HANDBOOK OF ELECTROENCEPHALOGRAPHY AND CLINICAL NEUROPHYSIOLOGY

EDITOR-IN-CHIEF A. REMOND

VOLUME 5

Evaluation of Bioelectrical Data from Brain, Nerve and Muscle, II

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Brain Research Institute, University of California, Los Angeles, Calif. (U.S.A.)

PART A

Frequency and Correlation Analysis

EDITOR: M. MATOUŠEK

The Sahlgren Hospital, Göteborg (Sweden)

ELSEVIER

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A great need has long been felt for a Handbook giving a complete picture of the present-day knowledge on the electrical activity of the nervous system.

The International Federation of Societies for EEG and Clinical Neurophysiology is happy to be able to present such a Handbook, of which this is a small part.

The decision to prepare this work was made formally by the Federation at its VIIth International Congress. Since then nearly two hundred specialists from all over the world have collaborated in writing the Handbook, each part being prepared jointly by a team of writers.

The Handbook begins with an appraisal of 40 years of achievements by pioneers in these fields and an evaluation of the current use and future perspectives of EEG and EMG. The work subsequently progresses through a wide variety of topics—for example, an analysis of the basic principles of the electrogenesis of the nervous system; a critical review of techniques and methods, including data processing; a description of the normal EEG from birth to death, with special consideration of the effect of physiological and metabolic variables and of the changes relative to brain function and the individual's behaviour in his environment. Finally, a large clinical section covering the electrical abnormalities in various diseases is introduced by a study of electrographic semeiology and of the rules of diagnostic interpretation.

The Handbook will be published in 16 volumes comprising 40 parts (about 2500 pages altogether). For speed of publication most of the 40 parts will be published separately and in random order.

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PART A

FREQUENCY AND CORRELATION ANALYSIS

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Preface

"When you can measure what you are speaking about and express it in numbers, you know something about it". The statement of Lord Kelvin is most pertinent for neurophysiological research and its future development. Signal analysis and subsequent quantification requires extraction of information which is considered useful. Very importantly, this implies rejection of information considered to be useless. Thus the type of analysis is determined by the question being asked. No universally applicable method of analysis exists because there are no universal questions.

The less experienced reader will find a comprehensive review of methods of EEG and EMG analysis in Section I of this Volume, where the theoretical background, applicability and critical remarks are briefly summarized. The following Sections are dealing with some of the methods in detail. The most advanced, most interesting or practically most important methods are discussed. It is believed that the reader will get a general impression of the history and of the future development of quantitative methods in neurophysiology.

Section I. Review of various methods of EEG analysis

A. INTRODUCTION

The development of various methods of EEG analysis has sometimes been as important for the advancement of electroencephalography as Berger's first experiments. Such an opinion is plausible when surveying the number of excellent theoretical papers which have appeared in the past twenty or thirty years. Some scepticism might arise, however, if the minimal profit for routine work is taken into consideration. Most probably, a new era has just begun; the number of new methods has decreased significantly, and the electroencephalographers are more interested in appropriate use and exploitation of existing techniques. Therefore, it is profitable to summarize the various methods of EEG analysis, and to supplement previous reviews (Knott 1953; Kozhevnikov 1958a; Burch 1959; Rémond 1960c; Storm van Leeuwen and Magnus 1961; Nebylicin 1962; Kozhevnikov and Mesherskij 1963; W. G. Walter 1963; Brazier 1965). Some international conferences have dealt exclusively with automatic EEG analysis (see Electroenceph. clin. Neurophysiol. Supplements 4, 20, 27) and the published proceedings of congresses yield detailed information on recent advances.

It is difficult, however, to find a logical system when considering various methods. The brain activity is registered as a simple amplitude-time distribution; the questions can only be asked about a fixed time interval and answered as amplitude variables, or examined in regard to fixed amplitude relationships and observed as variables in time. Thus, EEG analysis in the frequency domain and in the time domain[1] are distinguished (Burch 1959). A strictly logical classification is, on the other hand, somewhat less lucid, and does not include all methods. In the present review another classification is used. Basically, the various methods differ in two points:

1. They concern either the measuring of one EEG curve or several electric events;
2. they are based on the observation of all components or choose only specific ones.

