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# Portable Bio-Devices: Design of Electrochemical Instruments from Miniaturized to Implantable Devices

Jordi Colomer-Farrarons[1], Pere Ll. Miribel-Català[1],
A. Ivón Rodríguez-Villarreal[1,2] and Josep Samitier[1,2,3]
[1]*Department of Electronics, Bioelectronics and Nanobioengineering Research Group (SIC-BIO), University of Barcelona,*
[2]*IBEC-Institute for Bioengineering of Catalonia,Nanobioengineering group,*
[3]*CIBER-BBN-Biomedical Research Networking Center in Bioengineering, Biomaterials and Nanomedicine,*
*Spain*

## 1. Introduction

The integration of biosensors and electronic technologies allows the development of biomedical systems able to diagnose and monitoring pathologies by detecting specific biomarkers.

The chapter presents the main modules involved in the development of such devices, generically represented in Fig. 1, and focuses its attention on the essential components of these systems to address questions such as: how is the device powered? How does it communicate the measured data? What kind of sensors could be used?, and What kinds of electronics are used?

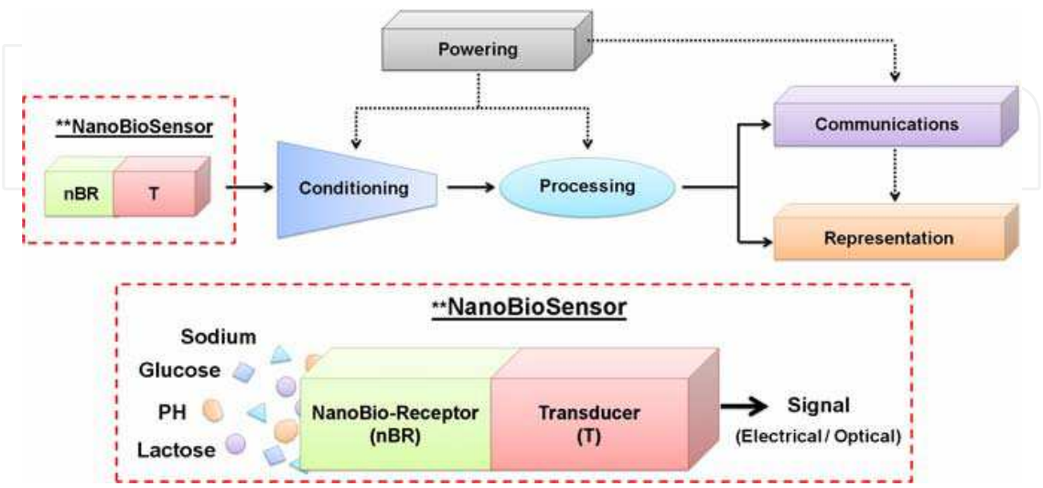


Fig. 1. Generic conception of the portable device specifying the different main components that are described throughout the chapter.

Two main fields of application are observed:
Health: Point of care technologies (POCT) can be defined as immediately actionable healthcare information outside the clinic laboratory in applications from diagnosis, to monitoring and therapy adjustment. A fundamental aspect of POCT versus clinical laboratory is the portability and the capacity to provide results in a shorter time frame. However, the higher costs of performing medical test at the point of care will only be accepted if the patient clinical condition strictly requires immediate results to guarantee more efficient and safer treatments. In the near future, healthcare systems will find a rational equilibrium for clinical laboratory and point of care utilization, where the most efficient technologies and systems will self-impose by factual clinical and economic evidences.
An evolution of these systems is the implantable lab-on-a-chip devices for in vivo continuous monitoring of the patients. In this case, the idea of the miniaturized devices is to integrate several functions in a microchip. The advances in biotechnology take us to the development of microdevices to detect proteins and/or ions suspended in blood/plasma related to specific pathologies or any other alteration of the standard health values. The integration of the detection and self-powered systems in the biological field are the basis of these new technologies. As a consequence, the major challenge of the electronic advances is to develop low powered consumption systems able to work under different environmental and physiological conditions. Besides, the devices should be covered or made with biocompatible and/or bioactive materials to reduce immune responses such as inflammation, thrombosis or any reaction induced by the implementation of the device. On the other hand, heat generated by the electronic devices must be controlled to avoid irreversible protein damage that could alter the measurements and/or necrosis caused by the implanted device.
Environment: The air and water pollutants are affecting the health of living beings (humans, animals, and plants), agriculture, fisheries and physical infrastructures (Cleven et al., 2005; Poyatos et al., 2010; Terbouche et al., 2011). Water pollution is present in all these fields. The hazardous residues of heavy metals, fertilizers, pesticides, toxic chemicals products, oil and other contaminants poured by companies all around the world, and humans waste such plastics; lubricants, etc., are contained in the drinking water, oceans, lakes and food. In the past years, it has become a global concern of associations such the U.S. and Scottish Environmental Protection Agency (EPA), American Water Resource Association (AWRA), the World Water Council, the European Environment Commission and others organizations. In response of the actual necessities, the research in systems designed to detect and monitor pollutants is exponentially increased. Devices able to detect in less time, in the point of care, handled by non-qualified personal and with lower cost in the fabrication process are the main aim of these research groups. In this way it is expected for example the detection of toxic drinking water that could cause health problems and in many cases the dead of living beings.
This chapter will discuss two approaches taking into account the envisaged fields of application: firstly, a discrete small and portable potentiostat amplifier integrated with detection and microfluidic systems result in a cheap and miniaturized device that can be applied for on-site simultaneous measurements of O2 and temperature values in water systems. Dissolved oxygen concentration (DO) is an important index of water quality and the ability to measure the oxygen concentration and temperature, at different positions and water depths, would be an important attribute for environmental analysis.

The second device presented is an approach for an in-vivo biomedical implantable device. The system is conceived to be implanted under the human skin. The powering and communication between this device and an external primary transmitter is based on an inductive link. The presented architecture is oriented for two different approaches defining a True/False alarm system, based on amperometric or impedance biosensors.

Two main problems from the point of view of the electronics, have to be overcome to obtain implantable devices (Colomer et al., 2009a), for true/false alarm, or event detector applications. The first, is how to transfer enough energy to power the devices, and the second, consists in the integration of the necessary instrumentation and communication electronics to control the sensors and to send the information provided by the sensors through human skin, avoiding excessively high levels of locally power dissipation. In this sense, our group works in the field of energy harvesting (Colomer et al., 2008), with experience of different sources (Juanola et al., 2010), which is one of our main interests. One experience is based on the use of an inductive coupling Radio Frequency (RF) power harvesting solution, to transmit energy to the implanted device, replacing the use of batteries or wires. Furthermore, this mechanism permits the establishment of a bidirectional communication between the implanted and the external interface devices.

In particular, the measurement of an electrical signal opens the second main field of interest, which is the instrumentation electronics. Looking for electrochemical instrumentation, the solutions vary from discrete to mixed and full custom-ASICs devices. The definition of the adopted solution is given by the size of the sensor, and the complexity of the system. For electrode areas greater than 1mm$^2$, electronics based on low-cost surface mount components alone can be adopted. On the other hand, for the use of smaller and multiplexed solutions, a valid approach is a full custom ASIC solution. If very low current levels are derived from the sensors, an ASIC interface near the electrodes is indicated. Other key indicators for an ASIC solution near the electrodes are not only the degree of miniaturization, but also the fact that EMI can be reduced avoiding external disturbances such as vibrations, moisture, sources of electrical noise, etc.

Experiences with amperometric sensors, calibration voltammetries and amperometric measurements, related to the presentation of the main techniques that can be used with such biosensors, are presented in this chapter, as well as the different results achieved in each case. A prototype to detect $O_2$ in water for environmental purposes is presented as an example of a discrete disposable (Colomer et al., 2009c). The architecture and implementation of the electronics for an implantable approach is introduced (Colomer et al., 2009b), and comments concerning the implantable devices are included.

## 2. Conception of a generic bio-portable device

### 2.1 Powering

From the point of view of an implantable electronic device, the first decision to make is regarding to the power system that should be used to produce the energy necessary for the system. Thereafter, this section summarizes the topic of batteries and fuel cells, and describes particularly the interest in using free available external energy sources for powering small electronic systems knows as energy harvesting. Subsequently, this section will be focused in the description of energy harvesting and the kind of sources available in the environment in order to recover energy, more explicit (or getting into more detail) in the one obtained from the human body.

### 2.1.1 Batteries and fuel cells

Battery technology has undergone tremendous progress since it was first discovered. This progress has enabled the explosion of a wide-range of new applications such as in mobile devices. However, new trends in technology added to some intrinsic limitations of batteries have motivated research into new energy generation solutions. An emerging generation of ultra-small rechargeable batteries can remain installed for decades if not the entire life of the system, restoring that promise of freedom. Many of these new-generation batteries are solid-state, thin-film lithium cells comparable in size to a large IC package. Now available, these thin-film batteries provide many design options in terms of storage capacity, output voltage, and size. Cymbet's EnerChip CBC3150 is a 9- by 9-mm, 3.3-V battery with 50 μA-H of capacity, figure 27, and its CBC012 provides 12 μA-H at 3.8 V in a 5- by 5-mm package.

Solicore provides the larger 26- by 29-mm Flexion battery with 3-V output and up to 14 mA-H of capacity. Similarly, Infinite Power Solutions is offering its Thinergy batteries which are just entering the product shipment phase. More introductions are likely to be forthcoming from companies that are now licensing thin-film battery technology developed at Oak Ridge Micro Energy.

An interesting field in storage elements is also covered by the micro-fuel cells. A micro fuel cell is a power source for electronic devices that converts chemical into electrical energy. Fuel cells differ from conventional electrochemical cells and batteries. Both technologies involve the conversion of potential chemical energy into electricity. But while a conventional cell or battery employs reactions among metals and electrolytes whose chemical nature changes over time, the fuel cell actually consumes its fuel, leaving nothing but an empty reservoir or cartridge. A fuel cell is replenished merely be refilling its reservoir, or by removing the spent fuel cartridge and replacing it with a fresh one. The micro fuel cells represent power for devices that include a range of PC, handset, PDA, and digital device segments in a variety of industry, military, and health care segments. The research in this field is very important. A popular fuel cell is direct methanol fuel cell. The methanol reacts electrochemically with water at the anode, producing free electrons and protons, with power levels reported as high as 47mW/cm$^2$. Specific fuel cells have a particular interest for the development of implantable devices. These devices can be achieved by using bodily fluids as the fuel source, such glucose and oxygen in blood (Sato et al., 2005).

### 2.1.2 Energy harvesting and ambient energy sources

There is a great interest in harvest the energy to power small electronic systems. We must distinguish between macro and micro energy harvesting scale. Macro harvesting, is related to energy recovery in the range from kilowatts to megawatts, which are fed to the grid. On the other hand, from the micro scale point of view, a limited amount of energy, in the range from nanowatts to milliwats, can be obtained from different types of external ambient sources and energy transducers (Niyato et al., 2007; Paradiso & Staner, 2005; Roundy et al., 2004), like vibrations (Garbuio et al., 2009; Kiziroglou et al., 2009; Le et al., 2006), heat (Carlson et al., 2009; Stark, 2006), and , light (Celik & Kusetogullari, 2010; Nasari et al., 2009), radio waves (Sogorb et al., 2008). Estimates of the energy available per unit area, or volume, for each harvesting source, are reported in Table 1.

