Encyclopedia of Biomedical Engineering

Biopotential Monitoring

Julián Oreggioni
Instituto de Ingeniería Eléctrica, Universidad de la República. Montevideo, Uruguay.
juliano@fing.edu.uy

Angel Ariel Caputi
Departamento de Neurociencias Integrativas y Computacionales, Instituto de Investigaciones Biológicas Clemente Estable. Montevideo, Uruguay.
acaputi@iibce.edu.uy

Fernando Silveira
Instituto de Ingeniería Eléctrica, Universidad de la República. Montevideo, Uruguay.
silveira@fing.edu.uy

Abstract
Biopotentials measurements are essential for biological research and biomedical monitoring of excitable tissues. This chapter provides an overview of biopotential monitoring, from the biological basis to the circuit and system techniques. Signal acquisition, processing and transmission are fundamental capabilities of biomedical research and medical devices development. In these topics, integrated, low power consumption systems for portable, wearable or implantable monitoring of neural signals is taken as study case, presenting both current research trends and established solutions. Starting from the biological sources of the biopotentials, the main observation levels are presented. The design of the integrated front-end amplifier, which must cope with the tougher trade-offs, is discussed and the system level requirements and alternatives for data acquisition, processing and wireless transmission are summarized.

Keywords
Analog front-end
Biomedical integrated circuit
Biopotential amplifier
Biopotential monitoring specifications
Biopotential organization levels
Biopotential sources
Low power wireless communication
Neural recording
Wireless biopotential monitoring

Abbreviations

ac = alternating current
ADC = analog-to-digital converter
BLE = Bluetooth low energy
BT = Bluetooth
CMOS = complementary metal oxide semiconductor
CMRR = common mode rejection ratio
dc = direct current
DDA = differential difference amplifier
IC = integrated circuits
IEEE = institute of electrical and electronics engineers
ISI = inter spike interval
ECG = electrocardiogram
EEG = electroencephalogram
EMG = electromyogram
EOG = electrooculogram
MOS = metal oxide semiconductor
OTA = operational transconductance amplifier
S/R = signal to noise ratio
RMS = root mean square.

Nomenclature

BW = bandwidth
δ = ADC input resolution
E = electromotive force (driving each ion)
ε_δ = ADC quantization error
g = ion channels conductance (though the membrane)
g_m = transistor transconductance
G_m = amplifier transconductance
k = Boltzmann constant
I_{DD} = total supply current
N_{BITS} = number of bits
q = electron charge
U_T = thermal voltage
T = absolute temperature
V = difference of potential between the inner and outer sides of the membrane
$v_{in,rms}$ = amplifier root mean square equivalent input noise
V_{REF} = ADC full scale range
S = noise power spectral density

Body text

This chapter provides an overview of biopotential monitoring, from the biological basis to the circuit and system techniques. Signal acquisition, processing and transmission are fundamental capabilities of biomedical research and medical devices development. In these topics, integrated, low power

consumption systems for portable, wearable or implantable monitoring of neural signals is taken as study case, presenting both current research trends and established solutions.

This chapter is organized as follows. Firstly, the biopotential sources and the specific requirements for recordings these signals at different levels will be described. Secondly, the design of the “front-end” circuits, particularly the first amplifying stage, also commonly referred as pre-amplifier, is considered. This stage must handle the toughest trade-offs in terms of low noise operation and rejection of undesired signals, while keeping consumption at a minimum when battery operated devices are targeted. Finally, the problem will be analyzed from the point of view of the biopotential acquisition system as a whole, focusing on wireless systems.

Biopotential sources

Electrophysiology is one of the most important sources of knowledge on the function of nerve and muscle tissues and the organs that such tissues construct. Some of these organs are involved with transduction of either “in” (sensory organs) or “out” (skeletal, visceral, and heart muscles) signals. Other organs, deal with the transmission (peripheral nerves) and processing of information (the brain and spinal cord) of such signals. Recordings of potential differences generated by excitable cells, provide data on the cell mechanisms of electrogeneration, inform about the localization, timing and waveform generation of biopotential sources and yield insights on the information flow through neural circuits and the activation of different muscle effectors.

The main source of biopotentials is a difference of potential (V) between the inner and outer sides of the cell membrane ranging from 50 to 100 mV. This difference of potential thermodynamically compensates a transmembrane pattern of ion gradients typical for each cell type. Although there are some exceptions, the most used model of cell membrane assumes: the constancy of the electromotive force driving each ion (E) and the relative independence of ion channels conductance though the membrane (g). As the cell surface is several orders of magnitude larger than its thickness, a constant capacity (C) in parallel is included (Fig 1). Moreover, for the same ion species more than one conductance may be present and show different voltage dependence (i.e. $E_1=E_2$ with $g_1 \neq g_2$).