In most cases, there is one or a few well-specified qualities which are responsible for the result of analysis. The classification system presented (see Table I) is based on these differences; it is more comprehensible and still does not exceed the necessary principles of logic.

The material compiled in each Subsection of this Section is arranged in the following order:

[1] Perhaps amplitude- and time-domains would seem more apt, but the terminology has already been established.

TABLE I

VARIOUS METHODS OF AUTOMATIC EEG ANALYSIS

Dominant quality	*Source of observation*	*Names and various types of analyses*	*Remarks*
Analysis of a single signal			
Amplitude	EEG in one derivation	*Amplitude analysis*: percentage time above a minimum level, integration, assessing amplitude distribution	Based on simple amplitude measurements Concerns all waves, neglecting wave length
Wave length	EEG in one derivation	*Periodometry* ("base-line-crossing", "interval analysis") and derived methods	Based on simple measurements of wave length Most methods neglect amplitudes and prefer the dominant activity EEG processed like a pure aperiodic signal
Frequency and amplitudes	EEG in one derivation	*Frequency analysis*: broad-band or narrow-band frequency analysis, spectral analysis	More or less accurate approximation to frequency spectrum, measuring amplitudes of various frequency components
Wave shape	EEG in one derivation	*Pattern recognition* and some simplified methods	Detection and counting specific waves and or wave complexes
Periodicity	EEG in one derivation	*Autocorrelation analysis* and related methods (reverse correlation, auto-averaging = auto-relation analysis)	Correlation between different parts of the same curve. Extraction of periodic signal.
Analysis of two simultaneously occurring signals			
Phase relations	EEG in two derivations	*Phase analysis*	Simple time relations, all waves regardless of frequency and amplitude concerned
Phase relations	EEG and external stimuli	*Registration of evoked potentials*: superposition (summation), averaging and similar methods	Extraction of signal which is time-locked to stimulation, suppression of "noisy" background activity
Correlation of two signals	EEG in two derivations or EEG and some other bioelectric phenomena	*Cross-correlation analysis* and related methods (cross-spectral analysis, coherence function, cross-averaging = cross-relation)	Extraction of periodic components which occur in common in both signals Phase relationships of these components
Analysis of more than two simultaneously occurring signals			
Phase relations	EEG in more than two derivations	*Toposcopy*	Topology and spreading of EEG potentials All waves included
Clinical normality	EEG in more than two derivations	*Attempts at automatic evaluation* of the EEG	Searching for complex parameters which correlate in the best way with normality or abnormality of the EEG curve

brief characteristics of the method,
technique and its development,
application, and
evaluation of the method (advantages and disadvantages).

The last, evaluation of the methods, is the most disputable. One can only gather the available literature and complement it with some quite subjective opinions. The reader's attention is called to the disproportion in length of treatment of the positive and negative features of each method. The former is usually shorter, since the disadvantages of various methods are more important and perhaps less known. They limit the application of the method in question. The author does not wish to appear too pessimistic in dealing with the problems arising in this subject. Many successful and significant papers treating any one of the discussed analytical methods prove the contrary.

B. ANALYSIS OF A SINGLE EEG SIGNAL

1. *Amplitude analysis*

(*a*) *Brief characteristics*

There are several methods, all of them with the following common features:

1. The analysis is provided separately for each EEG derivation,
2. all EEG waves appearing in the input signal are taken into account, regardless of wavelength, periodicity, etc., and
3. the analysis is based on measurement of amplitudes.

Amplitude analysis employs simple relay circuits, integrators and devices for measurement of amplitude distribution ("amplitude spectra").

(*b*) *Terminological remarks*

The term "analysis" is inaccurately used even in those cases when the whole curve is measured, not only its components (W. G. Walter 1963).

The term "amplitude" has various meanings. In routine electroencephalography it corresponds to the maximal peak-to-peak voltage in the recording (see Internat. terminology, *Electroenceph. clin. Neurophysiol.*, **1961**, *13*: 646–650). In connection with some forms of automatic analysis an average of the peak-to-peak voltage as it appears in certain short time periods is to be understood. Thus, the values are significantly lower in the latter instance. In some cases, only the voltage measured from the base-line is considered. Most methods of automatic EEG analysis concern all instantaneous values of amplitude, not only peak values.

