HANDBOOK OF ELECTROENCEPHALOGRAPHY AND CLINICAL NEUROPHYSIOLOGY

EDITOR-IN-CHIEF A. REMOND

VOLUME 4

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

EDITOR: M. A. B. BRAZIER
Brain Research Institute, University of California Medical Center, Los Angeles, Calif. (U.S.A.)

PART A

Sampling, Conversion and Measurement of Bioelectrical Phenomena

EDITOR: F. H. LOPES DA SILVA
Institute of Medical Physics T.N.O., Utrecht (The Netherlands)

ELSEVIER

HANDBOOK OF ELECTROENCEPHALOGRAPHY AND CLINICAL NEUROPHYSIOLOGY

Editor-in-Chief: **Antoine Rémond**
Centre National de la Recherche Scientifique, Paris (France)

VOLUME 4

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

Editor: **M. A. B. Brazier**
Brain Research Institute, University of California
Medical Center, Los Angeles, Calif. (U.S.A.)

PART A

Sampling, Conversion and Measurement of Bioelectrical Phenomena

Editor: **F. H. Lopes da Silva**
Institute of Medical Physics T.N.O., Utrecht (The Netherlands)

Elsevier Scientific Publishing Company – Amsterdam – The Netherlands

International Federation of Societies for EEG and Clinical Neurophysiology

ISBN 0-444-41418-5

Printed in The Netherlands

Sole distributor for Japan:
Igaku Shoin Ltd.
5-29-11 Hongo Bunkyo-ku
Tokyo

All other countries:
Elsevier Scientific Publishing Company
Amsterdam, The Netherlands

International Federation of Societies for EEG and Clinical Neurophysiology

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.

ISBN 0-444-41418-5

Elsevier Scientific Publishing Company, Jan van Galenstraat 335, Amsterdam
Printed in The Netherlands

Sole distributor for Japan:
Igaku Shoin Ltd.
5-29-11 Hongo Bunkyo-ku
Tokyo

All other countries:
Elsevier Scientific Publishing Company
Amsterdam, The Netherlands

Cover design by H. Sturris

PART A

SAMPLING, CONVERSION AND MEASUREMENT OF BIOELECTRICAL PHENOMENA

Editor: **F. H. Lopes da Silva**
Institute of Medical Physics T.N.O., Utrecht (The Netherlands)

Collaborators:

R. Cooper, *Burden Neurological Institute, Bristol (England)*

G. Dumermuth, *Children's Hospital, Zurich (Switzerland)*

A. Kamp, *Institute of Medical Physics T.N.O., Utrecht (The Netherlands)*

F. H. Lopes da Silva, *Institute of Medical Physics T.N.O., Utrecht (The Netherlands)*

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

Preface

This Part is dedicated to the treatment of the technical and methodological problems which arise at the stage in which electroencephalographic data are being prepared for use in the computer. In the last few years there has been a growing interest in the application of methods of digital computer analysis in EEG laboratories. The time when an EEG lab was limited to a set of ink-writers and included, possibly, some analogue or simple digital analyser is largely past. The new possibilities offered by computer analysis are being critically examined and in some places these are becoming part of the laboratory routine. Quite evidently these new possibilities force electroencephalographers to change their way of thinking about the organization of their laboratories; whether a small or medium computer is at their disposal in the neighbourhood, or a terminal is available, or simply their tape recorded EEGs can be brought to a computer centre, the central problem is the same: the EEGs have to be recorded in such a way that further computer data processing should be possible. This problem forms the essence of this Part. On the one hand it should be seen as a complement to Volume 3 where the main theme is the acquisition and recording of EEG data. On the other, it embraces the basic technical steps which permit EEG data to be treated by a digital computer, the topic which constitutes the central problem of Volume 4, Part B. Thus Volume 4, Part A occupies a strategic position between acquisition and analysis of data. It constitutes a real interface.

