

Copyright 1973. All rights reserved

## TOWARD DIRECT BRAIN-COMPUTER COMMUNICATION

9027

JACQUES J. VIDAL<sup>1</sup>

*Brain Research Institute,  
University of California, Los Angeles, California*

Electroencephalographic or EEG signals collected on the human scalp are sustained fluctuations of electrical potential that reflect corresponding variations in the upper layers of the brain cortex below the scalp surface. The signal structure is that of a stochastic time series with almost stationary epochs of various lengths separated by sharper transitions or disruptions. Amplitudes are small (up to a few tens of microvolts) and spectral decomposition reveals that very little power remains at frequencies above 30 Hz. Most of it is contained at very low frequencies ( $< 1$  Hz) and within the narrow bands of specific rhythms (and particularly of the 8–13 Hz alpha rhythm) that appear and disappear somewhat randomly in time. Signals collected on two or more electrodes exhibit changing levels of correlation, due either to physical proximity (that is, sharing of immediate influences from the cortical surface) or to actual coordination between different cortical sites, thus reflecting shared neuron activity within the brain itself. Spectral content and correlation have been related to various emotional and behavioral states.

Imbedded in this sustained "spontaneous" or "ongoing" electrical activity, short, distinctive (0.5–2 sec) waveforms can be found that are evoked, for instance, when a brief sensory message (stimulus) such as a brief illumination of the visual field or a tap on the forearm is received by the subject. These "evoked responses" are small (a few microvolts) and somewhat buried in the ongoing activity. The characteristics of the stimulus determine the evoked potential waveform together with the stimulus "environment," such as the level of attention of the subject, the "expectation set," and the meaning of the stimulus in the context of the experiment.

Can these observable electrical brain signals be put to work as carriers of information in man-computer communication or for the purpose of controlling such external apparatus as prosthetic devices or spaceships? Even on the sole basis of the present states of the art of computer science and neurophysiology, one may suggest that such a feat is potentially around the corner.

The Brain Computer Interface project, described later in this chapter, was meant to be a first attempt to evaluate the feasibility and practicality of utilizing the brain

<sup>1</sup> Research supported in part by NSF Grants GJ-32221, GK-31463X, and AFOSR 72-2384.

signals in a man-computer dialogue while at the same time developing a novel tool for the study of the neurophysiological phenomena that govern the production and the control of observable neuroelectric events.

The long-range implications of systems of that type can only be speculated upon at present. To provide a direct link between the inductive mental processes used in solving problems and the symbol-manipulating, deductive capabilities of the computer, is, in a sense, the ultimate goal in man-machine communication. It would indeed elevate the computer to a genuine prosthetic extension of the brain. To achieve that goal with adequate generality is a formidable task that will require considerable advances in neurophysiology (to identify appropriate correlates of mental states and decisions in external signals), in signal analysis techniques (to sort and identify the relevant information carriers from the garbled and diffuse mixture that reaches the scalp), and in computer science (to develop appropriate software within the constraints introduced by the nature of brain messages). While such major advances are still in the future, some progress in that direction is attainable with the present state of the art, which can open the door to a broad range of applications related to brain function and malfunction. By identifying those brain states that would optimize perception or learning, we can considerably increase the efficiency of computer-assisted learning programs. Studies of perception, investigations of dyslexia and epilepsy, studies of the effect of hallucinogenic drugs, and the development of early diagnosis of brain tumors that affect perception, are possible clinical applications, as would be the extension of such systems to the control of prosthetic devices.

## NEUROPHYSIOLOGICAL CONSIDERATIONS

In this section, the current theories for the phenomena responsible for generating EEG signals are briefly reviewed together with related work in computer processing and interpretation of these signals. The relatively recent development of operant conditioning of neural events is singled out as particularly relevant to our main topic.

### NEUROPHYSIOLOGICAL ORIGINS OF EEG SIGNALS

In 1929, Berger (1) demonstrated the possibility of recording brain waves from the intact skull. Since then, an enormous amount of brain wave data covering a variety of conditions has been accumulated by neurophysiologists, and in recent years, computers have been used extensively for analysis.

Scalp-recorded brain waves show a great deal of variability, reflecting the enormous number of influencing parameters. Overall characteristics of the wavetrains can be somewhat predicted in relation to the electrode site, the mental state of the subject, and the presence and type of sensory stimulation. Some of those characteristics are readily identified by eye. Well-known examples are recognition of alpha activity and the phenomenon of alpha blocking, sleep and barbiturate spindles, and the 3/sec spike and wave complex of petit mal epilepsy. More subtle information in the EEG activity, however, requires computer analysis.

The main source of scalp potentials is the electrical activity of the cerebral cortex, which constitutes the outside surface of the brain below the scalp. The cerebral cortex is a thin layer of gray matter containing nerve cells (neurons). Some of them (the pyramidal cells) are characterized by the so-called apical dendrites, which are long membranous tubes extending toward the surface where they branch out profusely and extend laterally for some distance. The result is a thin surface of "white matter" where a densely interwoven mesh of fine dendritic processes belonging to adjacent apical dendrites interconnect. Dendrites are electrolytic connectors that propagate electrical fields to the neuron body, where they eventually trigger the nerve impulse by "depolarizing" the nerve membrane. The impulse then propagates along another type of membranous connector, the axon.

The surface potentials observed are generated mainly at the apical dendrites and at the bodies (soma) of pyramidal cells. They correspond with alternate polarizations and depolarizations that occur somewhat in synchrony inside the cells below. (These potential changes are called postsynaptic as they result from the action of interneuron contacts or synapses.) Currents flowing vertically in the extracellular spaces are also thought to act as a feedback link between deep cells and dendrites. A positive variation recorded at the surface would correspond to a region of depolarization (greater excitability) in deeper regions and vice versa. It is important to note that postsynaptic potentials can be produced independently of any nerve impulse on the part of the neurons located in the vicinity of the electrode. Indeed, the exact correlation between neuronal firing and EEG waves is still controversial (Fox 2, Adey 3, von Euler et al 4, Dunlop et al 5, Widen & Marsan 6, Li 7, Gerstein & Kiang 8, Adey 9, and Buchwald et al 10). The waves occur even when all the cells concerned are prevented from firing altogether (Marshall et al 11, Li & Jasper 12).

On the other hand, correspondence between individual waves in the EEG signal and the postsynaptic potentials recorded intracellularly in adjacent neurons has been abundantly established (e.g., Purpura 13, Morrell 14, and Landau 15).

Due to the large concentration of dendrites at the surface, the potentials tend to be relatively large, but to account for their observed amplitudes, one must still assume that large numbers of underlying neurons are acting in synchrony, undergoing relatively slow fluctuations (compared with the time constant of a single neuron), in order to account for the long periods (30–500 msec).

This "spontaneous" or "ongoing" EEG activity (also called slow potentials, by contrast with neuronal spikes) is somewhat rhythmic in nature. The analysis of these rhythms has retained much of the early attention paid to brain waves in general. The cortical tissue itself has a tendency to oscillate rhythmically, in absence of any input. Cutting out small "islands" of tissue reduces or cancels spontaneous activity, but rhythmic ringing is still obtained in response to electrical impulses. The maintained oscillations that are observed in the intact brain are believed to reflect a "pacemaker" function probably mediated by the thalamus. It is increasingly evident (e.g., Morrell 16) that rhythmic activities cannot by themselves convey fine information and that their function resembles that of a carrier. The general picture is that idle nervous tissue will exhibit spontaneous oscillation or rhythm while activity or commitment of the same tissue to an active function will be denoted by desynchronized

random-like oscillations. The presence or absence of certain rhythms in a given EEG recording, however, will reflect gross differences in brain states such as sleep or wakefulness. There is evidence that these rhythms, and especially the (approximately) 10-cps alpha rhythm, reflect a scanning and recycling device controlling incoming sensory information (Pitts & McCulloch 17). Morrell (18) writes: "Changes in EEG frequency relate more to the balance between cellular synchrony and desynchrony than to the specific information content of a signal. If recorded with adequate resolution, they may indicate *where the action is*, but not *what the action is all about*." By contrast with the widespread character of oscillations, waveshapes are localized and correspond well with underlying postsynaptic potentials. Thus, beyond gross differentiation of brain states, it seems that information coding in the EEG wave should be sought in the specific waveforms generated in time. Locality and specificity also characterize the "evoked potential" discussed below.

A light flash, brief sound, or light touch of the skin generates in the corresponding sensory cortex (visual, auditory, or somesthetic) a localized electrical response betrayed on the cortical surface by a characteristic aperiodic waveform somewhat buried in the ongoing background activity and covering roughly one half a second. In general, repeated stimuli and averaging of the waveforms have been used to reveal the "evoked" response. When recorded directly on the cortical surface, these responses are made of either a positive or a positive-negative waveform of varying complexity. Again, the surface wave reflects the synchronous contribution of postsynaptic potentials in a large number of neurons in the vicinity of the electrode. The positive part of the response is attributed to the activity of the lower layers of the cortex (Li, Cullen & Jasper 19, von Euler, Green & Ricci 20, and Morrell 21), while the negative part is believed to represent a depolarization of the upper apical dendrites (von Euler, Green & Ricci 22).

