CRC Handbook of Engineering in Medicine and Biology

Section B
Instruments and Measurements
Volume I

Editor

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FOREWORD

In the process of preparing the material for the second volume of this Handbook Series, the editors became impressed by the rapid strides made in analytical and diagnostic instruments for health sciences. The ready availability of many computers and microprocesses has brought us to the threshold of a new generation of "smart" devices and systems in addition to the computerized axial tomographic systems, automated clinical laboratories, and patient-monitoring devices already in the market place.

On the other hand, progress in basic theory has shown few major advances since Volume I, and this observation should come as no surprise. Biomedical engineering is still a very young discipline and tends to operate largely at the descriptive level even when mathematical formulations are used. Consequently, with the notable exception of such areas as biomechanics and biomaterials, much of the data in the field better fits an encyclopedic rather than a handbook format. This conclusion is reflected in the style and content in Volumes I and II of the series. The editors anticipate a change in the style of future volumes as additional quantitative data becomes available in specialized areas of research and application.

The goal of this publishing effort as stated in Volume I is to organize and compile the body of knowledge which constitutes the core of engineering in medicine and biology. This locus inevitably reflects the interest and biases of the editors who are accutely aware of this limitation. Consequently, the advice and counsel of colleagues and friends from other fields is earnestly solicited. Subsequent volumes will be primarily thematic and will appear at appropriate times. We wish to express our gratitude to the contributors, our families, and the known and unknown people at CRC Press whose continuing encouragement and support made this task achievable.

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September 1978

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Dr. Feinberg received a B.S. in both Electrical Engineering and Mathematics from the University of Michigan in 1962. He received a Masters of Electrical Engineering from the University of Louisville in 1964, and a Ph.D. in Engineering from Case Institute of Technology at Case Western Reserve University in 1968.

Dr. Feinberg is a member of the Institute of Electrical and Electronic Engineers and the Association for the Advancement of Medical Instrumentation, as well as other honorary organizations. He is currently conducting research in clinical and biomedical engineering and has authored numerous papers in this area. He is also a Registered Professional Engineer and a Certified Clinical Engineer.

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From 1968 to 1970 Dr. Fleming was President of the IEEE Group on Engineering in Medicine and Biology. During the same time, Dr. Fleming also served as Chairman of the ASEE's Bio-and-Medical Engineering Committee. He also was a member of the Joint Committee on Engineering in Medicine and Biology from 1965 to 1970, acting as chairman in 1967.

Dr. Fleming's major research interest is biomedical instrumentation for high-risk infants and studies of physiological systems. He has authored many articles in these areas and holds numerous patents in the area of instrumentation

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TABLE OF CONTENTS

Electronics and Instrumentation

INSTRUMENTATION FOR BIOELECTRIC MEASUREMENTS

A. M. Dymond

INTRODUCTION

Most physiological processes result in the generation of electrical signals. The measurement and analysis of these biopotentials define the field of electrophysiology, which has provided much of the present knowledge of biological functioning. Bioelectric measurements are of fundamental importance not only to the basic researcher, but also to the clinician who uses these measurements for diagnosis and evaluation of patients. The purpose of this chapter is to summarize some of the considerations necessary for acquisition, signal conditioning, and storage of these biopotentials.

The basic series of steps which must be followed to obtain a biopotential in an analyzable form involve sensing the potential from the tissue, signal amplification and filtering, and signal display and storage. Sensing the biopotential involves placing electrodes in contact with the tissue and, depending on the application, many different types of electrodes are used. When recording a potential such as the electroencephalogram (EEG) from the surface of the skin, large electrodes which contact the subject through a conductive paste are generally used. When it is desired to record the potential from a single cell, such as an individual muscle fiber or a neuron in the brain, microelectrodes are used which may have tip diameters on the order of one micron. These electrodes are implanted inside of the body and make use of the conductive body fluids to interface between the electrode and the electrically active tissue.

