ABSTRACT

Sleep is a non-uniform biological state which has been subdivided into different stages. The basic criteria behind staging are the amplitude and frequency variations of sleep data. The sleep analysis is carried out by considering the characteristic variation of all three EEG, EOG and EMG signals. The polygraphic recording of nocturnal sleep is a method of research widely used in neurophysiology laboratories, both for the clinical study of sleep and for the evaluation of the therapeutic effectiveness of drugs acting on sleep. The analysis of this method is carried out by an expert individual whose depth of knowledge regarding the normal pattern of waveforms and the set of criteria used for staging reflects on the outcome of the analysis. With this approach there are always discrepancies among the individual scorers with respect to the method applied and as well as criteria considered.

Visual analysis of the EEG remains necessary and appropriate, but it is time consuming and lacks quantification. The alternative would be to develop an Computerized System for scoring the sleep stage data. Over these years automatic scoring of sleep stage data has promised increased understanding of pathological as well as normal sleep patterns. Computerized systems also act as an essential tool in describing the sleep process and to reflect the dynamic organization of human sleep.

The objective of the present work is to develop a Computerized System with an efficient algorithm to score the sleep stage data based on multiple set of criteria. The outcome of this study is then compared with the Visual Scoring data to find out the percentage of agreement between the human scorer and the computer algorithm.

COMPUTERIZED SCORING OF SLEEP STAGE DATA

by
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This thesis is dedicated to
Anna, Amma and to my loving Veena

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CHAPTER 1

INTRODUCTION

1.1 Introduction

Significant advances have been made in sleep disorder medicine, especially during the past ten years. The polygraphic recording of the nocturnal sleep is a widely used method in neurophysiology laboratories, both for the clinical study of the sleep and for the evaluation of the therapeutic effects of drugs acting on sleep. From these polygraphic data, we can identify pattern changes relating the characterization of sleep stages visually. Homogeneity of results, costs incurred and the time spent with visual scoring have opened the doors for automatic scoring method in recent years. The automatic scoring has promised increased understanding of pathological as well as normal sleep patterns. Despite publications of a number of encouraging results, few systems have been devised for routine sleep staging in a clinical environment. Several computerized sleep analysis systems have been commercialized [1] without any precise evaluation of their quality or reliability. The objective of work done in this thesis is to develop a computerized system for sleep stage scoring using a set of multiple criteria.

1.2 Clinical Sleep Disorders

Thousands of miles of sleep EEG data have been accumulated, and countless hours of effort have been expended by sleep researchers around the globe. Considerable information has emerged from the sleep laboratories which can be useful to the physician [2]. Some of the common disorders known are listed below .

a. Narcolepsy

This describes a condition of recurring, uncontrollable episodes of brief sleep. This disorder usually begins in adolescence or young adulthood, it continues throughout life but is generally thought to improve in later years [3]. In narcoleptics REM occurs at, or soon after, the onset of sleep when compared to normal sleep pattern. Many stimulant and antidepressant medications have been used in the treatment of true narcolepsy, but nothing replaces an understanding discussion with the patient and his family about the illness and ways they can adjust themselves to it.

b. Cataplexy

Characterized by brief episodes of muscular weakness which are precipitated by laughter, anger, or other emotional excitement. The degree of disability may range in scope from a mere subjective feeling of weakness to almost total paralysis.

c. Hypersomnia

The subject will have tendency to sleep for excessively long periods, either as an extension of nocturnal sleep into the late morning or past noon, or at various times during normal hours of wakefulness. Unlike narcoleptics, patients with hypersomnia do not display the auxiliary symptoms of cataplexy and rarely complain of disturbed nocturnal sleep [2].

d. Insomnia

Inability to fall asleep, frequent and prolonged awakenings, early morning awakenings, in the absence of gross physical or psychological pathology is probably one of the most common sleep disturbances. Sleep EEG studies indicate that there is a physiological basis for the insomniac's complaints and it has been found that these patients have significantly longer sleep latencies, shorter sleep times and less efficient sleep.

e. Sudden Infant Death Syndrome (SIDS)

Is a sleep related phenomenon that has been strongly supported by the evidence of a high incidence of infant mortality during sleep [4]. The typical clinical syndrome is that of a generally healthy infant of 2 to 4 months of age who is put to sleep in its crib at night and is found dead shortly thereafter or in the morning, having died several hours before. Autopsy examination reveals no abnormalities recognized as cause for death. The automatic inspiratory-expiratory rhythmic cycle is disrupted by recurrent periods of apnea. It is suggested that NREM sleep stages in the infant might be more prone to be correlated with a prolonged apnea than the REM sleep stage.

1.3 Automatic and Visual Scoring

Sleep is a nonuniform biological state which has been subdivided into different stages. The stage concept leads to inaccuracies if the underlying processes are continuous and vary gradually in time. This insufficient representation of sleep characteristics forced to use computers in sleep analysis. Analysis of the transient activity, in the EEG almost impossible without a computer, seems to give a good index to evaluate the quality of a night, especially when the patient is under pharmacological drugs. Numerical analysis of these transients may be considered as a future approach to describe the sleep process and to reflect the dynamical organization of sleep.

Large scale pharmacological screening of drug effects on EEG defined, sleep-waking behavior only becomes feasible when the normal laborious and time consuming visual scoring of sleep stages is circumvented by automatic analysis methods capable of unattended and reliable processing of many hours of data from large groups [5]. This also holds for systemic studies of general features of sleep-waking behavior, for which analysis of records from large

group of patients are required. The need to demonstrate the essential parameters and to simplify the interpretation of EEG data has led many investigators to intiate methods of analysis which opened the doors for Automatic Scoring.

In recent years a number of sleep variables have been defined that characterize sleep. These variables basically explain both the measurements which describe the evolution of sleep and the duration of the different states of sleep [6]. The physiological relationships between the various components of sleep are still largely unknown. Automatic Scoring helps in order to gain insight into the temporal and casual aspects of sleep mechanisms.

In visual scoring an individual with a good physiological background on sleep characteries the polygraphic records (for 30 seconds epoch) based on criteria that have been standardized for sleep staging. The scoring entirely depends upon individual insight into records and the standard sleep stage criteria applied. The visual scoring as a recording from various scorers could be different due to both the different application of standardized rules and the real difficulty in scoring the data with the standardized rules. Table 1 displays the data of a Inter-rater agreement of sleep stage scoring. Automatic scoring also results in small differences when the test is repeated on the same data which could be due to difficulties to precisely calibrate the amplitude of the signal with the available interface and also exactly assigning the same starting and end points. Except during critical evaluation these differences are accepted. Automatic scoring demands very strict recording conditions in order to avoid a confusion of the records by extraneous frequencies due to cardiac or respiratory activity or other phenomena which are not directly related to EEG activity. An additional drawback with manual scoring is that quantitative information concerning the frequency and density of specific waveforms is lost. Such wave count data are useful in assessing specific experimental interventions when the

Table 1 Inter-rater agreement of sleep stage scoring

		Scorer 1						
		W	1	REM	2	3	4	% agreement
Scorer 2	W	607	19	6	0	1	0	95.9
	1	80	496	90	44	0	0	69.9
	REM	9	38	2080	8	0	0	97.4
	2	2	63	103	4463	96	0	94.4
	3	0	0	0	274	940	141	69.4
	4	0	0	0	10	100	1288	92.1
% agreement		87.0	80.5	91.3	93.0	82.7	90.1	90.1

occurrence of dissociated or novel states render standard criteria for global assessment meaningless.

Although conventional sleep-wake stage scoring yields less extensive data than what is possible with computerized processing, the former has been more broadly studied. Visual scoring is considered as a reference for Automatic Scoring. When an algorithm is developed to score the data automatically, it is generally compared with the results obtained through visual scoring to check the performance of the algorithm. Fig 1. shows a [1] of a Barchart which depicts the performance of a Automatic scoring technique with Visual Scoring.

The edge that Automatic Scoring has over the Visual Scoring are the number of methods that are available for analysis. The Visual Scoring works only on the standard set of criteria that are defined, while Automatic Scoring employes methods like Period-Amplitude analysis, EEG power spectra analysis, amplitude analysis of EEG and EMG etc. The constant rhythmicity of the sleep cycle from day to day is a suitable physiological parameter for pharmacological studies. The use of Automatic data analysis of cortical or subcortical EEG recordings will provide a greater understanding of both physiological events and pharmacological effects. Keeping in mind the size of the test sample, the automated sleep analysis system has achieved a satisfactory performance level and may be considered as a useful alternative to visual sleep stage scoring for large scale investigation of sleep in man.

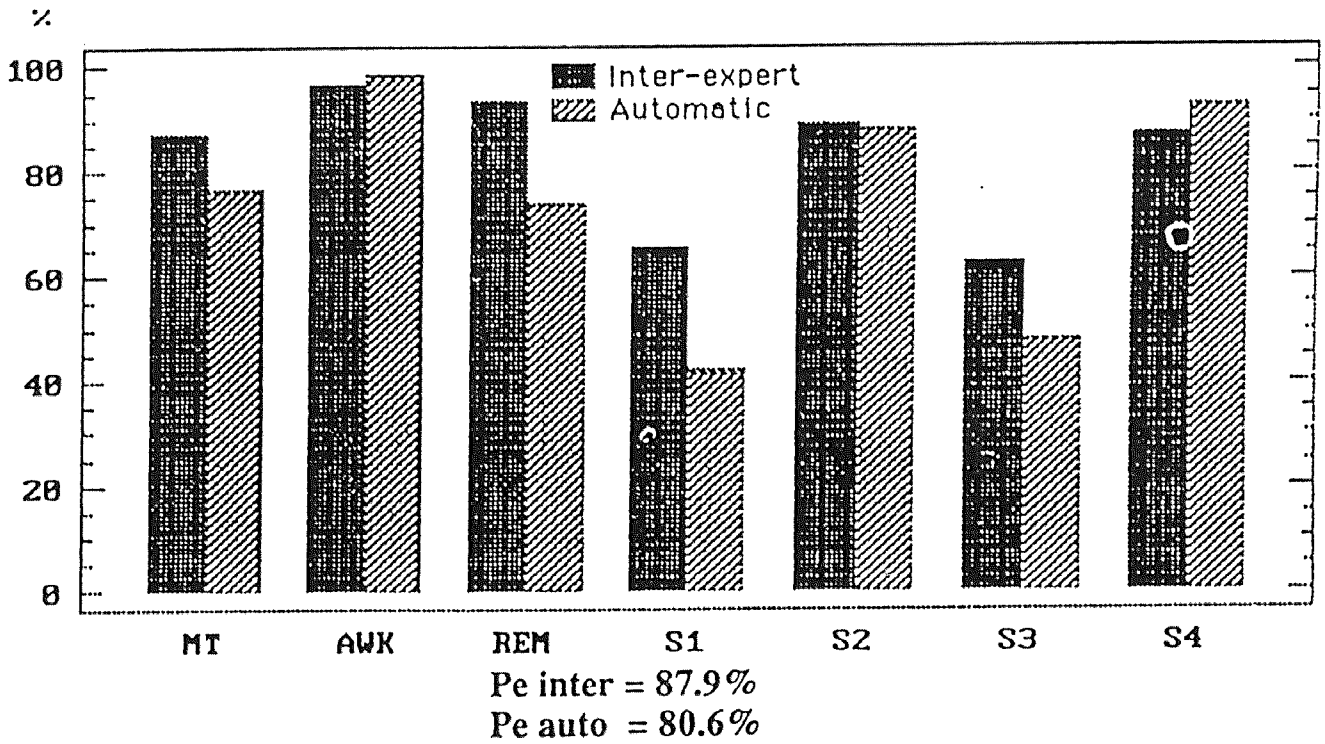

Figure 1 Interexpert and Computerized scoring agreement.

CHAPTER 2

SCORING AND ITS CRITERIA

2.1 Standard methods of data collection

Data should be acquired from the subject for further analysis and one has to follow a method for the same. Different techniques have to be employed to acquire different parameters depending on their characteristics. Without some standard procedures it would be useless to analyze the data with respect to designation criteria and scoring criteria. The standard methods employed for the data collection are listed below [7].

