTMBDD')) Call MCLOSE(IDCB)

CALL DTCLK(IDCBO,0,0,21) !STOP CLOCK

If (IDCB(11) .eq. 1) Go to 721

Call ERROR_MESSAGE(IDCBO)

Go to 1001

721 CALL DTAO(IDCBI,DAC4,1024,DAC1,30721)

If(IDCBI(1).EQ.1) Go to 722

CALL ERROR_MESSAGE(IDCBO)

Go to 1001

722 CALL BELL(' DATA ACQUISITION COMPLETE')

If (AUTO.EQ.0) Go to 813

If (AUTO.EQ.3) Go to 814

AUTO=AUTO+1

If (AUTO.EQ.3) Go to 815

FILENAME1(1:28)=FILENAME0(1:28)

Cdummy='P'

Ctypeo='L'

CPROC='A'

Go to 816

815 Call MSMBW3(IDCB, IW)

Call IERR1(IDCB,'MSMBW3')

Call MCLOSE(IDCB)

CALL DTCLK(IDCBO,0,0,21) !STOP CLOCK

If (IDCB(11) .eq. 1) Go to 721

Call ERROR_MESSAGE(IDCBO)

Go to 1001

722 CALL BELL(' DATA ACQUISITION COMPLETE')

If (AUTO.EQ.0) Go to 813

If (AUTO.EQ.3) Go to 814

AUTO=AUTO+1

If (AUTO.EQ.3) Go to 815

FILENAME1(1:28)=FILENAME0(1:28)

Cdummy='P'

Ctypeo='L'

CPROC='A'

Go to 816
FILENAME(1:32) = FILENAME(1:32)
CALL READ EEG(FILENAME1)
WRITE (6,'(A)') 'PRESS RETURN FOR NEXT PLOT'
READ (5,'(A)') IDUMMY2
CALL CHOP IT(FILENAME2)
CALL READ CHOP(FILENAME2,CPROC)
WRITE (6,'(A)') 'PRESS RETURN FOR NEXT PLOT'
READ (5,'(A)') IDUMMY2
CALL READ CHOP(FILENAME3,CPROC)
GO TO 1007
FILENAME(18:20) = 'LAT'
CALL CHOP IT(FILENAME)
CALL READ CHOP(FILENAME,CPROC)
GO TO 1001
Continue

CALL MSCLOS(IDCB)
CALL EXIT
STOP

SUBROUTINE CHOP IT(FILENAME)
IMPLICIT INTEGER*4(A-Z)
INCLUDE 'SYS$LIBRARY:VMSLIB.FOR'
INTEGER*2 IDCB(DCBLEN),MSCB(MSCBLEN)
PARAMETER IBFLIM=32768
INTEGER*2 IDTBUF(IBFLIM),IDATA(4096)
CHARACTER*32 FILENAME,ELYNAM
COMMON/IDTBUF/IDTBUF
DATA IEFN,III
CALL DTDEV(MSCB,'NLO:')
IF (MSCB(1).EQ.1) GO TO 10
CALL ERROR MESSAGE(MSCB)
GO TO 1000
CALL MSINIT(IDCB,MSCB)
IF (IERR1(IDCB,'MSINIT')) GO TO 1000
ELYNAM=FILENAME(1:27)//' .CHOP'
IBLOCK=125
IDISC=2000-1
CALL MSALOC(IDCB,-IDISC,-1)
IF (IERR1(IDCB,'MSALOC')) GO TO 1000
CALL MSOPNU(IDCB,ELYNAM)
IF (IERR1(IDCB,'MSOPNU')) GO TO 1000
CALL MSRWN(IDCB)
CALL MSCLOS(IDCB)
ITICKS=2000
EPOCHS=FLOAT(ITICKS)
IBFSIZ=32768
IBFSIZX=4096
IFLPTRO=-125 ! READING 32768-WORD BUFFERS
IFLPTRO=-15
DO 200 IBLOCK=1,IBLOCKUP
WRITE(6,302) IBLOCK
302 FORMAT(/X,'CHOPPING BLOCK # ',I3)
CALL MSOPNO(IDCB,FILENAME)
IF (IERR1(IDCB,'MSOPNO')) GO TO 1000
IFLPTRO=IFLPTRO+128
CALL MSPOS(IDCB,IFLPTRO)
CALL DTSBDB(IDCB,IEFN,IDTBUF,IBFSIZ)
CALL MSSBR(IDCB)
IF (IERR1(IDCB,'MSSBR')) GO TO 1000
CALL MSSBWB(IDCB)
IF (IERR1(IDCB,'MSSBWB')) GO TO 1000
CALL MSCLOS(IDCB)
CALL MSCLOS(IDCB)
CALL MSOPNO(IDCB,ELYNAM)
IF (IERR1(IDCB,'MSOPNO')) GO TO 1000
DO 100 J=1,16
INDEX=2048*(J-1)
INDEXO=256*(J-1)
DO 300 I=1,256
IDATA(INDEX+I)=IDTBUF(INDEX+I)
300 CONTINUE
100 CONTINUE
SUBROUTINE READ_CHOP(FILENAME, CPROC)  
IMPLICIT INTEGER*4 (A-Z)  
INCLUDE 'SYS$LIBRARY:VMSLIB.FOR'  
INTEGER*2 IDCB(DCBLEN), MSCB(MSCBLEN)  
PARAMETER (ADMAX=2047, ADMIN=2047)  
PARAMETER (MAXDAT=16384, MAXDT2=16386)  
REAL XARR(MAXDT2), YARR2(MAXDT2), EPOCHS  
REAL*4 DATA(MAXDT2), AMEAN(MAXDT2), SD(MAXDT2)  
INTEGER IFLAG(MAXDAT), IFLAG2(MAXDAT), IFLAG4(MAXDAT), NDATA(MAXDT2)  
INTEGER DENOM(MAXDAT)  
PARAMETER (PLTOUT=10)  
PARAMETER IBFLIM=32768  
INTEGER*2 IDTBUF(IBFLIM)  
COMMON IIDTBUFI  
DATA IEFN, ISTART  11, 301  
INTEGER COUNT  1 0 1  
CHARACTER*l CPROC  
CHARACTER*32 FILENAME, FILENAMEO  
CALL DTDEV(MSCB,'NLO:')  
IF (MSCB(l).EQ.1) GO TO 1  
CALL ERROR MESSAGE(MSCB)  
GO TO 1000  
1 CALL MSINIT(IDCBO, MSCB)  
IF (IERR1(IDCBO,'MSINIT')) GO TO 1000  
FILENAMEO=FILENAME(1:27)11'·CHOP'  
IF (FILENAME(18:20).EQ.'ELY') GO TO 12  
CALL MSOPNO(IDCBO, FILENAME)  
IF (IERR1(IDCBO,'MSOPNO')) GO TO 1000  
GO TO 13  
12 CALL MSOPNO(IDCBO, FILENAMEO)  
IF (IERR1(IDCBO,'MSOPNO')) GO TO 1000  
13 IF (FILENAME(18:20).EQ.'LAT') GO TO 10  
IBFSIZ=4096  
IFLPTR=15  
ITICKS=2000  
IBLOCKU=125  
NPTS=233  
JUP=NPTS  
INCR=16  
JUP=16  
JINCR=1  
I INCR=1  
INDEX=256  
GO TO 11  
10 IBFSIZ=32768  
IFLPTR=1  
IFLPTR=127  13 OCT 88  
ITICKS=100  
IBLOCKU=50  
NPTS=3226  
JUP=16130  
INCR=128  
JUP=2  
JINCR=1
I INCR=5
INDEX=16384
11 IF (CPROC.NE.'A') GO TO 14
ITICKS=ITICKS/2
JINCR=2
14 EPOCHS=FLOAT(ITICKS)
CC
DO 4 I = 1, MAXDAT
DATA(I) = 0.0
XARR(I) = FLOAT(I-1)
DENOM(I) = 0.0
IFLAG2(I) = 2
IFLAG4(I) = 4
4 CONTINUE
CALL MEANCU(DATA,IFLAG4,NPTS,DENOM,AMEAN,SD)
CC
DO 8 IBLOCK = 1, IBLOCKU
WRITE (6,5) IBLOCK
5 FORMAT (/X,'READING BLOCK # ',I3)
IFLPR = IFLPT+INCR
CALL MSPOS(IDC,B,IFLPR)
CALL DTSDBS(IDC,IEFN,IDTBUF,IBFSL)
CALL MSSBB(IDC)
IF (IER1(IDC,'MSSBR')) GO TO 1000
CALL MSSBB(IDC)
IF (IER1(IDC,'MSSBWB')) GO TO 1000
DO 7 J=1,JUP,JINCR
IZAK=0
INDEX=INDEX1*(J-1)
IF (CPROC.NE.'A') GO TO 15
IF (COUNT.EQ.0) GO TO 15
INDEX=INDEX+INDEX1
15 DO 6 I = 1,IUP,I INCR
INDEX = I+INDEX0
IF (FILENAME(18:20).EQ.'LAT')
POINTER=((I-1)/5)+1
IF (IDTBUF(INDEX).LT.ADMIN,AND.IDTBUF(INDEX).GT.ADMIN)THEN
IFLAG(POINTER) = 1
DATA(POINTER) = FLOAT(IDTBUF(INDEX))
ELSE
IZAK=1
ENDIF
6 CONTINUE
IF(IZAK.EQ.1) GO TO 7
CALL MEANCU (DATA,IFLAG,NPTS,DENOM,AMEAN,SD)
7 CONTINUE
8 CONTINUE
CC
DO 9 I = 1, NPTS
YARR2(I) = FLOAT(DENOM(I))
9 CONTINUE
CALL MEANCU (DATA,IFLAG2,NPTS,DENOM,AMEAN,SD)
666 CALL EPLT(XARR,AMEAN,YARR2,SD,NPTS,'CPROC,COUNT,ISTART,FILENAME)
CALL FLOT((0.0,0.0,0.999)
WRITE(6,*(A') ' REPEAT PLOT ?'
READ(5,*(A') ' YESNO
IF (YESNO .EQ. 'Y') THEN
CLOSE (PLOTOUT)
go to 666
ENDIF
COUNT=COUNT+1
IF ((COUNT.LE.1).AND.(CPROC.EQ.'A')) GO TO 13
CC
1000 CALL MSECLOS (IDCB)
1001 RETURN
END
CC
SUBROUTINE EPPLOT(XARR,YARR,YARR2,YARR3,NPTS,*CPROC,COUNT,ISTART,FILENAME)

DIMENSION XARR(1),YARR(1),YARR2(1),YARR3(1),DIVX(21),DIVY(14)

DIMENSION XGRID(4),YGRID(4),YTMP(5)

INTEGER DVR,PLTOUT,COUNT

LOGICAL AUTO

PARAMETER (PLTOUT=.TRUE.,XLEN=10.0,YLEN=4.0,DENSTY=2.0)

PARAMETER (FACTR=0.97,OFFSTX=0.37,OFFSTY=4.1)

PARAMETER (YLEN2=1.0,YLEN3=1.0,OFFSTY2=2.44,OFFSTY3=0.44)

CHARACTER*1 CPROC

CHARACTER*1 APPENDAGE0,APPENDAGE1

CHARACTER*32 FILENAME

CHARACTER*38 FILENAM0E0

BYTE NAME(38)

CHARACTER*80 MESSAGE

CHARACTER*5 RDWRT

CHARACTER*5 READ,WRITE

DATA AUTO! .TRUE. / 

DATA READ,WRITE! 'READ','WRITE'! / 

DATA EVOKS1,EVOKS2! 1984.0, 96.0! /

DATA DIVX(1),DIVX(2),DIVX(3),DIVX(4),DIVX(5)!.001,.002,.005,.01, .02! 

DATA DIVX(6),DIVX(7),DIVX(8),DIVX(9),DIVX(10)!.05,1.2,5.1, / 

DATA DIVX(11),DIVX(12),DIVX(13),DIVX(14),DIVX(15)! 2.,5.,10.,20, ! 

DATA DIVX(16),DIVX(17),DIVX(18),DIVX(19),DIVX(20)!.000,200.,500. ! 

DATA DIVX(21)! 5000. !

C X DIVISION ARRAY SET IN UNITS OF MILLISECONDS.

DATA DIVY(1),DIVY(2),DIVY(3),DIVY(4),DIVY(5)! 1.,2.,5.,10.,20. ! 

DATA DIVY(6),DIVY(7),DIVY(8),DIVY(9),DIVY(10)! 50.,100.,200.,500. ! 

DATA DIVY(11),DIVY(12),DIVY(13),DIVY(14)! 2000.,5000.,10000., * 

DATA DIVY(21)! 20000. /

C Y DIVISION ARRAY SET IN UNITS OF MILLIVOLTS.

C CHECK THAT OUTPUT FILE IS OPEN, IF NOT THEN OPEN.

MESSAGE(1:46) = ' Where would you like the plot?, (Txa6, etc.) ' 

RDWRT = WRITE 

CALL ISDEF (PLTOUT,MESSAGE,RDWRT) 

IF (COUNT.NE.1) GO TO 617 

WRITE (6, '(A)') , PRESS RETURN FOR THE NEXT PLOT' 

READ (5,618) IDUMMY 

618 FORMAT(I1)

C ------------------------ FIRST PLOT ------------------------

C FIND MIN AND MAX OF X AND Y ARRAYS.

617 YMAX = -2048.0 

YMIN = 2048.0 

XMAX = 0.0 

XMIN = 0.0 

DELYES = 0.0 

C YMAX = AMAX1(YMAX,YARR(1)) 

XMAX = AMAX1(XMAX,XARR(1)) 

C YMIN = AMIN1(YMIN,YARR(1)) 

XMIN = AMIN1(XMIN,XARR(1)) 

DO 10 I = ISTART, NPTS !FORMERLY I=2, NPTS 3 OCT 88 

YMAX = AMAX1(YMAX,YARR(I)) 

XMAX = AMAX1(XMAX,XARR(I)) 

YMIN = AMIN1(YMIN,YARR(I)) 

XMIN = AMIN1(XMIN,XARR(I)) 

DELYES = AMAX1(DELYES,YARR(I)-YARR(I-1))

10 CONTINUE 

DO 11 I=1,ISTART 

IF (YARR(I).GT.YMAX) YARR(I)=YMAX 

IF (YARR(I).LT.YMIN) YARR(I)=YMIN 

11 CONTINUE 

C SELECT APPROPRIATE X DIVISIONS FOR DISPLAY.
XTICK = (XMAX-XMIN)/XLEN
IDIVX = 1
DO 20 I = 1, 21
   IF (DIVX(I).LT.XTICK) IDIVX = I+1
20 CONTINUE
XDEL = DIVX(IDIVX)
CALL SCALE (XARR,XLEN,NPTS,1)
IF ((VAR(NPTS+2)).LT.DIVX(I)/(XLEN*DENSTY).OR. XARR(NPTS+2)).GT.DIVX(I)
   XDEL = XARR(NPTS+2)
C SELECT APPROPRIATE Y DIVISIONS FOR DISPLAY.
C BASED ON FIRST Y-ARRAY
YTICK = (YMAX-YMIN)/YLEN
IDIVY = 1
DO 30 I = 1, 14
   IF (DIVY(I).LT.YTICK) IDIVY = I+1
30 CONTINUE
YDEL = DIVY(IDIVY)
IF (DELYES .NE. 0.0 )CALL SCALE (YARR,YLEN,NPTS,1)
IF (YARR(NPTS+2)).LT.DIVY(1)/(YLEN*DENSTY).OR. YARR(NPTS+2)).GT.DIVY(14)
   THEN
      YMIN = YARR(NPTS+1)
      YDEL = YARR(NPTS+2)
ENDIF
C QUICK PATCH FOR SCALING
IF (AUTO) THEN
   CALL SCALE (YARR,YLEN,NPTS,1)
   YMIN = YARR(NPTS+1)
   YDEL = YARR(NPTS+2)
ENDIF
C GRAPHICS ROUTINES
WRITE (6,'(A)') , 'DEVICE DRIVER NUMBER?'
WRITE (6,'(A)') , 'TEKTRONIX' = 0'
WRITE (6,'(A)') , 'REGIS (DEC) = 2'
WRITE (6,'(A)') , 'HOUSTON INSTRUMENTS = 6'
WRITE (6,'(A)') , 'PRINTRONIX' = 7'
READ (5,*) DVR
CALL PLOTS (O,DVR,PLTOUT)
C SET FACTOR AND ORIGIN
CALL PLOT (OFFSTX,OFFSTY,-3)
CALL FACTOR (FACTR)
C TEMPLATE
DACVAL=48.828125 E-3  ; CONV. ADC VOLTS TO ELECTRODE VOLTS
YMINO=YMIN*DACVAL
YDELO=YDEL*DACVAL
IF (FILENAME(18:20).EQ. 'LAT') GO TO 615
XMINO=XMIN*0.043
XDELO=XDEL*0.043
GO TO 616
615 XMINO=XMIN*0.155
XDELO=XDEL*0.155
616 CALL AXS (0.0,0.0,19HTIME (MILLISECONDS),
   9,-19,XLEN,O.,XMIN0,XDELO,0)
C X AXIS, BOTTOM
CALL AXS (XLEN,0.0,9HADC VALUE,-9,YLEN,90.,YMIN,YDEL,3)
C Y AXIS, LEFT
CALL AXS (0.0,0.0,20HELECTRODE MICROVOLTS,+20,YLEN,90.,
   *YMIN0,YDEL0,3)
C X AXIS, TOP
CALL AXS (0.0,YLEN,1H ,+1,XLEN,0.,XMIN0,XDELO,0)
APPENDAGE0=' (SINGLE)'
APPENDAGE1=' (DOUBLE)'
FILENAME0=FILENAME(1:27)//APPENDAGE0(1:11)
FILENAME1=FILENAME(1:27)//APPENDAGE1(1:11)

601 DO 602 I=1,3
NAME(I)=CHAR(FILENAME0(I:I))

602 CONTINUE
IF (CPROC.EQ.'A') GO TO 610
IF (CPROC.EQ.'D') GO TO 600
CALL SYMBOL (0.1*XLEN,1.1*YLEN,0.2,NAME,0.0,+27)
GO TO 620

600 CALL SYMBOL (0.1*XLEN,1.1*YLEN,0.2,NAME,0.0,+27)
GO TO 620

610 IF (COUNT.EQ.1) GO TO 611
CALL SYMBOL (0.05*XLEN,1.1*YLEN,0.2,NAME,0.0,+38)
GO TO 620

611 CALL SYMBOL (0.05*XLEN,1.1*YLEN,0.2,NAME,0.0,+38)

C VERTICAL LINES

620 XGRID(3) = XMIN
XGRID(4) = XDEL
YGRID(3) = YMIN
YGRID(4) = YDEL
XM = XMIN*XLEN+XDEL
XM = YMIN+YLEN*YDEL
XMAXP = XMIN+XLEN*XDEL
YMAXP = YMIN+YLEN*YDEL
YEND = (IFIX(XLEN)*DENSTY-1)
DO 40 I = 1, YEND
XGRID(1) = XM*FLOAT(I)/DENSTY+XMIN
IF (I/2*2.EQ.I) THEN
YGRID(1) = YMIN
ELSE
YGRID(1) = YMAXP
ENDIF
CALL DLINE (XGRID,YGRID,2,1,1,1)
40 CONTINUE

C HORIZONTAL LINES

YGRID(3) = YMIN
YGRID(4) = YDEL
XGRID(3) = XMIN
XGRID(4) = XDEL
XMAXP = XMIN*XLEN+XDEL
XMAXP = XMIN+XLEN*XDEL
YM = (YMAXP-YMIN)/YLEN
YEND = (IFIX(YLEN)*DENSTY-1)
DO 50 I = 1, YEND
YGRID(1) = YM*FLOAT(I)/DENSTY+YMIN
IF (I/2*2.EQ.I) THEN
XGRID(1) = XMIN
ELSE
XGRID(1) = XMAXP
ENDIF
CALL DLINE (XGRID,YGRID,2,1,1,1)
50 CONTINUE

C HORIZONTAL LINE MARKING ZERO LEVEL

XGRID(1) = XGRID(1)
XGRID(2) = XGRID(2)
XGRID(3) = XGRID(3)
XGRID(4) = XGRID(4)
YGRID(1) = 0.0
YGRID(2) = YGRID(2)
CALL DLINE (XGRID,YGRID,2,15,05,1)
C SOLID LINES FOR GRID
C
YSO = YLEN/2.0
X2S = XLEN/4.0
X50 = XLEN/2.0
X7S = X2S*.30
MOVE = 3
IDRAW = 2
C
CALL PLOT (0.0,YLEN,MOVE)
CALL PLOT (XLEN,YLEN,IDRAW)
CALL PLOT (0.0,Y50,MOVE)
CALL PLOT (XLEN,Y50,IDRAW)
CALL PLOT (X7S,0.0,MOVE)
CALL PLOT (X7S,YLEN,IDRAW)
CALL PLOT (X50,0.0,MOVE)
CALL PLOT (X50,YLEN,IDRAW)
CALL PLOT (XSO,0.0,MOVE)
CALL PLOT (XSO,YLEN,IDRAW)
CALL PLOT (X2S,0.0,MOVE)
CALL PLOT (X2S,YLEN,IDRAW)

C DRAW WAVE FORM.
C
XARR(NPTS+1) .. XMIN
XARR(NPTS+2) .. XDEL
YARR(NPTS+1) .. YMIN
YARR(NPTS+2) .. YDEL
CALL LINERR (XARR,YARR,NPTS,l,O,O)
C
FACTRR = 1.0/FACTR
CALL FACTOR (FACTRR)
CALL PLOT (-OFFSTX,-OFFSTY,-3)
C
C ------------------------ SECOND PLOT -------------------------
C
C FIND MAX OF Y 2 ARRAY, SET MIN TO ZERO.
C
YMAX2 = 0.0
YMIN2 = 0.0
DELYES = 0.0
YMAX2 = AMAX1(YMAX2,YARR2(1))
DO 110 I = 2,NPTS
YMAX2 = AMAX1(YMAX2,YARR2(I))
DELYES = AMAX1(DELYES,YARR2(I)-YARR2(I-1))
110 CONTINUE
C ACTIVATE NEXT LINE TO FORCE SCALE TO GO FROM 0 TO THE SET POINT.
C IF (YMAX2 .LT. EVOKS1) YMAX2 = EVOKS1
C
C SELECT APPROPRIATE Y DIVISIONS FOR DISPLAY.
C BASED ON SECOND Y-ARRAY
C
YTMP(1) = YMIN2
YTMP(2) = YMAX2
CALL SCALE (YTMP ,YLEN2, 2 ,1)
IF (DELYES .NE. 0.0 )CALL SCALE (YARR2,YLEN2,NPTS,1)
YDEL2 = AMAX1 (YTMP(4),YARR2(NPTS+2))
C
C GRAPHICS ROUTINES
C
C SET FACTOR AND ORIGIN
C
CALL PLOT (OFFSTX,OFFSY2,-3)
CALL FACTOR (FACTR)
C
C TEMPLATE
C
CALL PLOT (OFFSTX,OFFSY2,-3)
CALL FACTOR (FACTR)
C
C X AXIS, BOTTOM
C
CALL AXS (0.0,0.0,15HDATA POINT ,15,XLEN,0.,XMIN,XDEL,0)
C
C Y AXIS, RIGHT
C
CALL AXS (XLEN,0.0,1H ,1,YLEN2,90.,YMIN2,YDEL2,3)
C
C Y AXIS, LEFT
C
CALL AXS (0.0,0.0, 4HNUM. ,+4,YLEN2,90.,YMIN2,YDEL2,3)
CALL AXS (0.0, YLEN2, 1H, +1, XLEN, 0., XMIN, XDEL, 0)

CALL SYMBOL (0.1 * XLEN, 1.1 * YLEN2, 0.2, 16H NUMBER AVERAGED, 0.0, +16)

GRID

VERTICAL LINES

XGRID(3) = XMIN
XGRID(4) = XDEL
YGRID(3) = YMIN2
YGRID(4) = YDEL2
XMAXP = XMIN + XLEN * XDEL
YMAXP = XMIN + XLEN2 * YDEL2
XM = (XMAXP - XMIN) / XLEN
YN2 = (YMAXP - XMIN) / YLEN2
IEND = (IFIX(XLEN) * DENSTY - 1)
DO 140 I = 1, IEND
   XGRID(1) = (XM * FLOAT(I) / DENSTY + XMIN)
   XGRID(2) = XGRID(1)
   IF (I/2*2.EQ.I) THEN
      YGRID(1) = YMIN2
      YGRID(2) = YMAXP
   ELSE
      YGRID(2) = YMIN2
      YGRID(1) = YMAXP
   ENDIF
   CALL DLNE (XGRID, YGRID, 2, .1, .1, 1)
140 CONTINUE

HORIZONTAL LINES

YGRID(3) = YMIN2
YGRID(4) = YDEL2
XGRID(3) = XMIN
XGRID(4) = XDEL
YMAXP = XMIN + XLEN2 * YDEL2
YMIN = (YMAXP - XMIN2) / YLEN2
YN2 = (YMAXP - XMIN) / YLEN2
IEND = (IFIX(YLEN2) * DENSTY - 1)
DO 150 I = 1, IEND
   YGRID(1) = (YM * FLOAT(I) / DENSTY + YMIN2)
   YGRID(2) = YGRID(1)
   IF (I/2*2.EQ.I) THEN
      XGRID(1) = XMIN
      XGRID(2) = XMAXP
   ELSE
      XGRID(2) = XMIN
      XGRID(1) = XMAXP
   ENDIF
   CALL DLNE (XGRID, YGRID, 2, .1, .1, 1)
150 CONTINUE

MARKING EVOKS1 AND EVOKS2 LEVEL

XMAXP = XMIN + XLEN * XDEL
XGRID(1) = XMAXP * 1.025
XGRID(2) = XGRID(1)
YGRID(1) = EVOKS1
YGRID(2) = EVOKS2
CALL LINE (XGRID, YGRID, 2, 1, 1, 3)

SOLID LINES FOR GRID

Y50 = YLEN2/2.0
X25 = XLEN/4.0
X50 = XLEN/2.0
X75 = X25*3.0
MOVE = 3
IDRAW = 2
CALL PLOT (0.0,YLEN2,MOVE)
CALL PLOT (XLEN,YLEN2,IDRAW)
CALL PLOT (X75,0.0,MOVE)
CALL PLOT (X75,YLEN2,IDRAW)
CALL PLOT (X50,YLEN2,MOVE)
CALL PLOT (X50,0.0,IDRAW)
CALL PLOT (X25,0.0,MOVE)
CALL PLOT (X25,YLEN2,IDRAW)
CALL PLOT (XLEN,0.0,MOVE)
CALL PLOT (XLEN,YLEN2,IDRAW)

DRAW WAVE FORM.

XARR(NPTS+1) = XMIN
XARR(NPTS+2) = XDEL
YARR2(NPTS+1) = YMIN2
YARR2(NPTS+2) = YDEL2
CALL LINERR (XARR,YARR2,NPTS,1,0,0)

RESET FACTOR AND ORIGIN
FACTRR = 1.0/FACTR
CALL FACTOR (FACTRR)
CALL PLOT (-OFFSTX,-OFFSY2,-3)

FIND MAX OF Y 3
ARRAY, SET MIN TO ZERO.

YMAX3 = 0.0
YMIN3 = 0.0
YMAX3 = AMAX1(YMAX3,YARR3(1))
DO 210 I = 2, NPTS
YMAX3 = AMAX1(YMAX3,YARR3(I))
DELYES = AMAX1(DELYES,YARR3(I)-YARR3(I-1))
210 CONTINUE

ACTIVATE NEXT LINE TO FORCE SCALE TO GO FROM 0 TO THE SET POINT.
IF (YMAX3 .LT. EVSD3) YMAX3 = EVSD3

SELECT APPROPRIATE Y DIVISIONS FOR DISPLAY.
BASED ON SECOND Y-ARRAY

YTMP(1) = YMIN3
YTMP(2) = YMAX3
CALL SCALE (YTMP ,YLEN3, 2 ,1)
IF (DELYES .NE. 0.0 )CALL SCALE (YARR3,YLEN3,NPTS,1)
YDEL3 = AMAX1 (YTMP(4),YARR3(NPTS+2))

GRAPHICS ROUTINES

SET FACTOR AND ORIGIN

CALL PLOT (OFFSTX,OFFSY3,-3)
CALL FACTOR (FACTRR)

TEMPLATE
X AXIS, BOTTOM
CALL AXS (0.0,0.0,15DATA POINT ,-15,XLEN,0.,XMIN,XDEL,0)

Y AXIS, RIGHT
CALL AXS (XLEN,0.0,1H ,,-1,YLEN3,90.,YMIN3,YDEL3,3)

Y AXIS, LEFT
CALL AXS (0.0,0.0, 4NUM. ,+4 ,YLEN3,90.,YMIN3,YDEL3,3)

X AXIS, TOP
CALL AXS (0.0,YLEN3,1H ,+1,XLEN,0.,XMIN,XDEL,0)

SYMBOL
CALL SYMBOL (0.1*XLEN,1.1*YLEN3,0.2,
& 19HSTANDARD DEVIATION ,0.0,+19)
C GRID
C VERTICAL LINES
C
XGRID(3) = XMIN
XGRID(4) = XDEL
YGRID(3) = YMIN3
YGRID(4) = YDEL3
XMAXP = XMIN+XLEN*XDEL
YMAXP = YMIN3+YLEN3*YDEL3
XMIN = (XMAXP-XMIN)/XLEN
IEND = (IFIX(XLEN)*DENSTY-1)
DO 240 I = 1, IEND
  XGRID(1) = (XMIN*FLOAT(I)/DENSTY+XMIN)
  IF (I/2.*2.EQ.I) THEN
    YGRID(1) = YMIN3
    YGRID(2) = YMAXP
  ELSE
    YGRID(2) = YMIN3
    YGRID(1) = YMAXP
  ENDIF
  CALL DLINEx (XGRID,YGRID,2, .1,.1,1)
240 CONTINUE
C HORIZONTAL LINES
C
YGRID(3) = YMIN3
YGRID(4) = YDEL3
XGRID(3) = XMIN
XGRID(4) = XDEL
YMAXP = YMIN3+YLEN3*YDEL3
YMIN3 = (YMAXP-YMIN3)/YLEN3
IEND = (IFIX(YLEN3)*DENSTY-1)
DO 250 I = 1, IEND
  YGRID(1) = (YMIN3*FLOAT(I)/DENSTY+YMIN3)
  IF (I/2.*2.EQ.I) THEN
    XGRID(1) = XMIN
    XGRID(2) = XMAXP
  ELSE
    XGRID(2) = XMIN
    XGRID(1) = XMAXP
  ENDIF
  CALL DLINEx (XGRID,YGRID,2, .1,.1,1)
250 CONTINUE
C + MARKING ZERO LEVEL
C
XMAXP = XMIN+XLEN*XDEL
XGRID(1) = XMAXP * 1.025
YGRID(1) = EVSD3
CALL LINEx (XGRID,YGRID,1,1,-1,3)
C SOLID LINES FOR GRID
C
X50 = YLEN3/2.0
X25 = XLEN/4.0
X50 = XLEN/2.0
X75 = X25*3.0
MOVE = 3
IDRAW = 2
CALL PLOT (0.0,YLEN3,MOVE)
CALL PLOT (XLEN,YLEN3,MOVE)
CALL PLOT (0.0,Y50,MOVE)
CALL PLOT (XLEN,Y50,MOVE)
CALL PLOT (X75,YLEN3,MOVE)
CALL PLOT (X50,YLEN3,MOVE)
CALL PLOT (X50,0.0,MOVE)
CALL PLOT (X25,0.0,MOVE)
CALL PLOT(XLEN,YLEN3,IDRAW)
CALL PLOT(XLEN,0.0,MOVE)
CALL PLOT(XLEN,YLEN3,IDRAW)

DRAW WAVE FORM.

CALL PLOT(XLEN,O.O,MOVE)
CALL PLOT(XLEN,YLEN3,IDRAW)

RESET FACTOR AND ORIGIN

FACTRR = 1.0/FACTR
CALL FACTOR (FACTRR)
CALL PLOT(-OFFSTX,-OFFSY2,-3)

RETURN
END

SUBROUTINE ISDEF (NUMBER,MESSAGE,RDWRT)

C THIS ROUTINE WILL CHECK IF FILE NUMBER "NUMBER" IS OPEN. IF
C IT IS THEN NO ACTION IS TAKEN.
C IF NOT THEN A WRITE STATEMENT IS ISSUED TRANSMITTING
C THE MESSAGE "MESSAGE" TO THE TERMINAL FOLLOWED BY A READ
C WHICH READS A FILE NAME TO BE OPENED.
C
C IF NUMBER EQUALS EITHER TTI OR TTO, NO ACTION IS TAKEN.

INTEGER NUMBER,TTI,TTO
PARAMETER (TTI=5,TTO=6)
CHARACTER(*) MESSAGE
CHARACTER(*) RDWRT
CHARACTER*50 FILE NAME
CHARACTER*5 READ,WRITE
LOGICAL TF
DATA READ,WRITE / 'READ ', 'WRITE'/

IF (NUMBER.EQ.TTI.OR.NUMBER.EQ.TTO) RETURN
INQUIRE (UNIT=NUMBER,OPENED=TF)
IF (.NOT.TF) THEN
WRITE (TTI,'(A,$)') MESSAGE
READ (TTI, '(Q,A)') LEN,FILE NAME(1:LEN)
IF (RDWRT(1:5).EQ.READ) THEN
OPEN (UNIT=NUMBER,FILE=FILE NAME(1:LEN),STATUS='old')
ELSE
IF (LEN.EQ.0) THEN
LEN = 6
FILE NAME(1:LEN) = 'TXA6:'
ENDIF
OPEN (UNIT=NUMBER,FILE=FILE NAME(1:LEN),STATUS='new',
    CARRIAGECONTROL='list',RECL=256)
ENDIF
ENDIF
RETURN
END

SUBROUTINE MEANCU (DATA,IFLAG,NSEP,NDATA,AMEAN,SD)

PARAMETER (NBITS=3, MAXDIF=16200)

INTEGER NDATA(*),IFLAG(*),BITS(NBITS),NDT(MAXDIF)
REAL*4 DATA(*),AMEAN(*),SD(*)
REAL*4 ASUM(MAXDIF),ASUMSQ(MAXDIF)

DATA FIRST / .TRUE. /

This subroutine determines mean and standard deviation.
It differs from MEANSD in that MEANSD receives an array for which the
mean and standard deviation are calculated and this routine is called
once for each value in the group for which the mean and sd is calculated.
This routine will keep track of "nsep" different groups of values.

USAGE:
VALUE OF IFLAG ON INPUT (ENTER AS DECIMAL)
FEATURE
DECIMAL
BINARY BIT
Accumulate values
Calculate mean and sd
Reset for new set of values

To select more than one feature, add the numbers together, i.e.: to calculate mean and sd and then reset, set iflag equal to 6.

If more than one feature is selected they are executed in the order listed above.

