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SIGNAL ANALYSIS TECHNIQUES FOR INTERPRETING ELECTROENCEPHALOGRAMS

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The principal objective of this study was to review and assemble the relevant signal processing literature for analyzing and interpreting EEG, especially steady-state visual evoked responses (VER). The principal Air Force objective is to investigate the usefulness of the VER as a tool in assessing the effects of visual stimuli upon the flier, especially stimuli which could lead to a temporary (or permanent) degradation of performance. This could include flashblindness, disorientation, or other physiological impairment caused by

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20. ABSTRACT (Continued)

visual stimuli. The study concentrated on those methods suitable for analysis of the spontaneous EEG. However, methods of modeling the spontaneous EEG have been considered, since by eliminating spontaneous EEG components, the VER should be more evident. The problem of measurement variability observed after signal processing was investigated, and a thorough literature search was conducted to look for neurophysiological evidence of variability and possible cures.

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SIGNAL ANALYSIS TECHNIQUES FOR INTERPRETING ELECTROENCEPHALOGRAMS

INTRODUCTION

Objective

The principal objective of this project was to review and assemble the relevant signal-processing literature for analyzing and interpreting electroencephalograms (EEG), especially visual evoked responses (VER). In the course of satisfying this objective, it was necessary to consider the goals of the U.S. Air Force; that is, to consider the fundamental U.S. Air Force objectives which led to this study.

The principal U.S. Air Force objective is to investigate the usefulness of the EEG/VER as a tool in assessing the effects of visual stimuli upon the flier, especially stimuli which could lead to a temporary (or permanent) degradation of performance. This could include flashblindness, disorientation, or other physiological impairment caused by visual stimuli.

Scope

This study has been, by necessity, somewhat limited in scope. We were concerned with assessing the state-of-the-art in digital signal processing as it relates to analysis and interpretation of the EEG, especially the VER. The nature of the EEG signal is very complex and for this reason the required tools may be quite sophisticated.

The study has concentrated on those methods suitable for analysis of visual evoked responses rather than those more suited for analysis of the spontaneous EEG. Thus, emphasis is not placed on tracking periodicities such as alpha, beta, or theta waves, since these tend to be missing in the VER. However, methods of modeling the spontaneous EEG have been considered since by eliminating spontaneous EEG components, the VER should be more evident.

In the course of this study, we have investigated the problem of measurement variability observed after signal processing. In particular, we have analyzed the current processing techniques used by the U.S. Air Force to determine whether the observed variability might be caused or aggravated by the processing. We have also conducted a thorough literature search to look for neurophysiological evidence of variability and possible cures. Finally, we have reviewed advanced signal-processing techniques to determine their potential for reducing variability.

The results of our efforts are encouraging. We have found reason to believe that some improvement is possible, although the magnitude of the improvement and the recommended processing techniques cannot be determined without a thorough analysis of the original (preprocessed) data. We suspect, however, that significant improvements may not be possible without more sophisticated processing and modified experimental practice and data collection.

General VER Signal Characteristics and Processing Implications

The characteristics of the VER signals we wish to analyze are not easily described using simple models. An example of an idealized VER is shown in Figure 1. The signal is clearly nonstationary and of high order. Furthermore, the VER cannot be modeled by a minimum-phase system since energy in the VER grows with time during the initial response. This complicates the modeling process.

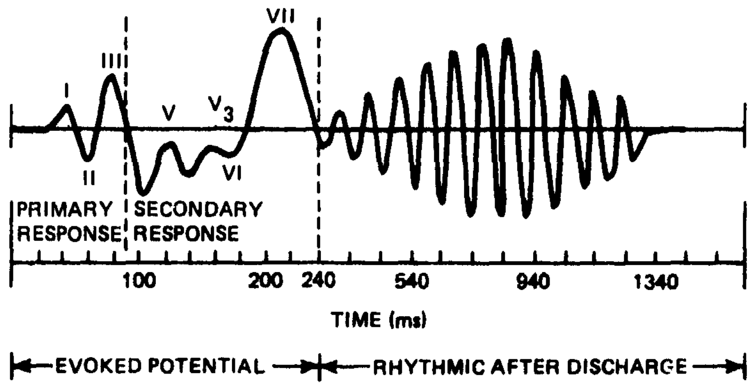

Figure 1. Schematic of a visual evoked potential. (after Desmedt (28, p. 18))

The VER is a stochastic process and any realistic analysis must include a consideration of stochastic effects. An example of a set of averaged VERs taken from the same human subject, but at different times, is shown in Figure 2. The variability between records is not systematic and follows no simple pattern. The problem is made more difficult by the fact that the VER is a collective process arising due to the action of many, variably coupled, cellular generators. This lack of determinism (predictability) in the VER suggests that stochastic effects are significant and that care must be taken when modeling them.

In designing VER signal-processing techniques, it is essential that the following points be kept in mind:

a) The VER signal is a stochastic process with a significant amount of unpredictability in time.

b) The VER signal is, at least in part, a nonstationary process. It is important that analysis techniques explicitly take this fact into account.

c) The information we seek may be spread over more than one electrode. Thus multivariate analysis techniques should be employed.

d) The relationship of input stimulus to output response we are analyzing will be nonlinear, especially the saturation (flash-blindness) reaction.

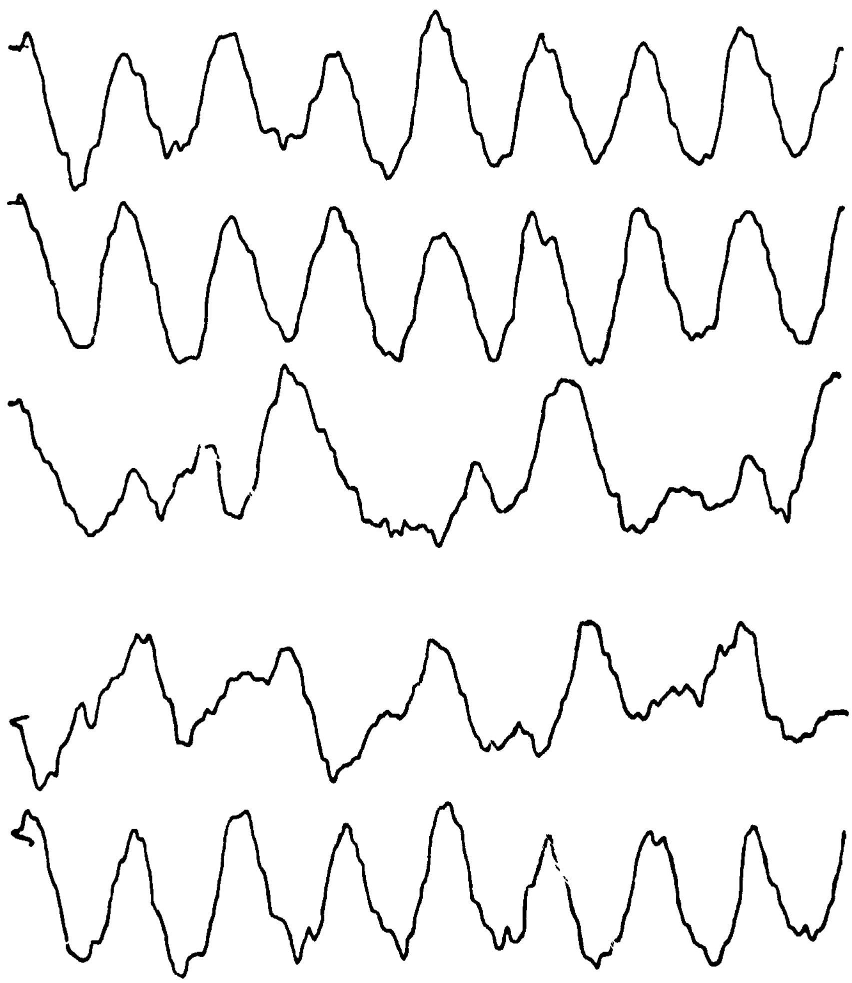

Figure 2. VER variability. Each tracing is an average of 240 successive 1-sec segments time-locked to a checkerboard pattern stimulus at a reversal rate of 4 per second. Data are for the human subject under the same controlled conditions during the same day, covering both morning and afternoon. Data supplied by the U.S. Air Force.

e) The corrupting noises we wish to filter out may be partially correlated over several adjacent electrodes. This is another argument for using multivariate signal analysis techniques.

With these points in mind, we can now broadly outline an overall approach to signal processing:

a) We may think of the EEG/VER signals as outputs of a system which we can model phenomenologically. That is, using all information at hand, we will use a system model to generate the evoked potentials.

b) We wish to take advantage of the known physiological characteristics of the eye and brain, insofar as they suggest particular model structures.

c) We will employ generic models which can be used to explain as many observed phenomena as possible.

d) We will take advantage of recent developments in the fields of system modeling and identification, time series analysis, adaptive Kalman filtering, spectral analysis, and pattern recognition.

e) We will suggest experiment design methods in order to enhance model identification by tailoring stimulus features to particular measurable reaction.

Overview

This report begins with a discussion of the signal-processing approach presently used by the U.S. Air Force for VER analysis, namely the Fast Fourier Transform (FFT). The observed variability in the periodogram is explained qualitatively and quantitatively via several simple signal and noise models. Based on these results, different signal processing techniques based on FFT analysis are suggested.

The physiological aspects of VER variability are discussed in the section "Aspects of EEG/VER Variability." A comprehensive literature search has been carried out in order to relate the U.S. Air Force problem to the work of other research groups and their findings. Several mechanisms for explaining the observed variabilities are presented. The important problem of how to determine an appropriate measure of VER activity is discussed.

The section "Improved Techniques for VER Analysis" is devoted to a discussion of alternate signal-processing techniques which are appropriate for VER signal processing. These include recently developed analytical methods and modeling approaches as well as more classical approaches. They have been culled from a comprehensive review of the EEG literature, as well as specific Scientific Systems, Inc. experience in biological signal processing.

Our conclusions and recommendations are given. Appendixes A through J are sections from our Interim Report that summarized our survey of signal-processing techniques applicable to EEG/VER analysis. This report began with a review of the physiological background of the problem and the general signal-processing objectives of the U.S. Air Force. We then discussed a number of signal-processing methods which may be useful in fulfilling the objectives. We concluded with a discussion of how these methods might be applied in VER experimentation.

ANALYSIS OF CURRENT PROCESSING

This section discusses some of the current signal-processing problems facing the U.S. Air Force researchers and outlines potential solutions and analysis techniques for reducing signal variability. This variability in the processed data, described in more detail below, is the major obstacle to developing accurate visual performance measures. We believe this obstacle can be reduced, if not removed.

The basic questions we tried to answer are: is the large amount of variability due to a signal characteristic or processing technique, and can it be reduced by alternate processing methods? Our answer, based on the available data and explained in this section, is: the variability is largely consistent with a noisy measurement model; that is, the variability is probably due to "noise" in the measured signal and is <u>not</u> a processing artifact, although different processing methods have <u>varying</u> sensitivities to the noise. Thus, the effect of the (signal) variability on a visual performance measure may be reduced by alternate processing techniques, some of which are quite simple and fast. In order to recommend a specific processing technique, however, an analysis of the raw data (measured EEG signals, with and without stimulus) is necessary.

Experiment Purpose

In order to evaluate potential processing techniques, an understanding of the purpose of the experiments is necessary. The immediate objective of the current experiments is to develop a measure of visual system (eye and brain) performance, using EEG data, that is accurate enough to distinguish between levels of visual acuity ranging from normal sight to flash-induced blindness. This measure must be computable in a reasonable amount of time (e.g., 1 min or less) in order to permit accurate tracking of the recovery for temporary flashblindness.

The achievement of this objective is hampered by certain experimental constraints (imposed in order to make the results relevant to the U.S. Air Force mission), such as narrow fields-of-view and anesthetized subjects, which reduce the amplitude of the VER and make it difficult to measure. To date, the observed variability in the processed data is sufficiently large to make accurate visual performance evaluation extremely difficult. We would like to examine whether this observed variability is due to the poor signal strength or other factors.

We begin by describing the observed variability and then investigating the processing used on the data. Next we discuss an alternate processing technique and compare its performance to that of the current method. We end this section with a summary of our conclusions to date.

Observed Variability

An example of the degree of variability is shown in Figure 3, which was made using actual data supplied by the Air Force. The figure shows the power (in undesignated units) of an evoked potential (left-hand data) and background noise (right-hand data) when processed in a particular manner, described in the next section. The experiment was performed on an anesthetized monkey, and the points have been reordered for this plot. Each point represents 60 sec worth of data, and the noise points were originally interspersed between signal points. Data were taken for approximately 5 hr, and only the first group--up to a rest period at 40 min--is shown. The rest of the data was qualitatively similar to that shown.

The experiment conducted was of the "steady-state" type, discussed in the section "Aspects of EEG/VER Variability," where the stimulus was a sinusoidal grate pattern which reversed 4 times per second. The processing employed tries to estimate the evoked response power (at 4 Hz) while suppressing the background EEG. The same processing is applied to each data group--the only change is the presence or absence of the stimulus pattern.

Current Signal Processing

In order to examine what the signal (EEG) characteristics are, we need to understand what the current processing technique does to the data. By inverting the processing operations, we would like to arrive at a signal model which can be used to obtain a better processor. Such an inversion is nearly impossible from the limited processed data available, of course, and a complete signal model must await the analysis of the original raw data. Nonetheless, much can be learned from simple potential models, as discussed below.

The basic processing approach currently used is a hybrid time-average and Fourier Transform which has several interesting properties. The raw signal (measured EEG), denoted by $x(t)$, is first averaged at 1-sec intervals, forming $\bar{x}(t)$.

$$\bar{x}(t) = \frac{1}{N} \sum_{n=0}^{N-1} x(t+n) \qquad t \in (0,1)$$

Thus, for the data of Figure 3, 60 sec worth of raw data is divided into 60, 1-sec intervals (each with 4 evoked responses) carefully aligned with the pattern reversal signal. These 60 records are then added together and divided by 60 to obtain an average evoked response 1 sec long, containing 4 individual average evoked responses. This average signal is then passed through an FFT algorithm (see Appendix C), which produces a complex sequence equally spaced in frequency (with 1 Hz resolution, in this case). The periodogram (power estimate formed with the magnitude of the FFT

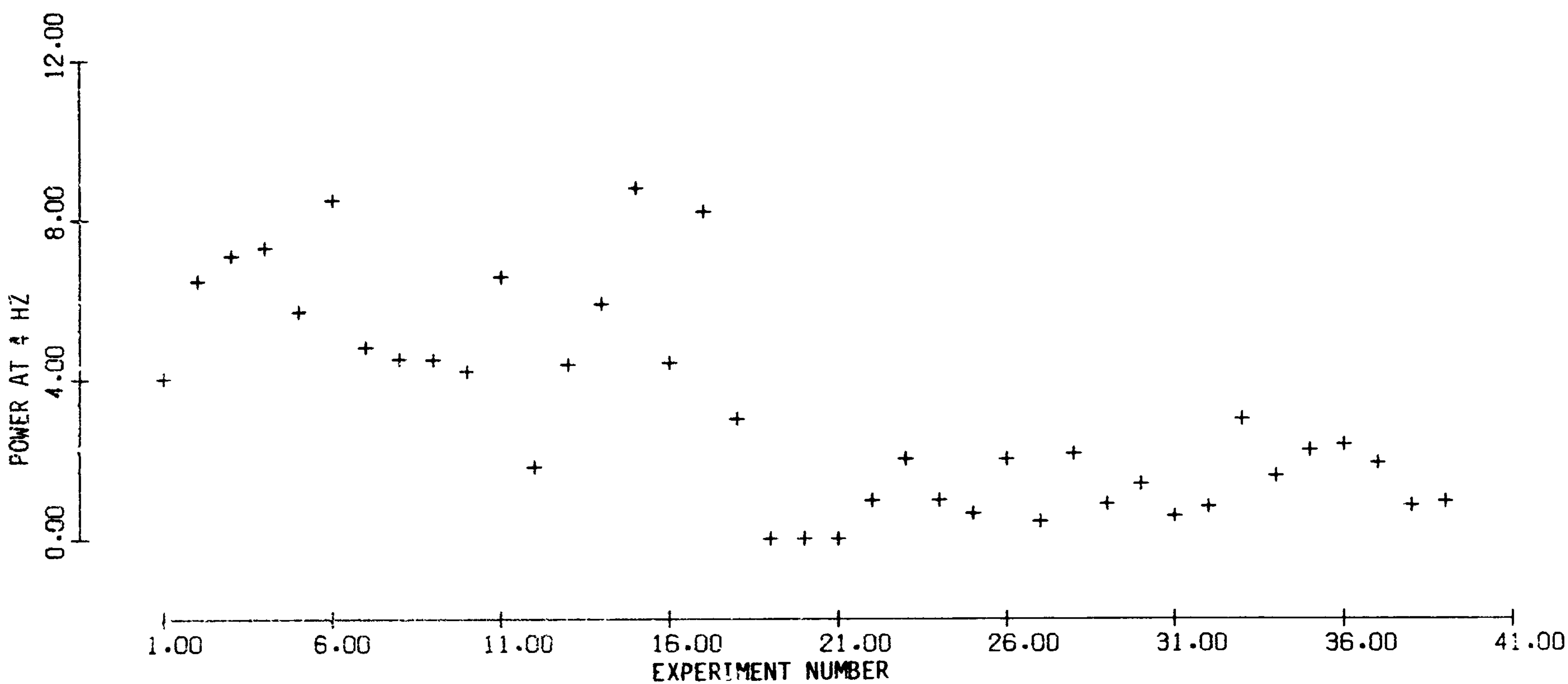

Figure 3. Evoked response (left) and background noise (right) power levels.

coefficients) is then computed, and the power component at 4 Hz is obtained. This power estimate is the data point used to summarize the 60-sec record, and these points are the ones shown in Figure 3. The processing sequence is shown in Figure 4.

$$\xrightarrow[x(t)]{\text{Time Series}} \overset{\text{Time Average}}{\boxed{\frac{1}{N}\sum_{n=1}^{N} x(t+n)}} \xrightarrow{\bar{x}(t)} \boxed{\text{FFT}} \xrightarrow[\bar{x}_1(\omega)+i\bar{x}_2(\omega)]{\bar{x}(\omega)} \overset{\text{Periodogram}}{\boxed{I(\omega_k)=\bar{x}_1^2(\omega_k)+\bar{x}_2^2(\omega_k)}} \xrightarrow{I(4)}$$

Figure 4. Processing sequence of time series.

The two-step processing (averaging, then taking the FFT) should reduce "noise" (spontaneous EEG not in phase with the stimulus for 60 sec) and enhance the typical evoked response. The averaging process will favor patterns that repeat at multiples of 1 Hz for the full 60 sec and suppress those signals, such as the background EEG, which naturally "wander" in phase. In particular, white Gaussian noise will have its variance reduced by a factor of 60; that is, if

$$x(t) = n(t)$$

$$E[n(t)] = 0$$

$$E[n(t)n(\tau)] = Q\delta(t-\tau)$$

where δ is the Dirac delta function, and Q is the height of the noise spectrum, then

$$E[\bar{x}(t)] = 0$$

$$E[\bar{x}(t)\bar{x}(\tau)] = \frac{Q}{60}\,\delta(t-\tau) \qquad (1)$$

Pure sinusoids at multiples of 1 Hz, however, will pass through the averages unaffected (i.e., with full power). Specifically, if

$$x(t) = \sqrt{2P}\,\sin \omega_0 t \qquad t \,\varepsilon\, (0,T)$$

then

$$I(\omega_0) = \frac{PT}{2}$$

for the scale factors used in our analysis. The application of the power estimator when more complex signals are present is not as straightforward, however.

FFT Operation

The FFT function often used to obtain power estimates is called the periodogram, as discussed in Appendix C. When pure sinusoids are processed in a periodogram, good power estimates are obtained, as discussed above. When noisy signals are processed by a single periodogram, however, very poor spectral estimates are obtained, with the error in the estimate often as large as the true power level. In particular, for a Gaussian spectrum, the standard deviation of the estimate is equal to the true spectrum height. Moreover, when both a pure sinusoid and a Gaussian process are observed, the estimation error (at the sinusoid's frequency) can be much larger than the Gaussian process alone might suggest.

Consider a signal of the form

$$z(t) = \sqrt{2P} \sin \omega_0 t + n(t)$$

where

$$E[n(t)n(\tau)] = Q\ \delta(t-\tau)$$

If n(t) is observed alone and an FFT (periodogram) power estimate obtained from it, the average power at each frequency would be

$$S(\omega) = Q$$

The variance of each power estimate would be Q^2. This results from the fact that the elements of the periodogram are Chi-squared random variables with 2 degrees of freedom. If the pure sinusoid were observed alone for T seconds, the power estimate at ω_0 would be

$$S(\omega_0) = \frac{PT}{2}$$

with zero error, as discussed above.

The question arises: if both components of z(t) are observed, what is the mean and variance of the spectral estimates?

To answer this question, we first note that the FFT is a linear operation (before the periodogram is computed) and that therefore the Fourier coefficients are normal random variables. Thus, for the signal above, we may model the Fourier components as[1]

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[1] $x \sim N(m,\sigma^2)$ implies that x is a normal (Gaussian) random variable with mean m and variance σ^2. $\overline{(\ )} = E(\ )$ is used to denote the mean of the quantity ( ). Var( ) is used to denote variance. The mean of the $x_i(\omega_0)$ components depends on the phase angle of the sinusoid, and we have assumed a 45° angle here. The spectral estimate $\hat{s}$ is, by design, independent of the phase.

$$x_i(\omega_j) \sim \begin{cases} N(0,\ Q/2); & \omega_j \neq \omega_0 \qquad i = 1,2 \\ N(\frac{1}{2}\sqrt{PT},\ Q/2); & \omega_j = \omega_0 \end{cases}$$

and the spectral estimate is

$$\hat{s}(\omega_j) = x_1^2(\omega_j) + x_2^2(\omega_j)$$

Thus, if Q = 0

$$x(\omega_0) = \frac{PT}{2}$$

and if P = 0

$$\overline{\hat{s}(\omega_j)} = Q$$

$$\text{var } \hat{x}(\omega_j) = Q^2$$

which agrees with our previous result.

When Q and P are both not zero,

$$\overline{\hat{s}(\omega_0)} = \frac{PT}{2} + Q \tag{2}$$

$$\text{Var } \hat{s}(\omega_0) = Q^2 + PTQ \tag{3}$$

as derived in Appendix K.

Thus, the mean spectral estimate is precisely the sum of the sinusoidal and white noise means. The variance, however, is larger than the white noise variance, and includes a cross-product (PTQ) that results from the squaring operation used for the power estimate. In the case of the data shown in Figure 3, the cross product term may be much larger than the white noise term (Q^2).

If the noise process is not white but colored (correlated), the results are similar. Indeed, if the noise spectrum is essentially flat over a bandwidth enclosing the sinusoid and as wide as the FFT resolution, the white noise model may be used. In the present case, if the FFT has frequency samples 1 Hz apart and the background spectrum is nearly flat from 3 to 5 Hz, then a white noise model may be used for examining the 4-Hz power component. Thus, the two noise spectra shown in Figure 5 have essentially the same effect on estimating the 4-Hz power component in an FFT. This observation may be used to justify a white noise model for much of our current analysis, where very little is known about the signal away from 4 Hz.

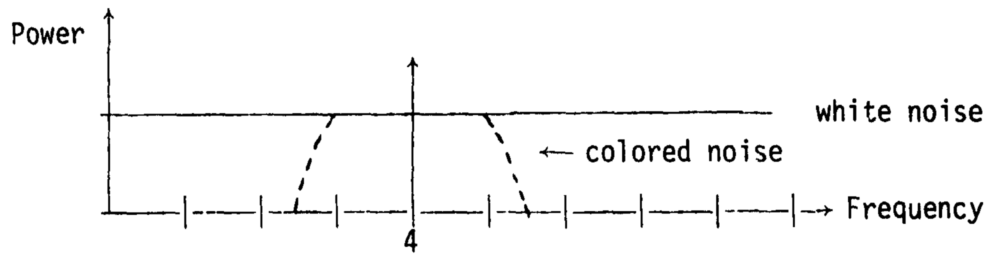

Figure 5. White and colored noise indistinguishable near 4 Hz.

Current U.S. Air Force Processing

With the above results, the performance of the current U.S. Air Force processing technique may be analyzed for simple signal models. The current technique can be divided into two steps: time series averaging and periodogram power estimation. As discussed above, the averaging step reduces the noise (broadband background EEG, measurement noise, etc.) variance by a factor of 60. The periodogram then produces a somewhat noisy power estimate from the averaged signal.

Specifically, we consider a signal composed of a pure sinusoid and white noise, i.e.,

$$z(t) = \sqrt{2P} \sin \omega_0 t + n(t)$$

as above. The current technique computes the <u>time</u> average

$$\bar{z}(t) = \frac{1}{N} \sum_{n=1}^{N} z(t+n) \qquad t \in (0,1)$$

The result of this averaging is to create a signal of the form

$$\bar{z}(t) = \sqrt{2P} \sin \omega t + \bar{n}(t)$$

where

$$E[\bar{n}(t)\bar{n}(\tau)] = \frac{Q}{N} \delta(t-\tau)$$

using the results of Eq. 1. Thus, the performance of the current estimator is:

$$\text{Mean} \qquad \hat{s}(\omega_0) = \frac{PT}{2} + \frac{1}{N} Q \tag{4}$$

$$\text{Variance} \quad \text{var}(\hat{s}(\omega_0)) = \frac{1}{N^2} Q^2 + \frac{1}{N} QPT \tag{5}$$

These results are shown in Figures 6 through 8.

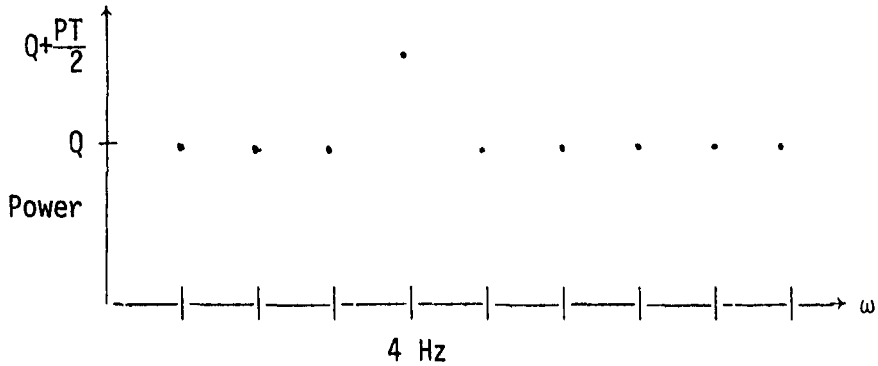

Figure 6. Original spectrum.

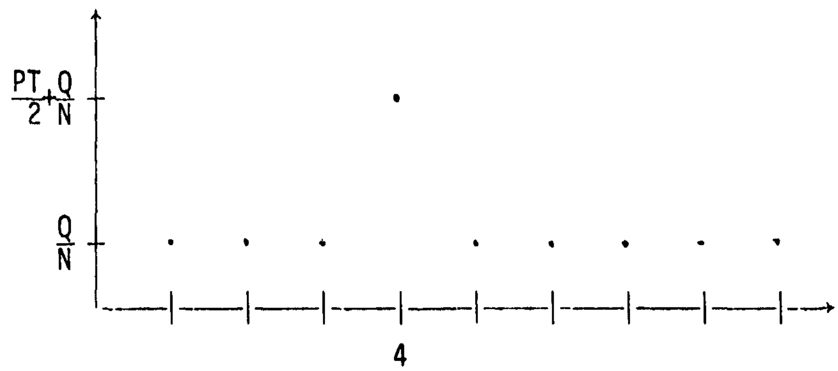

Figure 7. Spectrum of average time series.

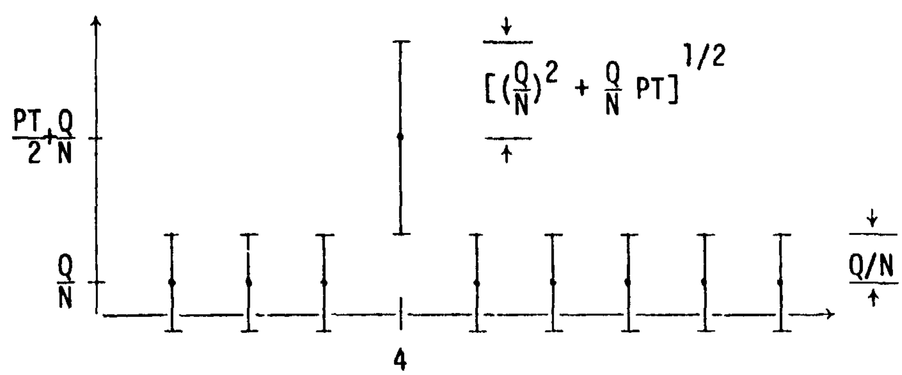

Figure 8. Variability of single periodogram ($\pm\sigma$).

Modeling Implications of Data

The sample statistics (mean and standard deviation) of the data shown in Figure 3 (18 points) are given in Table 1. Also shown in the table are the statistics for the full (5-hr, 84 and 85 points) data sequence from that experiment. The samples are reasonably close, so that a fairly high confidence can be placed in them.

TABLE 1. EXPERIMENT STATISTICS

	Stimulus on		Stimulus off	
	18 pts.	85 pts.	18 pts.	84 pts.
Mean	5.56	4.41	1.42	1.52
Standard deviation	1.94	1.69	0.74	0.85

We note in particular that the standard deviation-to-mean (σ/m) ratio for the background noise (stimulus off) case is approximately 1/2. A Chi-squared statistic, which would result from normally distributed samples ($x_i(\omega)$) being squared and summed (in the periodogram), would have a ratio of[2]

$$\frac{\sigma}{m} = \frac{2}{\sqrt{n}}$$

where n is the number of terms being summed. For $n = 2$, corresponding to the usual spectral estimate (real and complex parts of the FFT),

$$\frac{\sigma}{m} = 1$$

Thus, we see that there is less variability (proportionately lower σ) in the stimulus-off case than would be present in a white noise (or broadband noise) spectrum. This discrepancy, although not overly significant, indicates that a white noise model is relatively conservative (more variability than actually observed) and that time-varying spectra (e.g., from nonstationary signals) may not be needed.

If we believe that the stimulus creates a highly correlated (nearly deterministic) response in the EEG, then the observed signal might resemble a sinusoid (at the reversal rate--4 Hz) plus the background noise. Using noise values near the background noise levels (0.5 to 1) and a sinusoid power level (P) of 9 (to produce spectral heights on the order of 5 for T=1 sec), we see in Table 2 that the resulting mean and standard deviation (calculated using Eqs. 2 and 3) are close to those seen in Table 1.

Once again, the discrepancy between the simple model predictions and the observed values is not great, and indeed the model values are more pessimistic (higher σ) about estimating s than the observed data indicate. We also see that adding a <u>pure sinusoid</u> to low measurement noise results in a much larger spread in the spectral estimate than one might think. This is

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[2] In this case, σ^2 would equal Q/60 where Q was the original noise level.

a normal consequence of using a single periodogram for spectral estimation. The next section discusses one of the traditional ways of reducing this variability.

TABLE 2. THEORETICAL STATISTICS

Stimulus on		Stimulus off	
$\hat{\bar{s}}$	σ	$\hat{\bar{s}}$	σ
5	2.18	.5	.5
5.2	2.61	.7	.7
5.5	3.16	1	1

Classic Spectral Estimation

One of the standard techniques in spectral estimation is a slight variation on the current U.S. Air Force approach of computing the periodogram of a time series average. The classic technique computes a periodogram for each window in the total record length and then averages the periodograms to obtain a power spectrum estimate. This averaging reduces the error in the spectral estimate although it does not reduce the noise level in the signal. This is a fundamentally different result from that of the current U.S. Air Force processing: the classic technique tries to estimate the complete spectrum (signal plus noise), while the current approach tries to reduce the noise and then estimate the sinusoidal power.