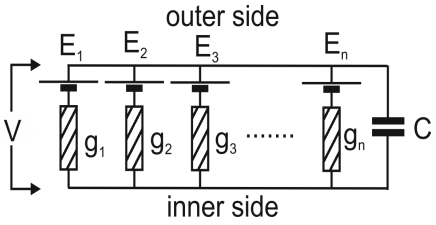

Fig. 1. Cell membrane electric model

In addition, ion dependent conductances are a non-linear function of the transmembrane voltage (V), which is in turn, a linear combination of the previous parameters, introducing complex dynamics. Furthermore, biochemical action (and also synthetic drugs) may affect each ion conductance in a different way in different cells.

Biopotentials originated at cells’ membranes can be observed at various levels of organization. The basic and most detailed level would be the ionic channels. A key question for researchers interested in pinpointing the mechanisms of cell electrogenesis is to investigate the parameters of each

elemental source driving each ionic current. This can be done either by indirectly measuring the contribution of one or several of these sources to the whole membrane voltage [1] or by directly measuring the conductance through isolated ion channels [2]. In both types of experiments a crucial aspect is the capability of recording devices to inject current into the cell and to control such amount of current in order to clamp the voltage either in a constant [1, 2] or dynamic way [3].

As most excitable cells are able to fire fast, all-or-none, events referred to as spikes, the second level of analysis consists in determining the firing time of single cells and their relationships with the firing time of other cells or behavioral events. Each cell is a closed surface (in most but not all cases geometrically spherical). Although the net current through the membrane is zero (Gauss' divergence theorem) any local difference in the transmembrane voltage (due to changes in some ion conductance) causes a localized current between membrane patches of opposite voltage polarity. As the electric field decays with the cube of distance from the emitting source, spikes are recorded only very close to the emitting cell and require electrode recording spots of tenths to hundreds of square micrometers.

The synchronic activity of groups of cells generates larger biopotentials that can be conceived as generated by distributed sources. Depending on the extension of the source and recording distance, two other forms of field potentials can be distinguished: local field potentials arising from the electrical activity of a group of closely located cells and global field potentials arising from the overall electrical activity of a whole structure. These last may be deeply buried in the background activity of other structures and may require to be evidenced by the cross correlation between the raw recorded signals and repetitive events (event related potentials).

Summarizing, different forms of electrophysiological research are focused at different levels of organization: a) to investigate the parameters of each elemental source driving each ionic current to pinpoint the mechanisms of cell electrogenesis; b) to evaluate the timing of activation of single cells by measuring the local currents generated by multiple single cells at the same time; c) to evaluate regional activities of a cell population by recordings of local differences of potential originated in the sum of currents arising from all neighbor cells; and, d) to record the "noise of the engine" of a whole structure (i.e. the brain, EEG; the heart, ECG; a group of muscles, surface-EMG) by measuring far field potential differences between points localized out of the structure. Although these approaches mostly rely on measuring the potential difference using electronic amplifiers (which is the focus of this article) other signal carriers should be mentioned: i) the magnetic field generated by biogenerated currents (a method used mainly at the organ level) and ii) the luminescence emitted by some substance in the presence of an electric field (a method used mainly at cellular level).

Specific requirements for recordings at different organization levels

Firstly, different number of channels is required when dealing with different organization levels. In the case of intracellular recordings only a few channels are required but when dealing with the extracellular activities (mentioned above in b, c, and d), it is often necessary to record simultaneously several signals to either assess information transmission between cells, or to compare generators occurring at different positions or orientations. In addition, it is also useful, in many cases, to correlate these signals with behavioral events external to the explored electric sources, imposing a need of additional acquisition channels for synchronism purposes.

Secondly, recording differences of potentials at different organization levels share commonalities, but there are also differences depending on the level and the purpose of the study (Table 1). These differences arise from the amplitude and bandwidth of the signals of interest and the electrode characteristics.

	Bandwidth (Hz)	Amplitude (μV_{PP})	Number of signals
ECG	0.1 - 150	100 - 15000	1-12
EEG	0.03 – 70	20 - 200	4 – 256
EEG (brain stem auditory evoked potential)	30 - 3k	0.05 - 4	2-4 (standard clinical use)
EEG (visual evoked potentials)	0.2- 200	0.5-20	2-4 (standard clinical use)
Intracellular recordings	dc-3k	10-250000	1-4
Local field potentials	1 – 500	10 - 5000	1-256
Spikes	0.3 - 5k	50 - 1000	1-256
Surface-EMG	25 - 3k	100 - 1000	1-10

Table 1: Main electrical characteristic of biopotentials (typical values).