IF (NSEP.GT.MAXDIF) STOP ' NSEP TOO LARGE IN S/R MEANCU.'
IF (.NOT.FIRST) GO TO 20
DO 10 J = 1, MAXDIF
   ASUM(J) = 0.0
   ASUMSQ(J) = 0.0
   NDT(J) = 0
10 CONTINUE
C DECODE IFLAG
20 DO 30 J = 1, NSEP
   CALL DECODE (IFLAG(J),BITS,NBITS)
C
ACCUMULATE VALUES
IF (BITS(1).EQ.1) THEN
   NDT(J) = NDT(J)+1
   ASUM(J) = ASUM(J)+DBLE(DATA(J))
   ASUMSQ(J) = ASUMSQ(J)+DBLE(DATA(J)*DATA(J))
ENDIF
CALCULATE MEAN AND SD
IF (BITS(2).EQ.1) THEN
   IF (NOT(J).GE.2) THEN
      AMEAN(J) = SNGL(ASUM(J)/FLOAT(NOT(J))
      SD(J) = SNGL((ASUMSQ(J)-(ASUM(J)*ASUM(J)/FLOAT(NDT(J))))
                    /FLOAT((NDT(J)-1)))
      SD(J) = SQRT(SD(J))
   ELSE
      AMEAN(J) = SNGL(ASUM(J))
      SD(J) = -1.0
   ENDIF
ENDIF
NDATA(J) = NDT(J)
RESET FOR NEW SET OF VALUES
IF (BITS(3).EQ.1) THEN
   ASUM(J) = 0.0
   ASUMSQ(J) = 0.0
   NDT(J) = 0
ENDIF
30 CONTINUE
FIRST = .FALSE.
RETURN
END

SUBROUTINE DECODE (IDEC,BITS,NBITS)
   Integer*2 INDEX
   Integer*4 DATA(NBITS)
   DO 20 I = 1, NBITS
      INDEX = mod(IDEC,2)
      IDEC = IDEC/2
20 Continue
RETURN
END

This routine receives a decimal number and converts it to binary,
placing zero's or one's in the array bits. The least significant
bit is placed in bits(1).

INUMB = IDEC
Do 20 I = 1, NBITS
   BITS(I) = mod(INUMB,2)
   INUMB = INUMB/2
20 Continue
RETURN
END

SUBROUTINE EGG(FILENAME)
   FRANK A. ZAK, 26 SEP 88
   Implicit Integer*4 (A-Z)
   Include 'SYS$LIBRARY:VMSLIB.FOR'
   Integer*2 DCB0(DCBLN),DCB1(DCBLN),DCB2(DCBLN)
   Integer*2 DCB3(DCBLN,4)


```fortran
Integer*2 MSCB(MSCBLEN)
Parameter IBFLIM = 4096
Integer*2 IDTBUF(IBFLIM)
Common/IDTBUF/IDTBUF
Character*4 ADNAME, CKNAME
Data ADNAME, CKNAME /'ASA0', 'KWA0'/
DATA IEFN, ISTART /1, 1/
Character*28 FILENAMEO

Call CHECK_PRIORITY (ensure real time priority)
Call DTDEV(IDCBO, ADNAME)
If (IDCB(1).eq.1) Go to 1
Call ERROR_MESSAGE(IDCBO)
Go to 1001
1 Call DTDEV(IDCBO, CKNAME)
If (IDCB(1).eq.1) Go to 2
Call ERROR_MESSAGE(IDCBO)
Go to 1001
2 CALL DTCIC(IDCBO, 0, 3)
IF (IDCB(1).EQ.-1) GO TO 1000
IDIV=11 KHz CLOCK (1 mSEC PERIOD)
CALL DTCLK(IDCBO,1,0,IDIV) !STOP THE CLOCK
CALL DTCLK(IDCBO,1,4,IDIV) !START THE CLOCK
CALL ERROR_MESSAGE(IDCBO)
Go to 1001
3 Call DTSDBB(IDCBO, IEFN, IDTBUF, IBFLIM)
If (IDCB(1).eq.1) Go to 5
Call ERROR_MESSAGE(IDCBO)
Go to 1001
5 Call MSINIT(IDCBO, MSCB)
If (IERR1(IDCBO, 'MSINIT')) Go to 1001
IDISC=(IBFLIM/256)+1
Call MSALLOC(IDCBO, -IDISC, -1) !IFZM
If (IERR1(IDCBO, 'MSALLOC')) Go to 1001
Call MSOPNU(IDCBO, FILENAMEO)
If (IERR1(IDCBO, 'MSOPNU')) Go to 1000
Call MSRWN(IDCBO)

ACQUIRE THE DATA AND STORE IT ON THE DISK FILE
Call DTSSBR(IDCBO)
If (IERR1(IDCBO, 'DTSSBR')) Go to 1000
CALL DTCLK(IDCBO,1,4,IDIV) !START THE CLOCK
IF (IDCB(1).EQ.1) GO TO 6
CALL ERROR_MESSAGE(IDCBO)
GO TO 1000
6 Call DTSBWB(IDCBO)
IF (IERR1(IDCBO, 'DTSBWB')) Go to 1000
Call MSSBH(IDCBO)
If (IERR1(IDCBO, 'MSSBH')) Go to 1000
Call MSSBWB(IDCBO)
If (IERR1(IDCBO, 'MSSBWB')) Go to 1000
CALL DTCLK(IDCBO,1,0,IDIV) !STOP THE CLOCK
IF (IDCB(1).EQ.1) GO TO 7
CALL ERROR_MESSAGE(IDCBO)
```

SUBROUTINE READ EEG(FILENAMEO)
    FRANK A. ZAK, 13 OCT 88
    Implicit Integer*4 (A-Z)
    Include 'SYSLIBRARY:VMSLIB.FOR'
    Integer*2 IDCB, IDCBO, IDCBl, IDCB(2), IDCBO(2), IDCBl(2)
    Integer*2 MSCB(2)
    Parameter IBFLIM = 4096
    Integer*2 IDTBUF(IBFLIM)
    Common/IDTBUF/IDTBUF
    REAL XARR(4099), YARR(4099)
    Character*28 ADNAME, CKNAME
    Data ADNAME, CKNAME /'AZAO', 'KWAO'/
    Character*28 FILENAME0
    Call CHECK_PRIORITY ensure real time priority
    Call DTDEVT(IDCBO, ADNAME)
      If (IDCB(l).eq. 1) Go to 1
      Call ERROR_MESSAGE(IDCBO)
      Go to 1001-
    Call DTDEVID(IDCBO, CKNAME)
      If (IDCB(l).eq. 1) Go to 2
      Call ERROR_MESSAGE(IDCBO)
      Go to 1001-
    Call DTICH(IDCBO, 0, 3)
      If (IDCB(l).eq. -1) Go to 1000
    DO 4 I=1, 4099
      XARR(I) = 0.0
      YARR(I) = 0.0
      CONTINUE
    Call MSINIT(IDCBO, MSCB)
      If (IERR1(IDCBO, 'MSINIT')) Go to 1001
    READ THE FILE BACK IN FROM THE DISK
    Call MSONO(IDCBO, FILENAME0)
      If (IERR1(IDCBO, 'MSONO')) Go to 1000
    Call DTSNDB(IDCBO, IEFN, IDTBUF, IBFLIM)
      If (IDCB(l).eq. 1) Go to 8
      Call ERROR_MESSAGE(IDCBO)
      Go to 1000-
    Call MSSBRR(IDCBO)
      If (IERR1(IDCBO, 'MSSBRR')) Go to 1000
    Call MSSBWB(IDCBO)
      If (IERR1(IDCBO, 'MSSBWB')) Go to 1000
    PROCESS THE DATA
    DO 9 I=1, 4096
      XARR(I) = FLOAT(I-1)
      YARR(I) = FLOAT(IDTBUF(I))
      CONTINUE
    NPTS = 4096
CALL OSCOPE(XARR,YARR,NPTS,ISTART,FILENAMEO)
CALL PLOT(0.0,0.0,0.0,999)

C
C 1000 CALL MSCLOS(IDCB)
1001 RETURN
END

C SUBROUTINE OSCOPE(XARR,YARR,NPTS,ISTART,FILENAMEO)
DIMENSION XARR(1), YARR(1), DIVX(21), DIVY(14)
DIMENSION YSMALL(5)
DIMENSION XGRID(4), YGRID(4)
LOGICAL AUTO
INTEGER DVR, PLTOUT
PARAMETER (PLTOUT=10,XLEN=10.0,YLEN=4.0,DENSTY=2.0)
PARAMETER (FACTR=0.97, OFFSTX=0.38, OFFSTY=3.50)
BYTE NAME(28)
CHARACTER*80 MESSAGE
CHARACTER*5 RDWRT
CHARACTER*28 FILENAMEO
DATA AUTO .TRUE., DATA READ, WRITE '/READ ', 'WRITE'/

C X division array set in units of milliseconds.
C DATA DIVX(1),DIVX(2),DIVX(3),DIVX(4),DIVX(5)
& / .001, .002, .005, .01, .02 /
DATA DIVX(6),DIVX(7),DIVX(8),DIVX(9),DIVX(10)
& / .05, .1, .2, .5, 1. /
DATA DIVX(11),DIVX(12),DIVX(13),DIVX(14),DIVX(15)
& / 2., 5., 10., 20., 50. /
DATA DIVX(16),DIVX(17),DIVX(18),DIVX(19),DIVX(20)
& / 100., 200., 500., 1000., 2000. /
DATA DIVX(21)
& / 5000. /

C Y division array set in units of millivolts.
C DATA DIVY(1),DIVY(2),DIVY(3),DIVY(4),DIVY(5)
& 1., 2., 5., 10., 20. /
DATA DIVY(6),DIVY(7),DIVY(8),DIVY(9),DIVY(10)
& / 50., 100., 200., 500., 1000. /
DATA DIVY(11),DIVY(12),DIVY(13),DIVY(14)
& / 2000., 5000., 10000., 20000. /

C Check that output file is open, if not then open.
C MESSAGE(1:46)
& = ' Where would you like the plot?, (T,x6, etc.) '
rdwrt = WRITE
CALL ISDEF(pltout,MESSAGE,RDWRT)
C Find min and max of x and y arrays.
C YMAX = 0.0
YMIN = 0.0
XMAX = 0.0
XMIN = 0.0
C DO 8 I = 1, ISTART-1
XMAX = AMAX1(XMAX, XARR(I))
XMIN = AMIN1(XMIN, XARR(I))
8 CONTINUE
C DO 10 I = ISTART, NPTS
YMAX = AMAX1(YMAX, YARR(I))
XMAX = AMAX1(XMAX, XARR(I))
YMIN = AMIN1(YMIN, YARR(I))
XMIN = AMIN1(XMIN, XARR(I))
10 CONTINUE
YSMALL(1) = YMIN
YSMALL(2) = YMAX
C CLIP ARRAY
C
DO 12 I = 1, ISTART-1
IF (YARR(I) .GT. YMAX) YARR(I) = YMAX
IF (YARR(I) .LT. YMIN) YARR(I) = YMIN
12 CONTINUE
C
C Select appropriate x divisions for display.
C
XTICK = (XMAX - XMIN) / XLEN
DIVX = 1
DO 20 I = 1, 21
IF (DIVX(I) .LT. XTICK) DIVX = I + 1
20 CONTINUE
XDEL = DIVX(DIVX)
CALL SCALE(XARR,XLEN,NPTS,1)
IF (XARR(NPTS+2) .LT. DIVX(1)/(XLEN*DENSTY)) &
.YOR. XARR(NPTS+2) .GT. DIVX(21)) XDEL = XARR(NPTS+2)
C
C Select appropriate y divisions for display.
C
YTICK = (YMAX - YMIN) / YLEN
DIVY = 1
DO 30 I = 1, 14
IF (DIVY(I) .LT. YTICK) DIVY = I + 1
30 CONTINUE
YDEL = DIVY(DIVY)
CALL SCALE(YARR,YLEN,NPTS,1)
CALL SCALE(YSMALL,YLEN,2,1)
YARR(NPTS+1) = YSMALL(3)
YARR(NPTS+2) = YSMALL(4)
YARR(NPTS+3) = YSMALL(5)
IF (YARR(NPTS+2) .LT. DIVY(1)/(YLEN*DENSTY)) &
.YOR. YARR(NPTS+2) .GT. DIVY(14)) YDEL = YARR(NPTS+2)
IF (AUTO) THEN
CALL SCALE (YARR,YLEN,NPTS,1)
YMIN = YARR(NPTS+1)
YDEL = YARR(NPTS+2)
ENDIF
C
Graphics routines
C
WRITE (6,'(A)') ' DEVICE DRIVER NUMBER?'
WRITE (6,'(A)') ' TECNTRONIX' = 0'
WRITE (6,'(A)') ' REGIS (DEC) = 2'
WRITE (6,'(A)') ' HOUSTON INSTRUMENTS = 6'
WRITE (6,'(A)') ' PRINTERONIX = 7'
READ (5,*) DVR
CALL PLOTS (0,DVR,PLTOUT)
C
Set factor and origin
C
CALL PLOT (OFFSTX, OFFSTY, -3)
CALL FACTOR (FACTR)
C
Template
DACVAL=48.828125E-3 CONVERT ADC VOLTS TO ELECTRODE VOLTS
YMIN=YMIN*DACVAL
XDEL=XDEL*DACVAL
XMIN=XMIN*1.0 CONVERT TO MILLISECONDS
XDEL=XDEL*1.0 CONVERT TO MILLISECONDS
DO 602 I=1,28
NAME(I)=ICHAR(FILENAME(1:I))
602 CONTINUE
C X axis, bottom
CALL AXS (0.0, 0.0, 
.19HTIME (MILLISECONDS),-19,XLEN,0.,XMIN,XDEL,0)
C Y AXIS, RIGHT
CALL AXS (XLEN,0.0,SHADC VALUE,-9,YLEN,90.,YMIN,YDEL,3)
C Y AXIS, LEFT
CALL AXS(0.0,0.0,20HELECTRODE MICROVOLTS,+20,YLEN,
*90.,YMIN,YDEL,3)
CALL AXS(0.0,YLEN,1H,+1,XLEN,0.,XMING,XDEL0,0.)
CALL SYMBOL(0.05*XLEN,1.1*YLEN,0.2,NAME,0.0,+28)

CALL DLINE(XGRID, YGRID, 2, .1, .1, 1)

CALL DLINE(XGRID, YGRID, 2, .1, .1, 1)

CALL DLINE(XGRID, YGRID, 2, .1, .1, 1)

CALL DLINE(XGRID, YGRID, 2, .1, .1, 1)

CALL DLINE(XGRID, YGRID, 2, .1, .1, 1)

CALL DLINE(XGRID, YGRID, 2, .15, .05, 1)

CALL PLOT(0.0, Y50, MOVE)
CALL PLOT(X75, 0.0, MOVE)
CALL PLOT(X75, YLEN, IDRAW)
CALL PLOT(X50, YLEN, IDRAW)
CALL PLOT(X50, 0.0, IDRAW)
CALL PLOT(X25, 0.0, MOVE)
CALL PLOT(X25, YLEN, IDRAW)

C

C Draw wave form.
CALL LINERR (XARR, YARR, NPTS, 1, 0, 0)

C Reset factor and origin

FACTRR = 1.0 / FACTR
CALL FACTOR (FACTRR)
CALL PLOT (OFFSTX, OFFSTY, -3)
RETURN
end

SUBROUTINE BELL(MESSAGE)
CHARACTER*(*) MESSAGE
CALL BUFOUT(7,1,6)
WRITE(6,'(A)') MESSAGE
RETURN
END

SUBROUTINE BUFOUT (IADE, N, IOUT)
CHARACTER*1 IADE(250)
DIMENSION IADE(1)
DO 10 J = 1, N
   CIADE(J) = CHAR(IADE(J))
CONTINUE
WRITE (IOUT,100) (CIADE(I),I=1,N)
100 FORMAT(1H,250A1)
RETURN
END
APPENDIX C

LATE_CHOP
PROGRAM LATE Chop
C REDUCES THE SIZE OF THE LATE FILES FROM 6400 BLOCKS TO 400 BLOCKS
C FRANK A. ZAK, 28 NOV 89
C
C IMPLICIT INTEGER*4 (A-Z)
C
PARAMETER (ADMAX=2047, ADMIN=-2047)
PARAMETER (MAXDAT=16384,MAXDT2=16386)
PARAMETER (PLTOUT=10)
PARAMETER (IBFLIM=32768)
C
CHARACTER*1 CPROC,CTYPE,SORD
CHARACTER*1 AOF,FILETYPE,READALL,STUDY
CHARACTER*2 CPERCENT
CHARACTER*5 INITIALS
CHARACTER*18 OUTFILE
CHARACTER*28 EEGFILE
CHARACTER*32 FILENAME,FILENAME0

IMPLICIT INTEGER*4
PARAMETER (ADMAX=2047, ADMIN=-2047)
PARAMETER (MAXDAT=16384, MAXDT2=16386)
PARAMETER (PLTOUT=10)
PARAMETER (IBFLIM=32768)
CHARACTER*l CPROC,CTYPE,SORD
CHARACTER*l AOF,FILETYPE,READALL,STUDY
CHARACTER*2 CPERCENT
CHARACTER*3 INITIALS
CHARACTER*18 OUTFILE
CHARACTER*28 EEGFILE
CHARACTER*32 FILENAME,FILENAME0

COMPLEX*16 A(8192)
DATA FILENAME /
DATA FILENAME0 /
C
INTEGER IFLAG(MAXDAT),IFLAG2(MAXDAT),IFLAG4(MAXDAT),NDATA(MAXDT2)
INTEGER DENOM(MAXDAT)
INTEGER COUNT,DAY
INTEGER*2 IDTBUF(IBFLIM)
LOGICAL ONDISK
REAL XARR(MAXDT2),YARR2(MAXDT2),EPOCHS
REAL*4 A0,A1,A2,A3,OFFSET,EDGE,PERCENT,AVERAGE,SCALE
REAL*4 AREA,MAG_AREA,PHASE_AREA,RMS,MAG_RMS,PHASE_RMS
REAL*4 RATIO,MAG_RATIO,PHASE_RATIO
REAL*4 AREA,RMS,MAG RMS,PHASE RMS
REAL*4 RATIO,AREA,MAG AREA, PHASE AREA
REAL*4 DATA(MAXDT2),AMEAN(MAXDT2),SD(MAXDT2),AMAX,V
REAL*4 F(8192),FM(8192),FP(8192),FR(8192),FI(8192)

WRITE (6,'(A)') ' ENTER 1 FOR PHASE 1 OR 2 FOR PHASE 2'
READ (5,'(') PHASE
IF (PHASE.EQ.1) THEN
   DAYUP=15
   SUBJUP=9
ELSE
   DAYUP=16
   SUBJUP=7
ENDIF

WRITE (6,'(A)') ' ENTER A FOR ALL-SUBJECT READ'
WRITE (6,'(A)') ' OR O FOR 1-SUBJECT READ'
WRITE (6,'(A)') ' OR F FOR 1-FILE READ'
READ (5, '(') AOF
IF (AOF.EQ.'A') GO TO 851
IF (AOF.EQ.'O') GO TO 855

WRITE (6, '(') ' STUDY SUBJECT? (Y=Yes,N=No)'
READ (5, '(') STUDY
IF (STUDY.EQ.'N') THEN
   WRITE (6, '(') ' ENTER FILENAME'
   READ (5, '(') FILENAME
   IF (FILENAME(18:20).NE.'LAT') GO TO 1001
   COUNT=0
   DAYINC=1
   FILETYPE(1:1)='L'
   GO TO 696
ELSE
   IF (PHASE.EQ.1) THEN
      WRITE (6, '(') ' ENTER DAY (0, 1-5, 10, OR 15)'
      READ(5, '(') DAY
   ELSE
      WRITE (6, '(') ' ENTER DAY (0-2, 5-6, 9, OR 12-16)'
      READ(5, '(') DAY
  ENDIF
WRITE (6,'(A)') ' ENTER SUBJECT INITIALS'
READ(5,'(A)') INITIALS

IF (PHASE.EQ.1) THEN
   IF (INITIALS(1:3).EQ.'MLR') SUBJECT=0
   IF (INITIALS(1:3).EQ.'SJD') SUBJECT=1
   IF (INITIALS(1:3).EQ.'TRB') SUBJECT=2
   IF (INITIALS(1:3).EQ.'SKW') SUBJECT=3
   IF (INITIALS(1:3).EQ.'DSC') SUBJECT=4
   IF (INITIALS(1:3).EQ.'DJC') SUBJECT=5
   IF (INITIALS(1:3).EQ.'DSG') SUBJECT=6
   IF (INITIALS(1:3).EQ.'RRC') SUBJECT=7
   IF (INITIALS(1:3).EQ.'DBH') SUBJECT=8
   IF (INITIALS(1:3).EQ.'JRH') SUBJECT=9
ELSE
   IF (INITIALS(1:3).EQ.'MDW') SUBJECT=0
   IF (INITIALS(1:3).EQ.'TRB') SUBJECT=1
   IF (INITIALS(1:3).EQ.'MWK') SUBJECT=2
   IF (INITIALS(1:3).EQ.'BLP') SUBJECT=3
   IF (INITIALS(1:3).EQ.'PEF') SUBJECT=4
   IF (INITIALS(1:3).EQ.'MWF') SUBJECT=5
   IF (INITIALS(1:3).EQ.'DDS') SUBJECT=6
   IF (INITIALS(1:3).EQ.'RFF') SUBJECT=7
ENDIF

ENDIF

IF (AOF.EQ.'F') GO TO 44
ENDIF

851 DAYINC=1
IF (PHASE.EQ.1) THEN
   WRITE (6,'(A)') ' ENTER 8 FOR 8-FILE READ OR 4 FOR 4-FILE READ'
   WRITE (6,'(A)') ' NOTE: 4 FILES = BASELINE + 3 STEADY-STATES'
   READ (5,'(A)') READALL
   IF (READALL.EQ.'4') DAYINC=5
ENDIF

44 IF (AOF.EQ.'O') GO TO 853
IF (AOF.EQ.'A') GO TO 301

301 DO 401 SUBJECT=0,SUBJUP
C
IF (PHASE.EQ.1) THEN
   IF (SUBJECT.EQ.0) INITIALS(1:3)=MLR'
   IF (SUBJECT.EQ.1) INITIALS(1:3)=SJD'
   IF (SUBJECT.EQ.2) INITIALS(1:3)=TRB'
   IF (SUBJECT.EQ.3) INITIALS(1:3)=SKW'
   IF (SUBJECT.EQ.4) INITIALS(1:3)=DSC'
   IF (SUBJECT.EQ.5) INITIALS(1:3)=DJC'
   IF (SUBJECT.EQ.6) INITIALS(1:3)=DSG'
   IF (SUBJECT.EQ.7) INITIALS(1:3)=RRC'
   IF (SUBJECT.EQ.8) INITIALS(1:3)=DBH'
   IF (SUBJECT.EQ.9) INITIALS(1:3)=JRH'
ELSE
   IF (SUBJECT.EQ.0) INITIALS(1:3)=MDW'
   IF (SUBJECT.EQ.1) INITIALS(1:3)=TRB'
   IF (SUBJECT.EQ.2) INITIALS(1:3)=MWK'
   IF (SUBJECT.EQ.3) INITIALS(1:3)=BLP'
   IF (SUBJECT.EQ.4) INITIALS(1:3)=PEF'
   IF (SUBJECT.EQ.5) INITIALS(1:3)=MWF'
   IF (SUBJECT.EQ.6) INITIALS(1:3)=DDS'
   IF (SUBJECT.EQ.7) INITIALS(1:3)=RFF'
ENDIF

C

853 DO 402 DAY=0,DAYUP,DAYINC
C
IF (PHASE.EQ.1) THEN
   * GO TO 402
ELSE
   IF ((DAY.EQ.3).OR.(DAY.EQ.4).OR.(DAY.EQ.7).OR.(DAY.EQ.8).OR.
   * (DAY.EQ.10).OR.(DAY.EQ.11))
   * GO TO 402
ENDIF
C
302 IF (PHASE.EQ.1) THEN

   IF ((INITIALS.EQ.'MLR').AND.(DAY.EQ.0)) THEN
      FILENAME(1:32)="MLR 14OCT88 0749 LAT ALT_X1.DATA"
      IF ((INITIALS.EQ.'MLR').AND.(DAY.EQ.1)) THEN
         FILENAME(1:32)="MLR 17OCT88 0743 LAT ALT_X1.DATA"
      ENDIF
      IF ((INITIALS.EQ.'MLR').AND.(DAY.EQ.2)) THEN
         FILENAME(1:32)="MLR 18OCT88 0750 LAT ALT_X1.DATA"
      ENDIF
      IF ((INITIALS.EQ.'MLR').AND.(DAY.EQ.3)) THEN
         FILENAME(1:32)="MLR 20OCT88 0751 LAT ALT_X1.DATA"
      ENDIF
      IF ((INITIALS.EQ.'MLR').AND.(DAY.EQ.4)) THEN
         FILENAME(1:32)="MLR 21OCT88 0842 LAT ALT_X1.DATA"
      ENDIF
      IF ((INITIALS.EQ.'MLR').AND.(DAY.EQ.5)) THEN
         FILENAME(1:32)="MLR 26OCT88 0756 LAT ALT_X1.DATA"
      ENDIF
      IF ((INITIALS.EQ.'MLR').AND.(DAY.EQ.6)) THEN
         FILENAME(1:32)="MLR_31OCT88_0744_LAT_ALT_X1.DATA"
      ENDIF
   ENDIF

   IF ((INITIALS.EQ.'SJD').AND.(DAY.EQ.0)) THEN
      FILENAME(1:32)="SJD 14OCT88 0819 LAT ALT_X1.DATA"
      IF ((INITIALS.EQ.'SJD').AND.(DAY.EQ.1)) THEN
         FILENAME(1:32)="SJD 17OCT88 0805 LAT ALT_X1.DATA"
      ENDIF
      IF ((INITIALS.EQ.'SJD').AND.(DAY.EQ.2)) THEN
         FILENAME(1:32)="SJD 19OCT88 0816 LAT ALT_X1.DATA"
      ENDIF
      IF ((INITIALS.EQ.'SJD').AND.(DAY.EQ.3)) THEN
         FILENAME(1:32)="SJD 20OCT88 0819 LAT ALT_X1.DATA"
      ENDIF
      IF ((INITIALS.EQ.'SJD').AND.(DAY.EQ.4)) THEN
         FILENAME(1:32)="SJD 21OCT88 0817 LAT ALT_X1.DATA"
      ENDIF
      IF ((INITIALS.EQ.'SJD').AND.(DAY.EQ.5)) THEN
         FILENAME(1:32)="SJD_31OCT88_0823_LAT_ALT_X1.DATA"
      ENDIF
   ENDIF

   IF ((INITIALS.EQ.'TRB').AND.(DAY.EQ.0)) THEN
      FILENAME(1:32)="TRB 10OCT88 0712 LAT ALT_X1.DATA"
      IF ((INITIALS.EQ.'TRB').AND.(DAY.EQ.1)) THEN
         FILENAME(1:32)="TRB 24OCT88 0710 LAT ALT_X1.DATA"
      ENDIF
      IF ((INITIALS.EQ.'TRB').AND.(DAY.EQ.2)) THEN
         FILENAME(1:32)="TRB 25OCT88 0707 LAT ALT_X1.DATA"
      ENDIF
      IF ((INITIALS.EQ.'TRB').AND.(DAY.EQ.3)) THEN
         FILENAME(1:32)="TRB 26OCT88 0710 LAT ALT_X1.DATA"
      ENDIF
      IF ((INITIALS.EQ.'TRB').AND.(DAY.EQ.4)) THEN
         FILENAME(1:32)="TRB 27OCT88 0713 LAT ALT_X1.DATA"
      ENDIF
      IF ((INITIALS.EQ.'TRB').AND.(DAY.EQ.5)) THEN
         FILENAME(1:32)="TRB 28OCT88 0749 LAT ALT_X1.DATA"
      ENDIF
      IF ((INITIALS.EQ.'TRB').AND.(DAY.EQ.6)) THEN
         FILENAME(1:32)="TRB_31OCT88_0719_LAT_ALT_X1.DATA"
      ENDIF
   ENDIF

   IF ((INITIALS.EQ.'SKW').AND.(DAY.EQ.0)) THEN
      FILENAME(1:32)="SKW 21OCT88 0721 LAT ALT_X1.DATA"
      IF ((INITIALS.EQ.'SKW').AND.(DAY.EQ.1)) THEN
         FILENAME(1:32)="SKW 24OCT88 0720 LAT ALT_X1.DATA"
      ENDIF
      IF ((INITIALS.EQ.'SKW').AND.(DAY.EQ.2)) THEN
         FILENAME(1:32)="SKW 25OCT88 0707 LAT ALT_X1.DATA"
      ENDIF
      IF ((INITIALS.EQ.'SKW').AND.(DAY.EQ.3)) THEN
         FILENAME(1:32)="SKW 26OCT88 0710 LAT ALT_X1.DATA"
      ENDIF
      IF ((INITIALS.EQ.'SKW').AND.(DAY.EQ.4)) THEN
         FILENAME(1:32)="SKW 27OCT88 0730 LAT ALT_X1.DATA"
      ENDIF
      IF ((INITIALS.EQ.'SKW').AND.(DAY.EQ.5)) THEN
         FILENAME(1:32)="SKW_01NOV88_0731_LAT_ALT_X1.DATA"
      ENDIF
      IF ((INITIALS.EQ.'SKW').AND.(DAY.EQ.6)) THEN
         FILENAME(1:32)="SKW_07NOV88_0743_LAT_ALT_X1.DATA"
      ENDIF
   ENDIF

   IF ((INITIALS.EQ.'DSC').AND.(DAY.EQ.0)) THEN
      FILENAME(1:32)="DSC 30OCT88 1012 LAT ALT_X1.DATA"
      IF ((INITIALS.EQ.'DSC').AND.(DAY.EQ.1)) THEN
         FILENAME(1:32)="DSC 31OCT88 0646 LAT ALT_X1.DATA"
      ENDIF
      IF ((INITIALS.EQ.'DSC').AND.(DAY.EQ.2)) THEN
         FILENAME(1:32)="DSC_01NOV88_0647_LAT_ALT_X1.DATA"
      ENDIF
   ENDIF