The cortical neurons are distributed in layers, each layer in a given area presumably having a particular integrative function. In a direction perpendicular to the cortical surface, cells above one another seem to subserve various subfunctions for a given sensory modality, while in a lateral direction, the functional properties of the cells exhibit sharp transitions. It has been advanced that the cortex offers a columnar organization of function although anatomists have been unable to this day to uncover a vertical structure in interneuronal connections that could be responsible for the columnar organization. At any rate, some experimental evidence exists for it in the visual and the somatosensory areas (Hubel & Wiesel 23) and to a lesser extent in the auditory cortex (Gerstein & Kiang 24). Function and modality vary with the cortical position. For example, at certain points of the visual cortex of the cat, single cells respond specifically to a line stimulus having given orientations on the retina. Functional specificity in relation to cortical sites is also reflected in the ongoing EEG: sensory stimuli of a given modality will desynchronize localized areas of the cortical surface. Thus, because various feature-extracting functions are mapped on the surface of the cortex, each different stimulus with its specific set of features will evoke distinguishable electrical "signatures" on the cortical surface and thus more diffusely on the scalp beyond. For instance, recording the scalp response to the brief flashing of a figure made of vertical lines will yield a waveform markedly different from that obtained from a set of circles. In fact, the presence in the evoked

waveforms of clear correlates of the modalities of sensory stimulation has been abundantly demonstrated. Of particular interest are studies dealing with visual stimuli (White & Eason 25, Harter & White 26, 27, Clynes & Cohn 28, and Spehlmann 29). The evoked electrical signature on the cortex does however include more than a mirror conversion of the stimulus content. In fact, only the early part of the response appears to be so related while the "late" components (100 msec and beyond) appear to relate to more complex integrations of the stimulus such as its perception and meaning.

### COMPUTER PROCESSING AND INTERPRETATION OF EEG DATA

The traditional strategies in utilizing the computer to analyze EEG data reflect the basic distinction between continuous "ongoing" activity and the short, time-locked disturbances of the EEG that constitute evoked responses to brief stimuli. To the former, the framework of brain rhythm and concepts such as spectral densities have been frequently applied. The latter, by contrast, are aperiodic events and the current processing practices vary from simple averaging of the waveforms to various functional expansions (including the classical Fourier spectrum). Some typical studies addressed to the ongoing EEG are listed below: descriptions of correlates of various states of consciousness in astronaut candidates (Walter, Rhodes & Adey 30); sorting of different phases of a tic-tac-toe game played by chimpanzees, including correct and incorrect decisions (Hanley et al 31); and coupling between brain structures in the visual and other systems (Galbraith 32, 33). In a recent study on patients with schizophrenia, some methods have characterized changes in the EEG induced by septal spiking (Hanley et al 34), identification of autistic behaviors in a child (Hanley et al 35), and discrimination between psychotic rituals and normal-appearing behavior in an adult with chronic disease (Hanley 36, Hanley et al 37). It has also been possible to distinguish between subjects before and after the inhalation of *cannabis sativa* and between subjects who are in normal and hypnotic states as well as within different suggestive hypnotic states (Hanley et al, in preparation). The basic tool that produced these differentiations is spectral decomposition, sometimes followed by discriminant analysis (Dixon 38). All required the selection by the experimenter of EEG epochs of various lengths (generally around 10 sec) and the subsequent correlation of the measured EEG parameters with the corresponding sequence of assumed behavior of the subjects. These studies have unquestionably demonstrated that some EEG changes can be detected by spectral methods. In their present form, however, the methods have produced somewhat erratic results and interpretation of the observed changes has been difficult, perhaps because traditional methods of frequency analysis destroy information about the temporal sequence of the EEG components.

A completely different approach was taken in a recent study by Nirenberg & Hanley (39). They found that a phase discontinuity in the ongoing EEG signaled the decision to flex a given set of muscles before the motor action occurred. The phase transition was detected by an optimally tuned phase-locked computer algorithm. A brief unlocking of the loop was obtained in response to the discontinuity, thereby providing a sharp, short pulse to signal the decision. This was the first time that phase-locked techniques had been applied to EEG signals and also

the first time that short electrical events were detected that seemed to reflect a mental decision. The phase-locked tracking filter thus offers a promising route for such applications as the control of prosthetic devices.

By contrast with the continuous EEG waves, evoked responses are short (0.5–2 sec) perturbations of the EEG, time locked to a stimulus, or to some well-defined neural or behavioral event. The time of occurrence of this event (e.g., presentation of the stimulus) is therefore an integral part of the data. Classically, the problem is to identify response waveshapes and to determine how these vary with what the experimenter assumes to be the stimulus parameters. Sometimes this is done by simple visual inspection, but the natural mathematical approach to this problem (classical with finite energy signals) is based on the expansion of the waveform on a function space with some appropriate choice of basis functions.

Orthogonal representation has been used by several investigators: Freeman (40–42) used sets of damped sinusoids. Lehmann & Fender (43) fitted a set of Gaussian curves aligned on the peaks of the waveform, the first component corresponding to the larger peak. Both of these approaches contain a heuristic element that can be avoided using the Karhunen–Loève expansion (Raviv & Streeter 44), in which the basis functions are not preassigned, but where the first component is constructed so as to account for the maximum variance in the data and additional components for additional portions of the remaining variance. The so-called *principal component* analysis method (John et al 45, Ruchkin et al 46, and Donchin 47) is equivalent to the Karhunen–Loève expansion. In all the studies above, the raw data is obtained by averaging the responses to several trials in an attempt to eliminate the “noise” due to many factors that escape experimental control but nevertheless affect brain-states. The averaging technique has often been assumed to eliminate the effects of the “background activity.” Mathematical models of the responses are thus obtained, but the expansion coefficients obtained for any single trial will, in general, differ greatly from those of the models. Donchin (48) showed that single trial classification was possible. In his approach, a few points in time are chosen by *discriminant analysis* that yield optimum discrimination. Subsequently, classification of single responses is based on the same points, ignoring all others. When both principal component and discriminant analyses are applied, it is found that the points selected appear to bear a simple relation to the peaks of the principal components, thus perhaps betraying an underlying mathematical relation between the two methods. Another successful treatment of single trial responses has also been reported (Palmer et al 49, Woody 50).

### OPERANT CONDITIONING OF NEURAL EVENTS

All the work reported above can be classified as “correlative.” To elucidate the way sensory input or behavioral output is represented or “coded,” neural events are observed that are coexistent with these stimuli or behaviors. At a later time the data is examined for correlation between arbitrary attributes of both the event and the stimuli. “Significant” correlation is generally considered a valid result. The data available from correlative studies would offer precious little hope that the variations detected in the brain signals could ever provide reliable indicators of brain states.



Considerable and sometimes seemingly hopeless variations are the rule rather than the exception. The reason for this variability can be traced to a number of causes; for instance:

a. The stimulus input is always incompletely characterized. Its "relevant" attributes are unknown as are the many possible indirect or concomitant influences elicited by the nominal input that are capable of influencing the neural output.

b. The "state" of the brain is unknown at the time the stimulus is presented (i.e., in the language of system engineering the system has undefined initial conditions) and even whatever state information is available (e.g., in the EEG potentials) is generally ignored.

A new approach to experimenting with brain signals has appeared in the last few years, namely the operant conditioning of neural events (OCNE), which alleviates some of these problems and brings a different perspective into the field. The key feature of the method is the use of the neural event itself as reference parameter while the experimental subject or animal is given a broad range of free behavior, from which he can choose the easiest or most effective means to reinforce the event. The approach has been applied both to spontaneous EEG (Carmona 51, Chase & Harper 52, Sterman et al 53, Black 54, Brown 55, 56, Green et al 57, Kamiya 58, 59, Paskewitz et al 60, Peper 61, and Peper & Mulholland 62), and to evoked responses (Fox & Rudell 63, 64, Rosenfeld 65). It has been suggested that using paradigms of this type will establish reliable and stable correspondences between behavioral (peripheral) events and the chosen neuroelectrical potentials. It is further proposed that this relationship will be a natural one as it has been selected naturally by the subject. While the validity and implications of these claims are still controversial, the method has shown tremendous efficiency in increasing the "reliability" of neural responses. For instance, in a study of human scalp potentials reported by Rosenfeld et al (66), a twofold increase was obtained in the frequency of occurrence of an arbitrarily selected potential in the evoked response. Typically, a rare event is arbitrarily selected in the neural response and reinforced until it becomes associated most of the time with the stimulus.