The authors of the different Sections agreed on dealing with this problem in a practical way by treating in succession the following items: (1) The present and foreseeable uses of computers in EEG and clinical neurophysiology; (2) The structure and function of computerized systems; (3) The structure of digital computers and computation; (4) Sampling and data reduction; (5) Time tracking; (6) Direct computer processing. This succession of items forms an attempt to give the reader an idea of why he should compute his EEGs, of how he has to prepare his recordings in order to enter the computer and select the epochs of interest and of the sort of computers he will find useful and, finally, on which types of results he may expect from actual computations. This volume has not, of course, the pretention of being exhaustive in the technical treatment of the subject. Many technical issues are also dealt with in other volumes and in technical literature. The objective is mainly to bring together into a readable digest a few of the relevant technical aspects from a wide range of sources. This may be useful to the electroencephalographer and clinical neurophysiologist who wish to obtain relevant information on the problems involved in the preparation of their data for use in a digital computer. A problem often encountered in this field is that of terminology. Therefore, it appeared useful to include a glossary of computer terminology, prepared by Donald Walter, which may help the electroencephalographer in the intricate jargon of the computer room.

Section I. Present and Foreseeable Uses of Computers in EEG and Clinical Neurophysiology

A. IN RESEARCH

Computer uses for research in EEG and clinical neurophysiology are almost as wide as the fields themselves. Indeed, it is difficult to mention a branch of those fields for which computers have not at least been proposed; and usually at least one laboratory has attempted the proposed application. Within this broad field, only two recent tendencies seem worth calling specifically to readers' attention: one is the increasing use of multi-channel, multi-function recording and processing; generally, this goes under the name of polygraphy, and has been widely applied in sleep research, psychophysiological studies of many kinds, and research into the causes of crib death, *i.e.*, sudden infant death, as well as in some clinical systems mentioned below. The second tendency, which has not spread so widely in present research as predicted it will in the near future, is the incorporation of computer technology as an integral part of systems which assist in preparing the subject in a more specific psychological state or series of states than has been customary heretofore. Outstanding examples are the work of the Bristol group (see W. Grey Walter 1975).

B. IN CLINICAL EEG

In the last several years, groups from several countries have proposed systems intended as contributions to standard clinical EEG practice; many of these were reported at the 8th International Congress of EEG and Clinical Neurophysiology (Sherwood and Wilson 1971; Ebe *et al.* 1973; Findji *et al.* 1973a; Gloor *et al.* 1973; Harner 1973; MacGillivray *et al.* 1973; Matoušek *et al.* 1973a; Samson-Dollfus *et* al. 1973). A few examples will be discussed in Section VI. These systems are quite varied in their goals and in their means. A useful classification scheme recently proposed by Lopes da Silva (1975b) considers separately those systems which are directed toward: (1) supporting; (2) extending; or (3) replacing the clinical EEGer in the usual exercise of his functions. Supporting systems, such as those of Sherwood and Wilson (1971) or of Harner (1973) have been directed principally toward computer-aided compilation and typing of the standard clinical EEG report; since they make a sensible division of labor between neurologist (perception and evaluation) and machine (accumulation, tabulation, typing a text which is mainly routine), they are immediately practical. They also tend to contribute both to EEG training and to communication between practitioners, because they encourage (though they do not insist on) gradually increasing standardization of terminology and criteria, while leaving to the neurologist's judgement the choice as to which of these improvements to incorporate in further adaptations of the system.

Those systems which seem intended for extending the capabilities of EEGers are numerous, partly perhaps because by directing themselves to new capabilities, they need not fit in immediately with current practice. The approaches nurtured by linear systems theory naturally lead to summation of successive amplitudes, matching with sinusoids, an analogous operation not directly resembling human perceptions. In contrast, the systems of Findji *et al.* (1973a, b) and of Samson-Dolfuss *et al.* (1973) attempt to replace such operations with more direct attention to the wave forms (or even half-wave forms). This approach is represented in research applications, also by several workers (Schenk 1972, 1973; Harner 1975a), and can be related to some developments in systems theory. The systems of Gloor *et al.* (1973) and of Matoušek *et al.* (1973a) are directed toward specific clinical extensions of EEG capabilities, the first toward hemispheric tumor detection and diagnosis, the second toward generalized or focal slowing, or other definite EEG finding. Both systems make a special effort to design their forms of communication with other medical specialists, in the attempt to produce output diagrams which can be relatively easily interpreted without special training.