2.1.1 EEG Recording

With the polygraphic tracing to record EEG a minimum paper speed of 10mm/sec is recommended as the slowest which will permit clear visual resolution of alpha and sleep spindle frequency. Time constants shorter than 0.3 seconds should be avoided. A minimal pen deflection of 7.5 mm for 50 microvolts is recommended; otherwise low amplitude sleep spindles may escape detection. Electrode resistance should not exceed 10K ohms at the beginning of recording.

EEG patterns, and therefore the scoring stages, may vary according to electrode placement and derivation. Ideally, a standard array, might include a large number of placements which would yield comprehensive regional information. However, regional differences are not critical for the scoring of sleep stages, except in so far as certain critical types of activity, i.e., alpha, vertex sharp waves, sleep spindles, K complexes, and delta waves are adequately registered. EEG information is limited to one channel and the recommended

derivation is C4/A1 or C3/A2 which is shown in Fig 2. Either the left or right side may be used, since the EEG patterns from homologous areas are generally synchronous. Sleep spindles, K complexes, and vertex shapes are clearly recorded from the C3 or C4 placements, and high voltage slow waves show maximal or nearly maximal if the referent maximizes interelectrode distance. Although alpha rhythm is better recorded from occipital areas, there is adequate registration at C3 or C4 to permit a precise evaluation of sleep onset according to EEG criteria. The opposite ear or mastoid placement is also used as the recommended reference for electrodes that record eye movement potentials. In addition to use of the ear or mastoid reference maximizes interelectrode distance and avoids mixing activity from two different scalp areas.

Sleep stages may be adequately scored using EEG information obtained from the recommended derivation. If multiple channel of EEG information can be recorded, and special studies make additional derivations desirable, the results from the additional placements should be compared with the results from C3/A2 and the C3/A2 potentials should be considered as reference. The EEG criteria for scoring sleep stages should always be based on tracings obtained from C4/A1 or C3/A2. A schematic illustration of these electrode placements is also shown in Fig 2 [7].

2.1.2 Eye movement recording (EOG)

To eliminate the confusion between eye movement potential and other signals which resemble them, at least two channels are necessary for recording eye movements. The recommended procedure is to record on one channel the potentials from an electrode approximately 1 cm above and slightly lateral to the outer canthus of one eye an a reference electrode on either the homolateral ear lobe or mastoid. On the second eye movement channel are recorded the

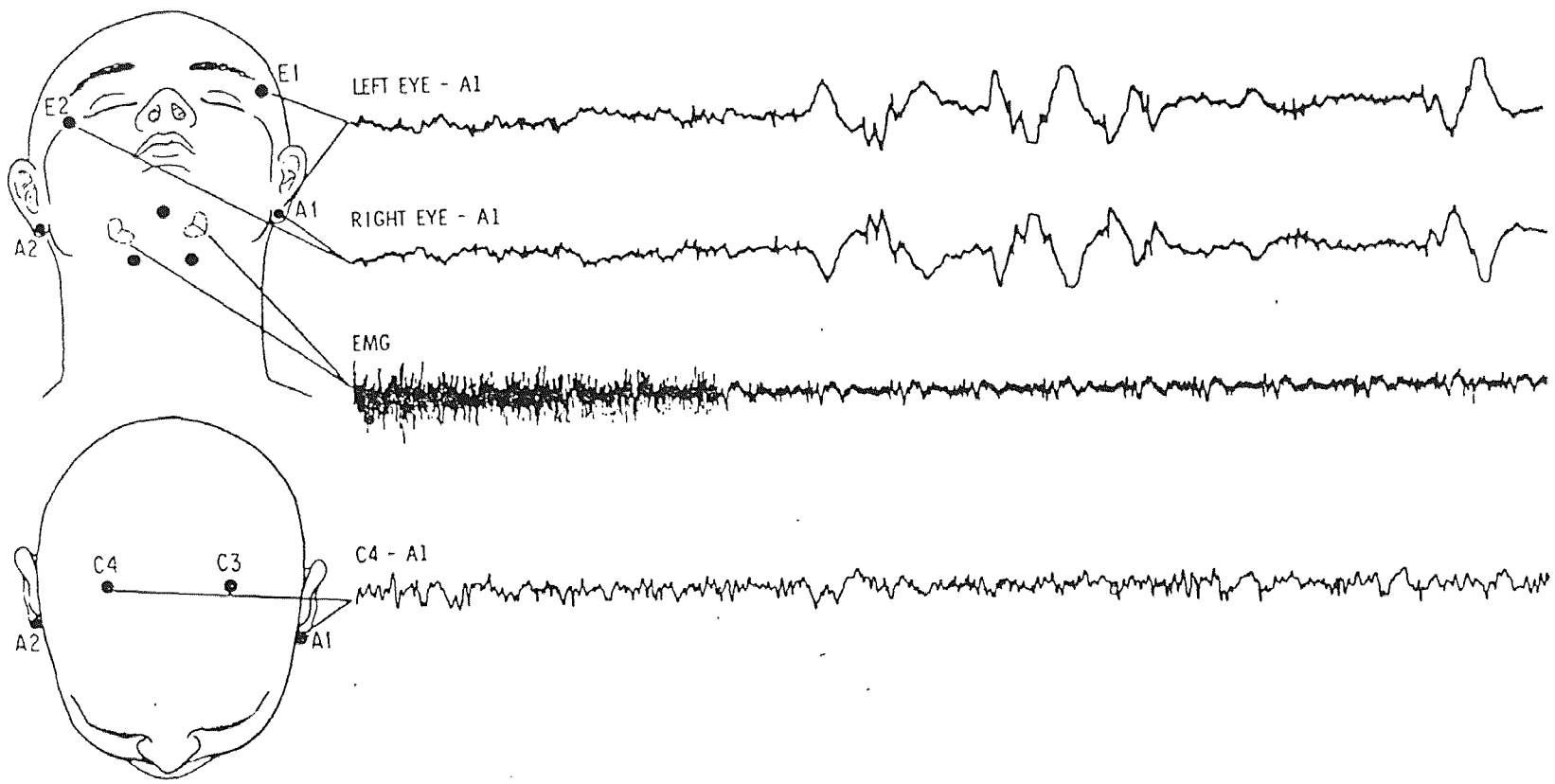

Figure 2 Electrode placements and standard waveforms

potentials from an electrode 1 cm below and slightly lateral to the outer canthus of the other eye referred to the contralateral ear or mastoid, i.e., both eyes are referred to the same ear or mastoid electrode.

When a specific information about the size and direction of eye movements is required, a four channel arrangement is suggested where electrodes horizontal to the outer canthi as well as infraorbital and supraorbital electrodes are each paired with the same ear or mastoid electrode and accorded a separate channel. DC recording is preferred when eye position is required. Time constants less than 0.3 seconds and a minimum gain of 7.5 mm for 50 microvolt is recommended.

2.1.3 EMG Recording

EMG has a major role in scoring of stage REM and the data is collected from the muscle areas on and beneath the chin. A gain of 20 microvolt/cm is preferred as the tonic activity is low during sleep. To avoid the noise a time constant of 0.1 sec or faster should be used. The type of electrodes, their position and firm contact with the skin are the critical factors in obtaining a good EMG.

2.2 Sleep Stages and their characteristics

From the research it is evident that sleep is not a steady state and that the sleep stages follow a fairly orderly cyclic pattern. The conceptualization of sleep stages or stages is based on the assumption that different physiological signs appear simultaneously for a certain period of time, displaying a specific and recognizable pattern [8]. This pattern is assumed to be unique and invariant for a certain time interval which lasts until a different unique pattern has been established. Since states or stages are conceptualized as discrete entities, they may successfully be used to represent the underlying physiological processes if

these processes consist of clearly discernible states with abrupt state changes. While knowledge of the significance of each stage of sleep is incomplete, specific physiological and behavioral correlates of the various have been found. These and other correlate may eventually provide more meaningful descriptions of sleep than the stages described in the following section [7] which emphasizes the EEG changes.

1. **Stage W** corresponds to the waking state. It is characterized by alpha activity and or a low voltage, mixed frequency EEG. Certain subjects may show little or no alpha activity and others may display a continuous alpha record. In this stage one can notice a high tonic EMG and often REM's and eye blinks are present in the EOG's tracing.

2. **Stage 1** is defined by a relatively low voltage, mixed frequency EEG with a prominence activity in the 2-7 Cps range. The term relatively low voltage refers to no rhythmic activity above 10 microvolts and no activity above 20 microvolts. This is required as the same pattern appears in stage REM. Stage 1 occurs most often in the transition from wakefulness to the other sleep stages or following body movements during sleep. During nocturnal sleep stage 1 tends to be relatively short, ranging from about 1 to 7 min. High amplitude vertex sharp waves of the order of 200 microvolts do appear later portions of the stage. Scoring of stage 1 requires an absolute absence of K complexes and sleep spindles. Sleep spindles are the rhythmic bursts that are clearly visible for at least 0.5 sec. Stage 1, especially following the wakefulness, is characterized by the presence of slow eye movements, each of several seconds duration, which are usually most prominent during the early portions of the stage. Rapid eye movements are absent. Tonic EMG levels are usually below those of relaxed wakefulness. The transition from an alpha record to stage 1 is characterized by decrease in the amount, amplitude, and frequency of alpha activity. When the

amount of record characterized by alpha activity combined with low voltage activity drops to less than 50% of the epoch and is replaced by relatively low voltage, mixed frequency activity, the epoch is scored as stage 1.

3. **Stage 2** is defined by the presence of K complexes and the absence of sufficient high amplitude, slow activity to define the presence of stages 3 and 4. The presence of a sleep spindle should not be defined unless it is of atleast 0.5 sec duration i.e., one should be able to count 6 or 7 distinct waves within the half-second period. K complexes are defined as EEG waveforms having a well delineated negative sharp wave which is immediately followed by a positive component. The total duration of the complex should exceed 0.5 sec. K complexes can occur as a response to a sudden stimuli, but they also frequently occur in the absence of any detectable stimuli. If the interval without sleep spindles or K complexes lasts 3 min or longer, the interval is scored as stage 1. If movement arousals or increases in muscle tone do occur during the interval, the piece of record prior to them should be scored as stage 2.

4. **Stage 3** is defined by an EEG record in which at least 20% but not more than 50% of the epoch consists of waves of 2 Cps or slower which have amplitudes greater than 75 microvolts from peak to peak. In actual practice, it will be necessary to make wave by wave measurements only for the epoches with borderline amounts of high amplitude, slow activity, i.e., about 20% and 50%. Differentiation between stage 3 and 4 can be made by comparison with the tracings shown in Fig 3 and Fig 4.

5. **Stage 4** is defined by an EEG record in which more than 50% of the epoch consists of waves of 2 Cps or slower which have amplitudes greater than 75 microvolts peak to peak. Intervals of lower amplitude, faster activity rarely persist for more than a few seconds in stage 4, but are usually prominent in stage 3 epoches.