The classic approach gained favor because of the severe sensitivity of a single periodogram to noise--even when the noise power is low. This sensitivity was discussed above, where it was shown that for white noise, the standard deviation of a <u>single</u> periodogram was as large as the mean value of the spectrum being estimated. The classic approach averages N periodograms to obtain a $\sqrt{N}$ reduction in standard deviation, while the average value converges to the actual power spectrum (sinusoid plus noise).

Specifically, we consider the N spectral estimates

$$\hat{s}_n(\omega_0) + x^2_{1_n}(\omega_0) + x^2_{2_n}(\omega_0) \qquad n = 1,\ldots,N$$

from the N windows:

$$z(t+n),\ t \in (0,1),\ n = 1,\ldots,N$$

For each window

$$x_{i_n}(\omega_0) \sim N(m,\sigma^2)$$

where

$$m = \frac{1}{2}\sqrt{PT}$$

$$\sigma^2 = \frac{Q}{2}$$

and then

$$\hat{s}(\omega_0) = \frac{1}{N}\sum_{n=1}^{N}\hat{s}_n(\omega_0)$$

is the average spectral estimate. The mean and variance of $\hat{s}$, as computed in Appendix K, are:

$$\bar{\hat{s}}(\omega_0) = \frac{PT}{2} + Q \qquad (6)$$

and

$$\text{var}\ \hat{s}(\omega) = \frac{Q^2 + PTQ}{N} \qquad (7)$$

This mean and standard deviation are shown in Figure 9.

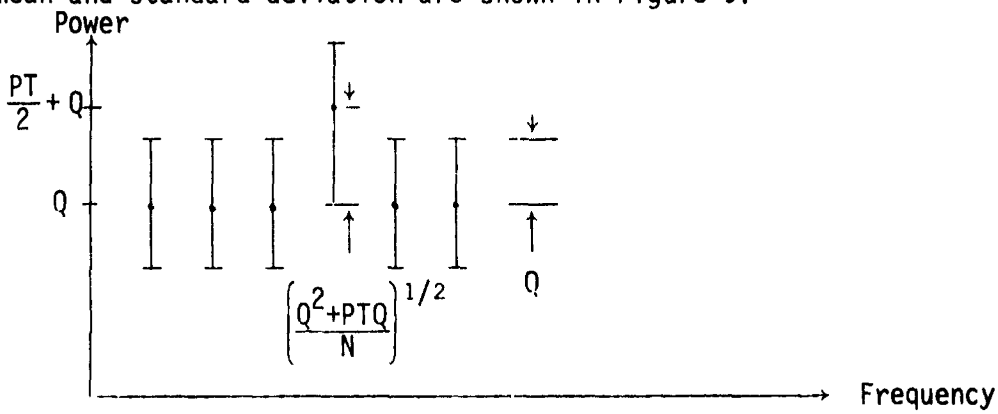


Figure 9. Classic estimator performance ($\pm\sigma$).

The classic technique is a somewhat ad hoc method which has proved to be very useful in unknown-signal applications. The method can be tuned to a particular problem by varying the window width, using window weighting functions, overlapping windows, or smoothing the frequency estimates as discussed in Appendix C.

Comparison of Approaches

In order to demonstrate the difference in these signal processing methods, we consider a sinusoid plus white noise model as discussed above, with the parameters adjusted to produce results similar to those of Figure 3. For clarity, the stimulus on (sinusoid plus noise) and stimulus off (noise only) simulation results are plotted separately in Figures 10 and 11. The first 10 points represent 10, 60-sec data records of signal plus noise,

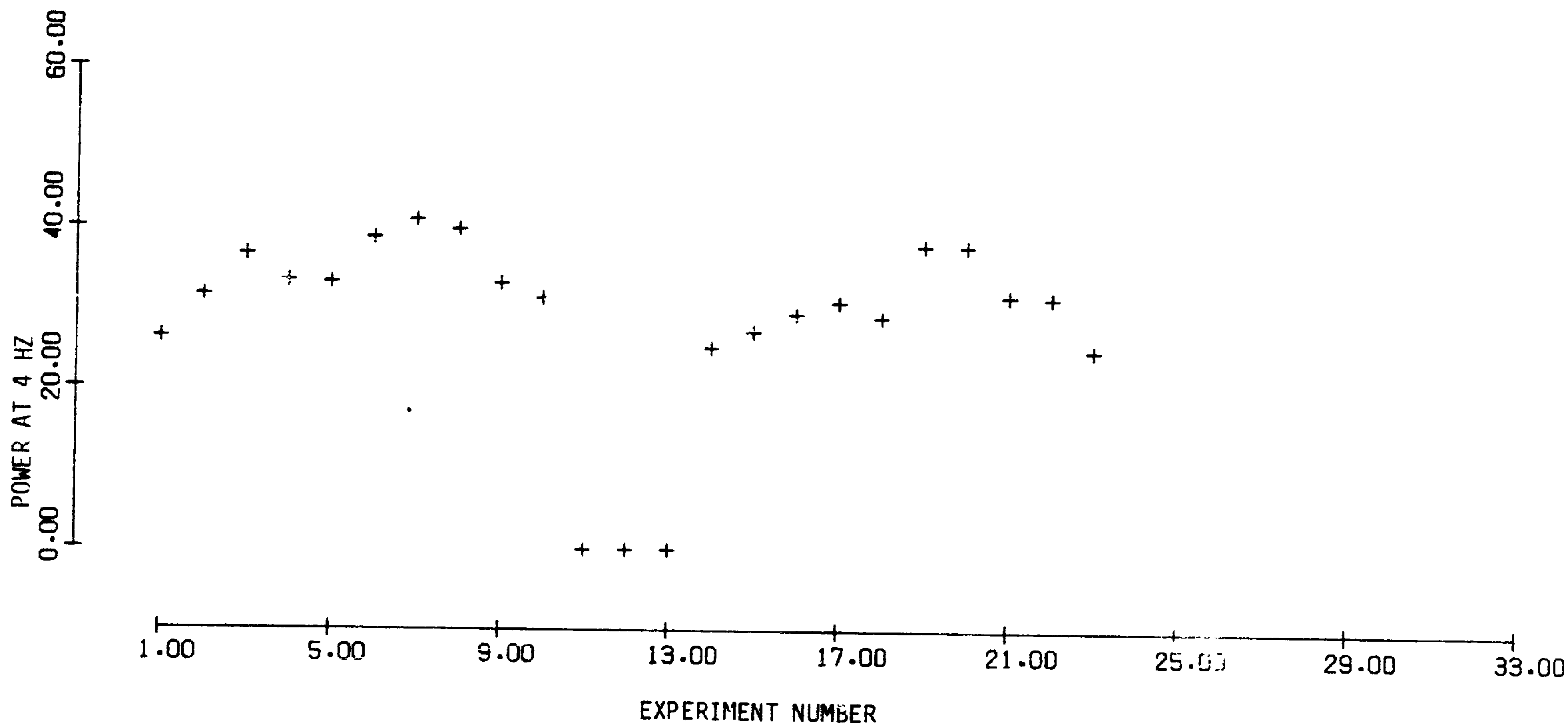


Figure 10. Classic estimator (simulation).

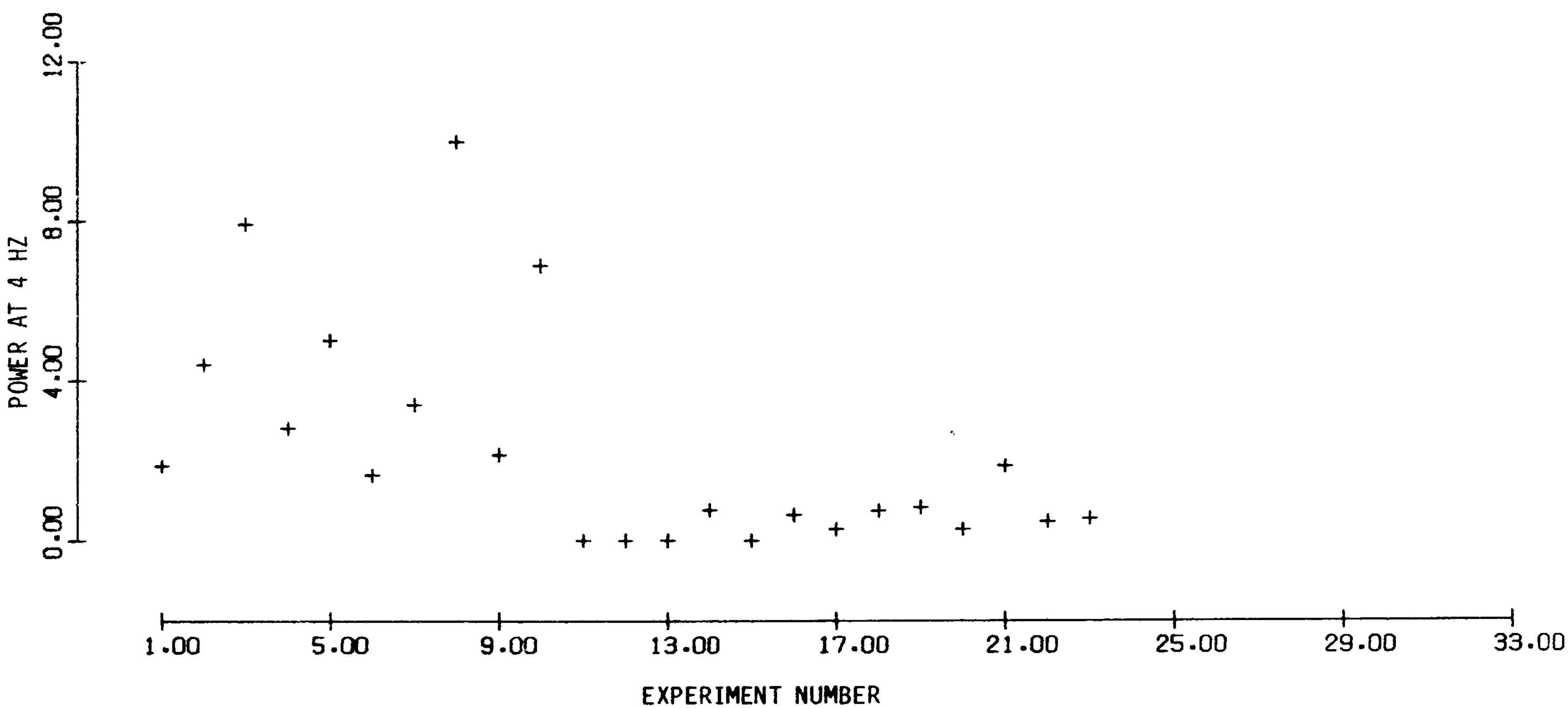


Figure 11. Current estimator (simulation).

followed by 3 min of quiet, and 10, 60-sec noise-only runs. Figure 10 shows the performance of the classic approach, and Figure 11 shows the current method. The same data were fed to both processors, and the simulation parameters were $P = 9$, $Q = 30$, $N = 60$ (60, 1-sec intervals per point for both techniques). The actual mean and standard deviation of the simulations, along with the predictions from Eqs. 4 through 7, are shown in Table 3.

TABLE 3. COMPARISON OF SPECTRAL ESTIMATORS

		Stimulus on		Stimulus off	
		mean	σ	mean	σ
Classic	Simulated	34.54	4.30	30.59	4.33
	Predicted	34.5	4.42	30.0	3.87
Current	Simulated	4.60	2.68	0.65	0.48
	Predicted	5.0	2.18	0.5	0.5

These results are quite revealing. The results using the current approach (Figure 11) demonstrate that merely adding a sinusoid to broadband noise drastically increases the spread of the data points in addition to raising the mean. The numbers are generally similar to those of Figure 3, as desired. The classic approach, on the other hand, has a much lower percentage variability, although the separation between signal plus noise and noise is not (proportionately) as great. Appendix K shows that the percentage variability (σ/m) for the classic method is always lower than that of the current processing scheme for a simple signal plus noise model. Whether this result is useful to the U.S. Air Force depends on the true signal characteristics.

The amount of noise in these simulations is quite large. Before averaging, the sinusoid ($P = 9$) power level is only 4.5 units above the background noise level of 30 (SNR = 0.15). If the noise--due to background EEG, measurement noise, processing errors, or physiological artifacts--is actually this bad or the signal this small, most processing schemes will be hard-pressed to drastically improve on these results. In order to determine whether substantial improvement is possible, we believe the raw data should be analyzed in detail.

We note in passing that the increased variability shown in the stimulus-on results appears due to the "cross term" PTQ (or PTQ/N) in the variance formulas. This term is a result of the squaring operation in the power estimates. If the signal shape is known (or easily approximated) and the phase lag (latency) is relatively constant, it may be possible to linearly filter the signals, thus avoiding the interference cross term. For example, for the sinusoid plus noise signal above, if we form

$$\hat{A} = \frac{1}{T}\int_0^T z(t) \sin \omega t \, dt$$

The mean of $\hat{A}$ is

$$\bar{\hat{A}} = \sqrt{P/2}$$

and

$$\text{var } \hat{A} = \frac{Q}{2T}$$

which is independent of P. For the parameters used in the simulation,

$$\bar{\hat{A}} = \sqrt{4.5} = 2.12$$

$$\text{var } \hat{A} = \sqrt{30/120} = 0.5$$

The degree of noise attenuation with this approach depends on the total integration time (60 sec in this case) which is the reciprocal of the bandwidth used. A longer averaging time corresponds to a narrower bandwidth for the noise to pass through. In the U.S. Air Force case, it may be possible to rearrange experiments to permit longer data lengths before stimulus-off readings. (If an accurate estimate of P is obtained, the stimulus-off readings might reduce to periodic baseline checks.) If 1-min response is needed (or even faster for the flash recovery tests), a sliding average may be used.

Finally, we note that the average of several logs of periodograms are sometimes used to estimate the log of the spectrum. This estimator has somewhat different properties (the variance becomes independent of the spectrum) which make it attractive in some circumstances. The scatter of the estimates is proportionately reduced, although the sensitivity to amplitude changes is also lowered.

Remarks

This analysis has described what the FFT (and periodogram) does in power spectrum estimation and how it is affected by noisy input signals. Using this knowledge, a simple signal model was constructed which qualitatively duplicates the experimental results at a single frequency (4 Hz). Alternate signal processing schemes which reduce the observed variability were then discussed.

These alternate techniques estimate different parameters than those of the current method, and the usefulness of any of these alternates can only be judged by considering the relevance of the estimated parameter as well as the accuracy achieved in estimating it. Thus, if the classic method (averaging periodograms) reduces variability (by better estimating the signal plus noise power) but does not help distinguish between two low-level signals of nearly the same power, it may not be useful in quantifying visual performance. Alternatively, by estimating all of the power near 4 Hz, the classic approach may find a signal component that was filtered out (e.g., due to phase jitter in the evoked response) in the current method, thereby reducing variability and improving sensitivity.

To determine what signals are really present, and what the best ways to estimate them are, a thorough analysis of the raw data (measured EEGs from many electrodes, as currently recorded) is necessary. Some of the tests that we recommend performing on this data are listed below.

First, the classic spectral estimation technique should be used to track the propagation of the full spectrum with time. (Other analysis tools, in addition to spectral techniques, may be needed if significant nonstationarities are noticed.) The changes in the spectrum between stimulus on and off should be noted. The response peaks (to the stimulus) should be examined to determine if they are broad enough to be measured by the classic technique but not by the current approach.

Examining the full spectrum will also determine whether any extraneous large peaks are present to corrupt the data and result in poor FFT scaling. Fixed-point FFT routines usually scale the signal to reduce error, which tends to be of a constant magnitude independent of the signal (i.e., if the signal weren't scaled, the maximum available signal-to-processing noise ratio would not be obtained.) A large peak away from 4 Hz might therefore govern the scaling operation, leaving the 4 Hz component with more noise than necessary. This may be cured by simply filtering the EEG around 4 Hz.

Also, we believe it is important to examine all the recorded electrodes for useful information. One channel will undoubtedly have most of the response power, but the other channels may be useful in obtaining an accurate EEG (background) signal which could be used to improve the VER resolution (e.g., by subtracting the background from the VER-plus-background channel before regular processing).

These tests, and others that may appear appropriate after an initial investigation, can all be performed on recorded data, and do not require special new experiments.

Conclusions

On the basis of analysis of the available data, we can conclude that the observed periodogram variability is consistent with FFT processing of a simple noisy measurement model. Therefore, it is entirely plausible that the observed variability is due to two principal factors: (1) a high "noise" level in the signal--most probably the spontaneous EEG, and (2) the extreme sensitivity of a single periodogram to the residual noise present after time-series averaging. In particular, the observed increased variability when the stimulus is present is probably caused by the nonlinearity in the processing technique (squaring signal and noise) rather than by an increase in the noise level.

We also believe that the variability in the processed signal may be reduced (i.e., the effect of the noise on a visual performance measure may be reduced) by alternate processing techniques. Two of the techniques discussed were: a simple modification to the current approach--altering the order of FFT and averaging operations--and a simple linear filter to estimate the VER amplitude. Selection of the most useful processing technique (or simply optimal tuning of the available techniques) must, however, await an analysis of the original measured data. Only then can an appropriate signal model and related processing scheme be chosen.

A thorough analysis of the raw data may reveal that our simple model is valid but that the signal to noise ratio ("signal" and "noise" as defined earlier) is simply too low to permit sufficient reduction of variability for the U.S. Air Force purposes. In this case, new information (e.g., through more electrodes) or revised experimental procedure may become necessary. The data analysis may also reveal that a more complex signal model, and sophisticated processing techniques, are required. In this event, improved performance may be obtained at the cost of some additional processing complexity. These issues are addressed in the next two sections.

ASPECTS OF EEG/VER VARIABILITY

In our Interim Report we developed the concept of an Eye-Brain-Electrode model (see also Appendix B). From information we obtained to date from the U.S. Air Force, it appears to us that a considerable effort is made by the U.S. Air Force to control for variability due to the experimental conditions and eye (especially for the monocular preparation). Thus, we will mainly address the variability due to the brain, discuss some apparently new aspects of the brain-electrode transmission, and aspects of improving the utilization of electrodes.

Roughly, the concept of variability of EEG and VER arose from experiments in which many factors are unknown and their combined effect on measurements appears random. But even when many experimental variables are controlled, successive measurements may differ in quality or in quantity. One attempts, of course, to control for as many factors as possible, but the number of potential factors in living systems is rather overwhelming. But even when the effect of some of the important factors is known individually for each factor, one can often not predict the effect of several simultaneously acting factors. All of the resulting changes in experimental outcomes may loosely be regarded as experimental variability.

Often a quantitative stochastic point of view is adopted in order to describe variability. This concept lends itself to a further subdivision of variability into variability due to sampling fluctuation (variability at fixed experimental conditions) and changes that are of a systematic nature such as adaptation or fatigue.

When quantifying variability, one should always be aware that the term is relative and the significance of a particular form of variability only attains relevance when predictions are formed. For example, variability of scalp potentials can be used to assess lateralization of the brain (Rebert and Low (84); Pfurtscheller et al. (81); Beaumont et al. (10)). In what follows we will not stress any particular measure of variability, but indicate in which sense a particular investigator perceived variability to be important.

In this section, we will first discuss the variability of EEG and VER under presumably fixed experimental conditions. Subsequently we will briefly discuss some anatomical and neurophysiological principles which have to be considered for the derivation of "good" measures (estimators) of VER.

General Considerations for Assessing Variability of Responses

For the purpose of quantifying responses as they are expressed in the EEG, four methodologies stand out:

1. Signal transfer (modeling characterization)

2. Steady-state responses (these often lead to signal transfer modeling)

3. (Single) response waveform analysis in space or in time (often one uses random stimulus intervals and averages waveform)

4. The use of "a measure" of EEG activity such as power spectral density estimation.

The first approach is a typical engineering approach and is geared for the prediction of an output (the response) given some input (the stimulus). In some instances the converse statement is also true, namely that the input can be estimated from the output. In principle such an analysis might appear to be the most attractive one. For practical matters, however, the method is only useful when fairly simple structures are analyzed or the set of possible inputs (stimuli) is small. The high complexity of living structures can set limits to the identifiability (e.g., too many variable components) of a given structure when only a "black box" approach is taken. Also, in order to construct a quantitative model for a particular input-output relation, much data has usually to be analyzed. For work in the direction of signal transfer modeling, see Desmedt (28).

The second approach, steady-state VER analysis, is in many cases an investigative stage prior to the above transfer-modeling approach. In steady-state VER analysis, a stimulus is applied periodically and the (usually) resulting periodic response is extracted. Typically amplitude and phase relation (related to latency) to the stimulus are studied at the fundamental frequency (e.g., reversal rate) and its harmonics. When hardware correlation filters are used for this purpose they may have adjustable bandwidth from about 1 Hz down to .001 Hz (Regan (85,86)). The narrow bandwidth is equivalent to taking a long averaging window and typically reduces "noise" or variability, but results on the other hand in slow tracking of possible true changes of a response. This method of analysis is used as a diagnostic tool in medical practice.

Single response waveform analysis is often done by averaging individual responses, all separated by large time intervals. Stimulation is done either in a periodic fashion, or preferentially with random time intervals between successive stimuli. Using randomized stimulus times is conceptually comparable to drawing randomized samples, a typical approach in statistical analysis. Such an approach is aimed at reducing variability (or cost) of decisions based on the sample (such as decision regarding the visual performance).

One may categorize a fourth approach in the evaluation of the response of the EEG to a stimulus. This approach is characterized by the use of "a measure" of EEG activity. The change of the measure in response to a stimulus is studied. The choice of a particular measure reflects the experience of the investigator or, in some instances, the properties of an algorithm (Sencaj et al. (101)). Frequently used measures are the power spectral density at specific frequencies or energy within a frequency band and the autocorrelation (or cross-correlation) at selected lags. When spatial distribution of EEG activity is measured, spatial spectra and correlation are used (Adey and Walter (3), Nunez (74)). The use of such measures must usually be regarded as somewhat nonspecific. Lack of well-defined objectives, insufficient understanding of underlying mechanisms but well-understood properties of above-mentioned (noncommittal) measures explain their preferential use.

In what follows we will consider evidence for the variability of any of the above-mentioned measures as necessary. The discussion of several measures relating to variability results directly from the U.S. Air Force objective to reduce variability in their measures: the goal to derive such measures (with respect to particular U.S. Air Force objectives) can only be accomplished when the properties and contributions of several ongoing physiological and physical mechanisms are clarified.

Variability of the VER

In the last decade the variability of the VER has become of increasing concern, especially in the context of establishing confidence in averaged VERs. Physiological variability as opposed to sampling fluctuations are often described in more specific terms such as adaptation, conditioning effects, habituation and dishabituation, sustained and transient responses, and response plasticity. To understand this physiological variability of the VERs, it was found important to investigate responses in relation to other ongoing brain activity such as various rhythms ($\alpha,\beta,\gamma,\delta,\mu$), the Bereitschafts potential, and the P-300 wave. For some new findings in this area using sophisticated signal analysis, see Chapman et al. (21). For improved understanding of the variability of responses, invasive microelectrode studies have become quite prevalent. In contrast to scalp potentials they provide drastically increased spatial and frequency resolution of electric nervous activity.

One of the early systematic studies of variability in the VER is found in Ciganek (25) who used O_z-P_z bipolar responses to flashes (.3 Joule, eyes closed) with random intervals (3-6 sec). Ciganek describes considerable intersubject differences analyzing mean amplitude (at peaks of response wave some 10 msec after stimulus) and standard deviation. The ratios of standard deviation over average peak amplitude lie between .24, for the "best" subject, up to about 10, for the "worst" subject. In that latter subject not only the mean amplitude decreased, but more importantly the standard deviation was increased by a factor of 8 compared to the "best" subject. Very interestingly, Ciganek reports also for some subjects a pronounced decrease of VER variability (standard deviation of potential) some 80 msec after the flash stimulus. Apparently this decrease in variability arises from a general response of the brain to the stimulus. The finding of modification of brain activity by stimuli is also in agreement with the investigations by Lansing and Barlow (61).

The relation between VER, adaptation attention fatigue, etc., has been studied quite extensively with invasive microelectrode techniques or microelectrodes attached to the scalp (Riggs and Wooten (90), Van de Grind et al. (112), Moise and Costin (71), Gould et al. (41), Salamy and McKean (96), Oatman and Anderson (75), Pay (79), Schafer (97), Halgren et al. (48), Rohrbaugh et al. (92), Kitajima (56), Kulikowski et al. (57), Drozdenko (33), Hennessy and Levine (51), Grunewald et al. (43)). There is general agreement on the importance of the limbic system (related to emotion and autonomic control) and hence in microelectrode studies recording sites often include the hypothalmus and hippocampal area in order to obtain indicators for the arousal state of the animal. The typical measurements to derive these indicators utilize transmembrane potentials (slow potential variations) and neural firing rates of single cells. By these techniques the effect of alertness or drowsiness of the test animal on the transfer characteristics of the lateral geniculate bodies (the first relay stations of the optic nerve, layered structures where binocular interactions first time take place) has been shown.

On an anatomical level (Hubel and Wiesel (52)) back projections of fibers from cortical layers to the lateral geniculate bodies have been shown. The complexity of this structure, lateral geniculate bodies and visual cortex, is further underlined by evidence for inputs from structures other than the lateral geniculate bodies (inferior and lateral pulvinar, Rezak and Benevento (89)) to the primary visual cortex (Brodman's area 17). The existence of these connections underlines the capability of VERs to produce a rich set of responses under seemingly identical experimental conditions. These findings also suggest not viewing the visual cortex as an "isolated unit" when trying to model certain aspects of it. Instead, activity in other areas may be important in explaining activity of area 17.

Along these considerations an interesting aspect of VER variability is the apparent influence of the phase relations between α-waves and stimulus on the VER. Work by Dustman and Beck (34), an extension of earlier psychophysical results, aids in understanding subjective brightness enhancement when flash stimuli are phase locked with α-waves. The importance of considering various components of the EEG is underlined by this finding.

The modulation transfer function (MTF) as a function of space and time has been studied by Van de Grind et al. (112), and they give their results in terms of isomodulation lines. However, their finding should be taken with some care since Harter and Previc (50), investigating variability of the MTF quite rigorously, found important adaptive processes in this transfer system. In essence they studied the susceptibility of the spatial MTF to changing attention to the stimulus and expectation of the individual. By analysis of response amplitudes at a specific latency, they were able to show an actual tuning of specific frequency channels. For evaluating the MTF the experimental sequence of stimuli is thus important. Negligence of this effect would clearly increase the unexplained variability of any results.

Several investigators have been concerned with the effect of simultaneous stimulation from different sensory modalities. The frequent finding of strong interactions of evoked responses to these paired stimuli (possibly with some intrastimulus time lag) (Oatman and Anderson (75), Fox (37), Stowell (106)) suggests the control of at least some of them, auditory stimuli in particular (Desmedt (29)).

Discussing variability of measures of VER also invites the question for modifications of measures which, in a particular context, improve performance. One of the possible augmentation of measures is the P300 wave shown to be a sensitive and significant indicator of attentiveness (Drodzenko (33)). However it appears that the use of the P300 wave limits stimulus rates to frequencies below 3 Hz.

Modifications of measures of VER which do not show this limitation are very desirable. Two findings concerning latency and spectral properties might be important for the U.S. Air Force. De Voe et al. (30) showed that predictions of stimulus luminance based on latency performs markedly better than when based on amplitude. Somewhat in contrast to this finding might appear the recent data by Osaka and Yamamoto (77) who show very high correlation between amplitude and latency when luminance is changed. Their particular stimulus condition, a 1° stimulus source, presumably very precise orientation of the eyeball, a well-motivated subject, and the analysis of very early response waves (P1) might in part account for their result. Regarding day-to-day variations they find reaction time and response amplitude to change less than 0.5 log units.

The second finding concerning different spectral components is discussed in Sokol (103). He summarizes that "low and medium frequency range reflect poorly the psychophysically determined spectral sensitivity functions, while the high frequency components show good agreement with photopic spectral sensitivity." These findings suggest the expansion of the measures derived from the scalp potentials. Specifically, high frequency components of the EEG and the phase relation (a relative of latency) of the VER to the stimulus should then be included in the analysis.

Spatial Properties of the VER

From basic neuroanatomic and physical considerations one expects to find local electric activity of the scalp to correlate with stimulus modality. Clearly, the combined consideration of spatial and time properties of the VER lead to some experimental and data acquisition difficulties and new aspects for data analysis. On the experimental side the main problems are reliable reproduction of multi electrode arrays and on the data acquisition side high digital to analog conversion rates. For careful mapping of the entire scalp potentials Ragot and Remond (83) recommend about 200 electrodes (human), spaced about 2 cm apart. Currently, however, development of potential maps is usually limited to tens of electrodes and hence some spatial smoothing has to be performed in order to arrive at such maps. Some of these maps are presented and discussed in Creutzfeld and Kuhnt (27), Allison et al. (6), and Goff et al. (40). These maps might provide guidance for selection of multiple electrode placement. In addition, timing windows for data acquisition may be specified in order to reduce the digital-to-analog conversion rate requirements.

The EEG of Restrained Monkeys

In many VER experiments the experimental animal is restrained in its body movements. Studies concerning the effect of restraint on EEG were conducted especially in the case of monkeys. It was found that with progressively more restraining conditions (head, legs, arms), the power spectral density of the EEG shows corresponding progressive changes (Bouyer et al. (13), Rougeul et al. (93)). In these studies the EEG of the experimental animal, the unrestrained condition (in the cage), was compared to the condition when the animal was strapped down in some device. Bouyer et al. (13) suggest the use of an anxiolytic drug (diazepam) in order to restore the highly abnormal EEG to near normal.

Anatomical and Neurophysiological Considerations of VER Changes

For studies of visual evoked responses one usually observes the electric potential near the occiput. The anatomical basis for the use of this electrode location is the proximity of the underlying visual cortex (area 17, 18, 19). Consequently, one finds relatively large electric VER potentials on the occiput when compared to the locations. It is necessary to obtain large potentials because of masking noise-like "background activity" of the brain.

From various field mapping techniques and neuroanatomic investigations (Szentagothai (107, 108), Brooks and Jung (15), Sokol (103), Hubel and Wiesel (52)) it is found that the visual world of upper half, lower half, left half, right half, and a macular area have to be distinguished. These areas map into corresponding areas in the visual cortex. Interestingly the macular area has a very large representation in terms of area on the cortex when compared to more peripheral regions. Sokol (103, p. 25) gives as a typical value for this representation near the fovea that 2 min of arc in the visual world correspond to 1 mm in the visual cortex.

Studies by Harter (49), in qualitative agreement with Riggs and Wooten (90, p. 715), show that the central 3° are mainly responsible for VER potentials on the scalp. Data by Sokol (103, Fig. 14) shows the small contribution of stimuli outside that central 3° range. From these experiments a relatively large response can be expected from low-diameter stimulus fields (compare Osaka and Yamamoto (77)) provided they are centered foveal. However, slight displacement (a few minutes of arc) may cause changes of observed potentials, because the electrode location does not follow the corresponding response location of cortical electric sources. An additional aspect arises when opposing dipole moments are nearly cancelling (possibly left versus right hemisphere). In such a case a slight spatial shift of the stimulus may either result in zero potential, or amplitude reversal. That such effects deserve attention follows from the distinct properties of the response components C1 (∿ 75 msec delay), C2 (∿ 100 msec delay), and C3

($\sim$ 150 msec delay) described by Jeffrey (in Desmedt, (28) p. 136). He shows that inversion of patterns produces corresponding inversion for some of the potentials. Hence, for at least certain patterns, cancellation of differential voltages may result. In principle such an effect may contribute to the finding of some researchers (Sokol (103)) of rather variable amplitude but fixed response times at a given luminance. This concept might also be related to the finding of "variable" narrow-band low-frequency components compared to "less variable" high-frequency components. (High-frequency components may never attain a very fixed phase relation with the stimulus and hence cancellation is not so obvious.) Anatomical considerations about the mirror image-like mappings between areas 17, 18, and 19 suggest that these contributions are separable by selecting appropriate electrode locations. In summary, analysis of scalp potentials by space, time, and frequency properties is important for the derivation of good measures of visual performance.