The systems of Ebe *et al.* (1973) and of MacGillivray *et al.* (1973, 1975) are frankly intended to replace the EEGer in his current practice, presumably for the purpose of freeing him for more difficult diagnostic or prognostic tasks, or perhaps for preparing the automation of those more difficult tasks. Their main difference from the "support" or "extension" systems is that "replacement" systems need to accept an unselected mixture of EEG examination results, and for each of them produce an acceptable diagnosis or other disposition (among which, "Needs human attention for interpretation" is acceptable only a small proportion of the time).

Another use of computers to extend the capabilities of the EEG is their use as aids in diagnosing brain death. Although the sometimes accepted criteria of such a diagnosis need not include the computer, it is natural to use a machine's addition to human sensitivity to increase the confidence which can be placed on such an essentially negative diagnosis. Some applications have used only an averager, to enhance any evoked potential (Gerin *et al.* 1969; Oftedal *et al.* 1971), but others have also sought in the power spectrum for additional confirmation (Bickford *et al.* 1971b). Further applications of computer processing in EEG and clinical neurophysiology are presented and discussed in Section VI of this Part.

C. IN OTHER ELECTROPHYSIOLOGICAL LABORATORIES

For EMG, special averagers are more common than general-purpose computers; these are treated in Volume 4 Part B.

A growing application of computers, at present represented principally by averagers, but which may be supplemented by software-programmed machines in the near future, is audiometry by evoked potentials. When the subject is uncooperative, either because of psychopathology, unconsciousness, or infancy, then a method of audiometry which depends only on physiological intactness of transmission pathways is valuable. Recently, Hecox and Galambos (1974) have proposed use of the recently discovered (Jewett and Williston 1971) short-latency auditory evoked potentials (in the range 2–10 milliseconds after a click) as a routine clinical test. One advantage of these waves from a physiological viewpoint is that they seem to test integrity of afferent nerves and brain-stem nuclei; from an operational viewpoint, they are convenient because they are essentially unaffected by attentiveness, drowsiness or sleep. The reason that averagers may soon be supplemented by more capable machines is the need to shorten the time required for such measurements; Krishman and Tuteur (1974) reported an application of frequency-domain computations which has just this effect in such audiometry.

Another special laboratory procedure which can be aided by computers in the case of uncooperative or non-verbal subjects is visual refraction correction (Harter and White 1968, 1970; White and Bonelli 1970). Here, particular features of the visually evoked potential are used as criteria for best refraction correction; in view of the recent demonstration, that long-uncorrected astigmatism can leave residual effects on cerebral visual sensitivity even after correction, it seems likely that early correction, at least of the most pronounced abnormalities, may be a valuable therapeutic possibility.

Other kinds of neurological diagnosis of sensory pathways have been mechanized by individual workers as a research effort, and it is this author's belief that such methods will penetrate increasingly into clinical practice; these areas include diagnosis of spinal shock, assessment of severity of sensory involvement in multiple sclerosis, etc. (see Sclabassi *et al.* 1974).

A slightly different area is automatic measurement and statistical evaluation of nystagmus in vestibular testing (Honrubia *et al.* 1971a, b, 1973). Here, the computer is programmed to make various measurements on the electroculographic (EOG) record, and is supplied with definitions of what constitutes nystagmus of any grade, and how to evaluate the grades separately.