Though a complete treatment of the topic of electrodes is out of the scope of this chapter, the following key considerations are presented. For instance: intracellular electrodes, multiple electrodes (from tetrode to Utah arrays), cuff electrodes and skin electrodes (Ag/AgCl or dry, capacitive, etc.) may behave as additional electric sources in series with the recording system. Usually a linear model of the electrode is sufficient to account their influence on the potential difference recorded by the amplifier, but in the general case, a non-linear model is required. This modeling of the electrode, among other effects, has sometimes to account for up to 100mV dc signals that can be generated at the skin- tissue- or cell- electrode interface. In the case of intracellular and deep placed extracellular, electrodes glass micropipettes, filled with appropriate solutions and having a tapered tip adapted to the purpose, have been the standard in the last 60 years [4]. For extracellular recordings of spikes and field potentials, multitrodes have recently improved the ability for recording multiple channels and also to separate several spikes recorded by the same electrode [5].

A particular challenge is posed in order to build small, easy-to-place electrodes and preferably embedded in wearable clothing, when small potentials have to be measured with electrodes in contact to the skin (EEG, EMG, EOG, etc.). Standard wet electrodes (Ag/AgCl) are attached to the skin by a conductive gel that improves the interface conditions. This placement process is slow, cumbersome and the result is uncomfortable for the user. On the other hand, dry electrodes have long been known, but their development remains limited to certain niches (fitness, games, etc.). While the main advantages of dry electrodes are their easier placement and use, the quality of the signals acquired with dry electrodes and traditional electronics has significant deficiencies in terms of noise and sensitivity to the electrode movements [6]. Despite this, the use of dry electrodes is clearly growing opening a wide field of research, including optimization methods for electrodes and signal acquisition circuits to alleviate the mentioned disadvantages of dry electrodes.

Third, in the case of freely behaving subjects, unobtrusive biopotential monitoring systems are required. Thus, a target system would be a wearable device (wireless, small and comfortable) with a

reasonable autonomy (low-power consumption), capable of acquiring, processing and transmitting biopotential signals. The use of wireless systems grants: a) more freedom to the user or subject under study, since wired systems restrict its movements; b) a simpler setup to the researcher; c) the correlation of the recorded potentials with behavior; and also helps to avoid the interference picked up by long cables between the electrode and the amplifier. There are commercial systems that are approaching to have wireless systems with the characteristics described above and much current research in the design of biopotential monitoring pursues that goal, as will be discussed in the rest of this chapter.

Challenges in the integrated acquisition of biopotentials

In recent years the trend on this area has been the use of solutions where most (or even all) of the circuitry is included in a single complementary metal oxide semiconductor (CMOS) integrated circuit (IC), instead of what we may call “discrete solutions”, where the circuitry is based on several standard off-the-shelf ICs and passive components. The use of ICs allows for very miniaturized devices that can be unobtrusively placed very close to the recording site (including implantable solutions) as well as to optimize the energy consumption. Following this trend, this work will focus on IC solutions because they pave the way for developing a broad range of new applications.

The analog front-end (also referred to as front-end) is the electronic circuit performing the signal conditioning (amplification and filtering) prior to digitize, process and/or transmit the acquired data (Fig. 2).

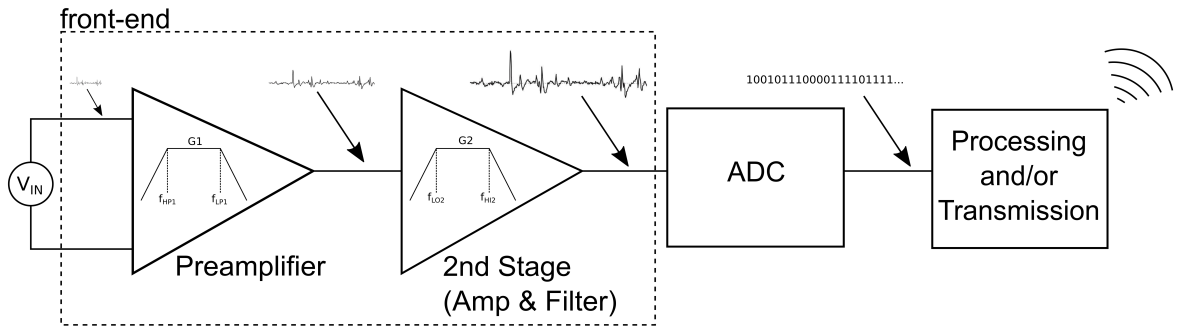

Fig. 2 Top-level schematic of a typical biopotential acquisition system (shown for only one channel and only the acquisition/transmitter side).

It is usual to tackle the front-end design with a filtering chain involving an amplifier with band-pass characteristic (pre-amplifier) and a programmable filtering second-stage [7].

Depending on the particular biopotential, it can be necessary that the second-stage provides additional amplification (because of the low amplitude of input signals). On the other hand, if the input signal was sufficiently amplified, the filter may need to deal with linearity issues, specially if rail-to-rail operation is desired in order to accommodate low supply voltages, as is the case in current IC technologies. Second-order roll off (40dB/decade) is usually sufficient to filter biopotentials. As can be seen from Table 1, cut-off frequencies are usually within the 0.1Hz to 10kHz range. Programmability of bandpass filters, which is easily achieved in ICs, is a useful mean for the user to focus the acquisition to the relevant phenomenon.