Signal Transmission from Cortex to Scalp

It has puzzled neuroscientists now for some time (F.G. Worden, 1979, Director, Neurosciences Research Program, M.I.T., personal communication; Pfurtscheller and Cooper (80)) that despite the large high-frequency content of intracortical recordings, high frequencies on the scalp are very small and are buried in electronic noise. Pfurtscheller and Cooper inserted microelectrodes into cortical regions, passing high-frequency currents through the tissue. No particularly selective suppression of high-frequency components, as recorded on the scalp, was observed; they call for an explanation other than tissue properties to be responsible for the surprisingly weak high-frequency components on the scalp as they arise from natural cortical activity.

To get a grip on this phenomenon, it appeared worthwhile to us to review properties of other bioelectric potentials, especially those which arise from a large number of similar cells. The muscle as a source of bioelectric potentials comes to mind. There too, one observes rather weak high-frequency components on the superficial skin, while internal activity contains strong high-frequency components. Some attempts have been made to account for this phenomenon (including false arguments about wave-guide phenomena), but the most successful and accurate work was done by Lindström and Magnusson (64). His theory predicts for fibers, conducting action potentials with a given velocity, a power spectral density on the skin (decreasing with increasing frequency), which is in good agreement with experiments. Without going into detail of his mathematical derivation, we just point out that the phenomenon of small high-frequency components is basically due to the travelling of action potentials. In Appendix L we give a simple outline of the concept which was solved by Lindström and Magnusson (64) for special geometries. The result suggests the possibility of tuning sensor electrodes to nearby sources by selecting high-frequency components. To exploit a range of frequencies rather than a single frequency, the frequency-dependent properties of electrodes become important and motivate the subsequent section.

Frequency-Dependent Properties of Macroelectrodes (and Amplifiers)

A good introductory treatment of the transfer characteristics of electrodes is given in Cobbold (26) and the relevant main points are reviewed in Appendix B. In summary, we recall that the typical impedance of these electrodes at low frequencies is around 10 kΩ (compare also Osaka and Yamamoto (77)). Interestingly, however, as higher frequencies are used, the impedance falls considerably. To assess impedances of electrodes empirically, electrodes array approaches similar to Robillard and Poussart (91) can be used.

It should be noted that the frequency-dependent transfer function characterization is insufficient to understand the limitations of recording. The frequency-dependent noise characteristics set the ultimate performance limit. With respect to these noise characteristics the work by Van der Ziel (113) is fundamental. He distinguishes several different mechanisms for noise, the most important ones in practice with electronic components (including electrodes) being the 1/f-noise (mainly due to quantum mechanical effects of tunneling), burst noise (with an insufficiently understood mechanism of origin), and Schottky-noise. The 1/f-noise, or flicker noise, has a power spectral density which falls with frequency f like 1/f and is of importance for very low-frequency noise (including drift) up to frequencies of a few hundred Hertz. The burst noise has similarly a moderately low-frequency power spectral density, while the Schottky-noise behaves like white noise from DC up to terahertz.

The characteristics of the noise suggest different limitations for the recording of low versus high frequencies. Van der Ziel (113) emphasizes the importance of matching amplifiers to the frequency band of interest (possibly using different amplifier units for different frequencies) and using amplifiers with certain technologies (e.g., use, in some cases, input pnp-transistors rather than npn transistors or FETs and use certain semiconductor cleavage planes). He also discusses a variety of aspects in connection with the design of amplifier input stages. It appears to us that many investigators (personal communications) are not aware of some of these fundamental principles. The view currently held (Cobbold (26)) is to use high-input impedance in order to insure good common mode rejection. However, in connection with sophisticated signal processing this need has not yet been demonstrated.

Summary

In summary, it is seen that there is considerable evidence for apparent VER variability with an origin other than just signal analysis. The origin of this variability is mainly neurophysiological. Ways to improve prediction or classification in the presence of variability must come from improved extraction of information from the scalp potential field. This can be accomplished with improved techniques for VER analysis (as discussed in the next section) by consideration of an increased number of electrodes and expanded frequency band for analysis (such as the analysis of higher harmonics in relation to frequencies between harmonics). It should be recognized that a priori restriction of analysis to only one component of

VER (such as the power of the sinusoidal 4 Hz component of one electrode) merely limits the potential to measure visual performance; some of the important facets relevant to good signal analysis were shown in this section. Finally, along the lines of information extraction we showed ultimate limitations for information extraction due to the electrode and amplifier design. Interestingly, it appears to us these limitations have not yet been reached (personal communications, F. G. Worden), and little is known about information extraction of high frequencies. As a result of these observations, we see considerable potential to aid in improving upon current results of the U.S. Air Force.

IMPROVED TECHNIQUES FOR VER ANALYSIS

The use of classical spectral analysis techniques for VER analysis has been discussed in the section on "Analysis of Current Processing." These methods are quite popular in EEG analysis and have the advantage of being almost universally understood in terms of their basic properties. However, they possess several drawbacks which are significant for VER analysis:

1. Nonstationary components are difficult to analyze. The VER contains significant nonstationarities.

2. Stochastic effects are not specifically accounted for. The VER contains significant stochastic effects.

3. Relatively long data epochs are required.

4. They implicitly assume that activity is wideband when, in fact, a more appropriate model may employ only a relatively few generators.

5. They are data-<u>independent</u>; that is, the decomposition is the same for all signals, since the measured signal is always represented as a weighted sum of sinusoids. This assumption is questionable for signals of the complexity of the VER, as indicated in 1 and 2.

A wide variety of techniques offer potential improvements over the use of classical spectral analysis. These will be briefly discussed in this section. More detailed discussions are presented in the appendixes.

Philosophy of Approach

The underlying philosophy of approach which is suggested for VER signal processing is based on the notion that all available prior information should be brought to bear on the problem. For example, if we wish to <u>model</u> the signal in some fashion, then we should use actual data to build the models. We should incorporate information relative to known spectral limits (upper and lower bounds), characteristics of disturbances, structure of underlying generators, etc. As an example, the discussion in the section "Aspects of EEG/VER Variability" has delineated several research results describing the importance of latency variations. Models which are utilized should thus be consistent with the observed latency data, in terms of its relation to amplitude, its possible rates of change, etc.

The approach we propose is model-based and is a combination of phenomenological and physiological components. Phenomenological modeling is a "black-box" approach which is often useful when trying to emulate complex signal processes for which no adequate models exist. Phenomenological models are developed without regard to underlying physiological structure; they depend only on trying to match observed phenomena. The simplest example of this approach would be modeling the alpha wave as an oscillator, with some additional nuances to allow for observed statistical variation. The physiological approach is based on the idea of using known structure or structural constraints in the model. Although we seek to use physiological information as appropriate (e.g., dynamics of the eye), it is felt that the overall model will, of necessity, be more a phenomenological one.

We seek parsimonious models; models which are too complex almost invariably lead to high noise sensitivity. In the section "Analysis of Current Processing," it was demonstrated that the variability observed in the U.S. Air Force data was consistent with very simple statistical models. Such simple models can form an important benchmark in design of models. For example, one needs to go to more sophisticated models only if the simple ones prove inadequate. In addition, the modeling errors can often reveal, by their nature, what the appropriate next modeling step is. By this process, a series of increasingly sophisticated models can be formed, as required, with reasonable assurance that the models are not overly sophisticated.

The approach we propose is not just based on analysis of the VER but utilizes the observed signal structure directly. Function is always linked to structure. In the past decade, much progress has been made towards understanding the ways in which information is communicated and processed in the brain. In addition, recent experiments have strongly suggested that the EEG itself is a "second signal system" (Adey (4)) to which the brain cells are tuned. That is, the EEG signal exerts an influence on the way in which information is communicated and processed within the brain. If this is indeed true, then it may be possible to eventually exert some stabilizing control over the brain through the use of weak external electric fields.

We will not pursue the implications of external control here. Rather, we wish to point out the importance of these experimental results on the philosophy of approach to EEG, especially VER, analysis. Consider the simple lumped parameter model shown in Figure 12. In Figure 12 (a), the EEG $e(t)$ is viewed as an output function consisting of noise-corrupted signal:

$$e(t) = S(t) + n(t) \tag{3}$$

In Figure 12 (b), the EEG is viewed as a second signal system; thus $e(t)$ contains <u>information</u>. The EEG depicted in Figure 12 (a) may contain almost no information, since there is no a priori bound on the noise power; thus, the EEG viewed as output could, in principle, be almost entirely buried in noise. On the other hand, the "second signal system" model puts practical upper limits on the signal-to-noise ratio. Since the brain utilizes the EEG as a source of information, the signal cannot be almost entirely buried in

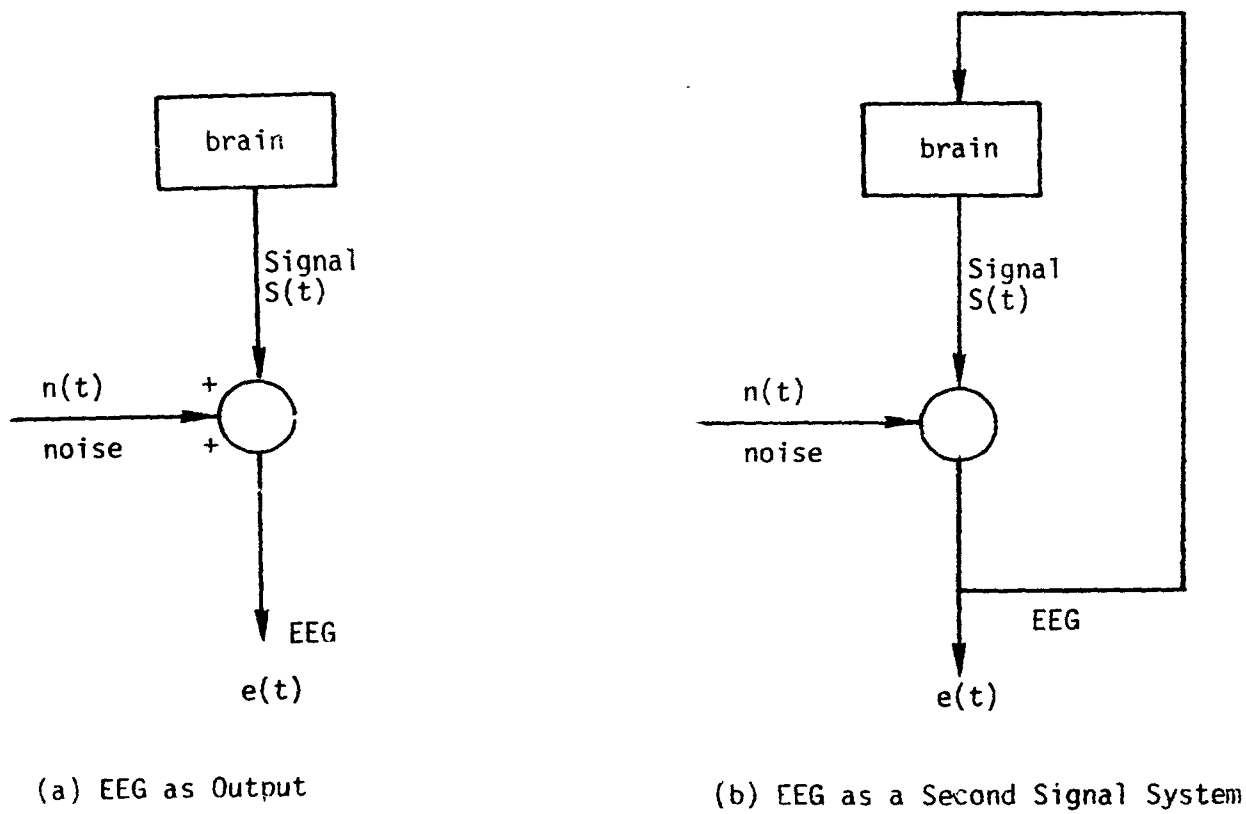


Figure 12. Implication of the EEG as a second signal system in EEG signal processing.

noise; extraction of information would be rendered extremely difficult. The implication of this result is that the EEG should, if viewed correctly, supply us with information related to on-going brain function. We are aware of no experimental results which would invalidate this conclusion. We wish to stress this point here since it has impact on the philosophy we wish to use in analyzing EEG data.

Since function is inevitably related to structure, we can conclude from the preceding argument that the EEG may provide information as to the states of groups of cells and, more importantly, to changes in the states of groups of cells. If this can, in fact, be done, it is strongly suggested that more sophisticated analytical methodologies will be required than have been used heretofore. In his paper Adey (4) says that

> lack of (new mathematical and statistical methods) remains a critical bottleneck, in which engineering application has seriously failed to keep pace with new physiological knowledge on the temporal and spatial organization of brain tissue and brain systems .... our paths to an understanding of brain function must surely falter and fail unless and until ways are found for mathematical expression and analysis of the multidimensional and hierarchical organization of cerebral information transaction.

We agree with this conclusion and would add the following points:

1. To our knowledge, EEG analysts have, as yet, not utilized several powerful analysis tools already available. These include several techniques of communication theory, adaptive filtering, and generalized state space modeling techniques. These are discussed in the appendixes.

2. More serious attention has to be given to the stochastic aspect of the problem, so that information-bearing signals are not treated as noise and true noise is filtered effectively.

3. A methodology is required to incorporate the idea of multiple, nonlinearly interacting, generators.

4. Since the EEG is a manifestation of a distributed communication and information processing network, a distributed process model should eventually be developed. This would probably require a large number of electrodes and models based on distributed network, or large scale systems, theory. These steps are in the future, of course, but are an indication of the large amount of work that yet needs to be done in EEG signal-processing development.

These points have been mentioned here to reinforce Adey's very important observation that the present state-of-the-art in EEG signal processing is seriously lacking. The methods which we discuss here are based on the present state-of-the-art in signal analysis. Thus, these techniques can be tried with a minimum of software development time.

EEG/VER Signal-Processing Objectives

Two types of objectives may be enumerated in EEG/VER signal processing. The first is a general set of objectives which would be applicable to a larger class of problems as well; for example, all biomedical signal-processing problems. The second type of objective relates to the specific problem at hand, i.e., EEG/VER signal processing, and includes determination of descriptive characteristics of the EEG/VER signal; e.g., characteristics not shared by other types of biological signals.

General Objectives. The general objectives of EEG/VER signal processing are:

1. provide tools for extracting useful information from the EEG signal;

2. perform information compression; and

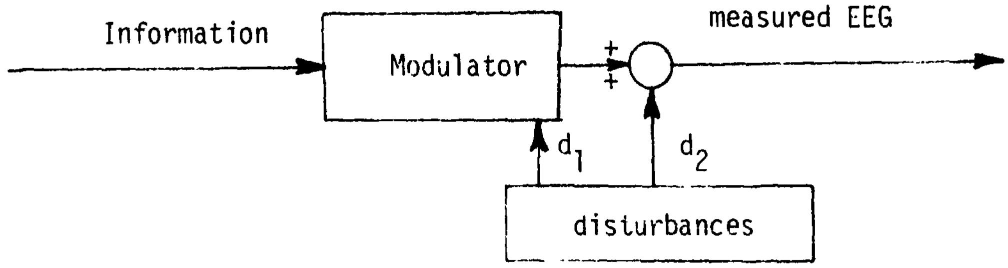
3. remove noise from the desired signal processes.

Tools to be sought for information extraction should be general and powerful. They will be determined on the basis of extensive analysis of the data to determine the character of the signal and/or noise. Note that the first objective implies that a measure of useful information be available. This may or may not be a mathematical function. It could be based on a statement such as "we wish to eliminate variability between these particular measured signals" or "we wish to obtain a smooth response to this flash impulse." In this case, information may be only vaguely defined mathematically; however, an improvement in information extraction will be readily apparent by visual evaluation of the output of the signal processor. In a more mathematical approach, measures such as entropy, rms fit error, or others may be used.

Information compression is a very important step. Raw VER data, sampled at a rate of 250 samples/sec, for example, quickly fills up a digital storage medium, especially when multiple electrodes are used. Not all of the data carries information. As a matter of fact, the information rate is probably very low. The implication is that if we can extract only the useful information, a tremendous reduction in storage can be realized. More importantly, however, is that this information is what we need in order to properly analyze the data. Information extraction is generally accomplished by employing modeling techniques, in which the signal is described with a parsimonious set of parameters. These parameters, then, are the carriers of information.

Once the signal process has been adequately described by, say, a parametric model, it remains to remove the undesired disturbances. Disturbance models may be utilized, which may be generated based on statistical analysis of the data. Some disturbances may have specific characteristics (spike and wave, e.g.) which can be used to advantage in detecting and removing them. The VER has, characteristically, a large amount of noise relative to signal, which is why a single VER is rarely used for analysis. Typically many VERs are averaged. Although this does tend to bring out a mean VER signal, any variations between responses which carry information tend to get averaged out. We propose to use techniques which can be used to process a single VER.

A general model of the process by which the measured EEG is generated is given below.



Information is thought of as being modulated by one or a set of modulating functions of unknown character. For example, if the EEG contains phase-modulated signals, then the information we seek would be carried by a phase process $\phi(t)$. Assuming simple sinusoidal carrier modulation at frequency ω, the EEG in the absence of disturbances would be $\sin(\omega t+\phi(t))$, and $\phi(t)$ could be recovered using phase-lock loop techniques described in Appendix D. Note that if $\phi(t)$ were a constant, the modulation transforms the constant ϕ into a continuous time process with infinite duration. The disturbances d_1 and d_2 may be correlated in practice. Using this general model, our objective is to:

1. remove disturbance d_2;
2. recover the undisturbed modulating function; and
3. demodulate to recover the desired information.

Specific Objectives. The specific objectives are predicated upon satisfaction of the general objectives just discussed. The objectives, along with analysis tools and subtasks, are listed below in approximate chronological order.

EEG/VER Data Analysis

compressed spectral arrays
correlation analysis
transient response
effect of VER averaging
cross-correlation analysis
(a) between patients
(b) same patient/different times

Model Development

- overall signal processor structure
- physiological considerations
- signal models
- noise/disturbance models

Performance Evaluation

- parameter identification
- model sensitivity determination
- model validation
- information extraction
- pattern recognition

Redefinition Phase

- project redefinition
- experiment design
  - (a) enhance model validation
  - (b) disturbance reduction
  - (c) enhance performance
- model redefinition
- performance evaluation criteria

This list is meant to represent an outline of objectives and there will be a synergism between the specific topics listed. For example, some modeling may be performed prior to data analysis to better define the data analysis objectives. Prefiltering may be necessary to reduce disturbances in regions outside the spectral bands of interest.

Data analysis is the initial information-gathering phase in which we seek to learn as much as possible about the measured data. An important aspect here is the sensitivity of the analysis to uncontrolled or unmeasured changes. Model development will proceed in earnest in the next phase. It is expected that both simple and sophisticated models will be developed. However, the preferred approach will be to utilize simple models initially and investigate the conditions under which these are inadequate. This approach will provide insight into development of more appropriate and complex models at a later stage.

Evaluation of performance will be assessed using a variety of techniques. Robustness and sensitivity will be evaluated. Artificial data will be generated, as required, to provide controlled inputs and disturbances. Pattern recognition techniques will be used, as necessary, to assist in evaluation of the signal processing results in case there are more than two or three parameters in the models (which we expect).

Redefinition of the problem and proposed solutions are expected to take place during all of the above phases, as new information, other research findings, test data, etc., become available.

Discussion of Techniques

We now present a brief discussion of several techniques which may be useful for VER interpretation and analysis. The reader is referred to the appropriate appendix for a more detailed description of the techniques.

Frequency-Domain Signal-Processing Techniques. There are several different types of frequency-domain signal-processing techniques, all of which are based on a decomposition of the data into a set of spectral components (sinusoids). Care must be taken, when using digital processing, that the sampling rates are high enough to capture the frequencies of interest without aliasing. In addition, sampling windows must be wide enough to capture the lowest frequencies of interest.

The Fast Fourier Transform (FFT) is perhaps the most popular spectral decomposition technique for EEG/VER analysis. A detailed discussion of the properties of the FFT when used for analysis of the VER under a periodic visual stimulation is given in the section "Analysis of Current Processing."

Recently, several alternate techniques have been developed for spectral estimation which offer advantages over the FFT in noisy environments and when the data epochs are rather short, perhaps only a partial cycle at the lowest frequencies of interest. These are the Maximum Entropy Method (MEM) and the Maximum Likelihood Method (MLM).

A detailed discussion of frequency-domain signal-processing techniques is given in Appendix C.

Communication-Theoretic Methods. These methods are model-based techniques of signal tracking and may prove useful in VER signal analysis. The models are based on the assumption that the VER or EEG is a process composed of signal and noise components. The signal components we wish to track are further assumed to be composed of one or more periodic processes which are modulated. The modulation which we wish to recover is the information carrier. As an example, latency variations in the VER could be tracked using this approach. It is well known that the phase coherence in the spontaneous EEG is affected by attention. This may also be true in the VER, although to a lesser extent.

It appears that the use of phase-lock loops is an attractive approach to the problem of signal tracking and recovery of modulation information. These can be designed to recover amplitude modulation (AM), phase modulation (PM), frequency modulation (FM), or a combination of these. In addition, other modulation models, such as phase or frequency shift keying, can be tried.

A detailed discussion of communication-theoretic methods and phase-lock loops is given in Appendix D.

Nonadaptive Time-Domain Analysis. Time-domain signal-processing techniques have the advantage of working directly with data as it evolves in time. Typically, time-domain techniques are recursive in nature; that is, the signal-parameter estimation process evolves in time along with the actual data. The most commonly used approaches utilize stochastic Markov process models for the observed data; these models are consistent with the need to build recursive signal processors.

Perhaps the most important class of time-domain models are auto-regressive moving-average (ARMA) processes. These have been used to model the spontaneous EEG (e.g., Bohlin (12), Zetterburg and Kjell (121), Segen and Sanderson(100)) and should have application to modeling of the VER as well.

A more general approach to time-domain tracking of signals is the Kalman Filter. This filter utilizes a linear Markov process model and a linear measurement model. The underlying dynamical process is driven by a white noise process and the measurements are assumed to be noisy. There are several advantages of Kalman Filters over the ARMA modeling approach. The structure of the filter is a more intuitive one, allowing the designer to better use his judgment in constructing the filter. An even more significant advantage is the fact that model identification is much simpler, and specialized software exists for determining the structure and estimating the parameters of the Kalman Filter directly from time-series data. Finally, a third advantage lies in the structure of the filter itself. It is relatively easy to model nonlinear effects and account for known time variation of model parameters. The Kalman Filter is backed by almost 20 years of theoretical study and application to a diverse set of problems in many fields including seismology, geology, biological signal processing, space navigation, economic and financial forecasting, meteorology, hydrology, image analysis, radar, and sonar tracking. In short, the Kalman Filter has proved to be beneficial in estimation and tracking problems where there are many variables to be simultaneously estimated and the signal process to be estimated evolves essentially as a stochastic Markov process. The EEG/VER signal-analysis problem should be amenable to this approach since it appears to satisfy these requirements.

A further discussion of nonadaptive time-domain approaches is given in Appendix E.

Nonlinear Systems Analysis. The techniques discussed to this point have been based on linear systems analysis in which the superposition principle holds; that is, it has been implicitly assumed that the evoked response is a superposition of several responses and that the total response is a linear combination of these responses. Furthermore, linearity implies the absence of saturation or hysteresis phenomena. It is well known that there are many nonlinear phenomena underlying evoked responses, most fundamentally in the generation of electrical potentials via the synapse. At a higher level, these nonlinear effects may not be apparent directly. However, they may manifest themselves in the evoked response via entrainment or saturation phenomena, which have been observed often in EEG analysis.

Nonlinear analysis is much more difficult than linear analysis and, for this reason, no general tools exist which are appropriate for all problems. However, several tools have been developed which may prove useful in analysis of the evoked potentials. Two of these are: (1) describing function analysis, (2) Volterra series analysis. These are described in some detail in Appendix F.

Adaptive and Robust Schemes. There is strong evidence that the nature of the evoked response may change significantly in time over both long and short epochs. The nature of these changes may be evidenced in several ways, including spectral content, amplitude, rms variation, etc. There may be short transient-like phenomena which may be part of the signal process or may be due to extraneous effects (artifacts) we wish to remove. All of these effects represent relatively unpredictable phenomena and the attendant evoked responses are then nonstationary processes. We need approaches which can adapt to information-bearing changes in the observed data and which are, at the same time, robust (i.e., insensitive to noise, artifact, and other extraneous clutter).

In order to track nonstationary processes, more sophistication is required than for stationary processes, since the observed data are qualitatively more complex. Several methods have been developed, however, which are felt to be particularly attractive for analysis of VER data. These methods can be utilized to analyze, simultaneously, data from multiple leads, and can do this without the requirement of growing memory for longer data epochs. In addition, real-time analysis may be possible for few leads and for simple models. Such (close to) real-time tracking and parameter estimation can be of great help in assessing the results and validity of a particular test shortly after or even during the test itself.

The methods which appear to have merit for nonstationary VER analysis are: (1) adaptive noise cancelling, (2) adaptive ARMA modeling (analysis of changing spectra), (3) adaptive Kalman filtering, (4) piecewise-stationary modeling.

Adaptive noise cancelling is a heuristic technique based on the assumption that the observed data in a particular lead consists of signal plus noise, with the signal and noise components correlated in a known qualitative way with signal and noise components in adjacent leads.

Adaptive estimation using ARMA modeling or Kalman filtering techniques employs more structure for the signal process; the underlying signal is modeled as a stochastic Markov process of known order and form. The parameters of the model are then estimated recursively and used to infer and track changes in the characteristics of the evoked response. Bohlin (12) has successfully applied adaptive AR modeling to tracking the spontaneous EEG, and it appears that this technique should also be applicable to the VER.

Piecewise stationary modeling of the VER is based on the idea that the VER can be adequately modeled as a stationary process over sufficiently short data epochs. These epochs are separated by points of transition of which the signal process is assumed to jump from one type to another type. Thus, changes in the behavior of the VER are assumed to occur in discrete steps rather than continuously over time. Several methods are available to handle this type of process. The most appropriate method to be used depends on the nature of the jump. If the time between jumps is relatively long, and the number of different signal types relatively distinct and small, multiple hypothesis testing methods involving a bank of Kalman Filters might be appropriate (Lainiotis and Park (59)). These have been successfully applied by Scientific Systems to ECG rhythm analysis (Gustafson et al. (45)).

If there are a large number of different signal types, multiple AR models can be derived using cluster analysis. This method has been successfully applied to analysis of the spontaneous EEG by Segen and Sanderson (100). If the time between jumps is relatively short or if there are transient artifacts, a generalized-likelihood ratios approach (Willsky and Jones (118)) may be more appropriate. This technique allows one to both eliminate artifacts and identify particular types of transients, as desired. This approach has been successfully applied to the detection and identification of cardiac rhythms using the ECG by Scientific Systems (Gustafson et al. (46)).

All of the techniques mentioned above have robustness properties, since they are designed to be insensitive to noise and other artifacts. The choice of the most appropriate technique must await detailed analysis of raw VER data on a variety of subjects and under a wide variety of conditions. A further discussion of adaptive and robust techniques is given in Appendix G.

Feature Extraction and Pattern Recognition Techniques. The previous subsections have been based on the notion that it is possible to generate structural models of the VER and then infer the VER characteristics from the parameters of the model. It may, in fact, turn out that it is not possible to generate adequate structural models of the VER. For example, the required number of parameters may be too large.

If this turns out to be the case, it might be more appropriate to utilize pattern recognition techniques. Pattern recognition may also be useful, if parametrized models are employed, to analyze the relationships between the parameters.

Pattern recognition is an approach which is essentially model-free; it depends, however, upon having a sufficiently large data base on hand. This approach has been found to be particularly useful in many biomedical signal processing problems, simply because of the inability to develop meaningful models of biomedical signals. The ECG is a good example of this. Although apparently more simple in nature than the EEG, no parametric model presently exists which can adequately capture the variations seen in the ECG signal. Recourse has inevitably been made to the tools of pattern recognition.

Pattern recognition generally takes place in two steps: (1) feature extraction wherein a parsimonious representation of the raw data is sought, (2) classification wherein the features are utilized in a decision rule to identify the pattern of the original data.

The feature extraction step is extremely important, since we wish to obtain an accurate representation of the data using as few parameters as possible. A particularly powerful technique which appears appropriate for VER analysis is the Karhunen-Loève expansion. By this technique it is possible to represent the time-synchronized VER (cf. Figure 2) as a weighted combination of predetermined basis functions. This technique has been successfully applied to representation of the ECG, and further discussion of this approach is given in Appendix M.

Once feature extraction has been performed it remains to extract the desired information from the numerical values of the features. Assuming there are more than two or three features, this information extraction can best be performed using pattern classification techniques. This involves the use of some type of decision logic to discriminate between patterns. This decision logic can be formed using two different types of approaches: (1) supervised learning, (2) unsupervised learning, or cluster analysis. In supervised learning, the pattern of each VER is known; that is, each VER can be labeled according to some typification. Decision rules are then generated to correctly classify each of the known cases. In unsupervised learning, such labeling is not used (generally it would not be available) and, in addition, the number of distinct classes of responses are not known. A wide variety of techniques are available for both supervised and unsupervised pattern recognition, and the choice of technique depends upon the nature of the problem at hand. It is generally true, however, that supervised learning is preferred assuming that labeling of the responses can be carried out. Further discussion of pattern recognition techniques is given in Appendix M.

CONCLUSIONS AND RECOMMENDATIONS

Based on our analysis of data supplied by the U.S. Air Force and a review of the relevant literature, we conclude that the observed variabi ity in the processed data is most probably due to the small averaged evoked response amplitude relative to the background EEG. This results in a low signal (response)-to-noise (EEG) ratio, which is a severe handicap to the current U.S. Air Force processing technique, as discussed in the section "Analysis of Current Processing." The basic problem of VER variability has been noted by many other researchers, however, although under different experimental conditions, as indicated in the section "Aspects of EEG/VER Variability." Nonetheless, we believe the variability may be reduced by alternate processing techniques and possible experiment modification.

To reduce the variability by modifying the signal processing, an analysis of the raw data (measured EEG and VER signals as currently recorded) is necessary. Some specific tests that should be performed are outlined in the subsection "Remarks" on page 21. The complete analysis procedure will depend on the results from these early tests, of course, and is hard to specify at this time. The analysis of the raw data is the most important step towards reducing variability. Using this data, a signal model can be developed and a processing technique selected from those described in the section "Improved Techniques for VER Analysis." If the performance of the improved techniques is not sufficient to meet the experiment objectives, modification of the experiment and redesign of the processing (to fit the new experiment) will be necessary.

A list of recommendations for reducing variability through experiment modification is given in Appendix N. These techniques have been extracted from the VER literature, and may be reviewed to determine whether any proven techniques are not now being used but may be incorporated without violating any experiment ground rules or constraints. If the use of these techniques does not sufficiently reduce variability, then a modification of the imposed constraints may be necessary to achieve higher signal-to-noise ratios.

Finally, if major modification of the experiment is needed, modern signal-processing techniques may be used to help design new experiments and their associated processing, as discussed in Appendix H.

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APPENDIX A

BACKGROUND OF VER/EEG EXPERIMENTS AND ANALYSIS

The analysis of electrical potentials from the surface of the human head is assuming increasing importance in the evaluation of brain functions, since these potentials reflect the activity of the brain. The use of surface potentials is also convenient for the investigation of brain functions from other primates because the technique is relatively noninvasive and hence many experiments can be carried out on a single subject. However, a price is paid for this convenience in terms of the information ultimately available, especially about the fine spatial distribution of neural activity.