A possible application, whose future growth one can also predict, is the use of the computer to perform more objective language assessment and perhaps therapy. Although the computer is essentially an auditory and graphemic receptive aphasic, it can present stimuli constituting many kinds of language tests, and record the patient's responses in various ways. Advantages of such testing would be conservation of the language-therapist's or linguist's time, especially if the patient were emotionally disturbed and likely to delay responding to a person; and that the testing is clearly documented and presented in an objectively repeatable manner. If such testing were to be combined with physiological recordings, accepted and analyzed in correlation with stimuli and responses, the result should be greatly increased diagnostic power, and perhaps therapeutic ability.

Section II. Structure and Function of Computerized Systems

A. THE DECISION TO COMPUTERIZE

As outlined in Volume 4, Part B, one valuable aspect of the attempt to decide whether or not to solve a particular problem by computer is the analysis of the problem which must be undertaken. The investigator sometimes realizes that his problem can be more economically solved otherwise than by computer. This is probably the most sensible conclusion if the problem is a one-time operation, with a rather low amount of continuing effort; in such a problem, the investment in "getting started" will be so great that it is quite unlikely to justify computerization.

In contrast, if the desired operation is long-continuing, fairly complicated (in the sense that there are many alternative paths in the flow chart of its operations) or is heavily computational by its definition (spectral analysis is a typical example of this type), and if the task is rather well-defined and unchanging (or only slowly changing), then a computerized system is likely to be a worthwhile investment. Of course, the degree to which a task seems "well-defined" may appear quite differently to the investigator, after he has tried to specify it to the computer (or the programmer), as investigators of sleep records quickly found. Indeed, the fact that very few centers actually use computers (even special-purpose ones) for automatic scoring of sleep records shows that an extremely high standard of definition is required, if computers are competing to perform tasks for which trained humans are well adapted.

B. AVAILABILITY OR ACCESSIBILITY OF EQUIPMENT AND PERSONNEL

Unless the personnel and equipment for the desired study are already present and functional in the laboratory, it will be necessary to consider their acquisition and maintenance. The same or different individuals may be required to study, design, produce, install, debug, maintain, operate, update, apply, and adjust any and all equipment ("hardware") and programs ("software") involved in the project. If the personnel for all these operations are not identical, then there will be need for communication and documentation, probably in fact for new learning and instruction (formal or informal), in order that the purpose, characteristics and operations of the new hardware and/or software will be sufficiently understood by all relevant personnel. If the equipment is anything but a standard item already used in other laboratories, there may well be additional problems of interfacing (designing, installing and debugging the connections between disparate equipment items), which require communication and common understanding between specialists in the two items interfaced.

C. OPERATING DEFINITION OF THE TOTAL SYSTEM

The major output of the design study should include a clear definition of the operation of the total system envisaged, within its environment. This will include inputs of data from the patient or subject's physiological functioning, inputs of identifying information such as the subject's name, along perhaps with other identifying numbers or codes such as medical record number, the data and perhaps time of day, possibly physicians' or nurses' comments or evaluations of the patient's condition, and perhaps an identification of the operator of the computerized system for that day. Also included in the operation specification should be a specification of outputs: computer-controlled stimuli to the patient or subject, graphical and typewritten results, perhaps intermediate verification of proper operation and data acquisition, numerical outputs for later use in summarizing across patients (these to be stored preferably on relatively safe and slow media such as magnetic tape or paper tape, rather than relatively volatile and fast media such as disks—these may be over-written by some other system user). Incidental outputs may include statistical data on the use of the computer system, accounting information for adding to the patient's bill, etc.

Other considerations in systems definition include availability and accessibility of the computer and the rest of the system: at what hours will it be needed for this use and for other uses? How rapidly and with what priority will operation need to be established? How reliably does the system need to be available—can availability of the computer be allowed to depend on visits of maintenance engineers, or must system reliability be guaranteed by having specialized personnel available at all times, as well as perhaps a duplicate computer system? Relative evaluation of costs and benefits of having the computerized system always available, *vs.* occasionally unavailable, *vs.* frequently unavailable, need examination; but computerized systems are not unique in being occasionally unavailable due to malfunction—the same may happen to electroencephalographs, X-ray systems, and any other device. Study of the adaptations in medical-system operations under malfunction of such previously known equipment can give guidance toward what relative costs and benefits to assign to different degrees of availability and reliability of computerized systems.