(*c*) *Technique and its development, application*

"*All-or-none*" *relay circuits.* The least complicated but nonetheless interesting method for the observation of amplitudes is relay circuits which respond when the EEG signal exceeds some predetermined voltage. They are used for monitoring or measuring the time occupied by the specific activity. It is possible, for instance, to detect decreased vigilance of the subject (Runnals 1963). Drowsiness causes a general flattening of the EEG, the relay circuits respond by switching on a stimulus (light), which attracts the subject's attention and arouses him. Similar devices are employed for the registration of episodic activity (Saslow and Sutton 1963) or for recording some specific rhythms; they register the time during which the amplitude of the alpha or other rhythm exceeds a certain limit (Kennedy and Travis 1948b; Armington 1958; Armington and Chapman 1959; Chapman *et al.* 1962; Kropel *et al.* 1962; Costa *et al.* 1965; Glass 1967; Vatter 1967; Chapman and Shelburne 1970). A computer program was used for similar measurements by Carrie (1972). Satterfield (1966) suggested registering artefacts according to their amplitude, using the same principle.

The main difficulty consists of correct setting of the critical amplitude level. Because such a point is always artificial, the method leads sometimes to over-simplification, replacing a continuous function by a dichotomy.

Integration and similar methods. A true measurement of amplitudes is provided most often by instruments which continuously add all instantaneous values of the amplitude as they appear in the EEG curve. The resulting value increases during the measurement and corresponds to the total area as circumscribed by the EEG curve and the base-line.

The basic principle of an analog integrator is very simple. The amplified input signal charges a condenser gradually, so that the potential difference on the condenser increases more or less proportionally to the integrated input voltage. If only a simple RC circuit is employed, it does not work linearly (even with constant input the charging current decreases gradually). In improved and practically applicable versions the linearity is acceptable, but only within certain limits. It is important to be aware of this because the working range is usually much more limited than that of EEG amplifiers.

During the measurement the positive as well as negative half-waves are considered equally significant, which from the mathematical point of view corresponds to integrating the absolute value of the input signal. The basic integrating circuit responds to DC signals and the integrator is connected with an electronic rectifier (usually a full-wave rectifier).

Another method is squaring the original input values of voltage (the square of the positive as well as the negative number is always positive). It is difficult to construct accurate analog circuits for this purpose ("squaring circuits") and the method is more common in digital processing. Presuming that there is constant resistance in the electrical circuit, the square of the voltage is in proportion to the electric power (watts). The power supplied by the electrode for the amplifier (approximately 10^{-13} W) is of course not connected with the actual energy output of the brain tissue. The difference between squared output values and output values of linearly working analog integrators (expressed in microvolt-seconds, or transformed for better understanding to mean amplitudes) should always be kept in mind.

Early instruments for automatic integration appeared not long after electroencephalography originated (Loomis *et al.* 1936; Freeman and Hoffman 1940). Drohocki's integrator (1948a) was widely employed and repeatedly improved to work with short time epochs (Drohocki 1956). The author suggested standard methods of "quantitative electroencephalography" (Drohocki 1948b, 1962a). Either a large number (*e.g.*, 200) of very short epochs is measured and the results serve as a basis for estimation of amplitude distribution, or measurement concerns a small number of longer epochs ("chronogram").

At about this same time, Davis (1948) published a paper on his work with an integrator. Later instruments were improved technically, *e.g.*, transitron connection (Bates and Cooper 1954) transistorized version (Ford 1954), electromechanical counter as an output device (Kozhevnikov 1954, 1958a; Kozhevnikov *et al.* 1959, 1963) and decimal divider of output pulses by means of magnetic cores (Dvořák 1963). For EMG purposes, the integrator has been equipped with an adjustable trigger circuit. Thus, the device responds only to signals exceeding some amplitude limit, and neglects the actual wave form (Bradley *et al.* 1967; Landolt and Milliken 1970).