The emerging role of operant conditioning of neural events was summarized by Black (67), who suggests that it opens new possibilities as an investigative tool in neurophysiology and neuroanatomy, as a way of control over neural processes, central (internal states) and peripheral (behavioral states), and as a process in itself to be studied in its relation to the phenomenon of learning. In our present perspective, a fourth function is proposed: that is, as a means of control over external processes, such as computers or prosthetic devices.

## A PILOT PROJECT IN DIRECT BRAIN-COMPUTER COMMUNICATION

### GENERALITIES

The remainder of this chapter is concerned with a specific attempt to test direct brain communication, namely, the Brain Computer Interface project conducted at the University of California, Los Angeles. This project was born of the conviction,

based on current evidence, that EEG waves contain usable concomitances of conscious and unconscious experiences and that the set of continuous electric signals observed does not for the most part consist of random noise as was often suggested, but on the contrary, constitutes a highly complex but significant mixture that reflects underlying neural events. This is not to say, obviously, that these neural events could always be separable on the basis of EEG alone, or that the EEG wave "signature" has to be unique with respect to any given brain "state." It has been shown (Fox 68) that slow wave phenomena, such as EEG and evoked potential, while surely due to the synchronous action of synaptic potentials, also reflect the momentary fluctuation in the probability of firing in the cell population in the vicinity of the electrode. It is then suggested that this sequence of shifting probabilities represents a sampling of the very language implemented at the surface of the cortex even if it is unlikely that any specific expression of this language be unique for a given experiment or subject.

The Brain Computer Interface system is geared to the use of both the spontaneous EEG and the specific evoked responses triggered by time-dependent (visual) sensory stimulation under various conditions. In addition, other biosignals that are of interest for interfacing the physiological man and the machine are to be included later in the project. Eye movements, muscle potentials, galvanic skin reflex, and heart rate are ready examples which hold promise for particular applications. Acoustic and somato-sensory evoked responses also need to be evaluated since the latter, in particular, affords less variability than the visual evoked responses. Of special interest also is the contingent negative variation (CNV), a slow negative baseline shift of the EEG signal that relates to expectation, attention, and arousal (e.g., Tecce 69). Any of these phenomena would find a natural place in particular applications. The first studies, however, are focusing on the control and conditioning of time-domain attributes of the EEG phenomena and of certain visual evoked responses. Indeed, for these experiments visual patterns are choice stimuli because they provide a potential support for nonverbal symbols in man-machine communication languages and in that respect afford much more flexibility than other modalities, including the acoustic.

#### DATA ACQUISITION AND PREPROCESSING

As indicated before, both ongoing EEG and evoked potential have exhibited considerable variability in most correlative studies. Clearly, a completely different approach is necessary if one is to extract reliable clues from the neural chatter. Our proposed approach, a combination of somewhat radical computer processing techniques with experimental strategies for operant conditioning under elaborate computer control, will now be discussed.

Early in the development of this project it had become obvious that most current methods and practices of EEG data acquisition and processing were utterly inadequate for the level of discrimination that was required in the proposed framework. Most of the early effort was invested in identifying the areas where improvement was realizable. First, the signals must be acquired with an absolute minimum of instrumentation noise. If finely structured information is available in the EEG, it must rest



in the miniature wavelets that remain in each channel after "common mode" rhythms and dominant signals have been removed. Ideally, input noise should fall below the microvolt level. The thermal noise limit within the usual range of bandwidth and electrode resistances is of the order of  $1/10 \mu\text{V}$  at body temperature. There are ominous indications, however, that the current arsenal of EEG instrumentation falls far behind in this respect. An unintended opportunity to measure this incident noise is often found in recorded EEG data (including some public data such as the *Normative Electroencephalographic Data Reference Library* 70) because recordings have been made with an electrode pattern that contains loops. For example, whenever three electrodes are used to produce three bipolar derivations, any one channel can be derived from the other two, neglecting instrumentation noise and distortion. In fact, each closed loop contains a redundant channel (i.e., linearly dependent upon the others). These practices suggest that many researchers in the past were not under excessive pressure to remove redundancies. Tests were carried out with our own data that suggest that even with the best EEG equipment available commercially, the noise figure is downright unacceptable to anyone interested in tracking down the waveforms beyond the dominant rhythms. Typically, a four-channel loop yielded residue power in the redundant channel that was of the order of one-third of the original (in theory it should have vanished). This noise level had nothing to do with the analog-to-digital conversion, which was performed to the tenth binary place (0.1%), but resided with the electroencephalography equipment. Perhaps relief will come from miniature low-noise amplifiers that can be attached directly to the electrodes and are currently being developed in various laboratories.

Once low noise preamplification has been achieved, the signals are transferred to digital format using multiplexers and analog-to-digital converters. A rate of 128 samples per second is a minimum that still generates over 2000 digital words per second for a 16-channel collection.

The first step in preparing the EEG signals for subsequent analysis is the removal of perturbations of nonneural origin such as ocular (EOG) artifacts. The problem has now been solved to a large extent. By contrast, the more elusive "muscle" artifacts remain unchallenged to this day. The EOG artifacts are a major source of extraneous disturbance originating in the electrical polarity of the eyeball. The effect is a reflection of the induced electrical field that moves when the eyes move in their orbits. They can be satisfactorily removed by subtracting an appropriate function of the horizontal and vertical component of the EOG signals from each electrode (Girton & Kamiya 71). Following EOG removal, the "raw" EEG samples are rearranged to provide "monopolar" channels that can be referred to a single electrode rather than to a pair. In Figure 1 only the vertex channel (CZ) is a monopolar lead, chosen because the vertex is relatively free from the muscle artifacts generated from facial or neck muscles. For all the other channels, a "bipolar" derivation is used to reduce these artifacts. The relative merits of monopolar and bipolar derivations have been the object of heated controversy among neurophysiologists. For instance, Landau (72) denounces monopolar recordings as meaningless. In the present context, however, they are strictly equivalent. The original choice is preferable from the standpoint of instrumentation but led to labeling difficulties that are

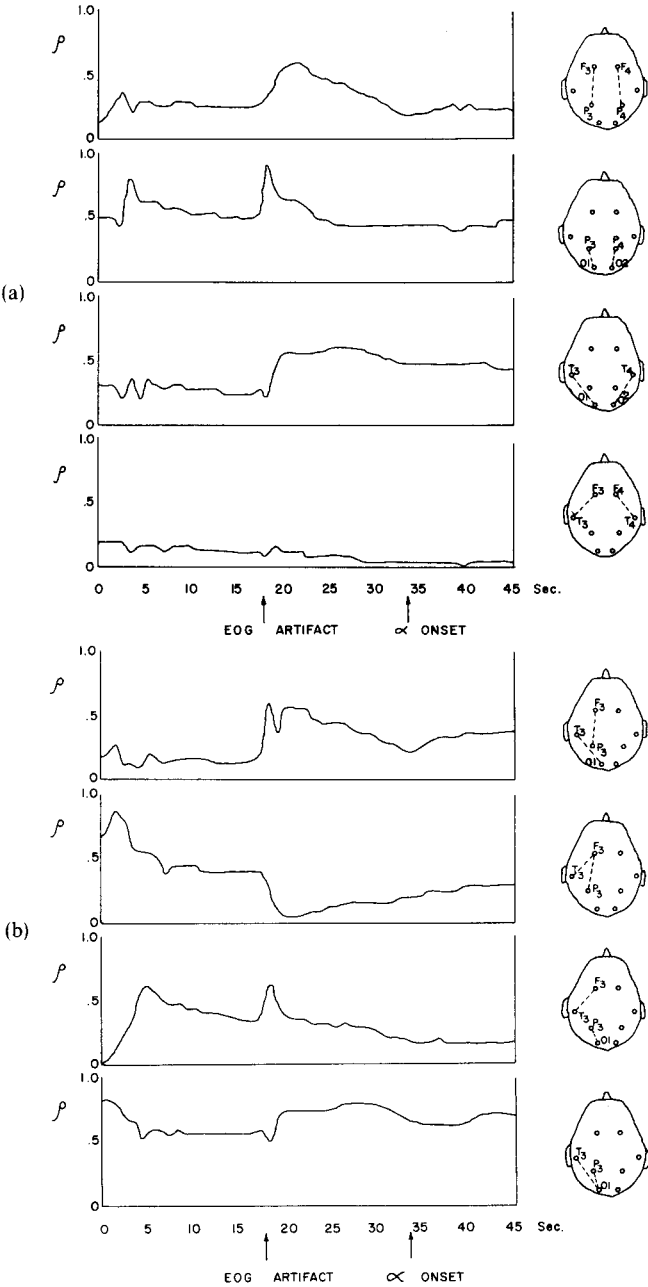


FIGURE 1 (a) and (b). Interchannel correlations versus time. These diagrams show some typical shifts of correlation levels following a brief eye movement (from Glassman 73).

removed by the subsequent transformation. No claims are made at this point that the chosen configuration facilitates the localization of the EEG sources.