At the input stage it is advisable to use analog amplification and analog filtering in order to achieve a reasonable signal to noise ratio (S/R) while maintaining energy efficiency [8] as well as providing the needed anti-alias filtering prior to sampling. On the other hand, from the point of view of energy consumption, flexibility and processing performance, it may be convenient to use digital processing in the subsequent stages.

The conditioning circuit is usually followed by a third stage consisting of an Analog-to-Digital Converter (ADC), where a typical maximum sample rate is 50ksamples/s. 10-bit or 12-bit ADCs usually provide an adequate resolution. For instance, a 12-bit ADC with a full scale range V_{REF}=3V and a front-end gain G=3000 V/V provides an input resolution δ:

$$\delta = \frac{V_{\mathrm{REF}}}{(2^{N_{\mathrm{BITS}}} - 1).G} = \frac{3V}{(2^{12} - 1).3000} = 244\mathrm{nV}$$

where the quantization error is less than:

$$\varepsilon_{\delta} = \delta/2 = 122\mathrm{nV}$$

This quantization error is comparable to the equivalent, intrinsic, input noise, which is later presented, therefore higher resolutions would be useless. When several channels are required the ADC may be shared among the channels by multiplexing all or a group of channels at the input.

Some topics related to the final block (processing and transmission) will be discussed in the next section. In the remaining of this section we will focus on the pre-amplifier, because is the part of the system in closer contact with the biological medium and it has to primary deal with the particular characteristics of the targeted biopotentials. ADCs and filters have a range of applications that far exceeds biopotentials, there is vast literature on them and therefore are out of the scope of this review. The interested reader may find further details in the selected readings.

According to the nature of the biopotentials and the target application, the pre-amplifier must meet challenging requirements, which usually are contradictory: ultra-low-power consumption, low noise, small size, high input impedance, high common mode rejection ratio (CMRR) and reject input dc values that are much higher than the input signal amplitude. These challenges are discussed in the next subsections.

Ultra-low-power consumption

Ultra-low-power consumption (up to tens of micro-amps per pre-amplifier) is a very important requirement in order to operate with small energy sources (in order to reduce size) and to not generate local heating of tissues. Next, it shall be considered how this can be accomplished in integrated implementations. These implementations shall be in CMOS processes, which are at present the prevailing ones and best suited for ultra low power implementations.

The MOS transistor has three regions of operation according to the prevailing mechanism in the current conduction. Firstly, the traditional strong inversion region, where the gate-source voltage is above threshold and the drain current in saturation varies quadratically with the gate-source voltage. Secondly, the weak inversion or sub-threshold region [9], where the gate-source voltage is below threshold and the drain current in saturation varies exponentially with the gate-source voltage.

Finally, the moderate inversion, where the gate-source voltage is near or around the threshold region and the drain current in saturation has a mixed behavior. In order to optimize power consumption, the best IC design approach is to exploit all the possibilities that the MOS transistor give us by using indistinctly all its regions of inversion, particularly weak and moderate inversion, because in several cases these provide the best compromise between transconductance generation and parasitic capacitance, leading to an optimum in power consumption [10].

Low noise

The MOS transistors, which are the basic component of these circuits, are sources of intrinsic electronic noise, mainly thermal noise and flicker noise. Thermal noise is produced by the random thermal motion of charge carriers, resulting in a power spectral density $S_{TN} \propto 1/g_m$ (independent of frequency), where g_m is the transistor transconductance. Flicker noise is a low-frequency noise related to the charge trapping in the silicon-oxide interface, thus it depends on how the transistor is manufactured, its power spectral density is $S_{FN} \propto 1/f$. The flicker noise can be made negligible in the frequency band of interest through adequate sizing of the transistors or special amplifier design techniques.

The noise added by the pre-amplifier is modeled as a voltage source ($v_{in,rms}$), which is usually referred to the input (equivalent input noise):

$$v_{in,rms} = \sqrt{\int_{BW} S_{in}(f).df}$$

where $S_{in}(f)$ is the power spectral density and BW is the bandwidth. $v_{in,rms}$ gathers all the contributions of the pre-amplifier noisy components.

The noise amplitude added by the pre-amplifier has to be lower than the biopotentials amplitude in a ratio related to the desired signal to noise ratio. In extracellular recordings this requirement often implies that $v_{in,rms}$ has to be lower than $1\mu V_{rms}$. As we discuss next, low noise pre-amplifiers design is ruled by two main trade-offs: noise increases as, on one hand, bandwidth increases and as, on the other hand, power consumption decreases. These dependencies are discussed next.