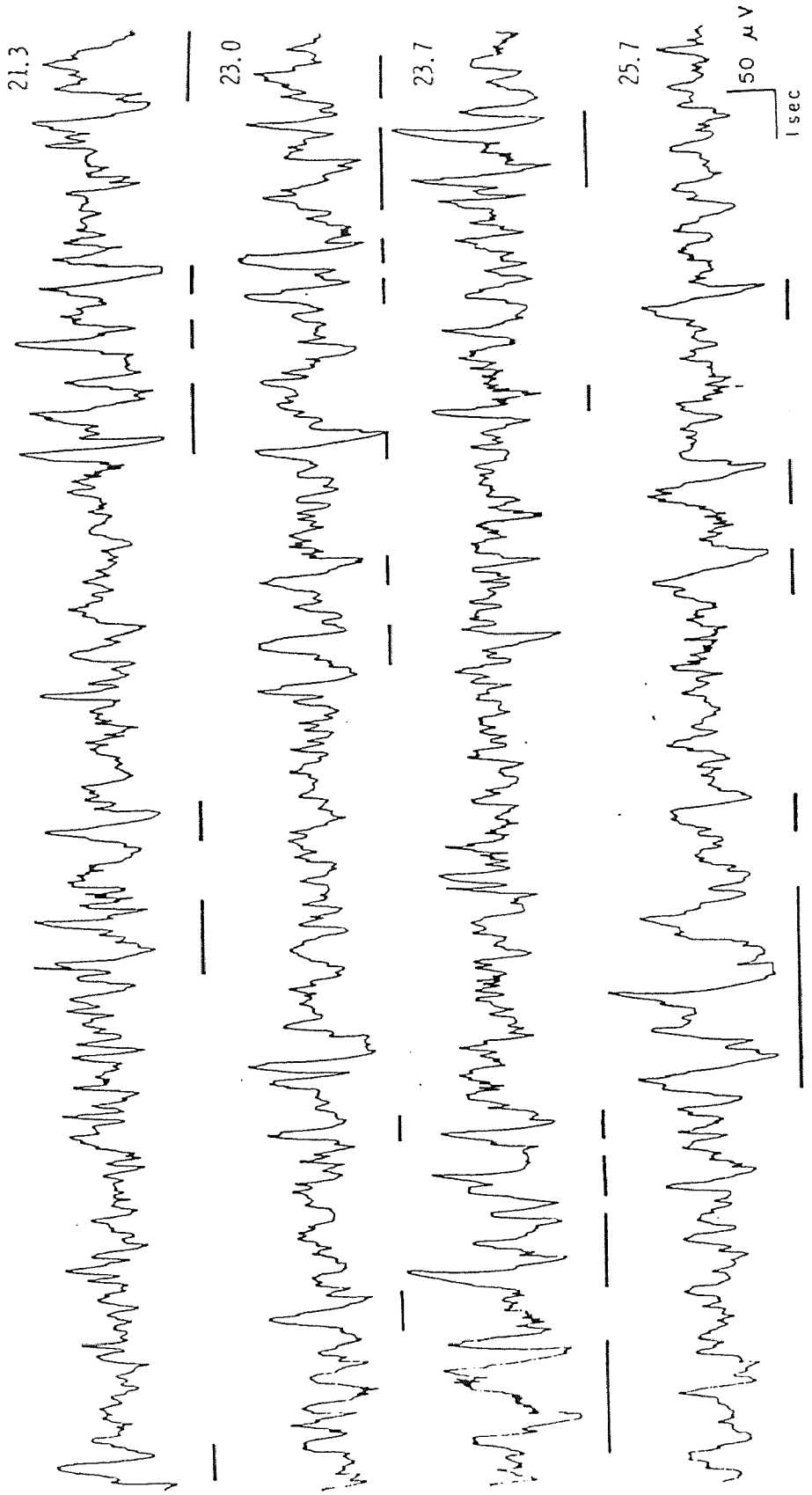

Figure 3 Standard tracings of sleep EEG in stage 3 for four continuous 30sec epoches

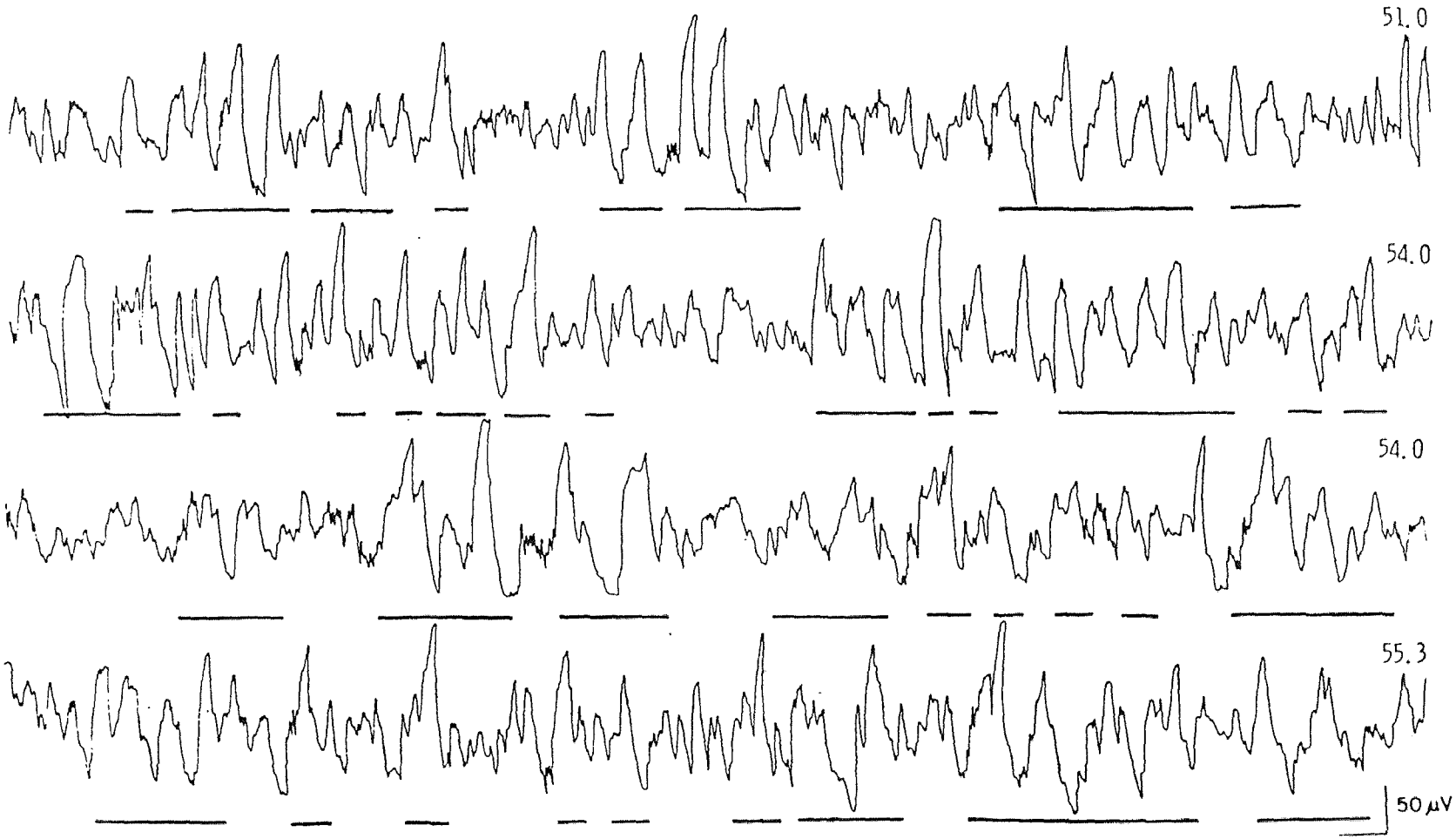

Figure 4 Standard tracings of sleep EEG in stage 4 for four continuous 30sec epoches

6. **Stage REM** is defined by the concomitant appearance of relatively low voltage, mixed frequency EEG activity and episodic REMs. The EEG pattern resembles the one described for stage 1, except that vertex sharp waves are not prominent in stage REM. Alpha activity is usually somewhat more prominent during stage REM than during stage 1, and the
frequency is generally 1-2 Cps slower than during wakefulness. Sleep spindles and K complexes are absent in this stage.

Stage REM should not be not be scored in the presence of a relatively elevated tonic mental-submental EMG. EMG tonic levels reach their lowest levels during the stage REM. These low levels may not be reached during other stages, but they are reached during unambiguous REM periods. Therefore, a low amplitude EMG contributes little to the scoring of sleep stages, but the presence of relatively elevated tonic EMG contributes to scoring information by precluding the scoring of stage REM.

At some stage there are situations where in sleep spindles are interspersed with REMs. During these situations the record is scored as REM if the EEG has relatively low voltage and EMG is at the REM level. If the record displays mixed frequency EEG between two sleep spindles or K complexes it is scored as stage 2 regardless of EMG level.

The major problem in scoring the stage REM is the determination of the precise points at which REM periods begin and end. This problem arises primarily from the fact that three indicators, EEG, EOG, and EMG activity, which are used to define stage REM may or may not change simultaneously. Rules for starting of the stage REM are schematically illustrated in Fig 5. The starting of the stage REM are identified by the following.

a. EEG changes to a relatively low voltage, Sleep spindles and K complexes stop.

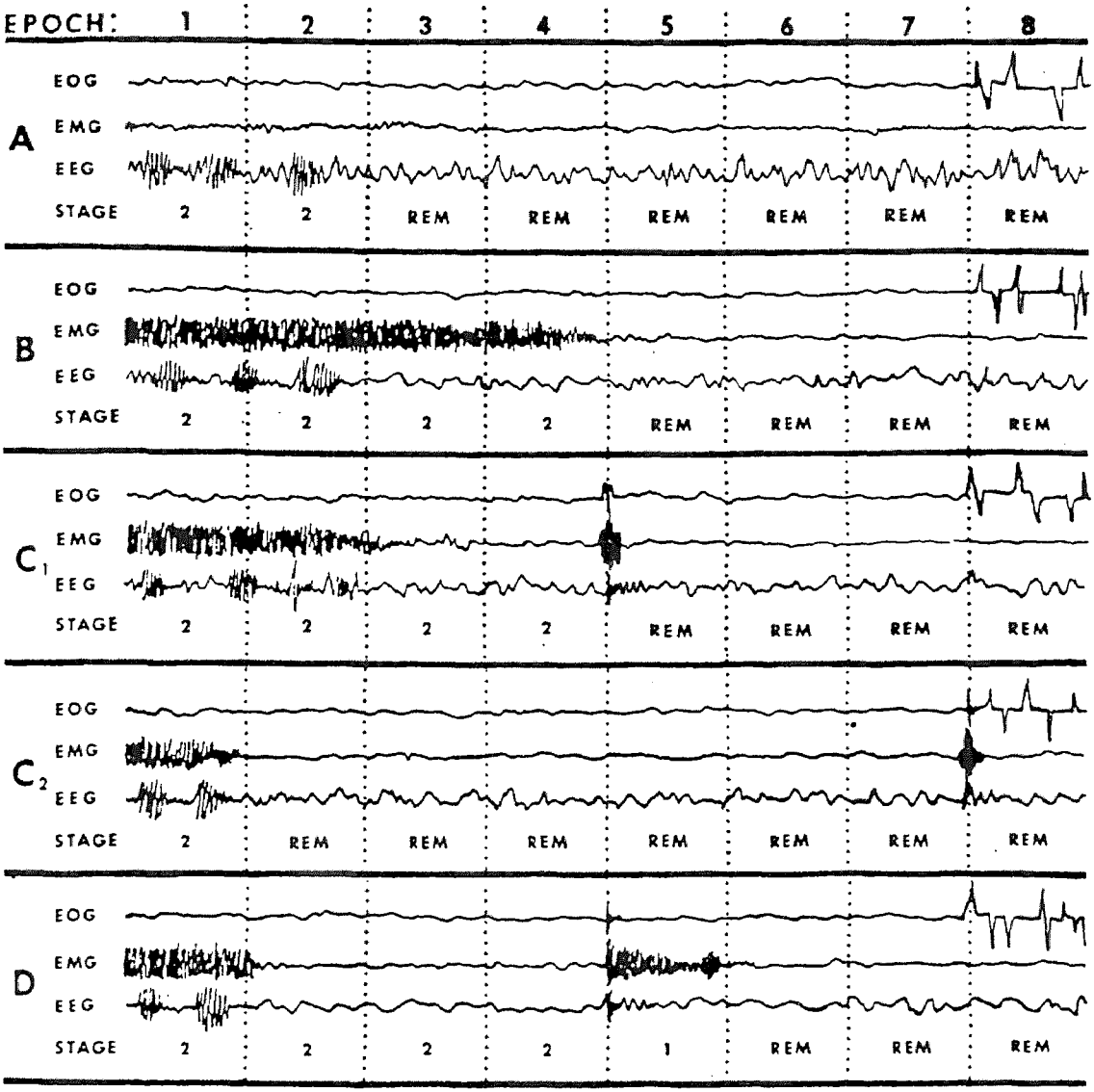

Figure 5 Illustrations of rules for scoring the start of REM

b. EMG amplitude drops. The record is scored as REM only at the instance where both the above said changes are noticed.

c. Whenever movement arousals appear the EMG activity is considered important as otherwise with high tonic EMGs those epoches are scored as stage 1.

The end of the stage REM is dictated by the following and it is schematically illustrated in Fig 6.

a. An interval of relatively low voltage, mixed frequency EEGs with an elevated EMG when compared to REM value.

b. There arises ambiguity when the movement arousals appear in the stage REM as to score the epoch as stage1 or REM stage. During these situations slow eye movements that are characteristic of stage 1 are considered as reference.