One advantage, from the user's viewpoint, of computerized systems, is that their malfunctions are total. This habit of computers comes from their serial organization, such that many operations serially use the same machine components; thus a malfunction will often produce obvious error. This is an advantage because if the system works at all, there is a good chance that it is working correctly.

Other system considerations include space for the system to operate in, and the somewhat specialized physical environments which many computing machines still require, including special demands on air-conditioning, temperature, and electric power.

A special aspect of outputs from a computerized system is the need to prepare the results in a form easily read and interpreted by all its potential users. Developers of systems intended for clinical use need to give special attention to creating comprehensible outputs, or else to training users and their associates in how to read and interpret the outputs which will be made available. In practice the critical difference between a successfully accepted computerized system and a failure may be localized solely in the comprehensibility of their outputs; of course, it may be that system designers who are willing to take the trouble to develop a comprehensible output form are also likely to consider the relations between their work and that of their users, and adapt their own work accordingly.

Discussion of the time on the computer needed to debug its programs is expanded on in a later Section (III.D.1).

D. STRUCTURE AND ARCHITECTURE OF COMPUTERIZED SYSTEMS IN EEG AND CLINICAL NEUROPHYSIOLOGY

Almost all physiologically important computer systems are the result of mixing at a gross level (grafting, rather than hybridization, in botanical terms) between simple analog processing (amplification, filtering, etc.), interfaces between analog and digital words (analog–digital converters, digital–analog converters), and the digital representations used within the computer. Other inputs and outputs, such as switches and indicator lamps, may be discrete and digital in effect, although their operation in fact incorporates analog action (moving the switch position from up to down, ...). Similarly, the digital representations internal to the computer are composed of exaggerated analog tendencies, in which amplifiers are driven into one extreme state or another; but the coding is entirely different, because the time-scale of operations is entirely different.

A system has input, action and output; but these can be conceived on various levels of generality. At one level, a computerized system will have as its input, data from the physiological functioning of the patient; its action will be to extract parameters placing that functioning on a scale of normality or adequacy or the like; its output is the printing or diagramming of these parameters. From a larger viewpoint, the input to the system is from patients having a certain class of diagnoses, which the system is intended to make more precise; the output is refined or improved diagnoses. From yet another viewpoint, the input of the system is from patients' medical records (and electric power and office and laboratory space); the action is to add to the medical record and to the technician's or operator's time card (as well as occasional items on the maintenance account); and the output is incremented medical records, and accounting documents requiring payment. Finally, the system can be viewed as a user of programs and a consumer of programming time, whose outputs are programs which can be distributed and used by other owners of machines sufficiently similar to the parent machine, and improved scientific or medical knowledge.

From the low-level viewpoint which considers only the visible hardware, most physiologically interesting computerized systems include sensors and/or transducers, a sensor-computer interface (often containing an analog–digital converter, when the computer is digital), the computer itself (viewed as a single item for the present discussion), output on typewriters, graph plotters or oscilloscopes, intermediate storage on media such as digital magnetic tape, and the operator who verifies generally correct operation. If the computer is analog, that is, one whose data transformations remain within the form of measurable voltages, the interface may consist only of impedance-matching amplifiers. Examples might be simple filters, active filters, analog averaging devices, oscilloscopes used for superposition studies, and the like. Such machines have sometimes been used for anesthesia monitoring, to ring an alarm whenever the amplitude of some frequency bands became too high.

Section III. Structure of Digital Computers and Computation

A. MACHINE ARCHITECTURE

Contemporary digital computers ("machines" will be our general terminology in this Section) have all opted for packaging their numbers and other information transactions exlusively in terms of "words", which are most easily identified by the fact that they have a single address in memory (which still is usually core memory), and are stored therein and fetched therefrom by a single instruction or machine command. The decimal number system is almost extinct internally, and is replaced by binary, with groupings in terms of octal or else hexadecimal groupings of the binary places, or bits.