Because of their small amplitudes, bioelectric signals require amplification. Amplifier specifications can vary substantially between different applications, but the requirement to obtain low-level signals in an electrically noisy environment has resulted in the use of the differential amplifier in many bioelectric amplification systems. The proper use of the differential amplifier, along with the identification of sources and control methods of interfering signals, must be considered when attempting to develop a signal amplification system. It must also be remembered that amplification is a process which can transform not only the amplitude of an input signal, but also the phase relationships. Any unwanted change in either of these parameters can result in significant data distortion.

Once the biopotential has been amplified to a useable level, it is necessary to record or display it in some format where it can be analyzed. This can be a relatively straightforward process, such as displaying a waveform on an oscilloscope. More frequently, however, it is desired to make a permanent record for a detailed visual examination and analysis.

There is also an increasing tendency to store the data in a format where it can be subjected at a later time to further analyses by analog or digital devices. The type of data storage necessary depends upon both the nature of the signal and the analysis requirements. Storage of data for visual examination may be satisfied through photographic techniques, ink or thermal writing recorders, or electrostatic recorders. Data storage in an electrical format suitable for later electronic analysis is most frequently done using magnetic tape. Here again, various approaches can be taken to recording the data. All of these modes of data storage have various advantages and disadvantages.

When complex data is being stored either on paper or electronically, it is often

desirable to include some type of coding information which will facilitate location and identification of data segments at a later time. This can be accomplished in a variety of ways, such as by putting marking pulses between segments of data or devoting a tape channel to a time-code generator.

In order to make successful bioelectric measurements, it is necessary to consider all of these different aspects and to view all of the instrumentation as a system, as well as focusing on each part of the instrumentation. The biomedical engineer developing bioelectric measurement systems must be familiar with the underlying physiological functions being measured, the electrochemistry of the recording electrodes, and the various aspects of electrical engineering involved in conditioning and storing the data. This instrumentation must be viewed as a system because its various components must be able to adequately function and interact while being able to withstand different interfering influences from the surrounding environment.

ACQUIRING THE BIOPOTENTIAL

Electrodes for Different Tasks

Biopotentials are sensed by placing electrodes in contact with the tissues. These electrodes are passive in the sense that they are not intended to pass current or otherwise stimulate the tissues, but, rather, they are intended to sense the potential between different points. As is shown in Figure 1, biopotential electrodes can be functionally separated into three classes: bare-metal electrodes, pipettes, and insulated electrodes.

The bare-metal electrodes are perhaps the most frequently used type and are characterized by having the bare surface of a metal probe in contact with the tissues through an electrolytic medium. An electrolyte is needed to provide a conductive pathway between the metal and the electrically active tissues. Various metals are used for recording electrodes, with noble metals and surgical-grade stainless steel being the most common. Systems such as the silver-silver chloride electrode can also be considered to belong to this group. Since metal electrodes have such an important role in monitoring, they will be discussed in more detail later.

Pipette electrodes make contact with the tissues through an electrolyte column

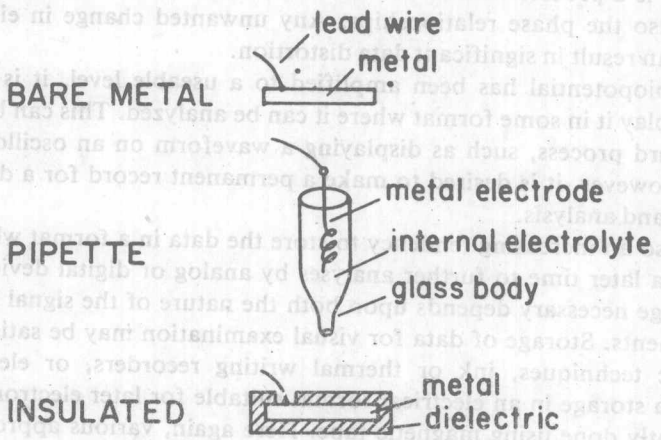

FIGURE 1. The three basic types of biopotential-recording electrodes. These electrodes can appear in many different forms, and only simple configurations are shown here.