These values are strongly dependent on the excitation conditions and the used technologies. From these different types of power sources and harvesting solutions, it is possible to recover peak power of 400μW for mechanical to electrical harvesting based on piezoelectric

| Energy Source | Performance | |
|---|---|---|
| **Ambient Light** | · Indoor 10μW/cm² (low illumination)<br>· Typical office 100μW/cm²<br>Outdoor 10mW/cm²<br>Full bright sun 10mW/cm² | · Solar cells (6830 lx 10W/m²)<br>· Indoor solar cells<br>(10lx to 1400 lx) |
| **Vibrational** | · 4 μW/cm³ (human motion Hz range)<br>· 800 μW/cm³ (machines-kHz ranges)<br>· These numbers depend heavily on size, excitations, technologies, etc.<br>Typically:<br>Piezoelectric ~ 200μW/cm³<br>Electrostatic ~ 50-100μW/cm³<br>Electromagnetic < 1μW/cm³ | · Microgenerators<br>350 μW<br>22μW<br>400 μW |
| **Radio Frequency (RF)** | · GSM 4 μW/cm²<br>· WiFi 0.001mW/cm²<br>· These numbers strongly depend on operation frequency and distance between the base station and the receiver. | · < 1μW/cm² unless near a transmitter<br>· ≈ 1mW for proximate stations (inductive coils)<br>· @900MHz, 1.1meter @ 24.98dBm (0.315W), ~ 20μW [48]<br>@4MHz, 25mm (subcutaneous powering) >5mW [62] |
| **Temperature Difference** | · Human 25 μW/cm²- 60 μW/cm²<br>· Industry 10mW/cm² | · Thermoelectric generators<br>60 μW/cm² Thermolife® ΔT=5°C. [7][14][48] |

Table 1. Energy Harvesting Sources and estimations.

MEMS, operating at 1kHz and generating voltages below 1V (Garbuio et al., 2009) for optimal load conditions, or as in (Le et al., 2006), based on micro-power generators based on a laminate piezoelectric membrane, generating 22μW of power and peak voltages up to 2.45V with no load. Following the objective to design energy-harvesting devices based on MEMS solutions, an electrostatic micro-generator is presented in (Le et al., 2006). In this case, a mechanical to electrical conversion based on an electrostatic solution instead of a piezoelectric or electromagnetic solution, the peak voltage generated can be up to 65V, and discrete electronics are used. In (Li et al., 2010), a piezoelectric cantilever working at lower frequencies of operation (65Hz), generating higher voltages (up to 15V) and in consequence presented a maximum power of 350μW. An interesting point of progress is shown in (Khaligh et al., 2008), where two power sources are combined: a piezoelectric and permanent magnetic energy scavenging. These elements are discrete and the total power theoretically generated is 44mW: 37mW from the electromagnetic source and 6mW from the piezoelectric source. In (Celik&Kusetogullari, 2010), the utilization of indoor cells for extreme low conditions of illumination, and low voltages of operation, is shown for a cell of 55mm x 20mm x 1.1mm with a power of 5μW@10lx to 200μW@1450lx for a voltage drop of 2V. The advances in semiconductor technologies related to the reduction of the transistor's size allow the industry to obtain more interest in the development of new self-powered portable electronic devices that incorporate a great variety of circuitry and functions as is stated in works like (Ferrari et al., 2009; Khaligh et al., 2010).

Energy harvesting, small-format batteries and power management ICs are technologies that will enable commercialization of the next-generation of ultra-low-power electronic devices and systems.

### 2.1.3 Body harvesting

In the particular case of energy scavenging in human beings, there are two approaches that are defined as passive or active power generation. Passive powering takes place when the user does not have to do any task different to normal tasks associated with the product, which is the main difference with an active generation. Generally speaking, higher amount of power can be generated actively than passively. A nice reference comes from (Paradiso& Starner, 2005), at the MIT.

There are different sources available in the body to harvest energy. The human body is a tremendous storehouse of energy, but some key aspects must be taken into account for its harvest. The first approach is related to the body heat. Since the human body emits energy as heat, it follows naturally to try to harness this energy. However, the efficiency of the Carnot thermodynamic cycle puts an upper limit on how well this waste heat can be recovered. Assuming normal body temperature and a relatively low room temperature (20 $^{o}$C), the Carnot efficiency is 5.5% at 25 $^{o}$C which drops to 3.2% in a warmer environment (27 $^{o}$C). Since the total amount of wasted heat can be turned into a power of 100W, the energy that can be recovered, using the Carnot engine, it is in the range of 2.4W to 4.8W. While a full wetsuit or even a torso body suit is inappropriate for many applications, the neck offers a good location for a tight seal, owing that access to major centres of blood flow, and could be easily removed by the user. The neck is approximately 1/15 of the surface area of the "core" region (those parts that the body tries to keep warm at all times). As a rough estimate, assuming even heat dissipation over the body, a maximum of 0.20-0.32W could be recovered conveniently by a neck brace for instance. There are different approaches to recover this energy thanks to thermoelectric generators. Low power thermoelectrically-driven products have appeared, for example, Applied Digital Solutions' Thermo Life, is a thermoelectric generator that measures 0.5 cm$^2$ in an area 1.6mm thick. Comprising a dense array of low-temperature thermopiles, it can generate 10 µA at 3 V (6 V open circuit) with only 5° C of temperature difference. In addition, the motion of the body could be also be an option for power harvesting. There are different approaches based on the movement of the human being to recover energy and studies that analyse this energy recovered from some human movements. Table 2 presents some references about the energy recovered from frequent human movements, Table 2.

In (Kazazian&Jansen, 2004) appears the idea of an energy fitness club where people could reload their portable device while getting in shape. They estimated that 10 minutes pedalling on a bicycle could generate 2 W, and therefore reload a mobile phone described by the authors as HUMAN POWERED. Moreover, the MIT Media Lab has developed a full system that harvests parasitic power in shoes employing piezoelectric materials (Shenck&Paradiso, 2001). The low-frequency piezoelectric shoe signals are converted into a continuous electrical energy source. The first system consists on harvesting the energy dissipated in bending the ball of the foot, placing a multilaminar PVDF bimorph under the insole. The second one consists on harvesting the foot strike energy by the curved, pre-stressed spring metal strips laminated with a semi-flexible form of PZT under the heel. Both devices were excited under a 0.9 Hz walking activity.

The e-health monitoring is a significant field in research which is related to the conception and definition of Body-sensor networks in the body, looking for external and internal biosensors implanted in the body. This approach of WBAN ubiquitous health monitoring is exposed in (Jovanov et al., 2005).
IMEC is one of the world leaders in smart textiles using the power harvesting technology. IMEC in Belgium associated with the laboratory of the Ghent University presented their newly developed UTCP (ultra-thin chip package) technology which can be seen as a big boost towards fully integrated, complex electronic into textiles. UTCP allows the integration of complete systems in a conventional low-cost flex substrate. IMEC demonstrated the integration technology with a flexible wireless monitored prototype that measures the heart rate and muscle activity. IMEC at Netherlands has presented the conception of an smart T-shirt, used to monitoring the cardiac activity, powered by body heat (Van Hoof, 2009), figure 2. Besides, IMEC has demonstrated the integration of a wireless autonomous sensor system in clothes. The system is fully autonomous for its entire life and requires no service - like replacing or recharging the battery - from the user. The shirt with integrated electronics can be washed in a regular washing machine. It occupies less than 1.5% of the shirt area and typically generates a power of 0.8–1mW at about 1V at regular sedentary office activity. However, if the user walks indoors, the power increases up to 2.7mW at 22°C due to forced convection. In colder environments where other clothes need to be worn on top of the shirt, the power generation is usually not affected.

| Activity | Power generation |
|---|---|
| Finger (pushing pen) | 0.3 W |
| Legs (cycling 25 km/h) | 100 W |
| Hand and arm (Freeplay) | 21 W |
| Hand (Aladdinpower) 3.6 W | 3.6 W |

Table 2. Examples of active human power generated by body movements.


Fig. 2. Smart T-shirt by IMEC-NL.

### 2.2 Communications

Referring to Fig. 1, communications are one of the last, but not the less important, steps when designing miniaturized equipment for environmental or BioMedical applications.

Basically, two main topologies can be studied, wired or wireless communications. Since wireless architectures are becoming more popular for such devices we will focus on them in more detail. It is well known that wireless communication consists on transmit data (information) over a short (few cm or meters) or long distance (kilometers or more) without the use of wires or electrical conductors. In a miniaturized device, the wireless information transmission process could represent an important part of the power consumption, so it is important to minimize the required power levels (Colomer & Miribel, 2011), with an accurate design of the antennas and associated circuits.

The basic communication scheme uses one antenna (and its associated circuits and modulations) to receive and transmit data (Fig. 3). It is tunned at the desired working frequency, typically one of the standards of the ISM (Industrial, Scientific and Medical radio bands) band for Wireless sensor networks like, Bluetooth or ZigBee for short communications range, or GPRS or WLAN for long ranges. Some low power transceivers are available from all major vendors like, Microchip® or Texas Instruments®.

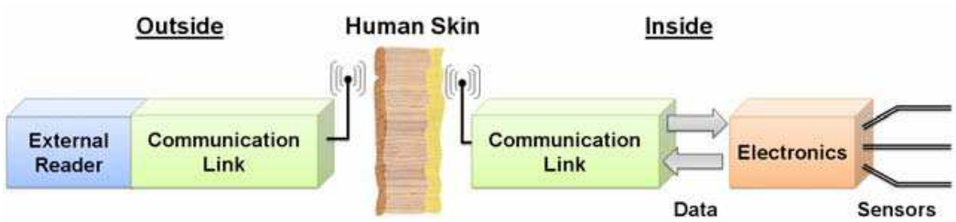


Fig. 3. Basic Communication scheme.

On the other side, if the applications require the design of a full-custom transceiver, some examples can be found in the literature (Roundy et al., 2004). Furthermore, magnetic induction communications based on the inductive coupling of two coils can be used to transmit bidirectional data i.g., Backscattering, with some implanted device (Colomer & Miribel, 2011), at the frequency operation of 1M to 15MHz range. One antenna is located under the skin while the other one is at the external side creating an inductive link used for communications and powering.

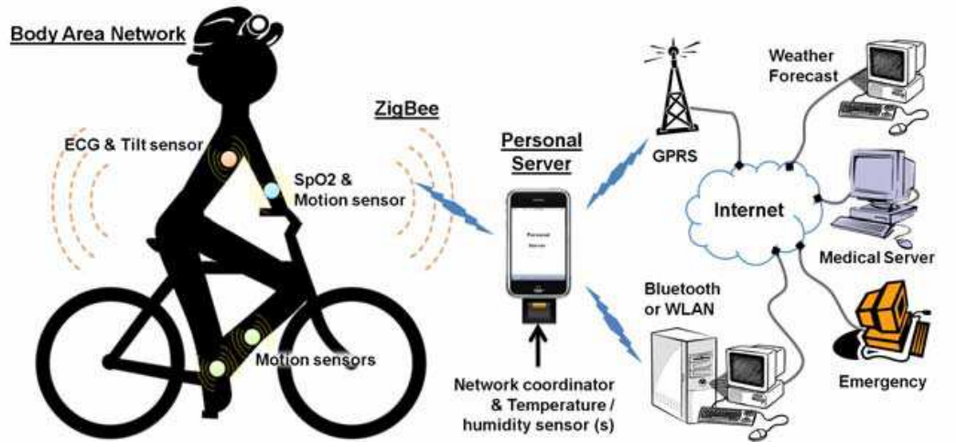


Fig. 4. Example of a distributed sensors networks and Wireless Body Area Networks (WBAN).

The combination of these standards allows the development of distributed sensors networks and Wireless Body Area Networks (WBAN). An example of WBAN is presented in Fig. 4. There, several sensors are distributed around the human body and use different type of protocols to communicate with a Central Control Unit or Personal Server. Then, this CCU module collects the data coming from all the sensors and transmits it to other users.