The above explained stages and the criteria for scoring are used as a reference by all sleep researchers, and further criteria have been added over the years by researchers throughout the world. Today sleep researchers are still busy in finding new methods and criteria for scoring to understand the enigma of sleep as it opens doors for the future research.

2.3 Scoring Methods

Various methods have been designed to score the data according to the rules explained in section 2.2. The methods devised depends on the application and the extent of analysis. Following are some of the methods adopted by several researchers to score the signal.

Paper Scoring [9] uses 20 sec epoches and follows the scoring rules explained in the previous section. The results totally depend on the scorers indepth knowledge and the rules he is applying. Paper scoring required 3 hours/polysomonogram, which averaged 8.4 h in length.

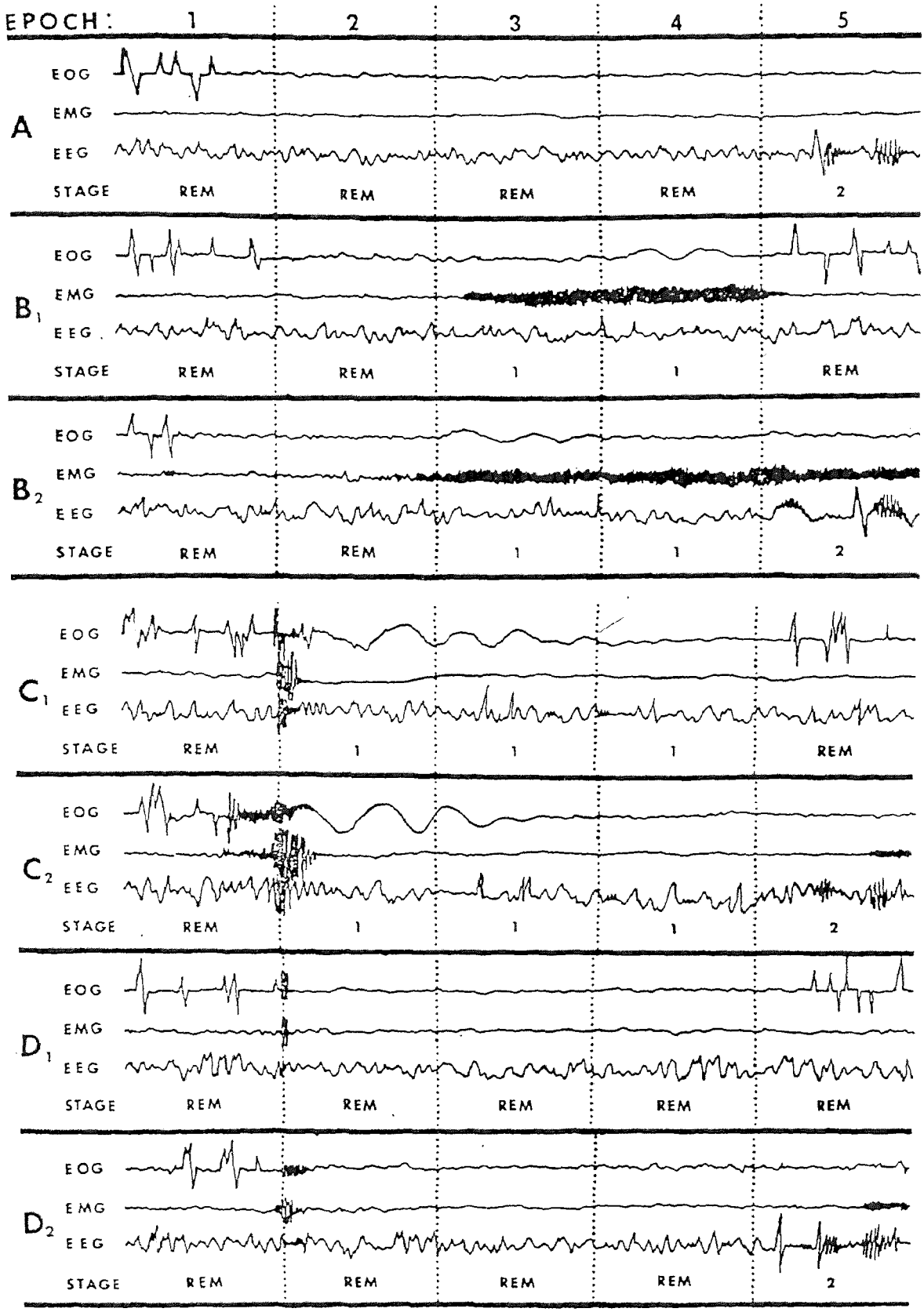

Figure 6 Illustrations of rules for scoring end of stage REM

Screen-by-Screen [9] scoring method closely paralleled for conventional paper scoring and involved scoring each individual 16-s epoch displayed bye the scanner. A sleep stage was assigned to each specific 16-s epoch. The scorer advanced the tape by paging forward, which advances the tape by 16-sec epoches. However, during periods in which the subject stayed in the same sleep stage for an extended period(e.g., during an extended awakening), the scorer reviewed the tape at 20 times the recorded speed and stopped the tape when the sleep stage has changed. The EEG signal amplitude used on the scanner is usually of the order of 5 microvolt/mm. Thus in scoring slow-wave sleep a deflection greater than 15 mm was required for scoring a delta wave. This scoring method required 3-4 h/polysomnogram.

In **Rapid Screen** [9] scoring the scorer played the tape at 20 times the recorded speed and noted the time of occurrence of sleep stage changes. Changes in sleep stage less than one minute were ignored. The scorer was free to stop the tape and further review and/or reply any portion of the tape that proved difficult to score. Sleep parameters were calculated by hand based on the recorded time of sleep stage changes. Movement time is not scored here and is tallied as a brief arousal. Including stops, replays, and calculation of sleep parameters, rapid screen scoring required an average scoring time of 1h/polysomnogram.

Friedman and Jones [10] generated scoring rules through their **Cluster analysis algorithm**. It was based on amplitude analysis of EEG and EMG, along with PGO spike rates to stage the sleep. An advantage of this system is its ability to adjust amplitude and period windows to obtain maximal agreement between visual and computer counts of PGO waves.

Neural Networks [1] have also been employed for staging. Multilayer neural network has been applied to all-night sleep stage scoring. The learning set is built from 12,455 sleep epoches extracted from 12 all-night sleep recordings.

CHAPTER 3

MATERIALS AND METHODS

3.1 Techniques of Signal Processing

3.1.1 Random Process Variables

A phenomenon is considered Random when each observation of the same is unique which cannot be described by an explicit mathematical relationship. In other words, any given observation will represent only one of many possible results which might have occurred.

Random processes may be categorized as being either stationary or nonstationary. The random process is said to be nonstationary if the mean value and the joint moment values vary with time. For special cases when mean and the joint moment do not vary as time varies, the random process is said to be weakly stationary or stationary in a wide sense [11]. When all possible moments and joint moments are time invariant, the random process is said to be strongly stationary. Four main types of statistical functions are used to describe the basic properties of random data.

1. Mean square value

The mean square value tries to describe the intensity of data. It is simply the average of the squared values of the time history. The mean square value for a sample time history $x(t)$ is given by

$$\Psi_x^2 = \lim_{T \to \infty} 1/T \int_0^T x^2(t)\, dt$$

Physical data is a combination of time-invariant component and a fluctuating component. The static component can be described by the mean value and

dynamic component by the variance which is the mean square value by the mean.

2. Probability density function

Probability density function furnishes the properties of data in the amplitude domain. It tries to describe the probability that the data will assume a value within some defined range at any instant of time. The probability that a sample time history $x(t)$ assumes a value within the range between x and $(x + \Delta x)$ may be obtained by taking the ratio of T_x/T, where T is the total amount of time that $x(t)$ falls inside the range $(x, x + \Delta x)$ during an observation time T. The probability density function $p(x)$ can defined as

$$p(x) = \lim_{\Delta x \to 0} \lim_{T \to \infty} 1 / T \left(T_x / \Delta_x \right)$$

The principal application for a probability density function measurement of physical data is to establish a probabilistic description for the instantaneous values of the data.

3. Autocorrelation Function

The autocorrelation function for random data describes the general dependence of the values of the data at one time at the values at another. An estimate for the autocorrelation between the values of a sample time history record $x(t)$ at times t and $t + \tau$ may be obtained by taking the product of the two values and averaging over the observation time T. The autocorrelation function can be represented mathematically as

$$R_x(\tau) = \lim_{T \to \infty} 1 / T \int_0^T x(t)\, x(t+\tau) dt$$

The autocorrelation function can be used to establish the influence of values at any time over values at a future time. Autocorrelation measurement clearly

provides a powerful tool for detecting deterministic data which might be masked in a random background.

4. Power spectral density function

Power spectral density function for random data describes the general frequency composition of the data in terms of the spectral density of its mean square value. A band-pass filter can be used to find the mean square value of a sample time history in a frequency range between f and $f + \Delta f$. The power spectral density function can be represented as

$$\Psi_x^2[\, f, f+\Delta f\,] = \lim_{T\to\infty} 1/T \int_0^T x^2(t, f, \Delta f)dt$$

Power spectral density function is used to establish the frequency composition of the data which inturn bears an important relationship to the basic characteristics of the physical system involved.

The processing techniques and the statistical formulas normally don't apply when the data is nonstationary. Special considerations and procedures are required for such analysis. Electroencephalograms tends to be nonstationary. Physical occurrence of nonstationary data can be represented by three parameters.

1. Time-varying mean value

For a nonstationary data the mean values can be estimated using a computer. If N sample functions $x_i(t)$; $i=1,2,3.....N$ represent a nonstationary process $x(t)$, the estimate of mean value will vary over different choices of the N samples. One must investigate how closely an arbitrary estimate will approximate the true mean value. This can be done in two steps. The first step is to obtain mean value for each record $x_i(t)$ as a function of t. After this has been done for N samples, the average is found out by adding the records together and dividing by N.

2. Time-varying mean square value

The same analysis given for the time-varying mean is carried out to determine the variation of nonstationary mean square value.

3. Time varying power spectra

The time-averaged power spectrum can be used for describing the time varying spectral characteristics of an important special class of nonstationary random processes which possess the following characteristics [11].

1. The lack of stationarity is due to deterministic time trends which are represented in every sample function.
2. The time trends are very slow relative to the instantaneous fluctuations of the data.

3.1.2 Transforms and their Applications

It is well known that when a quantity varies periodically with time it may be `Analyzed into its Harmonic components'. The variation in these quantities repeats itself at some basic frequency and the disturbances having repetition frequencies equal to the multiples of the basic frequency. Time and frequency appear as a related pair of variables in all these cases. Transformation is a technique used to change the representation of a parameter from one domain to another.

a. Fourier & Fast Fourier transforms

The basic essence of Fourier transform of a waveform is to decompose or separate the waveform into a sum of sinusoids of different frequencies. Figure 7 illustrates this interpretation. The pictorial representation of the Fourier transform is a diagram which displays the amplitude and frequency of each of the determined sinusoids [12]. Mathematically, this relationship is stated as

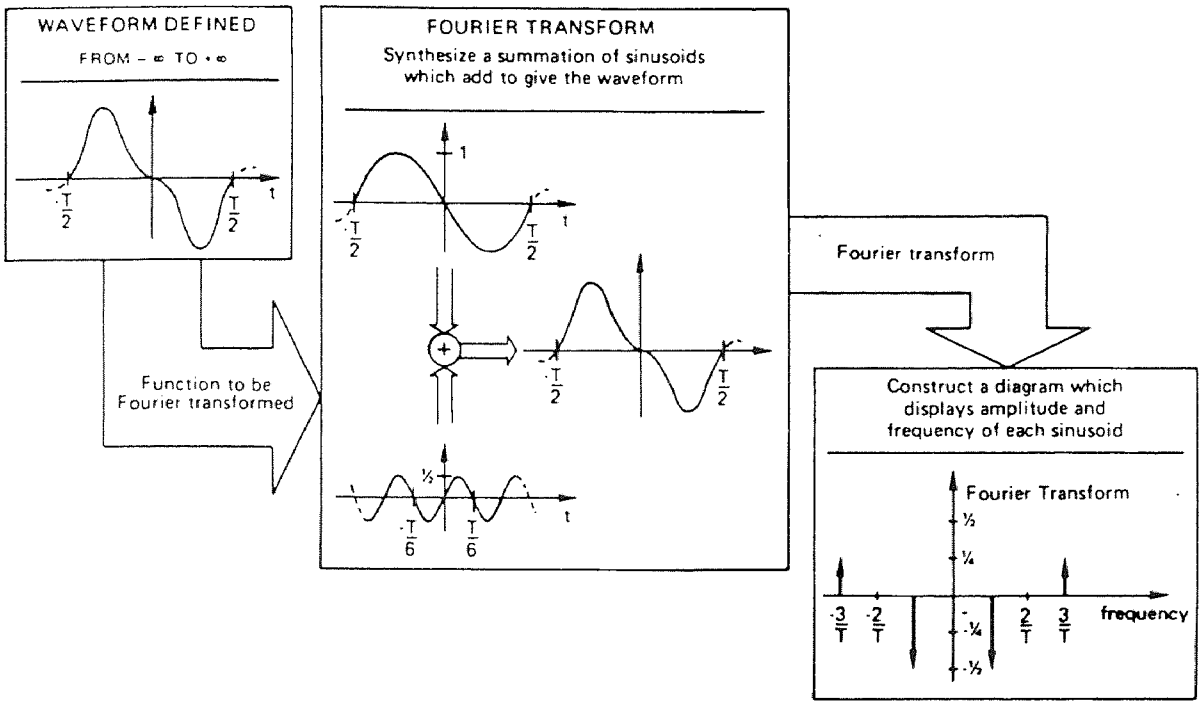

Figure 7 Interpretation of the Fourier Transform

$$s(f) = \int_{-\infty}^{\infty} s(t)\, e^{-j2\pi ft}\, dt$$

where $s(t)$ is the waveform to be decomposed into a sum of sinusoids, $S(f)$ is the fourier transform of $s(t)$.