The main problems experienced in the analysis of VER/EEG signals are high signal variability, complexity of patterns, and superimposed noise; noise is usually separated conceptually into noise of biological origin and noise due to recording equipment. The concept of biological noise should always be viewed with some suspicion; what might appear worthless variability of a signal to one investigator may be an informative feature to another investigator who is able to relate it to a neurophysiological mechanism.

From a more global point of view the problems experienced result from the complex and poorly understood neurophysiology of the brain with its many inputs, the large number of experimentally uncontrollable quantities, and the relatively small energy turnover ($\approx 10^{-11}$ W/nerve). Not all of the energy turned over by the brain is converted into electrical energy since only a few nerve fibers are electrically active (Abeles (1)), and usually they are quite distant from the recording electrodes. In addition, surface potentials do not have a one-to-one correspondence with internal brain activity which raises questions of observability (i.e., the capability of discriminating brain activity at different locations).

The high complexity of the structure to be analyzed leads to a variety of considerations about information gathering and processing schemes. Information gathering and processing cannot be separated into independent subproblems because of constraints imposed on experimental efforts, such as stimulus complexity, signal recording, and computational complexity. Thus, depending on special objectives, different compromises are sought.

In this appendix we will roughly outline several methodologies currently in use for VER/EEG analysis, including a discussion of the gross experimental structure, specific problems, experiment design with different objectives, and the "classical" as well as more modern methods of signal analysis. Physiological and physical considerations will be investigated in Appendix B.

SETUP OF VER/EEG ANALYSIS

A schematic of a typical VER/EEG analysis system is shown in Figure A-1, and the flow of information is indicated.

Stimulus: the discussion of the flow of information in the arrangement of Figure A-1 may naturally be started with the properties of the test stimulus since historically the feedback path was rarely used. In most instances, the stimulus pattern is two-dimensional, and basic geometric figures are used. The patterns (and background) have to be well defined in terms of brightness, onset-offset (or time course), color, and angular size. Care has to be taken to avoid production of simultaneous acoustic signals such as clicks from flash cubes or noises from static discharges of the TV screen. With use of a TV screen the time constant of the after-image may be of some importance, since the visual system may subconsciously process high-frequency (>60 Hz) information (Desmedt (28) p. 44). In general, when using TV stimuli, several technical characteristics of the images should be obtained from the manufacturer. With these precautions in mind, the use of a TV screen is still viewed as a very convenient and valuable source for stimuli (Desmedt (28) p. 8).

Subject: a subject of an experiment should be categorized following a standard procedure. Personal characteristics such as visual acuity, color vision, left- or right-handedness should be recorded as deemed necessary. Possibly the ears should be covered or background noise provided to mask event-related sounds.

Electrodes (Leads): electrodes should be placed on (selected) standard lead positions. Electrode type (cup, needle, capacitive) and the use of electrolyte paste are design quantities. Some aspects related to the choice of electrodes are discussed in Appendix B. These leads should be routed as close together as possible to avoid pickup of external electromagnetic or electrostatic interference.

Signal conditioning: typically the electric signal is fed into a high-impedance bandpass amplifier which suppresses DC and frequencies above 300 Hz (in some instances, such as spectral analysis, mixers, and narrow-band amplifiers are used). The choice of roll-off frequencies is usually determined by the signal-versus-noise bandwidth (where "signal" and "noise" are subject to interpretation, as discussed in Appendix B).

Signal conversion: the analog output of the signal conditioner is fed into an A/D converter which typically measures several leads (or channels) virtually simultaneously. The important characteristics of A/D converters include dynamic range, sampling rate, and the stability of the sampling rate. Note: actual sampling intervals may not follow precisely scheduled intervals when driving the sampling process through software executive commands. Digitizing a known waveform is thus recommended for performance evaluation.

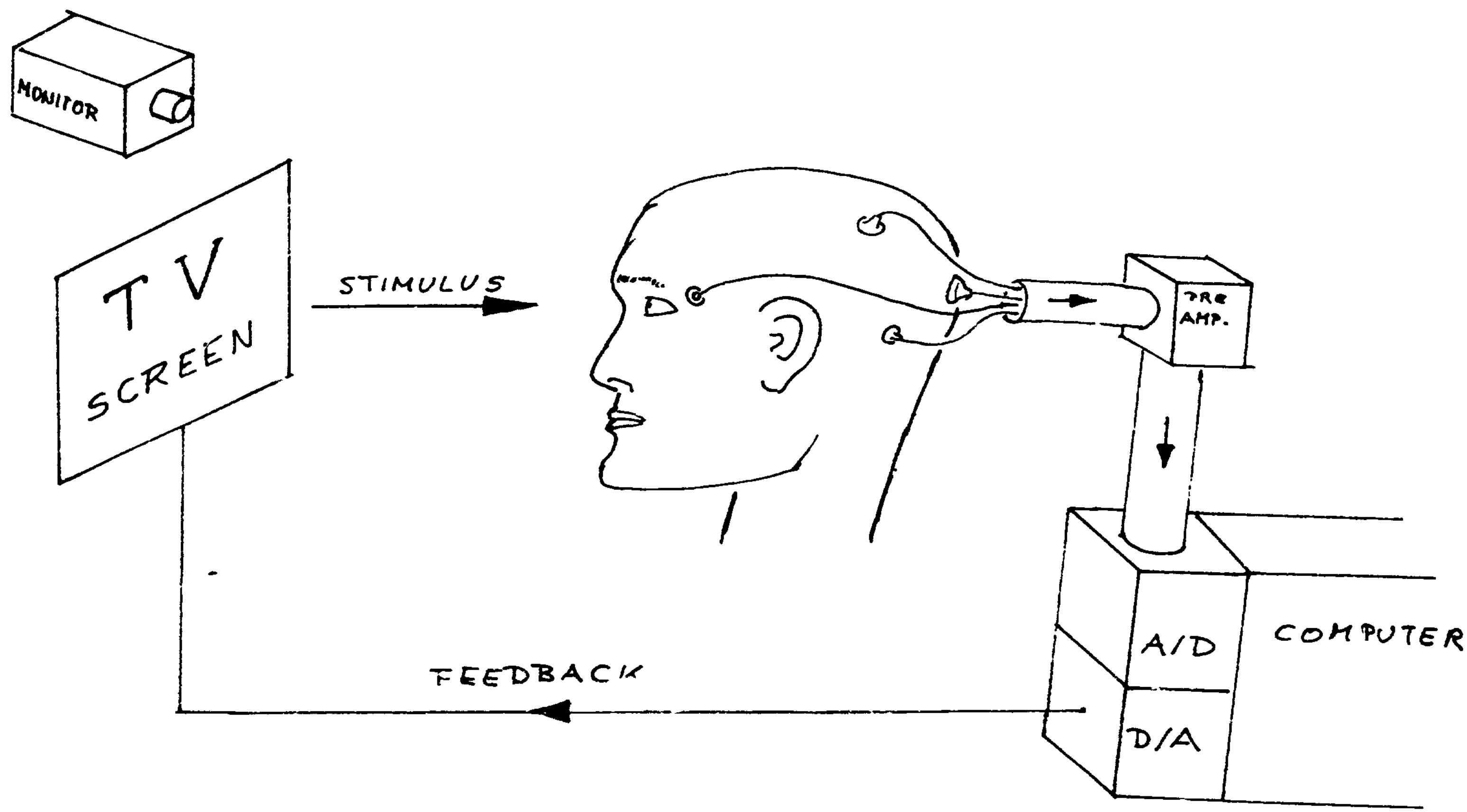

Figure A-1. VER test arrangement.

Computer: the digitized data is typically buffered and/or processed in the computer. Since information flow from many leads may lie in the kbyte/sec (8 bits/byte) range, on-line processing of all the data with sophisticated nondedicated software/hardware would be extremely difficult if required. Simple processing of the data (for example, detection of gross artifacts or lack of signal) may well proceed in real time, while more advanced signal analysis can be performed off-line on stored data. This data may be stored on either magnetic tape or disc. No difficulty due to limited transfer rates to the storage devices is anticipated.

During the recording, the computer may generate various test stimuli, possibly conditioned on a simple analysis of the data. Hence the loop shown in Figure A-1 may be closed in real time. An example for such a structure is given by Vidal (114).

SPECIFIC PROBLEMS IN VER/EEG ANALYSIS

Blinking, saccades, and lack of attention are some of the most deleterious disturbances in VER analysis when neglected. By means of separate information channels some compensation of these disturbances may be accomplished. For example, blinking and saccades are monitored with electrodes placed near the eye; the quick potential charges associated with these events provide reliable timing information to change the mode of analysis. Attention may be judged by separate human observer via a monitor. Clearly, the need for a human observer should be eliminated as much as possible.

The background EEG activity during VER studies provides a different form of disturbance. For example, the stationarity of EEG activity cannot be assumed following a stimulus. Indeed, there is indication of EEG activity entrainment or modulation by processes following stimulation (Lansing and Barlow (61)). Since EEG activity appears to be nonstationary in itself, it is hard to distinguish between random changes with superimposed VERs and nonlinear interaction between random changes and responses to a stimulus.

Fatigue and adaptation pose further problems, at least when stationary techniques are being used for signal analysis. Adaptive or piecewise stationary techniques are necessary to deal with this problem. The particular choice of adaptivity or segmenting requires some prior information about system behavior, especially for real time analysis; this prior knowledge may be represented in the form of a particular heuristic.

A difficulty on the hardware side in VER/EEG analysis might arise from uncertainty of electrode positioning when experiments are to be repeated or compared among subjects. One possibility to cope with this problem is to first study positioning sensitivity and selected points which appear to be insensitive. Alternatively one may position electrodes so as to obtain a specific transfer characteristic from the stimulus to the electrode. For example, signal processing tools may be used to give an indication of correct electrode placement. A completely different approach might involve photographic documentation or other more "physical means" to generate reproducible electrode placements.

CLASSICAL METHODS FOR VER/EEG ANALYSIS

The two classical methods of VER/EEG analysis are based on averaging and spectral analysis. These techniques were developed in other sciences, spectral analysis especially in engineering in the context of oscillating systems. These techniques are widely used today for the analysis of biological signals, mainly because of their well understood, usually fairly simple properties and simple implementation. They should be regarded as important techniques proved successful in a variety of areas. In some situations the methods are reasonably easily extended to approximately describe nonlinear and "moderately" nonstationary processes.

It should be noted that for the special case of analyzing linear processes, averaging and comb filtering (one of the spectral techniques analyzing a signal at integer multiples of the stimulus frequency) are intimately related via the Fourier transform.

These classical methods of signal analysis may be regarded as nonparametric. They provide a simple tool to describe input-output relations of dynamical systems. Often these techniques are inexpensively implemented on analog circuitry.

RECENT METHODS FOR VER/EEG ANALYSIS

With the advent of the computer and fast analog-to-digital converters, more complex techniques for the analysis of signals became feasible. These techniques are especially useful for treating the randomness of signals in natural processes. The Fast Fourier Transform, autoregressive modeling, and Karhunen-Loeve expansion are among the most prominent. For the purpose of spectral estimation the maximum entropy approach has drawn much attention. From the usual specification of the entropy induced by a filter (following Bartlett (9)) this form of spectral estimation leads essentially to autoregressive modeling. A close "relative" of the Karhunen-Loeve expansion is also well known in statistical analysis in slightly different setting under the title of principal component analysis. All of these methods are based on relatively strong linearity and stationarity assumptions. The use of these methods is widespread today and common in pattern classification.

It appears to us that many recent techniques are not fully exploited, in particular, techniques which allow modifications to test nonlinearities and certain forms of nonstationarities. For example, one of the important contributions of Box and Jenkins (14) was to develop systematic approaches to the use of time-series analysis in the time domain (with some reference to spectral representation) which can be followed by the statistical layman. The method advocated is the so-called autoregressive-moving average technique which can describe all possible (finite dimensional) linear time processes. Yet for reasons mentioned in this appendix and discussed in more detail in Appendix B, the modeling of VER/EEG may call for more general forms of nonlinearities and nonstationarities than those outlined by Box and Jenkins (14). Scientific Systems, Inc. has developed extensive expertise and automatic software to perform such analysis. In fact, the routines available to us are still more general in terms of modeling nonstationarity and nonlinearity.

The area of system identification in the engineering sciences has, of necessity, addressed the issues of fairly strong nonlinearities and nonstationarities. Important developments which allow consideration of these issues are extensions of the Kalman filter algorithm and modern control theory. These techniques are of vital importance today in aircraft trajectory estimation and control. As a supplement, describing function analysis, which developed in a rather straightforward fashion from classical spectral analysis and from certain statistical concepts, provides a good tool for modeling some of the interesting features of nonlinear systems such as the mixing of frequencies, limit cycles, subharmonics, and entrainment. For the successful application of these techniques considerable computational effort may be required. The high computational burden is in good part due to the iterative nature for solving the nonlinear equations associated with parameter estimation in these systems. The techniques in use today often require searches in a 10- to 50-dimensional parameter space to find the best fit.

Thus a variety of practical and theoretical problems related to numerical accuracy and uniqueness of solutions arise for the researcher. To deal effectively with these problems one should proceed stepwise in the augmentation of models, and, in our opinion, as much as possible start out with "meaningful" models. This approach can save considerable amounts of computation since it allows incorporation of prior knowledge about structure into the models. Diagnostic checking may then lead to approval, modification, and possibly augmentation of conjectured structures. In some instances one should also consider whether adding alternative forms of measurements may reduce computations through improved observability of parameters or decomposition of a model into simpler structures, thus simplifying the multidimensional searches. To show some of the possible considerations in this context, Appendix B is devoted to an investigation of the physiological and physical structure of VER/EEG analysis.

APPENDIX B

PHYSIOLOGICAL AND PHYSICAL CONSIDERATIONS IN VER/EEG SIGNAL ANALYSIS

In this appendix, we will give an outline of the overall signal structure under the special consideration of its physiological and physical origin. We start out with a review of physiological mechanisms responsible for electrical potentials and potential changes and turn then to what we term the Eye-Brain-Electrode model. This model is motivated by the different forms of information currently available about the eye, the brain, and properties of electrodes. In particular, such a partitioned model may be useful in analyzing specific saturations that take place in flash responses. Current literature appears to have disregarded this overall view of VER/EEG signals. Finally, the structure of the experimental setup is reviewed as it may pertain to the experiment design and data acquisition.

THE ELECTRICAL ACTIVITY OF LIVING CELLS

Living cells require an electric potential difference across the cell membrane. This bipolymer sheet of about 100 Å strength is by itself not capable of withstanding the high osmotic pressure of proteins in the cell interior; that osmotic pressure is balanced by the osmotic pressure and electric force of ions. Special sodium pumps shuttle sodium ions toward the cell exterior rendering the inside negative. Some of the ions leak back and hence the pumps must remain active.

Nerve cells utilize this potential difference to propagate actively (that is, in a regenerative fashion) variations of the potential along the cell body. These potential variations are regarded as action potentials, and they consist of a short reversal of the polarity of the (local) cell interior. Typically the duration for such an action potential is in the 1-msec range, and the spatial length of the potential reversal in the centimeter range. Propagation speeds vary, depending on myelination and diameter of an axon. The action potential follows an all-or-nothing law, and results always in a signature of the line and space distribution (Abeles (1)).

The initiation of an action potential may occur in several ways, for example, via specialized receptor cells or from another nerve cell via the dendritic tree. This dendritic tree serves as an approximate integrator of postsynaptic currents in time and space. These postsynaptic currents, in turn, result from chemical transmitter substances released by the synapses of other nerves. The effect of potential changes may either facilitate or inhibit the possibility of generating an action potential. The delay associated with the transmission of information from one nerve to the other may be as short as 1 msec per synapse-dendrite "relay." Thus response time can give a clue about the number of sequential relays and hence complexity of a neural pathway.

In contrast to the unit of information, the action potential which travels along a nerve axon, no such unit exists in the dendritic tree. As mentioned above, the dendritic tree functions more in an integrative linear fashion. Small inputs into many of these dendritic trees might thus be expected to result in changes of neural interaction. This view is supported by observed behavior changes in animals and the selective release of calcium ions (Adey (4)) in brain tissue by means of low-amplitude electric fields. He suggests demodulation of modulated high-frequency fields occurs on the (asymmetric) bipolymer sheet of cell membranes, inducing changed transmembrane potentials. This observation leads to the concept of slow electric potential changes serving as a possible second (electric) message system.

The nerve cells, composed of the dendritic tree, axon, and terminal branches, constitute the majority of cells in the brain. They are organized in bundles for signal transmission and in nuclei for information processing. The arrangements of dendrites and terminal branches appear to follow a random pattern (Abeles (1)). Electric activity among the various nerve cells also appears to follow random time processes, though not independent among nerve cells and with respect to stimuli.

In recording the electric activity of the brain through EEG and VER, it is the random superposition of extracellular farfields which is observed, since typically electrodes are separated from active cells by centimeters. It should be said that it is not clear today how much the voltage fluctuations observed result from action potentials and slow potential changes in dendrites, but both mechanisms are implicated.

Having set out some of the important aspects of bioelectrical potentials, we may turn to the eye-brain-electrode model and discuss the effect of these three components on the recorded signal.

THE EYE-BRAIN-ELECTRODE MODEL

The concept of the eye-brain-electrode model was motivated by the investigation of the stimulus-response path and the different properties and forms of prior knowledge about the components along that path. The eye appears to be physiologically fairly well understood in terms of its transmission properties and control. Thus some physiological modeling is suggested for the sake of stimulus design and transmission characterization.

In comparison with the eye, the brain is functionally extremely complex and information for the characterization of signal transmission is very incomplete. In addition, the neuroanatomy of the brain is highly species-specific, prohibiting simple extrapolation to other species. For example, the neuroanatomic structure of layers in the visual cortex of human and other closely related primates is quite different in quality and number. Hence, for the purpose of description, one is forced to resort to abstract models which may not resemble the underlying structure. Nevertheless, some information about potential pathways and processing mechanisms is available and should be considered in the selection and comparison of models.

Finally, it is realized that all signals recorded are affected by the transmission properties and location of the electrode. Hence they call for separate consideration. Proper use of electrodes, lead placement, and impedance matching may lead to improved signal quality and, potentially, to new information.

The Physiological Model of the Eye

The anatomy of the eye is shown in Figure B-1. Several of its components appear to be important factors in the signal transformation from

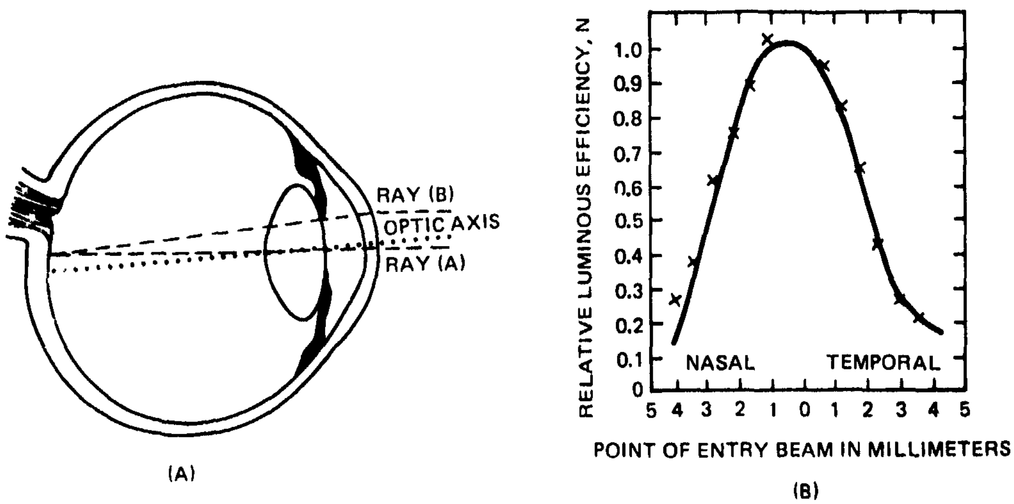

Figure B-1 (after Leibovic (63)). Optical arrangement in human eye and its luminance efficiency.

an optic image to the optic nerve: the iris, the lens, and the retina. The importance of the iris is due to not only its well-known control of illumination and consequent effect on image quality, but also its rather stochastic behavior. Stanten and Stark (105) demonstrated the considerable random fluctuations of pupil area at different levels of illumination; amplitudes may fluctuate about 20% (1 S.D.) and with a time constant of several seconds (cf. Figures B-2 and B-3). They also noted the strong correlation of left and right pupil area noise. This suggests a common pathway for the processing of illumination information, and they give a stochastic model for these processes.

Following the path of light, the lens is the second element-modulating image quality. Stanten and Stark (105) showed a dynamic limit cycle behavior of the focal length of the lens. For this they developed a deterministic nonlinear control model which accounts for oscillations around 2 Hz (cf. Figures B-4 and B-5). An obvious purpose of this system is to track focusing by testing blurs on the retinal image, much like automatic man-made systems do. These oscillations appear to be superimposed by a 1/f type (flicker) noise at still lower frequencies. For understanding properties of the retinal image one should be aware of these processes, especially since they are strong enough to drive an internal servo mechanism.

Another effect on retinal image associated with the lens results from its strong chromatic aberration. Thus not all colors are simultaneously in focus, and typically a 2-diopter myopic correction (50-cm negative focal length) is necessary to focus blue when red is focused (Desmedt (28)). Recall the common experience of the glare of blue lights (e.g., from emergency vehicles) at night. With the above-mentioned oscillatory lens control, focusing of different colors at different times occurs. Also, due to the geometry of the retina and the lens, sharp images are confined to the macula lutea with its fovea centralis. However, the area in focus may move (expanding and contracting) in connection with lens oscillations.

The retina, the organ which receives the optic image, is equipped with a large number of different receptors. Rods serve night vision (scotopic vision) and three types of cones serve daylight color vision (chromatic photopic vision). The dynamic range of this system is about 5 orders of magnitude in light intensity, far in excess of the dynamic range of the pupil, but with much slower adaptation (Figure B-6).

The highly regular arrangement of cells in the retina has an interesting effect on the electrical properties of the eye: it renders it an approximate dipole with the dipole moment approximately aligned with the optic axis. This property can be exploited to determine (within limits) eye position or at least eye movement.

For the purpose of investigating quick dynamic changes of illumination, the modeling of the kinetics of pigment synthesis in rods and cones is important since the recurrence of vision secondary to flash stimulation is limited by these kinetics (Leibovic (63)). The kinetics are probably different for rods and cones, and possibly even different for cones with different color pigments.

The lateral interaction between visual receptors is of special importance in color contrast experiments. Fortunately, in the case of the human retina, there seem to be no efferent neural networks. In cats such efferent networks voluntarily change retinal performance.

In addition to the above-mentioned nonlinearities and nonstationarities, a different kind of static nonlinearity is described by Leibovic (63). For intermediate light levels he supports the logarithmic-type Weber-Fechner law. However, for very low light levels a square root law is theoretically and experimentally more appealing. He also discusses the expected deviations from the Weber-Fechner law for very high light levels. These nonlinearities are interesting, because they allow the stimulus design to be such that the input to the optic nerve follows an arbitrary function, possibly a sinusoid.

Another interesting effect associated with the retinal image processing is its superresolution of lines: resolution of lines is not limited by the spacing of receptors. Instead, local spatial interaction via some sort of averaging allows considerably higher resolution.

Finally, we should consider changes of retinal image due to gross eye movement. Three mechanisms should be distinguished: a smooth system for smooth pursuit, a saccadic system for fast positioning and correction of errors, and a slow drift of the optical axis. Interestingly, the dynamics for the horizontal and vertical system are quite different. To avoid the blurring of images during saccades, visual perception is reduced (even some time after the movement is completed until the "wobbling" of the eyeball has sufficiently died out), for a total of about 30 msec (Leibovic (63, p. 118)).

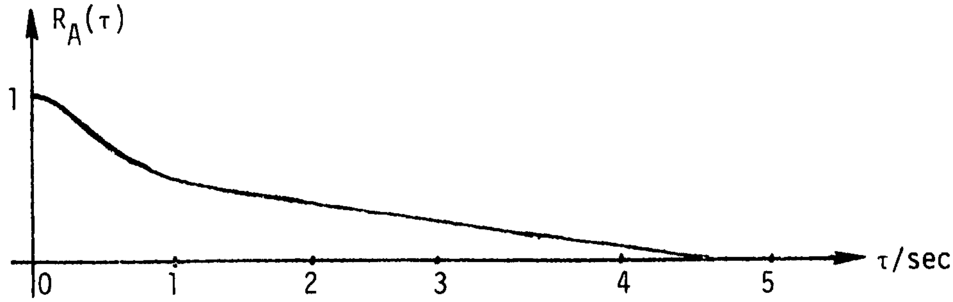

Figure B-2. Schematic of autocorrelation of pupil noise. The correlation between the two eyes is up to 95%.

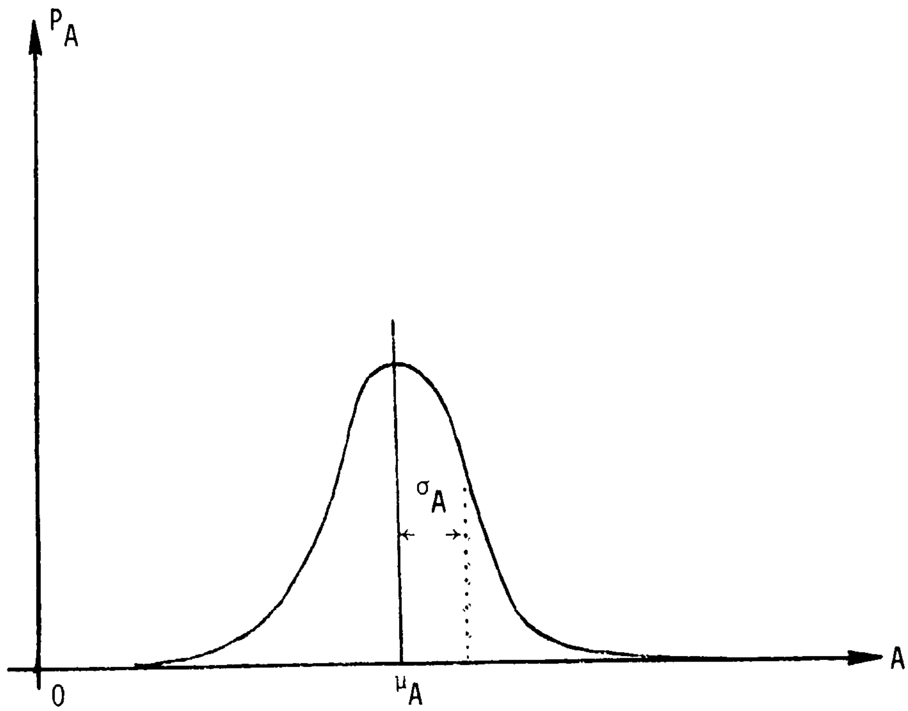

Figure B-3. Schematic of distribution of pupil area at constant illumination. Pupil area is also affected by various reflex mechanisms.

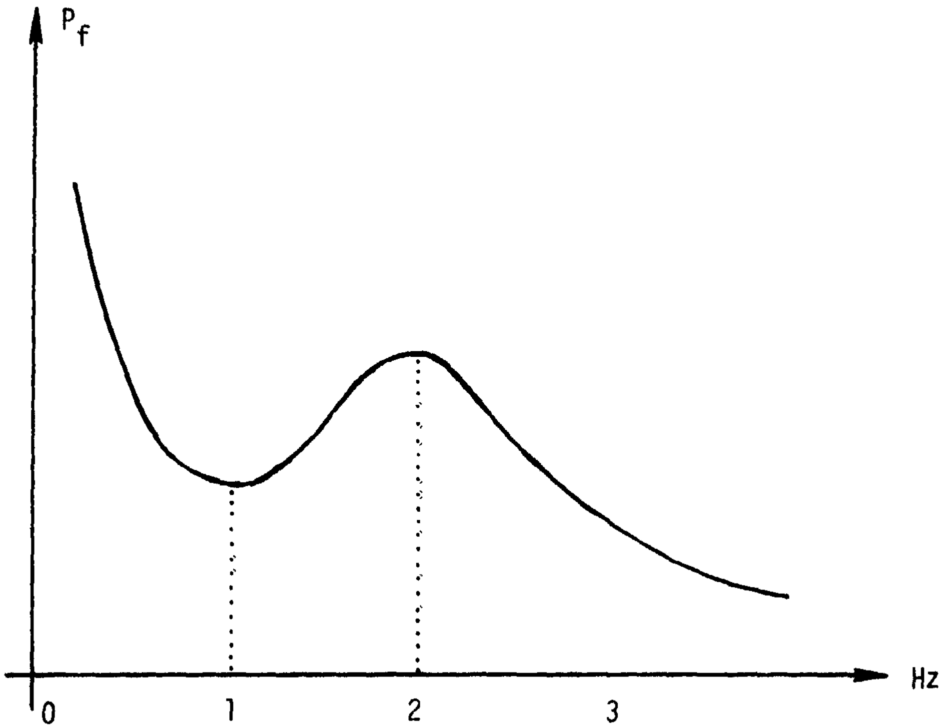

Figure B-4. Power spectrum of focal length of lens when sharp images are presented.

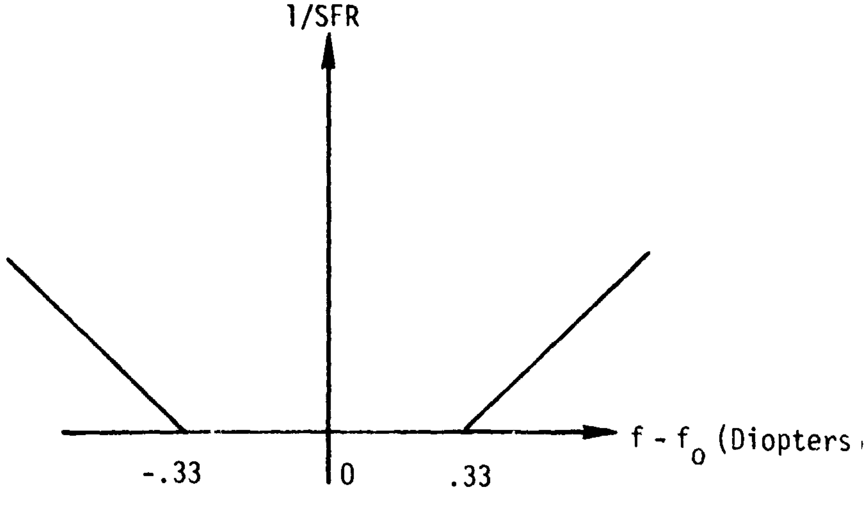

Figure B-5. Schematic of spatial frequency resolution (SFR) versus focal length of lens f.

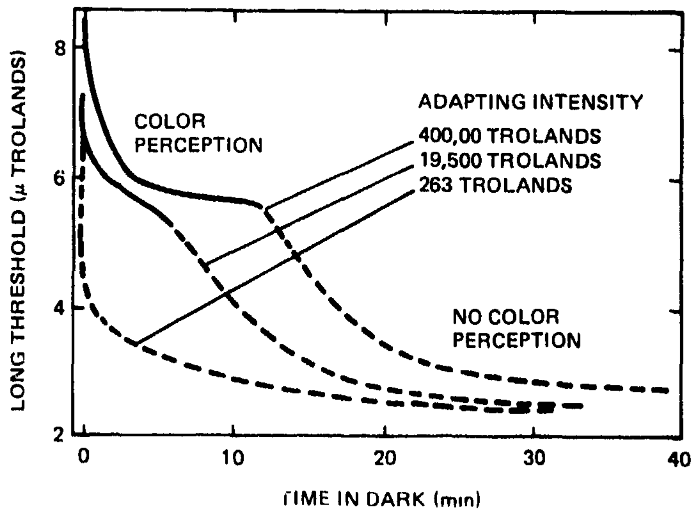

Figure B-6 (after Leibovic (63)). Variation of light detection threshold due to dark adaptation.

The drift phenomena, following Leibovic (63), is similar to Brownian motion of the optical axis. When certain critical limits of the positioning error are exceeded, correcting saccades are invoked automatically.