GO TO 402

IF (((INITIALS.EQ.'DSC').AND.(DAY.EQ.3))
  * GO TO 402
IF (((INITIALS.EQ.'DSC').AND.(DAY.EQ.4))
  * FILENAME(1:32)='DSC_04NOV88_0646_LAT_ALT_X1.DATA'
IF (((INITIALS.EQ.'DSC').AND.(DAY.EQ.5))
  * FILENAME(1:32)='DSC_04NOV88_0647_LAT_ALT_X1.DATA'
IF (((INITIALS.EQ.'DSC').AND.(DAY.EQ.6))
  * FILENAME(1:32)='DSC_04NOV88_0650_LAT_ALT_X1.DATA'
IF (((INITIALS.EQ.'DSC').AND.(DAY.EQ.7))
  * FILENAME(1:32)='DSC_04NOV88_0651_LAT_ALT_X1.DATA'
IF (((INITIALS.EQ.'DSG').AND.(DAY.EQ.0))
  * FILENAME(1:32)='DSG_14NOV88_0806_LAT_ALT_X1.DATA'
IF (((INITIALS.EQ.'DSG').AND.(DAY.EQ.1))
  * FILENAME(1:32)='DSG_14NOV88_0806_LAT_ALT_X1.DATA'
IF (((INITIALS.EQ.'DSG').AND.(DAY.EQ.2))
  * FILENAME(1:32)='DSG_14NOV88_0806_LAT_ALT_X1.DATA'
IF (((INITIALS.EQ.'DSG').AND.(DAY.EQ.3))
  * FILENAME(1:32)='DSG_14NOV88_0806_LAT_ALT_X1.DATA'
IF (((INITIALS.EQ.'DSG').AND.(DAY.EQ.4))
  * FILENAME(1:32)='DSG_14NOV88_0806_LAT_ALT_X1.DATA'
IF (((INITIALS.EQ.'DSG').AND.(DAY.EQ.5))
  * FILENAME(1:32)='DSG_14NOV88_0806_LAT_ALT_X1.DATA'
IF (((INITIALS.EQ.'DSG').AND.(DAY.EQ.6))
  * FILENAME(1:32)='DSG_14NOV88_0806_LAT_ALT_X1.DATA'
IF (((INITIALS.EQ.'DSG').AND.(DAY.EQ.7))
  * FILENAME(1:32)='DSG_14NOV88_0806_LAT_ALT_X1.DATA'
IF (((INITIALS.EQ.'RRC').AND.(DAY.EQ.0))
  * FILENAME(1:32)='RRC_15NOV88_0748_LAT_ALT_X1.DATA'
IF (((INITIALS.EQ.'RRC').AND.(DAY.EQ.1))
  * FILENAME(1:32)='RRC_15NOV88_0748_LAT_ALT_X1.DATA'
IF (((INITIALS.EQ.'RRC').AND.(DAY.EQ.2))
  * FILENAME(1:32)='RRC_15NOV88_0748_LAT_ALT_X1.DATA'
IF (((INITIALS.EQ.'RRC').AND.(DAY.EQ.3))
  * FILENAME(1:32)='RRC_15NOV88_0748_LAT_ALT_X1.DATA'
IF (((INITIALS.EQ.'RRC').AND.(DAY.EQ.4))
  * FILENAME(1:32)='RRC_15NOV88_0748_LAT_ALT_X1.DATA'
IF (((INITIALS.EQ.'RRC').AND.(DAY.EQ.5))
  * FILENAME(1:32)='RRC_15NOV88_0748_LAT_ALT_X1.DATA'
IF (((INITIALS.EQ.'RRC').AND.(DAY.EQ.6))
  * FILENAME(1:32)='RRC_15NOV88_0748_LAT_ALT_X1.DATA'
IF (((INITIALS.EQ.'RRC').AND.(DAY.EQ.7))
  * FILENAME(1:32)='RRC_15NOV88_0748_LAT_ALT_X1.DATA'
IF (((INITIALS.EQ.'DBH').AND.(DAY.EQ.0))
  * FILENAME(1:32)='DBH_15NOV88_0811_LAT_ALT_X1.DATA'
IF (((INITIALS.EQ.'DBH').AND.(DAY.EQ.1))
  * FILENAME(1:32)='DBH_15NOV88_0811_LAT_ALT_X1.DATA'
IF (((INITIALS.EQ.'DBH').AND.(DAY.EQ.2))
  * FILENAME(1:32)='DBH_15NOV88_0811_LAT_ALT_X1.DATA'
IF (((INITIALS.EQ.'DBH').AND.(DAY.EQ.3))
  * FILENAME(1:32)='DBH_15NOV88_0811_LAT_ALT_X1.DATA'
IF (((INITIALS.EQ.'DBH').AND.(DAY.EQ.4))
  * FILENAME(1:32)='DBH_15NOV88_0811_LAT_ALT_X1.DATA'
IF (((INITIALS.EQ.'DBH').AND.(DAY.EQ.5))
  * FILENAME(1:32)='DBH_15NOV88_0811_LAT_ALT_X1.DATA'
IF (((INITIALS.EQ.'DBH').AND.(DAY.EQ.6))
  * FILENAME(1:32)='DBH_15NOV88_0811_LAT_ALT_X1 DATA'
IF ((INITIALS.EQ.'DBH').AND.(DAY.EQ.15))
  FILENAME(1:32)="DBH_30NOV88_0806_LAT_ALT_X1.DATA"
ELSE
IF ((INITIALS.EQ.'JRH').AND.(DAY.EQ.0))
  FILENAME(1:32)="JRH_02DEC88_0815_LAT_ALT_X1.DATA"
IF ((INITIALS.EQ.'JRH').AND.(DAY.EQ.1))
  FILENAME(1:32)="JRH_03DEC88_0817_LAT_ALT_X1.DATA"
IF ((INITIALS.EQ.'JRH').AND.(DAY.EQ.2))
  FILENAME(1:32)="JRH_06DEC88_0814_LAT_ALT_X1.DATA"
IF ((INITIALS.EQ.'JRH').AND.(DAY.EQ.3))
  FILENAME(1:32)="JRH_07DEC88_0752_LAT_ALT_X1.DATA"
IF ((INITIALS.EQ.'JRH').AND.(DAY.EQ.4))
  FILENAME(1:32)="JRH_09DEC88_0753_LAT_ALT_X1.DATA"
IF ((INITIALS.EQ.'JRH').AND.(DAY.EQ.5))
  FILENAME(1:32)="JRH_06DEC88_0807_LAT_ALT_X1.DATA"
IF ((INITIALS.EQ.'JRH').AND.(DAY.EQ.6))
  FILENAME(1:32)="JRH_08DEC88_0807_LAT_ALT_X1.DATA"
IF ((INITIALS.EQ.'JRH').AND.(DAY.EQ.7))
  FILENAME(1:32)="JRH_09DEC88_0752_LAT_ALT_X1.DATA"
IF ((INITIALS.EQ.'JRH').AND.(DAY.EQ.8))
  FILENAME(1:32)="JRH_10DEC88_0812_LAT_ALT_X1.DATA"
ELSE
IF ((INITIALS.EQ.'MDW').AND.(DAY.EQ.0))
  FILENAME(1:32)="MDW_10AUG89_0604_LAT_ALT_X1.DATA"
IF ((INITIALS.EQ.'MDW').AND.(DAY.EQ.1))
  FILENAME(1:32)="MDW_10AUG89_0623_LAT_ALT_X1.DATA"
IF ((INITIALS.EQ.'MDW').AND.(DAY.EQ.2))
  FILENAME(1:32)="MDW_11AUG89_0610_LAT_ALT_X1.DATA"
IF ((INITIALS.EQ.'MDW').AND.(DAY.EQ.3))
  FILENAME(1:32)="MDW_12AUG89_0613_LAT_ALT_X1.DATA"
IF ((INITIALS.EQ.'MDW').AND.(DAY.EQ.4))
  FILENAME(1:32)="MDW_13AUG89_0611_LAT_ALT_X1.DATA"
IF ((INITIALS.EQ.'MDW').AND.(DAY.EQ.5))
  FILENAME(1:32)="MDW_14AUG89_0612_LAT_ALT_X1.DATA"
IF ((INITIALS.EQ.'MDW').AND.(DAY.EQ.6))
  FILENAME(1:32)="MDW_15AUG89_0612_LAT_ALT_X1.DATA"
IF ((INITIALS.EQ.'MDW').AND.(DAY.EQ.7))
  FILENAME(1:32)="MDW_16AUG89_0611_LAT_ALT_X1.DATA"
IF ((INITIALS.EQ.'MDW').AND.(DAY.EQ.8))
  FILENAME(1:32)="MDW_17AUG89_0611_LAT_ALT_X1.DATA"
IF ((INITIALS.EQ.'MDW').AND.(DAY.EQ.9))
  FILENAME(1:32)="MDW_18AUG89_0616_LAT_ALT_X1.DATA"
IF ((INITIALS.EQ.'MDW').AND.(DAY.EQ.10))
  FILENAME(1:32)="MDW_19AUG89_0614_LAT_ALT_X1.DATA"
IF ((INITIALS.EQ.'MDW').AND.(DAY.EQ.11))
  FILENAME(1:32)="MDW_20AUG89_0611_LAT_ALT_X1.DATA"
IF ((INITIALS.EQ.'MDW').AND.(DAY.EQ.12))
  FILENAME(1:32)="MDW_21AUG89_0611_LAT_ALT_X1.DATA"
IF ((INITIALS.EQ.'MDW').AND.(DAY.EQ.13))
  FILENAME(1:32)="MDW_22AUG89_0616_LAT_ALT_X1.DATA"
IF ((INITIALS.EQ.'MDW').AND.(DAY.EQ.14))
  FILENAME(1:32)="MDW_23AUG89_0614_LAT_ALT_X1.DATA"
IF ((INITIALS.EQ.'MDW').AND.(DAY.EQ.15))
  FILENAME(1:32)="MDW_24AUG89_0616_LAT_ALT_X1.DATA"
IF ((INITIALS.EQ.'MDW').AND.(DAY.EQ.16))
  FILENAME(1:32)="MDW_25AUG89_0614_LAT_ALT_X1.DATA"
ELSE
IF ((INITIALS.EQ.'TRB').AND.(DAY.EQ.0))
  FILENAME(1:32)="TRB_10AUG89_0649_LAT_ALT_X1.DATA"
IF ((INITIALS.EQ.'TRB').AND.(DAY.EQ.1))
  FILENAME(1:32)="TRB_11AUG89_0649_LAT_ALT_X1.DATA"
IF ((INITIALS.EQ.'TRB').AND.(DAY.EQ.2))
  FILENAME(1:32)="TRB_14AUG89_0704_LAT_ALT_X1.DATA"
IF ((INITIALS.EQ.'TRB').AND.(DAY.EQ.3))
  FILENAME(1:32)="TRB_15AUG89_0641_LAT_ALT_X1.DATA"
IF ((INITIALS.EQ.'TRB').AND.(DAY.EQ.4))
  FILENAME(1:32)="TRB_16AUG89_0646_LAT_ALT_X1.DATA"
IF ((INITIALS.EQ.'TRB').AND.(DAY.EQ.5))
  FILENAME(1:32)="TRB_17AUG89_0654_LAT_ALT_X1.DATA"
IF ((INITIALS.EQ.'TRB').AND.(DAY.EQ.6))
  FILENAME(1:32)="TRB_18AUG89_0658_LAT_ALT_X1.DATA"
IF ((INITIALS.EQ.'TRB').AND.(DAY.EQ.7))
  FILENAME(1:32)="TRB_19AUG89_0650_LAT_ALT_X1.DATA"
IF ((INITIALS.EQ.'TRB').AND.(DAY.EQ.8))
  FILENAME(1:32)="TRB_20AUG89_0650_LAT_ALT_X1.DATA"
IF ((INITIALS.EQ.'TRB').AND.(DAY.EQ.9))
  FILENAME(1:32)="TRB_21AUG89_0650_LAT_ALT_X1.DATA"
IF ((INITIALS.EQ.'TRB').AND.(DAY.EQ.10))
  FILENAME(1:32)="TRB_22AUG89_0650_LAT_ALT_X1.DATA"
IF ((INITIALS.EQ.'TRB').AND.(DAY.EQ.11))
  FILENAME(1:32)="TRB_23AUG89_0650_LAT_ALT_X1.DATA"
IF ((INITIALS.EQ.'TRB').AND.(DAY.EQ.12))
  FILENAME(1:32)="TRB_24AUG89_0650_LAT_ALT_X1.DATA"
IF ((INITIALS.EQ.'TRB').AND.(DAY.EQ.13))
  FILENAME(1:32)="TRB_25AUG89_0650_LAT_ALT_X1.DATA"
ELSE
IF ((INITIALS.EQ.'MVK').AND.(DAY.EQ.0))
  FILENAME(1:32)="MVK_29AUG89_0627_LAT_ALT_X1.DATA"
IF ((INITIALS.EQ.'MVK').AND.(DAY.EQ.1))
  FILENAME(1:32)="MVK_30AUG89_0637_LAT_ALT_X1.DATA"
IF ((INITIALS.EQ.'MVK').AND.(DAY.EQ.2))
  FILENAME(1:32)="MVK_31AUG89_0639_LAT_ALT_X1.DATA"
IF ((INITIALS.EQ.'MVK').AND.(DAY.EQ.3))
  FILENAME(1:32)="MVK_05SEP89_0630_LAT_ALT_X1.DATA"
IF ((INITIALS.EQ. 'HWK').AND.(DAY.EQ.6))
  FILENAME(1:32)='HWK 06SEP89 0645_LAT_ALT_X1.DATA'
IF ((INITIALS.EQ. 'HWK').AND.(DAY.EQ.7))
  FILENAME(1:32)='HWK 06SEP89 0638_LAT_ALT_X1.DATA'
IF ((INITIALS.EQ. 'HWK').AND.(DAY.EQ.8))
  FILENAME(1:32)='HWK 06SEP89 0654_LAT_ALT_X1.DATA'
IF ((INITIALS.EQ. 'HWK').AND.(DAY.EQ.9))
  FILENAME(1:32)='HWK 06SEP89 0643_LAT_ALT_X1.DATA'
IF ((INITIALS.EQ. 'HWK').AND.(DAY.EQ.10))
  FILENAME(1:32)='HWK 06SEP89 0658_LAT_ALT_X1.DATA'

GO TO 402
IF ((INITIALS.EQ. 'BLP').AND.(DAY.EQ.0))
  FILENAME(1:32)='BLP 29AUG89 0532_LAT_ALT_X1.DATA'
IF ((INITIALS.EQ. 'BLP').AND.(DAY.EQ.1))
  FILENAME(1:32)='BLP 30AUG89 0557_LAT_ALT_X1.DATA'
IF ((INITIALS.EQ. 'BLP').AND.(DAY.EQ.2))
  FILENAME(1:32)='BLP 01SEP89 0532_LAT_ALT_X1.DATA'
IF ((INITIALS.EQ. 'BLP').AND.(DAY.EQ.3))
  FILENAME(1:32)='BLP 02SEP89 0704_LAT_ALT_X1.DATA'
IF ((INITIALS.EQ. 'BLP').AND.(DAY.EQ.4))
  FILENAME(1:32)='BLP 03SEP89 0711_LAT_ALT_X1.DATA'
IF ((INITIALS.EQ. 'BLP').AND.(DAY.EQ.5))
  FILENAME(1:32)='BLP 04SEP89 0724_LAT_ALT_X1.DATA'
IF ((INITIALS.EQ. 'BLP').AND.(DAY.EQ.6))
  FILENAME(1:32)='BLP 05SEP89 0714_LAT_ALT_X1.DATA'

GO TO 402
IF ((INITIALS.EQ. 'PEF').AND.(DAY.EQ.0))
  FILENAME(1:32)='PEF 29AUG89 0556_LAT_ALT_X1.DATA'
IF ((INITIALS.EQ. 'PEF').AND.(DAY.EQ.1))
  FILENAME(1:32)='PEF 30AUG89 0705_LAT_ALT_X1.DATA'
IF ((INITIALS.EQ. 'PEF').AND.(DAY.EQ.2))
  FILENAME(1:32)='PEF 01SEP89 0719_LAT_ALT_X1.DATA'
IF ((INITIALS.EQ. 'PEF').AND.(DAY.EQ.3))
  FILENAME(1:32)='PEF 02SEP89 0734_LAT_ALT_X1.DATA'
IF ((INITIALS.EQ. 'PEF').AND.(DAY.EQ.4))
  FILENAME(1:32)='PEF 03SEP89 0717_LAT_ALT_X1.DATA'
IF ((INITIALS.EQ. 'PEF').AND.(DAY.EQ.5))
  FILENAME(1:32)='PEF 04SEP89 0724_LAT_ALT_X1.DATA'
IF ((INITIALS.EQ. 'PEF').AND.(DAY.EQ.6))
  FILENAME(1:32)='PEF 05SEP89 0732_LAT_ALT_X1.DATA'

GO TO 402
IF ((INITIALS.EQ. 'MWF').AND.(DAY.EQ.0))
  FILENAME(1:32)='MWF 29AUG89 0542_LAT_ALT_X1.DATA'
IF ((INITIALS.EQ. 'MWF').AND.(DAY.EQ.1))
  FILENAME(1:32)='MWF 30AUG89 0742_LAT_ALT_X1.DATA'
IF ((INITIALS.EQ. 'MWF').AND.(DAY.EQ.2))
  FILENAME(1:32)='MWF 01SEP89 0734_LAT_ALT_X1.DATA'
IF ((INITIALS.EQ. 'MWF').AND.(DAY.EQ.3))
  FILENAME(1:32)='MWF 02SEP89 0705_LAT_ALT_X1.DATA'
IF ((INITIALS.EQ. 'MWF').AND.(DAY.EQ.4))
  FILENAME(1:32)='MWF 03SEP89 0743_LAT_ALT_X1.DATA'
IF ((INITIALS.EQ. 'MWF').AND.(DAY.EQ.5))
  FILENAME(1:32)='MWF 04SEP89 0746_LAT_ALT_X1.DATA'
IF ((INITIALS.EQ. 'MWF').AND.(DAY.EQ.6))
  FILENAME(1:32)='MWF 05SEP89 0743_LAT_ALT_X1.DATA'
INQUIRE(FILE=FILENAME,EXIST=ONDISK)
IF(.NOT.ONDISK) THEN
  WRITE(6,'(1H0,A)') FILENAME//' IS NOT ON DISK.'
  GO TO 402
ENDIF
C
ENDF
C
INQUIRE(FILE=FILENAME,EXIST=ONDISK)
IF(.NOT.ONDISK) THEN
  WRITE(6,'(1H0,A)') FILENAME//' IS NOT ON DISK.'
  GO TO 402
ENDIF
C
ENDF
C
IF (INITIALS.EQ. 'MWF').AND. (DAY.EQ.14) THEN
  FILENAME(1:32) = 'MWF 14SEP89 0751 LAT ALT X1.DATA'
ENDIF
C
IF (INITIALS.EQ. 'DDS').AND. (DAY.EQ.1) THEN
  FILENAME(1:32) = 'DDS 06SEP89 0809 LAT ALT X1.DATA'
ELSE IF (INITIALS.EQ. 'DDS').AND. (DAY.EQ.2) THEN
  FILENAME(1:32) = 'DDS 07SEP89 0817 LAT ALT X1.DATA'
ELSE...
ENDIF
C
IF (INITIALS.EQ. 'RFF').AND. (DAY.EQ.1) THEN
  FILENAME(1:32) = 'RFF 06SEP89 0829 LAT ALT X1.DATA'
ELSE IF (INITIALS.EQ. 'RFF').AND. (DAY.EQ.2) THEN
  FILENAME(1:32) = 'RFF 07SEP89 0750 LAT ALT X1.DATA'
ELSE...
ENDIF
C
ENDF
C
696
INQUIRE(FILE=FILENAME,EXIST=ONDISK)
IF(.NOT.ONDISK) THEN
  WRITE(6,'(1H0,A)') FILENAME//' IS NOT ON DISK.'
  GO TO 402
ENDIF
C
ENDF
C
C
STYPE(1:1) = FILENAME(22:22)
FILENAME0(1:32) = FILENAME(1:27)://' CHOP,' OPEN (UNIT=1,FILE=FILENAME0(1:32),STATUS='NEW',
  FORM='UNFORMATTED')
OPEN (UNIT=2,FILE=FILENAME(1:32),STATUS='UNKNOWN',
  FORM='UNFORMATTED')
RDSIZ=16384
WRSIZ=1024
IBLOCKU=100
C
DO 8 IBLOCK = 1, IBLOCKU
  READ(2) (IDTBUF(K),K=1,RDSIZ)
  DO 7 J=1,WRSIZ
  C
C
END
IDTBUF(J) = IDTBUF(1 + (16*(J-1)))

7    CONTINUE
     WRITE(1) (IDTBUF(K), K=1, WRSIZ)
 8    CONTINUE

CLOSE (UNIT=2)
IF (AOF.NE.'F') GO TO 402
CLOSE (UNIT=1, STATUS='SAVE')
GO TO 1001

402    CONTINUE
CLOSE (UNIT=1, STATUS='SAVE')

401    CONTINUE

C 1001    STOP
   END
APPENDIX D
SAMPLE PACKET
Subiect Induction Flow Chart

Study Subject Candidate
Contacts PI or Co-PI

Study Subject Candidate receives “Subject’s Consent Form”

1. Study subject candidate contacts PI or Co-PI candidate.
2. Questions answered

1. PI or Co-PI contact physician (626-6254), 7th floor outpatient Psych. clinic,
2. Patient history & physical page placed in physicians box

Physician schedules physical

1. Study subject candidate signs “Subject’s Consent Form.”
2. Physician signs as witness
3. Physical done

Blood & urine samples sent to lab

Lab results received

Physician certifies on patient history and physical form
A) Study subject candidate not fit for Study
   Subject candidate’s involvement ends

or

B) Study subject candidate is fit for study, becomes a “study subject”.

Study Subject
Physician forwards patient history & physical form and signed "Subject's consent form"

Study Subject receives packet containing
1) "General Instructions for Lithium Study"
2) "Daily Medication Diary"
3) "Daily Side Effect Rating Scale"
4) Copy of "Subject's Informed Consent Form"

Subject contacts PI or Co-PI to schedule baseline levels

A) Baseline Levels (E.P. & blood) done
B) Study subject receives
   1) Dosing and measurement calendar
   2) Study drug
C) Dosing schedule and measurement schedule placed on master calendar

Study subject follows schedule for dosing and measurements
VOLUNTEERS NEEDED FOR A PHARMACOLOGICAL STUDY

Healthy males between ages of 18 and 45 are needed for this study. Subjects must have a normal physical and laboratory test and not take any medication, caffeine-containing beverages, alcohol or nicotine during the study.

Subjects will receive a 14-day treatment of sustained-release lithium carbonate Lithocid 500 mg tablets at three different doses (see Table 1). Subjects must come to eight scheduled appointments at the College of Pharmacy, Room 102, at the University of Arizona. The appointments will be scheduled between 7 a.m. and 9 a.m., and each appointment should last between 30 and 60 minutes. At each of the appointments, an EEG brain wave test will be recorded after a sound is heard over earphones. A lithium blood sample will be collected eight times during the study.

Subjects will be paid $15.00 upon completing the study.

If you are interested in participating in this study, please call Michael Karel, Ph.D., at 739-6888 at the College of Pharmacy. Please leave complete name and phone number in answering machine if no one answers.

Table 1: Measurements During the Study

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PHYSICIAN INSTRUCTIONS FOR LITHIUM STUDY

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Sign consent form - give a copy to the subject

Give subject "General Instructions about Study"

Patient history and physical

Laboratory tests
   SMAC - 1 red top tube, spin and transfer to tube
   CBC - 1 purple top tube (rotate)
   UA - transfer urine specimen to tube

Fill out National Health Labs requisition and call laboratory for pick-up in Outpatient Psychiatry Clinic

Instruct about no medications, caffeine-containing beverages (coffee, tea, sodas), alcohol, or nicotine for 7 days prior to start of study and throughout study

Call Mike Karol, Ph.D. at 626-4055 to schedule baseline tests and to receive study medication. Instruct about appointments at College of Pharmacy, Room 433 (4th Floor) at the corner of Mabel and Warren. Discuss parking available around the Arizona Health Sciences Center if needed.
DAILY MEDICATION DIARY

Name ___________________________ Date ___________________________

Dosage Instructions: Take one tablet at 7 p.m. for five days, then one tablet at 7 a.m. and 7 p.m. for five days, then one tablet at 7 a.m., 12 noon, and 7 p.m. for five days. Please note the time each dose is taken. Do not take your morning dose until after the blood draw.

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<th>Week No.</th>
<th>Dosage Instructions</th>
<th>Monday</th>
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**DAILY SIDE EFFECT RATING SCALE**

Name ___________________________ Date ___________________________

Please rate the side effects below with the following numbers each day.

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I am being invited to voluntarily participate in the above entitled research study. The purpose of this study is to determine the effect of the study drug (lithium) on the "brain waves" that occur after a sound is heard. The study will determine how different doses of the study drug and different amounts of the study drug in the blood (blood levels) affect these "brain waves". The "auditory evoked potential" measures these "brain waves". Approximately 12 subjects will be enrolled in this study.

If I agree to participate, I will be asked to agree to the following:

To participate in the study, you must be a nonsmoking male and be between the ages of 18 and 45 years. You will receive physical and laboratory tests before the study begins. A one-ounce blood sample (20 ml) and urine sample will be obtained for the laboratory evaluations. You will be excluded from the study if you have abnormal laboratory tests or a physical disorder (gastrointestinal tract disease, kidney or liver disease, epilepsy or mental illness, or allergy to lithium).

A week before the study and during the study, you will not be allowed to take any medication, caffeine-containing beverages, alcohol, or nicotine. You must maintain a consistent intake of Table salt and fluids during the study and not make any dietary or exercise changes.

The study will last approximately 18 to 21 days. You will be required to come to 8 appointments at the College of Pharmacy, Room 433, at the University of Arizona. The College of Pharmacy is located at the corner of Main and Warren. Your appointments will be scheduled between 7 a.m. and 8 a.m. and each appointment should last between 30 and 60 minutes.

At your first appointment, your baseline brain waves will be measured approximately 3 to 5 days before the study drug is started. Four electrodes (small objects with a wire attached) will be placed on your skin and held in place by a jelly-like substance called electrode paste. One electrode will also be attached to each earlobe. These connections will record the brain waves that occur naturally in the brain. You will also have earphones placed in each ear. A series of auditory clicks will be given over the earphones. The click will sound like a buzzing noise to the human ear and will be in the normal range of hearing sounds. During the procedure, you will be seated and asked to keep your eyes closed.

The evening before day 1 of the study, you will begin taking the lithium carbonate according to the schedule in Table 1 below. On days 1, 2, 3, 4, 5, 10, and 15 you will be scheduled for a brain wave test 12 hours after your last dose of lithium. You will have your blood drawn eight times for a lithium level on days 0, 1, 2, 3, 4, 5, 10, and 15 of the study. At these visits, four teaspoonsful of blood will be drawn for a lithium serum level. You will be required to complete a daily side effect form and chart when you take your doses of lithium.

During the study, you will receive three different daily doses of sustained-release lithium carbonate (Lithobid 300 mg tablet). The exact dosing schedule will vary depending on when you are scheduled to have the brain wave test. All brain wave tests will be
scheduled 12 hours after you have taken the previous evening dose. You SHOULD NOT take the morning dose of lithium until AFTER you have had the brain wave test. If you have intractable side effects during the study, or if there is too much lithium in your blood, you will be dropped from the study.

Table 1. Measurements During the Study

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All brain wave tests will be taken 12 hours after the evening lithium dose. You should not take the morning dose of lithium until after the brain wave test is completed.

I understand that my participation in this study may involve some risks. The most common side effects associated with early lithium therapy include increased thirst (30-50%), increased urinary frequency (30-50%), tremor (30-50%), fatigue (30%), nausea, vomiting and diarrhea (10-30%), and confusion (40%). The occurrence and severity of adverse reactions are generally directly related to higher serum lithium levels. Because this study will be starting with low doses of lithium, the side effects should be mild. The side effects of lithium stop when you stop taking lithium. Lithium may cause some initial drowsiness, so you should use caution when driving or operating heavy machinery or when doing other tasks which require mental alertness.

You will receive no direct benefit from participating in this study. You will receive a free physical and laboratory tests and $100.00 upon completion of the study. There will be no proration.

I understand that adverse reactions are possible in any research program despite the use of high standards of care and could occur through no fault of mine or the investigator involved. Reactions which can be foreseen have been described in this consent form. However, unforeseen harm may also occur and require care. I understand that money for research-related side effects or harm or for wages or time lost is not available. However, necessary emergency medical care will be provided without cost. I can obtain further information from Dr. Michael Karol at 826-4025. If I have questions regarding my rights as a research subject, I may call the Human Subjects Committee Office at 826-6721.

Every effort will be made to protect your confidentiality, and your name will not appear in publication.
I have read this subject consent form. The nature, demands, risks, benefits of the project have been explained to me. I understand that I may ask questions and that I am free to withdraw from the project at any time without incurring ill will or affecting my medical care. I also understand that this consent form will be filed in an area designated by the Human Subjects Committee with access restricted to the principal investigator or authorized representative of the particular department. I understand that I do not waive any of my legal rights by signing this form. A copy of this consent form will be given to me.

Subject's Signature ___________________________ Date __________

I have carefully explained to the subject the nature of the above project. I hereby certify that to the best of my knowledge the person who is signing this consent form understand clearly the nature, demands, benefits, and risks involved in his/her participation. A medical problem or language or educational barrier has not precluded this understanding.

Signature of person presenting this consent form ___________________________ Date __________
APPENDIX E

HAC_WINDOW
PROGRAM MAC_WINDOW

CALCULATION AND PLOT OF FAST FOURIER TRANSFORM AND AUTOCORRELATION OF EVOKED POTENTIAL INCLUDING A BLACKMAN-HARRIS WINDOW AROUND THE DATA.

FRANK A. ZAK, 19 DEC 88

MODIFIED FOR EEG READ ON 02 APR 89

MODIFIED FOR OPERATION ON HUGHES AIRCRAFT COMPANY - TUCSON BLDG. 805 VAX ON 13 OCT 89 (VIRUS D-DAY)

MODIFIED TO PERFORM AUTO CORRELATION ON 07 JAN 90, 4:16 PM

MODIFIED TO CALCULATE POWER SPECTRUMS ON 06 DEC 91

IMPLICIT INTEGER*4 (A-Z)

PARAMETER (ADMAX=2047, ADMIN=2047)
PARAMETER (MAXDAT=16384, MAXDT2=16386)
PARAMETER (PLTOUT=10)
PARAMETER (IBFLIM=32768)

CHARACTER*1 CPROC, CTYPE, SORD, TIMPLT, MAGFLT, CPHASE
CHARACTER*1 AOF, FILETYPE, READALL, STUDY, CFREQ, CAUTO
CHARACTER*2 CPERCENT, CDAY
CHARACTER*3 INITIALS
CHARACTER*5 CTEMP
CHARACTER*22 MAGFILE, PHAFILE, POWFILE
CHARACTER*27 MAGAVERFILE, PHAAVERFILE, POWAVERFILE
CHARACTER*27 MAGNORMFILE, PHANORMFILE, POWNORMFILE
CHARACTER*28 EGFFILE
CHARACTER*29 MAGNAME, PHANAME, FONAME
CHARACTER*30 AUTONAME, TIME NAME
CHARACTER*30 MEANHAGFILE, MEANPHASEFILE, MEANPOWERFILE
CHARACTER*30 MAGSECONFILE, PHASECONFILE, POWSECONFILE
CHARACTER*32 FILENAME, FILENAMED
CHARACTER*35 MAGSECONORMFILE, PHASECONORMFILE
CHARACTER*35 POWSECONORMFILE

COMPLEX*16 A(2048)

DATA FILENAME */
DATA FILENAMED */
DATA IEFN, ISTART, NUBASEAVE, NUDRUGAVE /1, 30, 0, 0/
DATA NUMBASEAVE, NUMANDRUG /0, 0/
DATA MEANBASEMAGEDGE, MEANBASEPHAEDGE /0.0, 0.0/
DATA MEANDRUGMAGEDGE, MEANDRUGPHAEDGE /0.0, 0.0/

INTEGER*2 IDTBUF(IBFLIM), DUMBUF(IBFLIM)
INTEGER*2 IFLAG(I MAXDAT), IFLAG2(MAXDAT), IFLAG4(MAXDAT)
INTEGER*2 NDATA(MAXDT2), DENOM(MAXDAT)
INTEGER*2 COUNT, DAY

LOGICAL ONDISK

REAL*4 XARR(MAXDT2), EPOCHS

REAL*16 YARR2(MAXDT2)
REAL*16 A0, A1, A2, A3, OFFSET, EDGE, PERCENT, AVERAGE, SCALE
REAL*16 AREA, MAG_AREA, PHASE_AREA, RMS, MAG_RMS, PHASE_RMS
REAL*16 RATIO, MAG_RATIO, PHASE_RATIO
REAL*16 DATA(MAXDT2), AMean(MAXDT2), AMAX, V
REAL*16 F(0:1024), FM(0:1024), FP(0:1024), FPOW(0:1024)
REAL*16 FR(0:1024), FI(0:1024)
REAL*16 AUTO(MAXDT2)
REAL*16 BASEMAGAVER(0:1024), BASEPHAVER(0:1024)
REAL*16 BASEPOWERAVER(0:1024)
REAL*16 DRUGMAGAVER(0:1024), DRUGPHAVER(0:1024)
REAL*16 DRUGPOWERAVER(0:1024)
REAL*16 BASEMAGEDGE, BASEPHAEDGE, BASEPOWEREDGE
REAL*16 DRUGMAGEDGE, DRUGPHAEDGE, DRUGPOWEREDGE
REAL*16 MAGEDGE, PHAEDGE, POWEREDGE
REAL*16 MEANBASEMAGEDGE, MEANBASEPHAEDGE, MEANBASEPOWEREDGE
REAL*16 MEANBASEMAGEDGE2, MEANBASEPHAEDGE2, MEANBASEPOWEREDGE2
REAL*16 MEANDRUGMAGEDGE, MEANDRUGPHAEDGE, MEANDRUGPOWEREDGE
REAL*16 MEANDRUGMAGEDGE2, MEANDRUGPHAEDGE2, MEANDRUGPOWEDGE2
REAL*16 BASEMAGVARIANCE, BASEPHAVARIANCE, BASEPOWVARIANCE
REAL*16 DRUGMAGVARIANCE, DRUGPHAVARIANCE, DRUGPOWVARIANCE
REAL*16 BASEMAG(0:16), BASEPHA(0:16), BASEPOW(0:16)
REAL*16 DRUGMAG(0:16), DRUGPHA(0:16), DRUGPOW(0:16)
REAL*16 MAGVSCONCX(0:16), PHAVSCONCY(0:16)
REAL*16 POWVSCONC(0:16), POWVSCON2
REAL*16 MAGVSCONCMIN, PHAVSCONCMIN, POWVSCONCMIN
REAL*16 MAGNORM, PHANORM, POWNORM
REAL*16 MAGVSCONCNORM, PHAVSCONCNORM, POWVSCONCNORM
REAL*16 TIMESCALE

DO 1 I=0,1024
BASEMAGAVER(I)=0.0
BASEPHAVER(I)=0.0
BASEPOWVER(I)=0.0
DRUGMAGAVER(I)=0.0
DRUGPHAVER(I)=0.0
DRUGPOWVER(I)=0.0
CONTINUE

WRITE (6,'(A)') '--- WINDOW.FOR'
WRITE (6,'(A)') 'PURPOSE: DETAILED ANALYSIS OF EEG AND AEP'
WRITE (6,'(A)') 'FREQUENCY DOMAIN ANALYSIS? (Y=YES, N=NO)'
READ (5,'(A)') CFREQ
WRITE (6,'(A)') 'AUTOCORRELATION ANALYSIS? (Y=YES, N=NO)'
READ (5,'(A)') CAUTO
WRITE (6,'(A)') 'ENTER THE % SPECTRAL EDGE (1 THRU 99)'
READ(5,'(A)') CPERCENT
READ(CPERCENT,*) PERCENT
WRITE (6,'(A)') 'ENTER 1 FOR PHASE 1 OR 2 FOR PHASE 2'
READ(5,'(A)*') PHASE
ENCOD(1,329,CPHASE) PHASE
IF (PHASE.EQ.1) THEN
DAYUP=15
SUBJUP=9
ELSE
DAYUP=16
SUBJUP=7
ENDIF
WRITE (6,'(A)') 'ENTER A FOR ALL-SUBJECT READ'
WRITE (6,'(A)') 'OR O FOR I-SUBJECT READ'
WRITE (6,'(A)') 'OR F FOR I-FILE READ'
READ (5,'(A)') AOF
IF (AOF.EQ.'A') GO TO 851
IF (AOF.EQ.'O') GO TO 855
WRITE (6,'(A)') 'STUDY SUBJECT? (Y=YES, N=NO)'
READ (5,'(A)') STUDY
IF (STUDY.EQ.'N') THEN
WRITE (6,'(A)') 'ENTER FILENAME'
READ (5,'(A)') FILENAME
IF (FILENAME(18:20).EQ.'EEG') THEN
FILETYPE(1:1)= 'G'
ELSE IF (FILENAME(18:20).EQ.'ELY') THEN
FILETYPE(1:1)= 'E'
ELSE IF (FILENAME(18:20).EQ.'LAT') THEN
FILETYPE(1:1)= 'L'
ENDIF
GO TO 852
ELSE IF (PHASE.EQ.1) THEN
WRITE (6,'(A)') ' ENTER DAY (0, 1-5, 10, OR 15)' READ(5,*) DAY
ELSE
WRITE (6,'(A)') ' ENTER DAY (0-2, 5-6, 9, OR 12-16)' READ(5,*) DAY
ENDIF
WRITE (6,'(A)') ' ENTER SUBJECT INITIALS' READ(5,'(A)') INITIALS
IF (PHASE.EQ.1) THEN
IF (INITIALS(1:3).EQ.'HLR') SUBJECT=0
IF (INITIALS(1:3).EQ.'SJD') SUBJECT=1
IF (INITIALS(1:3).EQ.'TRB') SUBJECT=2
IF (INITIALS(1:3).EQ.'SKW') SUBJECT=3
IF (INITIALS(1:3).EQ.'DSC') SUBJECT=4
IF (INITIALS(1:3).EQ.'DJS') SUBJECT=5
IF (INITIALS(1:3).EQ.'DSG') SUBJECT=6
IF (INITIALS(1:3).EQ.'RRC') SUBJECT=7
IF (INITIALS(1:3).EQ.'DBH') SUBJECT=8
IF (INITIALS(1:3).EQ.'JRH') SUBJECT=9
ENDIF
IF (AOF.EQ.'F') GO TO 44
ENDIF
851 DAYINC=1
IF (PHASE.EQ.1) THEN
WRITE (6,'(A)') ' ENTER 8 FOR 8-FILE READ OR 4 FOR 4-FILE READ'
WRITE (6,'(A)') ' NOTE: 4 FILES = BASELINE + 3 STEADY-STATES'
READ (5,'(A)') READALL
IF (READALL.EQ.'4') DAYINC=5
ENDIF
44 WRITE (6,'(A)') ' ENTER G FOR EEG, E FOR EARLY, OR L FOR LATE'
READ (5,'(A)') FILETYPE
852 IF (FILETYPE.EQ.'G') THEN
COUNT=1
REALN=1024.0
IL=1
IU=1024
N=10
NHI=1024
SCA=(2.0/QEXT(N))*(1.0/1.0E-3)/4.0)*(0.5)
ENDIF
IF (FILETYPE.EQ.'E') THEN
COUNT=0
REALN=128.0
IL=1
IU=152
N=35
NHI=162
SCA=(2.0/QEXT(N))*(1.0/1.0E-3)/16.0)*(0.5)
ENDIF
IF (FILETYPE.EQ.'L') THEN
COUNT=0
REALN=1024.0
IL=1
IU=1024
N=10
NHI=508
SCA=(2.0/QEXT(N))*(1.0/1.0E-3)/16.0)*(0.5)
ENDIF
WRITE (6,'(A)') ' PLOT THE INPUT TIME SERIES? (Y=YES, N=NO)'
READ (5,'(A)') TIMPLT
WRITE (6,'(A)') ' PLOT THE MAGNITUDE SPECTRUM? (Y=YES, N=NO)'
READ (5,'(A)') MAGLTL
DO 403 COUNT=COUNT, 1
IF ((FILETYPE.EQ.,'E').AND. (COUNT.EQ.1)) THEN
  ILOW=35
  IUP=162
ENDIF
IF (AOF.EQ.,'O') GO TO 853
IF (AOF.EQ.,'A') GO TO 301
IF (FILETYPE.EQ.,'G') THEN
  MAGFILE(1:18)=INITIALS//' EEG '//MAG '//CPERCENT//' .GRL'
  MAGNORMFILE(1:23)=INITIALS//' MAG _ '//MAG _ //
  CPERCENT//' NORM.GRL'
  MAGSECONCFILE(T:26)=MAGFILE(1:14)://' VS CONC.GRL'
  MAGSECONCNORMFILE(1:31)=MAGFILE(1:1147)://' VS CONC NORM.GRL'
  PHAFIELD(1:18)=INITIALS//' EEG '//PHA }//CPERCENT}//.GRL'
  PHANORMFILE(1:23)=INITIALS//' PHA _ }//PHA _ //
  CPERCENT//' NORM.GRL'
  PHASECONCFILE(T:26)=PHAFILE(1:14)://' VS CONC.GRL'
  PHASECONCNORMFILE(1:31)=PHAFILE(1:1147)://' VS CONC NORM.GRL'
  PowFILE(T:18)=INITIALS//' EEG '//POW }//CPERCENT}//.GRL'
  POWNORMFILE(1:23)=INITIALS//' POW _ }//POW _ //
  CPERCENT//' NORM.GRL'
  PowSECONCFIELD(1:30)=POWFILE(1:14)://' VS CONC.GRL'
  PowSECONCNORMFIELD(1:31)=POWFILE(1:1147)://' VS CONC NORM.GRL'
  EEGFILE(T:28)=FILENAME(1:28)
ENDIF
IF (FILETYPE.EQ.,'E') THEN
  IF (COUNT.EQ.0) THEN
    MAGFILE(1:22)=INITIALS//' ELY SGL '//MAG }//CPERCENT}//.GRL'
    MAGNORMFILE(1:27)=INITIALS//' ELY _ }//MAG _ //
    CPERCENT//' NORM.GRL'
    MAGSECONCFILE(1:30)=MAGFILE(1:18)://' VS CONC.GRL'
    MAGSECONCNORMFILE(1:35)=MAGFILE(1:1187)://' VS CONC NORM.GRL'
    PHAFIELD(1:22)=INITIALS//' ELY SGL }//PHA }//CPERCENT}//.GRL'
    PHANORMFILE(1:27)=INITIALS//' ELY _ }//PHA _ //
    CPERCENT//' NORM.GRL'
    PHASECONCFILE(1:30)=PHAFILE(1:18)://' VS CONC.GRL'
    PHASECONCNORMFILE(1:35)=PHAFILE(1:1187)://' VS CONC NORM.GRL'
    PowFILE(1:22)=INITIALS//' ELY SGL }//POW }//CPERCENT}//.GRL'
    POWNORMFILE(1:27)=INITIALS//' ELY _ }//POW _ //
    CPERCENT//' NORM.GRL'
    PowSECONCFIELD(1:30)=POWFILE(1:18)://' VS CONC.GRL'
    PowSECONCNORMFIELD(1:35)=POWFILE(1:1187)://' VS CONC NORM.GRL'
  ENDIF
  IF (COUNT.EQ.1) THEN
    MAGFILE(1:22)=INITIALS//' ELY DBL }//MAG }//CPERCENT}//.GRL'
    MAGNORMFILE(1:27)=INITIALS//' ELY _ }//MAG _ //
    CPERCENT//' NORM.GRL'
    MAGSECONCFILE(1:30)=MAGFILE(1:18)://' VS CONC.GRL'
    MAGSECONCNORMFILE(1:35)=MAGFILE(1:1187)://' VS CONC NORM.GRL'
    PHAFIELD(1:22)=INITIALS//' ELY DBL }//PHA }//CPERCENT}//.GRL'
    PHANORMFILE(1:27)=INITIALS//' ELY _ }//PHA _ //
    CPERCENT//' NORM.GRL'
    PHASECONCFILE(1:30)=PHAFILE(1:18)://' VS CONC.GRL'
    PHASECONCNORMFILE(1:35)=PHAFILE(1:1187)://' VS CONC NORM.GRL'
    PowFILE(1:22)=INITIALS//' ELY DBL }//POW }//CPERCENT}//.GRL'
    POWNORMFILE(1:27)=INITIALS//' ELY _ }//POW _ //
    CPERCENT//' NORM.GRL'
    PowSECONCFIELD(1:30)=POWFILE(1:18)://' VS CONC.GRL'
    PowSECONCNORMFIELD(1:35)=POWFILE(1:1187)://' VS CONC NORM.GRL'
  ENDIF
END
* IF (FILETYPE.EQ. 'L') THEN
  IF (COUNT.EQ.0) THEN
    MAGFILE(1:18) = INITIALS// 'LAT SGL'// 'MAG'// 'CPERCENT'// .GRL'
    NORMFILE(1:27) = INITIALS// 'LAT SGL'// '
    MAGSECONCFILE(1:30) = MAGFILE(1:18)// 'VS CONC.GRL'
    MAGSECONCFORMFILE(1:35) = MAGFILE(1:18)// '
    * VS CONC NORM.GRL'
    PHAFILE(1:127) = INITIALS// 'LAT SGL'// 'PHA'// 'CPERCENT'// .GRL'
    NORMFILE(1:27) = INITIALS// 'LAT SGL'// '
    PHASECONCFILE(1:30) = PHAFILE(1:18)// 'VS CONC.GRL'
    PHASECONCFORMFILE(1:35) = PHAFILE(1:18)// 'VS CONC NORM.GRL'
    POWFILE(1:127) = INITIALS// 'LAT SGL'// 'POW'// 'CPERCENT'// .GRL'
    NORMFILE(1:27) = INITIALS// 'LAT SGL'// '
    POWSECONCFILE(1:30) = POWFILE(1:18)// 'VS CONC.GRL'
    POWSECONCFORMFILE(1:35) = POWFILE(1:18)// 'VS CONC NORM.GRL'
  ENDIF
  IF (FILETYPE.EQ. 'N') THEN
    OPEN (UNIT=1, FILE=HAGFILE, STATUS='NEW')
    WRITE (1, *) 'TI ', MAGFILE(1:18)
    WRITE (1, *) 'SU '
    WRITE (1, *) 'HO DAY'
    WRITE (1, *) 'VE SPECTRAL EDGE (Hz)'
    OPEN (UNIT=8, FILE=PHAFILE, STATUS='NEW')
    WRITE (8, *) 'TI ', PHAFILE(1:18)
    WRITE (8, *) 'SU '
    WRITE (8, *) 'HO DAY'
    WRITE (8, *) 'VE SPECTRAL EDGE (Hz)'
    OPEN (UNIT=14, FILE=MAGSECONCFILE, STATUS='NEW')
    WRITE (14, *) 'TI ', MAGSECONCFILE(1:26)
    WRITE (14, *) 'SU '
    WRITE (14, *) 'HO [Li+] (mEq/L)'
    WRITE (14, *) 'VE SPECTRAL EDGE (Hz)'
    OPEN (UNIT=15, FILE=PHASESECONCFILE, STATUS='NEW')
    WRITE (15, *) 'TI ', PHASESECONCFILE(1:26)
    WRITE (15, *) 'SU '
    WRITE (15, *) 'HO [Li+] (mEq/L)'
    WRITE (15, *) 'VE SPECTRAL EDGE (Hz)'
    OPEN (UNIT=21, FILE=POWSECONCFILE, STATUS='NEW')
    WRITE (21, *) 'TI ', POWSECONCFILE(1:26)
    WRITE (21, *) 'SU '
    WRITE (21, *) 'HO [Li+] (mEq/L)'
  ENDIF
ENDIF
WRITE (21, *) 'VE SPECTRAL EDGE (Hz)'
GO TO 302