If there are N data points of a function and if we desire to determine the amplitude of N separate sinusoids, then the computation time is proportional to square of N. Even for high speed computers, computation of the discrete Fourier transformation requires excessive machine time for large N.

To reduce the computational time of discrete Fourier transformation a new mathematical algorithm known as Fast Fourier transformation was developed. This algorithm reduces the speed of computation to $Nlog_2N$ times. If a computer takes half an hour to do a Discrete fourier transformation on a data with N = 8192 samples, the calculation time required by Fast Fourier transformation is only about five seconds.

b. Walsh transformation

The complete set of Walsh functions are given by the following set of equations.

$w_j(t) = 0 \quad t < 0$ and $t < 1$

$w_0(t) = 1 \quad 0 < t < 1$

$w_{2j}(t) = w_j(2t) + (-1)^j\, w_j(2t-1)$

$w_{2j+1}(t) = w_j(2t) + (-1)^{j+1}\, w_j(2t-1)$

$j = 0, 1, 2.....$

The subscript j is the 'Sequency' which has the units of the number of zero crossings per unit time(z.p.s). The first eight functions are illustrated in Fig. 8.

By analogy with the sine and cosine functions in Fourier analysis, the finite sal and cal transforms are given by [6]

$$F_s(k) = 1/N \sum_{i=0}^{N-1} f(t_i)\, sal(k,t_i)$$

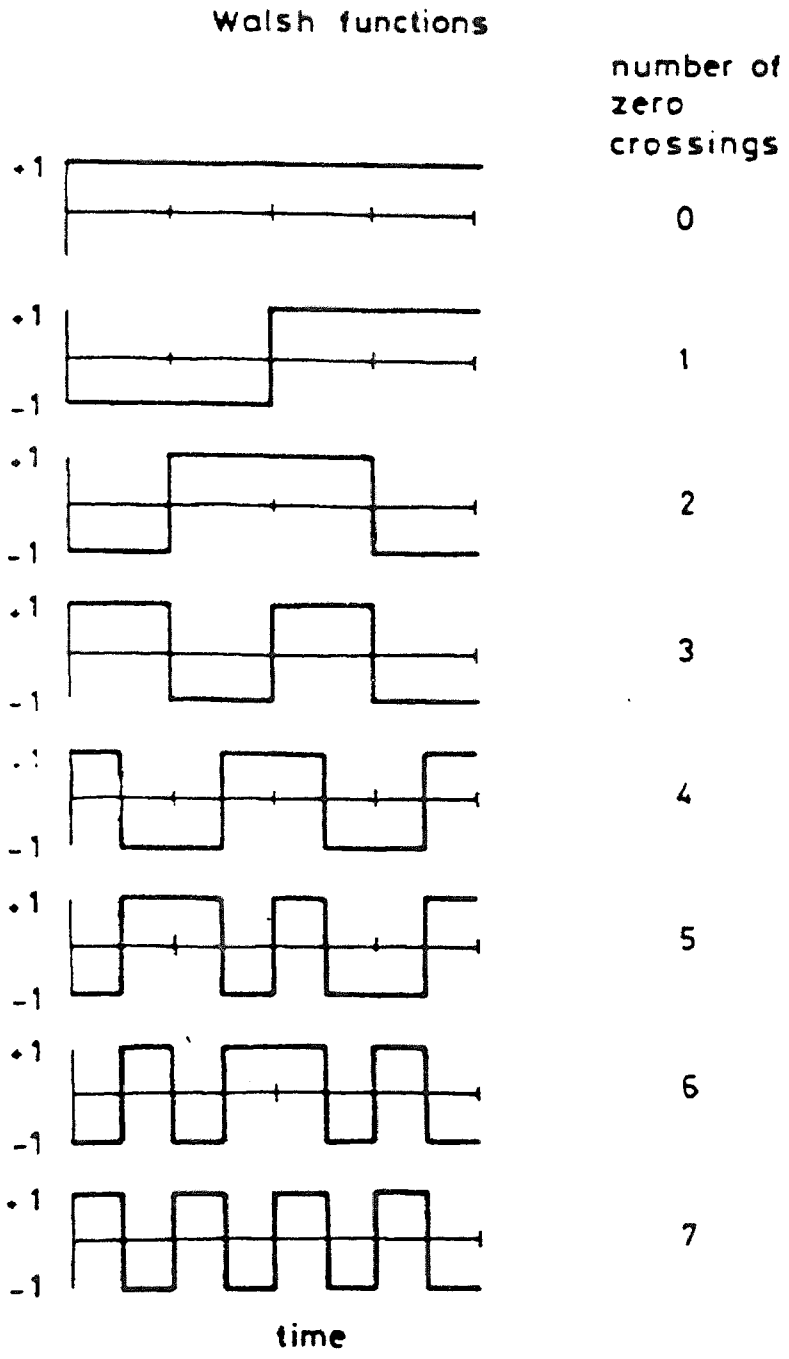

Figure 8 A set of walsh functions arranged in sequency order

$$F_c(k) = 1/N \sum_{i=0}^{N-1} f(t_i)\ cal(k,t_i)$$

where

$$sal(j,t) = w_{2j+1}(t)$$

$$cal(j,t) = w_{2j}(t)$$

Finally the Walsh power spectrum is written as

$$S(j) = F_c^2(j) + F_s^2(j).....$$

c. Haar Transform

Haar Transform like the Fourier and Walsh Transforms, form an orthogonal set of functions consisting of rectangular functions whose amplitudes assume a limited set of values: 0, 1, $\pm\sqrt{2}$, $\pm$ 2, $\pm 2\sqrt{2}$, + 4....etc. The first eight Haar functions are illustrated in Fig 9. The essential characteristic of the Haar function as shown in Fig 9 is seen as a constant value every where except in one sub-interval where a double step occurs. A given time function f(t) within the interval $0 \leq t \leq 1$ can be synthesized from the Haar series, by [13]

$$f(t) = \sum_{n=0}^{\infty} C_n\ HAR(n, t)$$

where

$$C_n = \int_{t=0}^{1} f(t)\ .\ HAR(n, t)\ .\ dt$$

Haar(n, t) is illustrated in Fig 9. From these equations, the discrete Haar Transforms and its inverse are stated as

$$F_n = 1/N \sum_{i=0}^{N-1} f_i\ HAR(n, i/N)$$

and

$$f_i = \sum_{n=0}^{N-1} F_n\ HAR(n, i/N)$$

i, n = 0, 1, 2.....(N-1)

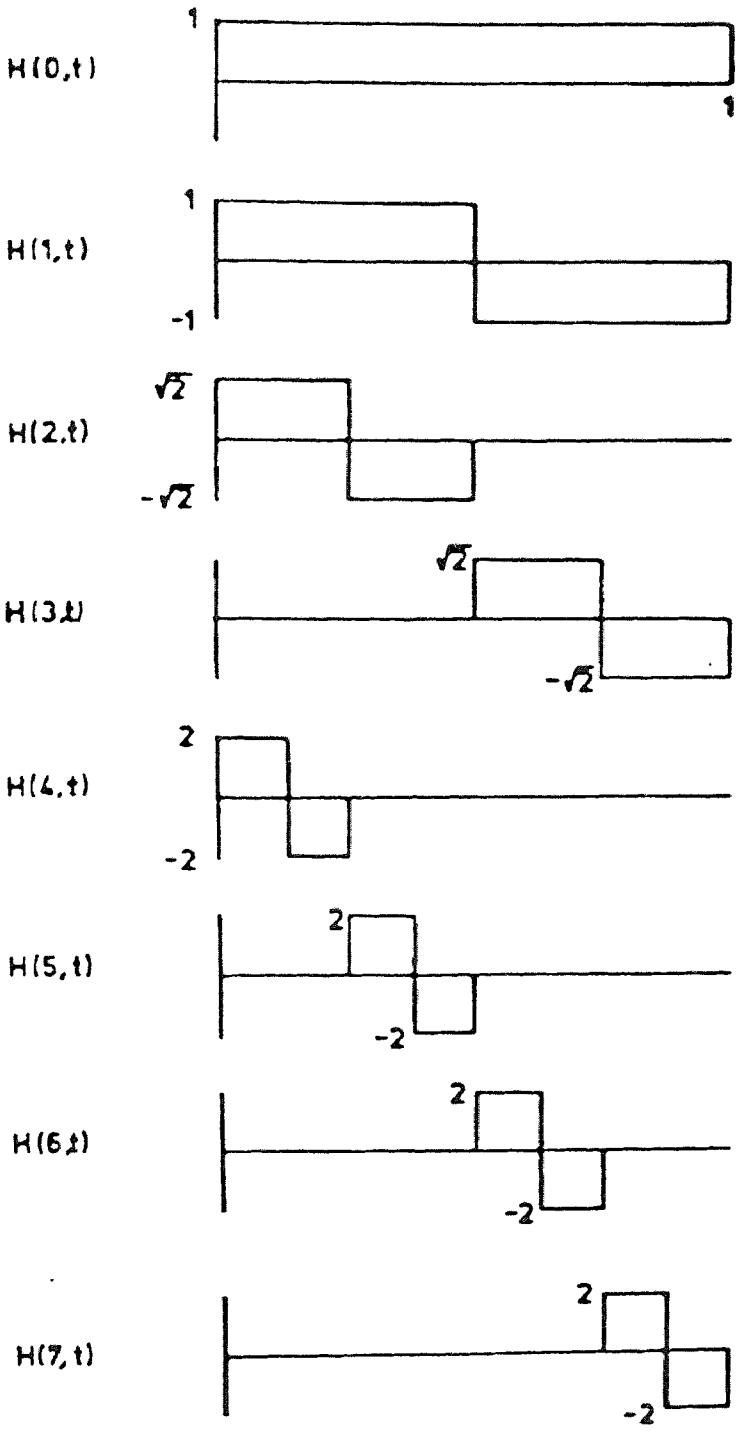

Figure 9 The first eight Haar functions

The Haar transform satisfies the Parseval's Theorem that is

$$f_2(t)\,.dt = \sum_{n=0}^{\infty} C_n^2$$

3.2 Experimental Setup

3.2.1 Subject

All-night EEGs, EOGs, and EMGs were recorded at the sleep laboratory of the Robertwood Johnson Research Center from a healthy 30-year old adult female. The recording was carried out in a sound-attenuated, ventilated, temperature-controlled room. The data was recorded by Medilog eight channel recorder for a period of six hours.