The monopolar transformations combined with EOG compensations are summarized in the following set of equations:

<i>Amplifier Inputs</i>	<i>EOG Correction</i>	<i>Corrected Monopolar Potentials</i>
$A1 = T3 - CZ$	$B1 = A1 - E1$	$T3' = B1 + B7$
$A2 = T4 - CZ$	$B2 = A2 - E2$	$T4' = B2 + B7$
$A3 = F3 - T3$	$B3 = A3 - E3$	$F3' = B3 + B1 + B7$
$A4 = F4 - T4$	$B4 = A4 - E4$	$F4' = B4 + B2 + B7$
$A5 = O1 - T3$	$B5 = A5 - E5$	$O1' = B5 + B1 + B7$
$A6 = O2 - T4$	$B6 = A6 - E6$	$O2' = B6 + B2 + B7$
$A7 = CZ$ [reference (ears)]	$B7 = A7 - E7$	$CZ' = B7$

where  $E1, E2 \dots E7$  represent the EOG correcting potentials, a fixed linear combination of the two components of the EOG as determined during a calibration run. It must be noted that the compensation can be implemented at the analog level (that is, before digital conversion) using potentiometers and differential amplifiers.

A second step, still part of the preprocessing phase, is a novel attack on common modes and redundancies of neural origin that are present in the EEG and especially in the scalp recordings considered in this study. It is readily apparent from even casual observation of EEG recordings that a large degree of redundancy is present between the different channels. Tissue conduction as well as functional connections between various areas of the brain contribute to this "crosstalk." Functional interactions are significant features that researchers would try to elucidate from the data. Tissue conduction across the skull and the scalp, on the contrary, constitutes a blurring factor. Because of it, it is generally considered unrewarding to place electrodes at less than 3 cm apart on the scalp. To alleviate these problems and isolate the sources of redundancies, an additional transformation is imposed on the raw EEG signals. In our opinion, this technique, which "orthogonalizes" the signals, offers considerable promise to clean up the EEG waveforms by isolating common rhythms and, to some extent, "deconvolving" the crosstalk effects. The original study (Glassman 73) was conducted as part of the present project. The method consists of calculating zero time correlations between channels as the data is collected and of orthogonalizing the time series in some arbitrary sequence with respect to each other. The first experiments with the "orthogonal derivation" have demonstrated that it has the power of removing considerable amounts of common activity between channels. The procedure can be summarized as follows:

Let

$$X = \{X_i(t)\} \quad i = 1, 2, \dots, N$$

represent the set of raw EEG waveforms for  $N$  channels.  $X$  is assumed to have zero mean, and

$$V = \{V_i(t)\} \quad i = 1, 2, \dots, N$$

to be the set of mutually orthogonal waveforms of unit variance, related to  $X$  by the relation

$$X = CV \quad 1.$$

where  $C$  is a lower triangular matrix of coefficients that must be computed. It is nonsingular, providing no diagonal element of  $C$  vanishes. That is, there must be no loop in the channel diagram.

Now let  $R(X)$  be the covariance matrix of  $X$ . By hypotheses,  $R(V) = I$ , the identity matrix. Then, assuming zero mean for  $X$ ,

$$R(X) = E\{XX^T\} = E\{CVV^TC^T\} = CC^T \quad 2.$$

where  $E$  denotes the expectation and the superscript  $T$  denotes the transpose of the corresponding matrix.

If an estimate of  $R(X)$  is obtained, then  $C$  can be evaluated recursively, using Equation 2, and subsequently inverted. Finally, since

$$V = C^{-1}X \quad 3.$$

the orthogonal set can be constructed. Because of the triangular form of all matrices concerned, calculations are greatly simplified. On the other hand,  $R(X)$  is evaluated directly by forming the cross products and estimating the expected values  $r_{ij}$  with a time-varying first-order filter that produces "infinite" memory, exponentially weighted past averages.

The full potential of the "orthogonal derivation" still remains to be assessed. Certainly, with respect to the present information yield of EEG data, it should at least provide a drastic data reduction. Conversely, if the decoding of the small fluctuation in the EEG should prove possible after all, the orthogonalization as a preprocessing technique should prove invaluable as an enhancing device because of the removal of the masking effects of the dominant influences. The expectation, which would have considerable clinical value, is that the orthogonal derivation may help in the spatial discrimination of EEG processes. In other words, it may become possible to identify activity specific to the site of the corresponding electrode. This may be achieved by performing several orthogonalization sequences in which each channel is placed in turn at the end of the sequence. Work is being pursued to evaluate these speculations.

#### COMPUTER ANALYSIS

The data transformations described in the previous paragraph constitute a preprocessing phase or preparation for final computer analysis. A major problem in EEG research is the enormous amount of raw data that is being produced. A 14-channel recording, for instance, sampled at the rate of 256 samples per second, creates over 3500 sample digital words per second. EEG experiments usually last from one-half hour to several hours (as in sleep studies), and it is easy to imagine the staggering size of the data sets that could be created during such experiments. Preprocessing techniques, such as the one just described, will do nothing to alleviate

the situation since the preprocessed data will occupy the same or even a larger volume than the original. To improve this situation, researchers have classically limited their analyses to short epochs of 10 seconds or less, either chosen arbitrarily during the stationary "state" of the experiment (for ongoing EEG) or, on the contrary, attached to an event that produces a time-locked, transient response (evoked response). In addition, extensive use has been made of magnetic tape recordings, both analog and digital. Indeed, the laboratory computers used for digitizing seldom had memories large enough to accommodate the data. After the recordings have been reduced to a set of finite epochs, spectral or functional analyses can be performed to further reduce the bulk.

In many cases, however, this is still not enough. A typical spectral analysis over  $N$  channels will produce  $N$  auto-spectral densities and  $[N(N - 1)]/2$  cross-spectral densities. Adding phase angle and coherences, we find that a 16-channel analysis will yield 376 numbers for each one of the frequencies considered in the analyses. If frequencies from 0 to 32 Hz are considered in 1-Hz steps, then over 12,000 numbers are generated for each epoch. If the epochs are 10 sec long, the data compression ratio is a modest 3 to 1, although the use of graphs to represent the results will help somehow. For final sorting of the results, stepwise discriminant analysis programs have been used extensively and sometimes carelessly. Similar techniques are used with evoked responses except that spectral transforms rather than spectral densities are used, since evoked responses are nonstationary time-locked events that can be brought into the category of finite energy signals. Integral transformations other than the Fourier transform can also be applied. A major characteristic of evoked response studies, however, is the almost universal practice of averaging to separate the responses from the ongoing background activity.

All these methods are geared to a type of computer procedure known as batch processing, where data sets are created during an experiment and analyzed later. None of them is readily amenable to the interactive, on-line, real-time feature extraction that the present project demands. To appreciate the difference, a few more words must be said about the constraints specific to this type of system, constraints that led to the special computer architecture described in the next paragraph.

Yourdon (74) defines computer systems as "on-line" when they accept input directly from the point where the input is generated and return the output directly to the point of consumption. They are also characterized by a randomly accessible memory, preferably one that is part of the core memory of the main computer. The on-line concept also implies man-machine interaction of which the system discussed in this chapter is an extreme example. Another concept applicable to brain-computer interaction is that of "real-time" as defined by Martin (75): "a real time computer system may be defined as one which controls an environment by receiving data, processing it and returning the results sufficiently quickly to affect the environment at that time." In terms of directly communicating brain messages, this would imply a round trip of less than 0.5 sec. For interactive work, the methods described above are bulky and costly, but above all, they are generally designed in a way that precludes real-time analyses. That is to say that they require a whole epoch of one to several seconds to be deposited in memory, or worse, that a large number of those

epochs be averaged together, before starting the computation. Averaging techniques are totally inapplicable in this project. Spectral methods, on the other hand, can be adapted to produce continuous estimates based on some span of past data. Nevertheless, one of the EEG correlates that appears the most promising at this time is the interchannel correlation coefficient, itself a by-product of the orthogonal derivation discussed earlier. Glassman (76) showed that those correlation coefficients behave smoothly and exhibit stable epochs separated by sharp transitions. Those stable epochs can be clearly identified without reference to spectra. Figure 1 illustrates the behavior of some of those functions over a period of 45 sec. The easy and immediate recognition of the times of transition may lead to substantial improvement in the processing. In particular, this knowledge will allow slicing the data in such a way that analysis always rests with data collected within those stable subepochs by uncoupling the computer program from data belonging to a past history characterized by a different state. The situation with evoked response also requires complete reevaluation. As mentioned before, there has been to this time very little work addressed to the identification of evoked response on the basis of a single event. However, to use the evoked response to a given sensory stimulus such as a visual pattern in an interactive man-machine dialogue, recognition must be made on the basis of a short section of EEG waveform containing the response.