### 2.3 Biosensors and measurement techniques

#### 2.3.1 What is a biosensor?

A biosensor is a measurement system for the detection of an analyte that combines a biological component with a physicochemical detector. The general function of a biosensor is to convert binding events between biological receptors and target agents into a signal thanks to a transducer (Fig. 5) which can be based on an optical, a thermal, a gravimetric or an electrochemical detection. This last one has gained increasing attention in the last years. The high sensitivity, low cost and easy miniaturization of the electronic detection taken in conjunction with the wide range of applications, has become these devices a perfect analytical tool in different fields, such as diagnosis of genetic diseases, detection of infectious agents, study of genetic predisposition, development of personalized medicine, detection of differential genetic expression, forensic science, drug screening, food safety and environmental monitoring. In order to develop portable systems, from discrete to integrated solutions for a discrete or continuous monitoring, electrochemical biosensors are the best choice. The generic components of a biosensor are depicted in Fig. 6.

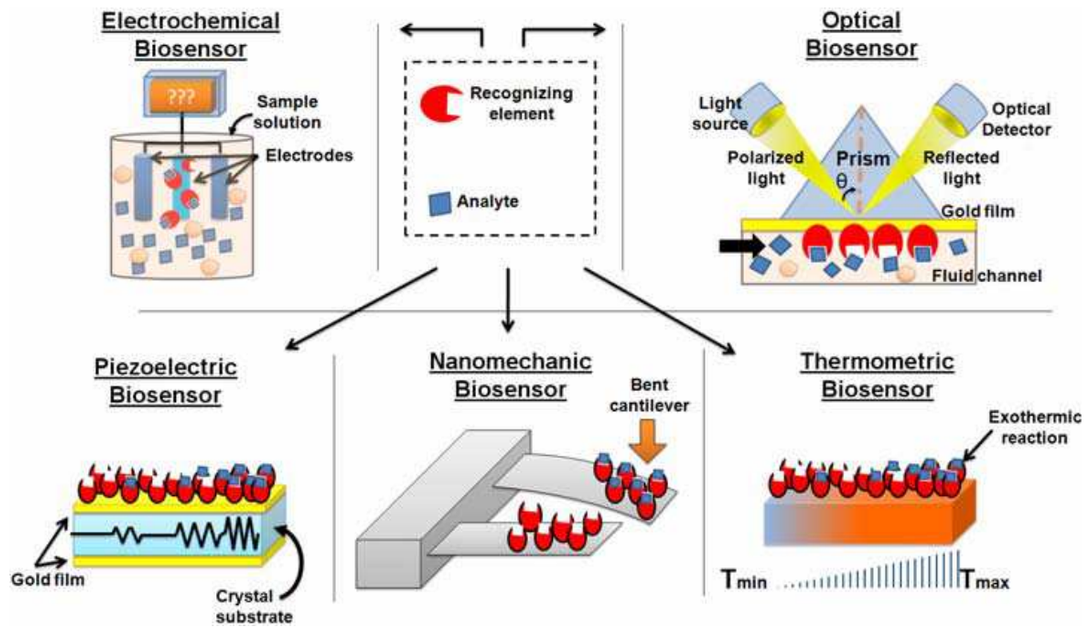


Fig. 5. Generic function of a biosensor is to convert binding events between biological receptors and target agents into a signal.

First we have the sensing element (a). It is where the biological system is immobilized. The agent can be an enzyme, antibody, DNA chains, etc, and is used for the recognition of the analyte. (b) is the transducer, where the biological signal is converted into a signal, which may be; optical, thermal, and electrical signal: current, potential, conductance, impedance,

etc. Then, such signal must me amplified and then processed. This amplifier module is the detector stage (c). Thinking in electrical signals, an amplifier stage is used to amplify the biological signal, which is generally very low. Then, (d) is the electronics module which has the role to process such measurements. Finally, (e), the results are presented thanks to a user-friendly interface to visualize the data.

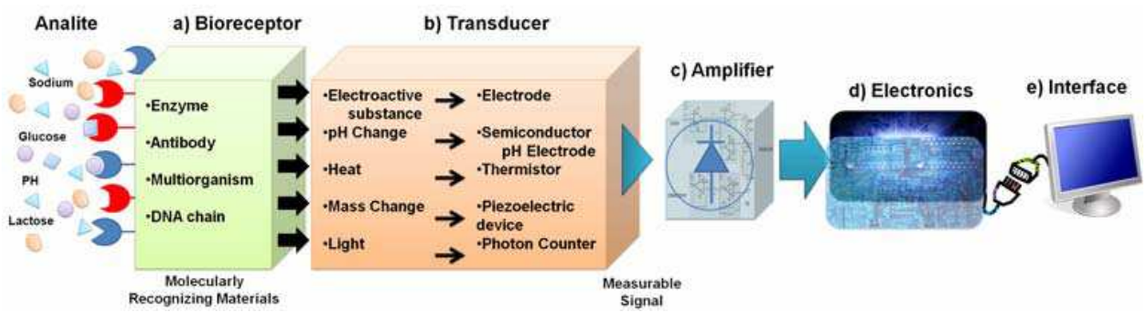


Fig. 6. Generic components of a biosensor.

### 2.3.2 Electrochemical biosensors

Electrochemical biosensors are the largest group of chemical sensors. All of them are based on fixing some variables of the electrochemical cell and check how the other variables change with the fluctuations of the controlled variables. These biosensors are normally based on enzymatic catalysis of a reaction that produces or consumes electrons (such as enzymes are rightly called redox enzymes). The sensor substrate usually contains three electrodes, a reference, an active or working and a counter or auxiliary electrode. Electrochemical sensors allow three main different configurations: voltammetric, potentiometric and conductrometric measurements. Voltammetric biosensors are those based on the measurement of the current-voltage variations. Voltammetric measurements typically consist of a three-electrode arrangement. Measurement of current occurs at the redox electrode as a function of the electrode potential. The solution must contain electro active species that can undergo electrode reaction. Amperometric biosensors are a particular case of them, where is determined electrical currents associated with a redox process where a fixed voltage in the sensor is applied. In potentiometric biosensors, the electrode and solution are in chemical equilibrium, the current flow is near zero and a voltage is measured relative to a reference electrode. Conductometric biosensors are based on the measurement of the variations of the conductance with the use on an alternating current at a fixed frequency of operation. Special interests, as is stated in more detail in the next section, have Impedance biosensors that determine variations of the impedance of the sensor.

For voltammetry biosensors, and in particular for amperometric biosensors, the most standard measurement method is based on the three-electrode configuration. By applying a proper fixed potential between them, a current is generated, which is related to the concentration of the electro active species in the sample solution. These species are generated by oxidation or reduction in the sample solution. The potentiostat amplifier, presented in 2.4.2, controls the voltage between the working and reference electrodes, and the current through the electrochemical cell formed by the three electrodes of the biosensor and the solution where the reaction takes place is conveyed through the counter electrode. Based on the use of the potentiostat amplifier, there are different kind of electrochemical test

that can be carried out in order to analyze the electrochemical cell formed by the biosensor and the solution media, Fig. 8. The most popular electrochemical technique used with electrochemical sensor is the cyclic voltammetry, depicted in Fig. 7.

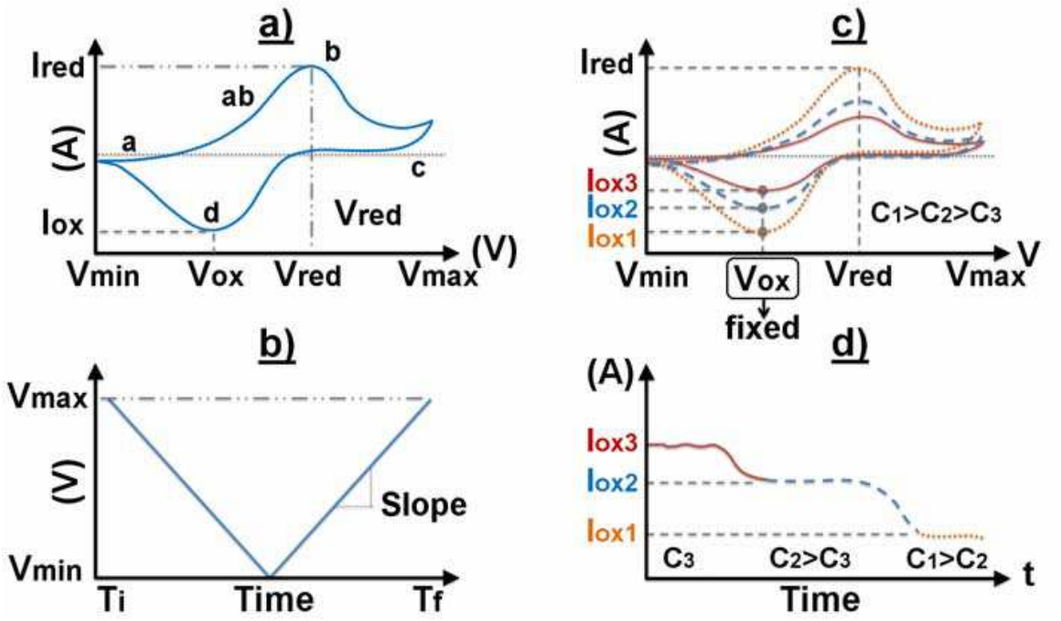


Fig. 7. Cyclic voltammetry.

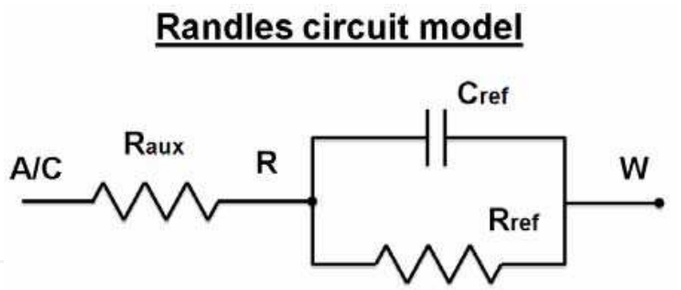


Fig. 8. Randles model.

The voltage applied in b) is fixed by the potentiostat between the working and reference electrodes. In a) is depicted the characteristic cyclic voltammetry, where the path between point (a) and (b) represent the reduction phase, that is, the electrons are derived to the solution from the electrodes. During the path (c) to (d) the oxidation takes place. The chemical species pass electrons to the electrode. Characteristic peaks for the oxidation and reduction are obtained, (d) and (a) respectively. Different voltage ramps define different reactions. Also, for different concentrations of the analytes the peaks of reduction and oxidation change, as depicted in c). Based on this technique the amperometric analysis is introduced. As it was mentioned above, a fixed voltage now is fixed and the current is directly measured. Usually this voltage is fixed at that point where the electrochemical response is maximized. In d) is depicted this situation of the maximum point of oxidation, and for different concentrations. Several other techniques are used for a voltammetric

analysis like staircase or sampled DC voltammetry, normal pulse voltammetry, differential pulse voltammetry, square wave voltametry and differential normal pulse voltammetry. All of these techniques are based in a potential that is scanned, defining an initial and final steps of voltage vs. time.