There are also other simple methods which yield information more or less comparable with the electronic integration. Some authors registered and measured the envelope curves of the EEG (Kennedy *et al.* 1948a; R. Walter and Yeager 1956; Prior *et al.* 1970). Bruck (1960) measured the space between envelope curves planimetrically. Interesting but obsolete is the use of electrolysis, where the volume of produced gas is proportional to the integrated value (Shminke 1954).

The method is most advantageous for measurement of EEG reactions to various external and internal stimuli and drug effects.

The integrator can quantify small shifts of vigilance level due to sensory stimuli (Drohocki 1962b; Krejčí 1964) or spontaneous falling asleep (Agnew *et al.* 1967). The influence of hyperventilation can be successfully measured, as it concerns amplitude rather than the frequency composition of the EEG (Drohocki 1962a). The integrators are typically used for the observation of drug effects: hypnotics and thymoleptics (Finckh and Kugler 1961), sedatives (Shagass *et al.* 1959), stimulants (L. Goldstein *et al.* 1963a; Pfeiffer *et al.* 1963), hallucinogens (L. Goldstein *et al.* 1963b) and neuroleptics (Murphree *et al.* 1964; Sugerman *et al.* 1964). The method of integration of total or prefiltered EEG activity is perhaps superior to all others in anesthesiology (Brazier 1960c), because the frequency structure of the EEG is of less importance than amplitudes, when monitoring the depth of narcosis (Bickford 1950). Thus, it is possible to control automatically the dosage of thiopental (Kiersey 1954), cyclopropane (Bellville *et al.* 1954), ether (Wyke 1957), nitrous oxide (Kavan 1959); there were attempts to use the integrator in following hypothermia (Clutton-Brock 1959) and in open thoracic surgery (Stephen 1959). All of these questions are discussed in the compiled works of Verzeano (1951), Dornette and Brechner (1959), Faulconer and Bickford (1960), Dornette (1964). The author's own experience shows that the use of EEG in anesthesiology is justified in those cases where the usual criteria for controlling narcosis are not available. As stated even in the literature (Martin *et al.* 1959), the main difficulty consists of inevitable artefacts (electrocautery, etc.). EEG changes after unilateral electroconvulsive therapy were followed by means of an integrator (d'Elia 1970). A very promising application of a simple registration of EEG amplitudes seems to be the long-term monitoring of patients suffering from cerebral anoxia (Prior *et al.* 1970).

The use of integrators is less adequate for mutual comparison of EEGs in various subjects. Thus, it was not possible to confirm any significant difference between a normal population and schizophrenics (Takahashi 1957). In similar studies, however, Bruck (1964) found higher voltage in normal controls.

Integrators are frequently employed in electromyography (for details, which could not be included here, see, *e.g.*, Yusevich 1970).

Amplitude distribution ("amplitude spectrum", "amplitude histogram"). The measurement may concern either a distribution of maximal amplitudes (*i.e.*, the peak values of each wave) or all instantaneous values of the voltage. The former method was used by Sato and Nakane (1948) who determined the amplitude of each wave and studied the statistical structure of values obtained. The latter is more usual, due to ease of technical realization; Lion and Winter (1953) devised a photoelectric apparatus, the method was simplified by Kozhevnikov and Mesherskij (1963), later by Tikal (1966). The measurement is based on densitometric evaluation of EEG activity, after multi-exposure photography from the CRO screen.