PASSIVE BIOPOTENTIAL ELECTRODES

FIGURE 2. Dimensions for further classifying the basic types of electrodes.

contained in glass or some other insulating material. The electrode tip is often pulled down to a small dimension to allow penetration of individual cells. A silver chloride electrode placed in the body of the tube provides the connection between the electrolyte within the tube and the electronic amplifying circuitry. The micropipette finds its major application in biology by being able to measure both DC and AC voltages from the inside of an individual cell.

Insulated electrodes sense biopotentials only by capacitive coupling across a dielectric and, therefore, do not require an electrolyte. The dielectric prevents any direct connection between the tissues and the recording circuitry. It also results in a very high impedance, and special high-input-impedance circuitry is required to record from these electrodes.

There are other dimensions which characterize recording electrodes, and Figure 2 illustrates one procedure for their further classification. Electrodes may be categorized according to their size as being either macroelectrodes or microelectrodes. Macroelectrodes tend to be large relative to the dimensions of the cells in the tissue under study, and they are generally used to record the combined potential arising from an aggregate of cells. An EEG disk electrode on the order of 1 cm^2 and situated on the scalp is an example of a macroelectrode. Microelectrodes, on the other hand, are intended to record the electrical activity arising from one or, at most, a few cells. In order to do this, it is necessary to get the electrode in close proximity to the cells. Either bare metal electrodes or pipettes are used in this application, where tip diameters on the order of one micron are frequently employed. Various procedures are used to fabricate these electrodes, such as electrical etching in the case of metal microelectrodes and heat pulling of capillary tubing in the case of micropipettes.

Electrodes can also be grouped depending on whether they will be used externally on the surface of the body or internally. External recordings are usually done using bare metal or insulated macroelectrodes. When used externally, the bare metal electrodes must be provided with some type of electrolyte to couple the electrode to the tissues. This electrolytic coupling is not necessary with internal bare metal electrodes since the electrolytic tissue fluid surrounding the electrode provides the necessary coupling.

Biopotential electrodes may be further subdivided on the basis of acute versus chronic use. Acute use implies a fairly short duration, while chronic application suggests the electrode would be used for a more prolonged period of time. There are no hard rules for defining acute versus chronic application, but a consensus might be to base this separation on whether the electrode would be used for more than 24 hr.

Chronic application of biopotential electrodes can pose difficulties, particularly with microelectrodes. When micropipettes are used, diffusion of the concentrated

electrolyte out of the pipette body will eventually degrade performance. With either bare metal or pipette microelectrodes, the necessary close proximity of the electrode tip to the cells being recorded poses a severe problem in localized tissue damage around the tip during chronic recordings. Cells such as the neurons in the brain have nominal diameters of μm, and the electrode tip must be adjacent to these cells in order to obtain recordings. Even small motions in the electrode-tissue system will result in whipping of the electrode tip and destruction of the cells immediately surrounding it. The problem is particularly severe for intercellular micropipette recordings where the pipette is actually inserted into the interior of the cell. Elaborate measures must be employed in these studies to decouple motion from the system.

Another problem which must be considered in chronic recordings is the condition of the electrolyte coupling the bare metal to the tissues.[1,2] This is not a problem when the electrode is implanted,[3] but it becomes a matter for some concern in the case of chronic external recordings. In this case, drying of the coupling paste can result in increasing source impedance and erratic behavior. Some conductive electrode pastes have been developed which have minimal degradation over time and are more suitable for long-term recordings. An alternative approach to this problem has been to use conductive paint applied directly to the skin. By using perspiration trapped between the conductive paint and the skin as an electrolyte, the need to apply and renew a conductive paste is eliminated.