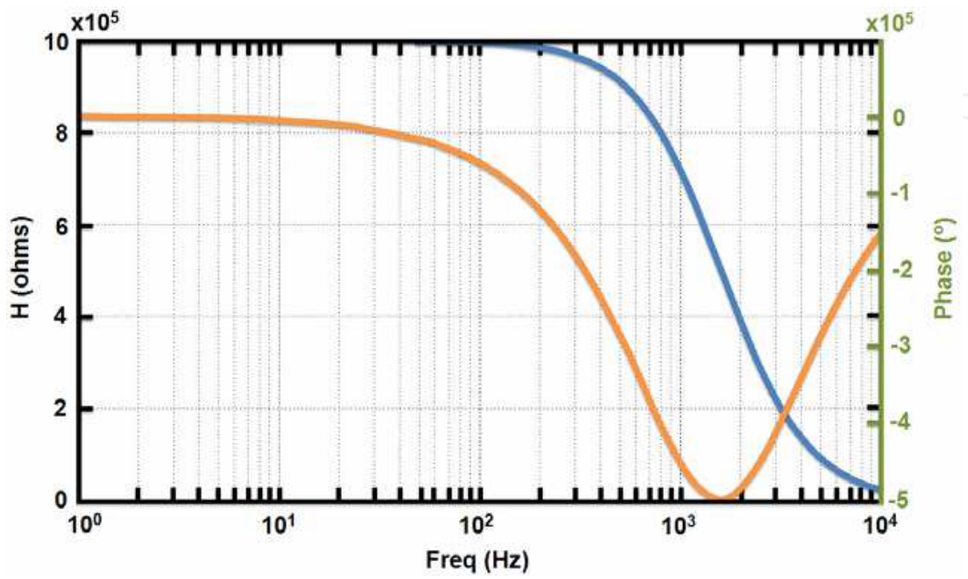


Fig. 9. Plof the Bode Polt for an EIS.

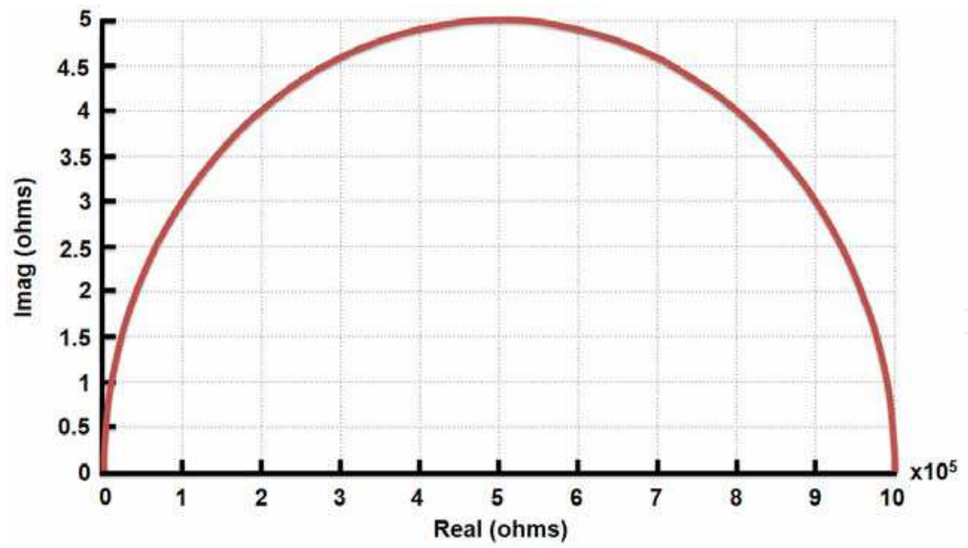


Fig. 10. Plot of the Nyquist Polt for an EIS.

The Electrochemical Impedance Spectroscopy (EIS), is a more effective method to probe the interfacial properties of the modified electrode through measuring the change of electron transfer resistance at the electrode surface, which is caused by the adsorption and desorption of chemical or biological molecules. There are different electrical models that represent the electrochemical cell, and the easiest one is the Randles model, Fig. 8, just

defined by three elements: by the double-layer capacitor in parallel with a polarization resistor, which is also described as a charge transfer resistor, and the solution resistor. In an electrochemical cell, electrode kinetics, redox reactions, diffusion phenomena and molecular interactions at the electrode surface can be considered analogous to the above components that impede the flow of electrons in an ac circuit. The measurement of the impedance variation of the cell can be depicted following two different approaches: a) the magnitude and phase of the impedance are depicted as a Bode plot, as depicted in Fig. 9, or b) a Nyquist plot, Fig. 10, where in the complex plane are depicted the real impedance component in the X coordinates, and the imaginary impedance component in the Y coordinates.

### 2.3.3 Some examples

Most of the biosensors are based on electrochemical transducer method. The clearest example is the blood glucose monitoring marker, based on amperometric enzyme biosensors. Here an enzyme glucose oxidise catalyses the conversion of the analyte to a molecule that can be detected by the transducer. First, it oxidises glucose and uses two electrons to reduce a component of the enzyme, FAD to FADH2, which is also oxidased. The resulting current in the electrode is a measurement of the concentration of glucose. Oxidades oxidize their substrates and they need oxygen as a co-substrate, re-oxidizing the enzyme to the initial state. The hydrogen peroxide produced is again oxidized at the electrode:

$$\text{Glucose} + O_2 \leftrightarrows \text{Gluconolactone} + H_2O_2$$

The glucose oxidase with its prosthetic group FAD

$$\text{Glucose} + \text{FAD} \leftrightarrows \text{Gluconolactone} + FADH_2$$

$$FADH_2 + O_2 \leftrightarrows H_2O_2 + \text{FAD}$$

And at the electrode takes place an anodic reaction, on platinum, @ 0.6V vs. Ag/AgCl; 3M.

$$H_2O_2 \leftrightarrows 2H^+ + O_2 + 2e^-$$

Then, the detected current by the potentiostat, which is proportional to the concentration of the analyte in the sample, is:

$$I_d = n \cdot A \cdot F \cdot D_s \cdot c^0 / \delta_N \quad (1)$$

Where A is the area of the electrode, $D_S$ is the diffusion coefficient of the analyte S, $c^0$ is the bulk solution concentration of the analyte and finally $\delta_N$ is the thickness of the stagnant layer.

The glucose biosensor (Fiorito and De Toresi, 2001; Hiller et al., 1996; Kros et al., 2001) is an example of this this applications. The biosensor is based on the electron transfer that occurs during the enzymatic reduction of glucose. Nowadays, there is an increasing interest in the field of glucose biosensors, looking for Glucose Continous Monitoring (GCM). In the last years several works have been published in the field like Patel et al., (2007), where it's presented an electro-enzymatic glucose sensor, (Xi Huang et al., 2009), where it is introduced a capacitive based MEMS affinity sensor for continuous glucose monitoring applications, (Teymoori, Mir Majid et al., 2009) introducing a MEMS for glucose and other generical sensors in medical applications and (Rodrigues et al., 2007) where it's developed a

new cell-based biochip dedicated to the real-time monitoring of transient effluxes of glucose and oxygen, using arrays of amperometric microsensors integrated in the inlet and the outlet of a PDMS cell chamber, and complete designs like (Rahman et al., 2009) where is presented the design, microfabrication, packaging, surface functionalization and in vitro testing of a complete electrochemical cell-on-a-chip (ECC) for the continuous amperometric monitoring of glucose, performing cyclic voltammetry, electrical impedance spectroscopy (EIS), and microscopic examination.
Special interest has the development of nanosensors applied in this field. Some examples are reported, like (Usman Ali, S.M et al., 2009), where ZnO Nanowires are used for a GCM application directly connected to the gate of a standard low-threshold MOSFET, (Lee Y.J. et al., 2009), where a flexible enzyme-free glucose micro-sensor with nanoporous platinum working electrode on a bio-compatible PET film was designed, (Goud et al., 2007), where it's presented nanobioelectronic system-on-package (SOP) with integrated glucose sensor based on carbon nanotubes working electrodes, (Jining Xie et al., 2007) where it's studied a platinum nanoparticle-coated carbon nanotubes for amperometric glucose biosensing, or in (Ekanayake, E.M.I et. al., 2007) where it's described fabrication and characterization of a novel nano-porous polypyrrole (PPy) electrode and its application in amperometric biosensors, with enhanced characteristics for glucose sensing.

### 2.4 Electronics for electrochemical biosensors

#### 2.4.1 Two and three electrodes configurations

Two are the minimum of electrodes that are required in order to control the interface between an electrode and a solution, forming a simple electrochemical cell. One of these electrodes is the working electrode (W), where the reaction of interest takes place. The other electrode is the reference electrode (R) where is fixed a constant potential reference. Generally for a voltammetry experience this approach it is not enough when the potential applied must be controlled owing to the equivalent resistance of the solution. Then, when a current circulates through the solution a voltage drop is generated. Also, when current is present at the reference electrode implies a variation of the voltage interface of it. This situation implies that the voltage difference between the reference and the working electrodes is not well defined. A simple solution is based on the use of a large reference electrode and a small working electrode but sometime this is not possible. The solution to this situation is the use of a three-electrode system, placing an extra electrode which is usually called counter (C) or auxiliary electrode, as is depicted in Fig. 11. The voltage difference is fixed between the (W) and (R) electrodes and the current is injected by the (C) electrode and the potential is well defined at the cell (Vcell). The potentiostat amplifier is the instrumentation that has the role to control this bias and read the current of the cell.

#### 2.4.2 The potentiostat amplifier

The main electronics involved in the design of the instrumentation are defined by the potentiostat amplifier, to drive and control the electrodes, and to measure the output signal and the processing electronics. The potentiostat amplifier is the electrochemical measurement technique to interface the biological elements with the electronics. Electronic measurement of the biochemical analyte concentrations is essential for diseases diagnose and study of biological systems.
Two different ways can be followed: a) the potentiometric configuration, where a fixed current it is applied and the output voltage is measured, or b) the amperometric

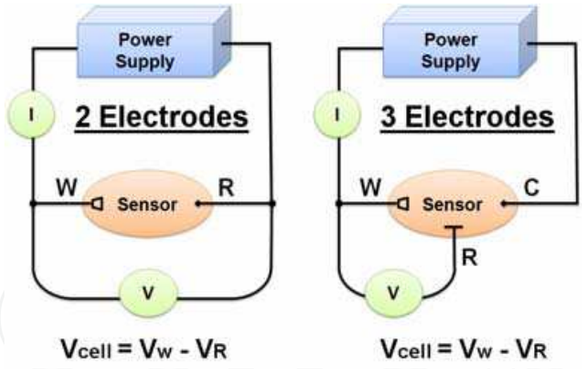


Fig. 11. Two and Three-electrode electrochemical measurement system.

configuration, where a fixed voltage is applied and the output current is read, and converted to a voltage signal by the transimpedance amplifier. If the size of the electrodes is decreased, defining micron-sized electrodes, the current level decreases up to femto-amperes. Some references are described in (Choi Myung-suk et al., 2007), in their work "Implantable Bio system design for displacement measurement of living life", in the work by (K.Kitamori, 2007), where he described micro and nano chemical sensors on-a-chip, and the by (Wen-Yaw Chung et al., 2007), where they present a low power readout circuit with an potentiostat amplifier for amperometric chemical sensors for a Glucose Meter Application. Other interesting biosensors are the piezoelectric immunosensors, like the developed for the rapid diagnosis of M. tuberculosis by (Eric Carnes et al., 2005).

The state of the art of the potentiostat amplifiers has evolved in such a different ways from discrete or integrated solutions. In order to design a portable system for standard electrochemical assays, discrete solutions become an extremely good choice in terms of portability, accuracy and economical cost. But, demands for increased functionality, reduced system size, reduced electrodes size, ultra-low current detection and versatility will force potentiostats to be designed on a system-on-chip (SoC) to be implemented in advanced CMOS processes. The scaled supply voltages in these processes (Kakerow et al., 1995; Kraver et al., 2001; Reay et al., 1994), however, seriously limit the chemical analysis range. The drive voltages of amperometric chemical sensors do not scale with electrode size, but are instead defined by the reduction/oxidation (redox) potentials of the analysis been investigated. In fact, many analysis are undetectable using standard potentiostats in a 0.18µm CMOS process due to its maximum supply voltage of 1.8V (Kissinger et al., 1996). Standard, single-ended (SE) potentiostats force the sensor's electrode to a fixed potential, Fig. 12, while fully differential (FD) potentiostat, employing a FD operational amplifier, dynamically controls the electrode's potential and doubles its voltage swing.