Drohocki (1962c) used large numbers of short epochs for integration, and the mean amplitudes served for similar studies on amplitude distribution. More advanced models of his integrator displayed the distribution (Drohocki 1970b). The amplitude distribution can easily be obtained as a part of complex data processing using a general-purpose or some special computer for bioelectrical data (*e.g.*, Cooper *et al.* 1968). Amplitude distribution is even used for control purposes during some computations. The resting EEG shows mostly a Gaussian distribution of amplitudes (Elul 1969b). Any influence changing the cooperative behaviour of the neuron population causes a deviation from the Gaussian distribution, according to Elul: the normal distribution is affected by mental activity and eye opening (Glass 1970) as well as during certain stages of physiological sleep (Adey *et al.* 1967c) but non-physiological factors like drugs (Drohocki 1970a), presence of paroxysmal events in the EEG (Dumermuth 1968) or localized brain lesions (Drohocki 1968a) are also detectable. Studies on the amplitude distribution increased the theoretical knowledge on relationships between micro- and macrogram (Elul 1967a; Frost and Elazar 1968; Lass 1968) and on the statistical nature of the background activity which resembles a filtered white noise (Saunders 1963). From the practical point of view, an interesting use of the method is the separation of various signals in multi-unit recordings (Dill *et al.* 1970). A simple on-line method for detection of the dependence between unit activity and amplitude of macropotentials has been described by Krekule and Walker (1971).

(d) Evaluation of the method

(Special methods like the use of relay circuits and computation of amplitude distribution are not included).

Positive features of integrators for EEG quantification may be summarized as follows:

1. The technique is perfectly elaborated and the probability of serious inaccuracies is minimal even in less equipped laboratories,
2. the result of measurement is quite understandable, well adapted to further statistical processing.

The following objections could arise:

1. The measurement concerns primarily the dominant activity and the information on less prominent components is suppressed.
2. Because the resulting information is limited to amplitudes, the examination should be carefully standardized and the output data cautiously evaluated. A general diminishing of amplitudes, for example, may accompany quite opposite functional states (arousal as well as drowsiness).
3. Various frequency components of the EEG have a different theoretical as well as practical significance but they are treated as equivalent parts of the brain activity.

2. *Period analysis*

(*a*) *Brief characteristics*

Periodometry ("base-line-crossing analysis", "interval analysis") is a method similar to amplitude analysis, dealing with wave-lengths (periods) instead of amplitudes:

1. The analysis is provided separately for each EEG derivation,
2. all EEG waves appearing in the input signal are taken into account, and
3. the method is based on measurement of wave-lengths.

Some more advanced modifications also concern amplitudes. Other modifications have improved the sensitivity to superposed EEG activity. Details on methodology and the theoretical background are described in Section IV.

(*b*) *Technique and its development*

A direct precursor of periodometry was the manual measuring of wave indices, *i.e.*, the percentage time occupied by the specified waves (alpha index—Davis and Davis 1936; delta index—Hoagland *et al.* 1938). Similar manual methods have been successfully applied recently (*e.g.* Glass 1967; Scheffner 1968; Giannitrapani 1969; Sulg 1969; Zhirmynskaya 1969; Otto 1971).

Various types of automatic devices which registered the period of waves were described independently by Prast (1951), Kozhevnikov (1955), Burch *et al.* (1956), Demetrescu (1957), Saltzberg *et al.* (1957b), Childers and Burch (1958), Zaander (1958) and Vieth *et al.* (1959). The analysis is based on determination of points where the EEG curve passes the zero level (base line). Distance between these points is considered the wave-length (Cohn 1963, 1967; MacIntyre *et al.* 1964), sometimes with amplitude limitation of the EEG signal (Shepalnikov and Shneiderov 1969).

Such a procedure could be easily done by digital processing (Burch 1964; Fink *et al.* 1964; Leader *et al.* 1967; Legewie and Probst 1969a).

The method was developed in various aspects. Firstly, some information on amplitudes was added. Some authors computed amplitude distribution independently (Fink *et al.* 1967; Bente and Ferner 1969). Tönnies (1961), later Schwarzer and Reetz (1966), Vatter *et al.* (1969) and Frost (1969) described more advanced methods which measure intervals between various points on the EEG curve at different amplitude levels. Marko and Petsche (1957) displayed the result of analysis as a graph with periods and amplitudes as coordinates. The method was later improved by Leader *et al.* (1967), Legewie and Probst (1969a) and Grémy *et al.* (1970). Some other authors combined the result of independent measurements of periods and amplitudes. It was possible to obtain quotients which corresponded well with small changes in the vigilance level (Riehl 1963; Nestianu and Bengelescu 1966; Voitinski and Prianishnikov 1966; Doroshensko *et al.* 1970). An effective data-reduction by measuring only mean periods and mean amplitudes has been published (Hjort 1970). A simple device for measuring the instantaneous frequency of the dominant activity has been described by Špunda and Radil-Weiss (1972).