Two EEG channels (C3/A1 & C4/A1), two EOG channels (A1, one cm vertically upward from outer canthus of left eye; A1, one cm vertically downward from outer canthus of right eye), and one EMG channel (two electrodes placed on the jawbone) were used which is schematically illustrated in Fig 10. The five channel data obtained from the subject was amplified by Gould Universal amplifier with Band-pass filter across 0.3 to 100 Hz, and continuously digitized at 256 Hz by a Data Translation Board. Fig 11 shows the experimental setup.

3.2.2 Data Porting

The digitized data had to be transferred from the recording center to the Sun workstation which had the requisite tools for analysis. The binary data file, the result of a six hour five channel recording was 66MB in size. Due to nonavailability of INTERNET access at the time of this work was carried out, other means for data transfer had to be thought of. An attempt to transfer the data through an optical disk failed due to the mismatch of optical reader formats.

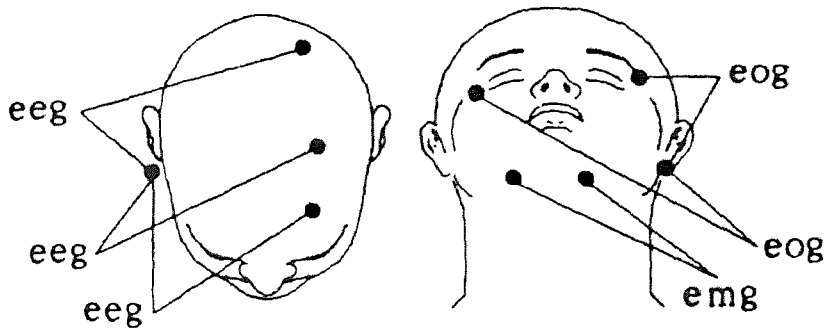

Figure 10 Electrode placement for data collection

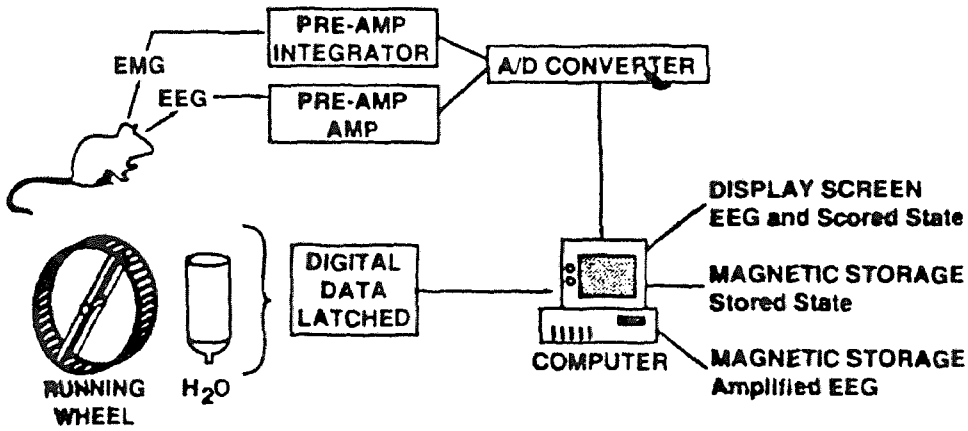

Figure 11 Experimental setup for data collection

Alternative ways of transferring were through Floppy Disks, Laptop with an ETHERNET card, Magnetic tapes etc. Storing onto floppy disks was not feasible considering the size of the data. Laplink, a package which supports the transfer of data between two computers, was used for this purpose. Laplink is a sophisticated package having capabilities to transfer any form of data. Data can be transferred to either a local or a remote machine. Local data transfer was achieved at a rate of 33Kb/sec. The data was loaded onto the Sun-Sparc Station using File Transfer Protocol. The binary file had to be converted into a readable form. The size of converted file was three times its counterpart which precluded its storage on the mainframe. Data Cartridge was employed to store the 200MB of readable data.

3.2.3 Procedure

Analysis of overnight recording of EEG, EMG, EOG was carried out on a Sun Sparc station. MATLAB was used as a tool for analysis since it was supported by sophisticated graphical and mathematical applications. Due to enormous size of the data and the computational problems, a smaller length of the signal was considered.

The data analysis was carried out using the Fast Fourier Transformation. The use of other orthogonal functions such as the Harr and Walsh was also considered, but Fourier Transform was applied in the present studies. Intially the digitized and filtered data was preprocessed by removing the DC component. The DC component inherent in the signal can be removed in two ways depending upon the type of analysis. One way is to take the mean of the epoch considered and subtracting from the epoch amplitudes. The other method is to calculate the overall mean of a signal and subtracting the calculated value from each epoch amplitudes. The signal was reduced by an amplitude factor of by

1000 to get a realistic scale. Fig 12 shows a sample signal with the above procedure applied on it.

While deciding the length of the epoch for the analysis few factors are important. The resolution one is looking for, computational capabilities, available memory space to store the results calculated etc. Considering the above factors and standardized techniques while analyzing a long stretch of data, an epoch length of thirty seconds is considered.

During the first phase of analysis an epoch of five seconds was used. Fast Fourier Transform was applied on each epoch and the individual Power Spectrums were calculated. The Fig 13 shows a sample of one of the Power Spectrums. To observe the overall frequency variations for the whole length of the signal, the calculated five second epoch spectrums were stacked. They were then plotted on a three dimensional plane with suitable frequency and time axes as shown in Fig 14.

In the real world of Fast Fourier Transforms the number of degree of freedom is a key factor in the analysis. With the first phase of analysis the Degree of Freedom was two and to increase the same to a higher number segmental averaging method was used. An epoch of thirty seconds in length was divided into fifteen segments and individual power spectrums were calculated. This resulted in the degree of freedom from two to thirty. While calculating the average Power Spectrum for an epoch the past segmental average is also considered. The calculated Power Spectrum was used as input to Scoring Algorithm.

3.2.4 Algorithm

The basic criterion used for the classification of an epoch as stage are the absolute magnitude of a sample signal and the calculated power spectrums of the epoch.

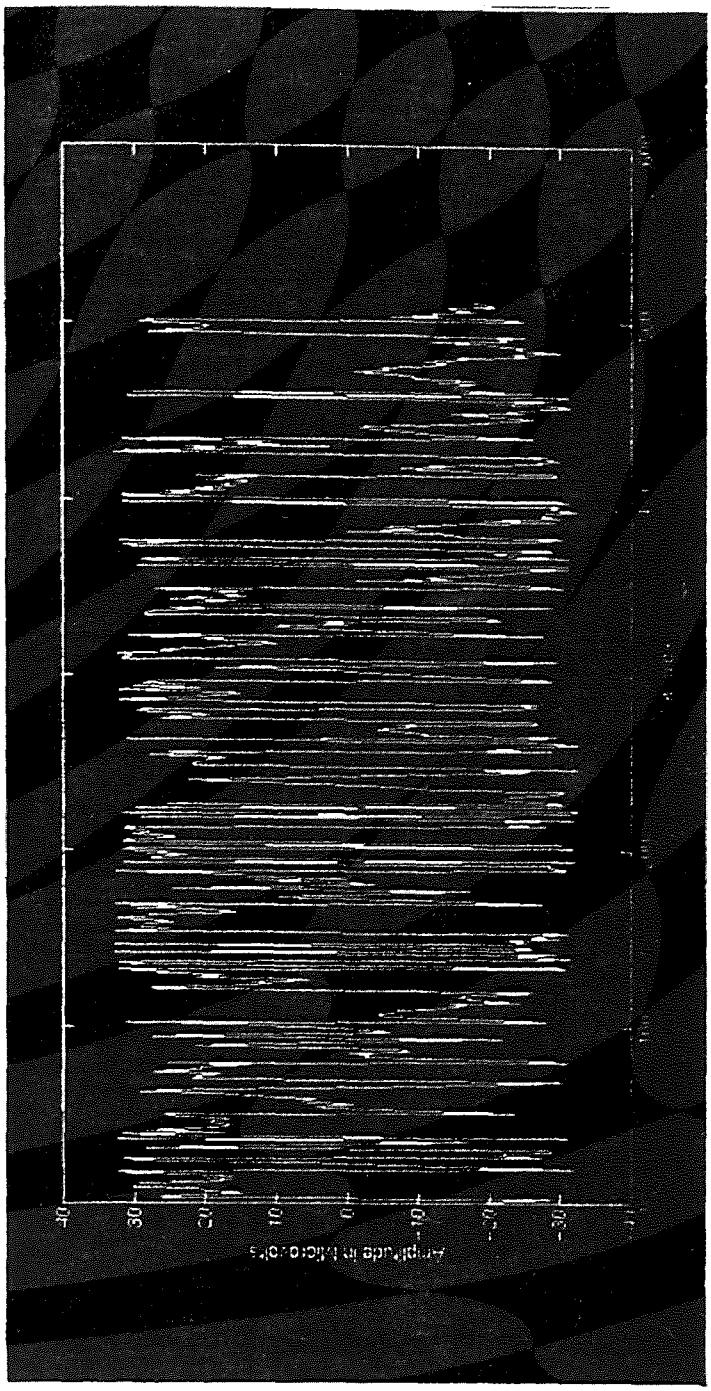

Figure 12 Sample EEG signal of two minutes used for analysis

Figure 13 Power Spectrum of EEG for a thirty second epoch

Figure 14 Three dimensional plot of power spectra of one hour EEG

In an epoch a set of five samples were used to calculate the highest frequency component. They are then compared with the next set of five samples and the process is repeated for the whole 30 second epoch.

The Algorithm is designed such that the computed highest frequency passes through conditional loops to score it as a stage. While deciding on the stages both the EEG & EMG absolute values and the percentage of occurrence of these values were considered, satisfying the basic criteria. The moving spectrum analysis was applied before concluding on the stages.

The whole signal is scored as wake, REM and NREM(subdivided as stage 1, 2, 3 and 4). The epoches which doesn't fit in any of the conditional statements are scored as stage 6. The absolute values were taken into account as the analysis demands peak-peak voltages. A time vector was generated corresponding to the number of epoches that were subjected to scoring which was used in the representation of stages on a two dimensional plane. Due to computational difficulties EOG could not be incorporated in the analysis. This Algorithm does not take in to account the appearance of K-complexes and the sleep spindles. Fig 15 and Fig 16 shows the Algorithm output for whole length of the data and with the time scale expanded respectively. Table 2 shows a list of criteria considered for this analysis. A flowchart has been shown in Fig 17 which explains the whole process. The conditional loops have been clearly shown with the absolute magnitude values and the frequency at which signal has to be present to score it as a stage. The algorithm doesn't detect the presence of K-complexes and sleep spindles. The percent factor in the flow chart refers to percentage of the epoch which satisfies the necessary criteria for that stage. The Algorithm was developed using the combined features of MATLAB and the object oriented language C++.