### 2.4.3 The lock-in amplifier

EIS is an ac method that describes the response of an electrochemical cell to a small amplitude sinusoidal voltage signal as a function of frequency. EIS technique consists on applying an AC voltage to the *R- W* electrodes and measure the resulting AC current at the *Working* electrode (Fig. 13). Then, it is possible to represent the impedance of the electrochemical cell. The resulting current sine wave differs in time (phase shift) with respect to the perturbing (voltage) wave, and the ratio V(t)/I(t) is defined as the impedance (Z), that accounts for the combined opposition of all the components within the

electrochemical cell (resistors, capacitors, inductors) to the flow of electrons. The variations in the electronic signal are due to the antibody-antigen (Ab-Ag) interactions. The signal processing circuitry has the role to obtain the real and imaginary components of the measurement of the Electrochemical Impedance.

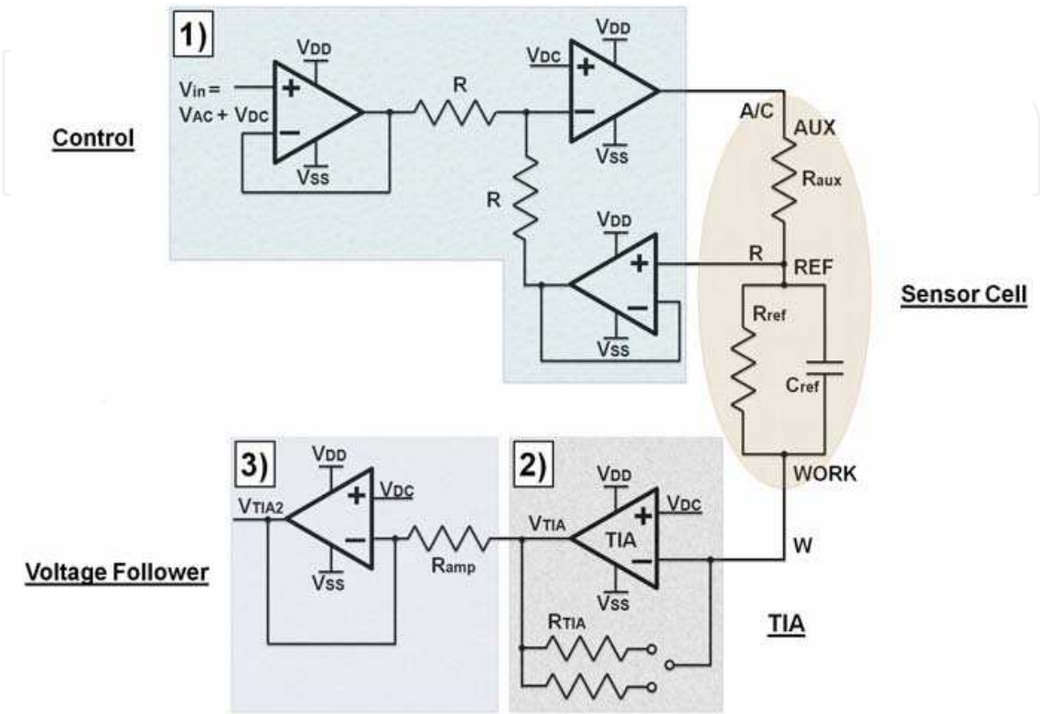


Fig. 12. Potentiostat Amplifier with electrochemical sensor's model.

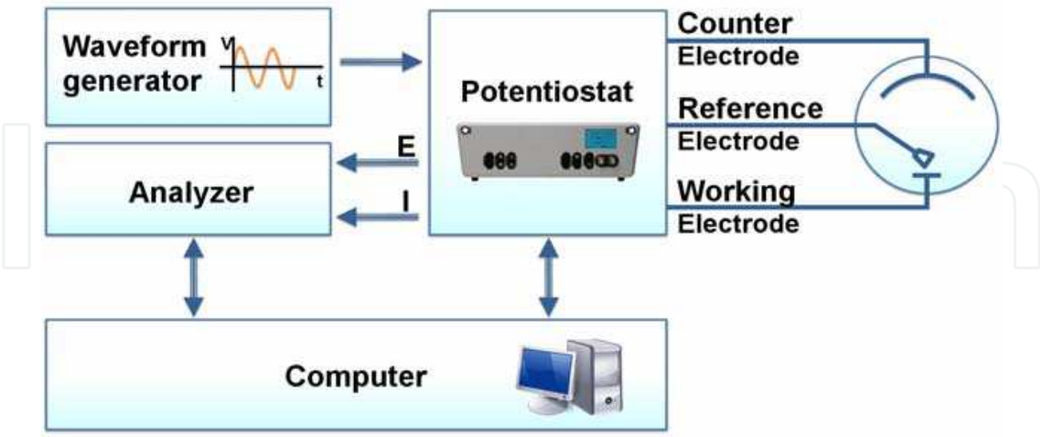


Fig. 13. Generic setup for an EIS experiment.

Based on the nature of the measured signal there are two main approaches: a) the capacitive immunosensors, where the surface of the electrode is completely covered by a dielectric layer and the whole electrode assembly behaves as an insulator. The variation of the capacitance is measured, in frequency ranges up to 100kHz, and b) the faradaic

immunosensors, which have the surface of the electrode partially or wholly covered by a non insulating layer or partially covered by an insulating layer, are able to catalyse a redox probe that exists in the measuring solution. In this case, the measured parameter is the charge transfer resistance (the real component of impedance at low frequency values, typically 0.1-1.0 Hz), and Ab-Ag interactions are expected to cause an increase in its value as the faradic reaction becomes increasingly hindered.

In order to proceed with the signal processing, there are mainly two approaches: a) the Fast Fourier Transform (FFT), and b) the Frequency Response Analyzer (FRA). In the case of the FFT, a pulse or step, -the approach to be followed is the ideal Dirac delta function-, is applied to the sample because it contains a wide frequency content. Then, the response of the sample is digitized and processed in a digital processor, for instance a DSP, and using the FFT algorithm, the different frequency components are obtained for their analysis. Also, other possibility that could be followed is the logarithmic sampling in the DFFT calculus, reducing the data that must be required in the process. A simpler solution is based on the FRA approach. In this case, a sine and cosine signals are adopted, and using two multipliers and a filter stage the real an imaginary components of the response are obtained. This measurement must be done for each frequency. Working with just one sensor and in terms of the size of the final product, the FFT option could be adopted, because the response for several frequencies is obtained. The FRA solution is a solution more oriented to multi-sensor approaches but also in the case of single sensors it is a nice option, in terms of the trade-off between complexity and speed, if not too low frequencies must be measured. This lock-in approach is more feasible.

### 2.5 Integration of lab on a chip devices

The fabrication of lab-on-a-chip devices require the integration of several systems such as microfluidic, detection (BioLED Technology, 2007), power supply (Colomer et al., 2008) and/or communication in a small and portable device.

The aim of the microfluidic system is to transport the fluid into the microcapillaries as well as its preparation for their proper analysis. The preparation step consists in the separation of the fluidic and/or suspended particles (Rodríguez-Villarreal et al., 2010), the mixing of the fluids for cell activation and/or mixing reactants for initiation. It could takes place along the capillaries or inside of created droplets (Xia et al. 2010), which can also be useful to encapsulate biological particles or chemical reagents. In some cases, the sample needs to be focalized (Rodríguez-Trujillo et al., 2008) before it flow through the electrical or optical detection system (Fig. 14) to achieve a better detection signal.

A complete portable lab-on-a-chip device required an integrated power supply for the functionality of the detection and the communications systems. The last one, has the objective to inform by sending the relevant results of the biological analysis.

The integration of all these Microsystems requires sophisticated microfabrication techniques such as photolithography, chemical vapour deposition, dry and wet etching and many more (Chen, 2006; Chinn, 2008) to create a final prototype made of biocompatible materials. The integration of the silicon, polymer or glass devices are the main concerns of research groups.

There are two ways of integrating such microdevices, the fabrication of all of them on the same device or the assembly of several microdevices previously fabricated as shown in Fig. 15. A). But up to now, although there are many portable devices, the lab on a chip technology still required of external sources for energy supply and the human-device interface.

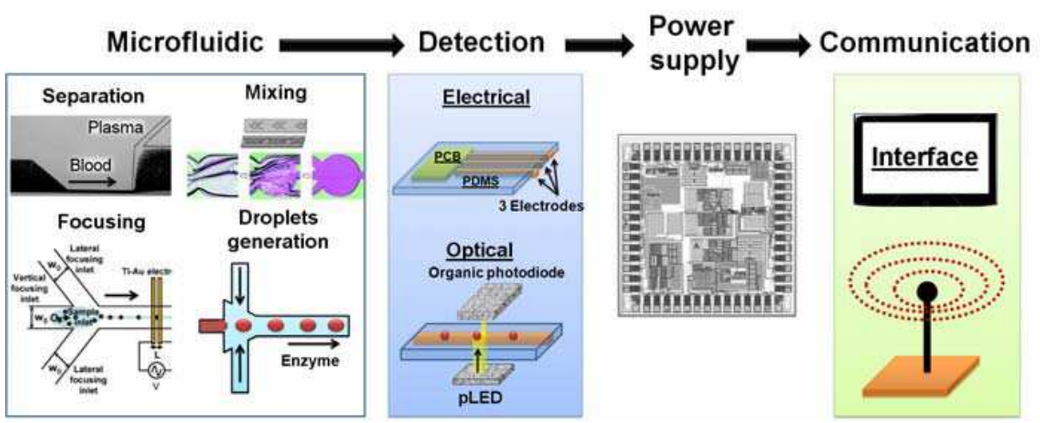


Fig. 14. Microsystems required for a complete Lab-on-chip device.

Different companies of biomedical devices such as Philips, Biosite Inc. and Medimate are developing small devices that integrate some fluidic/detection microsystems with portable power/interface macrosystems to commercialize analytical biomedical devices, Fig 15.B. Besides, the development of a full custom lab-on-a-chip device envisaged for implantable applications, keeps been the objective of the new medical technologies.

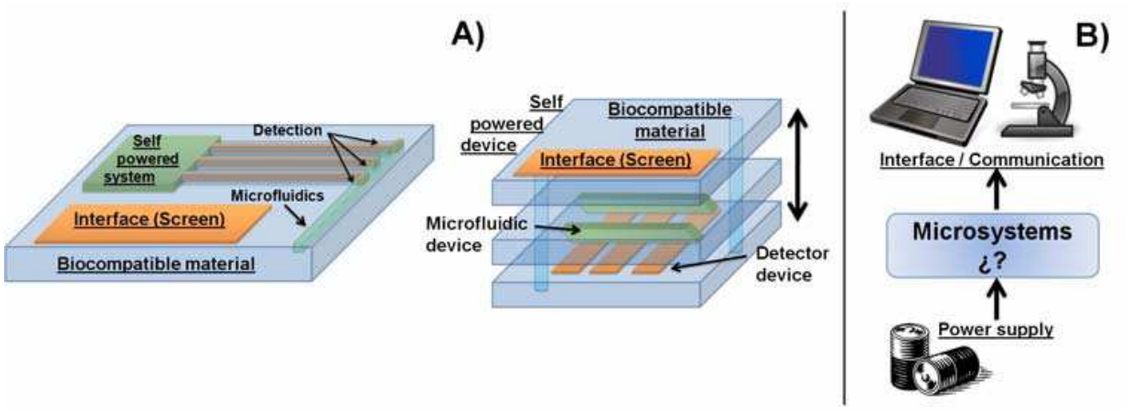


Fig. 15. Scheme of integration of A) full lab-on-a-chip devices and B) portable and microdevices.