C
301 DO 401 SUBJECT=0, SUBJUP
C
IF (PHASE.EQ.1) THEN
  IF (SUBJECT.EQ.0) INITIALS(1:3)='MLR'
  IF (SUBJECT.EQ.1) INITIALS(1:3)='SJD'
  IF (SUBJECT.EQ.2) INITIALS(1:3)='SJD'
  IF (SUBJECT.EQ.3) INITIALS(1:3)='SKW'
  IF (SUBJECT.EQ.4) INITIALS(1:3)='DSC'
  IF (SUBJECT.EQ.5) INITIALS(1:3)='DSC'
  IF (SUBJECT.EQ.6) INITIALS(1:3)='DSG'
  IF (SUBJECT.EQ.7) INITIALS(1:3)='HRC'
  IF (SUBJECT.EQ.8) INITIALS(1:3)='HRC'
  IF (SUBJECT.EQ.9) INITIALS(1:3)='JHR'
ELSE
  IF (SUBJECT.EQ.0) INITIALS(1:3)='MDW'
  IF (SUBJECT.EQ.1) INITIALS(1:3)='TRB'
  IF (SUBJECT.EQ.2) INITIALS(1:3)='MWD'
  IF (SUBJECT.EQ.3) INITIALS(1:3)='BLP'
  IF (SUBJECT.EQ.4) INITIALS(1:3)='PEF'
  IF (SUBJECT.EQ.5) INITIALS(1:3)='MWF'
  IF (SUBJECT.EQ.6) INITIALS(1:3)='DDS'
  IF (SUBJECT.EQ.7) INITIALS(1:3)='RFF'
ENDIF

C
853 IF (FILETYPE.EQ. 'G') THEN
  EEGFILE(1:26)=FILENAME(1:26)
  MAGFILE(1:14)=INITIALS// 'EEG // 'MAG // 'CPERCENT //'.GRL'
  MAGNORMFILE(1:23)=INITIALS// 'EEG // 'MAG // //
  * CPERCENT // NORM.GRL'
  MAGSECONCFILE(T:26)=MAGFILE(1:14) // VS CONC.GRL'
  MAGSECONCFILE(1:31)=MAGFILE(1:14) // VS CONC NORM.GRL'
  PHAFILE(1:18)=INITIALS// 'EEG // 'PHA // 'CPERCENT //'.GRL'
  PHANORMFILE(1:23)=INITIALS// 'EEG // 'PHA // //
  * CPERCENT // NORM.GRL'
  PHASECONCFILE(T:26)=PHAFILE(1:14) // VS CONC.GRL'
  PHASECONCFILE(1:31)=PHAFILE(1:14) // VS CONC NORM.GRL'
  POWFILE(1:18)=INITIALS// 'EEG // 'POW // 'CPERCENT //'.GRL'
  POWNORMFILE(1:23)=INITIALS// 'EEG // 'POW // //
  * CPERCENT // NORM.GRL'
  POWSECONCFILE(T:26)=POWFILE(1:14) // VS CONC.GRL'
  POWSECONCFILE(1:31)=POWFILE(1:14) // VS CONC NORM.GRL'
  IF (PHASE.EQ.2) THEN
    MAGAVERFILE(1:23)=MAGFILE(1:14) // 'AVER.GRL'
    MEANMAGFILE(1:26)=MAGFILE(1:14) // 'MEAN SE.GRL'
    PHAAVERFILE(1:23)=PHAFILE(1:14) // 'AVER.GRL'
    MEANPHASEFILE(1:26)=PHAFILE(1:14) // 'MEAN SE.GRL'
    POWAVERFILE(1:23)=POWFILE(1:14) // 'AVER.GRL'
    MEANPOWFILE(1:26)=POWFILE(1:14) // 'MEAN SE.GRL'
  ENDIF
ENDIF
IF (FILETYPE.EQ. 'E') THEN
  EEGFILE(1:26)=FILENAME(1:26)
  MAGFILE(1:14)=INITIALS// 'ELY_SGL // 'MAG // 'CPERCENT //'.GRL'
  MAGNORMFILE(1:27)=INITIALS// 'ELY_SGL // //
  * 'MAG // 'CPERCENT // NORM.GRL'
  MAGSECONCFILE(1:30)=MAGFILE(1:18) // VS CONC.GRL'
  MAGSECONCFILE(1:35)=MAGFILE(1:18) // VS CONC NORM.GRL'
  PHAFILE(1:12)=INITIALS// 'ELY_SGL // 'PHA // 'CPERCENT //'.GRL'
  PHANORMFILE(1:27)=INITIALS// 'ELY_SGL // //
  * 'PHA // 'CPERCENT // NORM.GRL'
  PHASECONCFILE(1:30)=PHAFILE(1:18) // VS CONC.GRL'
  PHASECONCFILE(1:35)=PHAFILE(1:18) // VS CONC NORM.GRL'
  POWFILE(1:27)=INITIALS// 'ELY_SGL // 'POW // 'CPERCENT //'.GRL'
  POWNORMFILE(1:27)=INITIALS// 'ELY_SGL // //
  * 'POW // 'CPERCENT // NORM.GRL'
  POWSECONCFILE(1:30)=POWFILE(1:18) // VS CONC.GRL'
  ENDIF
POWSECONCNORMFILE(1:35)=POWFILE(1:18)//
' VS CONC NORM.GRL'
IF (PHASE.EQ.2) THEN
  MAGAVERFILE(1:27)=MAGFILE(1:18)//' AVER.GRL'
  MEANMASEFILE(1:30)=MAGFILE(1:18)//' MEAN SE.GRL'
  PHAAVERFILE(1:27)=PHAFILE(1:18)//' AVER.GRL'
  MEANPHASEFILE(1:30)=PHAFILE(1:18)//' MEAN SE.GRL'
  POWAVERFILE(1:27)=POWFILE(1:18)//' AVER.GRL'
  MEANPOWSEFILE(1:30)=POWFILE(1:18)//' MEAN SE.GRL'
ENDIF
ENDIF
IF (COUNT.EQ.1) THEN
  MAGFILE(1:22)=INITIALS//' ELY DBL '//'MAG '//CPERCENT//'.GRL'
  MAGNORMFILE(1:27)=INITIALS//' ELY_DBL '//'MAG '//CPERCENT///NORM.GRL'
  PHASECONCFILE(1:30)=PHXFILE(1:18)//' VS CONC.GRL'
  PHASECONCNORMFILE(1:35)=PHXFILE(1:18)//' MEAN SE.GRL'
ENDIF
ENDIF
IF (FILETYPE.EQ.'L') THEN
  MAGFILE(1:22)=INITIALS//' LAT SGL '//'MAG '//CPERCENT//'.GRL'
  MAGNORMFILE(1:27)=INITIALS//' LAT-SGL '//'MAG '//CPERCENT///NORM.GRL'
  PHASECONCFILE(1:30)=PHXFILE(1:18)//' VS CONC.GRL'
  PHASECONCNORMFILE(1:35)=PHXFILE(1:18)//' MEAN SE.GRL'
ENDIF
ENDIF
IF (PHASE.EQ.2) THEN
  MAGAVERFILE(1:27)=MAGFILE(1:18)//' AVER.GRL'
  MEANMASEFILE(1:30)=MAGFILE(1:18)//' MEAN SE.GRL'
  PHAAVERFILE(1:27)=PHAFILE(1:18)//' AVER.GRL'
  MEANPHASEFILE(1:30)=PHAFILE(1:18)//' MEAN SE.GRL'
  POWAVERFILE(1:27)=POWFILE(1:18)//' AVER.GRL'
  MEANPOWSEFILE(1:30)=POWFILE(1:18)//' MEAN SE.GRL'
ENDIF
ENDIF
IF (COUNT.EQ.0) THEN
  MAGFILE(1:22)=INITIALS//' LAT SGL '//'MAG '//CPERCENT//'.GRL'
  MAGNORMFILE(1:27)=INITIALS//' LAT-SGL '//'MAG '//CPERCENT///NORM.GRL'
  PHASECONCFILE(1:30)=PHXFILE(1:18)//' VS CONC.GRL'
  PHASECONCNORMFILE(1:35)=PHXFILE(1:18)//' MEAN SE.GRL'
ENDIF
ENDIF
IF (PHASE.EQ.2) THEN
  MAGAVERFILE(1:27)=MAGFILE(1:18)//' AVER.GRL'
  MEANMASEFILE(1:30)=MAGFILE(1:18)//' MEAN SE.GRL'
  PHAAVERFILE(1:27)=PHAFILE(1:18)//' AVER.GRL'
  MEANPHASEFILE(1:30)=PHAFILE(1:18)//' MEAN SE.GRL'
  POWAVERFILE(1:27)=POWFILE(1:18)//' AVER.GRL'
  MEANPOWSEFILE(1:30)=POWFILE(1:18)//' MEAN SE.GRL'
ENDIF
ENDIF
IF (COUNT.EQ.1) THEN
  MAGFILE(1:22)=INITIALS//' LAT DBL '//'MAG '//CPERCENT//'.GRL'
  MAGNORMFILE(1:27)=INITIALS//' LAT-DBL '//'MAG '//CPERCENT///NORM.GRL'
  PHASECONCFILE(1:30)=PHXFILE(1:18)//' VS CONC.GRL'
  PHASECONCNORMFILE(1:35)=PHXFILE(1:18)//' MEAN SE.GRL'
ENDIF
ENDIF
IF (PHASE.EQ.2) THEN
  OPEN (UNIT=10,FILE=MAGAVERFILE,STATUS='NEW')
  WRITE (10,*) 'TI ',MAGAVERFILE(1:23)
  WRITE (10,*) 'SU ',MAGAVERFILE(1:23)
  WRITE (10,*) 'HO DAY',MAGAVERFILE(1:23)
  WRITE (10,*) 'VE SPECTRAL EDGE (Hz)',MAGAVERFILE(1:23)
  OPEN (UNIT=11,FILE=PHAAVERFILE,STATUS='NEW')
  WRITE (11,*) 'TI ',PHAAVERFILE(1:23)
  WRITE (11,*) 'SU ',PHAAVERFILE(1:23)
  WRITE (11,*) 'HO DAY',PHAAVERFILE(1:23)
  WRITE (11,*) 'VE SPECTRAL EDGE (Hz)',PHAAVERFILE(1:23)
  OPEN (UNIT=22,FILE=POWAVERFILE,STATUS='NEW')
  WRITE (22,*) 'TI ',POWAVERFILE(1:23)
  WRITE (22,*) 'SU ',POWAVERFILE(1:23)
  WRITE (22,*) 'HO DAY',POWAVERFILE(1:23)
  WRITE (22,*) 'VE SPECTRAL EDGE (Hz)',POWAVERFILE(1:23)
  OPEN (UNIT=12,FILE=MEANMAGSEFILE,STATUS='NEW')
  WRITE (12,*) 'TI ',MEANMAGSEFILE(1:26)
  WRITE (12,*) 'SU ',MEANMAGSEFILE(1:26)
  WRITE (12,*) 'HO DAY',MEANMAGSEFILE(1:26)
  WRITE (12,*) 'VE SPECTRAL EDGE (Hz)',MEANMAGSEFILE(1:26)
  OPEN (UNIT=13,FILE=MEANPHASEFILE,STATUS='NEW')
  WRITE (13,*) 'TI ',MEANPHASEFILE(1:26)
  WRITE (13,*) 'SU ',MEANPHASEFILE(1:26)
  WRITE (13,*) 'HO DAY',MEANPHASEFILE(1:26)
  WRITE (13,*) 'VE SPECTRAL EDGE (Hz)',MEANPHASEFILE(1:26)
  OPEN (UNIT=23,FILE=MEANPOWSEFILE,STATUS='NEW')
  WRITE (23,*) 'TI ',MEANPOWSEFILE(1:26)
  WRITE (23,*) 'SU ',MEANPOWSEFILE(1:26)
  WRITE (23,*) 'HO DAY',MEANPOWSEFILE(1:26)
  WRITE (23,*) 'VE SPECTRAL EDGE (Hz)',MEANPOWSEFILE(1:26)
ENDIF

ENDIF

IF (CFREQ.EQ."N") GOTO 562

...
WRITE (14,*) 'VE SPECTRAL EDGE (Hz)'
OPEN (UNIT=15,FILE=PHASECONCFILE,STATUS='NEW')
WRITE (15,*) 'TI ',PHASECONCFILE(1:26)
WRITE (15,*)
WRITE (15,*)
WRITE (15,* 'HO [Li+] (mEq/L)'
WRITE (15,*) 'VE SPECTRAL EDGE (Hz)'
OPEN (UNIT=21,FILE=POWSECONCFILE,STATUS='NEW')
WRITE (21,*) 'TI ',POWSECONCFILE(1:26)
WRITE (21,*)
WRITE (21,*)
WRITE (21,* 'HO (Li+J (mEq/L)'
WRITE (21,*) 'VE SPECTRAL EDGE (Hz)'
OPEN (UNIT=16,FILE=MAGNORMFILE,STATUS='NEW')
WRITE (16,*) 'TI ',MAGNORMFILE(1:23)
OPEN (UNIT=17,FILE=MAGSECONCNORMFILE,STATUS='NEW')
WRITE (17,*) 'TI ',MAGSECONCNORMFILE(1:31)
OPEN (UNIT=18,FILE=PHANORMFILE,STATUS='NEW')
WRITE (18,*) 'TI ',PHANORMFILE(1:23)
OPEN (UNIT=19,FILE=PHASECONCNORMFILE,STATUS='NEW')
WRITE (19,*) 'TI ',PHASECONCNORMFILE(1:31)
OPEN (UNIT=24,FILE=POWNORMFILE,STATUS='NEW')
WRITE (24,*) 'TI ',POWNORMFILE(1:23)
OPEN (UNIT=25,FILE=POWSECONCNORMFILE,STATUS='NEW')
WRITE (25,*) 'TI ',POWSECONCNORMFILE(1:31)

562 DO 402 DAY=0,DAYUP,DAYINC
  IF (PHASE.EQ.1) THEN
    IF (INITIALS.EQ.'MLR').AND.(DAY.EQ.O))
      EEGFILE(1:28)='MLR 140CT88 0748 EEG.DATA'
    IF (INITIALS.EQ.'RLR').AND.(DAY.EQ.1))
      EEGFILE(1:28)='RLR _140CT88_0748_EEG_DATA'
    IF (INITIALS.EQ.'MLR').AND.(DAY.EQ.2))
      EEGFILE(1:28)='MLR 150CT88 0749 EEG.DATA'
    IF (INITIALS.EQ.'MLR').AND.(DAY.EQ.3))
      EEGFILE(1:28)='MLR 160CT88 0750 EEG.DATA'
    IF (INITIALS.EQ.'MLR').AND.(DAY.EQ.4))
      EEGFILE(1:28)='MLR 170CT88 0751 EEG.DATA'
    IF (INITIALS.EQ.'MLR').AND.(DAY.EQ.5))
      EEGFILE(1:28)='MLR 180CT88 0752 EEG.DATA'
    IF (INITIALS.EQ.'MLR').AND.(DAY.EQ.6))
      EEGFILE(1:28)='MLR 190CT88 0753 EEG.DATA'
    IF (INITIALS.EQ.'MLR').AND.(DAY.EQ.7))
      EEGFILE(1:28)='MLR 200CT88 0754 EEG.DATA'
    IF (INITIALS.EQ.'MLR').AND.(DAY.EQ.8))
      EEGFILE(1:28)='MLR 210CT88 0755 EEG.DATA'
    IF (INITIALS.EQ.'MLR').AND.(DAY.EQ.9))
      EEGFILE(1:28)='MLR 220CT88 0756 EEG.DATA'
    IF (INITIALS.EQ.'MLR').AND.(DAY.EQ.10))
      EEGFILE(1:28)='MLR 230CT88 0757 EEG.DATA'
    IF (INITIALS.EQ.'MLR').AND.(DAY.EQ.11))
      EEGFILE(1:28)='MLR 240CT88 0758 EEG.DATA'
    IF (INITIALS.EQ.'MLR').AND.(DAY.EQ.12))
      EEGFILE(1:28)='MLR 250CT88 0759 EEG.DATA'
    IF (INITIALS.EQ.'MLR').AND.(DAY.EQ.13))
      EEGFILE(1:28)='MLR 260CT88 0760 EEG.DATA'
    IF (INITIALS.EQ.'MLR').AND.(DAY.EQ.14))
      EEGFILE(1:28)='MLR 270CT88 0761 EEG.DATA'
    IF (INITIALS.EQ.'MLR').AND.(DAY.EQ.15))
      EEGFILE(1:28)='MLR 280CT88 0762 EEG.DATA'
    IF (INITIALS.EQ.'MLR').AND.(DAY.EQ.16))
      EEGFILE(1:28)='MLR 290CT88 0763 EEG.DATA'
    IF (INITIALS.EQ.'MLR').AND.(DAY.EQ.17))
      EEGFILE(1:28)='MLR 300CT88 0764 EEG.DATA'
    IF (INITIALS.EQ.'MLR').AND.(DAY.EQ.18))
      EEGFILE(1:28)='MLR 310CT88 0765 EEG.DATA'
    IF (INITIALS.EQ.'MLR').AND.(DAY.EQ.19))
      EEGFILE(1:28)='MLR 320CT88 0766 EEG.DATA'
    IF (INITIALS.EQ.'MLR').AND.(DAY.EQ.20))
      EEGFILE(1:28)='MLR 330CT88 0767 EEG.DATA'
    IF (INITIALS.EQ.'MLR').AND.(DAY.EQ.21))
      EEGFILE(1:28)='MLR 340CT88 0768 EEG.DATA'
    IF (INITIALS.EQ.'MLR').AND.(DAY.EQ.22))
      EEGFILE(1:28)='MLR 350CT88 0769 EEG.DATA'
    IF (INITIALS.EQ.'MLR').AND.(DAY.EQ.23))
      EEGFILE(1:28)='MLR 360CT88 0770 EEG.DATA'
    IF (INITIALS.EQ.'MLR').AND.(DAY.EQ.24))
      EEGFILE(1:28)='MLR 370CT88 0771 EEG.DATA'
    IF (INITIALS.EQ.'MLR').AND.(DAY.EQ.25))
      EEGFILE(1:28)='MLR 380CT88 0772 EEG.DATA'
    IF (INITIALS.EQ.'MLR').AND.(DAY.EQ.26))
      EEGFILE(1:28)='MLR 390CT88 0773 EEG.DATA'
    IF (INITIALS.EQ.'MLR').AND.(DAY.EQ.27))
      EEGFILE(1:28)='MLR 400CT88 0774 EEG.DATA'
    IF (INITIALS.EQ.'MLR').AND.(DAY.EQ.28))
      EEGFILE(1:28)='MLR 410CT88 0775 EEG.DA
• IF (INITIALS.EQ.'TRB').AND.(DAY.EQ.1)
  EEGFILE(1:28)="TRB 24OCT88 0709 EEG x1.DATA"
  IF (INITIALS.EQ.'TRB').AND.(DAY.EQ.2)
  EEGFILE(1:28)="TRB 25OCT88 0706 EEG x1.DATA"
  IF (INITIALS.EQ.'TRB').AND.(DAY.EQ.3)
  EEGFILE(1:28)="TRB 26OCT88 0710 EEG x1.DATA"
  IF (INITIALS.EQ.'TRB').AND.(DAY.EQ.4)
  EEGFILE(1:28)="TRB 27OCT88 0713 EEG x1.DATA"
  IF (INITIALS.EQ.'TRB').AND.(DAY.EQ.5)
  EEGFILE(1:28)="TRB 28OCT88 0749 EEG x1.DATA"
  IF (INITIALS.EQ.'TRB').AND.(DAY.EQ.6)
  GO TO 402
• IF (INITIALS.EQ.'TRB').AND.(DAY.EQ.10)
  EEGFILE(1:28)="TRB_07NOV88_0718 EEG x1.DATA"
• IF (INITIALS.EQ.'TRB').AND.(DAY.EQ.15)
  EEGFILE(1:28)="TRB_07NOV88_0747 EEG x1.DATA"
• IF (INITIALS.EQ.'SKW').AND.(DAY.EQ.0)
  EEGFILE(1:28)="SKW 21OCT88 0721 EEG x1.DATA"
  IF (INITIALS.EQ.'SKW').AND.(DAY.EQ.1)
  EEGFILE(1:28)="SKW 24OCT88 0733 EEG x1.DATA"
  IF (INITIALS.EQ.'SKW').AND.(DAY.EQ.2)
  EEGFILE(1:28)="SKW 25OCT88 0737 EEG x1.DATA"
  IF (INITIALS.EQ.'SKW').AND.(DAY.EQ.3)
  EEGFILE(1:28)="SKW 26OCT88 0730 EEG x1.DATA"
  IF (INITIALS.EQ.'SKW').AND.(DAY.EQ.4)
  EEGFILE(1:28)="SKW 27OCT88 0736 EEG x1.DATA"
  IF (INITIALS.EQ.'SKW').AND.(DAY.EQ.5)
  EEGFILE(1:28)="SKW 28OCT88 0812 EEG x1.DATA"
  IF (INITIALS.EQ.'SKW').AND.(DAY.EQ.10)
  EEGFILE(1:28)="SKW_02NOV88 0735 EEG x1.DATA"
  IF (INITIALS.EQ.'SKW').AND.(DAY.EQ.15)
  EEGFILE(1:28)="SKW_07NOV88_0743 EEG x1.DATA"
• IF (INITIALS.EQ.'DSC').AND.(DAY.EQ.0)
  EEGFILE(1:28)="DSC 30OCT88 1012 EEG x1.DATA"
  IF (INITIALS.EQ.'DSC').AND.(DAY.EQ.1)
  EEGFILE(1:28)="DSC 31OCT88 0646 EEG x1.DATA"
  IF (INITIALS.EQ.'DSC').AND.(DAY.EQ.2)
  EEGFILE(1:28)="DSC 01NOV88 0647 EEG x1.DATA"
  IF (INITIALS.EQ.'DSC').AND.(DAY.EQ.3)
  EEGFILE(1:28)="DSC 03NOV88 0646 EEG x1.DATA"
  IF (INITIALS.EQ.'DSC').AND.(DAY.EQ.4)
  EEGFILE(1:28)="DSC 04NOV88 0647 EEG x1.DATA"
  IF (INITIALS.EQ.'DSC').AND.(DAY.EQ.5)
  EEGFILE(1:28)="DSC 05NOV88 0650 EEG x1.DATA"
  IF (INITIALS.EQ.'DSC').AND.(DAY.EQ.10)
  EEGFILE(1:28)="DSC_14NOV88_0650 EEG x1.DATA"
  IF (INITIALS.EQ.'DSC').AND.(DAY.EQ.15)
  EEGFILE(1:28)="DSC_14NOV88_0650 EEG x1.DATA"
• IF (INITIALS.EQ.'DJC').AND.(DAY.EQ.0)
  EEGFILE(1:28)="DJC 10NOV88 0653 EEG x1.DATA"
  IF (INITIALS.EQ.'DJC').AND.(DAY.EQ.1)
  EEGFILE(1:28)="DJC 11NOV88 0653 EEG x1.DATA"
  IF (INITIALS.EQ.'DJC').AND.(DAY.EQ.2)
  EEGFILE(1:28)="DJC 12NOV88 0708 EEG x1.DATA"
  IF (INITIALS.EQ.'DJC').AND.(DAY.EQ.3)
  EEGFILE(1:28)="DJC 13NOV88 0716 EEG x1.DATA"
  IF (INITIALS.EQ.'DJC').AND.(DAY.EQ.4)
  EEGFILE(1:28)="DJC 14NOV88 0701 EEG x1.DATA"
  IF (INITIALS.EQ.'DJC').AND.(DAY.EQ.5)
  EEGFILE(1:28)="DJC_14NOV88_0701 EEG x1.DATA"
  IF (INITIALS.EQ.'DJC').AND.(DAY.EQ.10)
  EEGFILE(1:28)="DJC_14NOV88_0701 EEG x1.DATA"
  IF (INITIALS.EQ.'DJC').AND.(DAY.EQ.15)
  EEGFILE(1:28)="DJC_28NOV88_0700 EEG x1.DATA"
• IF (INITIALS.EQ.'DSG').AND.(DAY.EQ.0)
  EEGFILE(1:28)="DSG 14NOV88 0606 EEG x1.DATA"
  IF (INITIALS.EQ.'DSG').AND.(DAY.EQ.1)
  EEGFILE(1:28)="DSG 15NOV88 0836 EEG x1.DATA"
  IF (INITIALS.EQ.'DSG').AND.(DAY.EQ.2)
  EEGFILE(1:28)="DSG 16NOV88 0836 EEG x1.DATA"
  IF (INITIALS.EQ.'DSG').AND.(DAY.EQ.3)
  EEGFILE(1:28)="DSG 17NOV88 0700 EEG x1.DATA"
  IF (INITIALS.EQ.'DSG').AND.(DAY.EQ.4)
  EEGFILE(1:28)="DSG 18NOV88 0700 EEG x1.DATA"
  IF (INITIALS.EQ.'DSG').AND.(DAY.EQ.5)
  EEGFILE(1:28)="DSG 19NOV88 0700 EEG x1.DATA"
  IF (INITIALS.EQ.'DSG').AND.(DAY.EQ.10)
  EEGFILE(1:28)="DSG_19NOV88_0700 EEG x1.DATA"
  IF (INITIALS.EQ.'DSG').AND.(DAY.EQ.15)
  EEGFILE(1:28)="DSG_19NOV88_0700 EEG x1.DATA"
  IF (INITIALS.EQ.'DSG').AND.(DAY.EQ.15)
  EEGFILE(1:28)="DSG_19NOV88_0700 EEG x1.DATA"
IF ((INITIALS.EQ.'DSG').AND.(DAY.EQ.5))
  EEGFILE(1:28)='DSG 19NOV88 0829 EEG X1.DATA'
IF ((INITIALS.EQ.'DSG').AND.(DAY.EQ.10))
  EEGFILE(1:28)='DSG 24NOV88 0742 EEG X1.DATA'
IF ((INITIALS.EQ.'DSG').AND.(DAY.EQ.15))
  EEGFILE(1:28)='DSG 29NOV88 0818 EEG X1.DATA'

IF ((INITIALS.EQ.'RRC').AND.(DAY.EQ.0))
  EEGFILE(1:28)='RRC 15NOV88 0748 EEG X1.DATA'
IF ((INITIALS.EQ.'RRC').AND.(DAY.EQ.1))
  EEGFILE(1:28)='RRC 20NOV88 0747 EEG X1.DATA'
IF ((INITIALS.EQ.'RRC').AND.(DAY.EQ.2))
  EEGFILE(1:28)='RRC 26NOV88 0904 EEG X1.DATA'
IF ((INITIALS.EQ.'RRC').AND.(DAY.EQ.3))
  EEGFILE(1:28)='RRC 29NOV88 0747 EEG X1.DATA'
IF ((INITIALS.EQ.'RRC').AND.(DAY.EQ.4))
  EEGFILE(1:28)='RRC 07DEC88 0806 EEG X1.DATA'
IF ((INITIALS.EQ.'RRC').AND.(DAY.EQ.5))
  EEGFILE(1:28)='RRC 14DEC88 0802 EEG X1.DATA'
ELSE
  IF ((INITIALS.EQ.'MDW').AND.(DAY.EQ.0))
    EEGFILE(1:28)='MDW 10AUG89 0603 EEG X1.DATA'
  IF ((INITIALS.EQ.'MDW').AND.(DAY.EQ.1))
    EEGFILE(1:28)='MDW 10AUG89 0622 EEG X1.DATA'
  IF ((INITIALS.EQ.'MDW').AND.(DAY.EQ.2))
    EEGFILE(1:28)='MDW 11AUG89 0610 EEG X1.DATA'
  IF ((INITIALS.EQ.'MDW').AND.(DAY.EQ.3))
    EEGFILE(1:28)='MDW 14AUG89 0612 EEG X1.DATA'
  IF ((INITIALS.EQ.'MDW').AND.(DAY.EQ.4))
    EEGFILE(1:28)='MDW 15AUG89 0611 EEG X1.DATA'
  IF ((INITIALS.EQ.'MDW').AND.(DAY.EQ.5))
    EEGFILE(1:28)='MDW 18AUG89 0612 EEG X1.DATA'
  IF ((INITIALS.EQ.'MDW').AND.(DAY.EQ.6))
    EEGFILE(1:28)='MDW 21AUG89 0613 EEG X1.DATA'
  ELSE
    EEGFILE(1:28)='MDW 22AUG89 0607 EEG X1.DATA'
IF (INITIALS.EQ.'MOW').AND.(DAY.EQ.14)
  EEGFILE(1:28)='MDW_23AUG89_0614_EEG_X1.DATA'
IF (INITIALS.EQ.'RDW').AND.(DAY.EQ.15)
  EEGFILE(1:28)='MDW_24AUG89_0702_EEG_X1.DATA'
IF (INITIALS.EQ.'ROW').AND.(DAY.EQ.16)
  EEGFILE(1:28)='MDW_25AUG89_0614_EEG_X1.DATA'

IF (INITIALS.EQ.'TRB').AND.(DAY.EQ.17)
  EEGFILE(1:28)='MDW_25AUG89_0614_EEG_X1.DATA'
IF (INITIALS.EQ.'BWB').AND.(DAY.EQ.18)
  EEGFILE(1:28)='MDW_26AUG89_0702_EEG_X1.DATA'
IF (INITIALS.EQ.'MBW').AND.(DAY.EQ.19)
  EEGFILE(1:28)='MDW_27AUG89_0614_EEG_X1.DATA'