To meet this challenge, each incoming response must be compared with a "reference set" and classified without benefit of averaging. A new method has been developed as part of this project (Schwartzmann 77) that allows the constitution of reference sets in a continuum of conditions rather than as discrete classifiers. Specifically, the approach consists of analyzing the family of reference-evoked responses (obtained during "training") to find the number of dominant input parameters that have varied through experimental (or accidental) realizations of the process (that is, presentation of the stimulus). At the end of the training phase, the reference set is described by  $M$  output responses corresponding to  $M$  separate presentations. Using an orthogonal basis, we represent them as points in a linear function space  $E_N$ .

An error due to this approximation will be made. The value of  $N$  is chosen such that most of the function energy is preserved (e.g., 95%). The choice of the basis is arbitrary but will influence heavily the performance of the method. Choices can be made, for instance, between Fourier and Walsh series, Karhunen-Loève expansion, or simply the raw sample values, which is equivalent to using delta functions as functional basis. One-to-one, piecewise continuous mapping of the input parameters into the output space is assumed. The minimum number  $K$  of "free" parameters needed to represent the output set is called the *intrinsic* dimensionality of the process. The problem reduces to the determination of the *topological* dimensionality of the cluster of points formed by the output functions in  $E_N$ . A minimum spanning tree is created by the computer to map the input influences into the cluster of points. This tree becomes a reference map or scale that can be used to label and compare any new response with the reference. Separately, an adjoint mapping procedure was developed that allows display in two dimensions of the cluster of points on the computer graphic terminal. This method provides a model-free description of evoked responses that avoids averaging or other loss of information.



### COMPUTER ARCHITECTURE OF THE BRAIN-COMPUTER INTERFACE PROJECT

The project is centered on the laboratory illustrated in Figure 2. Implementation of this system started late in 1971 and is still underway.

The main features are as follows: Subjects are monitored from a specially designed shielded enclosure that contains various input devices and output displays. The experimenter sits in an adjacent room containing the control terminals to the various computers as well as the recording equipment for EEG and other biosignals. This arrangement permits interplay between subject, experimenter, and computer in staging complex tasks and bringing feedback information to the subject. The EEG signals are preamplified by specially designed preamplifiers and monitored on conventional chart recorders. The amplified analog signals are routed directly to a digitizing station capable of handling 50 simultaneous channels. In the laboratory, a small dedicated XDS 920 computer acts as data input controller and real-time experiment scheduler. The data acquisition program deserves special attention: This program, called real-time data handling supervisor (DHS), enables the XDS 920 and its associated peripherals (analog-to-digital converters, digital-to-analog converters, multiplexers, relays, pulses, sense switches, and parallel logic lines) to coordinate the real-time collection, analysis, and display of EEG data. DHS operates via a remote station with a lighted panel display of its status. It can be operated alone or in conjunction with the rest of the system. The DHS can transmit data from up to 32 analog inputs at a rate of 128 samples per second (approximately 50 kilobits/sec). The data can be ordered in epochs of variable length with each epoch labeled for reference by subsequent data handling/processing programs. Simultaneous analog time marking signals are produced for the analog data records. An XDS Sigma 7 computer, whose main function is to serve the UCLA node of the ARPA Network, is used for general experiment control (which includes control of the 920 scheduler) and is operated through a terminal printer in the laboratory. It operates under a time-shared system (SEX), particularly well suited to the sophisticated handling and editing of small files.

The main computing power is provided by the campus IBM 360/91, which is equipped with an exceptionally large core memory of 4 M bytes. High-speed parallel data links connect all four computers involved in the system (Figure 3). The digitized data thus reaches the IBM 360/91 through a parallel port and is written directly into core. Feedback returns are retrieved the same way. A monitor program in the 360/91 controls the data flow and the processing protocol from a privileged position with respect to the 360/91 operating system software to optimize response time. Complex programs such as spectral or functional analysis of the signals can be performed in real time with results fed back to the laboratory in graphic form. The "awakening" of the software system and all subsequent file handling are performed under the campus-wide, time-shared system (URSA) and controlled by a CRT terminal (CCI) in the laboratory.

Finally, an IMLAC PDS-1 mini-computer and display terminal with 8 K of memory is reserved for the generation of visual feedback display and for other output functions. The PDS-1 derives great flexibility and speed from the combination of dual parallel processors sharing the same core memory. The display processor

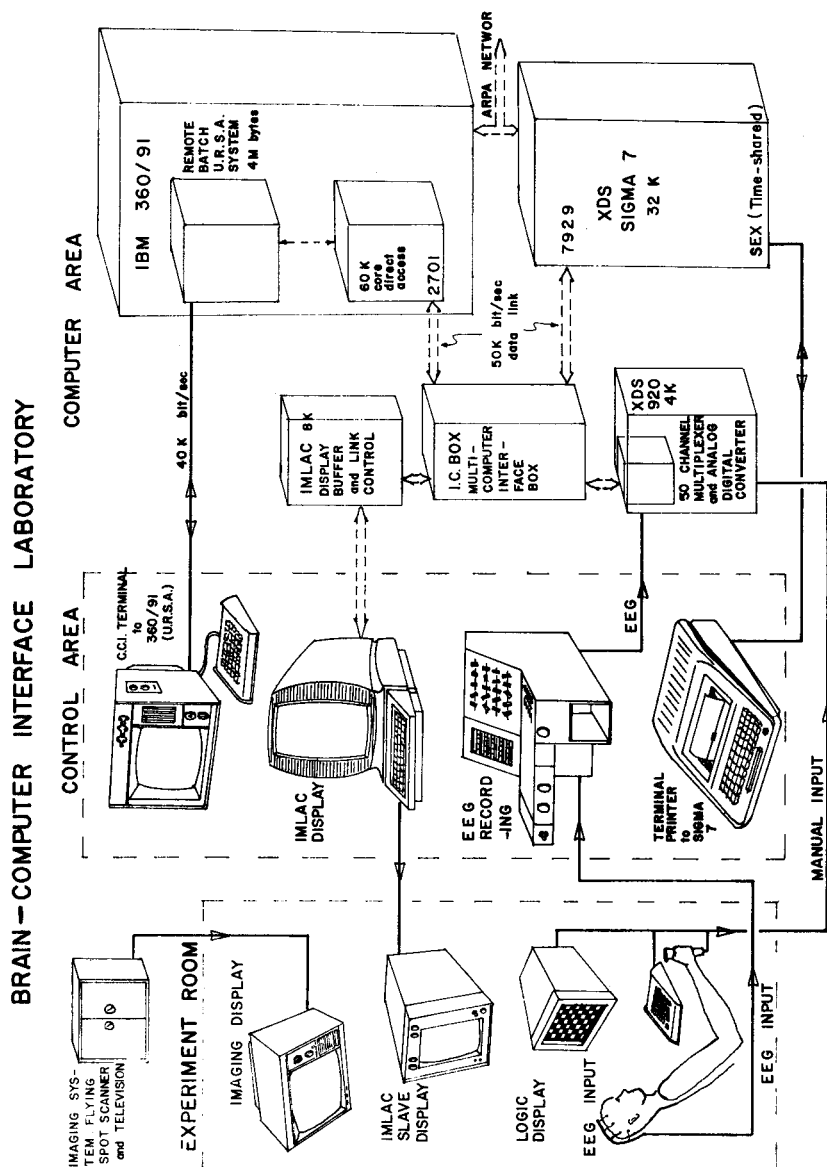


FIGURE 2. General organization and computer architecture of the Brain-Computer Interface Laboratory at UCLA.

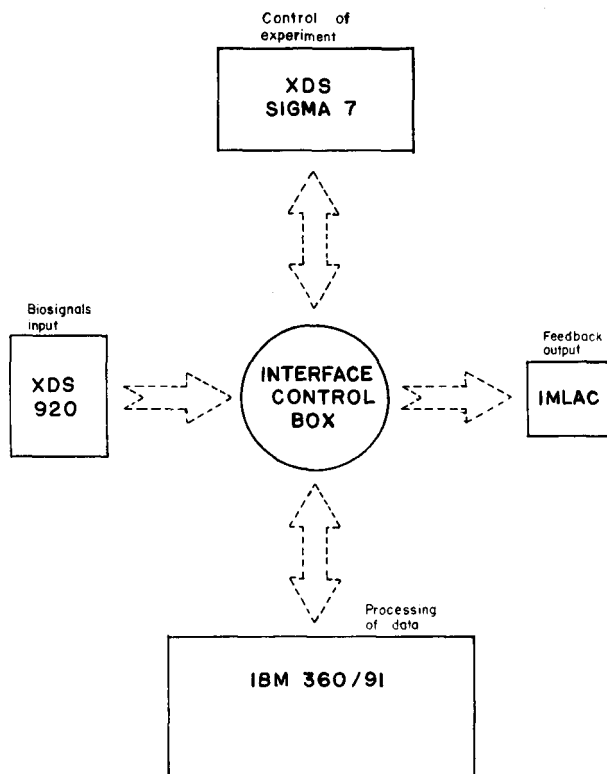


FIGURE 3. Brain Computer Interface Laboratory: The arrows indicate the direction of the data flow in the multiple computer structure.

interacts with the mini-computer only when it requires data from core to update graphical information on the screen. Smooth curves and figures can be displayed and manipulated while on-line with the processing computer (i.e., the 360/91). In addition, the PDS-1 can function as a stand-alone computer. A flying spot scanner (Dalto 500) is available to create background images that can be combined with computer outputs. A large computer display scope is associated with the scanner. The scanner and display can be placed under computer control and used in the creation of visual stimuli.