## 3. An example of a miniaturized electrochemical instrument for in- situ $O_2$ monitoring

The decrease of oxygen concentration in water is a clear indication of water pollution, which is one of the main concerns of the Water Framework directive in the European Union, as the pollution is mainly due to nitrogen-based fertilisers used in agriculture. One of the direct consequences of reduced levels of dissolved oxygen is suffocation especially in acute cases where fish live in well-oxygenated waters which suddenly become oxygen deficient, usually as a result of intervention by man rather than natural changes in oxygen levels (Kramer, 1987). In addition to pollution and biological processes including primary production and respiration, in open water systems, other sources of variation in the dissolved oxygen concentration come into play which includes physical mechanisms such as diffusion as a

function of wind and waves (Irigoien et al., 1999). Due to the complexity of these variables, the dissolved oxygen budget can be difficult to estimate requiring continuous and spatial on-line monitoring.

As a first approach a discrete PCB, covered with a hydrophobic polymer, has been designed based on commercial discrete electronics and specific oxygen sensors. The coated electronics (with PDMS), can be immersed in water without affecting its functionality.

This section presents the development of a low power portable potentiostat for In-Situ electrochemical measurements, covered by PDMS. The core of the electronics is defined by a potentiostat amplifier, as the structure presented in 2.4.2, Fig.12. The custom electronics, which includes a small printed circuit board (PCB) of 31mm X 21 mm, has been designed using commercial amplifiers, looking for the best performances, as described in the paper.

Some commercially available oxygen analyzers tend to be large, cumbersome and expensive. Here the electronics and sensors are miniaturized and placed in close proximity to each other and subsequently covered by a hydrophobic material. The size of the contact pads is 5mmX 2.5 mm, in order to have a good soldering area between the contacts and the electrodes, Fig. 16. The power consumption of this implementation is around 350 mW.

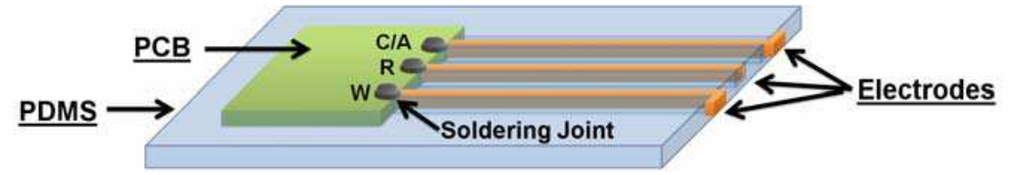


Fig. 16. PCB and connections of the electrodes.

The commercial amplifiers used, were the OPA 656 and the OPA 657 working as the transimpedance amplifier, both from Texas Instrument. These amplifiers were selected for their good characteristics in terms of high input impedance, low bias and offset input currents and voltages. It is important that the reference input has a high impedance in such a way that almost the same current flows between the counter/auxiliary electrode and the working electrode. The oxygen analyzer, coated with PDMS, is depicted in Fig.17. The PCB was tested before and after its introduction into water. Some experiments were carried out to analyze its performances compared with commercial equipment. The used instrument was the CH 1200A from CH Instruments.

Different fixed DC voltages were fixed, and the variation of O2 was measured in a programmed time interval. For testing purposes a three electrode electrochemical sensor (Advent Research Materials, UK), was fabricated using a 200µm platinum wire for the counter electrode, a 200µm silver wire for the pseudo reference electrode and a 75µm gold wire, with 18µm Teflon insulation, for the working electrode. The electrodes were cut into approximately 1cm lengths sections and soldered to the potentiostat. The insulated gold working electrode was cut so that the sensor tip was a 75 µm gold disc electrode. The gold electrode was cut each time with a new scalpel blade and the resulting disc electrode was checked under a microscope. The electrodes were placed approximately 1mm apart from each other during the experimental measurements. For the amperometry test, the gold working electrode was set at -1V where the oxygen was reduced to give a more negative current. Therefore, for high oxygen concentrations the current was more negative than for lower concentrations of oxygen. This was used as the main indicative of oxygen detection in water.

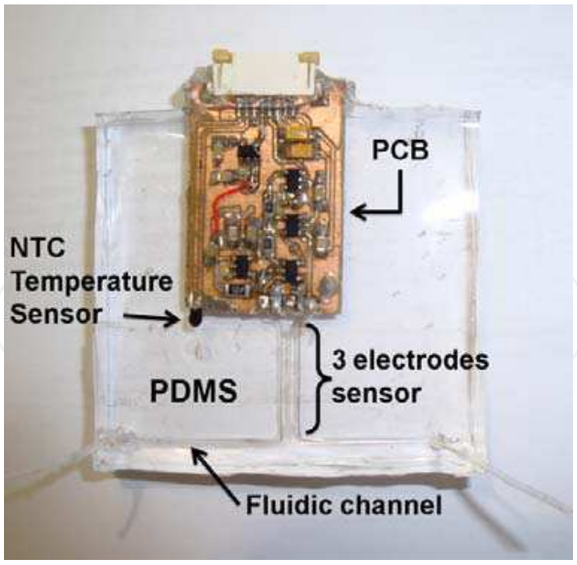


Fig. 17. PCB capture coated with PDMS.

The sensors were tested in different media solutions to detect changes in the oxygen concentration. The different media solutions used were Mili-Q water, TAP Water and 1mM PBS solution. All tests were performed at ambient temperature. The oxygen concentration in the solutions was reduced by applying nitrogen gas to the media for approximately 20 minutes. The measurements obtained are shown below, comparing the performance of the custom potentiostat with the commercial one. Fig. 18.A shows the experimental overlaid voltammograms obtained with tap water (with oxygen) concentration (Region A), and low $O_2$ concentration (Region B) using the commercial potentiostat and with the electronics coated with PDMS. The more negative peak shown in (A) results from the water sample that has been exposed to ambient air compared to the less negative peak (B) where the water sample has been bubbled with nitrogen to remove the oxygen.

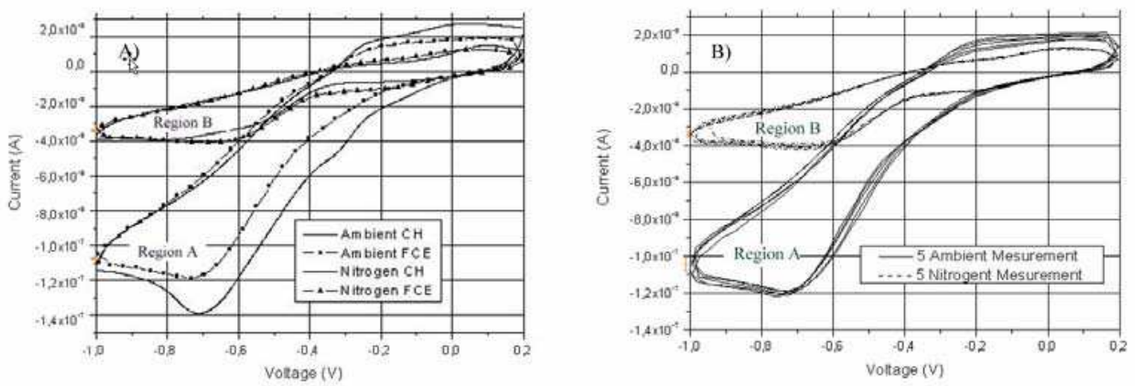


Fig. 18. A) Voltametry with CH Instrument and custom system in Ambient TAP Water and with nitrogen.; B) Custom Cyclic measurements, for different sensors and electronics, with tap water in the case of high and a very low concentration of oxygen.

Measurements with tap water have been carried out in order to characterise the custom potentiostat, as shown in Fig. 18.B) It can be noticed how the measurement of the current

level and the minimum operating voltage are very similar. We have measured a variation lower than 4.5% in the case of high level concentration of oxygen, and even a lower variation (2.5%), in the case of low level oxigen concentration.

## 4. An example of an in-vivo biomedical implantable device

In this section, the conception of a generic CMOS architecture for an implantable device, (Colomer&Miribel, 2011) is presented. Nowadays, special interest in nanobiosensors is increasing in the field of medical diagnosis. From the market point of view, the main opportunity of such sensors is focused on on-line devices and in-vivo or implantable devices. The impact of such devices for each individual being will open the possibility to define a personalized diagnosis, and monitoring each patient. The development of such devices and the derived telemedicine environments has a great market potential. Different approaches should be followed for a discrete, small $cm^3$ or for an implantable device, and performances, communications capabilities, etc, are very different. The size of this implantable device is envisaged as a capsule of an ideal size less than 4.5 cm long and 2.5 cm in diameter, following the same philosophy like some subcutaneous implantable devices like Norplant®, Jadelle® or Implanon®, as implantable contraceptives. A proposal would be a True/False implantable system, or event detector that works as an alarm. When the analyzed concentration level is out of a range of accepted values, a threshold value activates the alarm, and a mapping could be defined, but sizing the complexity and the required power. The proposed generic implantable architecture is presented in Fig. 19. It is composed by a three electrodes BioSensor, an antenna and the electronic modules.
Such system combines different modules introduced thought the chapter. The antenna and the AC/DC module that is used to supply energy to the device (inductive powering), and the communication set-up (backscattering), as stated in 2.2, defining and AM modulation. Then, an integrated a low-voltage and low-power potentiostat is placed, as described in 2.4.2. Finally, in the modulation/Data Processing module an analog lock-in amplifier can be integrated. In this case an FRA approach is followed. An interesting approach to work with in-vivo biosensors is to sense its impedance variation at one defined frequency, where the sensor is more sensitive to changes in its impedance. Not a full Electrochemical Impedance Spectroscopy is carried out. Just the variation of the impedance or capacitance of the biosensor when the target analyte is captured by the probe is of interest. Looking for this kind of implementations, there is a trade-off between complexity, area, power consumption, with the desired measurements and the electronic implementation. In this sense, a fully integrated DSP solution, as a digital lock-in amplifier, would present a big challenge. The design looks forward to very small power consumption, working at very low power supply. Following this assumption, an analogue lock-in amplifier is derived, Fig. 20, completely integrated and conceived in a commercial technology, as electronic interface with implantable biosensors in low-frequency applications. The integrated lock-in is based on two Synchronous Demodulated Channels. Both channels are used to find two DC components at the same time. These DC levels would be used by other two comparators, defining in the same way an alarm system, or two ADC converters to send its digital words by a backscattering method for monitoring the impedance. From these rectified signals are obtained two DC components, VREout and VIMout, after a low-pass filter placed for each channel. The magnitude and phase of the electrochemical cell are then obtained afterwards using (2) and (3).

