Autonomous Electrochemical Sensing Systems for Environmental and Bio Applications

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***Abstract*—The study describes the development of autonomous portable electrochemical sensing systems for environmental and bio applications by few examples of custom-designed systems. They include a swallowable capsule with wireless communication link for in-vivo gastrointestinal track investigation, an automatic chemical sensing system operating on-board of a robotic fish for detection pollution and monitoring of the water quality in seaport areas and multichannel electrochemical sensing instrumentation with fluidic control of flow-through system for screening the impact of nanomaterial on human health and the environment. The described apparatuses represent complete sensing systems comprising of a portable low-noise anolog front-end under microcontroller regulation which work in pare with a control PC equipped with corresponding signal processing software for handling the signal from a silicon microfabricated chip-based electrochemical sensors tailored to application specification and requirements. Key principles of the system design are considered and the systems operation and performance are discussed.**

Keywords-Electrochemical sensing system; electrochemical cell; microelectrode array; potentiostat; transimpedance amplifier; signal processing software.

I. INTRODUCTION

Nowadays, the necessity of monitoring and detecting different chemical and biochemical components (chemical anylytes, contaminants, toxicants, biomarkers, etc.) in environmental and bio application areas, such as food industry, clinical diagnostics, environmental protection, drug development and security has significantly increased [1]. Commonly, besides the classical for analytical sensing systems requirement on reliable and specific detection of extremely small quantities of chemical and biochemical targets an additional request on real-time autonomous operation at the point of needs moves to the forefront. This demand is often accompanied by the requirement that the sensing systems should be portable (have low weight and size, small power consumption) and be equipped with in-built signal processing and data interpretation algorithms to allow using the analytical system outside of specialised laboratories in an automatic mode with no-live operator. The role of the intelligent chemical sensing system capable of analyte quantification without user intervention is of great importance for emerging Internet of Things (IoT) devices, where they form an essential part of the IoT environment [2].

The most of traditional analytical methods, which are used to detect the chemical targets, are slow, expensive and require bulky and power hungry equipment demanding dedicated laboratories and highly skilled personnel to operate with it. In this regards, electrochemical sensing systems are of particular interest for in-situ autonomous applications as they can be implemented with relatively simple, portable and non-expensive apparatus that can provide for rapid and sensitive measurements in automatic mode. They can detect solid, liquid or gaseous analytes in different mediums including complex bio fluids with simple operating procedures without or with limited sample pre-treatment that is the essential condition for their implementation outside of the laboratory environment. Emerging microfabrication technologies allowing for manufacturing of micro and nano size electrodes and sensors are boosted an additional interest to electrochemical analytical systems.

Miniaturised electrochemical sensors offer a number of advantages over macroscopic devices including increased mass transport and hence improved sensitivity (due to the hemispherical diffusion), reduced *iR* drop and enhanced signal to noise ratio [3]. Thus, microfabricated electrochemical sensors can achieve the required limits of detection that could not be reached for portable in-field applications before. Additionally, in regards to bioanalytical applications, the micro- and nanobiosensors become comparable in dimensions to many of the biological entities (cells, enzymes, antibodies) appeared to be the detection targets that provides the potential to resolve many of currently unsolved challenges in biosensing.

The described circumstances explain the considerable recent attention that has focused on the development of analytical systems based on a range of electrochemical sensors and microsystems. These devices span diverse applications, including clinical diagnostics [4][5], monitoring of environmental pollutants [6][7], control of food safety [8], detection of bioterrorism agents [9], etc.

On instrumentation part there are a number of various commercial electrochemical equipment available on the market that can be used for lab based applications. At the same time, in many cases end-user and application requirements related to operability in field conditions, ease of use and maintenance, high reliability, fast analysis time, portability (small size, weight and power) and intelligence are so specific that cannot be met with available commercial

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hardware therefore necessitate custom development of the sensing system to comply with the application specification. In order to match these requirements, very often the full scale development of the sensing system should be undertaken including design of the electrochemical sensor, instrumentation hardware and software [9]-[15]. In the current study, the most attention will be given to instrumentation aspects of the electrochemical sensing systems. Although in recent time system-on-a-chip technologies are increasingly used in the design of the electrochemical instrumentation [12][16] the utilizing of-the-shelf component in the development is still relevant especially when a device series is not expected to be high and device cost is required to be low. Few examples of such custom hardware development are reported below.