### EXPERIMENTAL STRATEGY

Experimental possibilities with this system are unbounded. Generally speaking, one should seek to identify features in the EEG and in the evoked response signals that constitute potential codes for the direct communication of specific mental messages. These would be of the kind that occur in interactive man-computer communication such as: recognition of a clue (or matching), its acceptance and

rejection, choice between (visual) alternatives, arbitrary positioning of a pointer on a screen, etc. The next step would be to systematically evaluate the range and bandwidth (that is, the time penalty imposed by each distinguishable feature) in the EEG "signatures" and to determine the rules of association of those features (syntax). In addition, one should determine the natural modalities of sensory messages and conscious experiences that lead to easy discrimination and conditioning, or in other words, find some of the semantic constraints on this type of brain message. The study must involve the subject in an interactive or "game playing" situation that offers reward for performance and, therefore, constitutes a form of operant conditioning.

Experiments with ongoing EEG require a continuous analysis. Incoming data must be placed in a "push-down" memory store of adequate length in order to provide the processor with adequate epochs of data. Processing need not occur every time a new sample is added; however, the requirement of effective feedback still places severe constraints on the amount of processing that can be contemplated if the system is to keep up with the input data flow. In this respect, time domain analyses have distinctive advantages and the early experiments will be focusing on studies of this type. As mentioned earlier, interelectrode correlation coefficients have been shown to constitute promising correlates of brain activity. Early off-line experiments demonstrated definite shifts together with stable correlation levels between shifts. Such "states" of the correlation functions typically lasted for a few seconds. On-line experiments will determine if these functions do correlate naturally with mental states or if they are amenable to reinforcement by operant conditioning.

To implement the conditioning paradigm, a correlation map such as that illustrated in Figure 4 will be calculated continuously from the incoming data and displayed in real time.

Another promising route for feature extraction in ongoing EEG has been opened recently in experiments using phase-locked loops. Nirenberg, Hanley & Stear (78) showed that voluntary triggering of EEG phase transients was obtained in response to motor decisions (in this instance, a decision by the subject to clasp his hand). The original experiment was done with off-line processing on a graphic console IBM 2250. There was, therefore, no feedback to tell the subject of successful discrimination or any false alarm. The separation that was obtained then, although admittedly not perfect, did not benefit from reinforcement. The same experiment will be attempted, after adjustment to present hardware and software constraints, with a visual display of the open or closed hand according to the computer guesses. Performance scores will be taken to trace the influence of the conditioning procedure.

Two specific experiments centered on evoked response are also planned. With sensory stimuli (e.g., visual stimulus such as a geometric pattern), the evoked response depends on such factors as the geometric structure of the pattern (White 79, John et al 80, and Spehlmann 81), the light intensity and wavelengths (Clynes et al 82), the particular feature in the pattern to which the subject has selectively directed his attention (Gardiner & Walter 83, Steinberg 84), and the cognitive content of the stimulus such as the meaning of a pattern in the experimental context (Sutton et al 85, 86, Chapman 87). Autonomic influences such as those of the cardiac and respiratory cycles have also been reported (Callaway & Buchsbaum 88). Generally

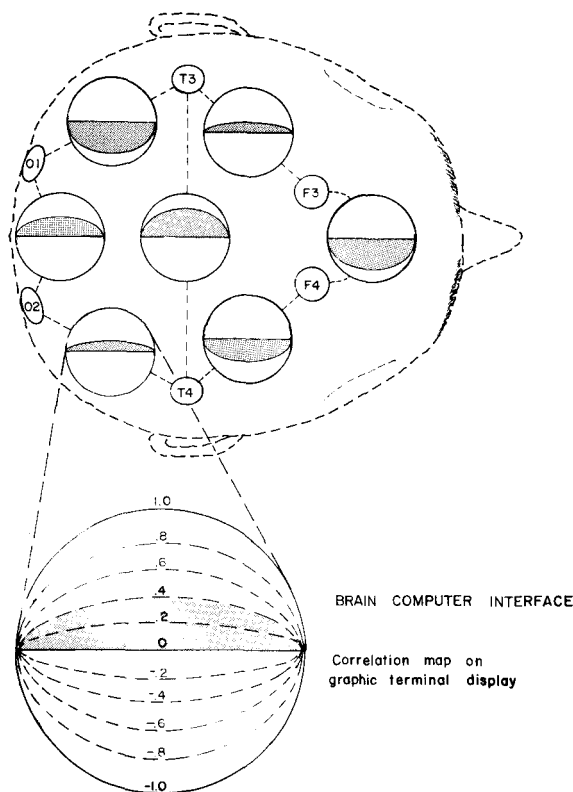


FIGURE 4. Interelectrode correlation map, as shown on computer graphic display.

speaking, anything that could affect the internal state of the brain is a potential factor of influence. This, of course, must include the state of the EEG itself at the time, or immediately before the delivery of the stimulus, since there is definite interaction between the evoked potentials and the ongoing activity. Indeed, the observed potentials betray, however incompletely, the "state" of the underlying cortex. Thus, by eliciting a response only at the time when a given "initial state" is observed, rather than at arbitrary instants, one removes a source of variability in the system response. That this is indeed the case has been shown in particular when the stimulus is applied at a given point in the time cycle of an alpha wave (Remond & Lesevre 89, Bremer 90) or under different states of correlation between brain structures (Galbraith 91, 92).

For the purpose of this project, the following experimental parameters will be considered:

(a) The "condition" upon the realization of which the stimulus is delivered. (At arbitrary time intervals, or upon the detection of a given feature in the EEG

signal such as a given phase in the alpha cycle or a given configuration of the correlation map.)

(b) The stimulus structure (pattern shape, sound pitch, etc).

(c) The particular feature in a complex stimulus to which the subject has selectively directed his attention (e.g., the set of vertical lines versus horizontal lines in a grid pattern).

(d) The meaning of the stimulus in the context of a given application, i.e., the degree of novelty (expectation) of the stimulus, or its acceptance or rejection in context (whether the occurrence of the stimulus represents a gain or a loss).

Each one of these factors may shape the evoked responses in a characteristic manner. In the system, the two first factors are selected by the control computer. In the man-machine dialogue, their selection represents the "questioning" strategy of the control program while the two last factors constitute either voluntary or subconscious "responses" from the human subject. Upon receiving the response, the processing computer will be asked to evaluate it against some reference measure and to generate the appropriate feedback to the subject. Parameters of type (a) and (b) are part of the design of the experiment and can, in principle, be selected arbitrarily. Parameters of type (c) and (d) reflect the subject's voluntary choices or the subject's reaction to the stimulus, i.e., precisely the mental information to be transmitted to the computer. In view of these facts, experiments will be planned along the following lines: Find the type of condition (a) and pattern structure (b) that "optimally" improve single response discriminability with respect to given "mental" parameters (c) and (d). The stimulus pattern and the conditions of presentation may be explored over a large spectrum for each "mental" parameter attached to the experimental paradigm. One procedure of each type (voluntary or "deliberate" versus subconscious) of mental parameter is being investigated.

*Selective attention (voluntary) to complementary features of a pattern.*—Grid patterns will be used first, since they have proven effective in ER work. The task will be to concentrate on either the horizontal or the vertical structure of the pattern.

This mental selection is analogous to the well-known phenomenon of figure-ground reversal in perception psychology (e.g., Gregory 93). Perceptually, the subject can ignore one of two complementary features of an image and concentrate on the other. Because evoked responses are in part related to perceptual phenomena, it is proposed that this shift of mental set will produce distinguishable evoked signatures in the EEG, in very much the same way as shown in the Gardiner-Walter experiments with tones. Furthermore, it is likely that those changes will somewhat parallel the differences observed in independent experiments with pure horizontal or pure vertical striped targets. Whether this holds true or not, however, would not directly affect the outcome of the experiment, although it may shed some light on the underlying neurophysiological phenomena. Response sensitivity to the stimulus parameters will be investigated first, using the topological dimensionality approach discussed earlier. This study will indicate if that choice of target is appropriate or if changes should be made. A continuum of grid patterns will be used in which the light intensity shifts progressively from the vertical to the horizontal components.