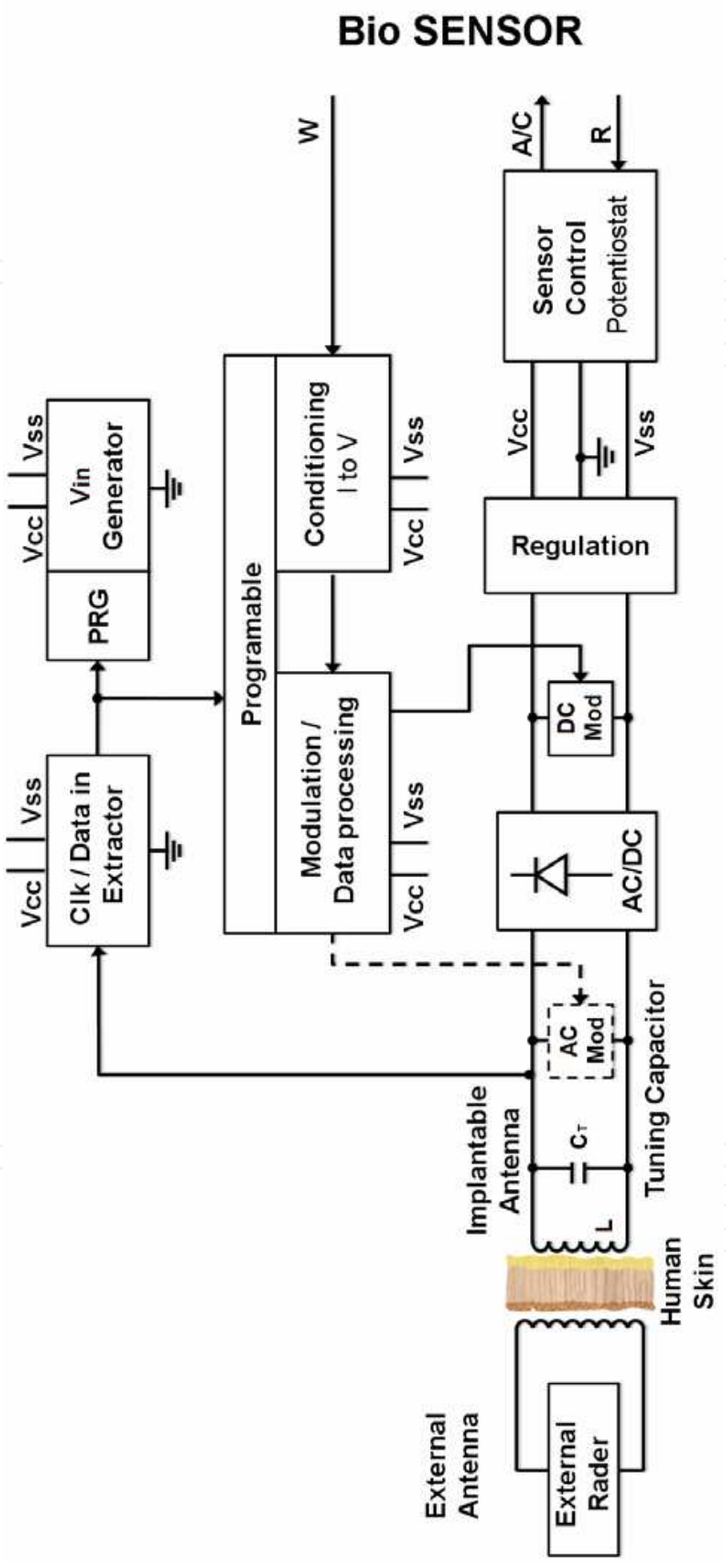


Fig. 19. Proposed generic implantable front-end architecture.

$$Magnitude = \sqrt{VREout^2 + VIMout^2} \tag{2}$$

$$Phase = Tan^{-1}\left(\frac{VIMout}{VREout}\right) \tag{3}$$

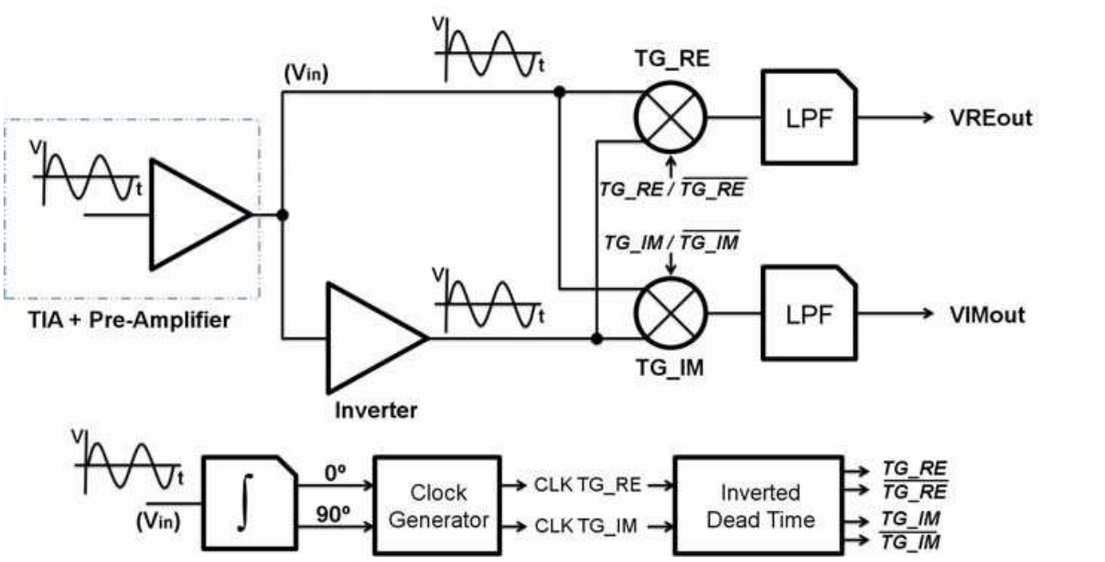


Fig. 20. Lock-in amplifier block diagram.

## 5. Summary and conclusions

In this chapter, we started with an introduction to the conception of a generic bio-portable device, which can be a miniaturized solution to an envisaged implantable device. This device is based on several components, which are basically represented by: the powering module, the communications module, the biosensors, the bioelectronics and the micro fluidics. These key elements have been introduced regarding the state-of-the-art and the trends involved in the development of such systems. In terms of the power module, special attention has been focused on the energy that can be harvested from ambient sources to body harvesting. A brief introduction to the communications module has been also presented. Biosensors and the needed bioelectronics involved in the design of such system were explained. Different approaches to work with electrochemical sensors, for potential control and measurement were introduced: potentiostat amplifiers and the use of a lock-in amplifier for an electrochemical impedance analysis. Finally, two implementations of electrochemical devices, from a discrete to an integrated approach, were also presented: an $O_2$ monitoring instrument and an approach for and In-vivo implantable device as an event detector.

## 6. References

Bender, S., and Sadik, O.A. (1998). Direct electrochemical immunosensor for polychlorinated biphenyls. *Environ. Sci. Technol*, vol. 32, pp. 788–797

BioLED Technology (2007). Internet Journal of emerging medical technologies, Available from http://www.medgadget.com/archives/2007/02/bioled_technolo.html

Carlson, E., Strunz, K., and Otis, B. (2009). 20mV input boost converter for thermoelectric energy harvesting. *Proc. of the 2009 Symposium on VLSI Circuits*, pp.162 – 163.

Carnes, E., and Wilkins, E. (2005). The development of a new, rapid, amperometric immunosensor for the detection of low concentrations of bacteria. *American Journal of Applied Sciences*.

Celik, T., and Kusetogullari, H. (2010). Solar-Powered Automated Road Survillance Systems for Speed Violation Detection. *IEEE Transactions on Industrial Electronics*, vol. 57, no. 9, pp. 3216– 3227.

Chen, Jingkuang. (2006). *Micro-machined medical devices, methods of fabricating microdevices, and medical diagnosis, imaging, stimulation, and treatment*. USPatent11/320921

Chinn, Douglas. (2008). Microfabricatin techniques for biologists: A Primer on Building Micromachines, In: *Microengineering in Biotechnology*. Michael P. Hugehs and Kai F. Hoettges. Springer. Methods in Molecular Biology, vol. 583, pp 1-53, ISBN:978-1-58829-381-7.

Chung, W.Y., Paglinawan, A.C., Wang, Y.H., and Kuo, T.T. (2007). A 600μW Readout Circuit with Potentiostat for Amperometric Chemical Sensors and Glucose Meter Applications. *Proc. of the IEEE Conference on Electron Devices and Solid- State Circuits*, pp. 1087 – 1090.

Cleven, R., Nur, Y., Krystek, P., and Van den Berg, G. (2005). Monitoring Metal Speciation in the Rivers Meuse and Rhine using DGT. *Water, air and Soil Pollution*, vol.165, pp. 249-263.

Colomer-Farrarons, J., Miribel-Catala, P., Saiz-Vela, A., Puig-Vidal, M., & Samitier, J. (2008). Power-Conditioning Circuitry for a Self-Powered System Based on Micro PZT Generators in a 0.13μm Low-Voltage Low-Power Technology. *IEEE Trans. on Industrial Electronics,* vol. 55, no. 9, Sept 2008, pp. 3249-3257.

Colomer-Farrarons, J., Miribel-Català, P., Rodríguez, I., & Samitier, J. (2009).CMOS Front-End Architecture for In-Vivo Biomedical Implantable Devices. *Proc. of the 35th Annual Conference of the IEEE Industrial Electronics*, Nov. 2009, pp.4437-4444.

Colomer, J., Miribel-Catala, P., Saiz-Vela, A., Rodriguez, I, &; Samitier, J. (2009). A low power CMOS biopotentiostat in a low-voltage 0.13 μm digital technology. 52nd IEEE International Midwest Symposium on Circuits and Systems, 2009. MWSCAS '09.

Colomer-Farrarons, J., Miribel-Català, P., Samitier, J., Arundell, M., & Rodríguez, I. (2009). Design of a miniaturized electrochemical instrument for in- situ O2 monitoring. (Proceedings Paper), *VLSI Circuits and Systems IV, Microtechnologies for the New Millennium*, Vol. 7363, Spie'09.

Colomer-Farrarons, J., Miribel-Català. P. (2011). *A CMOS Self-Powred Front-End Architecture for Subcutaneous Event-Detector Devices. Three-Electrodes Amperometric Biosensor Approach.* Springer, ISBN:978-94-007-0685-9, March 2011.

Ekanayake, E.M.I., Preethichandra, D.M.G., Kaneto, K. (2007). Fabrication and characterization of nano-structured conducting polymer electrodes for glucose biosensor applications. *Proc. Of the International Conference on Industrial and Information Systems*, pp. 63 – 66

Farace, G., Lillie, T., Hianik, P., Payne and Vadgama, P. (2002). Reagentless biosensing using electrochemical impedance spectroscopy. *Bioelectrochemistry*, vol. 55 , pp. 1–3.

Fiorito, P.A., and De Torresi, S.I.C. (2001). Glucose amperometric biosensor based on the co-immobilization of glucose oxidase (Gox) and ferrocene in poly(pyrrole) generated from ethanol/water mixtures. *J. Braz. Chem. Soc.*, vol. 12, pp. 729–733.

Garbuio, L., Lallart, M., Guyomar, D., Richard, C., and Audigier, D. (2009). Mechanical Energy Harvester With Ultralow Threshold Rectification Based on SSHI Nonlinear Technique. *IEEE Transactions on Industrial Electronics*, vol. 56, no. 4, pp. 1048 – 1056, April 2009.

Ghafar-Zadeh, E., Sawan, M., and Therriault, D. (2009).CMOS based capacitive sensor laboratory-on-chip: a multidisciplinary approach. *Analog Integrated Circuits and Signal Processing*, vol. 59, issue 1, pp. 1-12

Goud, J.D., Raj, P.M., Jin Liu, Narayan, R., Iyer, M., Tummala, R. (2007). Electrochemical Biosensors and Microfluidics in Organic System-on- Package Technology. *Proc. Of the Electronic Components and Technology Conference, 2007. ECTC '07, pp.* 1550 – 1555.

Hiller, M., Kranz, C., Huber, J., Bauerle, P., and Schuhmann, W. (1996). Amperometric biosensors produced by immobilization of redox enzymes at polythiophene-modified electrode surfaces. *Adv. Mater*, vol.8, pp. 219–222.

Huang, X., Li S., Schultz, J., Wang, Q., and Lin, Q. (2009).A capacitively based MEMS affinity glucose sensor. *Proc. of the International Solid-State Sensors, Actuators and Microsystems Conference*, TRANSDUCERS 2009, 21-25 June 2009, pp. 1457 – 1460.

Irigoien, X., Post, J., Castel, J., Pfeiffer ,K.F., HellmannB. (1999). Nycthemeral variations of the dissolved oxygen concentration in the turbidity maximum of three European estuaries: biological vs. physical processes. *Journal of Marine Systems,* vol. 22 , pp. 173-177.