The main problems of the instrumentation analog front-end design are discussed in section 2. Then the electrochemical sensing system development illustrated by custom-designed devices, such as a swallowable capsule with wireless communication link for in-vivo gastrointestinal track investigation, an automatic chemical sensing system operating on-board of a robotic fish for detection pollution and monitoring of the water quality in seaport areas and multichannel electrochemical sensing instrumentation with fluidic control of flow-through system for screening the impact of nanomaterial on human health and the environment.

II. ELECTROCHEMICAL INSTRUMENTATION

In general, an electrochemical sensing system comprises an electrochemical cell incorporating a sensor or sensor array and a mix signal instrumentation hardware. The latter consists of analog front-end, which includes two main electronic units, a potentiostat and a Trans Impedance Amplifier (TIA), and a microcontroller. The analog front-end connects to the microcontroller that controls the measurements and provides data acquisition and connectivity to a control computer. Depending on application requirements the control computer can be a laptop/desktop computer (PC) or a single board computer (i.e., Gumstix, Raspberry Pi, Aurdino, etc.). The electrochemical cell is usually a three electrode structure comprising a Counter Electrode (CE), a Reference Electrode (RE) and a Working Electrode/electrodes (WE) operating as a sensor, which is immersed into or covered by a sample solution to be analyzed. The potentiostat is responsible for setting a stimulation potential between the working and reference electrodes to initiate a redox reaction associated with electron transfer processes between the WE and the solution under investigation. The RE is used as a point of reference in the electrochemical cell; the CE is in charge of closing the current loop with the WE; and WE is the electrode on which surface the electrochemical reaction is happen. This reaction is accompanied with the current related to the target concentration. The current is measured by a TIA and after corresponding signal processing is used for extracting information on target concentration.

However, the signal processing is complicated by a non-faradaic current component attributed to charging of an electrical double layer capacitance and adsorption/desorption processes taking place at the interface of WE and surrounding solution. The double layer capacitance depends on a number of factors including electrode potential, temperature, ionic concentrations, types of ions, oxide layers, electrode roughness, impurity adsorption, etc. Its specific value falls within the range between 20 μF and 60 μF per cm^2 of electrode. Thus, the double-layer capacitance of a 1mm radius disk electrode can be between 0.6 μF and 1.9 μF. This is a significant value that has noticeable effect on performance of the analog front-end and extracting the Faradaic current which is a signal of interest for a great deal of applications.

On signal processing part a number of different electrochemical techniques were suggested to decrease masking effect of the charging current. These techniques use different shapes of the stimulation signal (e.g., DC for amperometry, staircase, square wave, etc. for voltammetry) and perform the current measurement (for voltammetric techniques) at the times when the charging current is significantly decayed after abrupt changes in the stimulation signal. On instrumentation part occurrence of the significant electrode capacitances connected to the analog front-end inputs lead to limitations in the circuit performance and can result in the circuit instability. Therefore, the circuit design should be performed with taking this circumstance into account.

A simplified schematic of the analog part of the electrochemical sensing system is shown in Figure 1

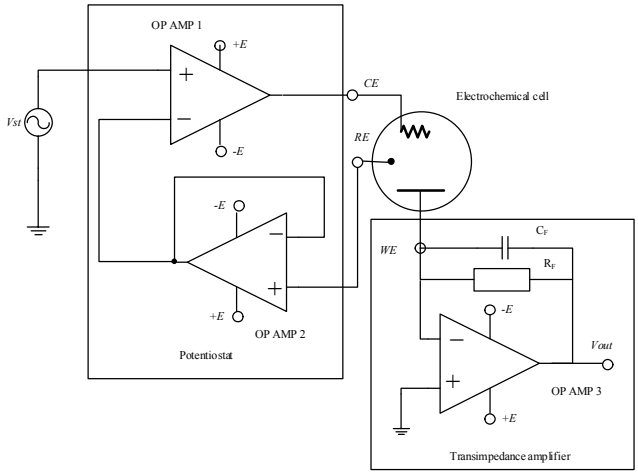

Figure 1. Simplified schematic of the potentiostatic sensing system

The potentiostat is composed of Operational Amplifiers 1 (OP AMP1) and 2 (OP AMP2). The OP AMP1 is the main amplifier that supplies current into the cell; the OP AMP2 serves as a voltage repeater that has high input impedance to eliminate a current flow through the RE. The feedback of the potentiostat is formed by a voltage divider made by the impedance *Zc* (between the CE and the RE) and impedance