GO TO 402
IF ((INITIALS.EQ.'PEF').AND.((DAY.EQ.0))
  EEGFILE(1:28)=PEF 29AUG89 0656 EEG X1.DATA'
  IF ((INITIALS.EQ.'PEF').AND.(DAY.EQ.1))
  EEGFILE(1:28)=PEF 30AUG89 0715 EEG X1.DATA'
  IF ((INITIALS.EQ.'PEF').AND.(DAY.EQ.2))
  EEGFILE(1:28)=PEF 31AUG89 0715 EEG X1.DATA'
  IF ((INITIALS.EQ.'PEF').AND.(DAY.EQ.3))
  EEGFILE(1:28)=PEF 05SEP89 0715 EEG X1.DATA'
  IF ((INITIALS.EQ.'PEF').AND.(DAY.EQ.4))
  EEGFILE(1:28)=PEF 06SEP89 0825 EEG X1.DATA'
  IF ((INITIALS.EQ.'PEF').AND.(DAY.EQ.5))
  EEGFILE(1:28)=PEF 08SEP89 0715 EEG X1.DATA'
  IF ((INITIALS.EQ.'PEF').AND.(DAY.EQ.6))
  EEGFILE(1:28)=PEF 11SEP89 0726 EEG X1.DATA'
  IF ((INITIALS.EQ.'PEF').AND.(DAY.EQ.7))
  EEGFILE(1:28)=PEF 12SEP89 0734 EEG X1.DATA'
  IF ((INITIALS.EQ.'PEF').AND.(DAY.EQ.8))
  EEGFILE(1:28)=PEF 13SEP89 0717 EEG X1.DATA'
  IF ((INITIALS.EQ.'PEF').AND.(DAY.EQ.9))
  EEGFILE(1:28)=PEF 14SEP89 0724 EEG X1.DATA'
  IF ((INITIALS.EQ.'PEF').AND.(DAY.EQ.10))
  EEGFILE(1:28)=PEF 15SEP89 0732 EEG X1.DATA'
  IF ((INITIALS.EQ.'MEF').AND.(DAY.EQ.0))
  EEGFILE(1:28)=MEF 29AUG89 0742 EEG X1.DATA'
  IF ((INITIALS.EQ.'MEF').AND.(DAY.EQ.1))
  EEGFILE(1:28)=MEF 30AUG89 0803 EEG X1.DATA'
  IF ((INITIALS.EQ.'MEF').AND.(DAY.EQ.2))
  EEGFILE(1:28)=MEF 31AUG89 0736 EEG X1.DATA'
  IF ((INITIALS.EQ.'MEF').AND.(DAY.EQ.3))
  EEGFILE(1:28)=MEF 05SEP89 0739 EEG X1.DATA'
  IF ((INITIALS.EQ.'MEF').AND.(DAY.EQ.4))
  EEGFILE(1:28)=MEF 06SEP89 0705 EEG X1.DATA'
  IF ((INITIALS.EQ.'MEF').AND.(DAY.EQ.5))
  EEGFILE(1:28)=MEF 08SEP89 0746 EEG X1.DATA'
  IF ((INITIALS.EQ.'MEF').AND.(DAY.EQ.6))
  EEGFILE(1:28)=MEF 11SEP89 0743 EEG X1.DATA'
  IF ((INITIALS.EQ.'MEF').AND.(DAY.EQ.7))
  EEGFILE(1:28)=MEF 12SEP89 0639 EEG X1.DATA'
  IF ((INITIALS.EQ.'MEF').AND.(DAY.EQ.8))
  EEGFILE(1:28)=MEF 13SEP89 0751 EEG X1.DATA'
  IF ((INITIALS.EQ.'MEF').AND.(DAY.EQ.9))
  EEGFILE(1:28)=MEF 15SEP89 0622 EEG X1.DATA'
  IF ((INITIALS.EQ.'DFSS').AND.((DAY.EQ.0))
  EEGFILE(1:28)=DFSS 29AUG89 0742 EEG X1.DATA'
  IF ((INITIALS.EQ.'DFSS').AND.(DAY.EQ.1))
  EEGFILE(1:28)=DFSS 30AUG89 0720 EEG X1.DATA'
  IF ((INITIALS.EQ.'DFSS').AND.(DAY.EQ.2))
  EEGFILE(1:28)=DFSS 31AUG89 0704 EEG X1.DATA'
  IF ((INITIALS.EQ.'DFSS').AND.(DAY.EQ.3))
  EEGFILE(1:28)=DFSS 05SEP89 0748 EEG X1.DATA'
  IF ((INITIALS.EQ.'DFSS').AND.(DAY.EQ.4))
  EEGFILE(1:28)=DFSS 06SEP89 0805 EEG X1.DATA'
  IF ((INITIALS.EQ.'DFSS').AND.(DAY.EQ.5))
  EEGFILE(1:28)=DFSS 08SEP89 0809 EEG X1.DATA'
  IF ((INITIALS.EQ.'DFSS').AND.(DAY.EQ.6))
  EEGFILE(1:28)=DFSS 11SEP89 0817 EEG X1.DATA'
  IF ((INITIALS.EQ.'DFSS').AND.(DAY.EQ.7))
  EEGFILE(1:28)=DFSS 12SEP89 0815 EEG X1.DATA'
  IF ((INITIALS.EQ.'DFSS').AND.(DAY.EQ.8))
  EEGFILE(1:28)=DFSS 13SEP89 0806 EEG X1.DATA'
  IF ((INITIALS.EQ.'DFSS').AND.(DAY.EQ.9))
  EEGFILE(1:28)=DFSS 15SEP89 0642 EEG X1.DATA'
  IF ((INITIALS.EQ.'RFF').AND.((DAY.EQ.0))
  EEGFILE(1:28)=RFF 29AUG89 0809 EEG X1.DATA'
  IF ((INITIALS.EQ.'RFF').AND.(DAY.EQ.1))
  EEGFILE(1:28)=RFF 30AUG89 0747 EEG X1.DATA'
  IF ((INITIALS.EQ.'RFF').AND.(DAY.EQ.2))
  EEGFILE(1:28)=RFF 31AUG89 0723 EEG X1.DATA'
  IF ((INITIALS.EQ.'RFF').AND.(DAY.EQ.3))
  EEGFILE(1:28)=RFF 05SEP89 0723 EEG X1.DATA'
  IF ((INITIALS.EQ.'RFF').AND.(DAY.EQ.4))
  EEGFILE(1:28)=RFF 06SEP89 0825 EEG X1.DATA'
  IF ((INITIALS.EQ.'RFF').AND.(DAY.EQ.5))
  EEGFILE(1:28)=RFF 08SEP89 0715 EEG X1.DATA'
  IF ((INITIALS.EQ.'RFF').AND.(DAY.EQ.6))
  EEGFILE(1:28)=RFF 11SEP89 0715 EEG X1.DATA'
  IF ((INITIALS.EQ.'RFF').AND.(DAY.EQ.7))
  EEGFILE(1:28)=RFF 12SEP89 0734 EEG X1.DATA'
  IF ((INITIALS.EQ.'RFF').AND.(DAY.EQ.8))
  EEGFILE(1:28)=RFF 13SEP89 0717 EEG X1.DATA'
  IF ((INITIALS.EQ.'RFF').AND.(DAY.EQ.9))
  EEGFILE(1:28)=RFF 14SEP89 0724 EEG X1.DATA'
  IF ((INITIALS.EQ.'RFF').AND.(DAY.EQ.10))
  EEGFILE(1:28)=RFF 15SEP89 0732 EEG X1.DATA'
  IF ((INITIALS.EQ.'RFF').AND.(DAY.EQ.11))
  EEGFILE(1:28)=RFF 16SEP89 0730 EEG X1.DATA'
  IF ((INITIALS.EQ.'RFF').AND.(DAY.EQ.12))
  EEGFILE(1:28)=RFF 17SEP89 0715 EEG X1.DATA'
  IF ((INITIALS.EQ.'RFF').AND.(DAY.EQ.13))
  EEGFILE(1:28)=RFF 18SEP89 0715 EEG X1.DATA'
  IF ((INITIALS.EQ.'RFF').AND.(DAY.EQ.14))
  EEGFILE(1:28)=RFF 19SEP89 0715 EEG X1.DATA'
  IF ((INITIALS.EQ.'RFF').AND.(DAY.EQ.15))
  EEGFILE(1:28)=RFF 20SEP89 0715 EEG X1.DATA'
  IF ((INITIALS.EQ.'RFF').AND.(DAY.EQ.16))
  EEGFILE(1:28)=RFF 21SEP89 0715 EEG X1.DATA'
  GO TO 402
* EEGFILE(1:28)='RFF 31AUG89 0835 EEG X1.DATA'
* EEGFILE(1:28)='RFF 06SEP89 0749 EEG X1.DATA'
* EEGFILE(1:28)='RFF 11SEP89 0758 EEG X1.DATA'
* EEGFILE(1:28)='RFF 08SEP89 0731 EEG X1.DATA'
* EEGFILE(1:28)='RFF 12SEP89 0755 EEG X1.DATA'
* EEGFILE(1:28)='RFF 13SEP89 0735 EEG X1.DATA'
* EEGFILE(1:28)='RFF 14SEP89 0828 EEG X1.DATA'
* EEGFILE(1:28)='RFF 15SEP89 0754 EEG X1.DATA'

ENDIF

INQUIRE(FILE=EEGFILE(1:28),EXIST=ONDISK)

IF(.NOT.ONDISK)

THEN

WRITE(6,'(1X,'EEGFILE//') IS NOT ON DISK.')

GO TO 402

ENDIF

CALL READ_EEG(EEGFILE,AMEAN)

GO TO 33

32 IF (FILETYPE.NE.'E') GO TO 34

IF (PHASE.EQ.1) THEN

* IF (INITIALS.EQ.'MLR').AND.(DAY.EQ.0)
* FILENAME(1:32)='MLR 14OCT88 0750 ELY ALT X1.CHOP'
* IF (INITIALS.EQ.'MLR').AND.(DAY.EQ.1)
* FILENAME(1:32)='MLR 17OCT88 0744 ELY ALT X1.CHOP'
* IF (INITIALS.EQ.'MLR').AND.(DAY.EQ.2)
* FILENAME(1:32)='MLR 18OCT88 0800 ELY ALT X1.CHOP'
* IF (INITIALS.EQ.'MLR').AND.(DAY.EQ.3)
* FILENAME(1:32)='MLR 21OCT88 0843 ELY ALT X1.CHOP'
* IF (INITIALS.EQ.'MLR').AND.(DAY.EQ.4)
* FILENAME(1:32)='MLR 23OCT88 0826 ELY ALT X1.CHOP'
* IF (INITIALS.EQ.'MLR').AND.(DAY.EQ.5)
* FILENAME(1:32)='MLR 31OCT88 0745 ELY ALT X1.CHOP'

* IF (INITIALS.EQ.'SJD').AND.(DAY.EQ.0)
* FILENAME(1:32)='SJD 14OCT88 0820 ELY ALT X1.CHOP'
* IF (INITIALS.EQ.'SJD').AND.(DAY.EQ.1)
* FILENAME(1:32)='SJD 17OCT88 0806 ELY ALT X1.CHOP'
* IF (INITIALS.EQ.'SJD').AND.(DAY.EQ.2)
* FILENAME(1:32)='SJD 18OCT88 0826 ELY ALT X1.CHOP'
* IF (INITIALS.EQ.'SJD').AND.(DAY.EQ.3)
* FILENAME(1:32)='SJD 21OCT88 0818 ELY ALT X1.CHOP'
* IF (INITIALS.EQ.'SJD').AND.(DAY.EQ.4)
* FILENAME(1:32)='SJD 23OCT88 0824 ELY ALT X1.CHOP'

* IF (INITIALS.EQ.'TRB').AND.(DAY.EQ.0)
* FILENAME(1:32)='TRB 14OCT88 0713 ELY ALT X2.CHOP'
* IF (INITIALS.EQ.'TRB').AND.(DAY.EQ.1)
* FILENAME(1:32)='TRB 17OCT88 0711 ELY ALT X2.CHOP'
* IF (INITIALS.EQ.'TRB').AND.(DAY.EQ.2)
* FILENAME(1:32)='TRB 19OCT88 0708 ELY ALT X2.CHOP'
* IF (INITIALS.EQ.'TRB').AND.(DAY.EQ.3)
* FILENAME(1:32)='TRB 23OCT88 0713 ELY ALT X2.CHOP'
* IF (INITIALS.EQ.'TRB').AND.(DAY.EQ.4)
* FILENAME(1:32)='TRB 25OCT88 0708 ELY ALT X2.CHOP'
* IF (INITIALS.EQ.'TRB').AND.(DAY.EQ.5)
* FILENAME(1:32)='TRB 27OCT88 0714 ELY ALT X2.CHOP'

ENDIF
IF (INITIALS.EQ.'T~B').AND.(DAY.EQ.5))
FILENAME(1:32)='TRB_07NOV88_0720_ELY_ALT_X2.CHOP'
IF (INITIALS.EQ.'SKW').AND.(DAY.EQ.0))
FILENAME(1:32)='SKW_21OCT88_0735_ELY_ALT_X2.CHOP'
IF (INITIALS.EQ.'SKW').AND.(DAY.EQ.7))
FILENAME(1:32)='SKW_25OCT88_0758_ELY_ALT_X2.CHOP'
IF (INITIALS.EQ.'SKW').AND.(DAY.EQ.4))
FILENAME(1:32)='SKW_29OCT88_0732_ELY_ALT_X2.CHOP'
IF (INITIALS.EQ.'SKW').AND.(DAY.EQ.3))
FILENAME(1:32)='SKW_02NOV88_0746_ELY_ALT_X2.CHOP'
IF (INITIALS.EQ.'SKW').AND.(DAY.EQ.1))
FILENAME(1:32)='SKW_07NOV88_0744_ELY_ALT_X2.CHOP'
IF (INITIALS.EQ.'DSC').AND.(DAY.EQ.0))
FILENAME(1:32)='DSC_30OCT88_1014_ELY_ALT_X2.CHOP'
IF (INITIALS.EQ.'DSC').AND.(DAY.EQ.7))
FILENAME(1:32)='DSC_01NOV88_0648_ELY_ALT_X2.CHOP'
IF (INITIALS.EQ.'DSC').AND.(DAY.EQ.6))
FILENAME(1:32)='DSC_09NOV88_0651_ELY_ALT_X2.CHOP'
IF (INITIALS.EQ.'DSC').AND.(DAY.EQ.5))
FILENAME(1:32)='DSC_14NOV88_0655_ELY_ALT_X2.CHOP'
IF (INITIALS.EQ.'DSC').AND.(DAY.EQ.4))
FILENAME(1:32)='DSC_10NOV88_0655_ELY_ALT_X2.CHOP'
IF (INITIALS.EQ.'DSC').AND.(DAY.EQ.3))
FILENAME(1:32)='DSC_16NOV88_0729_ELY_ALT_X2.CHOP'
IF (INITIALS.EQ.'DSC').AND.(DAY.EQ.2))
FILENAME(1:32)='DSC_23NOV88_0704_ELY_ALT_X2.CHOP'
IF (INITIALS.EQ.'DSC').AND.(DAY.EQ.1))
FILENAME(1:32)='DSC_28NOV88_0702_ELY_ALT_X2.CHOP'
IF (INITIALS.EQ.'DSC').AND.(DAY.EQ.0))
FILENAME(1:32)='DSC_30OCT88_1014_ELY_ALT_X2.CHOP'
GO TO 402
IF (INITIALS.EQ.'DSC').AND.(DAY.EQ.4))
FILENAME(1:32)='DSC_01NOV88_0648_ELY_ALT_X2.CHOP'
IF (INITIALS.EQ.'DSC').AND.(DAY.EQ.3))
FILENAME(1:32)='DSC_09NOV88_0651_ELY_ALT_X2.CHOP'
IF (INITIALS.EQ.'DSC').AND.(DAY.EQ.2))
FILENAME(1:32)='DSC_14NOV88_0655_ELY_ALT_X2.CHOP'
IF (INITIALS.EQ.'DSC').AND.(DAY.EQ.1))
FILENAME(1:32)='DSC_23NOV88_0704_ELY_ALT_X2.CHOP'
IF (INITIALS.EQ.'DSC').AND.(DAY.EQ.0))
FILENAME(1:32)='DSC_30OCT88_1014_ELY_ALT_X2.CHOP'
GO TO 402
IF (INITIALS.EQ.'DSC').AND.(DAY.EQ.4))
FILENAME(1:32)='DSC_01NOV88_0648_ELY_ALT_X2.CHOP'
IF (INITIALS.EQ.'DSC').AND.(DAY.EQ.3))
FILENAME(1:32)='DSC_09NOV88_0651_ELY_ALT_X2.CHOP'
IF (INITIALS.EQ.'DSC').AND.(DAY.EQ.2))
FILENAME(1:32)='DSC_14NOV88_0655_ELY_ALT_X2.CHOP'
IF (INITIALS.EQ.'DSC').AND.(DAY.EQ.1))
FILENAME(1:32)='DSC_23NOV88_0704_ELY_ALT_X2.CHOP'
IF (INITIALS.EQ.'DSC').AND.(DAY.EQ.0))
FILENAME(1:32)='DSC_30OCT88_1014_ELY_ALT_X2.CHOP'
GO TO 402
IF (INITIALS.EQ. 'RRC').AND.(DAY.EQ.2)
FILENAME(1:32)='RRC_17NOV88_0733_ELY_ALT_X2.CHOP'
IF (INITIALS.EQ. 'RRC').AND.(DAY.EQ.3)
FILENAME(1:32)='RRC_18NOV88_0756_ELY_ALT_X2.CHOP'
IF (INITIALS.EQ. 'RRC').AND.(DAY.EQ.4)
FILENAME(1:32)='RRC_19NOV88_0813_ELY_ALT_X2.CHOP'
 ELSE
 IF (INITIALS.EQ. 'DBH').AND.(DAY.EQ.2)
FILENAME(1:32)='DBH_17NOV88_0755_ELY_ALT_X2.CHOP'
 IF (INITIALS.EQ. 'DBH').AND.(DAY.EQ.3)
FILENAME(1:32)='DBH_18NOV88_0758_ELY_ALT_X2.CHOP'
 IF (INITIALS.EQ. 'DBH').AND.(DAY.EQ.4)
FILENAME(1:32)='DBH_19NOV88_0807_ELY_ALT_X2.CHOP'
 IF (INITIALS.EQ. 'DBH').AND.(DAY.EQ.5)
FILENAME(1:32)='DBH_20NOV88_0846_ELY_ALT_X2.CHOP'
 ELSE
 IF (INITIALS.EQ. 'JRH').AND.(DAY.EQ.2)
FILENAME(1:32)='JRH_02DEC88_0817_ELY_ALT_X2.CHOP'
 IF (INITIALS.EQ. 'JRH').AND.(DAY.EQ.3)
FILENAME(1:32)='JRH_05DEC88_0818_ELY_ALT_X2.CHOP'
 IF (INITIALS.EQ. 'JRH').AND.(DAY.EQ.4)
FILENAME(1:32)='JRH_06DEC88_0815_ELY_ALT_X2.CHOP'
 IF (INITIALS.EQ. 'JRH').AND.(DAY.EQ.5)
FILENAME(1:32)='JRH_07DEC88_0807_ELY_ALT_X2.CHOP'
 ELSE
 IF (INITIALS.EQ. 'MDW').AND.(DAY.EQ.2)
FILENAME(1:32)='MDW_10AUG89_0605_ELY_ALT_X2.CHOP'
 IF (INITIALS.EQ. 'MDW').AND.(DAY.EQ.3)
FILENAME(1:32)='MDW_11AUG89_0611_ELY_ALT_X2.CHOP'
 IF (INITIALS.EQ. 'MDW').AND.(DAY.EQ.4)
FILENAME(1:32)='MDW_12AUG89_0613_ELY_ALT_X2.CHOP'
 IF (INITIALS.EQ. 'MDW').AND.(DAY.EQ.5)
FILENAME(1:32)='MDW_13AUG89_0609_ELY_ALT_X2.CHOP'
 ELSE
 IF (INITIALS.EQ. 'TRB').AND.(DAY.EQ.2)
FILENAME(1:32)='TRB_10AUG89_0651_ELY_ALT_X2.CHOP'
 IF (INITIALS.EQ. 'TRB').AND.(DAY.EQ.3)
FILENAME(1:32)='TRB_11AUG89_0651_ELY_ALT_X2.CHOP'
 IF (INITIALS.EQ. 'TRB').AND.(DAY.EQ.4)
FILENAME(1:32)='TRB_12AUG89_0605_ELY_ALT_X2.CHOP'
 IF (INITIALS.EQ. 'TRB').AND.(DAY.EQ.5)
FILENAME(1:32)='TRB_13AUG89_0615_ELY_ALT_X2.CHOP'
 ELSE
 IF (INITIALS.EQ. 'MDW').AND.(DAY.EQ.2)
FILENAME(1:32)='MDW_14AUG89_0614_ELY_ALT_X2.CHOP'
 IF (INITIALS.EQ. 'MDW').AND.(DAY.EQ.3)
FILENAME(1:32)='MDW_15AUG89_0612_ELY_ALT_X2.CHOP'
 IF (INITIALS.EQ. 'MDW').AND.(DAY.EQ.4)
FILENAME(1:32)='MDW_16AUG89_0612_ELY_ALT_X2.CHOP'
 IF (INITIALS.EQ. 'MDW').AND.(DAY.EQ.5)
FILENAME(1:32)='MDW_17AUG89_0616_ELY_ALT_X2.CHOP'
 ELSE
 IF (INITIALS.EQ. 'TRB').AND.(DAY.EQ.2)
FILENAME(1:32)='TRB_17AUG89_0651_ELY_ALT_X2.CHOP'
 IF (INITIALS.EQ. 'TRB').AND.(DAY.EQ.3)
FILENAME(1:32)='TRB_18AUG89_0651_ELY_ALT_X2.CHOP'
 IF (INITIALS.EQ. 'TRB').AND.(DAY.EQ.4)
FILENAME(1:32)='TRB_19AUG89_0605_ELY_ALT_X2.CHOP'
 IF (INITIALS.EQ. 'TRB').AND.(DAY.EQ.5)
IF (INITIALS.EQ.'TRB').AND.(DAY.EQ.2)
  * FILENAME(1:32)='TRB 11AUG89 0650 ELY ALT X2.CHOP'
  IF (INITIALS.EQ.'TRB').AND.(DAY.EQ.3))
  * FILENAME(1:32)='TRB 14AUG89 0705 ELY ALT X2.CHOP'
  IF (INITIALS.EQ.'TRB').AND.(DAY.EQ.4)
  * FILENAME(1:32)='TRB 15AUG89 0642 ELY ALT X2.CHOP'
  IF (INITIALS.EQ.'TRB').AND.(DAY.EQ.5))
  FILENAME(1:32)=TRB 18AUG89 0647 ELY ALT X2.CHOP'
  IF (INITIALS.EQ.'TRB').AND.(DAY.EQ.6)
  * FILENAME(1:32)=TRB 21AUG89 0649 ELY ALT X2.CHOP'
  IF (INITIALS.EQ.'TRB').AND.(DAY.EQ.7)
  * FILENAME(1:32)=TRB 22AUG89 0656 ELY ALT X2.CHOP'
  IF (INITIALS.EQ.'TRB').AND.(DAY.EQ.8)
  * FILENAME(1:32)=TRB 24AUG89 0659 ELY ALT X2.CHOP'
  IF (INITIALS.EQ.'TRB').AND.(DAY.EQ.9)
  * FILENAME(1:32)=TRB 25AUG89 0651 ELY ALT X2.CHOP'
  IF (INITIALS.EQ.'TRB').AND.(DAY.EQ.10)

GO TO 402

IF (INITIALS.EQ.'MWK').AND.(DAY.EQ.0)
  * FILENAME(1:32)=MWK 29AUG89 0628 ELY ALT X2.CHOP'
  IF (INITIALS.EQ.'MWK').AND.(DAY.EQ.1)
  * FILENAME(1:32)=MWK 30AUG89 0630 ELY ALT X2.CHOP'
  IF (INITIALS.EQ.'MWK').AND.(DAY.EQ.2)
  * FILENAME(1:32)=MWK 31AUG89 0640 ELY ALT X2.CHOP'
  IF (INITIALS.EQ.'MWK').AND.(DAY.EQ.3)
  * FILENAME(1:32)=MWK 05SEP89 0631 ELY ALT X2.CHOP'
  IF (INITIALS.EQ.'MWK').AND.(DAY.EQ.4)
  * FILENAME(1:32)=MWK 06SEP89 0646 ELY ALT X2.CHOP'
  IF (INITIALS.EQ.'MWK').AND.(DAY.EQ.5)
  * FILENAME(1:32)=MWK 11SEP89 0649 ELY ALT X2.CHOP'
  IF (INITIALS.EQ.'MWK').AND.(DAY.EQ.6)
  * FILENAME(1:32)=MWK 15SEP89 0659 ELY ALT X2.CHOP'
  IF (INITIALS.EQ.'MWK').AND.(DAY.EQ.7)
  * FILENAME(1:32)=MWK 15SEP89 0659 ELY ALT X2.CHOP'
  IF (INITIALS.EQ.'MWK').AND.(DAY.EQ.8)
  * FILENAME(1:32)=MWK 15SEP89 0659 ELY ALT X2.CHOP'
  IF (INITIALS.EQ.'MWK').AND.(DAY.EQ.9)

GO TO 402

IF (INITIALS.EQ.'BLP').AND.(DAY.EQ.0)
  * FILENAME(1:32)=BLP 29AUG89 0833 ELY ALT X2.CHOP'
  IF (INITIALS.EQ.'BLP').AND.(DAY.EQ.1)
  * FILENAME(1:32)=BLP 30AUG89 0658 ELY ALT X2.CHOP'
  IF (INITIALS.EQ.'BLP').AND.(DAY.EQ.2)
  * FILENAME(1:32)=BLP 31AUG89 0659 ELY ALT X2.CHOP'
  IF (INITIALS.EQ.'BLP').AND.(DAY.EQ.3)
  * FILENAME(1:32)=BLP 06SEP89 0725 ELY ALT X2.CHOP'
  IF (INITIALS.EQ.'BLP').AND.(DAY.EQ.4)

GO TO 402

IF (INITIALS.EQ.'PEF').AND.(DAY.EQ.0)
  * FILENAME(1:32)=PEF 29AUG89 0657 ELY ALT X2.CHOP'
  IF (INITIALS.EQ.'PEF').AND.(DAY.EQ.1)
  * FILENAME(1:32)=PEF 30AUG89 0717 ELY ALT X2.CHOP'
  IF (INITIALS.EQ.'PEF').AND.(DAY.EQ.2)
  * FILENAME(1:32)=PEF 31AUG89 0716 ELY ALT X2.CHOP'
  IF (INITIALS.EQ.'PEF').AND.(DAY.EQ.3)
  * FILENAME(1:32)=PEF 05SEP89 0724 ELY ALT X2.CHOP'
  IF (INITIALS.EQ.'PEF').AND.(DAY.EQ.4)
  * FILENAME(1:32)=PEF 06SEP89 0826 ELY ALT X2.CHOP'
  IF (INITIALS.EQ.'PEF').AND.(DAY.EQ.5)
\begin{verbatim}
  IF (INITIALS.EQ.	'MWF').AND7(DAY.EQ.0)
  FILENAME(l:32)='MWF 29AUG89 0743 ELY ALT X2.CHOP'
  IF (INITIALS.EQ.	'MWF').AND7(DAY.EQ.1)
  FILENAME(l:32)='MWF 30AUG89 0804 ELY ALT X2.CHOP'
  IF (INITIALS.EQ.	'MWF').AND7(DAY.EQ.2)
  FILENAME(l:32)='MWF 31AUG89 0737 ELY ALT X2.CHOP'
  IF (INITIALS.EQ.	'MWF').AND7(DAY.EQ.3)
  FILENAME(l:32)='MWF 05SEP89 0741 ELY ALT X2.CHOP'
  IF (INITIALS.EQ.	'MWF').AND7(DAY.EQ.4)
  FILENAME(l:32)='MWF 06SEP89 0706 ELY ALT X2.CHOP'
  IF (INITIALS.EQ.	'MWF').AND7(DAY.EQ.5)
  FILENAME(l:32)='MWF 07SEP89 0747 ELY ALT X2.CHOP'
  IF (INITIALS.EQ.	'MWF').AND7(DAY.EQ.6)
  FILENAME(l:32)='MWF 11SEP89 0744 ELY ALT X2.CHOP'
  IF (INITIALS.EQ.	'MWF').AND7(DAY.EQ.7)
  FILENAME(l:32)='MWF 12SEP89 0620 ELY ALT X2.CHOP'
  IF (INITIALS.EQ.	'MWF').AND7(DAY.EQ.8)
  FILENAME(l:32)='MWF 13SEP89 0752 ELY ALT X2.CHOP'
  IF (INITIALS.EQ.	'MWF').AND7(DAY.EQ.9)
  FILENAME(l:32)='MWF 14SEP89 0753 ELY ALT X2.CHOP'
  IF (INITIALS.EQ.	'MWF').AND7(DAY.EQ.10)
  FILENAME(l:32)='MWF 15SEP89 0821 ELY ALT X2.CHOP'

  IF (INITIALS.EQ.	'RFF').AND. (DAY.EQ.0)
  FILENAME(l:32)='RFF 29AUG89 0810 ELY ALT X2.CHOP'
  IF (INITIALS.EQ.	'RFF').AND. (DAY.EQ.1)
  FILENAME(l:32)='RFF 30AUG89 0748 ELY ALT X2.CHOP'
  IF (INITIALS.EQ.	'RFF').AND. (DAY.EQ.2)
  FILENAME(l:32)='RFF 31AUG89 0836 ELY ALT X2.CHOP'
  IF (INITIALS.EQ.	'RFF').AND. (DAY.EQ.3)
  FILENAME(l:32)='RFF 05SEP89 0751 ELY ALT X2.CHOP'
  IF (INITIALS.EQ.	'RFF').AND. (DAY.EQ.4)
  FILENAME(l:32)='RFF 06SEP89 0732 ELY ALT X2.CHOP'
  IF (INITIALS.EQ.	'RFF').AND. (DAY.EQ.5)
  FILENAME(l:32)='RFF 11SEP89 0700 ELY ALT X2.CHOP'
  IF (INITIALS.EQ.	'RFF').AND. (DAY.EQ.6)
  FILENAME(l:32)='RFF 12SEP89 0757 ELY ALT X2.CHOP'
  IF (INITIALS.EQ.	'RFF').AND. (DAY.EQ.7)
  FILENAME(l:32)='RFF 13SEP89 0736 ELY ALT X2.CHOP'
\end{verbatim}
IF (INITIALS.EQ.'RFF').AND.(DAY.EQ.15))
  * FILENAME(1:32)=RFF_15SEP89_0830_ELY_ALT_X2.CHOP'
  IF (INITIALS.EQ.'RFF').AND.(DAY.EQ.16))
  FILENAME(1:32)=RFF_15SEP89_0755_ELY_ALT_X2.CHOP'
ENDIF
  
INQUIRE(FILE=FILENAME(1:32),EXIST=ONDISK)
IF(.NOT.ONDISK) THEN
  WRITE(6,'(I1H,A)') FILENAME//' IS NOT ON DISK.'
  GO TO 402
ENDIF
  
GOTO 35
  
34 IF (FILETYPE.NE.'L') GO TO 1001
IF (PHASE.EQ.1) THEN
  
IF (INITIALS.EQ.'MLR').AND.(DAY.EQ.0))
  * FILENAME(1:32)=MLR_14OCT88_0749_LAT ALT_X1.CHOP'
  FILENAME(1:32)=MLR_17OCT88_0743_LAT ALT_X1.CHOP'
  IF (INITIALS.EQ.'MLR').AND.(DAY.EQ.1))
  * FILENAME(1:32)=MLR_18OCT88_0759_LAT ALT_X1.CHOP'
  FILENAME(1:32)=MLR_20OCT88_0751_LAT ALT_X1.CHOP'
  IF (INITIALS.EQ.'MLR').AND.(DAY.EQ.2))
  * FILENAME(1:32)=MLR_26OCT88_0756_LAT ALT_X1.CHOP'
  
IF (INITIALS.EQ.'SJD').AND.(DAY.EQ.0))
  * FILENAME(1:32)=SJD_14OCT88_0819_LAT ALT_X1.CHOP'
  FILENAME(1:32)=SJD_17OCT88_0805_LAT ALT_X1.CHOP'
  IF (INITIALS.EQ.'SJD').AND.(DAY.EQ.1))
  * FILENAME(1:32)=SJD_18OCT88_0823_LAT ALT_X1.CHOP'
  FILENAME(1:32)=SJD_20OCT88_0819_LAT ALT_X1.CHOP'
  IF (INITIALS.EQ.'SJD').AND.(DAY.EQ.2))
  * FILENAME(1:32)=SJD_21OCT88_0821_LAT ALT_X1.CHOP'
  FILENAME(1:32)=SJD_24OCT88_0734_LAT ALT_X1.CHOP'
  IF (INITIALS.EQ.'SJD').AND.(DAY.EQ.3))
  * FILENAME(1:32)=SJD_25OCT88_0738_LAT ALT_X1.CHOP'
  FILENAME(1:32)=SJD_26OCT88_0731_LAT ALT_X1.CHOP'
  
IF (INITIALS.EQ.'TRB').AND.(DAY.EQ.0))
  * FILENAME(1:32)=TRB_20OCT88_0712_LAT ALT_X1.CHOP'
  FILENAME(1:32)=TRB_24OCT88_0710_LAT ALT_X1.CHOP'
  IF (INITIALS.EQ.'TRB').AND.(DAY.EQ.1))
  * FILENAME(1:32)=TRB_25OCT88_0707_LAT ALT_X1.CHOP'
  FILENAME(1:32)=TRB_28OCT88_0749_LAT ALT_X1.CHOP'
  IF (INITIALS.EQ.'TRB').AND.(DAY.EQ.2))
  * FILENAME(1:32)=TRB_27OCT88_0713_LAT ALT_X1.CHOP'
  FILENAME(1:32)=TRB_30OCT88_0719_LAT ALT_X1.CHOP'
  IF (INITIALS.EQ.'TRB').AND.(DAY.EQ.3))
  * FILENAME(1:32)=TRB_07NOV88_0719_LAT ALT_X1.CHOP'
  