There are four classes of digital computers, in current and near-future laboratory practice: fixed-program machines (almost exclusively averagers—these are treated in other volumes) and general-purpose computers in three subclasses: large computers (discussed in Volume 4, Part B), minicomputers (the conventional laboratory general computer of today) and microprocessors (which seem likely invaders of laboratories in the near future).

The microprocessors are not yet widely available; they can be considered as likely to replace minicomputers for large-volume, routine operations, such as data monitoring, analog–digital conversion and simple artifact suppression, and perhaps future averaging operations. Their disadvantages at present are their relatively lower speed and flexibility, and the difficulty of programming them; these factors make large-volume operations the most likely candidates for microprocessor application. Since previously known minicomputers are also being produced and marketed at continually decreasing prices, and already have programs written for their earlier versions, which can be adapted at little expense, the micro-processor market will have stiff competition from them, for other laboratory applications.

The most widespread kind of digital computer is the minicomputer. It typically consists of memory, central processing unit (CPU), and peripherals. Memory is usually a core memory capable of storing between 4,000 and perhaps 32,000 words, each word containing either one data value, or else one machine command (or in some machines, one-half a machine command). The CPU contains a few to several arithmetic registers, in which numbers can be written or read, added, complemented (changed in sign), and perhaps multiplied and divided. It also contains the command register, which holds the command currently being performed, and an address register which controls the arrival of the next command to be executed. Many variations and additions to this basic set of registers are made part of the CPU in various minicomputers.

1. Peripherals

Peripherals vary widely in function and include magnetic tape units, disks (fixed-head, moving-head, or nowadays, floppy disks), typewriters or line printers, plotters (ink-writing, electrostatic or cathode-ray tube), analog-to-digital and/or digital-to-analog converters, telephone modulator–demodulators ("modems") for inter-computer communication, computer-controlled relays, and computer-readable "sense lines", and probably other pieces of equipment in special circumstances. The reason for including all these under the single rubric "peripherals" is that, from the viewpoint of the CPU, they are all addressed and operated in rather similar ways. In this domain, as in that of the CPU itself, some modifications and special features in the design of particular machines may modify the relationship of particular peripheral units to the rest of the machine; for instance, some tape units and some analog–digital and digital–analog converters have, in addition to their control from the CPU, a direct access channel to the memory; such units, when started by the CPU, can then carry out data transmission to or from memory, without further commands from the CPU. Such a peripheral then "notifies" the CPU when it has finished the task initiated.

As implied above, minicomputers respond to commands, which are stored as sequences of bits in words, in various locations in the memory, just as, in other parts of the memory, data coded into strings of bits are stored. As will be explained in a later section, bit strings representing commands and especially the addresses of the data on which the commands are to operate *can be treated as data are treated, i.e.*, addresses within commands themselves can be incremented, and this capability adds great power to such machines.

2. Interfaces

Regardless of how simple or elaborate is the organization of what is considered as one individual digital computer, it can be thought of as analogous to a biological individual (some networks of computers now threaten to resemble weeds in the garden, but we will be concerned here only with clearly individual machines). Under this concept, each individual machine has some sensory, or input faces, and some effector, or output faces. In a typical laboratory minicomputer, the input faces are the A/DC, the sense lines, the typewriter keyboard, and in part, the magnetic tapes and disks. Its output faces may include those same tapes and disks, the typewriter paper, and the paper or CRT surface of the plotter. If the machine has a modem, this is usually both an input and output face.

Each input face has its own characteristics and limitations, in physical parameters (electronic and temporal) and in information-carrying capacity; matching these with the corresponding characteristics of the external devices (amplifiers, plotters, human users, etc.) constitutes the new specialty of "interfacing".