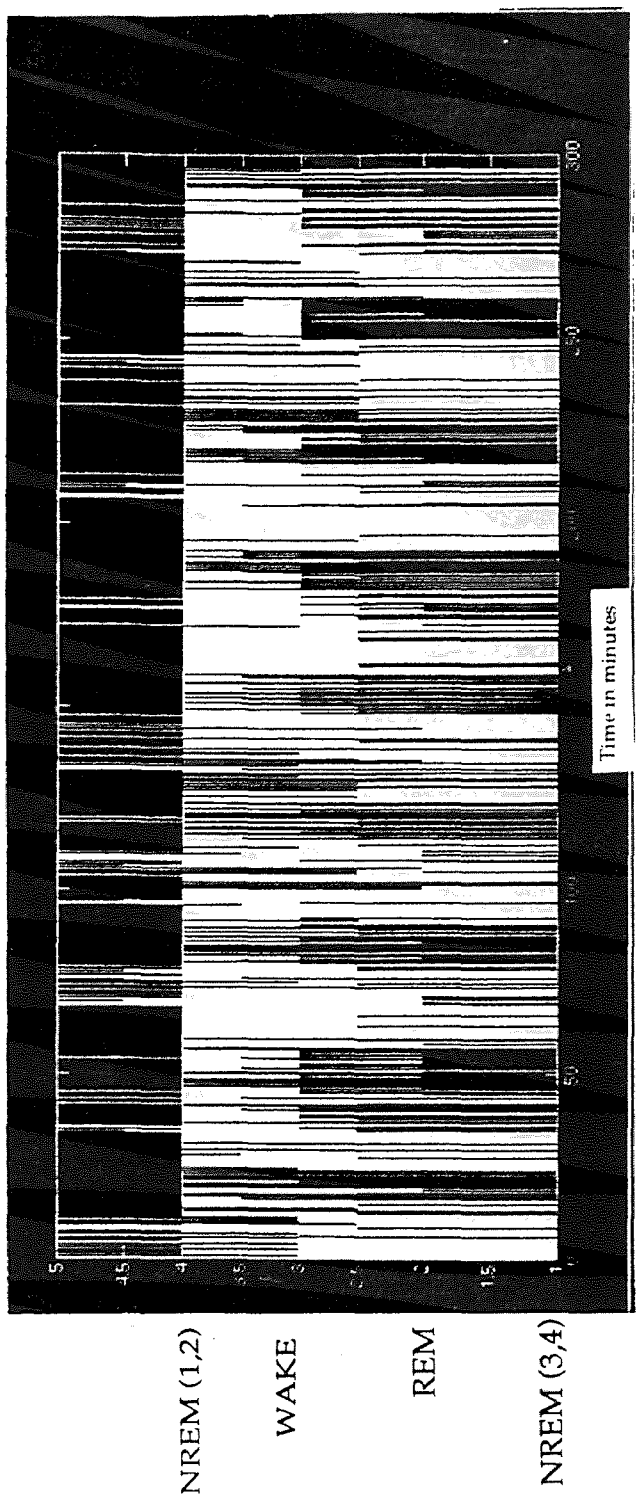

Figure 15 Algorithm output for five hours of data

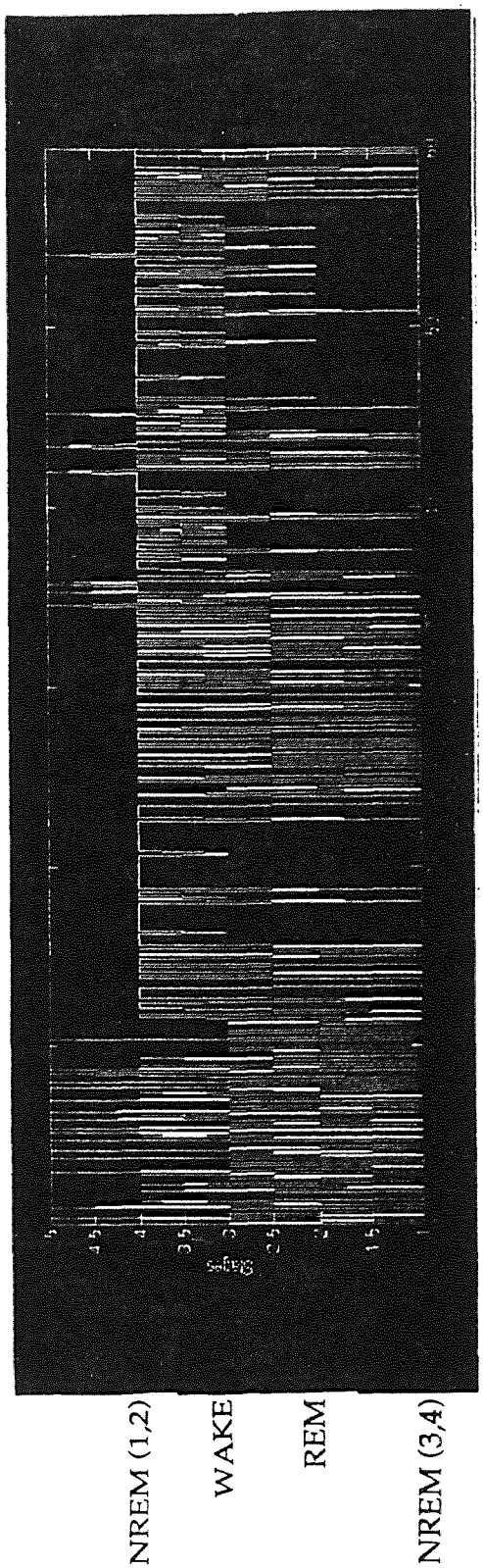

Figure 16 Algorithm output for first one hour of data

Table 2 Summary of criteria used for scoring

	EEG	EMG	EOG	% Epoch
STAGE WAKE	8-13Hz. Alpha activity is found over much of epoch. Waves around 20-30mmV	Not high - around 10mmV	Present	50%
STAGE 1	2-7Hz. Much activity around 3-4Hz. Low voltage during initial stages (10-20mmV) and vertex sharp waves during later portion of the epoch (75-200mmV)	Lower than wake	Slow eye movements, only during beginning of stage and are absent later. REMs absent	70%. Spindles and K complexes absent
STAGE 2	Vertex sharp waves are abundant with 2-7Hz. Sleep spindles and K complexes might be present. 75-200mmV	That of stage 1	Eye movements present	If sleep spindles do not appear for more than 3 min. in an epoch it is scored in stage 1
STAGE 3	2Hz. or slow wave with greater than 75mmV (p-p). Spindles may be present below 60%	EMG 10mmV	Slow eye movements	At least 20-50% of the epoch. If less than 20% score on stage 2
STAGE 4	--"--	--"--	--"--	Greater than 50% of epoch
STAGE REM	2-7Hz. activity. Low voltage 10-20mmV. Vertex sharp waves absent (from stage 2). When switching from stage 2 switches through a spindle. Spindles and K complexes absent. Appearance of saw tooth waves	EMG lowest throughout recording	REMs present but not as abundant and high in magnitude as that of stage 1	

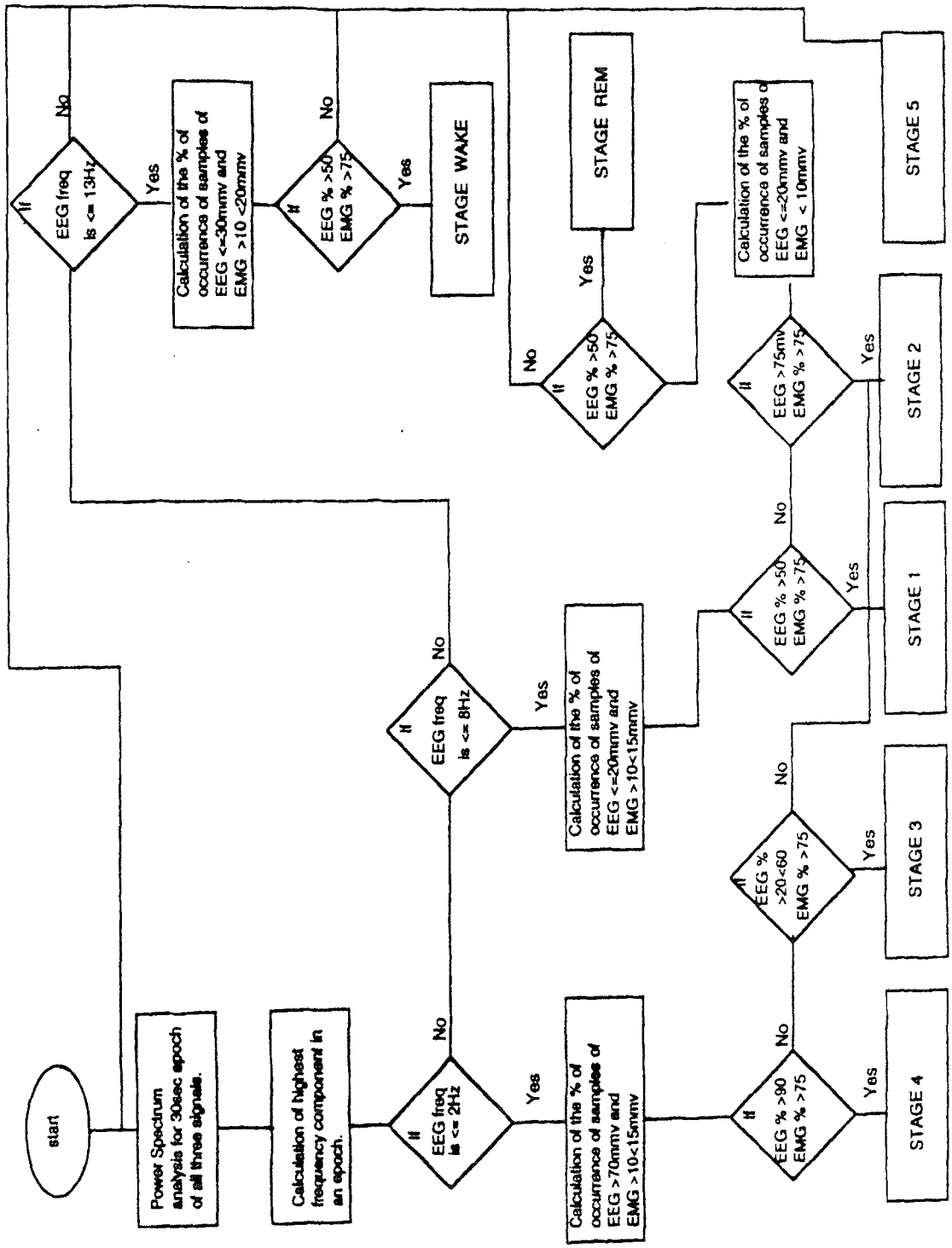

Figure 17 *Flowchart of the algorithm used for computerized scoring*

3.3. Results and Discussion

The EEG may be thought of as having two types of waveforms of interest. The first is the statistically regular waveform such as delta or theta rhythm which can be regarded as stationary and stoichiostic processes. The second are specific transients such as spindles, spikes or bursts. These latter, whole of major importance in human sleep EEG, have been studied by some researchers but in general use in sleep staging to a limited scope.

The stationary processes are characterized by their spectral properties which can be examined by techniques such as Autocorrelation, Cross correlation, Spectral Density and continuous frequency analysis using band pass filters. Auto and cross correlation are time domain statistics, while spectral density and continuous frequency analysis are frequency domain techniques. Time domain statistics are used to determine whether a signal is stationary and periodic. Frequency domain statistics assume these characteristics and resolve the signal into fundamental orthogonal components specified only by a frequency parameter. Auto and cross correlation techniques relay upon integration of the product of the signal and a delay signal, either the same signal or a second one, respectively. Both processes are more readily and reliably achieved in software than hardware due mainly to the delay required for the second signal.

Spectral density determines the power of a signal as a function of its frequency components without regard for either phase or temporal relationships. As the main parameter for scoring is frequency , spectral analysis was opted in this research. The spectral analysis determined by fourier analysis through FFT yielded very clear distinct variations in the power spectra for various sleep stages. Further in quantifying the effects of cerebral Ischemia on the EEG in a clinical setting, FFT proved superior to other methods, including period-amplitude analysis.

The results of the analysis are shown in the Fig 15. The whole five hours of data was evaluated through the algorithm which yielded around six hundred points with an epoch length of thirty seconds. One cannot appreciate the scored data with a large scale of time but can see the clearly the agreement with respect to visual scoring when expanded as shown in Fig 16. The manual scoring in the present context has been carried out with a standard epoch length of thirty seconds. The column displayed as page no in the visual scoring table as shown in Table 3 refers to polysomnograph recording sheet numbers. Each sheet corresponds to an epoch of thirty seconds. The stage values are named as 1, 2, 3, 4 ,REM as 5, and awake as A. The stage numbers display the onset of a stage and remain there till the next change. The individual pages of the polysomnograph record which represents 30sec epoch are represented as minutes in a separate column for the ready reference. The overall agreement between the visual and automatic scoring was satisfying for the whole length of the data. The correlation was the best for wake & NREM stages(for 1, 2, 3, and 4) and poor for REM sleep. Figure 18 shows sample power spectrums at the places where there is a match to prove the efficiency of the algorithm. The explanation for the above is discussed below.

Most classification errors occur when there is a transition between sleep stages and the errors generally consist of an exchange of temporally related sleep stages, especially quiet sleep and deep sleep. This is not surprising since the sleep is a nonstationary, continuous process. The frequent and fuzzy transitions between the artificial, discrete sleep stages are difficult to classify both by the computer and visually. It is judged that for fragments with stage transitions the computer scoring should be preferred, as it is more consistent than visual scoring.