IF (INITIALS.EQ.'SKW').AND.(DAY.EQ.0))
  * FILENAME(1:32)=SKW_21OCT88_0721_LAT ALT_X1.CHOP'
  FILENAME(1:32)=SKW_24OCT88_0734_LAT ALT_X1.CHOP'
  IF (INITIALS.EQ.'SKW').AND.(DAY.EQ.1))
  * FILENAME(1:32)=SKW_25OCT88_0738_LAT ALT_X1.CHOP'
  FILENAME(1:32)=SKW_28OCT88_0749_LAT ALT_X1.CHOP'
  IF (INITIALS.EQ.'SKW').AND.(DAY.EQ.2))
  * FILENAME(1:32)=SKW_26OCT88_0731_LAT ALT_X1.CHOP'
```
IF (INITIALS.EQ. 'SKW') .AND. (DAY.EQ.4)
  FILENAME(1:32) = 'SKW_27Oct88_0736_LAT_ALT_X1.CHOP'
IF (INITIALS.EQ. 'SKW') .AND. (DAY.EQ.5)
  FILENAME(1:32) = 'SKW_28Oct88_0812_LAT_ALT_X1.CHOP'
IF (INITIALS.EQ. 'SKW') .AND. (DAY.EQ.10)
  FILENAME(1:32) = 'SKW_02Nov88_0736_LAT_ALT_X1.CHOP'
IF (INITIALS.EQ. 'SKW') .AND. (DAY.EQ.15)
  FILENAME(1:32) = 'SKW_07Nov88_0743_LAT_ALT_X1.CHOP'

IF (INITIALS.EQ. 'S~W') .AND. (DAY.EQ.4)
  FILENAME(1:32) = 'SKW_27Oct88_0736_LAT_ALT_X1.CHOP'
IF (INITIALS.EQ. 'S~W') .AND. (DAY.EQ.10)
  FILENAME(1:32) = 'SKW_02Nov88_0736_LAT_ALT_X1.CHOP'
IF (INITIALS.EQ. 'S~W') .AND. (DAY.EQ.15)
  FILENAME(1:32) = 'SKW_07Nov88_0743_LAT_ALT_X1.CHOP'

IF (INITIALS.EQ. 'DSC') .AND. (DAY.EQ.0)
  FILENAME(1:32) = 'DSC_30Oct88_1012_LAT_ALT_X1.CHOP'
IF (INITIALS.EQ. 'DSC') .AND. (DAY.EQ.1)
  FILENAME(1:32) = 'DSC_01Nov88_0647_LAT_ALT_X1.CHOP'
IF (INITIALS.EQ. 'DSC') .AND. (DAY.EQ.3)
  FILENAME(1:32) = 'DSC_03Nov88_0646_LAT_ALT_X1.CHOP'
IF (INITIALS.EQ. 'DSC') .AND. (DAY.EQ.4)
  FILENAME(1:32) = 'DSC_04Nov88_0647_LAT_ALT_X1.CHOP'
IF (INITIALS.EQ. 'DSC') .AND. (DAY.EQ.5)
  FILENAME(1:32) = 'DSC_05Nov88_0650_LAT_ALT_X1.CHOP'
IF (INITIALS.EQ. 'DSC') .AND. (DAY.EQ.10)
  FILENAME(1:32) = 'DSC_09Nov88_0650_LAT_ALT_X1.CHOP'
IF (INITIALS.EQ. 'DSC') .AND. (DAY.EQ.15)
  FILENAME(1:32) = 'DSC_14Nov88_0651_LAT_ALT_X1.CHOP'

IF (INITIALS.EQ. 'D~C').AND. (DAY.EQ.0)
  FILENAME(1:32) = 'DSC_10Nov88_0654_LAT_ALT_X1.CHOP'
IF (INITIALS.EQ. 'D~C').AND. (DAY.EQ.1)
  FILENAME(1:32) = 'DSC_15Nov88_0700_LAT_ALT_X1.CHOP'
IF (INITIALS.EQ. 'D~C').AND. (DAY.EQ.3)
  FILENAME(1:32) = 'DSC_17Nov88_0701_LAT_ALT_X1.CHOP'
IF (INITIALS.EQ. 'D~C').AND. (DAY.EQ.4)
  FILENAME(1:32) = 'DSC_18Nov88_0703_LAT_ALT_X1.CHOP'
IF (INITIALS.EQ. 'D~C').AND. (DAY.EQ.5)
  FILENAME(1:32) = 'DSC_21Nov88_0703_LAT_ALT_X1.CHOP'
IF (INITIALS.EQ. 'D~C').AND. (DAY.EQ.7)
  FILENAME(1:32) = 'DSC_23Nov88_0703_LAT_ALT_X1.CHOP'
IF (INITIALS.EQ. 'D~C').AND. (DAY.EQ.8)
  FILENAME(1:32) = 'DSC_25Nov88_0705_LAT_ALT_X1.CHOP'
IF (INITIALS.EQ. 'D~C').AND. (DAY.EQ.9)
  FILENAME(1:32) = 'DSC_27Nov88_0705_LAT_ALT_X1.CHOP'

IF (INITIALS.EQ. 'D~G').AND. (DAY.EQ.0)
  FILENAME(1:32) = 'DSC_14Nov88_0806_LAT_ALT_X1.CHOP'
IF (INITIALS.EQ. 'D~G').AND. (DAY.EQ.1)
  FILENAME(1:32) = 'DSC_15Nov88_0836_LAT_ALT_X1.CHOP'
IF (INITIALS.EQ. 'D~G').AND. (DAY.EQ.3)
  FILENAME(1:32) = 'DSC_17Nov88_0821_LAT_ALT_X1.CHOP'
IF (INITIALS.EQ. 'D~G').AND. (DAY.EQ.4)
  FILENAME(1:32) = 'DSC_18Nov88_0821_LAT_ALT_X1.CHOP'
IF (INITIALS.EQ. 'D~G').AND. (DAY.EQ.5)
  FILENAME(1:32) = 'DSC_19Nov88_0830_LAT_ALT_X1.CHOP'
IF (INITIALS.EQ. 'D~G').AND. (DAY.EQ.7)
  FILENAME(1:32) = 'DSC_21Nov88_0829_LAT_ALT_X1.CHOP'
IF (INITIALS.EQ. 'D~G').AND. (DAY.EQ.8)
  FILENAME(1:32) = 'DSC_23Nov88_0819_LAT_ALT_X1.CHOP'
IF (INITIALS.EQ. 'D~G').AND. (DAY.EQ.9)
  FILENAME(1:32) = 'DSC_25Nov88_0819_LAT_ALT_X1.CHOP'

IF (INITIALS.EQ. 'RRC').AND. (DAY.EQ.0)
  FILENAME(1:32) = 'RRC_15Nov88_0748_LAT_ALT_X1.CHOP'
IF (INITIALS.EQ. 'RRC').AND. (DAY.EQ.1)
  FILENAME(1:32) = 'RRC_17Nov88_0722_LAT_ALT_X1.CHOP'
IF (INITIALS.EQ. 'RRC').AND. (DAY.EQ.3)
  FILENAME(1:32) = 'RRC_18Nov88_0755_LAT_ALT_X1.CHOP'
IF (INITIALS.EQ. 'RRC').AND. (DAY.EQ.4)
  FILENAME(1:32) = 'RRC_19Nov88_0812_LAT_ALT_X1.CHOP'
IF (INITIALS.EQ. 'RRC').AND. (DAY.EQ.5)
  FILENAME(1:32) = 'RRC_20Nov88_0747_LAT_ALT_X1.CHOP'
IF (INITIALS.EQ. 'RRC').AND. (DAY.EQ.7)
  FILENAME(1:32) = 'RRC_22Nov88_0805_LAT_ALT_X1.CHOP'
IF (INITIALS.EQ. 'RRC').AND. (DAY.EQ.8)
  FILENAME(1:32) = 'RRC_24Nov88_0742_LAT_ALT_X1.CHOP'
IF (INITIALS.EQ. 'RRC').AND. (DAY.EQ.9)
  FILENAME(1:32) = 'RRC_26Nov88_0747_LAT_ALT_X1.CHOP'
```
IF "INITIALS.EQ.'DBH').AND.(DAY.EQ.0"
FILENAME(1:32)='DBH 15NOV88 0811 LAT ALT X1.CHOP'
IF "INITIALS.EQ.'DBH').AND.(DAY.EQ.1"
FILENAME(1:32)='DBH 17NOV88 0754 LAT ALT X1.CHOP'
IF "INITIALS.EQ.'DBH').AND.(DAY.EQ.2"
FILENAME(1:32)='DBH 18NOV88 0737 LAT ALT X1.CHOP'
FILENAME(1:32)='DBH 19NOV88 0754 LAT ALT X1.CHOP'
FILENAME(1:32)='DBH 20NOV88 0806 LAT ALT X1.CHOP'
FILENAME(1:32)='DBH 26NOV88 0845 LAT ALT X1.CHOP'
FILENAME(1:32)='DBH_30NOV88_0806_LAT_ALT_X1.CHOP'
ELSE
IF "INITIALS.EQ.'JRH').AND.(DAY.EQ.0"
FILENAME(1:32)='JRH 02DEC88 0815 LAT ALT X1.CHOP'
FILENAME(1:32)='JRH 05DEC88 0817 LAT ALT X1.CHOP'
FILENAME(1:32)='JRH 06DEC88 0814 LAT ALT X1.CHOP'
FILENAME(1:32)='JRH 08DEC88 0807 LAT ALT X1.CHOP'
FILENAME(1:32)='JRH 09DEC88 0753 LAT ALT X1.CHOP'
FILENAME(1:32)='JRH 14DEC88 0802 LAT ALT X1.CHOP'
FILENAME(1:32)='JRH 16DEC88 0752 LAT ALT X1.CHOP'
FILENAME(1:32)='JRH 17DEC88 0807 LAT ALT X1.CHOP'
FILENAME(1:32)='JRH_19DEC88_0812_LAT_ALT_X1.CHOP'
ELSE
IF "INITIALS.EQ.'MDW').AND.(DAY.EQ.0"
FILENAME(1:32)='MDW 10AUG89 0604 LAT ALT X1.CHOP'
FILENAME(1:32)='MDW 10AUG89 0623 LAT ALT X1.CHOP'
FILENAME(1:32)='MDW 11AUG89 0610 LAT ALT X1.CHOP'
FILENAME(1:32)='MDW 14AUG89 0613 LAT ALT X1.CHOP'
FILENAME(1:32)='MDW 15AUG89 0611 LAT ALT X1.CHOP'
FILENAME(1:32)='MDW 18AUG89 0613 LAT ALT X1.CHOP'
FILENAME(1:32)='MDW 21AUG89 0612 LAT ALT X1.CHOP'
FILENAME(1:32)='MDW 22AUG89 0614 LAT ALT X1.CHOP'
FILENAME(1:32)='MDW 23AUG89 0614 LAT ALT X1.CHOP'
FILENAME(1:32)='MDW 24AUG89 0616 LAT ALT X1.CHOP'
FILENAME(1:32)='MDW_25AUG89_0614_LAT_ALT_X1.CHOP'
ELSE
IF "INITIALS.EQ.'TRB').AND.(DAY.EQ.0"
FILENAME(1:32)='TRB 10AUG89 0649 LAT ALT X1.CHOP'
FILENAME(1:32)='TRB 10AUG89 0703 LAT ALT X1.CHOP'
FILENAME(1:32)='TRB 11AUG89 0642 LAT ALT X1.CHOP'
FILENAME(1:32)='TRB 14AUG89 0704 LAT ALT X1.CHOP'
FILENAME(1:32)='TRB 15AUG89 0641 LAT ALT X1.CHOP'
FILENAME(1:32)='TRB 18AUG89 0646 LAT ALT X1.CHOP'
FILENAME(1:32)='TRB 21AUG89 0648 LAT ALT X1.CHOP'
FILENAME(1:32)='TRB_22AUG89_0654_LAT_ALT_X1.CHOP'
IF ((INITIALS.EQ.'TRB').AND.(DAY.EQ.14))
  FILENAME(1:32)='TRB 23AUG89 0641 LAT ALT X1.CHOP'
IF ((INITIALS.EQ.'TRB').AND.(DAY.EQ.15))
  FILENAME(1:32)='TRB 24AUG89 0658 LAT ALT X1.CHOP'
IF ((INITIALS.EQ.'TRB').AND.(DAY.EQ.16))
  FILENAME(1:32)='TRB 25AUG89 0650 LAT ALT X1.CHOP'
IF ((INITIALS.EQ.'MWK').AND.(DAY.EQ.0))
  FILENAME(1:32)='MWK 29AUG89 0627 LAT ALT X1.CHOP'
IF ((INITIALS.EQ.'MWK').AND.(DAY.EQ.1))
  FILENAME(1:32)='MWK 30AUG89 0637 LAT ALT X1.CHOP'
IF ((INITIALS.EQ.'MWK').AND.(DAY.EQ.2))
  FILENAME(1:32)='MWK 31AUG89 0639 LAT ALT X1.CHOP'
IF ((INITIALS.EQ.'MWK').AND.(DAY.EQ.3))
  FILENAME(1:32)='MWK 05SEP89 0630 LAT ALT X1.CHOP'
IF ((INITIALS.EQ.'MWK').AND.(DAY.EQ.4))
  FILENAME(1:32)='MWK 06SEP89 0645 LAT ALT X1.CHOP'
IF ((INITIALS.EQ.'MWK').AND.(DAY.EQ.5))
  FILENAME(1:32)='MWK 07SEP89 0638 LAT ALT X1.CHOP'
IF ((INITIALS.EQ.'MWK').AND.(DAY.EQ.6))
  FILENAME(1:32)='MWK 11SEP89 0648 LAT ALT X1.CHOP'
IF ((INITIALS.EQ.'MWK').AND.(DAY.EQ.7))
  FILENAME(1:32)='MWK 12SEP89 0656 LAT ALT X1.CHOP'
IF ((INITIALS.EQ.'MWK').AND.(DAY.EQ.8))
  FILENAME(1:32)='MWK 13SEP89 0702 LAT ALT X1.CHOP'
IF ((INITIALS.EQ.'MWK').AND.(DAY.EQ.9))
  FILENAME(1:32)='MWK 14SEP89 0704 LAT ALT X1.CHOP'
IF ((INITIALS.EQ.'MWK').AND.(DAY.EQ.10))
  FILENAME(1:32)='MWK 15SEP89 0714 LAT ALT X1.CHOP'
IF ((INITIALS.EQ.'MWK').AND.(DAY.EQ.11))
  FILENAME(1:32)='MWK 16SEP89 0715 LAT ALT X1.CHOP'
IF ((INITIALS.EQ.'MWK').AND.(DAY.EQ.12))
  FILENAME(1:32)='MWK 17SEP89 0727 LAT ALT X1.CHOP'
IF ((INITIALS.EQ.'MWK').AND.(DAY.EQ.13))
  FILENAME(1:32)='MWK 18SEP89 0729 LAT ALT X1.CHOP'
IF ((INITIALS.EQ.'HWK').AND.(DAY.EQ.14))
  FILENAME(1:32)='HWK 14SEP89 0643 LAT ALT X1.CHOP'
IF ((INITIALS.EQ.'HWK').AND.(DAY.EQ.15))
  FILENAME(1:32)='HWK 15SEP89 0658 LAT ALT X1.CHOP'
IF ((INITIALS.EQ.'BLP').AND.(DAY.EQ.0))
  FILENAME(1:32)='BLP 29AUG89 0832 LAT ALT X1.CHOP'
IF ((INITIALS.EQ.'BLP').AND.(DAY.EQ.1))
  FILENAME(1:32)='BLP 30AUG89 0657 LAT ALT X1.CHOP'
IF ((INITIALS.EQ.'BLP').AND.(DAY.EQ.2))
  FILENAME(1:32)='BLP 06SEP89 0724 LAT ALT X1.CHOP'
IF ((INITIALS.EQ.'BLP').AND.(DAY.EQ.3))
  FILENAME(1:32)='BLP 07SEP89 0716 LAT ALT X1.CHOP'
IF ((INITIALS.EQ.'BLP').AND.(DAY.EQ.4))
  FILENAME(1:32)='BLP 08SEP89 0718 LAT ALT X1.CHOP'
IF ((INITIALS.EQ.'BLP').AND.(DAY.EQ.5))
  FILENAME(1:32)='BLP 09SEP89 0720 LAT ALT X1.CHOP'
IF ((INITIALS.EQ.'BLP').AND.(DAY.EQ.6))
  FILENAME(1:32)='BLP 10SEP89 0722 LAT ALT X1.CHOP'
IF ((INITIALS.EQ.'BLP').AND.(DAY.EQ.7))
  FILENAME(1:32)='BLP_15SEP89_0732_LAT_ALT_X1.CHOP'
GO TO 402
IF ((INITIALS.EQ.'PEF').AND.(DAY.EQ.0))
  FILENAME(1:32)='PEF 29AUG89 0656 LAT ALT X1.CHOP'
IF ((INITIALS.EQ.'PEF').AND.(DAY.EQ.1))
  FILENAME(1:32)='PEF 30AUG89 0716 LAT ALT X1.CHOP'
IF ((INITIALS.EQ.'PEF').AND.(DAY.EQ.2))
  FILENAME(1:32)='PEF 31AUG89 0715 LAT ALT X1.CHOP'
IF ((INITIALS.EQ.'PEF').AND.(DAY.EQ.3))
  FILENAME(1:32)='PEF 06SEP89 0723 LAT ALT X1.CHOP'
IF ((INITIALS.EQ.'PEF').AND.(DAY.EQ.4))
  FILENAME(1:32)='PEF 07SEP89 0725 LAT ALT X1.CHOP'
IF ((INITIALS.EQ.'PEF').AND.(DAY.EQ.5))
  FILENAME(1:32)='PEF 08SEP89 0715 LAT ALT X1.CHOP'
IF ((INITIALS.EQ.'PEF').AND.(DAY.EQ.6))
  FILENAME(1:32)='PEF 09SEP89 0727 LAT ALT X1.CHOP'
IF ((INITIALS.EQ.'PEF').AND.(DAY.EQ.7))
  FILENAME(1:32)='PEF_15SEP89_0732_LAT_ALT_X1.CHOP'
GO TO 402
IF ((INITIALS.EQ.'PEF').AND.(DAY.EQ.14))
  FILENAME(1:32)='PEF 13SEP89 0717 LAT ALT X1.CHOP'
IF ((INITIALS.EQ.'PEF').AND.(DAY.EQ.15))
  FILENAME(1:32)='PEF 14SEP89 0724 LAT ALT X1.CHOP'
IF ((INITIALS.EQ.'PEF').AND.(DAY.EQ.16))
  FILENAME(1:32)='PEF 15SEP89 0732 LAT ALT X1.CHOP'
C
IF (INITIALS.EQ.'MWF').AND.(DAY.EQ.0)
FILENAME(1:32)='MWF 29AUG89 0742 LAT ALT X1.CHOP'
IF (INITIALS.EQ.'MWF').AND.(DAY.EQ.1)
FILENAME(1:32)='MWF 30AUG89 0803 LAT ALT X1.CHOP'
IF (INITIALS.EQ.'MWF').AND.(DAY.EQ.2)
FILENAME(1:32)='MWF 05SEP89 0739 LAT ALT X1.CHOP'
IF (INITIALS.EQ.'MWF').AND.(DAY.EQ.3)
FILENAME(1:32)='MWF 06SEP89 0744 LAT ALT X1.CHOP'
IF (INITIALS.EQ.'MWF').AND.(DAY.EQ.4)
FILENAME(1:32)='MWF 08SEP89 0740 LAT ALT X1.CHOP'
IF (INITIALS.EQ.'MWF').AND.(DAY.EQ.5)
FILENAME(1:32)='MWF 09SEP89 0736 LAT ALT X1.CHOP'
IF (INITIALS.EQ.'MWF').AND.(DAY.EQ.6)
FILENAME(1:32)='MWF 11SEP89 0743 LAT ALT X1.CHOP'
IF (INITIALS.EQ.'MWF').AND.(DAY.EQ.7)
FILENAME(1:32)='MWF 12SEP89 0737 LAT ALT X1.CHOP'
C
IF (INITIALS.EQ.'DDS').AND.(DAY.EQ.0)
FILENAME(1:32)='DDS 29AUG89 0720 LAT ALT X1.CHOP'
IF (INITIALS.EQ.'DDS').AND.(DAY.EQ.1)
FILENAME(1:32)='DDS 30AUG89 0731 LAT ALT X1.CHOP'
IF (INITIALS.EQ.'DDS').AND.(DAY.EQ.2)
FILENAME(1:32)='DDS 05SEP89 0806 LAT ALT X1.CHOP'
IF (INITIALS.EQ.'DDS').AND.(DAY.EQ.3)
FILENAME(1:32)='DDS 06SEP89 0809 LAT ALT X1.CHOP'
IF (INITIALS.EQ.'DDS').AND.(DAY.EQ.4)
FILENAME(1:32)='DDS 08SEP89 0804 LAT ALT X1.CHOP'
IF (INITIALS.EQ.'DDS').AND.(DAY.EQ.5)
FILENAME(1:32)='DDS 09SEP89 0817 LAT ALT X1.CHOP'
IF (INITIALS.EQ.'DDS').AND.(DAY.EQ.6)
FILENAME(1:32)='DDS 11SEP89 0817 LAT ALT X1.CHOP'
IF (INITIALS.EQ.'DDS').AND.(DAY.EQ.7)
FILENAME(1:32)='DDS 13SEP89 0806 LAT ALT X1.CHOP'
C
IF (INITIALS.EQ.'RFF').AND.(DAY.EQ.0)
FILENAME(1:32)='RFF 29AUG89 0809 LAT ALT X1.CHOP'
IF (INITIALS.EQ.'RFF').AND.(DAY.EQ.1)
FILENAME(1:32)='RFF 30AUG89 0747 LAT ALT X1.CHOP'
IF (INITIALS.EQ.'RFF').AND.(DAY.EQ.2)
FILENAME(1:32)='RFF 05SEP89 0826 LAT ALT X1.CHOP'
IF (INITIALS.EQ.'RFF').AND.(DAY.EQ.3)
FILENAME(1:32)='RFF 06SEP89 0750 LAT ALT X1.CHOP'
IF (INITIALS.EQ.'RFF').AND.(DAY.EQ.4)
FILENAME(1:32)='RFF 08SEP89 0731 LAT ALT X1.CHOP'
IF (INITIALS.EQ.'RFF').AND.(DAY.EQ.5)
FILENAME(1:32)='RFF 11SEP89 0759 LAT ALT X1.CHOP'
IF (INITIALS.EQ.'RFF').AND.(DAY.EQ.6)
FILENAME(1:32)='RFF 12SEP89 0756 LAT ALT X1.CHOP'
IF (INITIALS.EQ.'RFF').AND.(DAY.EQ.7)
FILENAME(1:32)='RFF 13SEP89 0735 LAT ALT X1.CHOP'
C
ENDIF
C
INQUIRE(FILE=FILENAME(1:32),EXIST=ONDISK)
IF (.NOT. ONDISK) THEN
WRITE(6,'(1H ,A)') FILENAME//' IS NOT ON DISK.'
GO TO 402
ENDIF
CTYPE(1:1)=FILENAME(22:22)
FILENAMEO(1:32)=FILENAME(1:27)//'.CHOP'
OPEN (UNIT=2, FILE=FILENAMEO(1:32), STATUS='UNKNOWN',
* FORM='UNFORMATTED')
IF (FILETYPE.EQ.'L') GO TO 10
IBFSIZ=4096
ITICKS=2000
IBLOCKU=125
IBLOCKINC=1
NPTS=256
JUP=16
JINCR=1
INDEX1=256
GO TO 11
10 IBFSIZ=1024
ITICKS=100
IBLOCKU=100
IBLOCKINC=2
NPTS=1024
JUP=1
JINCR=1
INDEX1=0
11 IF (CTYPE.NE.'A') GO TO 14
ITICKS=ITICKS/2
JINCR=2
14 EPOCHS-REAL(ITICKS)
DO 4 I = 1, MAXDAT
  DATA(I) = 0.0
  XARR(I) = REAL(I-1)
  DENOM(I) = 0.0
  IFLAG(I) = 0
  IFLAG2(I) = 2
  IFLAG4(I) = 4
  CONTINUE
CALL MEAN (DATA,IFLAG4,NPTS,AMEAN)
DO 8 IBLOCK = 1,IBLOCKU,IBLOCKINC
  IF ((FILETYPE.EQ.'L'),AND.(COUNT.EQ.1)) THEN
    READ(2) (DUMBUF(K),K=1,IBFSIZ)
  ENDIF
  READ(2) (IDTBUF(K),K=1,IBFSIZ)
  IF ((FILETYPE.EQ.'L'),AND.(COUNT.EQ.0)) THEN
    READ(2) (DUMBUF(K),K=1,IBFSIZ)
  ENDIF
  DO 7 J=1,JUP,JINCR
    IZAK=0
    INDEX0=INDEX1*(J-1)
    IF (CTYPE.NE.'A') GO TO 15
    IF (COUNT.EQ.0) GO TO 15
    INDEX0=INDEX0+INDEX1
  15 DO 6 I = 1,NPTS
    INDEX = I+INDEX0
    POINTER=I
    IFLAG(POINTER) = 0
    IF(IDTBUF(INDEX).LT.ADMAX
      .AND.IDTBUF(INDEX).GT.ADMIN)THEN
      IFLAG(POINTER) = 1
      DATA(POINTER) = QEXT(IDTBUF(INDEX))
    ELSE
      IZAK=1
      ENDIF
  6 CONTINUE
  IF(IZAK.EQ.1) GO TO 7
  CALL MEAN (DATA,IFLAG,NPTS,AMEAN)
  CONTINUE
CALL MEAN (DATA,IFLAG2,NPTS,AMEAN)
CODE ADDED ON 30 MAR 89 TO CENTER AMEAN ABOUT 0
AVERAGE=0.0
DO 323 I=ILOW,IUP
AVERAGE=AVERAGE+AMEAN(I)
323 CONTINUE
AVERAGE=AVERAGE/REALN
DO 324 I=ILOW,IUP
AMAX=AMEAN(I)-AVERAGE
324 CONTINUE

CODE ADDED ON 27 MAY 89 TO MAKE PEAK MAGNITUDE = 1
AMAX=2048.0
DO 355 I=ILOW,IUP
IF (ABS(AMEAN(I)).GT.AMAX) AMAX=ABS(AMEAN(I))
355 CONTINUE
AMAX=AMEAN(I)/AMAX
356 CONTINUE

IF (CAUTO.EQ. 'N') GO TO 560
CALL AUTCOR(AMEAN,AUTO,ILOW,IUP,N)
560 IF (CFREQ.EQ. 'N') GO TO 561
A0=0.35875
A1=0.48829
A2=0.14128
A3=0.01168
V=(2.0*3.14159)/QEXT(N)
DO 112 I=1,N
XARR(I)=I-1
IF (.FILETYPE.EQ. 'G') THEN
   A(I)=DCMPLX(AMEAN(I))
   *(A0-(A1*COS(V*QEXT(I)))
   *(A2*COS(2.0*V*QEXT(I))-(A3*COS(3.0*V*QEXT(I)))))
ELSE
   A(I)=DCMPLX(AMEAN(I)+ILOW-1)
   *(A0-(A1*COS(V*QEXT(I)))
   *(A2*COS(2.0*V*QEXT(I))-(A3*COS(3.0*V*QEXT(I)))))
ENDIF
112 CONTINUE

CALL FFT1(A,M,N)
DO 554 I=1,N
FM(I)=QEXT(ABS(A(I)))
FPow(I)=20.0*QLOG10(FM(I)+2048.0)
IF ((DREAL(A(I)).LT.1E-38).AND.(DREAL(A(I)).GT.-1E-38)) THEN
   FM(I)=0.0
   FPow(I)=0.0
   ENDIF
553 IF (I.EQ.NHI) THEN
   FM(I)=0.0
   FPow(I)=0.0
   ENDIF
554 CONTINUE

CALL NUMINT(F,NUMNUM,PERCENT,EDGE,SCALE,AREA,RMS)
WRITE (1,*) 'DAY, ', SNGL(EDGE)
MAGEDGE=EDGE
IF (PHASE.EQ.1) THEN
   BASEMAGEDGE=EDGE
   BASEMAG(DAY)=EDGE
ENDIF
554 CONTINUE
}

416
* IF ((DAY.EQ.0).OR.(DAY.EQ.1).OR.(DAY.EQ.2).OR.
  (DAY.EQ.5).OR.(DAY.EQ.6)) THEN
  BASEMAG(DAY)=EDGE
ENDIF
* IF ((DAY.EQ.9).OR.(DAY.EQ.12).OR.(DAY.EQ.13).OR.
  (DAY.EQ.14).OR.(DAY.EQ.15).OR.(DAY.EQ.16)) THEN
  DRUGMAG(DAY)=EDGE
ENDIF

DO 577 I=1,N
F(I)=FP(I)
577 CONTINUE
CALL NUMINT(F,HNUMHUM,PERCENT,EDGE,SCALE,AREA,RMS)
WRITE (8,*) DAY,',',SNGL(EDGE)
PHASE=EDGE
IF (PHASE.EQ.1) THEN
  IF (DAY.EQ.0) THEN
    BASEPHASE=EDGE
    BASEPHA(DAY)=EDGE
  ENDIF
  IF ((DAY.EQ.1).OR.(DAY.EQ.2).OR.(DAY.EQ.3).OR.
   (DAY.EQ.4).OR.(DAY.EQ.5).OR.(DAY.EQ.10).OR.
   (DAY.EQ.15)) THEN
    ORUGPHA(DAY)=EDGE
  ENDIF
ENDIF
IF (PHASE.EQ.2) THEN
  IF ((DAY.EQ.0).OR.(DAY.EQ.1).OR.(DAY.EQ.2).OR.
   (DAY.EQ.5).OR.(DAY.EQ.6)) THEN
    BASEPHA(DAY)=EDGE
  ENDIF
  IF ((DAY.EQ.9).OR.(DAY.EQ.12).OR.(DAY.EQ.13).OR.
   (DAY.EQ.14).OR.(DAY.EQ.15).OR.(DAY.EQ.16)) THEN
    DRUGPHA(DAY)=EDGE
  ENDIF
ENDIF

DO 578 I=1,N
F(I)=FPW(I)
578 CONTINUE
CALL NUMINT(F,HNUMHUM,PERCENT,EDGE,SCALE,AREA,RMS)
WRITE (20,*) DAY,',',SNGL(EDGE)
POWEDGE=EDGE
IF (PHASE.EQ.1) THEN
  IF (DAY.EQ.0) THEN
    BASEPOWEDGE=EDGE
    BASEPOW(DAY)=EDGE
  ENDIF
  IF ((DAY.EQ.1).OR.(DAY.EQ.2).OR.(DAY.EQ.3).OR.
   (DAY.EQ.4).OR.(DAY.EQ.5).OR.(DAY.EQ.10).OR.
   (DAY.EQ.15)) THEN
    ORUGPOW(DAY)=EDGE
  ENDIF
ENDIF
IF (PHASE.EQ.2) THEN
  IF ((DAY.EQ.0).OR.(DAY.EQ.1).OR.(DAY.EQ.2).OR.
   (DAY.EQ.5).OR.(DAY.EQ.6)) THEN
    BASEPOW(DAY)=EDGE
  ENDIF
  IF ((DAY.EQ.9).OR.(DAY.EQ.12).OR.(DAY.EQ.13).OR.
   (DAY.EQ.14).OR.(DAY.EQ.15).OR.(DAY.EQ.16)) THEN
    DRUGPOW(DAY)=EDGE
  ENDIF
ENDIF

TEMPDAY=DAY
ENCOD(2,328,CDAY,TEMPDAY)
328 FORMAT(22)
IF (COUNT.EQ.0) CTEMP(1:5)=' SGL ',
IF (COUNT.EQ.1) CTEMP(1:5)="DBL ",
IF (TIMELT.EQ. "N") GO TO 330-
TIMEINC=1
IF (FILETYPE.NE."E") TIMEINC=4
TIMENAME(1:130)=FILENAME(1:14)//'PH'//CPHASE(1:1)///'DAY'//
*CDAY(1:2)//FILENAME(17:20)//CTEMP(1:5)//'TIME.GRL'
IF (FILETYPE.EQ.'G')
  TIMENAME(1:30)=EEGFILE(1:4)//'PH'/CPHASE(1:1)//'_DAY'//' TIME.GRL'
OPEN (UNIT=4, FILE=TIMENAME, FORM='FORMATTED', STATUS='NEW')
WRITE (4,*), 'TI //',TIMENAME(1:26)
WRITE (4,*), 'SU//' IF (FILETYPE.EQ.'G') THEN
  WRITE (4,*), 'HO TIME (mSEC)'//
ELSE
  WRITE (4,*), 'HO TIME (SEC)'//
ENDIF
WRITE (4,*), 'VE ADC AMPLITUDE'
IF (FILETYPE.EQ.'G') THEN
  TIMESCALE=4.0E-3
ENDIF
IF (FILETYPE.EQ.'E') THEN
  TIMESCALE=43.0E-6*1000.0
ENDIF
IF (FILETYPE.EQ.'L') THEN
  TIMESCALE=496.0E-6*1000.0
ENDIF
DO 325 I=ILOW,IUP,TIMEINC
  WRITE (4,*) SNGL(QEXT(I)*TIMESCALE)
325 CONTINUE
WRITE (4,*), 'YL'
DO 326 I=ILOW,IUP,TIMEINC
  WRITE (4,*) SNGL(AMEAN(I)*TIMESCALE)
326 CONTINUE
CLOSE (UNIT=4,STATUS='SAVE')
C
330 IF (MAGPLT.EQ.'N') GO TO 327
  MAGNAME(1:29)=FILENAME(1:4)//'PH'//CPHASE(1:1)//'_DAY'//' TIME.GRL'
  PNAME(1:29)=FILENAME(1:4)//'PH'//CPHASE(1:1)//'_DAY'//' TIME.GRL'
  PNAME(1:29)=FILENAME(1:4)//'PH'//CPHASE(1:1)//'_DAY'//' TIME.GRL'
  PNAME(1:29)=FILENAME(1:4)//'PH'//CPHASE(1:1)//'_DAY'//' TIME.GRL'
  PNAME(1:29)=FILENAME(1:4)//'PH'//CPHASE(1:1)//'_DAY'//' TIME.GRL'
  PNAME(1:29)=FILENAME(1:4)//'PH'//CPHASE(1:1)//'_DAY'//' TIME.GRL'
ENDIF
OPEN (UNIT=7, FILE=MAGNAME, FORM='FORMATTED', STATUS='NEW')
IF (FILETYPE.NE.'G') THEN
  WRITE (7,*), 'TI //',MAGNAME(1:25)
ELSE
  WRITE (7,*), 'TI //',MAGNAME(1:25)
ENDIF
WRITE (7,*), 'SU//' IF (FILETYPE.EQ.'G') THEN
  WRITE (7,*), 'VE FREQUENCY (Hz)'//
WRITE (7,*), 'VE ADC MAGNITUDE'
ELSE
  WRITE (7,*), 'X'//
ENDIF
OPEN (UNIT=27, FILE=PNAME, FORM='FORMATTED', STATUS='NEW')
IF (FILETYPE.NE.'G') THEN
  WRITE (27,*), 'TI //',PNAME(1:25)
ELSE
  WRITE (27,*), 'TI //',PNAME(1:25)
ENDIF
WRITE (27,*), 'SU//' IF (FILETYPE.EQ.'G') THEN
  WRITE (27,*), 'HO FREQUENCY (Hz)'//
WRITE (27,*), 'VE PHASE (DEGREES)'//
WRITE (27,*), 'X'//
ENDIF
OPEN (UNIT=26, FILE=PNAME, FORM='FORMATTED', STATUS='NEW')
IF (FILETYPE.NE.'G') THEN
  WRITE (26,*), 'TI //',PNAME(1:25)
ELSE
  WRITE (26,*), 'TI //',PNAME(1:25)
ENDIF
WRITE (26,*), 'SU//' IF (FILETYPE.EQ.'G') THEN
  WRITE (26,*), 'HO FREQUENCY (Hz)'//
WRITE (26,*), 'VE 20 LOG [Vadc]'//
C
WRITE (26,*) 'X'
NSKIP=1
IF ((FILETYPE.EQ.'G').OR.(FILETYPE.EQ.'L')) NSKIP=4
DO 331 I=1,NHI,NSKIP
WRITE (27,*) SNGL(I*SCALE)
WRITE (26,*) SNGL(I*SCALE)
331 CONTINUE
WRITE (27,*) 'YL'
WRITE (26,*) 'YL'
WRITE (27,*) 'YL'
DO 332 I=1,NHI,NSKIP
WRITE (27,*) SNGL(FM(I))
WRITE (26,*) SNGL(FP(I))
332 CONTINUE
CLOSE (UNIT=7,STATUS='SAVE')
CLOSE (UNIT=27,STATUS='SAVE')
CLOSE (UNIT=26,STATUS='SAVE')
C
327 IF (CAUTO.EQ.'N') GO TO 564
*AUTONAME(1:30)=FILENAME(1:4)//'PH'//CPHASE(1:1)//' DAY'//
*DAY(1:2)//FILENAME(17:20)//CTEMP(1:5)//' AUTO.GRL'
*IF (FILETYPE.EQ.'G')
*AUTONAME(1:30)=EEGFILE(1:4)//'PH'//CPHASE(1:1)//' DAY'//
*DAY(1:2)// EEG AUTO.GRL
OPEN (UNIT=9,*FILE=AUTONAME, FORM='FORMATTED', STATUS='NEW')
WRITE (9,*) 'TI',AUTONAME(1:26)
WRITE (9,*) 'SU'
WRITE (9,*) 'NO DELAY DATA POINT'
WRITE (9,*) 'VE NORMALIZED AMPLITUDE'
WRITE (9,*) 'X'
DO 565 I=1,N
WRITE (9,*) I
565 CONTINUE
CLOSE (UNIT=9,STATUS='SAVE')
564 CLOSE (UNIT=2)
C
IF (PHASE.EQ.2) THEN
* IF ((DAY.EQ.0).OR.(DAY.EQ.1).OR.(DAY.EQ.2).OR.(DAY.EQ.5).OR.(DAY.EQ.6)) THEN
NUBASEAVE=NUBASEAVE+1
NUMEANBASE=NUMEANBASE+1
MEANBASEMAGEDGE=MEANBASEMAGEDGE+MAGEDGE
MEANBASEPHAEDGE=MEANBASEPHAEDGE+(PHAEDGE**2)
MEANBASEPOWEDGE=MEANBASEPOWEDGE+POWEDGE
ELSE
NUDRUGAVE=NUDRUGAVE+1
NUMEANDRUG=NUMEANDRUG+1
MEANDRUGMAGEDGE=MEANDRUGMAGEDGE+MAGEDGE
MEANDRUGPHAEDGE=MEANDRUGPHAEDGE+(PHAEDGE**2)
MEANDRUGPOWEDGE=MEANDRUGPOWEDGE+POWEDGE
ENDIF
ENDIF
DO 476 I=1,NIMUM
* IF ((DAY.EQ.0).OR.(DAY.EQ.1).OR.(DAY.EQ.2).OR.(DAY.EQ.5).OR.(DAY.EQ.6)) THEN
BASEMAGAVER(I)=BASEMAGAVER(I)+FM(I)
BASEPHAAVER(I)=BASEPHAAVER(I)+FP(I)
ENDIF
BASEPOWAVE(I) = BASEPOWAVE(I) + FP(I)
ELSE
DRUGMAGAVER(I) = DRUGMAGAVER(I) + FM(I)
DRUGPHAAVER(I) = DRUGPHAAVER(I) + FP(I)
DRUGPOWAVE(I) = DRUGPOWAVE(I) + FP(I)
ENDIF
CONTINUE