By definition, the noise is related to bandwidth. When thermal noise is dominant, we have:

$$v_{in,rms} = \sqrt{\int_{BW} S_{in}(f).df} = \sqrt{S_{TN}.BW}$$

If the pre-amplifier input-stage is implemented with a differential pair operating in weak inversion and these transistors are the only source of noise (noise contributions of other transistors are made negligible):

$$v_{in,rms} = \sqrt{S_{TN}.BW} \propto \sqrt{\frac{BW}{g_m}} \Rightarrow v_{in,rms} \propto \sqrt{\frac{BW}{I_{DD}}} \quad (1)$$

where $v_{in,rms}$ is the pre-amplifier input-referred noise, BW is the bandwidth and I_{DD} is the total supply current. Eq. 1 highlights the noise-consumption trade-off and the noise-bandwidth trade-off. For

instance, in order to decrease 10 times the noise level, it will be necessary to increase 100 times the power consumption.

In order to quantify the current consumption efficiency in achieving low noise at a given bandwidth, as well as guide design decisions, the following NEF (Noise Efficiency Factor) [11] is a figure of merit that is widely used in integrated biopotential amplifiers (the lower it is the better):

$$NEF = v_{in,rms} \cdot \sqrt{\frac{I_{DD}}{2k\pi TU_T BW}}$$

where I_{DD} is the total supply current, BW is the bandwidth, U_T=kT/q is the thermal voltage, k is the Boltzmann constant, T is the absolute temperature and q is the electron charge. An amplifier using a single bipolar transistor can reach a NEF=1.

Some examples from actual published results, which are representative of the state-of-the-art, are presented in Table 2.

Application	Neural	ECG	EEG
Input-referred noise ($v_{in.rms}$)	3.8μV_{rms}	26μV_{rms}	2.8μV_{rms}
Bandwidth (BW)	6.7kHz	370Hz	100Hz
Power consumption (I_{DD})	1.6µA	1.7µA	33nA
NEF	2.2	2.1	2.0

Table 2. State-of-the-art biopotential pre-amplifier performance.

Small size

Size is largely reduced by resorting to integrated implementations. Nevertheless, size reduction in integrated form is limited by the low frequency of biopotentials. On one hand, the integration of the associated large time constants tends to require large capacitors, which occupy large silicon area. On the other hand, one of the most interesting challenges posed by processing biopotentials is to observe a high number of channels. This requirement would not be an issue regarding the silicon area if the pre-amplifier could be shared with multiple electrodes through an analog multiplexer. However, the large time constants involved in the pre-amplifier prevent a fast enough changeover of the pre-amplifier among channels, leading to the need of one pre-amplifier per channel.

High input impedance

High input impedance is necessary in order to guarantee that the output impedance of the electrode and/or the electrode-tissue impedance do not significantly affect the signal conditioning. This requirement is critical when one electrode is connected to several amplifiers, for example the reference in a multichannel recording. Depending on the application, the output impedance of electrodes, in the frequencies of interest, ranges from a few kilo-ohms (i.e. wet EEG electrodes) to hundreds of mega-ohms (i.e. dry EEG electrodes). In the case of dry electrodes, is very challenging that the front-end input impedance (including connections and packages) be actually much higher than the electrode output impedance, thus some small signal degradation might occur.

High CMRR

Biopotential monitoring require to separate the low-amplitude signals of interest from other biological or external interfering signals appearing in common mode. A CMRR greater than 80 dB, is required because these common mode interfering signals can have amplitudes much more larger than the monitored biopotential. The high CMRR requirement becomes critical in the acquisition of low amplitude extracellular biopotential in which the signal waveform carries significant information.

Reject dc input artifacts

The tissue-electrode interface often develops undesired dc voltages up to 100mV, which are superposed to the low-amplitude biopotential of interest. To avoid such artifact, it is possible to use capacitors between the electrode and the pre-amplifier to eliminate the dc voltage, leading to “ac-coupled circuits”. Due to the slow-nature of biopotentials, this option requires large capacitors or large resistors, which can’t be integrated because occupy a large silicon area. One way to overcome this problem is to use a MOS-bipolar pseudo-resistor. The pseudo-resistor can be thought as a transistor “almost off” that presents a very high resistance. In contrast, the resistance of this nonlinear element is difficult to model and control, and can also suffer from drift. Alternatively, there are “dc-coupled circuits” that rely on feedback instead on capacitors for eliminating the undesired dc voltage.

Main biopotential integrated pre-amplifier architectures

Harrison et al. [12] present a bandpass pre-amplifier architecture that in the last decade has become a very important reference. At that time, Harrison reported the best noise-consumption compromise, and in some aspects the circuit is still in the state-of-the-art of biopotentials amplifiers. The core of Harrison’s circuit (see Fig. 3a) is based on a symmetrical resistor-less differential amplifier based on an operational transconductance amplifier (OTA). To minimize noise, the architecture relays in a careful design of all the OTAs transistors, particularly those of the input differential pair (using wide transistors, working in weak inversion). The circuit has several interesting aspects. The gain is set by a ratio of capacitors, avoiding the use of resistors that are a source of noise and consumption. The high-pass characteristic, which requires high valued resistors, is defined by a MOS-bipolar pseudo-resistor (M1, M2, M3 and M4 in Fig. 3a). Therefore, although this architecture can reach high-pass frequency values less than 0.1Hz, this can only be done with a low accuracy. A workaround on the accuracy problem is to modify the pseudo-resistor arrangement so that the equivalent resistance can be controlled through the gate voltage of the MOS transistors that operates in weak inversion. This allows for an off- or on-chip tuning of the high-pass frequency. However, even if the accuracy issue is solved, a second drawback of this architecture remains. This drawback is the intrinsically low CMRR, which is limited by the capacitor matching that set the amplifier gain. While acceptable values of CMRR (60dB) are obtained, it is not possible to obtain very high values (greater than 80dB).