A different type of optical signal is created by blinking. Electrical potentials associated with this muscle activity might be detected by electrodes placed near the eye; these electrodes may simultaneously be used to detect saccadic eyeball movements. Since the mechanisms for generating these potentials are somewhat different, discrimination may be possible.

Finally, the stereoscopic vision should be considered. The long evolution of the visual system seems to have led to a strong integration of individual components. Thus, Stark (personal note) found a correlation of the angle of the optic axis with the focusing of the lens. The angle, in turn, is driven by the difference in retinal images. He also discusses the importance of considering the rotation of the eyeball around the optic axis during these dynamic maneuvers.

Modeling the Brain

The fast processing of information within the brain is based on electrochemical processes. Some of these processes, such as neural action potentials, are of short duration and fixed waveform but occur with variable time intervals. The intervals, even though random, are not independent. Thus, even though individual responses to stimuli seem to fluctuate, there is a consistent relation between them. In particular, in the case of VERs, variable amplitudes and latencies are observed. Little is known about the dynamics of these variations, but their importance for signal enhancement is recognized (McGillem and Aunon (69)). In some situations, as in acoustic click stimuli experiments, a relation between signal amplitudes and latencies was found (Moller (72)), in agreement with elementary models of synaptic signal transmission (Eccles (36)). The establishment of such models and their incorporation into estimation schemes may be very helpful in developing powerful and efficient techniques.

Some of the difficulties which are suggested by our understanding of the functioning of the brain should also be emphasized. For example, the transmission of signals is apparently accomplished via different pathways, each "modulating" the signal in its own fashion in terms of amplitudes and latencies, possibly even influenced by some of the other pathways. An example of this mechanism is the processing of different colors in "color channels" (Regan (87)) and the complex evoked sensation (Land (60)).

Another diffuculty arises due to the nonlinear behavior of information processing: in some cases, it is not clear whether evoked potentials result from the stimulus directly or from the modulation (entrainment) of other electrical activity of the brain, such as the modulation of the EEG (Lansing and Barlow (61)).

One of the potentially interesting, but more speculative aspects of the EEG and VER analysis, is the consideration of frequencies above the currently used values (say between 50 Hz and 1000 Hz). It is usually argued that the power of the spectrum falls off quickly above 50 Hz, hence higher frequencies do not represent much information. From an information theoretic point of view, this interpretation is incorrect. The crucial quantity to be looked at is the signal-to-noise ratio. As mentioned earlier, only thermal electronic noise can safely be regarded as noise. Another interesting aspect is the possible effect of a dielectric constant of the brain on high-frequency transmission. For low frequencies currently studied, this dielectric effect can safely be disregarded (Desmedt (28)); for higher frequencies up to the kHz range, however, we have not yet found relevant information. The interest in high frequencies is due to 1) their existence: the spectrum of action potentials reaches into the kHz range, and 2) their possible value in locating signal sources. Globally, increasing the signal bandwidth of analysis implies increased information flow.

On physical grounds, one may expect a different character in signals at high frequencies: first, because of the above-mentioned dielectric effect; second, because of the loss of the phase relation with respect to stimuli as a result of latency variations (often called jitter). The different properties may call for different processing techniques, but also preprocessing for digitizing and for the design of electrodes and preamplifiers. The following section should serve to clarify some of these considerations.

Considerations About Electrodes

Roughly, the use of electrodes is characterized by 1) their electrochemical characteristics (type), 2) number used, 3) placement, and 4) size. The important electric properties of (external) electrodes are well described by the linearized characterization of the electric half cell. They imply an interesting small signal frequency character: for increasing frequencies their impedance reduces (Figure B-1). Many investigators dislike this frequency-dependent characteristic of electrodes and reduce its effect by the use of a high-input impedance amplifier. However, increased input impedance results in an effective thermal electronic noise power (excluding flicker noise at the moment) in the final signal, proportional to that input impedance. For the purpose of sophisticated signal analysis such noise sets a limit for the performance of any scheme, but the frequency dependency does not. In fact, since the electrode characteristics can easily be modeled, they would not significantly decrease performance of sophisticated signal analysis.

For the purpose of high frequency measurements with a given sampling interval of the analog-to-digital converter a frequency shift is necessary. That shift may be done at the output of the analog preamplifier. It should be mentioned that a separate preamplifier may be desirable for high-frequency amplification to match the lower electrode impedance in that frequency range (compare Figure B-7). A consequence of the use of low-input impedance amplifiers is an increased sensitivity to electrode and scalp interface impedance changes. This sensitivity may be overcome by periodic (recalibration) sampling of the impedance, but care must be taken to limit the calibration-signal amplitude to avoid interference with brain activity.

The number and placement of electrodes are interesting experiment design features. The number may be limited by convenience of application, available preamplifiers, and the analog-to-digital conversion capability of the computer. Data storage may impose further practical limits on the number of electrodes used. The placement should clearly follow some anatomical considerations about the origin of various signals. The determination of "good" locations may proceed interactively with the signal analysis. In this context the issue of placement sensitivity and reproducibility plays an important role. The location of the ground, or reference, electrode is also important in specifying the differential potentials actually measured (see Cobbold (26, p. 431)).

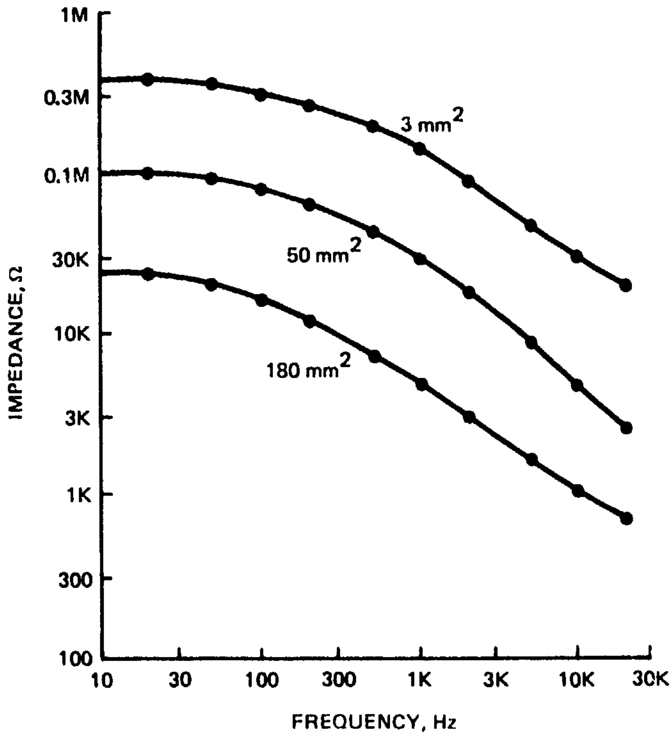

Figure B-7a (after Cobbold (26)). Frequency and size dependence of impedance in skin electrodes.

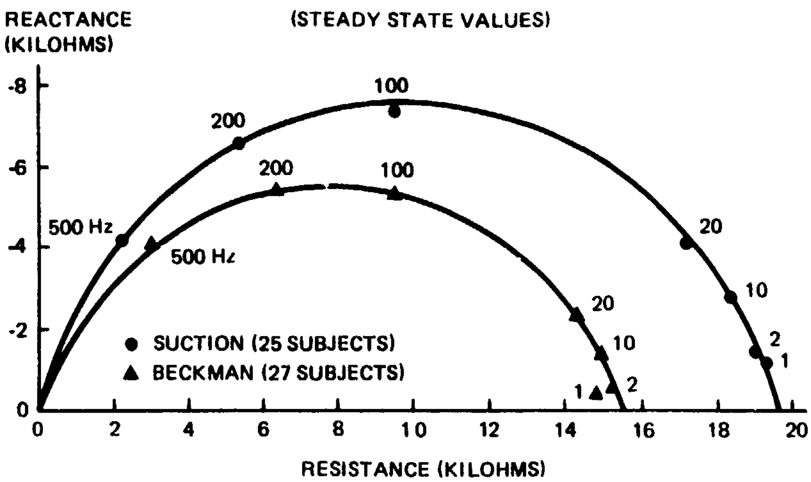

Figure B-7b (after Cobbold (26)). Frequency dependence of complex impedance in skin electrodes.

The size of electrodes seems to be a further important design factor. Clearly, for low impedances which reduce thermal electronic noise, large diameters are desirable. Even though spatial resolution may be lost, there are some indications that information for the purpose of response classification may not so much be contained in spatial characterization (Squires and Donchin (104)). In that study of schemes which classified different stimuli based on evoked responses, a classifier based on a linear superposition of tracings from different leads performed nearly as well as the "optimal" classifier (a Karhunen-Loeve representation was used in both cases). Furthermore, assuming dipole models for generators of electric fields, the distance of electric dipoles to the electrode should affect the choice of electrode use. A pragmatic approach might be based on trying different size electrodes and determining performance in conjunction with various signal analysis schemes.

In summary, the current methods of data acquisition and signal analysis should be rethought in view of the flexibility and adaptability of modern computerized signal analysis. Demands different from traditional VER and EEG analysis are present today.

APPENDIX C

FREQUENCY DOMAIN SIGNAL-PROCESSING TECHNIQUES

DIGITAL PROCESSING CONSIDERATIONS

Several practical considerations arise in the digital processing of analog (continuous) data. These issues concern the relationship between the digital numbers being computed and the analog data, spectrum, or other information originally sought. Excellent general references for this subject are Oppenheim and Schafer (76) and Papoulis (78).

Sampling

An analog-to-digital (A/D) converter accepts a continuous input and creates a discrete (in time and range) output. Several types of A/D converters and sampling circuits are available, but the casual user is most concerned with the rate of sampling (discrete time) and quantization (discrete level or state) of the digital work. The usual precaution taken in digital processing is to ensure that the sampling rate is above the Nyquist frequency, which is twice the maximum frequency in the signal being analyzed. If this is true, then no "aliasing," or folding of high signal frequencies into low-frequency digital artifacts, will occur.

To avoid aliasing when high-frequency noise (or signal) is present, an anti-aliasing filter must be placed before the A/D converter. The corner frequency of the filter should be above the maximum desired signal bandwidth and at least a factor of 2 below the sampling frequency. A factor of 3 or 4 is usually desirable since the anti-aliasing filter passes some noise, although attenuated, above its corner (-3dB) frequency. If enough is known about the filter and noise properties, the exact consequences of aliasing can be computed.

The second effect of sampling--quantization or discretization of the signal level (amplitude)--is harder to examine. In general, the quantization should be fine (small) enough so that the discrete signal is an accurate representation of the analog process. The adequacy of the representation may be analyzed by assuming that uniformly distributed quantization errors are added to the desired signal. A second quantization error occurs in the processing of digital data. This error is harder to analyze, but bounds have been developed for FFT algorithms as a function of the number of data points (and therefore multiplications) that are used.

In general, the cost and speed of very accurate A/D converters prevent their use in many applications, and the computer work lengths are much longer than the input signal. This extra computer work length is desirable, however, since processing increases the required word length (e.g., during the sequential multiplication and subtraction of many numbers) at intermediate steps in the analysis.

Data Windows

The use of digital processors on finite-length data intervals results in errors caused by the sudden appearance and disappearance of the data. These errors are greatest for short intervals and become negligible for very large data sets. The errors can be reduced, however, by weighting the data in a manner that simulates the gradual turning on and off of the information. Such weighting functions are called windows, since they represent the finite boundaries through which the computer views the (presumably) infinite data stream.

For an input f(n), n=0,...,N-1, the window function a(n) is used to create a processing input b(n):

$$b(n) = f(n)a(n), \quad n=0,\dots,N-1$$

For long data sets, a(n) may be unity, forming a rectangular window:

$$a(n) = 1, \quad n=0,\dots,N-1$$

The simplest alternate to the rectangular window is the triangular, or Bartlett, window:

$$a(n) = \begin{cases} \dfrac{2n}{N-1}, & 0 \le n \le \dfrac{N-1}{2} \\[2ex] 2 - \dfrac{2n}{N-1}, & \dfrac{N-1}{2} < n < N-1 \end{cases}$$

A slightly better type of window employs a cosine weighting to the data. The two most popular are the Hanning window

$$a(n) = \tfrac{1}{2}\left[1 - \cos\left(\frac{2\pi n}{N-1}\right)\right], \quad 0 \le n \le N-1$$

and the similar Hamming window

$$a(n) = 0.54 - 0.46 \cos\left(\frac{2\pi n}{N-1}\right), \quad 0 \le n \le N-1$$

The Blackman window provides even better performance, when needed, at the cost of a second cosine term:

$$a(n) = 0.42 - 0.5 \cos\left(\frac{2\pi n}{N-1}\right) + 0.08 \cos\left(\frac{4\pi n}{N-1}\right), \quad 0 \le n \le N-1$$

and finally, Kaiser (54) suggests a family of windows using the modified Bessel function of the first kind $I_0(\ )$:

$$a(n) = \frac{I_0\left[\omega_a \sqrt{\left(\frac{N-1}{2}\right)^2 - \left[n - \left(\frac{N-1}{2}\right)\right]^2}\,\right]}{I_0\left[\omega_a\left(\frac{N-1}{2}\right)\right]} \qquad n=0,\dots,N-1$$

where ω_a is an adjustment parameter, usually in the range

$$4 < \omega_a\left(\frac{N-1}{2}\right) < 9$$

Window choice is usually a matter of convenience if the data frame size is large enough. For very small data blocks, however, more care must be taken in window design. Windows may be examined and compared in the frequency domain, of course, where some of their features are most easily understood. In particular, when using windows to smooth periodograms for spectral estimation, some windows can produce negative power estimates (for some frequencies) because of the negative spectrum of portions of the window, as discussed in Tretter (109).

FAST FOURIER TRANSFORM (FFT)

The Fast Fourier Transform (FFT) is one of the most popular signal-processing techniques. The method gets its name from one of several algorithms available for quickly and efficiently obtaining the discrete Fourier Transform of a given time series. The discrete transform is useful for power-spectrum estimation, signal characterization, signal detection, and analysis of model performance. For further reading, the books by Oppenheim and Schafer (76) and Tretter (109) are well written and informative.

Definition of Fourier Transform

Given a time series f(t), and a sampled version of the signal f(nT), the Fourier Transform (of the sampled signal) may be written as

$$F(e^{j\omega}) = \sum_{n=-\infty}^{\infty} f(nT)e^{-j\omega nT}$$

where $f(nT) = \frac{1}{2\pi}\int_{-\pi}^{\pi} F(e^{j\omega})e^{j\omega n}\, d\omega$

Discrete Fourier Series

For periodic signals of period N or limited sample signals x(n), n=0,...,N-1 that may be assumed to repeat after N steps, we may write

$$x(n) = \frac{1}{N}\sum_{k=0}^{N-1} X(k)\, e^{j(2\pi/N)nk}$$

$$X(k) = \sum_{n=0}^{N-1} x(n)\, e^{-j(2\pi/N)nk}$$

$$\omega_N = e^{-j(2\pi/N)}$$

$$X(k) = \sum_{n=0}^{N-1} x(n)\,\omega_N^{kn}$$

$$x(n) = \frac{1}{N}\sum_{k=0}^{N-1} X(k)\,\omega_N^{-kn}$$

$X(k)$ may be thought of as samples on the unit circle, equally spaced in angle, of the z-transform of (one period of) $x(n)$.

If the input is thought of as periodic, then the operations above are usually called the discrete Fourier series; if the input is considered finite duration, then the operations are called the Discrete Fourier Transform (DFT). The transform (with no computation errors) is an exact representation (one-to-one mapping) of the input, but may not be a good approximation of the continuous transform due to sampling and spectral estimation considerations.

Efficient algorithms for computing DFTs are known as Fast Fourier Transforms (FFTs). These algorithms have greatly expanded the use of Fourier transforms in signal processing, and permit the computation of parameters that were considered impractical a short while ago.

SPECTRAL ESTIMATION WITH FFT ALGORITHMS

In many instances, one wants to estimate the power-density spectrum of the process which generated the data sample. The Fourier Transform may be used in several ways to obtain such an estimate. The most direct estimate is the periodogram, which is the square of the amplitude of the DFT, i.e.,

$$I_N(\omega) = \frac{1}{N}|X(e^{j\omega})|^2$$

Unfortunately, this estimate is not usually a good use of the available N data points. The periodogram is a biased estimate of the spectrum, with a bias which decreases with N but a variance which approaches a constant for large N. For a Gaussian spectrum, the variance of the periodogram approaches the square of the spectrum which results in rapid fluctuations (in the periodogram from one frequency point to the next) about the true spectrum. Since the resolution in frequency also increases with N, there is an inevitable trade-off between resolution and variance.[3]

[3] The resolution of an FFT calculation is equal to the bandwidth of interest divided by twice the number of data samples used (since two data points are used to produce amplitude and phase information at each frequency).

Two common ways of improving the periodogram estimates are averaging and smoothing. The averaging method breaks the data block into several smaller blocks, usually not overlapping, and computes a periodogram for each smaller block. These periodograms are then averaged, at each frequency, to obtain a spectrum estimate. This estimate has the low resolution and large bias of the short block size, with a reduced variance from the averaging.[4] The estimate is affected by any data window used, of course, and other effects dominate for very short data blocks.

An alternate technique for improving spectral estimates is to "smooth" the large-N periodogram. The smoothers used correspond to window types, and the remaining errors relate to window shape. The same types of trade-offs exist as in averaging, and smoothing method is not used as much as averaging now that FFTs permit fast periodogram calculations.

These techniques assume, of course, that the desired spectrum does not change during the data interval (N steps, above). This assumption of stationarity is implicit in most Fourier Transform analysis. The DFT will always be a unique transform of a given data set, but it may or may not be the spectrum of interest. Several complex tests for stationarity exist and should be used if there is doubt about the signal characteristics. A change in the measured windowed spectrum gives an indication of nonstationarity, of course, but, in general, FFTs provide a poor means for measuring changing spectra.

SPECTRAL ESTIMATION VIA ENTROPY AND LIKELIHOOD

Maximum Entropy Method and Maximum Likelihood Method (MEM and MLM) for spectral estimation are modern procedures (Childers (24)) often considered superior to various alternatives. The value of these methods lies in providing tools which, at least in principle, do not impose strong assumptions about the underlying structure of the process being examined. This is of importance since other parametric tools of statistical analysis require checks of their appropriateness, of which practitioners are often not aware. Much of the success of MEM and MLM is due to their minimal structural assumptions, and hence the properties of the data come to bear, rather than a possible incorrectly implemented procedure. There are still open questions in this area, but the concepts are appealing and turn out to be related to certain forms of statistical modeling, showing the latter in a still different light.

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[4] A bias indicates that the estimated spectrum converges to the wrong spectrum, independent of the number of periodograms averaged. The bias is a function of the number of data points and window function used in each periodogram. The degree of convergence to the (biased) spectrum estimate is indicated by the variance, which decreases with the number of periodograms in the average.

The Maximum Entropy Method (MEM)

The Maximum Entropy Method is based on a result by Bartlett (9), who showed a simple relation between the power-transfer characteristics of a linear filter and the change of entropy of the signal transferred. Burg (17) then raised the question of which spectrum estimate has the largest entropy, given autocorrelation values of a signal. The idea of maximizing entropy is appealing since it is "least committal" (Ables (2)), that is, few prior assumptions have to be made about the data. The question leads to a constrained optimization problem. The entropy change is given by Bartlett's

$$\Delta H = \int_F \ln S(\nu) \, d\nu$$

and the constraints resulting from the (usually estimated) autocorrelation values satisfy

$$g(k) = \int_F S(\nu) \exp[-i2\pi\nu k] \, d\nu, \quad i = \sqrt{-1}$$

Interestingly, the Lagrangian multipliers in this problem can be interpreted as autoregressive coefficients (Childers (23, p. 92)), identical to those described in Box and Jenkins (14). Burg (17) suggests certain procedures to estimate these coefficients in a recursive way, without resorting to estimates of the autocorrelation of the process, as is done by the use of Yule-Walker (120) equation. Thus, the importance of "end-effects" of the finite data window is reduced. For example, by use of the Yule-Walker equation, there is finite probability of obtaining (for autoregressive models of higher than second order) a non-semi-positive definite (Toeplitz) autocorrelation matrix (regarding the definition of the autocorrelation matrix, see Box and Jenkins (14, p. 31)). Hence, autoregressive coefficients (or Lagrangian multipliers) may be estimated which correspond to an explosive process. Clearly, spectra which correspond to such a process are meaningless, since limits by which spectra are defined do not exist under such circumstances. The problem is exacerbated when observations are missing.

Various extensions of Burg's (18) MEM are in use today. These extensions concern, for example, multidimensional image processes, processes containing white noise, and vector processes. The remaining main problem for practical applications results from questions about the order M of the autoregressive model (or more generally, the number of Lagrangian multipliers) which should be used. This question is not answered by the current maximum entropy methodology. Some guidance is derived from classical statistical procedures or criteria such as those given by Akaike (5) or Schwarz (98).

The importance of the MEM approach lies in avoiding the imposition of any particular structural assumptions on the spectral estimation (except for linearity when Bartlett's formula is used). In some instances, however, certain assumptions about a spectrum are reasonable. One might expect superior estimation if these prior assumptions are incorporated into spectral estimation. This idea leads to the method of maximum likelihood spectral estimation.

The Maximum Likelihood Method (MLM)

The maximum likelihood method is derived from a structure shown in Figure C-1. The goal is to adjust filter coefficients in such a way that the single frequency of the signal z(t) is optimally (unbiased) estimated by the filter output x(t). Thus the filter is to be adjusted in such a way that the signal z(t) is transferred without distortion, and all other frequencies are suppressed as much as possible (Lacoss, (58)). Obviously, the procedure has certain optimality properties when a single frequency is to be estimated. However, for the practitioner it is interesting to see performance of that scheme when some assumptions are not satisfied--for example, when the spectrum contains two frequencies, possibly "close" together. It turns out that in such a situation the "noncommittal" MEM method is superior in detecting two spectral lines when compared to MLM. Thus, as one might expect, MLM should only be used when there is strong prior evidence for the existence of only a single frequency in an otherwise continuous spectrum. Burg (19) noted a simple relation between MEM and MLM spectral estimation which accounts for some of the properties of MLM estimation, for example, the "smeared out" estimation of a pair of spectral lines.

When two or more spectral lines are expected in an otherwise continuous spectrum, one might of course generalize the MLM approach. The value of such generalizations can be seen in Siegel's (102) generalized test of periodicities in a white spectrum. Even though Fisher's test is known to be optimal in certain settings for the detection of a single frequency, it is outperformed by Siegel's method when multiple lines are present in a spectrum. At the same time very little power for detecting single lines, compared to Fisher's optimal test, is lost.

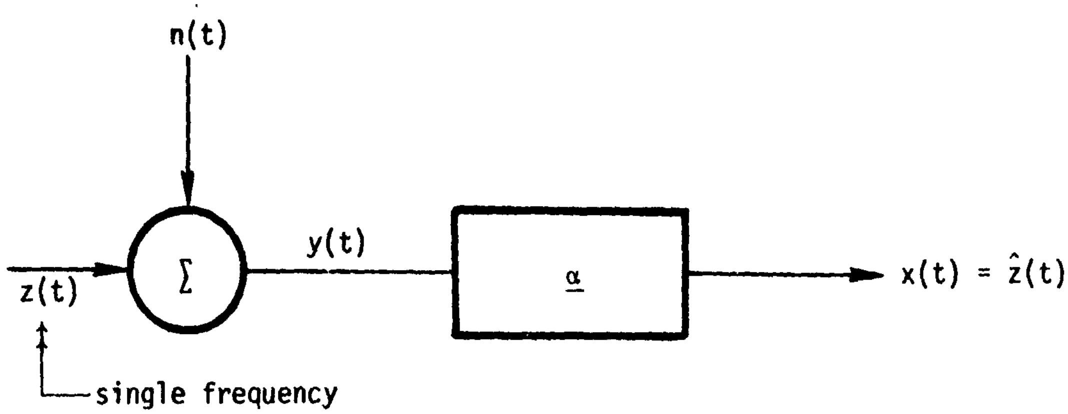


Figure C-1. Structure for maximum likelihood spectral estimation (MLM).

APPENDIX D

COMMUNICATION-THEORETIC METHODS

MODULATION

Several concepts in communication theory may prove to be useful in understanding or characterizing EEG signals. In particular, modulation and heterodyning may be used to transform an EEG analysis task into a domain where linear signal processing is more appropriate. Modulation, in general, is the encoding of a signal of interest in another, more easily transmitted signal. The process is designed to be reversible so that the original signal may be retrieved (demodulated) by the receiver. An excellent reference for communication systems is Wozencraft and Jacobs (119).

The most common forms of modulation--amplitude and frequency modulation (AM and FM)--are achieved by the multiplication of a sinusoidal (carrier) signal s(t) by an information process of interest a(t). The new signal (usually thought of as a "transmitted" signal) z(t) is then

$$z(t) = a(t)s(t)$$

or a linearly filtered version of the above.

Amplitude modulation is produced by the operation

$$z(t) = A(t) \sin\omega t$$

where A(t) is the process of interest and ω is known, while frequency modulation (or, more generally, angle modulation) may be written

$$z(t) = A \sin(\omega t + \theta(t))$$

Where $\theta(t)$ contains information and A is a fixed amplitude.

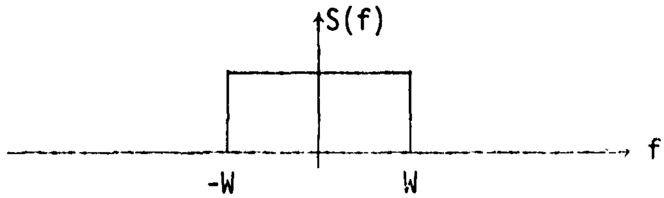
Although we are not interested in communication systems in general, it is useful to examine typical transmitted signal types and the means of demodulating them. Demodulation is a transformation to recover a signal of interest from the transmitted wave. In many instances of signal processing , it is useful to transform a signal (whether originally modulated or not) to simplify subsequent processing. In addition, demodulation may be used to extract certain information (e.g., phase coherency) of interest even though the corresponding modulation process is not thought to be present.

The basic goal of most demodulation systems is to mathematically recover the signal (i.e., functionally invert the modulation) while removing as much transmission noise as possible. The noise may be wideband (nearly white) due to receiver thermal noise or very narrowband due to specific interference or jamming. For EEG analysis, noise sources include thermal noise from the electrodes and amplifiers, 60 Hz "line" noise from the power system, and possibly a related 120 Hz noise from fluorescent lights. For VER detection, the spectrally similar background EEG itself may be considered "noise."

Heterodyning

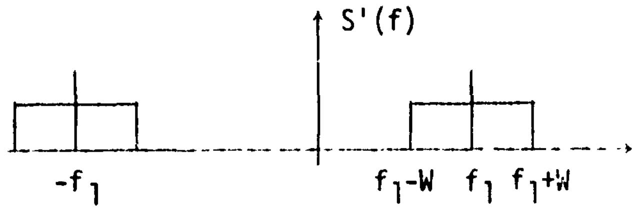
Heterodyning is a modulation process which frequency-shifts the signal of interest to facilitate transmission or processing. The technique relies on standard trigonometric identities and high, low, or band-pass filtering to manipulate the signal spectrum in the frequency domain.

As an example, consider a signal of bandwidth W, as shown below:

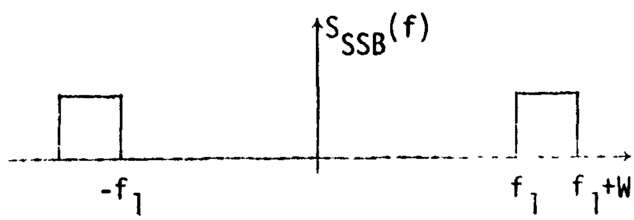


where S(f) is the 2-sided power spectrum.

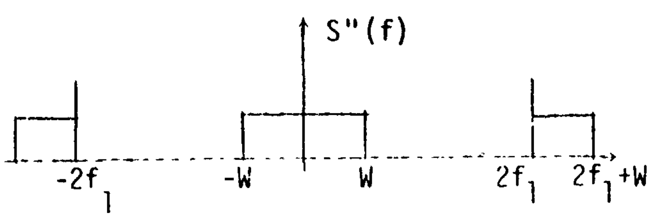
If this signal is multiplied by 2 cos$\omega_1 t$, the new product has spectrum:



where $f_1 = \frac{\omega_1}{2\pi}$. The information in the range f_1-W to f_1 is redundant and sometimes filtered out (in single side-band modulation) to produce the spectrum:



If this signal is transmitted, received, and multiplied by 2 cos$\omega_1 t$ again, the spectrum below results:



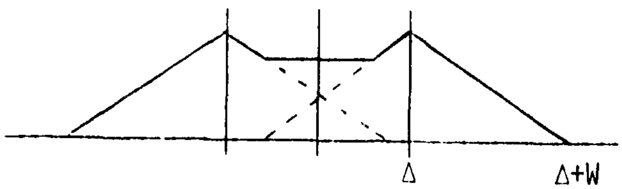
This signal may now be low-pass filtered to remove the component above $2f_1$ and recover the original information.

This type of manipulation, while invaluable in communications, must be approached with caution in signal analysis in general, where no control may exist over the original modulation. For example, if a narrowband signal exists as shown:

and the signal is multiplied by $2\cos\omega_2 t$ where

$$f_2 = \frac{\omega_2}{2\pi} = f_1 - \Delta, \qquad \Delta<W$$

and then low-pass filtered to remove the $f_1+f_2-\Delta$ component, the distorted spectrum shown below results:



When "demodulating" a narrowband signal whose modulation is uncertain, one must be careful to preserve the information in the signal. One way to assure this preservation is to carefully bandpass filter the signals before heterodyning, to assure that no unanticipated aliasing, or frequency ambiguity (as shown above), occurs.

One way to use such distortion to advantage is in power spectrum estimation. For example, if we multiply a measured EEG by a cosine wave at 10 Hz and pass the result through a low-pass filter with a bandwidth of 1 Hz, the resulting signal is a mixture of the original signal between 9 and 11 Hz. By rectifying and averaging (low-pass filtering) this signal, an estimate of the power in the original signal, between 9 and 11 Hz, may be obtained. This estimator has independent control ov · the bandwidth (the first low-pass filter after heterodyning) and response (the averager low-pass filter) of the spectral estimate, subject to the restriction that the averager should not be faster (higher bandwidth) than the first filter.

PHASE-LOCK LOOPS

Phase-lock loops are communications receivers that lock-on, or synchronize, to the transmitted signal, thus permitting excellent performance even during transmitter or receiver drift in frequency. These devices naturally demodulate phase- or frequency-modulated signals, while being almost completely insensitive to amplitude modulation--which may be due to interference in normal communication channels.

Usually, phase-lock loops assume a signal input of the form:

$$z(t) = A \sin(\omega t + \theta(t))$$

where A and ω are known and $\theta(t)$ is the information process of interest. If $z(t)$ is multiplied by a signal of the form

$$2 \cos(\omega t + \hat{\theta}(t))$$

and the product is then low-pass filtered to remove the double-frequency component $(A \sin(2\omega t + \theta + \hat{\theta}))$[5], the result is

$$A \sin(\theta - \hat{\theta})$$

If $\hat{\theta}$ is "close" to θ, this signal may be approximated by

$$A(\theta - \hat{\theta})$$

and a linear filter then used (in servo fashion) to compute $\hat{\theta}$, an estimate of θ, from the error signal $\theta - \hat{\theta}$. The loop is (usually) completed by a voltage-controlled oscillator, which takes $\hat{\theta}$ as an input and produces $2 \cos(\omega t + \hat{\theta})$ as an output. The loop thus looks like Figure D-1, and performs like the linear system of Figure D-2.