Table 3 Visual Scoring data table for the subject used in the analysis

DATE RUN 5-13-92 NONBLIND BLIND
LIGHTS OUT 11:07PM EPOCH 009 UPTIME 5:13 EPOCH 744

PAGE NO	MINUTES	STAGE	PAGE NO	MINUTES	STAGE	PAGE NO	MINUTES	STAGE
9	4.5	A	294	147	1	433	216.5	2
56	28	1	298	149	2	435	217.5	3
58	29	2	299	149.5	1	437	218.5	2
59	29.5	1	300	150	2	438	219	A
60	30	2	301	150.5	1	440	220	1
62	31	1	302	151	2	444	222	2
63	31.5	2	352	176	3	450	225	1
81	40.5	3	353	176.5	2	452	226	5
83	41.5	2	359	179.5	3	467	233.5	1
85	42.5	3	360	180	2	468	234	5
****	****	*****	365	182.5	3	474	237	1
160	80	A	366	183	2	475	237.5	5
164	82	1	368	184	3	488	244	A
165	82.5	2	373	186.5	2	489	244.5	1
183	91.5	1	376	188	3	493	246.5	2
184	92	2	378	189	2	597	298.5	A
215	107.5	A	379	189.5	3	604	302	1
224	112	1	384	192	2	606	303	2
237	118.5	A	385	192.5	3	669	334.5	5
243	121.5	1	387	193.5	2	670	335	A
248	124	2	388	194	3	671	335.5	1
249	124.5	1	390	195	2	675	337.5	5
250	125	2	392	196	3	689	344.5	A
256	128	5	399	199.5	2	692	346	1
271	135.5	1	401	200.5	3	699	349.5	2
274	137	5	415	207.5	2	700	350	A
276	138	1	419	209.5	3	701	350.5	1
277	138.5	5	420	210	2	703	351.5	2
283	141.5	1	421	210.5	3	710	355	5
284	142	5	425	21.5	2	744	372	5
288	144	A	426	213	3	END		

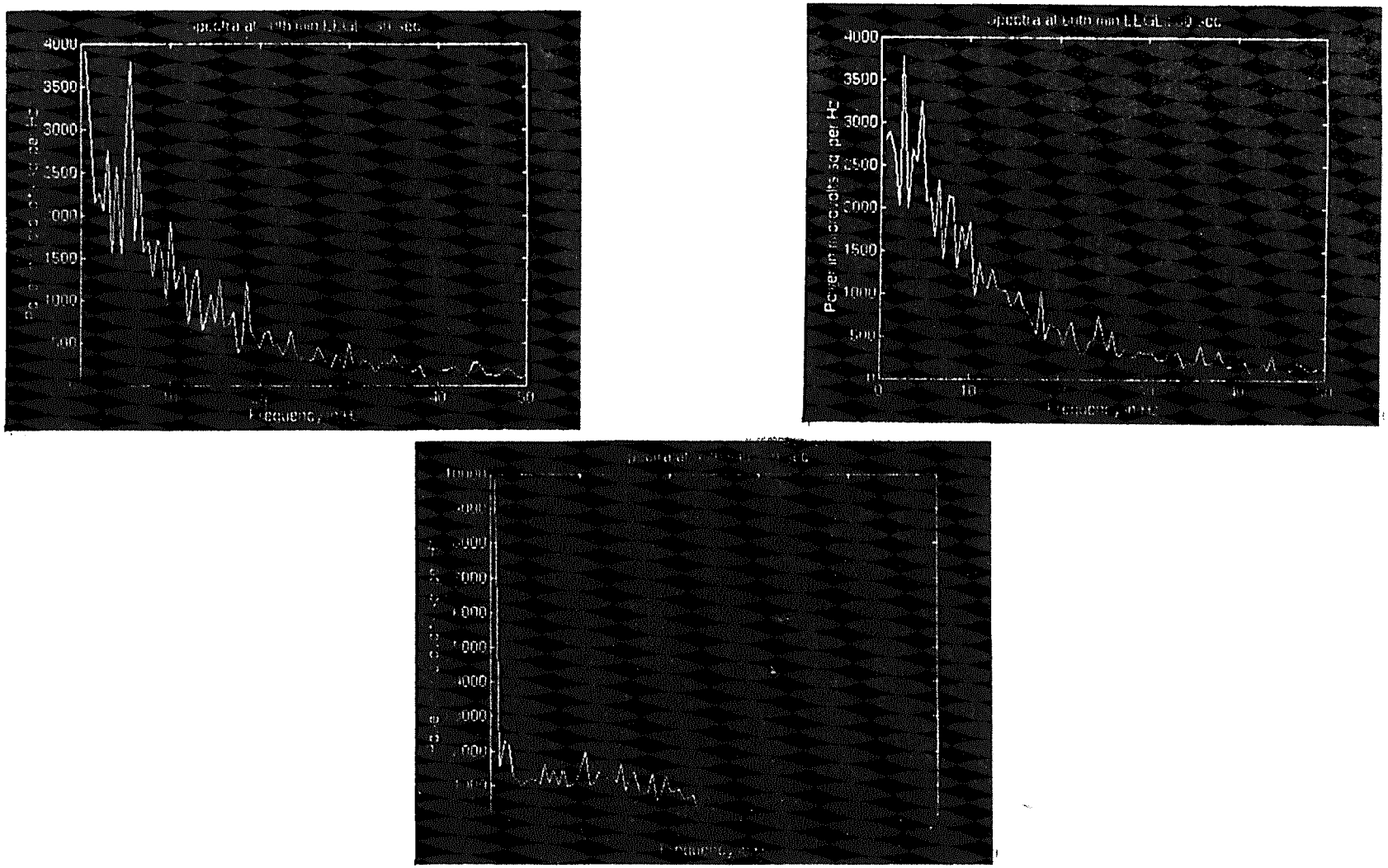

Figure 18 Samples of Power Spectra of EEG where there is a good agreement with the computerized scoring

One shortcoming in this approach is that the automatic scoring algorithm cannot discriminate short bursts of phasic activity from tonic, more prolonged but less intense activity. Since the algorithm cannot discriminate brief bursts of EMG activity, the short bursts of EMG activity due to muscle twitches sometimes lead the algorithm to erroneously score as awake. The possible reason for poor REM scoring can be justified by applying the above fact to EEG, as sleep spindles do appear in stage 2 before switching on to REM. Fortunately such epoches are small in number resulting in a minor effect as scoring error. The irregularities that appear intermittently can be accounted for electrophysiological effects and movement artifacts. There could also be an error due to patient movement.

Although spectral was best suited for this analysis it had drawbacks when compared to other methods. Averaging of spectra occurring over long intervals of time has the disadvantage of ignoring short term changes in the EEG. In addition power spectral analysis doesn't separate the relative contributions of changes in amplitude and incidence of a given wave form. If elevated power spectral density is identified, this may be secondary to an increase in the amplitude of the waveform, a greater incidence of that waveform, or a combination of both factors.

3.3.1 Extensions and Improvements

The analysis which was carried out only with analog filtering of 256 Hz can be improved considerably using an algorithm for artifact rejection. The algorithm should be able to detect the noise pattern and if the noise percentage is large in an epoch it should be discarded. If the staging algorithm is used on the data from which the noisy epoches have been eliminated, there will be an increment in the percentage of agreement between visual scoring and computerized scoring.

An attempt should be made to design an algorithm to detect the K-Complexes and sleep spindles. The use of such an algorithm should help to achieve in attaining a higher percentage of agreement. The algorithm can be designed to find a typical K-Complex pattern to use it as a template for further matching through the signal.

This can be expanded to an on-line scoring system running on a personnel computer with the front-end developed using Microsoft Windows. This helps a physician to see the sleep stages when the subject is sleeping at the other end. To achieve the required speed for the real time system one can use the faster transformations like Haar and Walsh which are ideal for non-stationary signals.

APPENDIX A

MATLAB

MATLAB is a technical computing environment for high performance numeric computation and visualization. MATLAB integrates numerical analysis, matrix computation, signal processing, and graphics in an easy-to-use environment where problems and solutions are expressed just as they are written mathematically - without traditional programming.

The name MATLAB stands for Matrix laboratory. MATLAB was originally written to provide easy access to matrix software developed by LINPACK and EISPACK projects, which together represent the state of the art in software for matrix computation.

MATLAB is an interactive system whose base data element is a matrix that does not require dimensioning. This allows you to solve many numerical problems in a fraction of time it would take to write a program in a language such as FORTRAN, Basic, or C.

MATLAB has evolved over a period of years with input from many users. In university environments, it has become the standard instructional tool for introductory courses in applied linear algebra, as well as advanced courses in other areas. In industrial settings MATLAB is used for research and to solve practical engineering and mathematical problems. Typical uses include general purpose numeric computation, algorithm prototyping, and special purpose problem solving with matrix formulations that arise in disciplines such as automatic control theory, statistics, and digital signal processing.

MATLAB also features a family of application-specific solutions that it calls as Toolboxes. Very important to most users of MATLAB, toolboxes are

comprehensive collections of MATLAB functions(M-files) that extend the MATLAB environment in order to solve particular classes of problems. Areas in which toolboxes are available include signal processing, control system design, dynamic systems simulation, systems identification, neural networks, and others.

Probably the most important feature of MATLAB, and the one that MATLAB people took care to perfect, is its easy extensibility. This allows us to become a contributing author too, creating our own applications. In the years that MATLAB has been available, the company has enjoyed watching many scientists, mathematicians, and engineers develop new and interesting applications, all without writing a single line of low level code.

External Interfaces to MATLAB

Although MATLAB is a complete, self-contained environment for programming and working with data, it is often very useful to interact with data and programs external to MATLAB. Shell escape functions and MEX-files are the two methods for calling your own C or Fortran subroutines.

a. Shell Escape Functions

Shell escape functions use shell escape command ! to make external stand alone programs act like new MATLAB functions. A shell escape M-function is an M-file that

1. Saves the appropriate variables on disk.
2. Runs an external program (which reads the external data file, processes the data, and writes the result back out to disk.
3. Loads the processed file back into the workplace. Shell escape functions are less efficient than MEX- files because they incur the overhead associated with invoking an external program each time they are called and because their arguments are passed via disk files. In situations where relatively large amount

of processing is performed in the external program, this overhead can be negligible, and converting to MEX-files offer no real advantage.

If the computation time of the external program is short compared to the time spent loading the program and passing the variables, MEX-files may be more suitable since the object code of a MEX-file is physically linked into MATLAB.

b. Dynamically Linked Subroutines: MEX-Files

One can also call C and Fortran subroutines from MATLAB as if they were built-in functions. MATLAB-callable C and Fortran programs are referred to as MEX-files. MEX-files are dynamically linked subroutines that the MATLAB interpreter can automatically load and execute. MEX-files have several applications:

1. Large pre-existing Fortran and C programs can be called from MATLAB without having to be rewritten as M-files.
2. Bottleneck computations (usually for-loops) that do not run fast enough in MATLAB can be recorded in C or Fortran for efficiency.
3. A/D cards, D/A cards, and other hardware can be accessed directly for data acquisition and control applications.

MEX-files are not appropriate for all applications. MEX-files offer an avenue that unsuspecting users may follow when they would be much better of programming in the MATLAB language. MATLAB is a high-productivity system whose specialty is eliminating time consuming, low-level programming in compiled languages like C and Fortran.

Techniques for importing and exporting data to and from the MATLAB environment are also available. The most important approach is MAT-files-the file format that MATLAB uses for saving data to disk. MAT-files offer a simple and convenient mechanism for transporting our data between different platforms.

APPENDIX B

`SIGNA' SIGNAL PROCESSING PACKAGE

The package supports a biomedical signals processing system. As a research tool the system offers the potential to acquire and analyze experimental and clinical data obtained in the form of photographs, polygraphic paper charts etc. In its role as an adjunct to biomedical education, several self-teaching features are implemented which enable the student of biomedical signals processing to gain hands-on experience in the application of signals processing methodologies to the analysis of clinical and experimental data. These features include a software function generator and a help option. The modular approach employed in the system design provides a great deal of flexibility to the investigator such that when a new analysis is desired one can simply add on the particular user-developed module to the system without causing any undue system constraints.

The types of analyses that are currently implemented include numerical integration, curve fitting, Fourier, Walsh and Haar transformations, spectral analysis and frequency response measurements. The system is being used for a wide range of applications which include the analysis of electrical signals generated at the neuromuscular junction, the computation of input impedance of the arterial system, the analysis of pressure waveforms obtained during anesthesia and in the characterization of respiratory dynamics in studies pertinent to asthma.

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