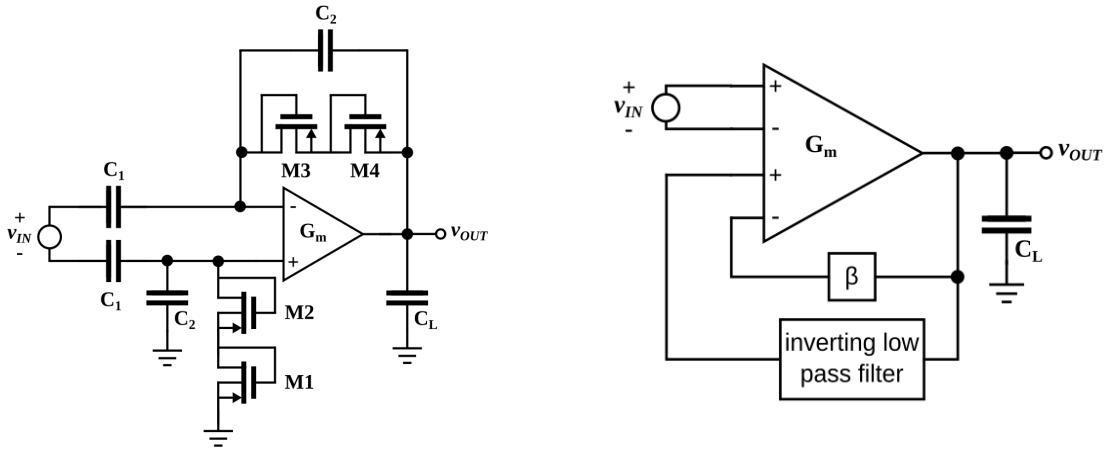

Fig. 3. Main biopotential integrated pre-amplifier architectures: a) Harrison et al. [12]; b) based on a DDA [13].

Other biopotential amplifier architectures, though not as popular as Harrison's, have been proposed over the years. An important subset of these uses as input stage a differential difference amplifier (DDA). A DDA is an OTA with two differential inputs that are added [13]. One architecture for implementing an instrumentation amplifier by means of a DDA is shown in Fig. 3b. It uses one differential input for the signal to be amplified, and the other differential input for the feedback that fixes the gain (feedback factor β) and high-pass characteristic (inverting low-pass filter). This architecture is intrinsically suitable for high CMRR, and the gain and bandpass cut-off frequencies are fixed by means of parameters that are, respectively, very accurate (i.e. ratios of transconductances) or can be easily and automatically tuned (i.e. ratios of transconductance over capacitances).

Challenges for biopotential multichannel wireless recordings

The most important challenge that faces the design of biopotential wireless recording systems is handling an enormous amount of information that is generated in a small device, with severe power and processing constraints. To acquire signals of 10 kHz bandwidth, a minimum sampling frequency of 20 ksamples/s per channel is required. Then, 8 channels and 12-bit samples imply an effective data throughput of 1.92Mbps. If it were 100 channels, the effective data rate should be greater than 24Mbps. No low-power wireless standard communication protocol reaches these transmission rates nowadays.

In the last 20 years, there have been several proposals for providing a solution for solving this problem, for example [14] and [15]. Fischer et al. [14] present a discrete two channel system for acquiring flying locusts EMG signals. The acquired analog signal is directly transmitted in the 145MHz band within a range of 20 meters. The system weighs 0.55 grams and has 7.3 hours autonomy powered from a 1.5V battery, which is overall an impressive performance for the date it was designed and not using custom integrated circuits. Harrison et al. [15] present an integrated four channel telemetry system, which acquires neural signals and EMGs in flying locusts and weakly

swimming electric fish, and transmits them wirelessly in the 900MHz band within a range of 2 meters. The samples are digitized with 9 bits and the useful date rate is 104kbps. The system weighs 0.17 grams and has 5 hours autonomy powered from a 1.5V battery. Table 3 presents some selected examples of commercially-available biopotential wireless recording systems.