Zw (between RE and WE) followed by the voltage repeater. If there is no Faradaic reaction on the electrodes, an equivalent circuit of impedances *Zc* and *Zw* can be represented by serial connection of the corresponding double layer capacitances associated with the corresponding electrodes and liquid resistance between counter or working and reference electrodes. The liquid resistance depends on solution, type of analyte and its concentration, temperature, and the geometry of the electrode system (shape, area and the distance between electrodes). It increases if the distance increases and the electrode area decreases. The potentiostat transfer functions of the stimulation signal to the counter and the reference electrodes are described by eq. (1) and eq. (2) where G_1 and G_2 are frequency dependent open gains of the corresponding OP AMPs, and *Zo* is output resistance of OP AMP1.

$$G_{CE} = \left(1+\frac{Zc}{Zw}\right) \Bigg/ \left[\frac{1}{1+1/G_2}+\frac{1}{G_1}\left(1+\frac{Zc+Zo}{Zw}\right)\right] \quad (1)$$

$$G_{RE} = 1 \Bigg/ \left[\frac{1}{1+1/G_2}+\frac{1}{G_1}\left(1+\frac{Zc+Zo}{Zw}\right)\right] \quad (2)$$

Due to serial connection of the two operational amplifier the phase margin can reduce and cause ringing and even instability of the potentiostatic circuit. To avoid it, the repeater amplifier should have the bandwidth significantly larger than the main amplifier. If the circuit stability is secured and DC gains for OP AMPs are significant (|G2|>>1 and |G1|>>|1+(Zc+Zo)/Zw|, the signal at reference electrode will follow stimulation signal with a small shift that is the smaller, the larger G2 and G1. In this case, the signal at the counter electrode will be defined by 1+Zc/Zw and therefore it can exceed the stimulation signal (if |Zc/Zw |>>1). Thus the electrochemical cell should be designed in such a manner that to avoid it.

The presence of the large capacitance in the impedance of the WE connected to the input of the transimpedance amplifier is also can cause instability and ringing of the circuit. The standard approach to optimize the TIA performance is to add a bypass capacitor C_F in parallel with the TIA feedback resistance R_F in order to compensate phase shift and to guarantee sufficient phase margin for stable operation of TIA [17]. However, overcompensation reduces the usable bandwidth of the amplifier thus in case of application requirement on frequency bandwidth the selection of the C_F should be made very carefully.

III. EXAMPLES OF THE ELECTROCHEMICAL SENSING SYSTEM

Electrochemical sensing system with wireless communication link implemented in a swallowable capsule format [15] was developed for in-vivo investigation of gastrointestinal track (GI). The capsule approach, which is as an alternative to the classical invasive methods of GI tract analysis such as endoscopy and colonoscopy, is receiving more research attention in recent years [18]. The suggested solution differs from other capsule based technologies and proposes for examination of GI status to use an electrochemical signature of different GI tract areas instead of taking their images. The solution is represented a complete electrochemical sensing system comprising of electrode system on chip, analog front-end discussed above, microcontroller, wireless transmitter with antenna, and power unit with a single lithium-ion cell battery. These functional units integrated were assembled on a polyimide flexible substrate which was arranged in a fold manner and encapsulated in polyether ether ketone (PEEK) material to fit a capsule with dimensions 12 mm in diameter and 28 mm in length (volume is 3.2 cm3, weight is 7.4 g) (Figure 2). The sensing electrode structure was realized as a 6 x 6 mm2 square silicon die. The largest electrode is a counter electrode. It is a 2 mm diameter disk made of platinum. Four smaller electrodes are 1 mm disks made of gold. Three of these small electrodes connected together were played role of the working electrodes; the fourth disk was plated with platinum and was used as a pseudo reference electrode. The analog front-end of the system was realized with low power, precision JFET AD8643 amplifiers; the microcontroller was PIC18F microcontroller that was chosen for design due to its small package size (6×6 mm^2) and low power consumption; wireless communication link was performed with the help of TH72015, which is a Melexis communication solution implemented in a 3×3 mm^2 QFN package. It has integrated PLL and operates with frequency shift key modulation in the 433 MHz ISM band. The developed capsule was capable of performing cyclic, differential pulse voltammetries in autonomous mode.