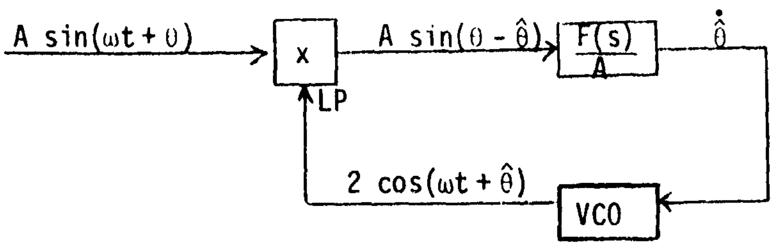


Figure D-1.[6] Phase-lock loop.

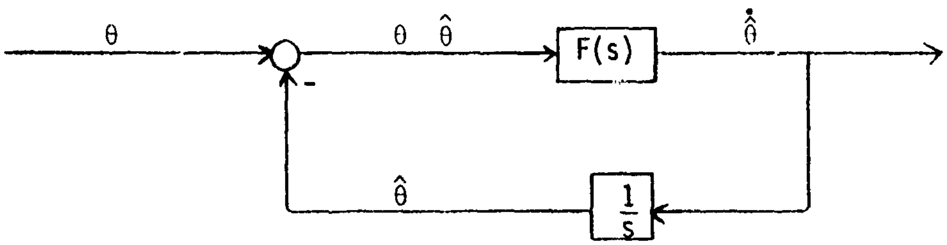


Figure D-2. Linearized PLL model.

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[5] We temporarily suppress the time dependence of θ and $\hat{\theta}$ for convenience.

[6] LP by the multiplier refers to the low-pass filtering which removes the double-frequency terms.

Several assumptions are implicit in the PLL model. The frequency and amplitude are assumed known, but this may be relaxed somewhat. For example, the filter may be designed to acquire and lock to a frequency different from that expected (within limits, of course). Also, practical considerations usually require that a hard limiter be used on the input (usually in the multiplier). Thus, the received amplitude may be an unknown A but the input amplitude to the PLL will be the known limiter amplitude (L), provided that

$$A > L$$

If $A < L$ and A is an unknown function of time, then A can significantly degrade loop performance or make the loop completely lose lock. The degree to which the original signal can be amplified to make $A > L$ is limited by the receiver noise.

Phase-lock loops have been suggested for use of EEGs to track an expected phase modulation. This model assumes that the single-sideband type of phase modulation (shown above) is in fact present, and that double-sided modulation, i.e.,

$$z(t) = A \sin(\omega t + \theta) + A \sin(\omega t - \theta)$$

is not. It also requires that A be known or limited (as above). It is generally prudent to narrowband filter the input before the PLL, to assure that no out-of-band components corrupt the processing. The narrowband filter should have at least the bandwidth of the loop filter (calculated from the linear model) and be centered around the band of interest.

These bandwidth considerations become very important when the PLL filter bandwidth is a large fraction of the carrier frequency, for example, for low frequency EEGs. For instance, if a PLL is tracking an EEG component at 8 Hz, and the loop filter is 1 Hz wide, then the loop will be susceptible to other EEG components present between 7 and 9 Hz. Unless the EEG is known to represent only one phase-modulated process, it is dangerous to use a wideband PLL to track the "EEG phase."

One final aspect of PLLs is the inherent lock indication available. By multiplying the original limited input by $2 \sin(\omega t + \hat{\theta})$ and low-pass filtering, the signal $L \cos(\theta - \hat{\theta})$ is obtained. An averaged value of this signal provides an indication of lock since, for $\theta - \hat{\theta}$ small, the cosine $\rightarrow 1$. A threshold detector easily may be set to trigger on this signal, often called the "quadrature" channel since it results from a signal 90° out-of-phase to the original feedback channel.

In general, if $\theta(t)$ can be described as a linear process and if the acutal measurement

$$z(t) = A \sin(\omega t + \theta(t)) + n(t)$$

has low enough noise $n(t)$, then a phase-lock loop will perform very well. For cases where more noise is present, other filters may be developed (see, e.g., Bucy and Mallinckrodt (16), Willsky (117), Gustafson and Speyer (44)). For the EEG, measurement noise is not as much of a problem as amplitude modulation, and two simple approaches to phase and amplitude demodulation are worth noting.

The first technique uses linear filters in the measurement space, i.e., filters which take

$$x(t) = A(t) \sin(\omega t + \theta)$$

or the "base band" (heterodyned by 2 $\sin\omega t$ and 2 $\cos\omega t$ and low-pass filtered) pair

$$x_1(t) = A(t) \sin\theta$$

$$x_2(t) = A(t) \cos\theta$$

as signals of interest (states). These filters assume that the measurement is of the form

$$z(t) = x(t) + n(t)$$

where $n(t)$ is white Gaussian noise, and then

$$z_1(t) = x_1(t) + n_1(t)$$

$$z_2(t) = x_2(t) + n_2(t)$$

are the inputs fed to linear filters, where n_1 and n_2 become (after heterodyning) independent white Gaussian noise processes. The linear filters produce estimates $\hat{x}_1(t)$ and $\hat{x}_2(t)$, and phase and amplitude estimates are constructed by

$$\hat{\theta} = \tan^{-1} \hat{x}_1(t)/\hat{x}_2(t)$$

$$A(t) = (x_1^2(t) + x_2^2(t))^{\frac{1}{2}}$$

An alternate technique for amplitude estimation is to use the quadrature channel of a PLL discussed above. If a limiter is used for the normal PLL, and $A(t) > L$, then the normal loop will be insensitive to $A(t)$, and a good phase estimate will be obtained. Also, the quadrature signal

$$2 \cos(\omega t + \hat{\theta}(t))$$

may be used to heterodyne the input (without limiting) to create

$$A(t) \cos(\theta - \hat{\theta})$$

If $\hat{\theta}$ is close to θ, this signal produces a good amplitude estimate.

It should be noted that all of these demodulation techniques assume an original modulation. If the amplitude or phase of an EEG is easier to track, classify, or reproduce than the measured wave, then such demodulation will be justified. If, however, the demodulation reveals no new insight, it may be a needless complication, and other techniques should be considered.

APPENDIX E

NONADAPTIVE TIME-DOMAIN ANALYSIS

Time Domain Analysis is a tool to compress data efficiently, that is, with little loss of information and if possible by a simple scheme. In some sense the compression then describes the properties of the data. The compressed information may be used to forecast, classify patterns, or for design changes (e.g., when a system appears "sluggish").

For the purpose of VER/EEG analysis we will concentrate on the stochastic modeling of time processes. An important class of these models is given by the Markov processes. In these processes the future statistics of a process are fully specified from knowledge of the present statistics. This concept is also referred to as a generalized causality principle. In good part the importance of these processes arises from their flexibility and mathematical convenience. The transition from the present to the future may proceed in a linear or nonlinear fashion and the process may or may not be stationary.

An important class of linear and stationary models is given by autoregressive (AR), moving average (MA), and autoregressive-moving average (ARMA) processes. Their importance in a variety of fields and a systematic approach to selecting proper models is described by Box and Jenkins (14). An important and still more general tool was developed by Kalman (55). Increased generality and applicability are due to considering nonstationary linear processes which also allow approximation of many nonlinear processes through nonstationarity.

In this appendix we outline model assumption for AR, MA, and ARMA structures together with their characteristics. Then we outline the Kalman model and discuss its advantages over other procedures, but also some important problems related to its structural generality.

AUTOREGRESSIVE AND MOVING AVERAGE MODELS

The use of AR models goes back to Yule (120) when he attempted to predict sunspot activity. It had been observed from Wölfer's (Box and Jenkins (14)) sunspot data that the sunspot activity was nearly periodic with a cycle length of about 11 years. However, there was fluctuation in amplitude and period of these numbers. Yule (120) attempted to describe these fluctuations by a causal random process of the type:

$$x(t) = \alpha_1\, x(t-1) + \alpha_2 x(t-2) + \ldots + \alpha_p\, x(t-p) + \varepsilon(t)$$

where $\varepsilon(t)$ expresses random shocks driving the linear process. They assumed $\varepsilon(t)$ to be a white process with constant power; that is, the covariance of $\varepsilon(k)$ and $\varepsilon(\ell)$ are given by

$$\mathrm{cov}\,[\varepsilon(k), \varepsilon(\ell)] = \delta_{k\ell}\, \sigma^2 .$$

Yule found for such a process a closed form estimate for $\alpha_1, \ldots, \alpha_p$ and σ^2 based on estimates of the autocorrelation function. Asymptotically, as the observed data grows infinitely long, his estimate is equivalent to the maximum likelihood estimate. Observe that for an AR process any disturbance propagates infinitely long (even though the amplitude may decrease).

An alternative linear process with slightly different characteristics can be written as

$$y(t) = \varepsilon(t) - \beta_1 \varepsilon(t-1) - \ldots \beta_q \varepsilon(t-q)$$

$$\text{cov } [\varepsilon(k), \varepsilon(\ell)] = \delta_{k\ell} \sigma^2$$

This linear process is known as moving average (MA) process. An apparent difference to the AR process is its finite memory of lag q; that is, after more than q steps any disturbance has died out.

For purposes of modeling it appears attractive to combine the AR with MA structure to obtain a still more flexible model. The combination may be written as

$$y(t) = \alpha_1 y(t \quad \ldots - \alpha_p y(t-p) = \varepsilon(t) - \beta_1 \varepsilon(t-1) - \ldots - \beta_q \varepsilon(t-q)$$

$$\text{cov } [\varepsilon(k), \varepsilon(\ell)] = \delta_{k\ell}\sigma^2,$$

and is called an autoregressive-moving average (ARMA) process. Since this model may be viewed as a polynomial, in a delay operator, on y(t) and $\varepsilon(t)$, the representation is only unique up to common roots in these polynomials (known to engineers as pole-zero cancellation). This is of importance when parameters are to be estimated since such common roots are not identifiable.

As an example for an ARMA process, Zetterberg and Kjell (121) have modeled the EEG signal as:

$$y(k) = \sum_{i=1}^{m} a_i \, y(k-i) + \sum_{j=1}^{n} b_i \, e(k-i) + e(k) \qquad \text{(E.1)}$$

where y(k) is the EEG signal at time $t_k = kT$, and e(k) is an assumed white noise input process. This ARMA model parametrizes the EEG in a set of m+n parameters $(a_1, \ldots, a_m; b_1, \ldots, b_n)$. The residual process e(k) (the modeling error) can be computed to determine goodness-of-fit, for example, by variance tests. The advantage of a model of the form of (E.1) is that it may be possible to model the EEG signal using a few parameters. Zetterberg found that $m \leq 5$, $n<m$, gave satisfactory performance in most cases for the spontaneous EEG. Bohlin (12) has also considered models of this form. Since many parameters are free to choose, a significant computational simplification is accomplished by assuming the moving average parameters $(b_1, \ldots, b_n)$ to be constant for all signals, so that signal variations could be accounted for by using only the autoregressive coefficients $(a_1, \ldots, a_m)$. For the purpose of multilead recording the modeling can easily be extended to vector ARMA processes and covers then all linear stationary finite dimensional Markov processes.

The basic theory using (E.1) assumes stationarity of the EEG signals. However, it is well known that the character of the EEG may change spontaneously. Furthermore, when the change in character is induced by stimuli, the nature of the change is of interest.

In order to treat this more general problem effectively a different notation, known as the Kalman message model (Kalman (55)) was introduced. The model with the observation $\underline{z}(t)$ is given by

$$\underline{z}(t) = H_t\, \underline{x}(t) + v(t) \qquad \text{observation model}$$

$$\underline{x}(t) = F_t\, \underline{x}(t-1) + w(t) \qquad \text{process model}$$

$$\left.\begin{aligned} &\mathrm{cov}(\underline{v}_k, \underline{v}_\ell) = \delta_{k\ell}\, V_v(k) \\ &\mathrm{cov}(\underline{w}_k, \underline{w}_\ell) = \delta_{k\ell}\, V_w(k) \\ &\mathrm{cov}(\underline{v}_k, \underline{w}_\ell) = 0 \\ &E[\underline{w}(t)] = E[\underline{v}(t)] = \underline{0} \end{aligned}\right\} \quad \text{moment assumptions}$$

Kalman (55) showed a computationally efficient way to track in real time $\underline{x}(t)$. The algorithm, in combination with nonlinear parameter estimation is easily extended to find also estimates of the transition matrix F_t, observation matrix H_t, the variance of the measurement noise $V_v(t)$, and the process noise $V_w(t)$. Moderately nonlinear processes may be approximated by nonstationarities (Jazwinski (53)). The scheme is also easily extended to be adaptive (see Appendix G, "Adaptive Filtering") and robust (see Appendix G, "Artifact Detection and Robustness").

Clearly, with increasing generality of schemes, theoretical and computational problems arise. For example, while for the estimation of AR-parameters the solution is unique and found by elementary matrix operations, estimating parameters in the Kalman model must be preceded with an analysis whether these are at all observable (such as in the problem: what is a given c, where c = a + b?). In other words, parameters are mutually dependent, sometimes such that they cannot be distinguished. (Note: this observability problem arose already in ARMA models with the pole-zero cancellation).

When estimation of parameters is possible, one still has to be aware of possible nonuniqueness, a result of the complex (usually nonlinear) relation of parameter with the data. Hence, when nonlinear parameter estimation is used, one has not only to recursively optimize the fit of a model, but also to verify uniqueness by using a sufficient number of different starting points of the estimation scheme. Since, in addition, many model structures are possible, they all have to be compared.

S^2I is in possession of routines which perform this task automatically, but application to models with many parameters (high dimensionality) is computationally expensive and requires potentially high computational accuracy. S^2I is also working on methods to relax some of the computational requirements, further automate these routines, and improve their performance for high dimensional problems. It will not be advisable, however, to use these routines in a completely unsupervised manner.

One of the conveniences in the use of the Kalman filter lies in the simplicity with which physical models are converted into filter coefficients. For example, one may have good a priori knowledge of the noise power in measurements; this quantity can be directly entered in the Kalman model. If this knowledge is to be expressed in the ARMA structure, a nonlinear relation to ARMA parameters arises. Clearly, this further exacerbates the problem of untangling the "components" in biological signals.

A danger in the use of the Kalman filter for the layman lies in the rather overwhelming freedom of structures he may choose from. He is then easily tempted to "overfit" the data (Box and Jenkins (14)). Thus their use requires experience with modeling, beginning with statistical analysis of residuals to an understanding of controllability and observability and appreciation of numerical complexities.

APPENDIX F

NONLINEAR SYSTEMS ANALYSIS

The nonlinearity of responses of living systems to stimuli, such as VERs for visual stimulation, is well documented. Nonlinearity is also seen on more microscopic levels--for example, in the generation and propagation of action potentials or the quantum release of chemical transmitter substances of synapses. The importance of nonlinearity can be appreciated in different ways: on the one hand, it is a means to enrich the input-output relations of systems and often it is a tool to perform certain tanks very reliably and inexpensively. In some instances, it is indeed the optimal approach to certain constrained problems such as the force constraint in saccadic eye movements. On the other hand, the richness of input-output relations poses considerable analytical problems; hence, analysis is typically limited to approximations. These approximations will often require simulations and iterative numerical procedures to check and improve solutions.

For the understanding of such systems special tools were developed in the engineering sciences. Typically the tools are based on an expansion such as Taylor or Volterra series. Special forms of linearization are used for the describing function analysis or extensions to the Kalman filter algorithm. Applications of Volterra series expansions for system analysis were pioneered by Wiener (116) and subsequently somewhat modified by others (Marmarelis (67)).

We may start out with the describing function approach, mainly because it provides insight into some of the important properties of nonlinear systems. As such, it is mainly developed for the evaluation of known nonlinear structures, such as the description of transfer characteristics or oscillations, as opposed to the estimation of underlying structure, given the transfer characteristics. On the contrary, extensive Kalman filter methods and Volterra series representations have been developed for the estimation and identification of unknown structures given input-output relations. However, in this appendix we will not discuss the Kalman filter algorithms or its extensions, since it is based on linear estimation and only its extensions deal with nonlinearity. The reader is referred to Appendix G where approximations to nonlinearities and nonstationarities are treated jointly.

DESCRIBING FUNCTIONS ANALYSIS

Describing function analysis was mainly developed in the engineering sciences and resulted from the need to describe nonlinear devices such as on-off controllers in an analytical fashion jointly with other possible linear circuitry. Often these on-off controllers are implemented more reliably or economically than continuous alternatives. It should thus not be surprising that similar principles are also favored in biological systems. As a matter of fact, in many hormonal control schemes (Martin (68)) the on-off approach is rather "popular." However, the usual context of describing function is with dynamical mechanical or electrical elements from engineering. In that field, specification of elements and overall structure are known and performance characteristics are of interest.

For our purpose here, the situation is somewhat different. Nevertheless, we believe the describing function analysis provides a tool to gain insight into processes such as limit cycles, sub- and superharmonics, and intermodulation. It may also provide guidance in the design of stimuli and aid in the discrimination of competing hypotheses.

The main thrust of describing function arises from the convenience of describing a nonlinearity by its transfer of the fundamental frequency and/or the transfer of mean and variance of the input signal. The sufficiency of such a description arises from the memory-behavior of practical linear components within a system. Firstly, the memory will result in spectral selectivity and secondly, via the central limit theorem, it suggests Gaussian output amplitude densities (Wozencraft and Jacobs (119)). Hence the signal flow and characterization may be accomplished by the consideration of only few spectral lines and the propagation of only the first two moments of the amplitude distribution functions (which are given by the mean and variance).

The methodology of the describing function analysis provides thus moderately simple means to understand oscillations of biological systems (recall the oscillation of the focal length of the lens of the eye), and to predict their frequencies and amplitudes as well as sensitivity to external perturbations. Mechanisms like variable gain and the effect of dither signals (signals which have a linearizing effect on nonlinearities) can all be studied within that framework. For hypothesized structures the methodology may suggest signals which emphasize a particular feature of a system, or guide one to test signals which allow improved estimation of certain components, or possibly to discriminate between alternatives. There is considerable freedom in the design and modification of signals because of their freedom in space and time. Some guidance about the way in which such changes should be made appears very important and may in part be answered by that methodology.

VOLTERRA SERIES

The Volterra series representation for the analysis of nonlinear dynamical networks was first developed by Wiener (116). The concept evolves easily from the generalization of the impulse response characterization of linear networks, an approach widely used in engineering. In linear networks (assume for simplicity scalar input and output) the general response (the output) is completely characterized by the response to a unit Dirac impulse. Basically any input other than the Dirac impulse may be viewed as a limiting superposition of infinitely many impulses shifted in time. Due to the superposition principle of linear networks to the response to this arbitrary input, waveform is also the limiting superposition of the individual impulse responses, since no "interaction" takes place between impulse responses.

The generalization to nonlinear system characterization is then realized by incorporating the possibility of interaction of impulse responses. This concept is precisely what is expressed by the Wiener series. To simplify the characterization, Wiener chose orthogonal functionals. In general, an infinite number of functionals (and their associated kernels) have to be considered. In practice, this infinite expansion must be truncated; but from current methodology (Lee and Schetzen, (62)) it is not clear how many kernels have to be calculated for adequate system characterization. For rather practical computational reasons only first- and second-order kernels are usually calculated.

In the application of the approach other considerations are also of importance. Instead of a Gaussian white input signal (which carries, roughly speaking, infinitely many (Dirac) impulses with a particular amplitude distribution) some other amplitude distribution and nonwhite signal which can be generated by physical means (finite power) must be used. Under limiting conditions a Gaussian white signal is usually reached.

Marmarelis (67) points also to other practical limitations of the method. In particular, he notes the strong dependence of kernel values on input (stimulus) power. Great experimental care has to be taken since the dependency becomes more pronounced with increasing order of the kernel. He discusses a variety of practical considerations and suggests methods for computing error bounds on the performance of such analysis. Some theoretical difficulties associated with kernel computation in dependence on input function are also presented. A good example of the application of the method to quantification of multiple sclerosis is shown in Sclabassi et al. (99). In this example, the intuitive meaning of the second-order kernel as a measure of interaction between a pair of stimuli is quite appealing to the clinician, for the evaluation of the integrity of portions of the nervous system is certainly characterized by such interactions.

APPENDIX G

ADAPTIVE AND ROBUST SCHEMES

ADAPTIVE NOISE CANCELLING

One of the principal objectives in the EEG signal-processing task under consideration is the elimination of spurious signals (noise) from the desired VER. The problem is complicated by the fact that there are no simple methods for modeling the nature of the noise or the interrelationships of the signals present at the various scalp electrode locations. In this case, we need to be very careful in any modeling assumptions we make to ensure that they do not place unnecessarily severe limitations on the quality of the results; that is, we seek techniques that are robust to modeling errors. In a general sense, we can enhance robustness by using a minimum number of assumptions in our models and by using a minimal number of parameters as well.

One technique which uses a very minimal number of assumptions as to the nature of the data is the adaptive noise-cancelling technique of Widrow et al. (115). The form of the problem and its solution are shown in Figure G-1 using, for simplicity in presentation, a single signal channel and a single noise channel. In the figure, the signal S is corrupted by noise n_0. Two electrodes are used; the first electrode records signal plus noise $(S + n_0)$ and the second electrode records the noise n_1. n_0 and n_1 are related by an unknown transformation which is dependent upon the properties of the medium through which the noise travels. Clearly if $n_0 = n_1$, the signal can be recovered directly by subtraction $(S = S + n_0 - n_1)$

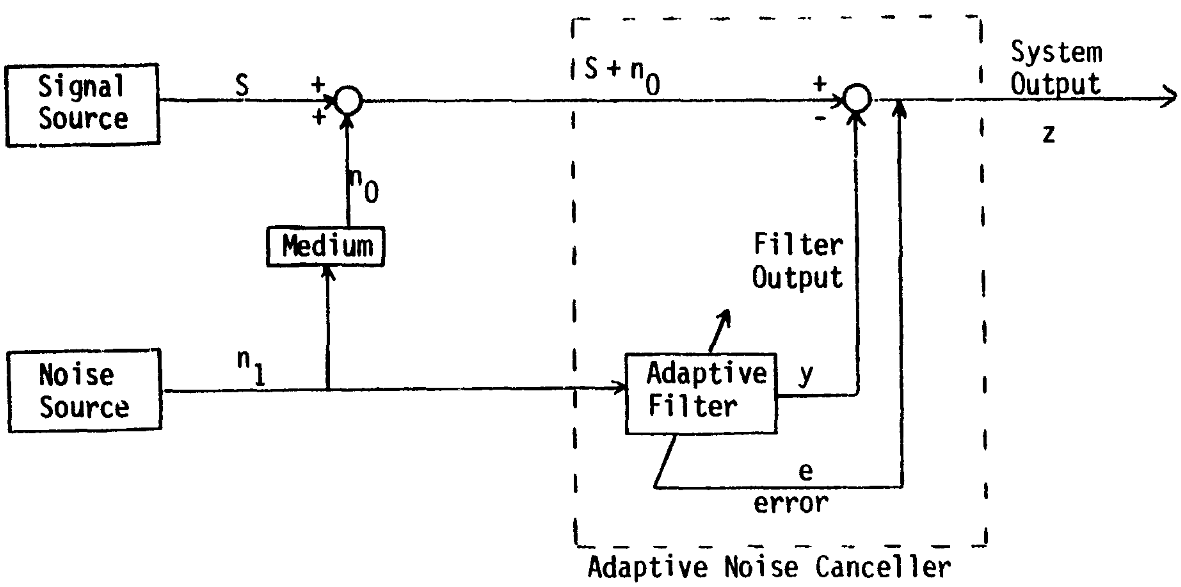

Figure G-1. Adaptive noise-cancelling concept.

Thus, we see that the problem of recovery of the signal is related to the properties of the conducting medium and, it turns out, the properties of the noise itself. Since the spurious signals we wish to estimate may change dramatically in character with time, we need a method to adapt to these unpredictable changes. The Adaptive Noise Cancelling method is an appropriate technique for this problem.

By inspection of Figure G-1 it is clear that we wish to make y "track" the unknown noise n_0 as closely as possible. If we make the crucial assumption that the signal S is uncorrelated with n_0 and y, then the problem is solved by adjusting y to give minimum output power (the power in z).

The adaptive noise canceller may be used in various ways. By assuming that the desired signal is the VER, we can attempt to cancel disturbances and make z a good estimate of the VER. Another approach would be to treat a desired response (such as flash response) as the signal and make z a good estimate of the response. In this case, the noise would include the VER.

The adaptive noise canceller has found many applications, as a result of its very general nature. These include estimation of fetal ECG by elimination of maternal ECG, elimination of radar sidelobes, notch filtering, noise cancelling in speech, self-tuning filters, and spectral estimation.

LONGINI'S NOISE CANCELLATION VIA ORTHOGONAL BASIS FUNCTIONS

A particular type of adaptive algorithm is based on orthogonal basis function representation; it has thus some similarity with the Karhunen-Loeve expansion and may be viewed as a communication theoretic approach. The method applies to models of the structure assumed by Widrow's adaptive noise cancellation. The solution proceeds, however, in a different fashion and provides fast convergence. For nearly periodic interferences of noise with the signal a further advantage over Widrow's method arises, since nonstationarity can easily be accounted for by rather primitive windowing. Due to the better convergence properties of Longini's over Widrow's method, less danger of system instability exists. Clearly a price has to be paid for these conveniences in terms of computational complexity.

Just as in Widrow's LMS-algorithm the linear but structurally unknown transmission characteristics for noise and the direct observation of the noise sources are exploited in a least-squares sense. The basic version of Longini's (65) method is based on the selection of sequential frames of data; within each of these frames the noise cancellation is done independently. The selection of frames is often given in a very natural way by periodic "events" such as heart beats, artificial stimuli, or other oscillation.

The procedure then calls for the estimation of noise transmission via estimation of covariances. Knowledge of these covariances may then be exploited to construct an orthogonal set of waveforms via the Gram-Schmidt procedure. Minimization of the noise in the signal then results directly from subtraction of these orthogonal waveforms from the observed data containing the signal. It is the use of the orthogonal set of waveforms which leads in this quadratic minimization to a one-step "convergence." Since Widrow's method does not orthogonalize his waveforms, convergence via his particular (nonlinear parameter) estimation scheme is slow if noise sources are correlated (either in space or time--depending on the particular problem). On the other hand, when noise sources may be assumed independent, nothing can be gained by Longini's orthogonalization approach, but much computation is saved by Widrow's algorithm. Longini's method requires n(n-1)/2 correlations for n-correlated noise sources.

For the purpose of real-time noise cancellation a fairly simple modification exists for Longini's approach. Instead of using frames of data, an exponential weighting function, aging past data can be used. In this form the algorithm is considered for implementation on a clinical instrument for removing maternal ECG signals (noise) from the abdominal fetal ECG signal (Longini et al. (65)).

ADAPTIVE FILTERING

The adaptive estimation technique given in Appendix G, "Adaptive Noise Cancelling," was predicated only on several vague assumptions concerning the character of the EEG; specifically, signal and noise components were assumed uncorrelated. No particular signal structure was presumed. In Appendix E, it was shown that the EEG (particularly the spontaneous EEG) does have certain definable statistical characteristics and that autoregressive models may be useful in EEG analysis. It would appear to follow naturally that the VER would have even more definable structure due to the controlled nature of the input signal. If this is so, then it also follows that adaptive algorithms should have more structure than allowed by Widrow's method. This subsection will discuss a potentially powerful approach to adaptive filtering using more highly structured models.

The basic theory, discussed in Appendix E, assumes stationarity of the EEG signals. However, it is well known that the character of the EEG may change spontaneously. Furthermore, when the change in character is induced by stimuli, the nature of the change is of interest.

An example of the variable character of the spontaneous EEG is shown in Figure G-2. The resultant time-variable spectra are shown in Figure G-3. Each curve in this plot is a power spectral density, averaged over 1.6 sec, and taken over successive 1.6-sec intervals. Figure G-3, sometimes called a compressed spectral array (CSA), is often used to analyze the time-varying nature of biological signals. The figure can give us qualitative information as to the nature of the nonstationarities in the EEG. However, we need to obtain quantitative information in order to study the problem more precisely. To do this, we now turn to a discussion of analysis of nonstationary EEG signals.

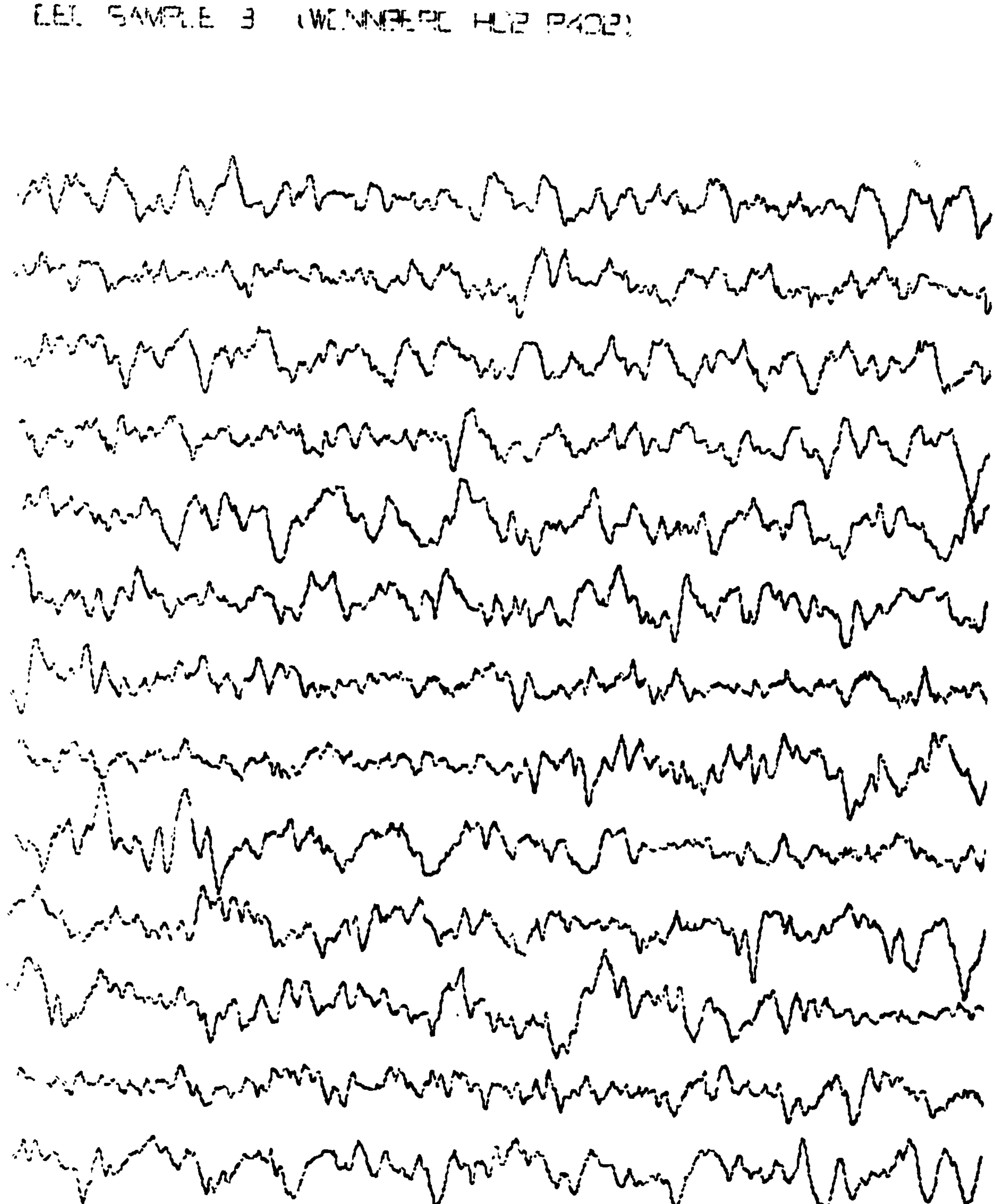

Figure G-2. Sample EEG.