Application	Neural Recording	EEG	EEG	EEG/EMG
Number of channels	128	64	8	64
Weight (grams)	7.5	>800	360	500
Autonomy (hours)	1-3	12-24	25-100	5
Effective data rate per channel	30 ksamples/s	4 ksamples/s	256 samples/s	2 ksamples/s
Input-referred noise (v_{in_rms})	8.5μV_{rms}	2μV_{PP}	N/A, <500μV_{PP}	1μV_{rms}
Communication protocol	Proprietary, analog 4-meters range	WiFi	Bluetooth	WiFi

Table 3. Commercial biopotential wireless recording systems

Regarding digital communication, it is important to distinguish between “effective data rate” and “raw data rate”. The effective data rate (also named useful data rate) refers to the information that the user or the application needs to receive or transmit. The raw data-rate (also referred as the over-the-air data rate) is the total number of transferred bits per second over the communication link, this data-rate take into account not only the useful data, but also any other transmitted data (i.e. protocol overhead). Some digital wireless communication standards are discussed next.

Typical implementations of Bluetooth (BT) and its low-power version “Bluetooth low energy” (BLE), are designed to operate in short distances (from a few meters to several tens of meters). BT can achieve an effective data rate of up to 800kbps while consuming an average current in the order of 20mA. BLE typically achieves a maximum effective data rate of 200kbps while consuming an average current less than 10mA. These protocols typically communicate two devices (host and client), don’t require infrastructure and are easy to install and configure.

The IEEE 802.15.4 standard specifies the low level layers of a low power (less than 10 mA), low effective data rate (up to 50kbps), and short distance (from a few meters to several tens of meters) wireless communication protocol. Zigbee is a protocol based on this standard. These protocols typically communicate several devices (sensor nodes) and don’t require infrastructure since they organize “ad hoc” networks.

In the same range of distances, options like WiFi, can be used to monitor biopotentials. In this case, an effective data rate of 5Mbps is easily achieved, but current consumption of hundreds of milliamperes has to be tolerated. WiFi typically communicates several devices by means of additional infrastructure (i.e. router).

A promising way to solve the problem of having to transmit such a high volume of data is to incorporate data processing to reduce the amount of transmitted data. In some applications, the data processing consist of methods for detecting the relevant information contained in the biopotential signal. To illustrate this, let us consider the particular example of the detection of the spikes that indicate neurons activation, where several methods for reducing the amount of information to be transmitted have been proposed. Some of them compare the acquired signal

against a template (called “template matching”). These methods are particularly effective when the waveform of the target spike is known or can be estimated. There are also methods that measure (and transmit) the energy of the signal. Although in many cases it is sufficient to send the inter spike interval (ISI), there are works that have proposed to send more data (without sending the complete stream). For example, in a "feature extraction" data compression scheme, where the spike is detected by two thresholds (one negative and one positive), and instead of sending the complete signal, either a short epoch of about 2 ms long including the spike waveform or a few points can be transmitted.

An alternative approach is to apply general data compression techniques, which have been proposed in the past 20 years. Methods ranging from simple dictionary-based approaches to more sophisticated context modeling techniques, methods that exploit the biopotential particularities (i.e. temporal and/or spatial correlation) or methods that don't.

Another way to deal with a high volume of data is to perform some data processing in order to take decisions “in situ” (for example to give an alarm or to stimulate), thus completely avoiding the need to transmit data.

Conclusions

We have presented an overview of biopotential monitoring, from the biological basis to the electronic circuits and systems techniques, focusing in the challenges and bottlenecks that have to be faced.

Summarizing, we introduced the specific requirements of the transduction stage for biopotential recordings (number of channels, electrical characteristics of the signals, type of electrodes, etc.). Next, we presented the front-end in charge of the biopotential acquisition, making emphasis on the preamplifier stage, where the toughest trade-offs in terms of low noise and rejection of undesired signals must be handled, while keeping energy consumption at a minimum. Finally, at the recording system level, we discussed one of the most important challenge faced, which is to handle the enormous amount of information that is generated in a small device, with severe power and processing constraints.

In the years to come, neuroscience research will heavily depend on multi-unitary recording performed in parallel to behavior recording. Developing and applying methods for large scale monitoring of neural activity sensory images and behavioral in synchrony, would produce a dynamic picture of the brain function, which is essential for understanding the brain in action. The develop of a wearable, wireless, multichannel and small-size device offering to the user a synchronism mechanism, allowing the correlation between neural activity, sensory images and behavior signals recorded by other devices is a problem still not fully solved. Event related potentials and unit probability after sensory stimulus and before motor actions are currently recorded in neurosciences, medicine and psychology, among others disciplines. In the case of event related potentials the increase in channel number with small size and low power consumption would improve the possibility of source reconstruction. Large-scale multi-unitary recordings will allow scientists to search for correlations between the activities of neurons belonging to the same local circuitry and deciphering their functional connectivity and also to evaluate the effects on other brain regions

through long connections. Peripheral studies, as for example Holter recordings of heart or skeletal muscle activities in medicine and sports, would benefit from the same type of recording devices and simultaneous synchronous monitoring of physical activity. Finally, concerning EEG, an important challenge is electrode development. The use of dry electrodes will continue to grow boosted by applications in Brain-machine interface, wearable devices and Internet of Things, among others. This will push further the research on optimization methods for electrodes and signal acquisition circuits to alleviate the disadvantages of dry electrodes.