Quite another type of modification was intended to improve the information on superimposed activity. For special purposes it was profitable to extract some components by prefiltering the EEG signal (Schwarzer and Reetz 1966; Šimonová and Scheich 1968; Frost 1969). In an effort to arrive at a better definition of the waveform and thus to involve the superimposed activity, even mid-points and points of maximal deflection were considered (Leader *et al.* 1967). Similar important points could be determined more precisely by using also the first and second derivatives (primary, intermediate and minor zero crossing points—Silverman *et al.* 1956; Saltzberg and Burch 1957a, 1959; Burch and Childers 1961; Burch 1964).

(*c*) *Application*

As will be shown later (see Section IV) the method is very suitable for drug studies (Fink *et al.* 1967; Itil 1968; Saltzberg *et al.* 1970; Schwartz *et al.* 1971). Effects of bilateral and unilateral electroconvulsive treatment were studied by Volavka *et al.* (1972). Besides that, measurements of wave-periods enabled the dynamics of physiological sleep to be followed (Burch *et al.* 1955; Roessler *et al.* 1970; Itil and Saletu 1971) as well as small shifts of the vigilance level during various mental tasks (Cohen *et al.* 1963; Shmavonian *et al.* 1964; Grünewald *et al.* 1968; Šimonová and Scheich 1968; Koukou *et al.* 1969; Legewie and Probst 1969a). The median period of dominant activity seems to be a simple but efficient age-dependent parameter (Pechstein 1970; Manovskij and Belonog 1971). Period analysis was used even in theoretical studies on slow and "ultra-slow" fluctuation of EEG background activity (Voitinski 1964; Scheich 1969) and for correlation between EEG and ECG (Cohn 1963). Due to neglect of amplitudes, the method was profitable even in following very fast frequencies (MacIntyre *et al.* 1964). Less known is the possible applicability of period analysis in electromyography (Dowling *et al.* 1968).

(d) Evaluation

The advantages of period analysis are most often discussed in comparison with frequency analysis:

1. Some authors believe that neglecting amplitudes improves the correlation with clinical data (Friedländer 1958; Obrist and Henry 1958; Creutzfeldt *et al.* 1969).

2. Some advantages of processing the EEG as an aperiodic signal have been pointed out (Forbes 1950).

3. According to various authors the method gains relevant data in a less complicated, or better defined way, when compared with digital or analog filtering (Cohn 1967; Reetz 1969; Saltzberg and Burch 1971).

4. This could be explained by the fact that the information on amplitudes is often redundant because the periods and amplitudes of EEG waves are proportional (Travis and Knott 1937; Brazier *et al.* 1944; Carrie 1969).

5. The method is very effective when using digital computers.

Possible objections:

1. The original method of analysis prefers EEG components of comparatively high amplitude (Wiener 1953) and – if the amplitudes are similar—of short duration (Chapman 1964). Therefore, a complicated relationship between amplitudes of various EEG components influences the resulting data.

2. The use of derivatives solves most of these problems, but the results are hardly interpretable in conventional EEG terminology.

3. Of less importance perhaps is the fact that only waves exceeding a certain amplitude limit are considered. Thus, the results are influenced by a factor which is artificial.

4. Some empirical as well as statistical findings are contradictory to the opinion that the information on amplitudes of EEG waves is redundant (Berkhout 1965). This is true particularly in pathological recordings where the amplitude distribution deviates from the Gaussian.

3. *Frequency analysis*

(a) Brief characteristics

1. The analysis is provided independently for each EEG derivation.

2. Periodically occurring components are preferentially represented, but distinguishing between periodic and aperiodic activity is of little practical significance in the final result.

3. The method is based on dividing various EEG components according to their frequency; the amount of activity is evaluated more or less separately in each frequency band.

There are two practical differences between frequency and period analysis. Firstly, both dominant and superimposed activity are evaluated independently in frequency analysis, and secondly, the information on amplitudes is included in the result of frequency analysis.