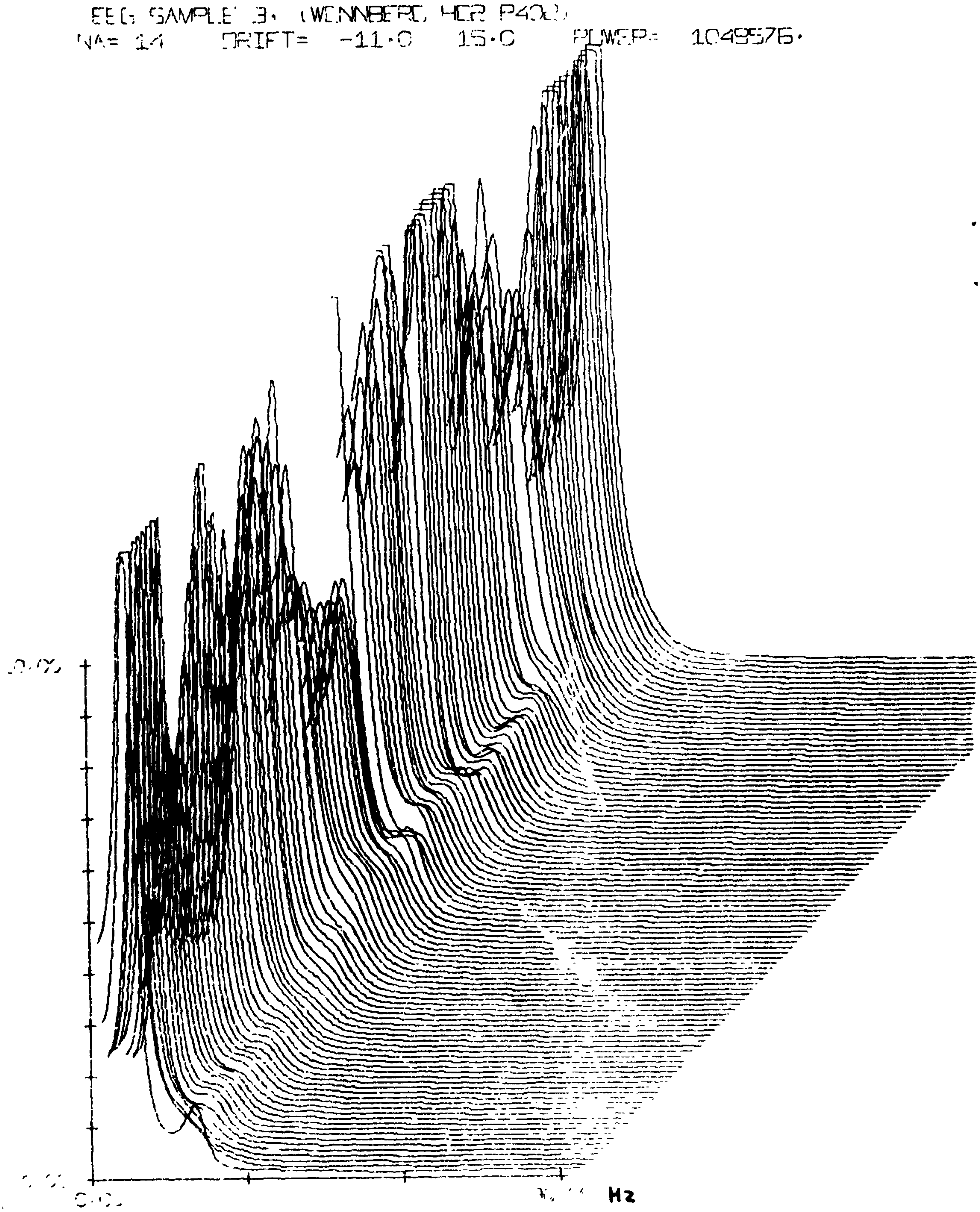

Figure G-3. Compressed spectral array for sample EEG.

Nonstationary Models

For the nonstationary case, it is useful to think of the ARMA model as time-varying; that is, the coefficients now become time functions. These functions are unknown, due to the unpredictability of the EEG signal. Thus, we need a way of estimating them from the data. The most powerful and general methodology for accomplishing this is adaptive filtering.

Before discussing adaptive filtering, we wish to remark that the ARMA model causes difficulties if the moving average parameters also change in time. ARMA modeling is very difficult for nonstationary processes. Bohlin (12) has developed an adaptive filter for tracking the AR parameters, while keeping the MA parameters constant; he did not consider time-varying MA parameters. It is possible, however, to resolve this problem by using a different problem formulation called state-space modeling. The state-space models we will consider are of the form:

$$y(k) = H\, x(k) + r(k) \qquad \text{(G.1)}$$

$$x(k) = \Phi(k)\, x(k-1) + G(k)\, u(k-1) \qquad \text{(G.2)}$$

where

$y(k)$ is the output (measured EEG),

$x(k)$ is the $n \times 1$ state vector,

H is a $1 \times n$ measurement matrix,

$\Phi(k)$ is an $n \times n$ state transition matrix, and

$G(k)$ is an $n \times 1$ input vector.

The output $y(k)$ may be a vector. The noise input $u(k)$ produces uncertainties in $x(k)$, while the noise $r(k)$ acts as channel noise.

The state vector $x(k)$, and hence the output $y(k)$, may be estimated using modern estimation theory. If we assume that $\{u(k)\}$ and $\{r(k)\}$ are zero-mean white Gaussian processes with known second moments, that $x(k)$ is Gaussian, and that H, $\Phi(k)$, and $G(k)$ are known, then the best estimator is a Kalman filter which is of the form

$$\hat{x}(k) = \Phi(k)\, \hat{x}(k-1) + K(k)\, \nu(k) \qquad \text{(G.3)}$$

$$\nu(k) = y(k) - H\, \Phi(k)\, \hat{x}(k-1) \qquad \text{(G.4)}$$

Here $\hat{x}(k)$ is the minimum-variance estimate of $x(k)$, and $\nu(k)$ is the measurement residual, or innovation, which represents the new information brought in by the measurement $y(k)$. The last term in (G.4) is the predicted value of $y(k)$; hence, if $\nu(k) = 0$, we are not getting any new information from $y(k)$. The matrix $K(k)$ is a gain matrix which controls the rate at which new information is incorporated into the estimate $\hat{x}(k)$. It is computed as a function of $\Phi(k)$, H, $G(k)$, and the noise covariance matrices.

With this brief background, we are now finally in a position to discuss adaptive filtering.

Adaptive Kalman Filtering

Since the models we are discussing here have a particular parametric structure, we expect that development of adaptive techniques will be more complex than the Widrow algorithm. This is indeed the case. Adaptive filtering based on a Kalman filtering methodology has been an active field of research for at least a decade. A good review is given in Mehra (70).

Perhaps the most generally powerful technique is the maximum likelihood approach, in which we attempt to compute the most likely set of parameters in time. Bohlin (12) has used this approach for EEG analysis (while restricting his study to AR models) and developed adaptive filters in a special integer arithmetic implementation to maximize computational speed. His results indicated that the approach could provide a useful man-readable interpretation of the EEG.

Duval (35) has developed a more general adaptive algorithm which can be used for the model of (G.1)-(G.2). He considered only the problem of adapting the gain matrix $K(k)$. More recently, Gustafson and Ledsham (47) have developed an adaptive filter for tracking the transition matrix $\Phi(k)$ in real time. The form of these adaptive filters is similar. To illustrate the technique, suppose we are interested in tracking only $\Phi(k)$. Then the adaptive filter takes the recursive form:

$$\text{filter} \quad \begin{cases} \nu(k) = y(k) - H\,x'(k) \\ \hat{x}(k) = x'(k) + K(k)\,\nu(k) \end{cases}$$

$$\text{adaptor} \quad \begin{cases} \Phi^*(k) = \Phi^*(k-1) - f(\nu(k)) \\ \hat{\Phi}(k+1) = \hat{\Phi}(k) + \beta[\Phi^*(k) - \hat{\Phi}(k)] \end{cases}$$

$$\text{propagation} \quad \{x'(k+1) = \hat{\Phi}(k+1)\,\hat{x}(k)$$

The first two equations ("filter") incorporate the measurement $y(k)$ into the state estimate $\hat{x}(k)$. The quantity $x'(k)$ is the predicted value of the state $x(k)$ prior to incorporating the measurement $y(k)$.

Adaptation of $\Phi(k)$ takes place in two steps. First, the optimal estimate $\Phi^*(k)$ is found using the maximum likelihood equations. The function $f(\nu(k))$ is linear in $\nu(k)$. Next, the estimate $\hat{\Phi}(k+1)$ is computed using an update rate parameter β. If $\beta=1$, then $\hat{\Phi}(k+1) = \Phi^*(k)$. If $\beta = 0$, $\Phi(k+1) = \hat{\Phi}(k)$ and the estimate does not change from its previous value. Thus β controls the speed of adaptation.

The final step is propagation of the state estimate using the new estimate $\hat{\Phi}(k+1)$.

This algorithm is easily extended to include simultaneous adaptation of $\Phi(k)$, $K(k)$, and $G(k)$, although the equations become more complex. As mentioned previously, S^2I has applied these algorithms to other problems and is quite experienced in their use.

PIECEWISE STATIONARY MODELING

Another approach to the analysis of nonstationary signals is to segment them into stationary, or quasi-stationary, segments. It is undoubtedly true that the nonstationarity of the VER, using almost any nonstationarity measure, increases as the data epoch increases. It has been experimentally verified (e.g., McGillem and Aunon (69)) that segmenting the VER and using latency-correcting techniques for each segment results in higher signal energies and more sharply defined responses. More recently, Segen and Sanderson (100) have used piecewise stationary autoregressive models for the spontaneous EEG. The data were segmented using a cluster analysis of the model parameters. Their results demonstrate clearly the possible improvement in signal tracking attainable using segmentation of the EEG. This same technique should be applicable as well to the modeling of the VER (cf. Figure G-2 for an example of the nonstationarity of the VER).

ARTIFACT DETECTION AND ROBUSTNESS

Large real-world data sets will always tend to be corrupted by artifacts, some of which cannot be accounted for. When the occurrence of artifacts is rare and of little power, they may be ignored. In VER/EEG analysis, however, rather large artifacts such as from frequent saccades of the eye, periodic blinking of the eyelid, and loosening of electrodes may occur. Analysis of VER/EEG data should include these effects.

Robustness expresses the concept of good system performance when structured or other deviations from the assumed model arise. The concept has received much attention in control theory and statistics in the last decade. The objective when making a particular procedure robust is to trade little of known good properties of a particular procedure against resistance to model errors. The general theoretical treatment is very hard or even intractable in all but the most trivial situations. Consequently investigation of robustness properties is guided by consideration of limiting cases, possibly expressed in bounds and typically checked by simulation. Usually only robustness against a few types of model deviations is accomplished, but never against all.

Applied to VER/EEG analysis this could mean an algorithm is capable of continued good performance, despite saccades, blinks, or other erratic events; possibly the algorithm might also cope with an occasionally misplaced electrode. The robust scheme will typically "suspect" or "detect" model deviations and reduce the weight in considering such data. A good example of such a robust method is given by Athans et al. (7) where a ballistic reentry vehicle produces an ionic wake; when observing the vehicle by radar, the wake may also reflect the radar beam resulting in erratic measurements. Based on a likelihood argument, the well-known Kalman filter algorithm is modified to be "cautious" in incorporating such erratic data. In a comparison, the "optimal" Kalman filter algorithm lost track of the vehicle; the robustified version did not. Furthermore, when there was no wake, there was little difference in the performance of the two versions of the algorithm.

Lately, the concept of robustness is also combined with the concept of adaptivity. For example, one would like to make a procedure more robust when there is evidence of model deviation, but approach the optimal method if there is no such indication. Some theoretical work in this direction has been done by Prescott (82) for adaptive trimming proportions for the estimation of means.

Some experience related to adaptive trimming in dynamical system was also gained by one of the authors. There the problem arose to describe dynamic fluctuations (arrhythmia) of the fetal heart rate in the presence of erratic artifacts due to maternal heart beat, uterine contraction during labor, and electrode imperfections.

Examples: Adaptive Spectral Line Enhancing

Adaptive methods are quite useful in extracting periodic components from broadband noise. For example, this approach could be used to track VER frequencies at or near the input frequency.

As a result of random, unknown modulation effects within the brain, the counterphase frequency component may be changed slightly within the measured VER. This "detuning" is something we would like to be able to track. As a simple example, suppose that the counterphase frequency is $f_0=2\pi/\omega_0$ Hz. The fundamental signal component is

$$S_0(t) = \cos \omega_0 t$$

Now assume that a phase modulation of the form

$$\Phi(t) = \alpha \sin \omega_0 t$$

is introduced. The signal then becomes

$$S(t) = \cos(\omega_0 t + \alpha \sin \omega_0 t)$$

The Fourier coefficient at frequency f_0 is

$$a_{f_0}(\alpha) = J_0(\alpha) - \frac{\alpha}{\pi} J_1(\alpha)$$

where $J_\nu(\alpha)$ is the Bessel function of order ν. For α small

$$a_{f_0}(\alpha) \simeq 1 - 0.75\alpha - 0.159\alpha^2$$

The parameter α represents the maximum phase deviation one would expect over one counterphase cycle. For example, McGillem and Aunon (69) found phase deviations of up to 20 msec over VER segments of 100 msec. For a counterphase frequency of 8 Hz this gives α = .16 and

$$a_{f_0}(.16) \doteq .88$$

Thus, expected small latency shifts give rise to significant reductions in output signal power (here 23%) at the counterphase frequency.

Frequency tracking may be accomplished by the Adaptive Line Enhancer (ALE) (cf. Tufts et al. (110)). An example of the performance improvement relative to the FFT is shown in Figure G-4. The probability of detecting a constant frequency signal in wideband Gaussian noise is plotted vs. input signal/noise ratio for several values of false alarm probability (P_{FA}). Performance improvement at low P_{FA} is quite significant.

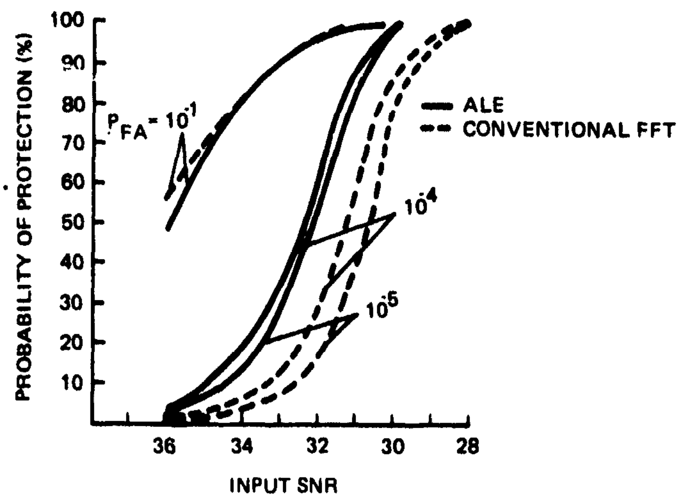

Figure G-4. A comparison of receiver operation characteristic (ROC) curves of the conventional and ALE detectors.

(after Dentino et al., Proc. IEEE Conf. on Decision and Control, p. 1377, 1978.)

APPENDIX H

EXPERIMENT DESIGN

The design and operational details of a VER experiment can have a significant impact on the effectiveness of signal processing. In particular, critical parameters in the signal source, subject condition, and experimental procedure should be regarded as valuable data inseparable from the measured EEG. These parameters may be classified as a) controlled, b) uncontrolled but measured, and c) important but unmeasured. Of course, the same parameter may be controlled in one experiment but an unmeasured disturbance in another. Desmedt (28) contains (in chapter I on methodology) a good description of such parameters in VER research.

The first group of parameters contains all of the factors directly controlled by the experimenter. These parameters include a) stimulus details, for example, color, pattern characteristics, flash frequency, and eye illumination; b) subject details, for example, concentration points and task performance during the experiment; and c) measurement details, such as electrode placement and characteristics, analog processing before digitization, and digitization parameters.

Other parameters may be equally important, although uncontrolled (or even uncontrollable) but measured. Included in this category are subject blinking or eye movement, time of day (patient awareness), and electrode impedance characteristics. The effect of some parameter variations may be reduced rather than measured, by proper experiment design. For instance, impedance variations may be reduced by using a high-impedance amplifier at the sacrifice of noise level (see Appendix B).

The last group of parameters, uncontrolled and unobserved, contains the most troublesome variables for the experimenter. Subject attention and focal point, random stimulus variations (e.g., frequency jitter), pupil dilation, and electrode noise can all add unaccounted variability to an experiment session. The potential damage is much worse when the data is processed long after it is taken, possibly ending in a wasted session rather than merely one bad run. Data processing techniques which give instant results, not unlike instant pictures, are quite valuable even if inferior in quality to post-processing.

Proper experiment design may test for the sensitivity of the results to any questioned parameter and modify the experiment when necessary. For example, a simple VER extraction technique (for removing the background EEG) in real time can be used to position electrodes for maximum response and may reduce day-to-day variability in the data, thus providing better data for later, more sophisticated, post-processing.

Experiment design may also prevent unmeasured disturbances from corrupting the data. For example, a Maxwellian view technique may be used to prevent random pupil dilations (see Appendix B) from unintentionally amplitude-modulating the stimulus. Another example is the possibility of (deliberately) frequency-modulating the pattern reversal rate in the α wave region to prevent the EEG from locking to the stimulus. If the response to a blinding flash is measured by sychronously demodulating (see Appendix D) the pattern response, a much different result from constant-rate experiment--with EEG entrainment--may be obtained. This may permit EEG entrainment time-constants to be distinguished from flashblindness recovery times.

APPENDIX I

EVALUATION OF PERFORMANCE

Evaluation of the performance of a signal-processing method or experiment is inherently based on costs and benefits (negative costs, also considered utility). Ideally, an evaluation should aid in modifying the structure analyzed, so as to improve overall utility or reduce costs. A difficulty exists in that utility and cost are usually not fixed as a project progresses, and often they are hard to specify at all. Thus the best one can do initially is to discuss aspects related to these costs as they pertain to the balance between signal analysis and other research objectives.

Typically simpler structures can be evaluated more objectively, complex problems more subjectively. In this appendix we will start out with a discussion of simple structures and turn to more complex situations.

EVALUATION OF PERFORMANCE OF SIMPLE STRUCTURES

Earlier, in Appendix A, we discussed the general philosophy of signal analysis as a task to separate information in data from its random component. The separation is rarely complete; in many cases, complete separation is not even necessary to meet one's goals, while in other uses it may be mandatory.

Special tools have been developed in statistics to identify when separation is nearly complete. The tests concern the residuals of the model: that random part not accounted for by the model. A variety of tests for the mutual independence of residuals (from one sample point to another) have been developed, each with a specific diagnostic value and power to discriminate against certain alternatives. For Gaussian distributions, which are very important in much of signal analysis, a test for uncorrelated residuals is equivalent to a test for their mutual independence.

For example, consider an EEG tracing. We select a window-subsection in order to fit a model and would like to detect when in subsequent windows a significant model change occurred, so that we may update our model. In this case, we may, for example, simply compute the one-lag autocorrelation value of the residuals for any of these new data windows; when a critical value is exceeded we are willing to proceed with the possibly costly (in terms of computer time) reestimation of our model.

The importance of mutually independent residuals is intuitively very appealing in case of sequences of events, such as in time series. For example, when we forecast an observation based on present and past, and the difference between our forecast and the eventual observation is independent of all our knowledge (including all past forecasts and observations), we have done the best possible job--all structural information in the ongoing process is known to us. It is only the randomness of nature which surprises us and creates an innovation. On the contrary, if the difference between forecast and eventual observation depends on the past, we could use this dependency to improve our forecast; hence we did not use the optimal scheme.

The importance of this concept was emphasized by Wiener (116). In the case of linear dynamical structures and Gaussian densities, testing for uncorrelated innovation is equivalent to testing for optimality of the scheme. Such uncorrelated sequences are usually called white sequences (they need not be Gaussian) in resemblance to the stochastic properties of white light. Observe, that colored light such as from lasers is highly structured as expressed by the coherence properties. Again, in resemblance to colored light, (innovation) sequences which are correlated and hence contain much structure are regarded as colored (see Sage and Melsa (94, 95)).

For cases other than linear structures, checking correlation is in general insufficient to detect dependency. But in many statistical models local linearizations are possible and hence "moderately" nonlinear problems may still be analyzed by correlation procedures. Possibly one might also use Dewan's (31) generalized procedure. Thus testing correlation remains one of the most important and also diagnostic procedures to establish optimality of a scheme.

An alternative to checking for the "optimality" of a signal-processing scheme in terms of residuals is to look at the usefulness of one's scheme to express gross features. For example, the second-order (linear) AR-model describes gross oscillations in an EEG waveform but does not account for the asymmetry in that particular waveform. When these oscillations entrain another mechanism, it may not be very interesting to have the "optimal" model. It may be sufficient to specify roughly the (possibly somewhat drifting) modulating power and frequency of these oscillations to predict the behavior of the entrainment.

For other purposes one might not be interested in the predictive value of a scheme, but as in pattern recognition, one wishes to have a parameterization of observation which allows separation into different classes, sometimes even into distinct clusters. When such separation is accomplished with low enough error rates, one may well regard a particular scheme as good. Clearly, when error rates are not low enough, examination of model residuals may tell whether there is (still) possibly useful information left in the original data which might be "extracted" by improved modeling.

SUBJECTIVE EVALUATION AND EVALUATING A LARGE SYSTEM

Subjective performance evaluation will often occur in preliminary evaluation of simple structures or will result from subjective cost structures. For the preliminary evaluation of simple models, plots of model residuals and their visual (subjective) evaluation are very important; a good treatment of this topic is given by Draper and Smith (32). As structures become more complex, their evaluation requires approximations (they are subjective) especially because of nonlinear interactions (such as limitation and decisions) of system components and changing objectives.

The most important performance measures of large systems we will use are based on:

1. Reproducibility

2. Speed of processing--real time versus off line

3. Numerical stability and sensitivity

4. Automatic versus manually supervised operations (selection of starting values)

5. Robustness against artifacts

6. Resistance to operator command errors

7. Structural clarity--e.g., relation of parameters to physical or physiological processes

8. Ease of modification (e.g., model changes)

Their mutual weighting in the evaluation of a particular component is essentially a quite subjective task.

In an environment with the goal to improve these essentially subjective performance measures, we ask first for diagnostic procedures to detect components which perform poorly. Detection of such components (e.g., a spike/wave detector) and their importance in the overall scheme will tend to be more valuable (because of simplicity) than a complete ranking of the performance of all components: delineation of poorly performing components invites immediate treatment. In view of changing objectives and costs it is unlikely that the effects of a poorly performing component will improve with time. Hence this approach of detecting "bad" components is one of the important aspects of the philosophy of trouble shooting which ultimately may reduce costs or improve utility.

Then, once all "bad" components have been taken care of, one may proceed to examine more carefully the cost effectiveness of components. Possibly one determines also their relations and the potential to tune components in terms of tradeoffs.

APPENDIX J

OVERVIEW OF APPLICATIONS

The varied techniques of signal processing discussed earlier in this report can be applied at several points, and on several levels in VER experimentation. This appendix outlines some obvious applications and discusses some of the more promising processing techniques for each area.

OVERALL EXPERIMENTATION

The basic experimental process may be structured as in Figure J-1. The first step in the design of an experiment is to define objectives; i.e., to specify what one hopes to learn in the experiment. With these objectives in mind, one forms a model for the process under investigation and then designs an experiment to test the model. The actual preparation and conduction of the experiment may include the minor feedback loop, from data analysis to experiment set-up, as shown. This loop represents the real-time use of signal processing in "calibrating" the experiment or reducing unwanted variations in experimental conditions, for example, the use of EEG amplitude measurements to repeatably place electrodes.

DATA PROCESSING AND ANALYSIS FOR VER EXPERIMENTS

The data-processing block of Figure J-1 contains the usual functions of signal analysis in experimentation. For VER experiments, this block may be subdivided into several subtasks, each of which may be accomplished by a different signal-processing technique. The subdivision will also be different for "transient" (single flashes or patterns) testing than for "steady-state" (pattern reversal) experiments.

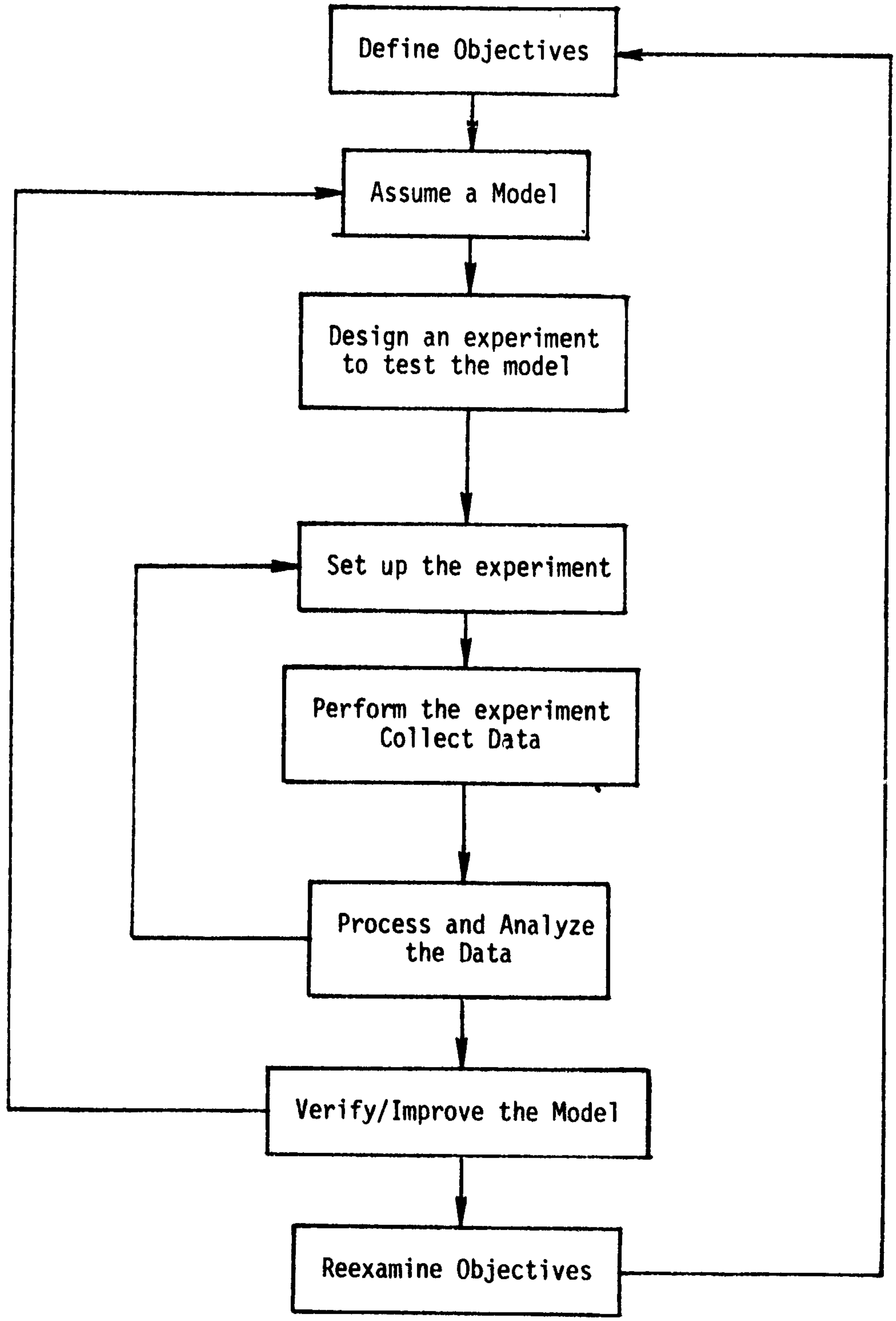

Figure J-1. Experiment overview.

Steady-State Experiments

For steady-state experiments, the measured data from one or more electrodes will be used to compute the instantaneous spectrum of the EEG (or a single component of the spectrum at the pattern reversal frequency). This instantaneous spectrum may then be tracked in time, and any changes (especially in response to blinding flashes) noted. The first task--that of computing the instantaneous spectrum--is a problem in spectral estimation as discussed in Appendix C. It is particularly difficult in this experiment because the spectrum is changing with time, and one must inevitably trade off the accuracy of larger data windows against the error caused by spectral changes during the window.

Once the instantaneous spectrum is computed, the modeling and tracking of the spectrum changes (in response to a stimulus) may be more appropriately handled in the time domain as discussed in Appendix E. This two-part analysis is shown in Figure J-2.

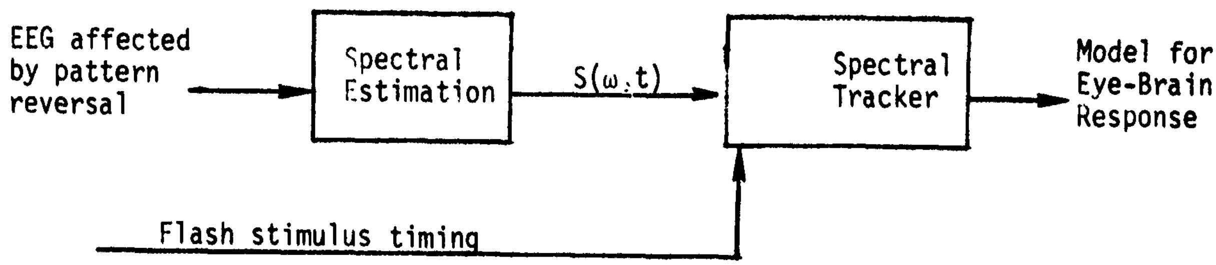

Figure J-2. Steady-state analysis.

Transient Experiments

In transient experiments, the EEG is measured at one or more scalp locations, and the data is used to identify a brain response to a visual stimulus. The data processing may be separated into two parts, as above, but in this case the goals are decidedly different. The first task is to take the measurements and extract the evoked response from the background (spontaneous) EEG. Several different techniques for this removal of the EEG may be considered. The second task is to analyze the VER, as shown in Figure J-3.

Traditionally, the background EEG is averaged out by superimposing several responses all synchronized by the stimulus times. This technique, unfortunately, removes some high-frequency VER information and ignores any response (VER) change from one stimulus to the next. Two other techniques seem useful for VER extraction and do not possess these drawbacks. The first would use time series filtering (e.g., ARMA) to track the EEG before the flash and subtract an estimated EEG from the measurements during the expected response. The residual should be the VER alone. The second approach would use multi-lead information (ideally one lead with EEG plus VER and one with EEG alone) to extract the VER via, for example, Widrow's

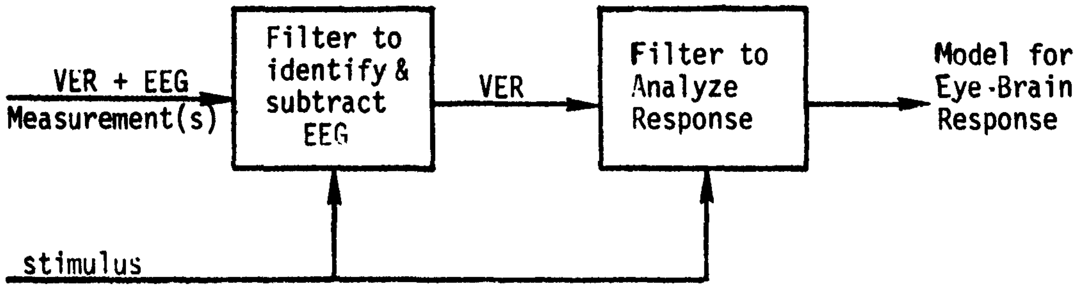

Figure J-3. Transient analysis.

method (see Appendix G). The first suggested approach requires temporal correlation of the background EEG, while the second looks for spatial correlation of the EEG (but not VER).

Once the (pure) VER is obtained, any manner of signal processing, feature extraction, and pattern recognition techniques may be used to examine the stimulus-response behavior. The choice of technique will depend on the stimulus and response characteristics, but should be greatly facilitated by the visibility of the VER after its extraction in the above stage.