References

[1] Hodgkin, A. L. and Huxley, A. F. (1952). A quantitative description of membrane current and its application to conduction and excitation in nerve. J Physiol. 117, 500-544.

[2] Sakmann, B. and Neher, E. (1984). Patch clamp techniques for studying ionic channels in excitable membranes. Annual review of physiology, 46(1), 455-472.

[3] Le Masson, G., Renaud-Le Masson, S., Debay, D. and Bal, T. (2002). Feedback inhibition controls spike transfer in hybrid thalamic circuits. Nature 417, 854-858,

[4] Ling, G., and Gerard, R. W. (1949). The influence of stretch on the membrane potential of the striated muscle fiber. Journal of cellular physiology 34(3), 397-405.

[5] Cheung, K. C. (2007). Implantable microscale neural interfaces. Biomedical microdevices 9(6), 923-938.

[6] Chi, Y. M., Jung, T. P. and Cauwenberghs, G. (2010). Dry-contact and noncontact biopotential electrodes: methodological review. IEEE Reviews in Biomedical Engineering 3, 106-119.

[7] Oreggioni, J. and Silveira F. (2014). Integrated programmable analog front-end architecture for physiological signal acquisition. In Proceedings of the International Instrumentation and Measurement Technology Conference, 108-112. Place: IEEE.

[8] Vittoz, E. and Tsividis, Y. (2002). Frequency-dynamic range-power. In Tournazou, C., Moschytz G. and Gilbert B. (eds.) Trade-Offs in Analog Circuit Design: the designer's companion. Place: Kluwer Academic Publishers.

[9] Vittoz, E. and Fellrath, J. (1977). CMOS analog integrated circuits based on weak inversion operations. IEEE Journal of Solid-State Circuits 12(3), 224-231.

[10] Silveira, F., Oreggioni, J. and Castro-Lisboa, P. (2015). Constraints and design approaches in analog ICs for implantable medical devices. In Proceedings of the International Symposium on VLSI Design, Automation and Test. Place: IEEE.

[11] Steyaert, M. S. J. and Sansen, W. M. C. (1987). A micropower low-noise monolithic instrumentation amplifier for medical purposes. IEEE Journal of Solid-State Circuits 22(6), 1163-1168.

[12] Harrison, R. R. and Charles, C. (2003). Low-power low-noise CMOS amplifier for neural recording applications. IEEE Journal of Solid-State Circuits 38(6), 958-965.

[13] Sackinger, E. and Guggenbuhl, W. (1987). A versatile building block: the CMOS differential difference amplifier. Journal of Solid-State Circuits, vol. 22(2), 287-294.

[14] Fischer, H., Kautzb, H. and Kutscha, W. (1996). A radiotelemetric 2-channel unit for transmission of muscle potentials during free flight of the desert locust, Schistocerca Gregaria. Journal of Neuroscience Methods, 64(1), 39-45.

[15] Harrison, R. R. et al. (2011). Wireless neural/EMG telemetry systems for small freely moving animals. IEEE Transactions on Biomedical Circuits and Systems 5(2), 103-111.

Further Reading

Johnston, D. and Wu. S. M. (1994). Foundations of cellular neurophysiology. MIT press.

Lewicki, M. S. (1998). A review of methods for spike sorting: the detection and classification of neural action potentials. Network: Computation in Neural Systems 9(4), 53-78.

Maloberti, F. (2007). Data converters. Springer Science & Business Media.

Martinsen, O. G. and Grimnes, S. (2011). Bioimpedance and bioelectricity basics. Academic press.

Nicolelis, M. A. L. (2001). Actions from thoughts. Nature 409(6818), 403-407.

Nicolelis, M. A. L. (2007). Methods for neural ensemble recordings. CRC press.

Nunez, P. L. and Srinivasan, R. (2006). Electric fields of the brain: the neurophysics of EEG. Oxford University Press Inc.

Ogden, D. (1994). Microelectrode techniques: the Plymouth Workshop handbook. Company of Biologists.

Sedra, A. S. and Smith, K. C. (2009). Microelectronic circuits. 6th Edition. Oxford University Press.

Schaumann, R., Xiao, H. and Van Valkenburg, M. A. (2009). Design of Analog Filters. Oxford University Press Inc.

Schneider, M. C. and Galup-Montoro, C. (2010). CMOS analog design using all-region MOSFET modeling. Cambridge University Press.

Tsividis, Y. and McAndrew, C. (2011). Operation and Modeling of the MOS Transistor. Oxford University Press Inc.

Yoo, H. J. and van Hoof, C. (2010). Bio-Medical CMOS ICs. Springer Science & Business Media.

Webster, J. G. (2010). Medical Instrumentation. John Wiley and Sons Inc.