Evoked responses along this continuum will be studied by dimensionality analysis to establish the reference functions in the computer. The pattern generation as well as the evoked response analysis programs will be placed under the control of the processing computer. The subject will be presented with repeated flashing of a grid pattern on the graphic terminal screen. The task will consist of reducing the pattern to a set of either horizontal or vertical lines by exercising control over the figure-ground perception in the appropriate direction. The preliminary experiments will have provided the computer memory with a functional nonlinear map relating the response "trajectory" with the input parameters. Therefore, any incoming evoked response can be labeled from its functional projection on the trajectory. The next target flashed will then be modified in the corresponding direction. In other words, if the response is such that some of the "horizontal" features have been suppressed, the next target will reflect that fact by displaying the horizontal lines with less intensity. The subject is, therefore, given a real-time score of this performance and can evaluate the control that he gains over the phenomenon. Meanwhile, the responses are automatically incorporated in an updated reference set in order to account for the adjustment in the response produced by the operant conditioning.

In this particular experiment, the computer can choose the instants at which the stimulus is presented. Therefore, by choosing appropriate EEG conditions to determine each time of presentation, one hopes to reduce the uncertainties associated with single response discrimination. As mentioned earlier, Galbraith has shown that evoked responses were dependent upon the state of correlation between various parts of the brain. Although this study was confined to correlation between cortical and deep structures, it is conceivable that the same holds for correlation between different cortical sites. Therefore, time of presentation will be tentatively linked to the state of the correlation coefficients (as shown on the correlation map) to determine their effect on response stability.

*Evoked-response experiments with cognitive parameters.*—In the experiment discussed in the previous paragraph, the computer discrimination of the evoked responses was based on the reinforcement by conditioning of response features that were bound to the physical structure of the stimulus or to its perception. By contrast, the second type relies on the cognitive influences that would modify the waveform evoked by an otherwise identical stimulus. A first implementation of this type of paradigm will incorporate a well-known graphic program (space war) in which subjects are given an opportunity to fire "missiles" at opponents' space ships. A visual event that will create an associated evoked potential is provided by the "explosion" of either ship on the display screen. Thus, the same visual event will be associated with a different state of mind or expectation whenever the subject witnesses the destruction of his opponent's ship rather than his own. In the implementation, the opponent's ship is controlled by the computer, which plays a fairly aggressive albeit standard strategy in attempting to destroy the subject's spaceship. When an explosion occurs, an interrupt signal is generated by the display processor for the benefit of the real-time data handler program, and an epoch of EEG data time-bound to the explosion is entered into the system. The epochs are defined on both sides of the triggering event

to include some lead time. Again, the procedure starts with a learning period during which the computer establishes its reference data. A score is displayed that is originally determined by the number of games won by the subject versus those won by the computer. When enough points have been acquired for a decision rule to emerge with acceptable confidence limits, the scoring rules are modified and gains are doubled if accompanied by correct classification of the evoked response, cancelled otherwise. Losses are cancelled for correct classification and doubled otherwise. This rule is intended to provide an operant conditioning paradigm where the operant neural events are correlates of cognitive parameters in the stimulus. Similar experiments could conceivably be designed to investigate the flash or "hitch" of recognition arising from novelty or the various abrupt arousals which it has been speculated make learning possible (assuming, for instance, that only those events that cause internal satisfaction or dissatisfaction are specifically perceived and conducive to learning). The above experimental procedure although admittedly simpler in scope would be a first step in this direction.

## CONCLUSION

As the reader undoubtedly realizes, direct brain-computer communication still lies somewhat in the future. Even the relatively modest experimental program outlined in this paper may take several years to reach maturity, at which time new directions probably will have emerged.

In summary, it can be said that the feasibility of the communication concept rests on three basic assumptions. The first assumption is that mental decisions and reactions can be probed, in a dimension that both transcends and complements overt behavior, from the array of observable bioelectric signals and, in particular, from the electroencephalographic potential fluctuations as measured on the human scalp. A second assumption is that all meaningful EEG phenomena should be viewed as a complex structure of elementary wavelets, similar in nature to components of evoked responses, that sequentially reflect individual cortical events and create a continuous flow of neuroelectric messages. The third assumption is that operant conditioning procedures can increase the reliability and stability of these time signatures and patterns.

Admittedly the validity and implications of these assumptions are far from universally accepted. The view, for instance, that the EEG is organized in sequential waveforms reflecting brain states on a moment-to-moment basis contrasts somewhat with a portion of the classical literature that concentrates on brain rhythms. On the other hand, considerable experimental evidence lends credence to the proposed concepts.

The program outlined in this paper constitutes a first systematic attempt to clarify these concepts and to establish their possibilities and limitations.

# LITERATURE CITED

1. Berger, H. 1931. Ueber das Elektrenkephalogramm des Menschen. *Arch. Psychiat.* 94:16-60
2. Fox, S. S., O'Brien, J. H. 1965. *Science* 147:888-90
3. Adey, W. R. 1958. *Reticular Formation of the Brain*, ed. H. H. Jasper, L. D. Proctor, R. S. Knighton, W. C. Noshay, R. T. Costello, 621-44. Boston: Little, Brown
4. von Euler, C., Green, J. D., Ricci, G. 1958. *Acta Physiol. Scand.* 42:87-111
5. Dunlop, C. W., Killam, K. F., Brazier, M., Adey, W. R. 1959. *Fed. Proc.* 18:38
6. Widen, L., Marsan, C. A. 1960. *Arch. Ital. Biol.* 98:248-74
7. Li, C. -L. 1963. *J. Cell. Comp. Physiol.* 61:165-79
8. Gerstein, G. L., Kiang, N. Y.-S. 1964. *Exp. Neurol.* 10:1-18
9. Adey, W. R. 1966. *Progress in Physiological Psychology*, ed. E. Stellar, J. M. Sprague, 1-43. New York: Academic
10. Buchwald, J. S., Halas, E. S., Schramm, S. 1966. *Electroencephalogr. Clin. Neurophysiol.* 21:227-38
11. Marshall, W. H., Talbot, S. A., Ades, H. W. 1943. *J. Neurophysiol.* 6:1-15
12. Li, C. -L., Jasper, H. H. 1953. *J. Physiol.* 121:117-40
13. Purpura, D. P. 1967. *The Neurosciences: A Study Program*, ed. G. C. Quarton, T. Melnuechuk, F. O. Schmitt, 372-93. New York: Rockefeller Univ. Press
14. Morrell, F. 1967. *The Neurosciences: A Study Program*, ed. G. C. Quarton, T. Melnuechuk, F. O. Schmitt, 452-69. New York: Rockefeller Univ. Press
15. Landau, W. M. 1967. *The Neurosciences: A Study Program*, ed. G. C. Quarton, T. Melnuechuk, F. O. Schmitt, 469-82. New York: Rockefeller Univ. Press
16. Morrell, F. See Ref. 14
17. Pitts, W., McCulloch, W. S. *Bull. Math. Biophys.* 9:127-47
18. Morrell, F. See Ref. 14
19. Li, C. -L., Cullen, C., Jasper, H. H. 1956. *J. Neurophysiol.* 19:131-43
20. von Euler, C. See Ref. 4
21. Morrell, F. See Ref. 14
22. von Euler, C. See Ref. 4
23. Hubel, D. H., Wiesel, T. N. 1962. *J. Physiol.* 160:106-54
24. Gerstein, G. L., Kiang, N. Y.-S. See Ref. 8
25. White, C. T., Eason, R. G. 1966. *Psychol. Monogr.* 80:24, whole no. 632
26. Harter, M. R., White, C. T. 1968. *Vision Res.* 8(6):701-11
27. Harter, M. R., White, C. T. 1970. *Electroencephalogr. Clin. Neurophysiol.* 28(1):48-54
28. Clynes, M., Kohn, M. 1968. *Computers and Electronic Devices in Psychiatry*, ed. N. S. Kline, E. Laska, 206-37. New York: Grune & Stratton
29. Spehlmann, R. 1965. *Electroencephalogr. Clin. Neurophysiol.* 19:560-69
30. Walter, D. O., Rhodes, J. M., Adey, W. R. 1967. *Electroencephalogr. Clin. Neurophysiol.* 22:22-29
31. Hanley, J., Walter, D. O., Rhodes, J. M., Adey, W. R. 1968. *Nature* 220:879-81
32. Galbraith, G. C. 1966. *Proc. Symp. Biomed. Eng.* 1:341-44
33. Galbraith, G. C. 1966. *IEEE Trans. Biomed. Eng.* 4(4):223-29
34. Hanley, J., Berkhout, J., Crandall, P. H., Rickles, W. R., Walter, R. D. 1970. *Electroencephalogr. Clin. Neurophysiol.* 28:90
35. Hanley, J., Walter, D. O., Rhodes, J. M., Adey, W. R. See Ref. 31
36. Hanley, J. 1969. *Automatic recognition of psychotic and normal appearing behavior in a chronic schizophrenic patient by EEG criteria*. Presented at Society for Biological Psychiatry, Miami, Florida
37. Hanley, J., Berkhout, J., Crandall, P. H., Rickles, W. R., Walter, R. D. See Ref. 34
38. Dixon, W. F. 1968. *BMD Computer Programs*. Los Angeles Health Sciences Computing Facility, Department of Preventive Medicine and Public Health, School of Medicine, University of California
39. Nirenberg, H. M., Hanley, J. 1969. *Music and the EEG*. Presented at Winter Conference on Brain Research, Snowmass in Aspen
40. Freeman, W. J. 1962. *Exp. Neurol.* 5:477-99
41. Freeman, W. J. 1964. *Exp. Neurol.* 10:475-92
42. Freeman, W. J. 1968. *J. Neurophysiol.* 31:1-13
43. Lehmann, D., Fender, D. H. 1968. *Electroencephalogr. Clin. Neurophysiol.* 24:542-53
44. Raviv, J., Streeter, D. N. 1965. *IBM Res. Rep. RC 1577*
45. John, E. R., Ruchkin, D. S., Villiegas, J. 1964. *Ann. NY Acad. Sci.* 112:362-420
46. Ruchkin, D. S., Villiegas, J., John, E. R. 1964. *Ann. NY Acad. Sci.* 115:779-826