Jining Xie; Shouyan Wang; Aryasomayajula, L.; Varadan, V.K. (2007).Material and electrochemical studies of platinum nanoparticle-coated carbon nanotubes for biosensing. *Proc. Of the IEEE Conference Nanotechnology*, pp.1077 – 1080

Johannessen, E.A., Wang, L., Cui, L., Tang, T.B., Astaras, A., Ahmadian, M., Cooper, J.M. (2004). Implementation of Multichannel Sensors for Remote Biomedical Measurements in a Microsystems Format. *IEEE Tran. Biomedical Engineering,* vol.51, issue 3, pp. 525-535.

Jovanov, E., Milenkovic, A., Otto, C., de Groen, P. (2005). A wireless body area network of intelligent motion sensors for computer assisted physical rehabilitation. *Journal of NeuroEngineering and* Rehabilitation, March, pp.2-6.

Juanola, E., Miribel-Català, P., Colomer-Fararrons, J., & Samitier, J. (2010). New green market opportunities from novel autonomous low power systems by energy harvesting. XXVII World Conference on Science and Technology Parks, IASP1020,

Kakerow, R., Kappert, H., Spiegel, E., and Manoli, Y. (1995). Low-power single-chip CMOS potentiostat. *Proc. of the International Conference on Solid-State Sensors and Actuators*.

Katz, E., and Willner, I. (2003). Probing biomolecular interactions at conductive and semiconductive surfaces by impedance spectroscopy: routes to impedimetric immunosensors. DNA-sensors, and enzyme biosensors. *Electroanalysis,* vol. 15, pp. 913–947.

Kazazian T., and Jansen, A.J. (2004). Eco-desing and human-powered products. *Proceedings of the Electronics Goes Green* 2004, 6-10 September 2004.

Khaligh, A., Zeng P., Xiaochun, W., and Yang, X. (2008). A hybrid energy scavenging topology for human-powered mobile electronics. *Proc. of the 34th Annual Conference of IEEE Industrial Electronics*, Nov. 2008 pp. 448 - 453.

Khaligh, A., Zheng, P., and Zheng, C. (2010). Kinetic Energy Harvesting Using Piezoelectric and Electromagnetic Technologies-State of the Art. *IEEE Transactions on Industrial Electronics*, vol.57, no. 3, March 2010, pp. 850-860.

Kissinger, P., Preddy, C., et.al. (1996*). Laboratory Techniques in Electroanalytical Chemistry.* Second Edition, P. Kissinger, and W. Heineman Eds., Marcel Dekker, Inc.,ISBN: 0-8247-9445-1, New York.

Kitamori, K. (2007). Micro and Nano Chemical System on Chip. *Proc. of the International Solid-State Sensors, Actuators and Microsystems Conference*, pp. 11 – 16

Kiziroglou, M.E., He, C., and Yeatman, E.M. (2009). Rolling Rod Electrostatic Microgenerator. *IEEE Transactions on Industrial Electronics*, vol. 56, no. 4, pp. 1101 – 1108.

Kramer,D.L. (1987). Dissolved oxygen and fish behavior. Environmental Biology of Fishes, vol.18, pp. 81-92 .

Kraver, K., Guthaus, M., Strong, T., Bird, P., Cha, G., Hold, W., and Brown, R. (2001). A mixed-signal sensor interface microinstrument. *Sensors and Actuators A*, vol. 91, pp. 266-277.

Kros, A., Van Hovell, W.F.M, Sommerdijk, N.A.J.M., and Nolte, R.J.M. (2001). Poly(3, 4-thylenedioxythiophene)-based glucose biosensors. *Adv. Mater*, vol. 13, pp. 1555–1557.

Laureyn, W., Nelis, D., Van Gerwen, P., Baert, K., Hermans, L., Magnee, R., Pireaux, J.J., and Maes, G. (2000). Nanoscaled interdigitated titanium electrodes for impedimetric biosensing. *Sens. Actuators B-Chem*, vol. 68, pp. 360–370

Le, T.T., Han, J., Jouanne, A. Von., Mayaram, K., and Fiez, T.S. (2006). Piezoelectric Micro-Power Generation Interface Circuits. *IEEE Journal of Solid-State Circuits*, vol.41, no.6, pp. 1411-1420, June 2006.

Lee, Y.J., Kim, J.D., Park, J.Y., (2009). Flexible enzyme free glucose micro-sensor for continuous monitoring applicati*ons. Proc. Of the Solid-State Sensors, Actuators and Microsystems Conference, 2009, pp.* 1806 - 1809

Li, W., He, S., and Yu, S. (2010). Improving Power Density of a Cantilever Piezoelectric Power Harvester Through a Curved L-Shape Proof Mass. *IEEE Transactions on Industrial Electronics*, vol.57, no.3, pp. 868-876.

Lillie, G., Payne, P., and Vadgama, P. (2001). Electrochemical impedance spectroscopy as a platform for reagentless bioaffinity sensing. *Sens. Actuators B-Chem, vol.* 78, pp. 249–256.

Liu, Y., Chakrabartty, S., and Alocilja. E.C. (2007). Fundamental building blocks for molecular biowire based forward error-correcting biosensors. *Nanotechnology*, vol. 18, 424017, pp. 1-6.

Mohseni, P., Najafi, K., Eliades, S.J., Xiaoqin Wang, (2005). Wireless multichannel biopotential recording using an integrated FM telemetry circuit. *IEEE Tran. on Neural Systems and Rehabilitation Engineering*, vol. 13, issue 3, pp. 263-271

Murari, K., Sauer, C.M., Stanacevic, M., Cauwenberghs, G., and Thakor, N. (2005). Wireless Multichannel Integrated Potentiostat for Distributed Neurotransmitter Sensing. *Prof. Of the Engineering in Medicine and Biology Conference.*

Myung-suk, C., Sang-won, L., Jong-chul, K., Jun-dong, C., Jin-kwon, K., Hang-sik. S., Myung-ho, L., Un-sun, C., and Jae-seok, K. (2007). Implantable Bio system design for displacement measurement of living life. *Proc. of the International Conference on Advanced Communication Technology,* vol. 1, pp.299 – 304

Nasiri, A., Zabalawi, S.A., and Mandic, G. (2009). Indoor Power Harvesting Using Photovoltaic Cells for Low-Power Applications. *IEEE Transactions on Industrial Electronics*, vol. 56, no. 11, pp. 4502 – 4509.

Niyato, D., Hossain, E., Rashid, M.M., and Bhargava, V.K. (2007).Wireless sensor networks with energy harvesting technologies: a game-theoretic approach to optimal energy management. *IEEE Wireless Communications*, vol.14, no. 4, pp.90-96.

Paradiso, J.A. Starner, T. (2005). Energy scavenging for mobile and wireless electronics. *IEEE Pervasive Computing*, vol.4, Issue 1, pp. 18-27.

Patel, J.N., Kaminska, B., Gray, B., Gates, B.D. (2007). Electro-Enzymatic Glucose Sensor Using Hybrid Polymer Fabrication Process. *Proc. Of IEEE International Conference the Electronics, Circuits and Systems, 2007. ICECS 2007,* pp. 403 – 406

Poyatos, J.M., Muñio, M.M., Almecija, M.C., Toress, J.C., Hontoria, E., and Osorio.F. (2010). Advanced Oxidation Processes for Wastewater Treatment: State of the Art. *Water Air Soil Pollut*, vol.205, pp. 187-204.

Rahman, A.R.A., Justin, G., Guiseppi-Wilson, A., Guiseppi-Elie, A., (2009). Fabrication and Packaging of a Dual Sensing Electrochemical Biotransducer for Glucose and Lactate Useful in Intramuscular Physiologic Status Monitoring. *Sensors Journal*, vol. 9, issue 12, pp. 1856 – 1863

Reay, R., Kounaves, S., and Kovacs, G. (1994). An integrated CMOS potentiostat for miniaturized electroanalytical instrumentation. *Proc. of the IEEE Solid-State Circuits Conf*.

Rodrigues, N.P., Kimura, H., Sakai, Y., Fujii, T. (2007). Cell-Based Microfluidic Biochip for Electrochemical Real-Time Monitoring of Glucose and Oxygen. *Proc. Of the Solid-State Sensors, Actuators and Microsystems Conference*, pp. 843 - 846

Rodríguez-Trujillo, R., Castillo-Fernandez, O., Garrido, M., Arundell, M., Valencia, A., Gomila, G. (2008). High-Speed particle detection in a micro-Coulter counter with two-dimensional adjustable aperture. *Biosensors and Bioelectronics*. vol 24:2, pp. 290-296

Rodríguez-Villarrea, A.I., Arundell, M., Carmona, M., Samitier, J. (2010) -High flow rate microfluidic device for blood plasma separation using a range of temperaturas. *Lab on a Chip*, vol 10, pp. 211-219.

Roundy, S. Steingart,D., Frechette, L., Wright, P., and Rabaey, J. (2004). Power sources for wireless sensors networks. *Proc. of the 1st European Workshop on Wireless Sensors Networks*, Jan.2004, pp. 1-17.

Sato, F., Togo, M., Islam, MK., Matsue, T., Kosuge, J., et al. (2005). Enzymebased glucose fuel cell using Vitamin K-3-immobilized polymer as an electron mediator. *Electrochemistry Communications*, vol.7, no.7, pp. 643-647.

Shenck, N.S., and Paradiso, J. (2001). Energy scavenging with shoe-mounted piezoelectrics. *IEEE Micro*, Vol. 21, No. 3, May-June 2001, pp. 30-42.

Sogorb, T., Llario, J.V., Pelegri, J., Lajara, R., and Alberola, J. (2008).Studying the Feasibility of Energy Harvesting from Broadcast RF Station for WSN. *Proc. of the IEEE Instrumentation and Measurement Technology Conference,* May 2008, pp. 1360 – 1363.

Stark, J. (2006). Thermal Energy Harvesting with Thermo Life. *Proc. of the International Workshop on Wearable and Implantable Body Sensor Networks*, pp.19 – 22.

Teymoori, M.M., Asadollahi, H. (2009). MEMS Based Medical Microsensors. *Proc. Of the Computer and Electrical Engineering International Conference,* vol. 1, pp.158 – 162.

Terbouche, A., Djebbar, S., Benali-Baitich, O., and Hauchard, D. (2011). Complexation Study of Humic Acids Extracted from Sahara Soils with Zuinc (II) and Cadmium (II) by Differential Pulse Anodic Stripping Voltammetry (DPASV) and Conductimetric Methods. Water Air Soil Pollut, vol.216, pp. 679-691.

Thewes, R., Hofmann, F., Frey, A., Holzapfl, B., Schienle, M., Paulus, C., Schindler,P., Eckstein, G., Kassel, C., Stanzel, M., Hintsche, R., Nebling, E., Albers, J., Hassman, J., Schülein, J., Goemann, W., and Gumbrecht, W. (2002). Sensor Arrays for Fully-Electronic DNA Detection on CMOS. *Proc. Of the IEEE International Solid-State Circuits Conference.*

Usman Ali, S.M., Nur, O., Willander, M., Danielsson, B. (2009). Glucose Detection With a Commercial MOSFET Using a ZnO Nanowires Extended Gate. *IEEE Transactions on Nanotechnology*, vol. 8, issue 6, pp. 678 – 683.

Van Hoof, C., Leonov, V., Vullers, R.J.M. (2009). Thermoelectric and Hybrid Generators in Wearable Devices and Clothes. *Sixth International Workshop on Wearable and Implantable Body Sensor Networks*. 3-5 June, pp. 195 – 200.


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A biosensor is a detecting device that combines a transducer with a biologically sensitive and selective component. Biosensors can measure compounds present in the environment, chemical processes, food and human body at low cost if compared with traditional analytical techniques. This book covers a wide range of aspects and issues related to biosensor technology, bringing together researchers from 12 different countries. The book consists of 20 chapters written by 69 authors and divided in three sections: Biosensors Technology and Materials, Biosensors for Health and Biosensors for Environment and Biosecurity.

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