476
ELSE
DRUGMAGAVER(I) = DRUGMAGAVER(I) + FM(I)
DRUGPHAAVER(I) = DRUGPHAAVER(I) + FP(I)
DRUGPOWAVE(I) = DRUGPOWAVE(I) + FP(I)
ENDIF
CONTINUE

486
ENDIF
C
IF (AOF.NE. 'F') GO TO 402
IF ((FILETYPE.EQ. 'E').AND.(COUNT.EQ.0)) GO TO 403
IF (CFREQ.EQ. 'N') GO TO 1001
CLOSE (UNIT=1,STATUS='SAVE')
CLOSE (UNIT=8,STATUS='SAVE')
CLOSE (UNIT=20,STATUS='SAVE')
GO TO 1001
402
CONTINUE
C
IF (AOF.EQ. 'F') GOTO 226
IF (PHASE.EQ. 2) THEN
DO 486 I = 1, NUMNUM
BASEMAGAVER(I) = (BASEMAGAVER(I) / QEXT(NUBASEAVE))
BASEPHAAVER(I) = (BASEPHAAVER(I) / QEXT(NUBASEAVE))
BASEPOWAVE(I) = (BASEPOWAVE(I) / QEXT(NUBASEAVE))
DRUGMAGAVER(I) = (DRUGMAGAVER(I) / QEXT(NUDRUGAVE))
DRUGPHAAVER(I) = (DRUGPHAAVER(I) / QEXT(NUDRUGAVE))
DRUGPOWAVE(I) = (DRUGPOWAVE(I) / QEXT(NUDRUGAVE))
END IF
CONTINUE
C
DO 222 I = 1, NUMNUM
F(I) = BASEMAGAVER(I)
222
CONTINUE
CALL NUMINT(F, NUMNUM, PERCENT, EDGE, SCALE, AREA, RMS)
BASEMAGEDGE = EDGE
DO 223 I = 1, NUMNUM
F(I) = BASEPHAAVER(I)
223
CONTINUE
CALL NUMINT(F, NUMNUM, PERCENT, EDGE, SCALE, AREA, RMS)
BASEPHAEDGE = EDGE
DO 227 I = 1, NUMNUM
F(I) = BASEPOWAVE(I)
227
CONTINUE
CALL NUMINT(F, NUMNUM, PERCENT, EDGE, SCALE, AREA, RMS)
BASEPOWEDGE = EDGE
DO 224 I = 1, NUMNUM
F(I) = DRUGMAGAVER(I)
224
CONTINUE
CALL NUMINT(F, NUMNUM, PERCENT, EDGE, SCALE, AREA, RMS)
DRUGMAGEDGE = EDGE
DO 225 I = 1, NUMNUM
F(I) = DRUGPHAAVER(I)
225
CONTINUE
CALL NUMINT(F, NUMNUM, PERCENT, EDGE, SCALE, AREA, RMS)
DRUGPHAEDGE = EDGE
DO 228 I = 1, NUMNUM
F(I) = DRUGPOWAVE(I)
228
CONTINUE
CALL NUMINT(F, NUMNUM, PERCENT, EDGE, SCALE, AREA, RMS)
DRUGPOWEDGE = EDGE
WRITE (10, *) '1', SNGL(BASEMAGEDGE)
WRITE (10, *) '2', SNGL(DRUGMAGEDGE)
CLOSE (UNIT=10, STATUS='SAVE')
WRITE (11, *) '1', SNGL(BASEPHAEDGE)
WRITE (11, *) '2', SNGL(DRUGPHAEDGE)
CLOSE (UNIT=11, STATUS='SAVE')
WRITE (22, *) '1', SNGL(BASEPOWEDGE)
WRITE (22, *) '2', SNGL(DRUGPOWEDGE)
CLOSE (UNIT=22,STATUS='SAVE')
NBASESAVE=0
NDARUGSAVE=0
DO 911 I=1,N
BASEMAGAVER(I)=0.0
BASEPHAVER(I)=0.0
BASEPOWAVER(I)=0.0
DRUGMAGAVER(I)=0.0
DRUGPHAVER(I)=0.0
DRUGPOWAVER(I)=0.0
CONTINUE

BASEMAGVARIANCE=((QEXT(NUMEANBASE))*MEANBASEMAGEDGE**2)/
* (QEXT(NUMEANBASE)**2)
MEANBASEMAGEDGE=(QEXT(NUMEANBASE)**2)
MEANBASEMAGEDGE/QEXT(NUMEANBASE)
BASEPHAVARIANCE=((QEXT(NUMEANBASE))*MEANBASEPHAEDGE**2)/
* (QEXT(NUMEANBASE)**2)
MEANBASEPHAEDGE=MEANBASEPHAEDGE/QEXT(NUMEANBASE)
BASEPOWVARIANCE=((QEXT(NUMEANBASE))*MEANBASEPOWEDGE**2)/
* (QEXT(NUMEANBASE)**2)
MEANBASEPOWEDGE=MEANBASEPOWEDGE/QEXT(NUMEANBASE)
DRUGMAGVARIANCE=((QEXT(NUMEANDRUG))*MEANDRUGMAGEDGE**2)/
* (QEXT(NUMEANDRUG)**2)
MEANDRUGMAGEDGE=(QEXT(NUMEANDRUG)**2)
MEANDRUGMAGEDGE/QEXT(NUMEANDRUG)
DRUGPHAVARIANCE=((QEXT(NUMEANDRUG))*MEANDRUGPHAEDGE**2)/
* (QEXT(NUMEANDRUG)**2)
MEANDRUGPHAEDGE=MEANDRUGPHAEDGE/QEXT(NUMEANDRUG)
DRUGPOWVARIANCE=((QEXT(NUMEANDRUG))*MEANDRUGPOWEDGE**2)/
* (QEXT(NUMEANDRUG)**2)
MEANDRUGPOWEDGE=MEANDRUGPOWEDGE/QEXT(NUMEANDRUG)
WRITE (12,*) 'BASE MAG SE MEAN = ',SNGL(MEANBASEMAGEDGE)
WRITE (12,*) 'BASE MAG SE VARIANCE = ',SNGL(BASEMAGVARIANCE)
WRITE (12,*) 'DRUG MAG SE MEAN = ',SNGL(MEANDRUGMAGEDGE)
WRITE (12,*) 'DRUG MAG SE VARIANCE = ',SNGL(DRUGMAGVARIANCE)
CLOSE (UNIT=12,STATUS='SAVE')
WRITE (13,*) 'BASE PHA SE MEAN = ',SNGL(MEANBASEPHAEDGE)
WRITE (13,*) 'BASE PHA SE VARIANCE = ',SNGL(BASEPHAVARIANCE)
WRITE (13,*) 'DRUG PHA SE MEAN = ',SNGL(MEANDRUGPHAEDGE)
WRITE (13,*) 'DRUG PHA SE VARIANCE = ',SNGL(DRUGPHAVARIANCE)
CLOSE (UNIT=13,STATUS='SAVE')
WRITE (23,*) 'BASE POW SE MEAN = ',SNGL(MEANBASEPOWEDGE)
WRITE (23,*) 'BASE POW SE VARIANCE = ',SNGL(BASEPOWVARIANCE)
WRITE (23,*) 'DRUG POW SE MEAN = ',SNGL(MEANDRUGPOWEDGE)
WRITE (23,*) 'DRUG POW SE VARIANCE = ',SNGL(DRUGPOWVARIANCE)
CLOSE (UNIT=23,STATUS='SAVE')
ENDIF

IF (PHASE.EQ.1) THEN
IF (INITIALS.EQ.'MLR') THEN
XVSCONC=5
WRITE (14,*) ' 0.0',SNGL(BASEMAGEDGE)
MAGVSCONC(1)=0.0
MAGVSCONC(1)=SNGL(BASEMAGEDGE)
DRUGMAGTEMP=(DRUGMAG(1)+DRUGMAG(2))/2.0
WRITE (14,*) ' 0.2',SNGL(DRUGMAGTEMP)
MAGVSCONC(2)=0.2
MAGVSCONC(2)=SNGL(DRUGMAGTEMP)
DRUGMAGTEMP=(DRUGMAG(3)+DRUGMAG(4)+DRUGMAG(5))/3.0
WRITE (14,*) ' 0.3',SNGL(DRUGMAGTEMP)
MAGVSCONC(3)=0.3
MAGVSCONC(3)=SNGL(DRUGMAGTEMP)
WRITE (14,*) ' 0.4',SNGL(DRUGMAG(10))
MAGVSCONC(4)=0.4
MAGVSCONC(4)=SNGL(DRUGMAG(10))
WRITE (14,*) ' 0.5',SNGL(DRUGMAG(15))
MAGVSCONC(5)=0.5
MAGVSCONC(5)=SNGL(DRUGMAG(15))
WRITE (15,*) ' 0.0',SNGL(BASEPHAEDGE)
PHAVSCONC(1)=0.0
PHAVSCONC(1)=SNGL(BASEPHAEDGE)
ENDIF

ENDIF

IF (INITIALS.EQ.'SJD') THEN

XVSCONC=5

WRITE (14,*) '0.0', SNGL(BASEMAGEDGE)
MAGVSCONCX(1)=0.0
MAGVSCONCY(1)=SNGL(BASEMAGEDGE)
DRUGMAGTEMP=(DRUGMAG(1)+DRUGMAG(2))/2.0
WRITE (14,*) '0.2', SNGL(DRUGMAGTEMP)
MAGVSCONCX(2)=0.2
MAGVSCONCY(2)=SNGL(DRUGMAGTEMP)
DRUGMAGTEMP=(DRUGMAG(3)+DRUGMAG(4)+DRUGMAG(5))/3.0
WRITE (14,*) '0.3', SNGL(DRUGMAGTEMP)
MAGVSCONCX(3)=0.3
MAGVSCONCY(3)=SNGL(DRUGMAGTEMP)
WRITE (14,*) '0.4', SNGL(DRUGMAG(10))
MAGVSCONCX(4)=0.4
MAGVSCONCY(4)=SNGL(DRUGMAG(10))
WRITE (14,*) '0.6', SNGL(DRUGMAG(15))
MAGVSCONCX(5)=0.6
MAGVSCONCY(5)=SNGL(DRUGMAG(15))

WRITE (15,*) '0.0', SNGL(BASEPHAEDGE)
PHAVSCONCX(1)=0.0
PHAVSCONCY(1)=SNGL(BASEPHAEDGE)
DRUGPHATEMP=(DRUGPHA(1)+DRUGPHA(2))/2.0
WRITE (15,*) '0.2', SNGL(DRUGPHATEMP)
PHAVSCONCX(2)=0.2
PHAVSCONCY(2)=SNGL(DRUGPHATEMP)
DRUGPHATEMP=(DRUGPHA(3)+DRUGPHA(4)+DRUGPHA(5))/3.0
WRITE (15,*) '0.3', SNGL(DRUGPHATEMP)
PHAVSCONCX(3)=0.3
PHAVSCONCY(3)=SNGL(DRUGPHATEMP)
WRITE (15,*) '0.4', SNGL(DRUGPHA(10))
PHAVSCONCX(4)=0.4
PHAVSCONCY(4)=SNGL(DRUGPHA(10))
WRITE (15,*) '0.5', SNGL(DRUGPHA(15))
PHAVSCONCX(5)=0.5
PHAVSCONCY(5)=SNGL(DRUGPHA(15))

POWVSCONCX(1)=0.0
POWVSCONCY(1)=SNGL(BASEPOWEDGE)
DRUGPOWTEMP=(DRUGPOW(1)+DRUGPOW(2))/2.0
WRITE (21,*) '0.2', SNGL(DRUGPOWTEMP)
POWVSCONCX(2)=0.2
POWVSCONCY(2)=SNGL(DRUGPOWTEMP)
DRUGPOWTEMP=(DRUGPOW(3)+DRUGPOW(4)+DRUGPOW(5))/3.0
WRITE (21,*) '0.3', SNGL(DRUGPOWTEMP)
POWVSCONCX(3)=0.3
POWVSCONCY(3)=SNGL(DRUGPOWTEMP)
WRITE (21,*) '0.4', SNGL(DRUGPOW(10))
POWVSCONCX(4)=0.4
POWVSCONCY(4)=SNGL(DRUGPOW(10))
WRITE (21,*) '0.5', SNGL(DRUGPOW(15))
POWVSCONCX(5)=0.5
POWVSCONCY(5)=SNGL(DRUGPOW(15))
WRITE (21,*) '0.6', SNGL(DRUGPOW(15))
POWVSCONCX(3)=0.3
POWVSCONCY(3)=SNGL(DRUGPOWTEMP)
WRITE (21,*) '0.4',SNGL(DRUGPOW(10))
POWVSCONCX(4)=0.4
POWVSCONCY(4)=SNGL(DRUGPOW(10))
WRITE (21,*) '0.6',SNGL(DRUGPOW(15))
POWVSCONCX(5)=SNGL(DRUGPOW(15))
ENDIF
IF (INITIALS.EQ.'TRB') THEN
  XVSCONC=5
  WRITE (14,*) '0.0',SNGL(BASEMAGEDGE)
  MAGVSCONCX(1)=0.0
  MAGVSCONCY(1)=SNGL(BASEMAGEDGE)
  WRITE (14,*) '0.2',SNGL(DRUGMAG(4))
  MAGVSCONCX(2)=0.2
  MAGVSCONCY(2)=SNGL(DRUGMAG(4))
  DRUGMAGTEMP=(DRUGMAG(1)+DRUGMAG(3)+DRUGMAG(5))/3.0
  WRITE (14,*) '0.3',SNGL(DRUGMAGTEMP)
  MAGVSCONCX(3)=SNGL(DRUGMAGTEMP)
  MAGVSCONCY(3)=SNGL(DRUGMAG(1))
  WRITE (14,*) '0.4',SNGL(DRUGMAG(10))
  MAGVSCONCX(4)=0.4
  MAGVSCONCY(4)=SNGL(DRUGMAGTEMP)
  WRITE (14,*) '0.6',SNGL(DRUGMAG(15))
  MAGVSCONCX(5)=SNGL(DRUGMAG(15))
ENDIF
IF (INITIALS.EQ.'SKW') THEN
  XVSCONC=5
  WRITE (14,*) '0.0',SNGL(BASEMAGEDGE)
  MAGVSCONCX(1)=0.0
  MAGVSCONCY(1)=SNGL(BASEMAGEDGE)
  WRITE (14,*) '0.2',SNGL(DRUGMAG(4))
  MAGVSCONCX(2)=0.2
  MAGVSCONCY(2)=SNGL(DRUGMAG(4))
  DRUGMAGTEMP=(DRUGMAG(3)+DRUGMAG(4)+DRUGMAG(5))/3.0
  WRITE (14,*) '0.3',SNGL(DRUGMAGTEMP)
  MAGVSCONCX(3)=SNGL(DRUGMAGTEMP)
  MAGVSCONCY(3)=SNGL(DRUGMAG(1))
  WRITE (14,*) '0.4',SNGL(DRUGMAG(10))
  MAGVSCONCX(4)=0.4
  MAGVSCONCY(4)=SNGL(DRUGMAGTEMP)
  WRITE (14,*) '0.6',SNGL(DRUGMAG(15))
  MAGVSCONCX(5)=SNGL(DRUGMAG(15))
ENDIF
MAGVSCONCX(4)=0.4
WRITE (14,*), '0.5', SNGL(DRUGMAG(15))
MAGVSCONCX(5)=0.5
MAGVSCONCY(4)=SNGL(DRUGMAG(15))
WRITE (15,*), '0.0', SNGL(BASEPOWEDGE)
PHAVSCONCX(1)=0.0
PHAVSCONCY(1)=SNGL(BASEPHAEDGE)
DRUGPHATEMP=(DRUGPHA(3)+DRUGPHA(4)+DRUGPHA(5))/3.0
WRITE (15,*), '0.2', SNGL(DRUGPHATEMP)
PHAVSCONCX(2)=0.2
PHAVSCONCY(2)=SNGL(DRUGPHATEMP)
WRITE (15,*), '0.3', SNGL(DRUGPHATEMP)
PHAVSCONCX(3)=0.3
PHAVSCONCY(3)=SNGL(DRUGPHATEMP)
DRUGPHATEMP=(DRUGPHA(2)+DRUGPHA(10))/2.0
WRITE (15,*), '0.4', SNGL(DRUGPHATEMP)
PHAVSCONCX(4)=0.4
PHAVSCONCY(4)=SNGL(DRUGPHATEMP)
WRITE (15,*), '0.5', SNGL(DRUGPHA(15))
PHAVSCONCX(5)=0.5
PHAVSCONCY(5)=SNGL(DRUGPHA(15))
POWVSCONCX(1)=0.0
POWVSCONCY(1)=SNGL(BASEPOWEDGE)
DRUGPOWTEMP=(DRUGPOW(3)+DRUGPOW(4)+DRUGPOW(5))/3.0
WRITE (21,*), '0.2', SNGL(DRUGPOWTEMP)
POWVSCONCX(2)=0.2
POWVSCONCY(2)=SNGL(DRUGPOWTEMP)
WRITE (21,*), '0.3', SNGL(DRUGPOWTEMP)
POWVSCONCX(3)=0.3
POWVSCONCY(3)=SNGL(DRUGPOWTEMP)
DRUGPOWTEMP=(DRUGPOW(2)+DRUGPOW(10))/2.0
WRITE (21,*), '0.4', SNGL(DRUGPOWTEMP)
POWVSCONCX(4)=0.4
POWVSCONCY(4)=SNGL(DRUGPOWTEMP)
WRITE (21,*), '0.5', SNGL(DRUGPOW(15))
POWVSCONCX(5)=0.5
POWVSCONCY(5)=SNGL(DRUGPOW(15))
ENDIF
IF (INITIALS.EQ.'DSC') THEN
XVSCONC=5
WRITE (14,*), '0.0', SNGL(BASEMAGEDGE)
MAGVSCONCX(1)=0.0
MAGVSCONCY(1)=SNGL(BASEMAGEDGE)
DRUGMAGTEMP=(DRUGMAG(1)+DRUGMAG(2))/2.0
WRITE (14,*), '0.1', SNGL(DRUGMAGTEMP)
MAGVSCONCX(2)=0.1
MAGVSCONCY(2)=SNGL(DRUGMAGTEMP)
DRUGMAGTEMP=(DRUGMAG(3)+DRUGMAG(4)+DRUGMAG(5))/3.0
WRITE (14,*), '0.2', SNGL(DRUGMAGTEMP)
MAGVSCONCX(3)=0.2
MAGVSCONCY(3)=SNGL(DRUGMAGTEMP)
WRITE (14,*), '0.3', SNGL(DRUGMAG(10))
MAGVSCONCX(4)=0.3
MAGVSCONCY(4)=SNGL(DRUGMAG(10))
WRITE (14,*), '0.4', SNGL(DRUGMAG(15))
MAGVSCONCX(4)=0.4
MAGVSCONCY(4)=SNGL(DRUGMAG(15))
WRITE (15,*), '0.0', SNGL(BASEPOWEDGE)
PHAVSCONCX(1)=0.0
PHAVSCONCY(1)=SNGL(BASEPHAEDGE)
DRUGPHATEMP=(DRUGPHA(1)+DRUGPHA(2))/2.0
WRITE (15,*), '0.1', SNGL(DRUGPHATEMP)
PHAVSCONCX(2)=0.1
PHAVSCONCY(2)=SNGL(DRUGPHATEMP)
DRUGPHATEMP=(DRUGPHA(3)+DRUGPHA(4)+DRUGPHA(5))/3.0
WRITE (15,*), '0.2', SNGL(DRUGPHATEMP)
PHAVSCONCX(3)=0.3
PHAVSCONCY(3)=SNGL(DRUGPHATEMP)
WRITE (15,*), '0.3', SNGL(DRUGPHA(10))
PHAVSCONCX(4)=0.3
PHAVSCONCY(4)=SNGL(DRUGPHA(10))
WRITE (15,*), '0.4', SNGL(DRUGPHA(15))
PHAVSCONCX(5)=0.4
PHAVSCONCY(5)=SNGL(DRUGPHA(15))
POWVSCONCX(1)=0.0
POWVSCONC(1)=SNGL(BASEPOWEDGE)

DRUGPOWTEMP=(DRUGPOW(1)+DRUGPOW(2))/2.0
WRITE (21,*),'0.1',SNGL(DRUGPOWTEMP)

POWVSCONC(2)=0.1

POWVSCONC(2)=SNGL(DRUGPOWTEMP)

DRUGPOWTEMP=(DRUGPOW(3)+DRUGPOW(4)+DRUGPOW(5))/3.0
WRITE (21,*),'0.2',SNGL(DRUGPOWTEMP)

POWVSCONC(3)=0.3

POWVSCONC(3)=SNGL(DRUGPOWTEMP)

WRITE (21,*),'0.3',SNGL(DRUGPOW(10))

POWVSCONC(4)=0.3

POWVSCONC(4)=SNGL(DRUGPOW(10))

WRITE (21,*),'0.4',SNGL(DRUGPOW(15))

POWVSCONC(5)=0.4

POWVSCONC(5)=SNGL(DRUGPOW(15))

ENDIF

IF (INITIALS.EQ.'DSC') THEN

XVSCONC=5
WRITE (14,*),'0.0',SNGL(BASEMAGEDGE)

MAGVSCONC(1)=0.0

MAGVSCONC(1)=SNGL(BASEMAGEDGE)

DRUGMAGTEMP=(DRUGMAG(1)+DRUGMAG(2))/2.0
WRITE (14,*),'0.1',SNGL(DRUGMAGTEMP)

MAGVSCONC(2)=0.1

MAGVSCONC(2)=SNGL(DRUGMAGTEMP)

WRITE (14,*),'0.2',SNGL(DRUGMAG(5))

MAGVSCONC(3)=0.2

MAGVSCONC(3)=SNGL(DRUGMAGTEMP)

WRITE (14,*),'0.3',SNGL(DRUGMAG(10))

MAGVSCONC(4)=0.3

MAGVSCONC(4)=SNGL(DRUGMAGTEMP)

WRITE (14,*),'0.4',SNGL(DRUGMAG(15))

MAGVSCONC(5)=0.4

MAGVSCONC(5)=SNGL(DRUGMAG(15))

WRITE (15,*),'0.0',SNGL(BASEPHAEDGE)

PHAVSCONC(1)=0.0

PHAVSCONC(1)=SNGL(BASEPHAEDGE)

DRUGPHATEMP=(DRUGPHA(1)+DRUGPHA(2))/2.0
WRITE (15,*),'0.1',SNGL(DRUGPHATEMP)

PHAVSCONC(2)=0.1

PHAVSCONC(2)=SNGL(DRUGPHATEMP)

WRITE (15,*),'0.2',SNGL(DRUGPHA(5))

PHAVSCONC(3)=0.2

PHAVSCONC(3)=SNGL(DRUGPHATEMP)

WRITE (15,*),'0.3',SNGL(DRUGPHA(10))

PHAVSCONC(4)=0.3

PHAVSCONC(4)=SNGL(DRUGPHATEMP)

WRITE (15,*),'0.4',SNGL(DRUGPHA(15))

PHAVSCONC(5)=0.4

PHAVSCONC(5)=SNGL(DRUGPHA (15))

POWVSCONC(1)=0.0

POWVSCONC(1)=SNGL(BASEPOWEDGE)

DRUGPOWTEMP=(DRUGPOW(1)+DRUGPOW(2))/2.0
WRITE (21,*),'0.1',SNGL(DRUGPOWTEMP)

POWVSCONC(2)=0.1

POWVSCONC(2)=SNGL(DRUGPOWTEMP)

WRITE (21,*),'0.2',SNGL(DRUGPOWTEMP)

POWVSCONC(3)=0.2

POWVSCONC(3)=SNGL(DRUGPOWTEMP)

WRITE (21,*),'0.3',SNGL(DRUGPOWTEMP)

POWVSCONC(4)=0.3

POWVSCONC(4)=SNGL(DRUGPOWTEMP)

WRITE (21,*),'0.4',SNGL(DRUGPOW(15))

POWVSCONC(5)=0.4

POWVSCONC(5)=SNGL(DRUGPOW(15))

ENDIF

IF (INITIALS.EQ.'DSG') THEN

XVSCONC=6
WRITE (14,*),'0.0',SNGL(BASEMAGEDGE)

MAGVSCONC(1)=0.0
MAGVSCONCX(1) = SNGL(BASEMAGEDGE)
WRITE (14, *) '0.1', SNGL(DRUGMAG(1))
MAGVSCONCX(2) = 0.1
MAGVSCONCX(3) = SNGL(DRUGMAG(1))
DRUGMAGTEMP = (DRUGMAG(2) + DRUGMAG(4))/2.0
WRITE (14, *) '0.2', SNGL(DRUGMAGTEMP)
MAGVSCONCX(3) = 0.2
MAGVSCONCX(5) = SNGL(DRUGMAGTEMP)
DRUGMAGTEMP = (DRUGMAG(3) + DRUGMAG(5))/2.0
WRITE (14, *) '0.3', SNGL(DRUGMAGTEMP)
MAGVSCONCX(4) = 0.3
MAGVSCONCX(6) = SNGL(DRUGMAGTEMP)
WRITE (14, *) '0.4', SNGL(DRUGMAG(10))
MAGVSCONCX(5) = 0.4
MAGVSCONCX(6) = SNGL(DRUGMAG(10))
WRITE (14, *) '0.5', SNGL(DRUGMAG(15))
MAGVSCONCX(7) = 0.5
MAGVSCONCX(9) = SNGL(DRUGMAG(15))
WRITE (15, *) '0.0', SNGL(BASEPHAEDGE)
PHAVSCONCX(1) = 0.0
PHAVSCONCX(2) = SNGL(BASEPHAEDGE)
WRITE (15, *) '0.1', SNGL(DRUGPHA(1))
PHAVSCONCX(3) = 0.1
PHAVSCONCX(4) = SNGL(DRUGPHA(1))
DRUGPHATEMP = (DRUGPHA(2) + DRUGPHA(4))/2.0
WRITE (15, *) '0.2', SNGL(DRUGPHATEMP)
PHAVSCONCX(5) = 0.2
PHAVSCONCX(6) = SNGL(DRUGPHATEMP)
WRITE (15, *) '0.3', SNGL(DRUGPHATEMP)
PHAVSCONCX(7) = 0.3
PHAVSCONCX(8) = SNGL(DRUGPHATEMP)
WRITE (15, *) '0.4', SNGL(DRUGPHA(10))
PHAVSCONCX(9) = 0.4
PHAVSCONCX(10) = SNGL(DRUGPHA(10))
WRITE (15, *) '0.5', SNGL(DRUGPHA(15))
PHAVSCONCX(11) = 0.5
PHAVSCONCX(12) = SNGL(DRUGPHA(15))
WRITE (15, *) '0.6', SNGL(DRUGPHA(15))
PHAVSCONCX(13) = 0.6
POWVSCONCX(1) = SNGL(BASEPOWEDGE)
WRITE (21, *) '0.1', SNGL(DRUGPOW(1))
POWVSCONCX(2) = 0.1
POWVSCONCX(3) = SNGL(DRUGPOW(1))
DRUGPOWTTEMP = (DRUGPOW(2) + DRUGPOW(4))/2.0
WRITE (21, *) '0.2', SNGL(DRUGPOWTTEMP)
POWVSCONCX(4) = 0.2
POWVSCONCX(5) = SNGL(DRUGPOWTTEMP)
WRITE (21, *) '0.3', SNGL(DRUGPOWTTEMP)
POWVSCONCX(6) = 0.3
POWVSCONCX(7) = SNGL(DRUGPOWTTEMP)
DRUGPOWTTEMP = (DRUGPOW(3) + DRUGPOW(5))/2.0
WRITE (21, *) '0.4', SNGL(DRUGPOWTTEMP)
POWVSCONCX(8) = 0.4
POWVSCONCX(9) = SNGL(DRUGPOWTTEMP)
WRITE (21, *) '0.5', SNGL(DRUGPOW(10))
POWVSCONCX(10) = 0.5
POWVSCONCX(11) = SNGL(DRUGPOW(10))
WRITE (21, *) '0.6', SNGL(DRUGPOW(15))
POWVSCONCX(12) = 0.6
POWVSCONCX(13) = SNGL(DRUGPOW(15))
WRITE (21, *) '0.6', SNGL(DRUGPOW(15))
ENDIF