APPENDIX K

CURRENT AND CLASSIC SIGNAL PROCESSOR PERFORMANCE

This appendix derives some of the numerical results used in the section "Analysis of Current Processing." We begin by noting a number of relations for a Gaussian random varable (x) with mean m and variance σ^2, denoted by

$$x \sim N(m, \sigma^2)$$

Then the first four moments of x are

$$\overline{x} = m$$

$$\overline{x^2} = m^2 + \sigma^2$$

$$\overline{x^3} = m^3 + 3m^2\sigma^2$$

$$\overline{x^4} = m^4 = 3\,\sigma^4 + 6m^2\sigma^2$$

We consider the spectral estimate s:

$$s = x_1^2 + x_2^2 ,$$

where $x_i \sim N(m, \sigma^2)$, $i = 1,2$

x_1 and x_2 are independent, and

$$m = \frac{1}{2}\sqrt{PT}$$

$$\sigma^2 = Q/2$$

<u>Mean of s</u>

The mean of the random variable s is

$$\overline{s} = E(x_1^2) + E(x_2^2) = 2(m^2 + \sigma^2)$$

and, substituting from above

$$\overline{s} = \frac{PT}{2} + Q$$

<u>Variance of s</u>

We may find the variance of s from the relation

$$\text{Var } s = E[(s-\overline{s})^2] = E(s^2) = \overline{s}^2$$

From above we know that

$$\overline{s}^2 = 4(m^2 + \sigma^2)^2$$

We have that

$$E(s^2) = E(x_1^4 + 2x_1^2 x_2^2 + x_2^4)$$

$$= 2E x_1^4 + 2(E x_1^2)^2$$

$$= 2(3\sigma^4 + m^4 + 6m^2\sigma^2) + 2(\sigma^2 + m^2)^2.$$

Then

$$\text{Var } s = 2[\,3\sigma^4 + m^4 + 6m^2\sigma^2 - (\sigma^2 + m^2)^2\,]$$

$$= 4\sigma^4 + 8m^2\sigma^2.$$

And, substituting for m and σ,

$$\text{Var } s = Q^2 + P\,T\,Q$$

Classic Spectral Estimation

The classic technique computes N estimates

$$\hat{s}_n = x_{1_n}^2 + x_{2_n}^2 , \quad n = 1,\ldots,N$$

from the N windows:

$$z(t+n), \quad t \in (0,T), \quad n = 1,\ldots,N.$$

For each window, the components at 4 Hz are

$$x_{i_n} \sim N(m, \sigma^2)$$

where

$$m = \frac{1}{2}\sqrt{PT}$$

$$\sigma^2 = Q/2$$

and then

$$\hat{s} = \frac{1}{N}\sum_{n=1}^{N} \hat{s}_n$$

is the spectral estimate. We wish to compute the mean and variance of $\hat{s}$.

Mean

$$\overline{\hat{s}} = \frac{1}{N} \sum_{n=1}^{N} \overline{\hat{s}_n}$$

and,

$$\overline{\hat{s}_n} = \overline{x_{1_n}^2} + \overline{x_{2_n}^2} = 2(m^2 + \sigma^2)$$

Therefore

$$\overline{\hat{s}} = \frac{PT}{2} + Q.$$

Variance

To compute the variance of s we need $(\overline{\hat{s}})^2$ and $\overline{\hat{s}^2}$.

$$\overline{\hat{s}^2} = \frac{1}{N^2} \sum_{n=1}^{N} \sum_{r=1}^{N} \overline{\hat{s}_n \hat{s}_r}$$

$$E[\hat{s}_n \hat{s}_r] = E(x_{1_n}^2 + x_{2_n}^2)(x_{1_r}^2 + x_{2_r}^2) = 4\,E\,x_1^2\,x_2^2 = 4(\sigma^2 + m^2)^2, \; n \neq r$$

and

$$E[(\hat{s}_n)^2] = E(x_1^4 + 2\,x_1^2\,x_2^2 + x_2^4) = 2(2\sigma^4 + 4m^2\sigma^2) + 4(m^2 + \sigma^2)^2.$$

Therefore

$$\overline{\hat{s}^2} = \frac{1}{N^2} \sum_{n=1}^{N} \sum_{r=1}^{N} 4(\sigma^2 + m^2)^2 + \frac{1}{N^2} \sum_{n=1}^{N} 2(2\sigma^4 + 4m^2\sigma^2)$$

$$= 4(\sigma^2 + m^2)^2 + \frac{1}{N}(4\sigma^4 + 8m^2\sigma^2)$$

and

$$(\overline{\hat{s}})^2 = 4(m^2 + \sigma^2)^2$$

so that

$$\mathrm{Var}\,\hat{s} = \frac{1}{N}(4\sigma^4 + 8m^2\sigma^2)$$

and, substituting for m and σ, we have

$$\mathrm{Var}\,\hat{s} = \frac{Q^2 + PTQ}{N}.$$

Comparison

Consider the following measure of a spectral estimator:

$$M = \frac{\text{standard deviation}}{\text{mean}}$$

where the lower M is, the better. Then the current estimator has

$$M_c = \frac{\left[\frac{Q^2}{N^2} \quad \frac{Q}{N} PT\right]^{1/2}}{\frac{PT}{2} + \frac{Q}{N}}$$

and the classic estimator has

$$M_{cl} = \frac{[\frac{1}{N} (Q^2 + P\ T\ Q]^2}{\frac{PT}{2} + Q}$$

We note in passing that the current estimator performance is independent of T (the window length), and depends only on the total record length NT. To see this we let the record length be

$$L = NT$$

Then

$$M_c = \frac{[Q^2 + QPL]^{1/2}}{(PL/2) + Q}$$

Of course, different window lengths result in different frequency resolutions and thus different responses to noise outside of the 4-Hz band that we consider. Thus this result should be approached with caution.

An interesting point, however, is that the classic estimator performance improves as more windows are taken. This improvement is limited, however, by the low-frequency resolution available at short window lengths and by the eventual correlation (lack of whiteness) of the noise for short times.

Finally, we are ready to consider the ratio of the measures

$$\eta = M_{cl}/M_c$$

where small η (<1) implies the classic technique is better while large η (>1) favors the current method. We let T and N be the same for both techniques, so that frequency resolution and total data lengths are the same for both.

We have,

$$\eta = \left\{ \frac{[(1/N)(Q^2 + PTQ)]}{[(Q^2/N^2) + (Q/N)PT]} \right\}^{1/2} \left\{ \frac{(PT/2) + (Q/N)}{(PT/2) + Q} \right\}$$

Letting α represent a signal to "noise" ratio

$$\alpha = PT/2Q$$

we have

$$\eta^2 = \left\{ \frac{(1/N)(1+2\alpha)}{(1/N^2) + (2\alpha/N)} \right\} \left\{ \frac{(1/N) + \alpha}{1+\alpha} \right\}^2$$

$$= \left\{ \frac{1 + 2\alpha}{(1/N) + 2\alpha} \right\} \left\{ \frac{(1/N) + \alpha}{1 + \alpha} \right\}^2 .$$

As shown in Figure K-1, η^2 is always less than 1, although for large α, $\eta^2 \to 1$.[7] Thus, if a pure sinusoid of sufficient power is present, both techniques will give equally good performance. For low α, however, the classic technique is better by a factor of

$$\eta = 1/\sqrt{N}.$$

[7] For convenience the asymptotes of the $\ln(\eta^2)$ versus $\ln\alpha$ have been plotted by analogy with Bode techniques.

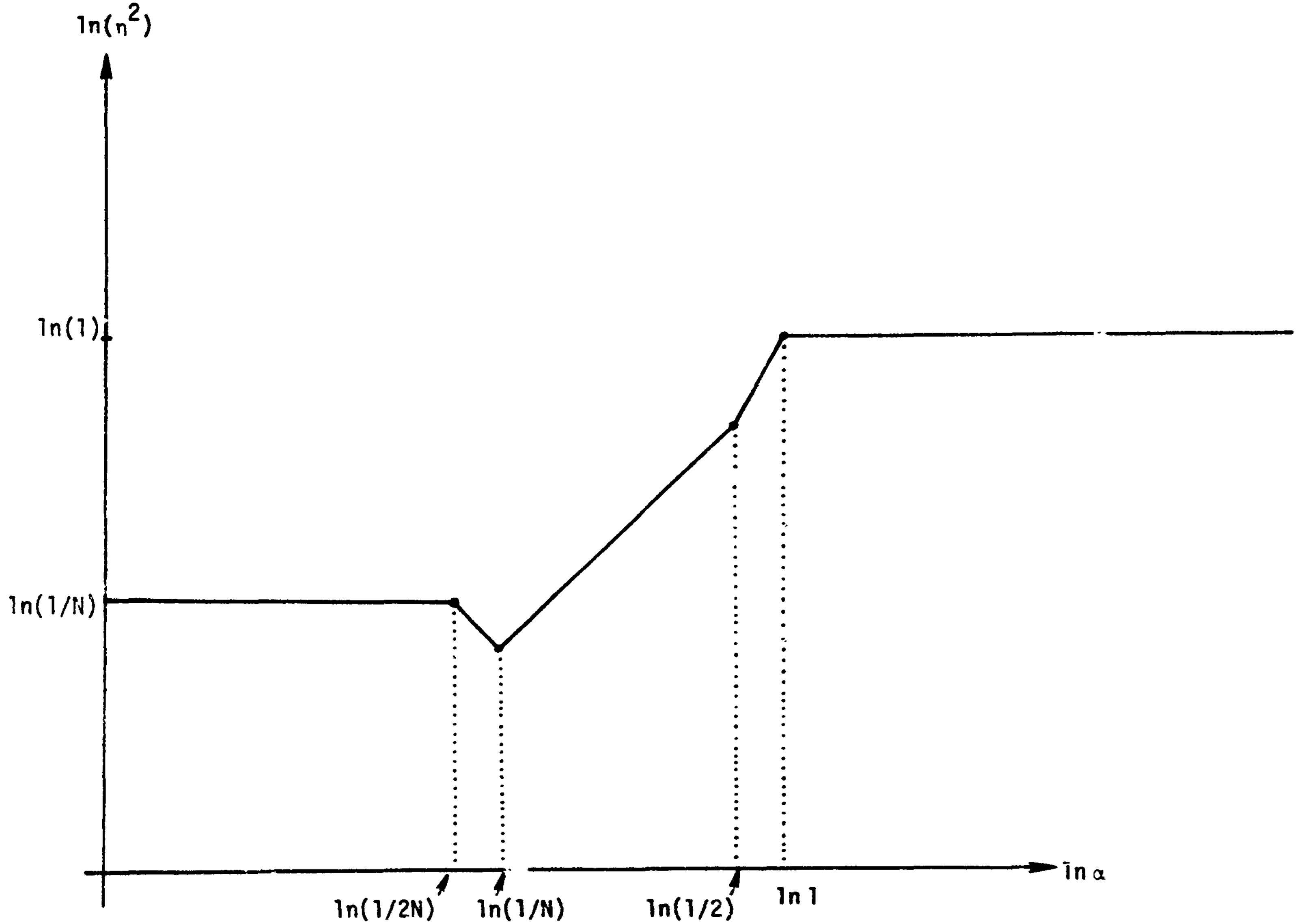

Figure K-1. Asymptotes of relative performance measure.

APPENDIX L

A MODEL FOR WEAK HIGH-FREQUENCY COMPONENTS OF TRAVELLING WAVES, MODIFIED FROM LINDSTRÖM (64)

Lindström's model is based on a Fourier analysis and Coulomb's law for quasi-stationary fields (wave propagation velocity $v \ll c = 1/\sqrt{\epsilon\mu}$). The explanation we give here is a simplified qualitative geometric consideration.

We may start out by considering a wave, such as an action potential, as composed of a continuum of infinitely long sinusoidal waves. For simplicity, we will only consider far-field effects ($h \gg \lambda$), as shown for two sinusoidal waves in Figure L-1.

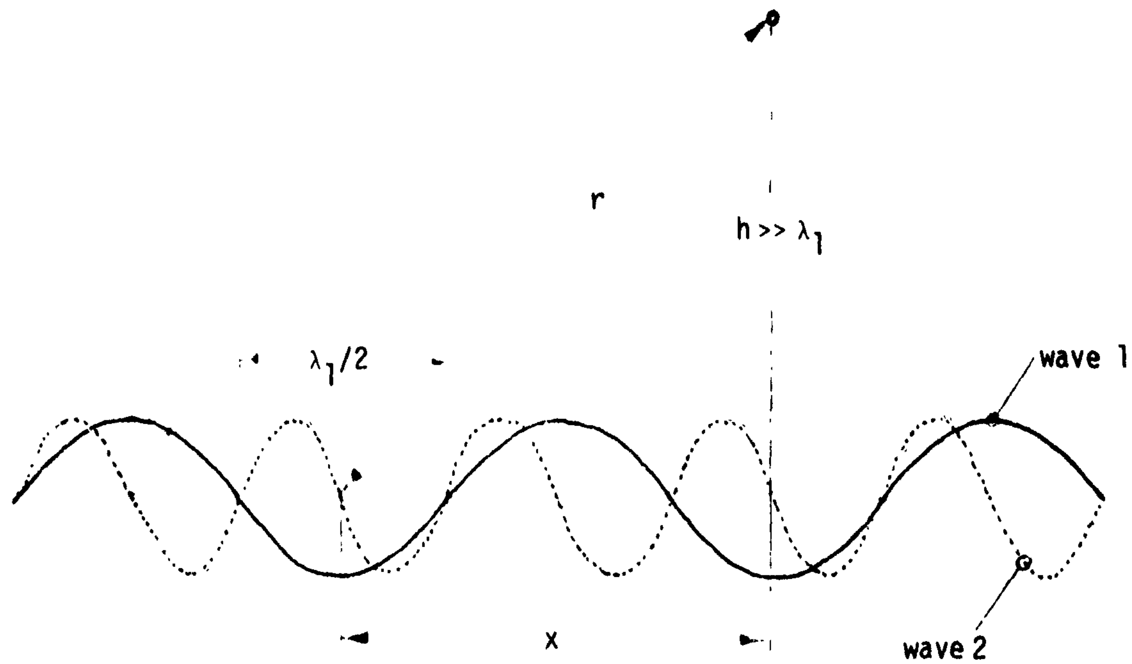

Figure L-1. The far-field contribution of two waves with different spatial frequencies.

From Coulomb's law we realize that the contribution of the positive halfwave #1 (darkened area), shown in the Figure L-1, will decrease like $1/r$ as the distance of that halfwave #1 from the point P is increased. However, the contribution of the wave #2 within the window shown (with twice that spatial frequency) will simultaneously decrease like $1/r^2$ since it contributes a dipole. Correspondingly the contribution of higher spatial frequency components, say of order p, will decrease like $1/r^p$. However, these higher spatial frequency components are also the components generating the high-frequency components in time, since they all travel with the same velocity as the underlying wave (such as the action potential). A drastic decrease of high-frequency component due to dealing with waves, all traveling with constant velocity, is thus to be expected. Integration (Lindström and Magnusson (64)) for the infinitely long structure yields for the far-field "transfer function"

$$\psi(j\omega) = C[K_0(\omega h/v)] \exp(-j\omega x_0/v),$$

where K_0 is the Bessel function of the second kind. For large arguments, one can use the approximation $K_0(u) \approx (\pi/2u)^{1/2} \exp(-u)$, showing a predominantly exponential decline of the transfer with increasing frequency. Note, there is no need to consider only a single fiber for this model; there could be many synapsing fibers in series giving rise to the propagation of a potential wave. Qualitatively, the above equation shows how quickly with increasing distance h and increasing frequency ω the transfer of potentials decreases. This result is interesting since it suggests the possibility to tune sensor electrodes to nearby sources by selecting high-frequency components. With such a goal in mind, methods to reduce electronic noise of currently used equipment become important (see subsection "Frequency-Dependent Properties of Macroelectrodes (and Amplifiers)").

APPENDIX M

PATTERN RECOGNITION TECHNIQUES

Pattern recognition techniques have been developed to provide computer assistance to the problems of analyzing, detecting, recognizing, and describing patterns in apparently erratic data. As a result, an entire field of study has evolved which has found application in diverse fields, including engineering, computer science, biology, psychology, and medicine. The techniques of pattern recognition have been especially useful in the biomedical area, due to lack of appropriate physical models with which to describe the processes of interest.

Pattern recognition is generally divided into several sequential steps, as illustrated in Figure M-1. The raw data is first conditioned

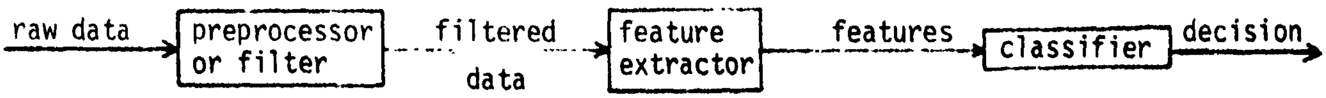

Figure M-1. Information flow in typical pattern recognition process.

(e.g., remove unwanted frequency components or artifacts), with the proviso that no information is lost in the process. The next step is feature extraction, where the desire is to extract a minimal set of information-bearing parameters. This step may be viewed as a process of data compression. The final step is the classification process, where decision rules are utilized to classify the features. Since the features contain (ideally) the same information as the raw data, the classifier actually classifies the raw data.

We discuss briefly here approaches to feature extraction and pattern recognition which might be particularly useful for VER analysis.

FEATURE EXTRACTION

Perhaps the most important part of any pattern recognition scheme is the feature extractor. In this appendix, a mathematical model will be derived which will generate signals that closely approximate measured VERs. The model can account for the information-carrying signal components, along with the various noises corrupting them. The model can be derived from a training set via the Karhunen-Loeve expansion technique. The coefficients of the expansion then become the features of the VER.

A model of the VER must be able to account for the variations from cycle to cycle (i.e., each time the stimulus pattern is repeated) in both amplitude and period (stimulus rate). Moreover, it must be able to take advantage of the possibly strong correlation between signals from different electrodes. Any variation in the stimulus rate means that the time origin must be reset with onset of each stimulus. The model to be developed attempts to describe the VER and the identifiable sources of noise as observed by measurements on the head surface. For ease of implementation on a digital computer, only linear discrete time models will be considered.

First, we consider the VER model. An efficient means of characterizing a sample waveform from an ensemble of statistically nonstationary waveforms in terms of a set of parameters α_i is:

$$y(n) = \overline{y}(n) + \sum_{i=1}^{M} \alpha_i \phi_i(n) + \varepsilon(n); \qquad n=1,2,\ldots,N_R \qquad \text{(M.1)}$$

where

1) $\overline{y}(n)$ is the average value of the waveforms at the n^{th} sample.
2) $\varepsilon(n)$ is the truncation error corresponding to M terms.
3) $\phi_i(n)$; $n = 1,2,\ldots,N_R$ are a complete set of orthonormal basis functions.
4) N_R is the number of samples in the heartbeat (assumed of standard duration).

The coefficients α_i can be assembled into a vector $\underline{\alpha}$ called the pattern vector of a particular VER. Of the several techniques for generating the desired basis functions, the method chosen is the Karhunen-Loeve expansion, which has the following desirable properties (Fukunaga (39)):

1) It minimizes the expected value of the error energy

$$J = E\{\sum_{i=1}^{N_R} \varepsilon^2(i)\}.$$

2) It maximizes the distance between independent samples from a single distribution, as defined by the scatter measure

$$\overline{d_\alpha^2} = E\{\| \alpha_i - \alpha_j \|^2\}.$$

3) It minimizes the population entropy, defined by

$$h = -E\{\ln p(\underline{\alpha})\},$$

where $p(\underline{\alpha})$ is the probability density function of $\underline{\alpha}$.

4) The coefficients α_i are statistically uncorrelated.

The basis functions are determined as follows. Let

$$\underline{\delta y} \triangleq [\delta y(1)\delta y(2)\ \ldots\ \delta y(N_R)]^T$$

$$\underline{\phi}_i \triangleq [\phi_i(1)\phi_i(2)\ \ldots\ \phi_i(N_R)]^T; \qquad i = 1,2,\ldots,N_R$$

$$\underline{\varepsilon} \triangleq [\varepsilon(1)\varepsilon(2)\ \ldots\ \varepsilon(N_R)]^T$$

where $\delta y(n) \triangleq y(n) - \bar{y}(n)$. Then (M.1) can be expressed as

$$\delta\underline{y} = \sum_{i=1}^{M} \alpha_i \underline{\phi}_i + \underline{\varepsilon} = \underline{\underline{\phi}}\underline{\alpha} + \underline{\varepsilon} \tag{M.2}$$

where $\underline{\phi} = [\underline{\phi}_1 \underline{\phi}_2\ \ldots\ \underline{\phi}_M]$. The eigenfunctions are orthonormal in the sense that

$$\underline{\phi}_i^T \underline{\phi}_j = \delta_{ij}$$

where δ_{ij} is the Kronecker delta function. Therefore,

$$\underline{\alpha} = \underline{\phi}^T \delta\underline{y} \tag{M.3}$$

Let the covariance matrix of $\delta\underline{y}$ be

$$\underline{R} = E[\delta\underline{y}\delta\underline{y}^T] \tag{M.4}$$

where $E(\delta\underline{y}) = 0$ by definition. Then the basis functions are the eigenvectors of the covariance matrix $\underline{R}$. A particular eigenvalue is the expected value of the energy associated with its eigenfunction.

If $y(n)$ is a sample function from one of k different stochastic processes (i.e., generated by different brain processes), the Karhunen-Loeve expansion is still optimal in that it minimizes the mean residual energy and the population entropy, when the covariance matrix is defined appropriately (Chien and Fu (22)):

$$\underline{R} = \sum_{i=1}^{k} p_i \underline{R}_i$$

where R_i is the covariance of the i^{th} stochastic process, which has probability of occurrence p_i.

For a vector stochastic process (we are simultaneously measuring different components of the VER with multiple electrodes), the expansion can be easily extended.

An example of the use of a Karhunen-Loeve expansion for ECG data is given in Figure M-2. Three different types of heartbeats are shown and compared to a 10^{th} order expansion (RECON). Since there were 200 samples in the original data, the data compression is a factor of 20:1. Furthermore, the reconstruction error is seen to be very small, in this case not large enough to give a different cardiac diagnosis.

PATTERN CLASSIFICATION

A wide variety of techniques are available for classifying a set of feature vectors. They may be conveniently divided on the basis of the process used to determine the location of classes in feature space (learning). Supervised learning implies that all data are labeled according to class. In unsupervised learning, the data are unlabeled and classes are typically generated using cluster analysis.

Many supervised learning techniques are available. However, the ones which are most widely applicable to relatively unstructured data such as the VER are the so-called nonparametric methods. Among these, the partitioning decision tree approach of Friedman (38) is particularly powerful, as well as being ideally suited to computer implementation. This method will construct decision trees to any arbitrary accuracy on the training set and can handle multiple classes in a straightforward manner. It is presently being applied to classification of ECGs by Scientific Systems, Inc.

Cluster analysis might be particularly useful in the early stages of investigation of the properties of the VER. By using this technique, it may be possible to gain insight into the structure of the data and determine whether the VERs tend to fall into distinct types. The most popular and generally applicable clustering techniques are iterative ones, using similarity measures between points in feature space, and employing hierarchical or nearest-neighbor decision rules. A good review is given by Ball (8). More recently, the use of fuzzy set theory has been proposed for unsupervised learning, in order to eliminate the necessity of using zero-one membership functions (a point is either in the class or not). This work has led to a class of "Fuzzy ISODATA" algorithms (Bezdek (11)) which are easily implementable and are particularly applicable to problems in which there are smooth transitions from one class to another (e.g., slightly overlapping classes). Since the results are completely data-dependent, it is not possible to present results or even predict the outcome of using such techniques on the VER. However, they do represent the most generally powerful approach to data clustering and thus have potential for VER analysis.

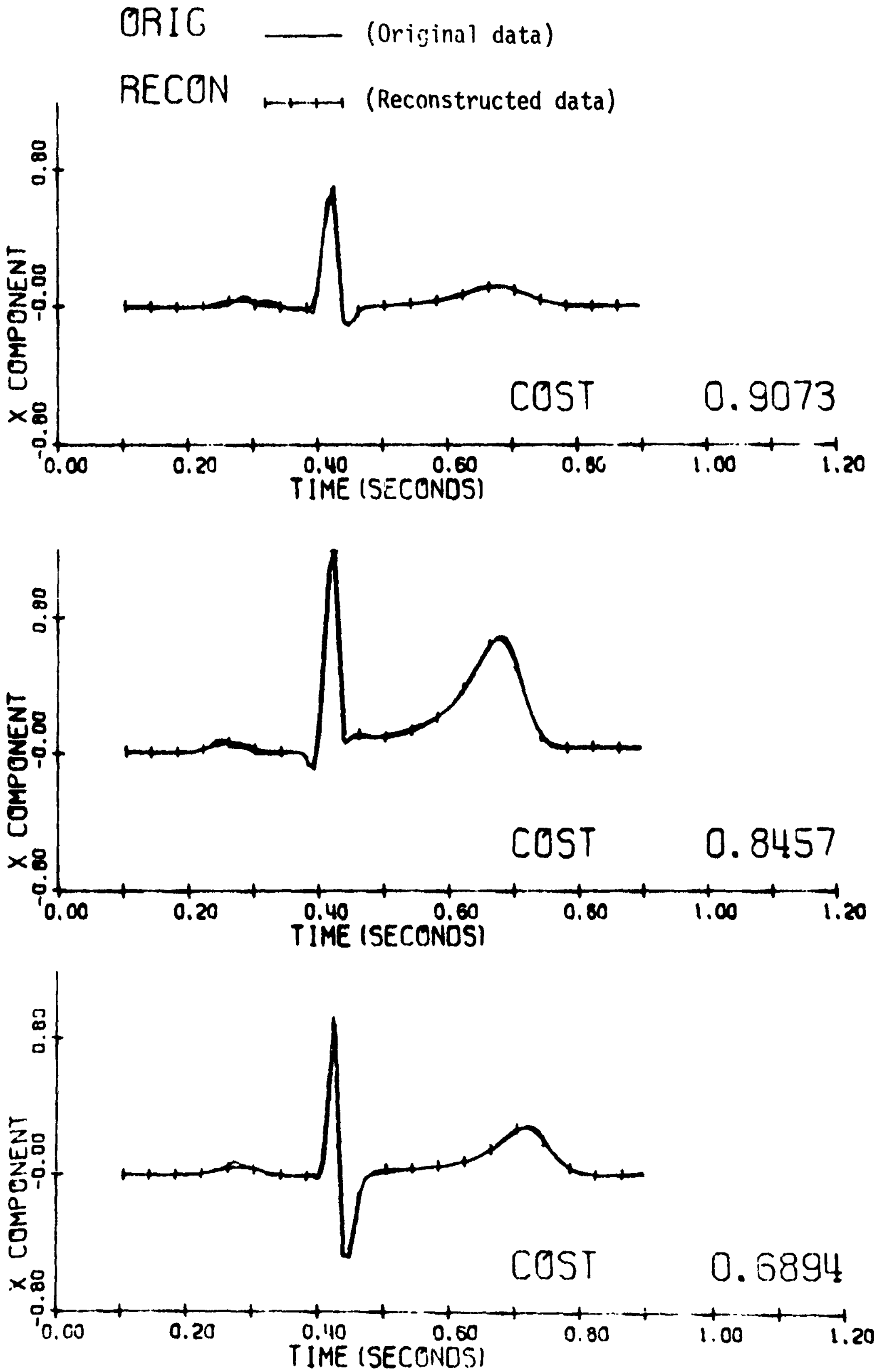

Figure M-2. Illustrating the data-compression capability of the Karhunen-Loeve expansion, ECG data with variable morphology. Compression ratio 20:1.

APPENDIX N

A SET OF RECOMMENDATIONS FOR SEVERAL PROBLEM AREAS

The recommendations given below are derived from our analysis of the pertinent literature, especially literature concerning the evidence for certain properties of EEG/VER signals and literature on experimental procedures and considerations. The recommendations fall into the following groups: signal analysis, stimulus design/experiment design, choice of electrode location, medical/psychophysical, and future aspects. Within each group we followed (tentatively) some ordering corresponding to the apparent increase in complexity of the recommendation and/or decreasing expected pay-off in terms of reduced variability.

SIGNAL ANALYSIS

1. Incorporate information from frequencies other than the fundamental pattern reversal rate. Especially harmonics and frequencies between harmonics should be considered in the development of measures of visual performance. To distinguish between experimental conditions (e.g., preflash vs. postflash), learning schemes such as Friedman algorithm (38) [developed at the Stanford Linear Accelerator Center for similar purposes], which selects by itself the important features (given a set of measures) could be useful.

2. Variability in itself should not be regarded as adverse. Variability itself may provide a measure of visual performance as concluded from studies by Ciganek (25) and recently by Callaway (20).

3. The general techniques for signal analysis as described in Appendixes C-G should be applied. The importance and power of the use of these (statistical) techniques are demonstrated in the recently published report by Chapman et al. (21) which used a principal component analysis for the simultaneous extraction of <u>known</u> (well established) and discovery of new VER properties.

EXPERIMENT DESIGN

1. The overall performance of the data-acquisition system has to be verified. By that we mean to set up experiments (complete simulation including TV)--possibly with a dummy subject (some conductive material fed with active electrodes) which generates known waveforms. These waveforms must be retrievable truthfully from the collected data base before any further data collection on actual subjects should be conducted. From time-to-time the reliability of that system has to be checked.

2. The best brightness level should be determined. Studies by Riggs and Wooten (90, p. 707) suggest that very stable amplitudes of VER are obtained at 0.3 log units of brightness above threshold, while with increasing brightness variability increases. Nachimas (73, p. 71) gives similar results for cat (microelectrode studies).

One way to increase possibly weak responses might be to use zig-zag lines as recommended by MacKay and Jeffreys (66).

3. Use masking noise in the experiments and verify its effectiveness. In most of the literature this point is stressed.

4. Use stimuli with random intervals. Investigate the importance and variability of the CI,...CIII (complex) waveform (Jeffrey, in Desmedt (28)) and P10-P150 (or N) as described above in the section for signal analysis recommendations.

5. Check the importance of dipole reversal by pattern (mirror image) reversal, similar to Jeffrey (in Desmedt (28)).

ELECTRODE LOCATION

1. The earlobes should not be regarded as "ground" and should not mutually be connected. Instead the differential voltage for the left and right side (e.g., inion vs. left or right ear) should be recorded. When a grounding for the subject is necessary (especially with high-input impedance amplifiers), any point of the body may be tried. Care should be taken in shielding of cables and avoiding magnetic loops.

2. The number of electrodes for recording should be increased. Especially we are thinking of four additional electrodes slightly (2 cm) above and below, to the left and right of the currently used electrode. Since analog-to-digital conversion rate may be limited, the amplifier bandwidth and sampling rate for A/D should be reduced as necessary.

3. Search for optimal electrode location individually for each subject. Grass (42) argues that many investigations rely too much on standard lead arrangements. One possible way to speed up such a search is to use an array (e.g., horizontal linear array) which is applied at different locations. Signals from the data analysis scheme could indicate the adequacy of the location and/or select the "best" electrodes.

4. Monitor saccades, eyeblinks, and other muscle potentials (jaws, heart, etc.).

MEDICAL-PSYCHOLOGICAL ASPECTS

1. The use of (additional) drugs like the anxiolytic diazepam should be considered for the restrained animal, in order to restore near normal EEG.

2. The subject should be assigned an appropriate task. As MacKay and Jeffreys (66) point out, a subject without a task is not in a "neutral" state.

FUTURE POSSIBILITIES

1. Electrode impedance can be calibrated automatically and periodically (for safety standards, see Underwriter Labs. Manual (111)).

2. Low-input impedance amplifiers should be tried (Van der Ziel (113)). This approach may necessitate the above periodic recalibration.

3. Extension of the currently used frequency band up to higher frequencies. This approach, if of value, will probably require low-input impedance amplifiers.