Engineering Characteristics of Metal Electrode Systems

A key point to note in understanding electrode behavior is that when biopotential measurements are being made, some current must flow through the entire amplifier-electrode-tissue system. This current is carried by electrons through the metal, wiring, and electronic circuitry of the electrode system. However, the current is carried by ions in the tissue, and, in order for the current to be continuous, there must be some type of charge transfer mechanism in operation at the electrode surface.

Metal electrodes are used most frequently for recording biopotentials.[4] The behavior of these electrodes is controlled by the physical and chemical properties of the metal-tissue interface,[5] which is shown in an idealized form in Figure 3. When the bare-metal surface of the electrode is placed in contact with either the electrode paste or the tissue fluids, thermodynamic forces attempt to bring the two mediums into electrochemical equilibrium. Various chemical reactions underly this process for obtaining equilibrium, and an electrical potential is usually developed between the metal and the electrolyte. This potential causes an ordering of ions in the electrolyte. These ions are usually arranged in two layers called the inner, or Helmholtz, layer and the outer, or diffuse, layer.[6]

When viewed at a microscopic level, the surface of the metal electrode is not homogeneous. Different microregions on the metal surface can have different chemical and physical properties, and small currents can flow between them. As is shown in Figure 3, the surface of the electrode may also be contaminated by adsorbed material and by various films, oxides and precipitants.

The electrode interface presents an electrical impedance in the path of the signal being recorded. This impedance can be modeled by a series resistor and capacitor, and values of 10^2 Ω and 10 μF are representative for an electrode having a 1-cm^2 surface area. This impedance physically arises in part due to the double-layer capacitance formed by the charged ions facing the metal surface. Other components of the electrode impedance are due to diffusional factors, the energy required to move reacting species up to the electrode surface, and the energy involved in chemical reactions.

The interface physicochemistry of metal electrodes affects their behavior in bioe-

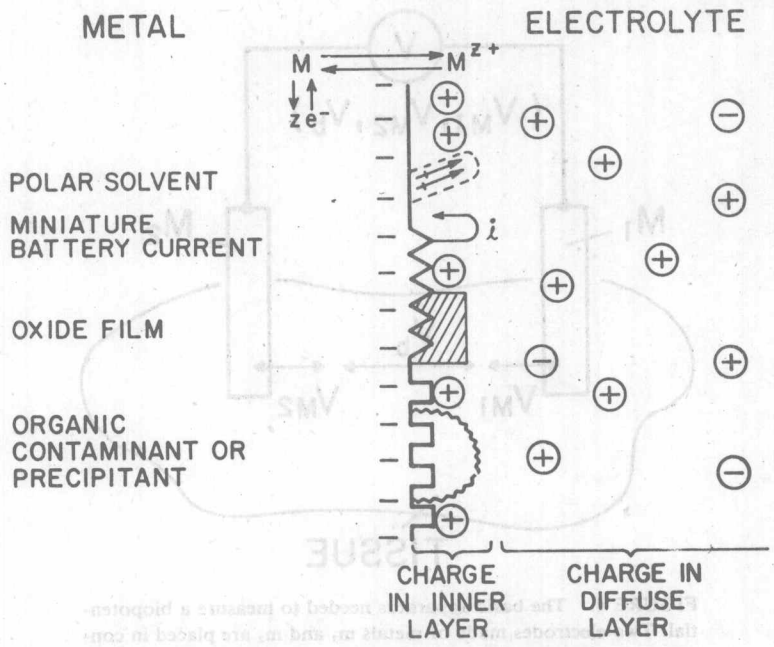

FIGURE 3. An idealized cross-sectional view of the metal-electrolyte interface of a metal recording electrode. Three different microregions of the metal surface are depicted. Various materials can cover parts of the surface and the potential across the interface causes an attraction and ordering of ions in the electrolyte. (From Dymond, A.M., *IEEE Trans. Biomed. Eng.*, 23, 274, 1976. With permission.)