IF (INITIALS.EQ.'RC') THEN
  XVSCONC = 5
  WRITE (14, *) '0.0', SNGL(BASEMAGEDGE)
  MAGVSCONCX(1) = 0.0
  MAGVSCONCX(2) = SNGL(BASEMAGEDGE)
  DRUGMAGTEMP = (DRUGMAG(1) + DRUGMAG(3) + DRUGMAG(5))/3.0
  WRITE (14, *) '0.2', SNGL(DRUGMAGTEMP)
  MAGVSCONCX(3) = 0.2
  MAGVSCONCX(4) = SNGL(DRUGMAGTEMP)
  WRITE (14, *) '0.3', SNGL(DRUGMAGTEMP)
  MAGVSCONCX(5) = 0.3
  MAGVSCONCX(6) = SNGL(DRUGMAGTEMP)
  WRITE (14, *) '0.4', SNGL(DRUGMAG(10))
  MAGVSCONCX(7) = 0.4
  MAGVSCONCX(8) = SNGL(DRUGMAG(10))
  WRITE (14, *) '0.6', SNGL(DRUGMAG(15))
  MAGVSCONCX(9) = 0.6
ENDIF
MAGVSCONCY(5) = SNGL(DRUGMAG(15))
WRITE (15, *) '0.0', SNGL(BASEPHAEDGE)
PHAVSCONCX(1) = 0.0
PHAVSCONCY(1) = SNGL(BASEPHAEDGE)
DRUGPHATEMP = (DRUGPHA(1) + DRUGPHA(3) + DRUGPHA(5))/3.0
WRITE (15, *) '0.2', SNGL(DRUGPHATEMP)
PHAVSCONCX(2) = 0.2
PHAVSCONCY(2) = SNGL(DRUGPHATEMP)
DRUGPHATEMP = (DRUGPHA(2) + DRUGPHA(4) + DRUGPHA(5))/2.0
WRITE (15, *) '0.3', SNGL(DRUGPHATEMP)
PHAVSCONCX(3) = 0.3
PHAVSCONCY(3) = SNGL(DRUGPHATEMP)
WRITE (15, *) '0.4', SNGL(DRUGPHA(10))
PHAVSCONCX(4) = 0.4
PHAVSCONCY(4) = SNGL(DRUGPHA(10))
WRITE (15, *) '0.5', SNGL(DRUGPHA(15))
PHAVSCONCX(5) = 0.5
PHAVSCONCY(5) = SNGL(DRUGPHA(15))
POWVSCONCX(1) = 0.0
POWVSCONCY(1) = SNGL(BASEPOWEDGE)
DRUGPOWTEMP = (DRUGPOW(1) + DRUGPOW(3) + DRUGPOW(5))/3.0
WRITE (21, *) '0.2', SNGL(DRUGPHATEMP)
POWVSCONCX(2) = 0.2
POWVSCONCY(2) = SNGL(DRUGPOWTEMP)
DRUGPOWTEMP = (DRUGPOW(2) + DRUGPOW(4) + DRUGPOW(5))/2.0
WRITE (21, *) '0.3', SNGL(DRUGPOWTEMP)
POWVSCONCX(3) = 0.3
POWVSCONCY(3) = SNGL(DRUGPOWTEMP)
WRITE (21, *) '0.4', SNGL(DRUGPOW(10))
POWVSCONCX(4) = 0.4
POWVSCONCY(4) = SNGL(DRUGPOW(10))
WRITE (21, *) '0.5', SNGL(DRUGPOW(15))
POWVSCONCX(5) = 0.5
POWVSCONCY(5) = SNGL(DRUGPOW(15))
ENDIF
IF (INITIALS.EQ.'DBH') THEN
XVSCONC = 4
WRITE (14, *) '0.0', SNGL(BASEMAGEDGE)
MAGVSCONCX(1) = 0.0
MAGVSCONCY(1) = SNGL(BASEMAGEDGE)
DRUGMAGTEMP = (DRUGMAG(1) + DRUGMAG(2) + DRUGMAG(3) + DRUGMAG(4) + DRUGMAG(5))/5.0
WRITE (14, *) '0.2', SNGL(DRUGMAGTEMP)
MAGVSCONCX(2) = 0.2
MAGVSCONCY(2) = SNGL(DRUGMAGTEMP)
WRITE (14, *) '0.4', SNGL(DRUGMAG(10))
MAGVSCONCX(3) = 0.4
MAGVSCONCY(3) = SNGL(DRUGMAG(10))
WRITE (14, *) '0.5', SNGL(DRUGMAG(15))
MAGVSCONCX(4) = 0.5
MAGVSCONCY(4) = SNGL(DRUGMAG(15))
WRITE (14, *) '0.0', SNGL(BASEMAGEDGE)
PHAVSCONCX(1) = 0.0
PHAVSCONCY(1) = SNGL(BASEMAGEDGE)
DRUGPHATEMP = (DRUGPHA(1) + DRUGPHA(2) + DRUGPHA(3) + DRUGPHA(4) + DRUGPHA(5))/5.0
WRITE (15, *) '0.2', SNGL(DRUGPHATEMP)
PHAVSCONCX(2) = 0.2
PHAVSCONCY(2) = SNGL(DRUGPHATEMP)
WRITE (15, *) '0.4', SNGL(DRUGPHA(10))
PHAVSCONCX(3) = 0.4
PHAVSCONCY(3) = SNGL(DRUGPHA(10))
WRITE (15, *) '0.5', SNGL(DRUGPHA(15))
PHAVSCONCX(4) = 0.5
PHAVSCONCY(4) = SNGL(DRUGPHA(15))
WRITE (15, *) '0.0', SNGL(BASEPHAEDGE)
POWVSCONCX(1) = 0.0
POWVSCONCY(1) = SNGL(BASEPOWEDGE)
DRUGPOWTEMP = (DRUGPOW(1) + DRUGPOW(2) + DRUGPOW(3) + DRUGPOW(4) + DRUGPOW(5))/5.0
WRITE (21, *) '0.2', SNGL(DRUGPOWTEMP)
POWVSCONCX(2) = 0.2
POWVSCONCY(2) = SNGL(DRUGPOWTEMP)
WRITE (21, *) '0.4', SNGL(DRUGPOW(10))
POWVSCONCX(3) = 0.4
POWVSCONCY(3) = SNGL(DRUGPOW(10))
WRITE (21, *) '0.5', SNGL(DRUGPOW(15))
POWVSCONCX(4)=0.5
POWVSCONCY(4)=SNGL(DRUGPOW(15))
ENDIF
IF (INITIALS.EQ. 'JRH') THEN
  XVSCONC=5
  WRITE (14, *) '0.0', SNGL(BASEMAGEDGE)
  MAGVSCONCX(1)=0.0
  MAGVSCONCY(1)=SNGL(BASEMAGEDGE)
  DRUGMAGTEMP=(DRUGMAG(1)+DRUGMAG(4)+DRUGMAG(5))/3.0
  WRITE (14, *) '0.2', SNGL(DRUGMAGTEMP)
  MAGVSCONCX(2)=0.2
  MAGVSCONCY(2)=SNGL(DRUGMAGTEMP)
  WRITE (14, *) '0.3', SNGL(DRUGMAG(3))
  MAGVSCONCX(3)=0.3
  MAGVSCONCY(3)=SNGL(DRUGMAG(3))
  DRUGMAGTEMP=(DRUGMAG(2)+DRUGMAG(10))/2.0
  WRITE (14, *) '0.4', SNGL(DRUGMAGTEMP)
  MAGVSCONCX(4)=0.4
  MAGVSCONCY(4)=SNGL(DRUGMAGTEMP)
  WRITE (14, *) '0.6', SNGL(DRUGMAG(3))
  MAGVSCONCX(5)=0.6
  MAGVSCONCY(5)=SNGL(DRUGMAG(3))
ENDIF
IF (PHASE.EQ.2) THEN
  IF (INITIALS.EQ. 'MDW') THEN
    XVSCONC=6
    WRITE (14, *) '0.00', SNGL(MEANBASEMAGEDGE)
    MAGVSCONCX(1)=0.00
    MAGVSCONCY(1)=SNGL(MEANBASEMAGEDGE)
    WRITE (14, *) '0.41', SNGL(DRUGMAG(9))
    MAGVSCONCX(2)=0.41
    MAGVSCONCY(2)=SNGL(DRUGMAG(9))
    WRITE (14, *) '0.46', SNGL(DRUGMAG(16))
    MAGVSCONCX(3)=0.46
    MAGVSCONCY(3)=SNGL(DRUGMAG(16))
    WRITE (14, *) '0.47', SNGL(DRUGMAG(14))
    MAGVSCONCX(4)=0.47
    MAGVSCONCY(4)=SNGL(DRUGMAG(14))
    DRUGMAGTEMP=(DRUGMAG(13)+DRUGMAG(15))/2.0
    WRITE (14, *) '0.48', SNGL(DRUGMAGTEMP)
    MAGVSCONCX(5)=0.48
    MAGVSCONCY(5)=SNGL(DRUGMAGTEMP)
  ENDIF
ENDIF
IF (PHASE.EQ.2) THEN
  IF (INITIALS.EQ. 'MDW') THEN
    XVSCONC=6
    WRITE (14, *) '0.00', SNGL(MEANBASEMAGEDGE)
    MAGVSCONCX(1)=0.00
    MAGVSCONCY(1)=SNGL(MEANBASEMAGEDGE)
    WRITE (14, *) '0.41', SNGL(DRUGMAG(9))
    MAGVSCONCX(2)=0.41
    MAGVSCONCY(2)=SNGL(DRUGMAG(9))
    WRITE (14, *) '0.46', SNGL(DRUGMAG(16))
    MAGVSCONCX(3)=0.46
    MAGVSCONCY(3)=SNGL(DRUGMAG(16))
    WRITE (14, *) '0.47', SNGL(DRUGMAG(14))
    MAGVSCONCX(4)=0.47
    MAGVSCONCY(4)=SNGL(DRUGMAG(14))
    DRUGMAGTEMP=(DRUGMAG(13)+DRUGMAG(15))/2.0
    WRITE (14, *) '0.48', SNGL(DRUGMAGTEMP)
    MAGVSCONCX(5)=0.48
    MAGVSCONCY(5)=SNGL(DRUGMAGTEMP)
  ENDIF
ENDIF
WRITE (15,*), '0.78', SNGL(DRUGPHA(14))
PHAVSCONCX(5)=0.78
PHAVSCONCY(5)=SNGL(DRUGPHA(14))
WRITE (15,*), '0.83', SNGL(DRUGPHA(13))
PHAVSCONCX(6)=0.83
PHAVSCONCY(6)=SNGL(DRUGPHA(13))
WRITE (15,*), '0.88', SNGL(DRUGPHA(15))
PHAVSCONCX(7)=0.88
PHAVSCONCY(7)=SNGL(DRUGPHA(15))
POWVSCONCX(1)=0.00
POWVSCONCY(1)=SNGL(MEANBASEPOWEDGE)
WRITE (21,*), '0.55', SNGL(ORUGPOW(9))
POWVSCONCX(2)=0.55
POWVSCONCY(2)=SNGL(ORUGPOW(9))
WRITE (21,*), '0.76', SNGL(DRUGPOW(12))
POWVSCONCX(3)=0.76
POWVSCONCY(3)=SNGL(DRUGPOW(12))
WRITE (21,*), '0.77', SNGL(DRUGPOW(16))
POWVSCONCX(4)=0.77
POWVSCONCY(4)=SNGL(DRUGPOW(16))
WRITE (21,*), '0.78', SNGL(DRUGPOW(14))
POWVSCONCX(5)=0.78
POWVSCONCY(5)=SNGL(DRUGPOW(14))
WRITE (21,*), '0.83', SNGL(DRUGPOW(13))
POWVSCONCX(6)=0.83
POWVSCONCY(6)=SNGL(DRUGPOW(13))
POWVSCONCX(7)=0.88
POWVSCONCY(7)=SNGL(DRUGPOW(15))
ENDIF
IF (INITIALS.EQ. 'MWK') THEN
XVSCONC=7
WRITE (14,*), '0.00', SNGL(MEANBASEMAGEDGE)
MAGVSCONCX(1)=0.00
MAGVSCONCY(1)=SNGL(MEANBASEMAGEDGE)
WRITE (14,*), '0.61', SNGL(DRUGMAG(9))
MAGVSCONCX(2)=0.61
MAGVSCONCY(2)=SNGL(DRUGMAG(9))
WRITE (14,*), '0.67', SNGL(DRUGMAG(13))
MAGVSCONCX(3)=0.67
MAGVSCONCY(3)=SNGL(DRUGMAG(13))
WRITE (14,*), '0.70', SNGL(DRUGMAG(14))
MAGVSCONCX(4)=0.70
MAGVSCONCY(4)=SNGL(DRUGMAG(14))
WRITE (14,*), '0.71', SNGL(DRUGMAG(12))
MAGVSCONCX(5)=0.71
MAGVSCONCY(5)=SNGL(DRUGMAG(12))
WRITE (14,*), '0.72', SNGL(DRUGMAG(15))
MAGVSCONCX(6)=0.72
MAGVSCONCY(6)=SNGL(DRUGMAG(15))
WRITE (14,*), '0.73', SNGL(DRUGMAG(16))
MAGVSCONCX(7)=0.73
MAGVSCONCY(7)=SNGL(DRUGMAG(16))
WRITE (15,*), '0.00', SNGL(MEANBASEPHAEDGE)
PHAVSCONCX(1)=0.00
PHAVSCONCY(1)=SNGL(MEANBASEPHAEDGE)
WRITE (15,*), '0.61', SNGL(DRUGPHA(9))
PHAVSCONCX(2)=0.61
PHAVSCONCY(2)=SNGL(DRUGPHA(9))
WRITE (15,*), '0.67', SNGL(DRUGPHA(13))
PHAVSCONCX(3)=0.67
PHAVSCONCY(3)=SNGL(DRUGPHA(13))
WRITE (15,*), '0.70', SNGL(DRUGPHA(14))
PHAVSCONCX(4)=0.70
PHAVSCONCY(4)=SNGL(DRUGPHA(14))
WRITE (15,*), '0.71', SNGL(DRUGPHA(12))
PHAVSCONCX(5)=0.71
PHAVSCONCY(5)=SNGL(DRUGPHA(12))
WRITE (15,*), '0.72', SNGL(DRUGPHA(15))
PHAVSCONCX(6)=0.72
PHAVSCONCY(6)=SNGL(DRUGPHA(15))
WRITE (15,*), '0.73', SNGL(DRUGPHA(16))
PHAVSCONCX(7)=0.73
PHAVSCONCY(7)=SNGL(DRUGPHA(16))
POWVSCONCX(1)=0.00
POWVSCONCY(1)=SNGL(DRUGPOW(16))
WRITE (21, *) '0.61', SNGL(DRUGPOW(9))
POWVSCONCX(2) = 0.61
POWVSCONCY(2) = SNGL(DRUGPOW(9))
WRITE (21, *) '0.67', SNGL(DRUGPOW(13))
POWVSCONCX(3) = 0.67
POWVSCONCY(3) = SNGL(DRUGPOW(13))
WRITE (21, *) '0.70', SNGL(DRUGPOW(14))
POWVSCONCX(4) = 0.70
POWVSCONCY(4) = SNGL(DRUGPOW(14))
WRITE (21, *) '0.71', SNGL(DRUGPOW(12))
POWVSCONCX(5) = 0.71
POWVSCONCY(5) = SNGL(DRUGPOW(12))
WRITE (21, *) '0.72', SNGL(DRUGPOW(15))
POWVSCONCX(6) = 0.72
POWVSCONCY(6) = SNGL(DRUGPOW(15))
WRITE (21, *) '0.73', SNGL(DRUGPOW(16))
POWVSCONCX(7) = 0.73
POWVSCONCY(7) = SNGL(DRUGPOW(16))
ENDIF

IF (INITIALS.EQ. 'BLP') THEN

ENDIF
IF (INITIALS.EQ.'PEF') THEN
  XVSCONC=7
  WRITE (14,*), '0.00', SNGL(MEANBASEMAGEDGE)
  MAGVSCONCX(1)=0.00
  MAGVSCONCY(1)=SNGL(MEANBASEMAGEDGE)
  WRITE (14,*), '0.47', SNGL(DRUGMAG(9))
  MAGVSCONCX(2)=0.47
  MAGVSCONCY(2)=SNGL(DRUGMAG(9))
  WRITE (14,*), '0.97', SNGL(DRUGMAG(15))
  MAGVSCONCX(3)=0.97
  MAGVSCONCY(3)=SNGL(DRUGMAG(15))
  WRITE (14,*), '0.98', SNGL(DRUGMAG(12))
  MAGVSCONCX(4)=0.98
  MAGVSCONCY(4)=SNGL(DRUGMAG(12))
  WRITE (14,*), '0.99', SNGL(DRUGMAG(16))
  MAGVSCONCX(5)=0.99
  MAGVSCONCY(5)=SNGL(DRUGMAG(16))
  WRITE (15,*), '1.01', SNGL(DRUGMAG(14))
  MAGVSCONCX(6)=1.01
  MAGVSCONCY(6)=SNGL(DRUGMAG(14))
  WRITE (15,*), '1.02', SNGL(DRUGMAG(13))
  MAGVSCONCX(7)=1.02
  MAGVSCONCY(7)=SNGL(DRUGMAG(13))
  WRITE (15,*), '0.00', SNGL(MEANBASEPHAEDGE)
  PHAVSCONCX(1)=0.00
  PHAVSCONCY(1)=SNGL(MEANBASEPHAEDGE)
  WRITE (15,*), '0.47', SNGL(DRUGPHA(9))
  PHAVSCONCX(2)=0.47
  PHAVSCONCY(2)=SNGL(DRUGPHA(9))
  WRITE (15,*), '0.97', SNGL(DRUGPHA(15))
  PHAVSCONCX(3)=0.97
  PHAVSCONCY(3)=SNGL(DRUGPHA(15))
  WRITE (15,*), '0.98', SNGL(DRUGPHA(12))
  PHAVSCONCX(3)=0.98
  PHAVSCONCY(3)=SNGL(DRUGPHA(12))
  WRITE (15,*), '0.99', SNGL(DRUGPHA(16))
  PHAVSCONCX(4)=0.99
  PHAVSCONCY(4)=SNGL(DRUGPHA(16))
  WRITE (15,*), '1.01', SNGL(DRUGPHA(14))
  PHAVSCONCX(5)=1.01
  PHAVSCONCY(5)=SNGL(DRUGPHA(14))
  WRITE (15,*), '1.02', SNGL(DRUGPHA(13))
  PHAVSCONCX(6)=1.02
  PHAVSCONCY(6)=SNGL(DRUGPHA(13))
  WRITE (16,*), '0.00', SNGL(MEANBASEPOWEDGE)
  POWVSCONCX(1)=0.00
  POWVSCONCY(1)=SNGL(MEANBASEPOWEDGE)
  WRITE (21,*), '0.47', SNGL(DRUGPOW(9))
  POWVSCONCX(2)=0.47
  POWVSCONCY(2)=SNGL(DRUGPOW(9))
  WRITE (21,*), '0.97', SNGL(DRUGPOW(15))
  POWVSCONCX(3)=0.97
  POWVSCONCY(3)=SNGL(DRUGPOW(15))
  WRITE (21,*), '0.98', SNGL(DRUGPOW(12))
  POWVSCONCX(3)=0.98
  POWVSCONCY(3)=SNGL(DRUGPOW(12))
  WRITE (21,*), '0.99', SNGL(DRUGPOW(16))
  POWVSCONCX(4)=0.99
  POWVSCONCY(4)=SNGL(DRUGPOW(16))
  WRITE (21,*), '1.01', SNGL(DRUGPOW(14))
  POWVSCONCX(5)=1.01
  POWVSCONCY(5)=SNGL(DRUGPOW(14))
  WRITE (21,*), '1.02', SNGL(DRUGPOW(13))
  POWVSCONCX(6)=1.02
  POWVSCONCY(6)=SNGL(DRUGPOW(13))
ENDIF
WRITE (15,*) '0.53', SNGL(DRUGPHA(15))
PHAVSCONCX(4)=0.53
WRITE (15,*) '0.57', SNGL(DRUGPHA(15))
PHAVSCONCX(5)=0.57
WRITE (15,*) '0.58', SNGL(DRUGPHA(15))
PHAVSCONCX(6)=0.58
WRITE (15,*) '0.61', SNGL(DRUGPHA(16))
PHAVSCONCX(7)=0.61
WRITE (15,*) '0.61', SNGL(DRUGPHA(16))
POWVSCONCX(1)=0.15
POWVSCONCX(2)=SNGL(DRUGPOW(9))
WRITE (21,*) '0.43' ,SNGL(DRUGPOW(9))
POWVSCONCX(3)=SNGL(DRUGPOW(14))
WRITE (21,*) '0.51' ,SNGL(DRUGPOW(14))
POWVSCONCX(4)=SNGL(DRUGPOW(15))
WRITE (21,*) '0.53' ,SNGL(DRUGPOW(15))
POWVSCONCX(5)=SNGL(DRUGPOW(12))
WRITE (21,*) '0.57' ,SNGL(DRUGPOW(12))
POWVSCONCX(6)=SNGL(DRUGPOW(13))
WRITE (21,*) '0.58' ,SNGL(DRUGPOW(13))
POWVSCONCX(7)=SNGL(DRUGPOW(16))
WRITE (21,*) '0.61' ,SNGL(DRUGPOW(16))
ENDIF
IF (INITIALS.EQ.'RFF') THEN
XVSCONC=7
WRITE (14,*) '0.00', SNGL(MEANBASEMAGEOGE)
MAGVSCONCX(1)=0.00
MAGVSCONCX(2)=SNGL(MEANBASEMAGEOGE)
WRITE (14,*) '0.50', SNGL(DRUGMAG(9))
MAGVSCONCX(3)=SNGL(DRUGMAG(9))
WRITE (14,*) '0.64', SNGL(DRUGMAG(15))
MAGVSCONCX(4)=SNGL(DRUGMAG(15))
WRITE (14,*) '0.70', SNGL(DRUGMAG(14))
MAGVSCONCX(5)=SNGL(DRUGMAG(14))
WRITE (14,*) '0.71', SNGL(DRUGMAG(12))
MAGVSCONCX(6)=SNGL(DRUGMAG(12))
WRITE (14,*) '0.72', SNGL(DRUGMAG(16))
MAGVSCONCX(7)=SNGL(DRUGMAG(16))
WRITE (15,*) '0.00', SNGL(MEANBASEPHAGEOE)
PHAVSCONCX(1)=0.00
PHAVSCONCX(2)=SNGL(MEANBASEPHAGEOE)
WRITE (15,*) '0.50', SNGL(DRUGPHA(9))
PHAVSCONCX(3)=SNGL(DRUGPHA(9))
WRITE (15,*) '0.64', SNGL(DRUGPHA(15))
PHAVSCONCX(4)=SNGL(DRUGPHA(15))
WRITE (15,*) '0.70', SNGL(DRUGPHA(14))
PHAVSCONCX(5)=SNGL(DRUGPHA(14))
WRITE (15,*) '0.71', SNGL(DRUGPHA(12))
PHAVSCONCX(6)=SNGL(DRUGPHA(12))
WRITE (15,*) '0.72', SNGL(DRUGPHA(16))
PHAVSCONCX(7)=SNGL(DRUGPHA(16))
PHAVSCONCX(7)=0.73
ENDIF
ENDIF
CLOSE (UNIT=14, STATUS='SAVE')
CLOSE (UNIT=15, STATUS='SAVE')
CLOSE (UNIT=21, STATUS='SAVE')

NUMBASE=0
NUMDRUG=0
MEANBASEMAGEDGE=0.0
MEANBASEMAGEDGE2=0.0
MEANBASEPHAEDGE=0.0
MEANBASEPHAEDGE2=0.0
MEANBASEPOWEDGE=0.0
MEANBASEPOWEDGE2=0.0
MEANDRUGMAGEDGE=0.0
MEANDRUGMAGEDGE2=0.0
MEANDRUGPHAEDGE=0.0
MEANDRUGPHAEDGE2=0.0
MEANDEERUGPOWEDGE=0.0
MEANDRUGPOWEDGE2=0.0

MAGMIN=1E12
PHAMIN=1E12
POWMIN=1E12
DO 607 DAY=0, DAYUP, DAYINC
IF (PHASE.EQ.1) THEN
  IF (DAY.EQ.0) THEN
    IF (BASEMAG(DAY).LT.MAGMIN) THEN
      MAGMIN=BASEMAG(DAY)
    ENDIF
    IF (BASEPHA(DAY).LT.PHAMIN) THEN
      PHAMIN=BASEPHA(DAY)
    ENDIF
    IF (BASEPOW(DAY).LT.POWMIN) THEN
      POWMIN=BASEPOW(DAY)
    ENDIF
  ENDIF
  IF (DAY.EQ.1).OR.(DAY.EQ.2).OR.(DAY.EQ.3).OR.
  ((DAY.EQ.4).OR.(DAY.EQ.5).OR.(DAY.EQ.10)).OR.
  (DAY.EQ.15) THEN
    IF (DRUGMAG(DAY).LT.MAGMIN) THEN
      MAGMIN=DRUGMAG(DAY)
    ENDIF
    IF (DRUGPHA(DAY).LT.PHAMIN) THEN
      PHAMIN=DRUGPHA(DAY)
    ENDIF
    IF (DRUGPOW(DAY).LT.POWMIN) THEN
      POWMIN=DRUGPOW(DAY)
    ENDIF
  ENDIF
ENDIF
IF (PHASE.EQ.2) THEN
  IF (DAY.EQ.0).OR.(DAY.EQ.1).OR.(DAY.EQ.2).OR.
* (DAY.EQ.5).OR.(DAY.EQ.6)) THEN
  IF (BASEMAG(DAY).LT.MAGMIN) THEN
    MAGMIN=BASEMAG(DAY)
  ENDIF
  IF (BASEPHA(DAY).LT.PHAMIN) THEN
    PHAMIN=BASEPHA(DAY)
  ENDIF
  IF (BASEPOW(DAY).LT.POWMIN) THEN
    POWMIN=BASEPOW(DAY)
  ENDIF
ENDIF
* IF ((DAY.EQ.9).OR.(DAY.EQ.12).OR.(DAY.EQ.13).OR.
  (DAY.EQ.14).OR.(DAY.EQ.15).OR.(DAY.EQ.16)) THEN
  IF (DRUGMAG(DAY).LT.MAGMIN) THEN
    MAGMIN=DRUGMAG(DAY)
  ENDIF
  IF (DRUGPHA(DAY).LT.PHAMIN) THEN
    PHAMIN=DRUGPHA(DAY)
  ENDIF
  IF (DRUGPOW(DAY).LT.POWMIN) THEN
    POWMIN=DRUGPOW(DAY)
  ENDIF
ENDIF
ENDIF
CONTINUE
WRITE (16,616) ,
616 FORMAT (1H ,A8,F8.2,lX,A2)
WRITE (16,616) 'SU a =',SNGL(MAGMIN),'Hz'
WRITE (16,616) 'VE SPECT. EDGE (Hz) - a'
WRITE (16,616) 'SU a =',SNGL(PHAMIN),'Hz'
WRITE (16,616) 'VE SPECT. EDGE (Hz) - a'
WRITE (16,616) 'SU a =',SNGL(POWMIN),'Hz'
WRITE (16,616) 'VE SPECT. EDGE (Hz) - a'
C DO 608 DAY=0,DAYUP,DAYINC
IF (PHASE.EQ.1) THEN
  IF (DAY.EQ.0) THEN
    MAGNORM=BASEMAG(DAY)-MAGMIN
    PHANORM=BASEPHA(DAY)-PHAMIN
    POWNORM=BASEPOW(DAY)-POWMIN
  ENDIF
  IF ((DAY.EQ.1).OR.(DAY.EQ.2).OR.(DAY.EQ.3).OR.
    (DAY.EQ.4).OR.(DAY.EQ.5).OR.(DAY.EQ.10).OR.
    (DAY.EQ.15)) THEN
    MAGNORM=DRUGMAG(DAY)-MAGMIN
    PHANORM=DRUGPHA(DAY)-PHAMIN
    POWNORM=DRUGPOW(DAY)-POWMIN
  ENDIF
ENDIF
IF (PHASE.EQ.2) THEN
  IF ((DAY.EQ.0).OR.(DAY.EQ.1).OR.(DAY.EQ.2).OR.
    (DAY.EQ.5).OR.(DAY.EQ.6)) THEN
    MAGNORM=BASEMAG(DAY)-MAGMIN
    PHANORM=BASEPHA(DAY)-PHAMIN
    POWNORM=BASEPOW(DAY)-POWMIN
  ENDIF
  IF ((DAY.EQ.9).OR.(DAY.EQ.12).OR.(DAY.EQ.13).OR.
    (DAY.EQ.14).OR.(DAY.EQ.15).OR.(DAY.EQ.16)) THEN
    MAGNORM=DRUGMAG(DAY)-MAGMIN
    PHANORM=DRUGPHA(DAY)-PHAMIN
    POWNORM=DRUGPOW(DAY)-POWMIN
  ENDIF
ENDIF
IF (PHASE.EQ.1) THEN
    (DAY.EQ.11).OR.(DAY.EQ.12).OR.(DAY.EQ.13).OR.(DAY.EQ.14))
    GO TO 608
ELSE
  IF ((DAY.EQ.3).OR.(DAY.EQ.4).OR.(DAY.EQ.7).OR.(DAY.EQ.8).OR.
    (DAY.EQ.10).OR.(DAY.EQ.11))
    GO TO 608
ENDIF
WRITE (16,611) DAY,SNGL(MAGNORM)
CONTINUE

WRITE (17, 616) 'SU', SNGL(MAGVSCONCMIN), 'Hz'
WRITE (17, *) 'HO (Li+) (mEq/L)'
WRITE (17, *) 'VE SPECT. EDGE (Hz) - a'
WRITE (19, 616) 'SU', SNGL(PHAVSCONCMIN), 'Hz'
WRITE (19, *) 'HO (Li+) (mEq/L)'
WRITE (19, *) 'VE SPECT. EDGE (Hz) - a'
WRITE (25, 616) 'SU', SNGL(POWVSCONCMIN), 'Hz'
WRITE (25, *) 'HO (Li+) (mEq/L)'
WRITE (25, *) 'VE SPECT. EDGE (Hz) - a'

DO 610 VSCONCX=1,VSCONC
MAGVSCONCMIN=MAGVSCONC(VSCONCX)
PHAVSCONCMIN=PHAVSCONC(VSCONCX)
POWVSCONCMIN=POWVSCONC(VSCONCX)
WRITE (17, 613) SNGL(MAGVSCONCMIN), SNGL(MAGVSCONCNORM)
WRITE (19, 613) SNGL(PHAVSCONCMIN), SNGL(PHAVSCONCNORM)
WRITE (25, 613) SNGL(POWVSCONCMIN), SNGL(POWVSCONCNORM)

CONTINUE

CLOSE (UNIT=17, STATUS='SAVE')
CLOSE (UNIT=19, STATUS='SAVE')
CLOSE (UNIT=25, STATUS='SAVE')

IF (CFREQ.EQ.'N') GO TO 563
CLOSE (UNIT=1, STATUS='SAVE')
CLOSE (UNIT=8, STATUS='SAVE')

563 IF ((AOF.EQ.'O').AND.(COUNT.EQ.0)) GO TO 403
IF ((AOF.EQ.'O').AND.(COUNT.EQ.1)) GO TO 1001
401 CONTINUE
403 CONTINUE

1001 STOP

END

SUBROUTINE NUMINT(F, NUMNUM, PERCENT, EDGE, SCALE, AREA, RMS)

REAL*16 F(*), NUMNUM
REAL*16 PERCENT, EDGESCALAE, AREA, RMS
REAL*16 AREA0, RMSAREA0, TEMPAREA(512), WIDTH, SLOPE, XL, XR, FXL, FXR

AREA=0.0
RMSAREA=0.0

DO 10 I=1, NUMNUM-1
TEMPAREA(I)=(F(I)+F(I+1))/2.0
AREA=AREA+TEMPAREA(I)
RMSAREA=RMSAREA+((F(I)**2)+(F(I+1)**2))/2.0
10 CONTINUE
EDGE = (PERCENT/100.0) * AREA
RMS = SQRT(RMSAREA/(QEXT(NUMNUM)))
AREA = 0.0
NODIV = 10000
WIDTH = 1.0/(QEXT(NODIV))

DO 30 I = 1, NUMNUM - 1
    AREA = AREA + TEMPAREA(I)
    IF (AREA.GT.EDGE) THEN
        SLOPE = F(I+1) - F(I)
        AREA = AREA + TEMPAREA(I)
    ENDIF
    DO 20 J = 1, NODIV
        XL = (QEXT(J-1))*WIDTH
        XR = (QEXT(J))*WIDTH
        FXL = FXR
        FXR = FXR + (SLOPE * WIDTH)
        AREA = (WIDTH/2.0) * (FXL + FXR)
        IF (AREA.GT.EDGE) THEN
            EDGE = (QEXT(I) + XL) * SCALE
            AREA = AREA - AREA0
        ENDIF
    20 CONTINUE
30 CONTINUE

C

STOP
END

SUBROUTINE ISDEF (NUMBER, MESSAGE, RDWRT)

C THIS ROUTINE WILL CHECK IF FILE NUMBER "NUMBER" IS OPEN.
C IF IT IS THEN NO ACTION IS TAKEN.
C IF NOT THEN A WRITE STATEMENT IS ISSUED TRANSMITTING
C THE MESSAGE "MESSAGE" TO THE TERMINAL FOLLOWED BY A READ
C WHICH READS A FILE NAME TO BE OPENED.
C
C IF NUMBER EQUALS EITHER TTI OR TTO, NO ACTION IS TAKEN.

INTEGER NUMBER, TTI, TTO
PARAMETER (TTI=5, TTO=6)
CHARACTER*1 DDNAME
CHARACTER*10 MESSAGE
CHARACTER*16 RDWRT
CHARACTER*40 FILE NAME
CHARACTER*5 READ, WRITE
LOGICAL TF
DATA READ, WRITE / 'READ', 'WRITE' /

IF (NUMBER.EQ.TTI OR NUMBER.EQ.TTO) RETURN
INQUIRE (UNIT=NUMBER, OPENED=TF)
IF (.NOT. TF) THEN
    WRITE (TTI, '(A, $)') MESSAGE
    READ (TTI, '(Q, A)') LEN, FILE_NAME(1:LEN)
    IF (RDWRT(1:5).EQ. READ) THEN
        OPEN (UNIT=NUMBER, FILE=FILE_NAME(1:LEN), STATUS='old')
    ELSE
        IF (LEN.EQ.0) THEN
            LEN = 5
            FILE_NAME(1:LEN) = 'TXA6:'
        ENDIF
        OPEN (UNIT=NUMBER, FILE=FILE_NAME(1:LEN), STATUS='new',
            CARRIAGECONTROL='1ist', RECL=256)
    ENDIF
ENDIF
RETURN
END

SUBROUTINE FFT1(A, M, N)
COMPLEX*16 A(N), U, W, T
REAL*16 PI
IN-PLACE REVERSAL OF INPUT DATA

J=1
DO 20 I=1,NM1
IF (I.GE.J) GO TO 5
T=A(J)
A(J)=A(I)
A(I)=T
5 K=HV2
10 IF (K.GE.J) GO TO 15
J=J-K
K=K/2
GO TO 10
15 J=J+K
20 CONTINUE

CRUNCH TWIDDLE FACTORS AND BUTTERFLIES

DO 30 L=1,M
LE=2*I
LE1=LE/2
U=(1.0,0.0)
W=DCMPLX(QCOS(PI/LE1),QSIN(PI/LE1))
DO 30 J=1,LE1
DO 2S I .. J,N,LE
IP=I+LE1
T=A(IP)*U
A(IP)=A(I)-T
A(I)=A(I)+T
2S CONTINUE
U=U*W
30 CONTINUE

RETURN
END

SUBROUTINE READ EEG(FILENAME0,AMEAN)
FRANK A. ZAK, 13 OCT 88

Parameter IBFLIM = 4096
Integer*2 IDTBUF(IBFLIM)
REAL*16 XARR(4099),YARR(4099)
REAL*16 AMEAN(*)
DATA IEFN,ISTART /11,11/
CHARACTER*28 FILENAME0

OPEN (UNIT=3,FILE=FILENAME0,STATUS='UNKNOWN',FORM='UNFORMATTED')

DO 4 I=1,4099
XARR(I)=0.0
YARR(I)=0.0
4 CONTINUE

READ THE FILE BACK IN FROM THE DISK

READ (3) (IDTBUF(I),I=1,4096)

PROCESS THE DATA (MULTIPLY SAMPLING FREQUENCY BY 1/4)

DO 9 I=1,1024
XARR(I)=REAL(I-1)
AMEAN(I)=QEXT(IDTBUF((4*(I-1))+1))
9 CONTINUE

RETURN
END
SUBROUTINE AUTCOR(AMEAN, AUTO, ILOW, IUP, N)
C
C ROUTINE FOR COMPUTING THE AUTOCORRELATION OF AMEAN(I)
C
C IMPLEMENTS Rxx[k] EQUATION ON PAGE 61 OF 'SIGNAL PROCESSING' BY
D. BROOK AND R.J. WINNE
C
C COMPUTES AUTOCORRELATION FOR k=N VALUES OF DELAY
C
FRANK A. ZAK, 09 DEC 89
C
REAL*16 AMEAN(*), AUTO(*)
K=N

DO 10 I=1,K
AUTO(I)=0.0
10 CONTINUE

DO 40 J=0,K-1
  DO 20 I=ILOW-1, IUP-1
    IF ((I-ILOW+J).EQ.N) GO TO 30
  AUTO(I)=AUTO(I)+((AMEAN(I+J))**2)(AMEAN(I+1+J))
20 CONTINUE
30 AUTO(J+1)=AUTO(J+1)/QEXT(I-ILOW)
40 CONTINUE

RETURN
END

SUBROUTINE BELL(MESSAGE)
CHARACTER*(* ) MESSAGE
CALL BUFOUT(7,1,6)
WRITE(6,'(A)') MESSAGE
RETURN
END

SUBROUTINE BUFOUT(IADE, N, IOUT)
CHARACTER*250 CIADE
DIMENSION IADE(250)

DO 10 J=1, N
  CIADE(J)=CHAR(IADE(J))
10 CONTINUE
WRITE(IOUT,100)(CIADE(I),I=1,N)
100 FORMAT(1H,250A1)
RETURN
END

SUBROUTINE MEAN (DATA, IFLAG, NSEP, AMEAN)
PARAMETER (MAXDIF=16200)
INTEGER*2 IFLAG(*), NDT(MAXDIF)
REAL*16 DATA(*), AMEAN(*), ASUM(MAXDIF)

DO 30 J=1, NSEP
  ACCUMULATE VALUES
  IF (IFLAG(J).EQ.1) THEN
    NDT(J)=NDT(J)+1
    ASUM(J)=ASUM(J)+QEXT(DATA(J))
  ENDIF
  CALCULATE MEAN AND SD
  IF (IFLAG(J).EQ.2) THEN
    IF (NDT(J).GE.2) THEN
      AMEAN(J)=ASUM(J)/QEXT(NDT(J))
    ELSE
      AMEAN(J)=ASUM(J)
    ENDIF
  ENDIF
  RESET FOR NEW SET OF VALUES
  IF (IFLAG(J).EQ.4) THEN
    ASUM(J)=0.0
    NDT(J)=0
END
ENDIF

C 30 CONTINUE
C
RETURN
END
APPENDIX F

t_TEST
PROGRAM T_TEST

IMPLICIT REAL*16 (A-Z)

REAL*16 BEFORE(10), AFTER(10), DIFF(10)

INTEGER N, J

TPT05 = 1.895
N = 8
MEAN = 0.0
SUM = 0.0

DO 10 J = 1, N
WRITE (6, *) 'ENTER BEFORE DATA POINT', SNGL(J)
READ (5, *) BEFORE(J)
WRITE (6, *) 'ENTER AFTER DATA POINT', SNGL(J)
READ (5, *) AFTER(J)
DIFF(J) = BEFORE(J) - AFTER(J)
10 CONTINUE

MEAN = MEAN / REAL(N)
DO 20 J = 1, N
SUM = SUM + (DIFF(J) - MEAN)**2
20 CONTINUE
STANDEV = SQRT(SUM / REAL(N-1))

T = (MEAN * SQRT(REAL(N))) / STANDEV

WRITE (6, *) 'MEAN = ', SNGL(MEAN)
WRITE (6, *) 'STANDEV = ', SNGL(STANDEV)
WRITE (6, *) 'T = ', SNGL(T)
IF (T.GT.TPT05) THEN
WRITE (6, *) 'SIGNIFICANT DRUG EFFECT'
ELSE
WRITE (6, *) 'NO SIGNIFICANT DRUG EFFECT'
ENDIF

STOP
END
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