47. Donchin, E. 1966. *IEEE Trans. Biomed. Eng.* 13:131-39
48. Donchin, E. *Electroencephalogr. Clin. Neurophysiol.* 27(3):311-14
49. Palmer, C. W., Derbyshire, A. J., Lee, A. W. 1966. *Electroencephalogr. Clin. Neurophysiol.* 20:204-6
50. Woody, C. D. 1967. *Med. Biol. Eng.* 5:539-53
51. Carmona, A. B. 1967. *Diss. Abstr.* 28: 1157B-58B
52. Chase, M. H., Harper, R. M. 1971. *Electroencephalogr. Clin. Neurophysiol.* 31:85-92
53. Sterman, M. B., Howe, R. C., MacDonald, R. 1969. *Science* 167:1146-48(a)
54. Black, A. H. 1971. *Am. Sci.* 59:236-45
55. Brown, B. 1970. *Psychophysiology* 6: 442-52
56. Brown, B. 1971. *Psychophysiology* 7: 451-64
57. Green, E. E., Green, A. M., Walters, E. D. 1970. *Progress of Cybernetics: Proceedings of the International Congress of Cybernetics*, ed. J. Rose. London: Gordon & Breach
58. Kamiya, J. 1968. *Psychol. Today* 1:57-60
59. Kamiya, J. 1969. *Altered States of Consciousness*, ed. C. Tart, 507-17. New York: Wiley
60. Paskewitz, D., Lynch, J., Orne, M., Costello, J. 1970. *Psychophysiology* 6(5): 637
61. Peper, E. 1970. *Kybernetik* 7:107-12
62. Peper, E., Mulholland, T. 1970. *Kybernetik* 7:10-13
63. Fox, S. S., Rudell, A. P. 1968. *Science* 162(3859):129-30
64. Fox, S. S., Rudell, A. P. 1970. *J. Neurophysiol.* 33(4):548-61
65. Rosenfeld, J. P. 1969. *Science* 165:821-23
66. Rosenfeld, J. P., Rudell, A. P., Fox, S. S. 1969. *Science* 165(3895):821-23
67. Black, A. H. In press
68. Fox, S. S. 1970. *The Neurosciences: Second Study Program*, ed. F. O. Schmitt, 243-57. New York: Rockefeller Univ. Press
69. Tecce, J. J. In press
70. National Aeronautics and Space Administration (NASA). *Normative Electroencephalographic Data Reference Library*. Final Report prepared by Baylor University College of Medicine and the Methodist Hospital
71. Girtton, D., Kamiya, J. 1972. *Electroencephalogr. Clin. Neurophysiol.* In press
72. Landau, W. M. See Ref. 15
73. Glassman, J. A. 1972. *An empirical study into the efficient processing of electroencephalographic data*. PhD dissertation. Univ. California, Los Angeles. 229 pp.
74. Yourdon, E. 1972. *Design of On-Line Computer Systems*. Englewood Cliffs, N.J.: Prentice-Hall
75. Martin, J. 1967. *Design of Real-Time Computer Systems*. Englewood Cliffs, N.J.: Prentice-Hall
76. Glassman, J. A. See Ref. 73
77. Schwartzmann, H. G. 1972. *Black box system identification via the topological dimensionality approach with applications to neurophysiological problems*. PhD dissertation. Univ. California, Los Angeles. 173 pp.
78. Nirenberg, H. M., Hanley, J., Stear, E. B. 1971. *IEEE Trans. Biomed. Eng.* 19:389-98
79. White, C. T. 1969. *Amer. Psychol.* 24:211-14
80. John, E. R., Ruchkin, D. S., Villiegas, J. See Ref. 45
81. Spehlmann, R. See Ref. 29
82. Clynes, M., Kohn, M., Gradijan, J. 1967. *IEEE Convention Record, Biomed.*, ETAI
83. Gardiner, M. F., Walter, D. O. 1969. *Averaged Evoked Potentials*, ed. E. Donchin, D. B. Lindsley, 335-42. Washington, DC: NASA SP-191
84. Steinberg, R. H. 1965. *Electroencephalogr. Clin. Neurophysiol.* 18:378-91
85. Sutton, S., Braren, M., Zubin, J., John, E. R. 1965. *Science* 150:1187-88
86. Sutton, S., Tueting, P., Zubin, J., John, E. R. 1967. *Science* 155:1436-39
87. Chapman, R. M. 1971. *Conference on Psychophysiology of Thinking*, ed. F. J. McGuigan. Virginia: Hollins College
88. Callaway, E., Buchsbaum, M. 1965. *Electroencephalogr. Clin. Neurophysiol.* 19:476-80
89. Rémond, A., Lesèvre, N. 1967. *Electroencephalogr. Clin. Neurophysiol. Suppl.* 26:42-52
90. Bremer, F. 1958. *Physiol. Rev.* 38:357-88
91. Galbraith, G. C. 1966. *Proc. Symp. Biomed. Eng.* 1:341-44
92. Galbraith, G. C. 1966. *IEEE Trans. Biomed. Eng.* 4:223-29
93. Gregory, R. L. 1970. *The Intelligent Eye*. London: Weidenfeld & Nicolson

## CONTENTS

AHARON (KATZIR) KATCHALSKY.....	1
FREQUENCY DYNAMICS OF PERIPHERAL VASCULAR BLOOD FLOW, <i>E. O. Attinger and F. M. Attinger</i> .....	7
ELECTRIC AND MAGNETIC FIELD OF THE HEART, <i>David B. Geselowitz</i> .....	37
INTERPRETATION OF SOME MICROELECTRODE MEASUREMENTS OF ELECTRICAL PROPERTIES OF CELLS, <i>A. Peskoff and R. S. Eisenberg</i> .....	65
CLUSTERING, <i>J. A. Hartigan</i> .....	81
TECHNOLOGY OF MULTIPHASIC PATIENT SCREENING, <i>Morris F. Collen and Joseph F. Terdiman</i> .....	103
OPTIMIZATION OF THE MAMMALIAN RESPIRATORY GAS TRANSPORT SYSTEM, <i>Fred S. Grodins and Stanley M. Yamashiro</i> .....	115
PRIMARY PROCESSES IN BACTERIAL PHOTOSYNTHESIS, <i>Roderick K. Clayton</i> ....	131
TOWARD DIRECT BRAIN-COMPUTER COMMUNICATION, <i>Jacques J. Vidal</i> .....	157
BIOPHYSICS OF FLAGELLAR MOTILITY, <i>J. J. Blum and J. Lubliner</i> .....	181
LONG-RANGE PHYSICAL FORCES IN THE BIOLOGICAL MILIEU, <i>V. Adrian Parsegian</i> .....	221
STRUCTURE AND SYMMETRY OF OLIGOMERIC ENZYMES, <i>B. W. Matthews and S. A. Bernhard</i> .....	257
REPRINT INFORMATION.....	319
INDEXES	
AUTHOR INDEX.....	321
CUMULATIVE INDEX OF CONTRIBUTING AUTHORS, VOLUMES 1-2.....	331
CUMULATIVE INDEX OF CHAPTER TITLES, VOLUMES 1-2.....	332