lectric measuring systems. One important consideration is the DC potential of the electrode. Figure 4 outlines the experimental arrangement encountered when two electrodes made of metals m_1 and m_2 are used to attempt to measure the voltage v_b in a biological preparation. The total voltage sensed from this circuit includes the DC half-cell potentials from the two metal electrodes ($v = v_{m1} + v_b + v_{m2}$). An investigator trying to measure the DC tissue potential would normally try to simplify the situation by making both electrodes of the same metal, in which case the half-cell potentials would be equal and opposite and would cancel. In practice, making both electrodes of the same material does not guarantee that the half-cell potentials are the same to start with or that either of the half-cell potentials will remain the same as a function of time.

Why this is so can be seen by a closer consideration of the chemical reactions which underly the electrode half-cell potential.[7] Half-cell potentials reflect the energy associated with a dominant chemical reaction at an electrode. Each electrode sensing potential in an electrolyte has a half-cell potential, and, therefore, a voltage measurement between two electrodes involves two half-cell potentials. Voltages characterizing one half-cell alone are possible by making this measurement relative to an electrode whose half-cell has been arbitrarily defined as zero. The hydrogen reference electrode serves this purpose, and tables of half-cell potentials of various metals measured relative to this reference are available from many texts. These tables describe the metal half-cell potentials for the general reaction

$$M_m \rightleftharpoons M_e^{z+} + ze_m \qquad (1)$$

where M_m is an atom in the bulk metal which dissolves to become an ion M_e^{z+} with $z+$ charge in the electrolyte, while z electrons remain behind in the metal.

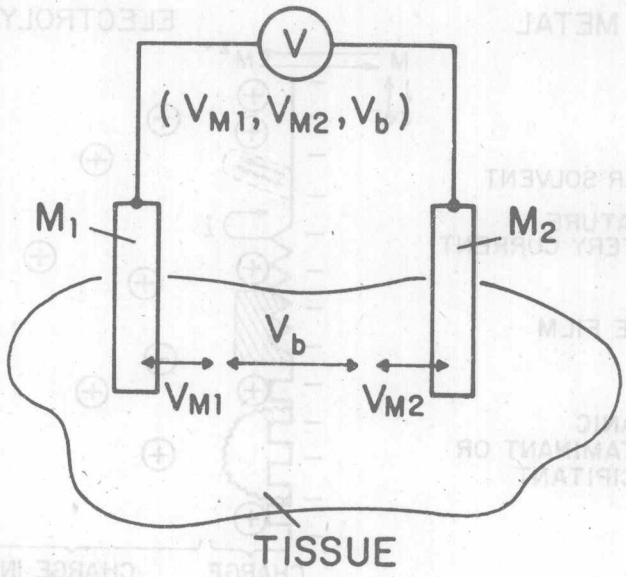

FIGURE 4. The basic apparatus needed to measure a biopotential. Two electrodes made of metals m_1 and m_2 are placed in contact with the tissue and are connected to a voltage-measuring device. The voltage sensed by this device is the sum of the two electrode half-cell potentials, v_{m1} and v_{m2}, and the biopotential v_b.

The half-cell voltage v_{m1} associated with this reaction for metal m_1 is given by

$$v_{m1} = v_{m10} + f(a_{m1}) \qquad (2)$$

where v_{m10} is the potential when the metal ions have unity activity in the electrolyte ($a_{m1} = 1$). The last term in Equation 2 is related to the solvation energy of the metal ions.

The v_{m10} term represents energies for taking a metal atom from the bulk metal, ionizing it, and then dissolving the metal ion in the electrolyte and the electrons in the metal. This term has hidden dependence upon factors such as the ionization and electronic work function energies of the metal. These are both dependent upon the state of the metal surface. Differences in stress or crystal structure occur to some extent on any solid metal surface and result in differences in these energies. If, over a period of time, different regions of the surface are covered or exposed by films or other protective layers, different parts of the surface with different v_{m10} can be exposed, resulting in changes in the overall potential with time. The different electrochemical energies of different regions on the surface can also cause miniature battery currents to flow between these regions. These currents can result in a slow etching of the surface or in the formation or removal of protective layers causing changes in v_{m10}.

The DC potential measured in the arrangement shown in Figure 4 is dependent upon the biopotential v_b and the two half-cell potentials v_{m1} and v_{m2}, which reflect energies from several sources. Since it is difficult to equalize the electrochemical potential between different regions on the surface of a bare-metal electrode, it is not surprising that the mean potential of two different electrodes would be different or that the potential of either electrode would change as a function of time.

In practice, it is unlikely that the simple mechanism involving release of metal ions into the electrolyte plays a significant role in determining the half-cell potential of noble metal electrodes. Other more energetic reactions, perhaps involving layers

of adsorbed oxygen on the metal surface, are more likely to be the true potential controlling mechanisms.[8,9] This role of oxygen in controlling measured tissue potential has been demonstrated by Carter and Phillips[10] in studies involving respired gases.

Other influences of adsorbed gases on potential have been demonstrated in studies where the tissue was subjected to X-ray irradiation while the potential was being recorded with electrodes made of different metals. X-rays have been shown to cause a fall in potential recorded by platinum electrodes, while no change in potential was detected from adjacent gold electrodes. These effects may be due to differences in the adsorption characteristics of the different metal surfaces.[11,12]

The consideration of the underlying energetics determining the half-cell potential for the simple metal dissolution reaction is generally applicable to other reaction mechanisms. The point to be made is that reactions which require an interaction between the chemical species and the metal surface will be dependent upon the physical characteristics of the surface. In practice, this electrode surface is heterogeneous and can undergo dynamic changes over a period of time, resulting in changes in the electrode half-cell potential.

No simple bare-metal electrode has sufficient DC potential stability to allow it to be used for fine DC measurements. When stable DC measurements are required, the worker in electrophysiology most frequently employs the Ag-AgCl electrode.[13] The reaction of this electrode is

$$AgCl \rightleftharpoons Ag^{+} + Cl \qquad (3)$$

The electrode essentially operates by an exchange of chloride ions between the electrolyte and the AgCl salt. This mechanism has a lower DC resistance and higher DC voltage stability than is found with simple bare metals.

Although the Ag-AgCl electrode performs well enough to be of value in many experimental situations, these electrodes are by no means exactly reproduceable or stable. As with the solid metal electrodes, the thermodynamic properties of the Ag-AgCl surface are variable and affect electrode performance. In addition, silver is moderately toxic in tissues, prohibiting direct application of this type of electrode to the body for a prolonged period.[14]

Other characteristics of bare metal electrodes affect biopotential measurements. One of the most common and troublesome problems is electrode movement artifact.[15] This appears as an artifact potential originating from the electrode whenever it is mechanically disturbed. The electrode movement artifact arises because of the interdependence of the potential across the metal-tissue interface and the structure of the interface, as is depicted in Figure 3. Mechanical disruption of this interface will cause changes in its potential and impedance,[16] and this will result in artifact potentials in the recording.

Transient artifact potentials can also occur from bare-metal electrodes which are not being subjected to movement. These types of artifacts are probably related to some of the electrochemical mechanisms discussed in relation to the electrode half-cell potential. Such artifacts could, for example, be explained by the rupture of an oxide layer covering part of the electrode surface, or by the loosening of some other type of contamination. The transient potentials would be the result of the newly exposed region on the metal surface coming to equilibrium with the rest of the electrode.[17]

An often unconsidered source of artifact during biopotential measurement is due to spontaneous polarography[18,19]. Referring to Figure 4, the basic arrangement for measuring biopotentials from tissues requires sensing the potential between two electrodes by some type of device which is presumed to have a high input impedance.