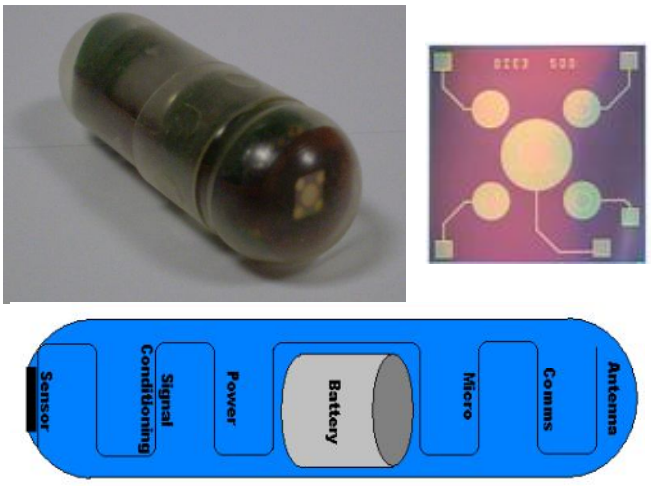

Figure 2. Electrochemical sensing system with wireless communication implemented in capsule format

Laboratory evaluation of the capsule performance confirmed that it could operate over 72 h (estimation of the maximum time of capsule passage through GI tract) and provide at least 500 measurement cycles followed by corresponding wireless data transmission from inside of body at a distance of 1.5 m from the patient.

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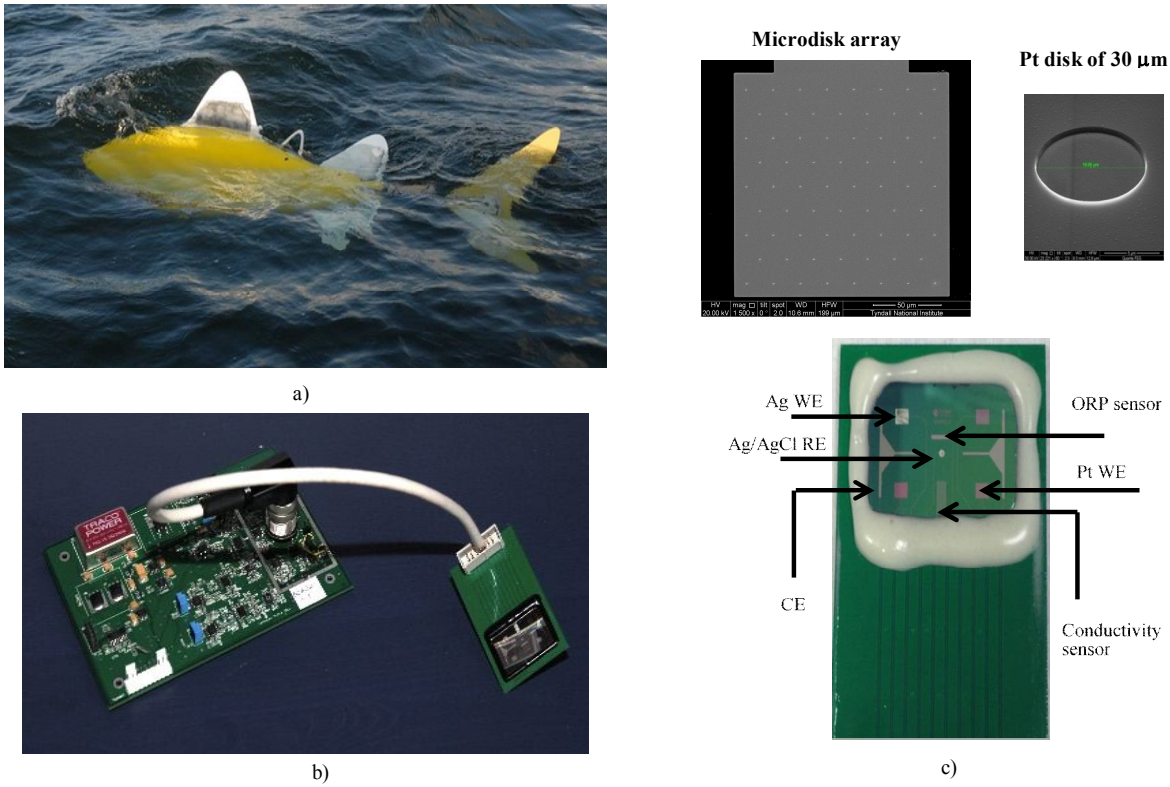

Figure 3. Robotic fish (a) with smart electrochemical sensing instrumentation hardware (b) and packaged sensor chip (c)

The smart chemical sensing system (Figure 3) capable of autonomous operation on-board of a robotic fish for monitoring and detection pollution in water area of seaports was developed to provide real time in-situ detection and measurement of contaminants including heavy metals (ions of Cu2+) and phenol derivatives and sea water quality parameters: dissolved oxygen, oxidation-reduction potential (ORP) and sea water conductivity [14]. The sensing system consisted of four channel potentiostatic system for quantification of chemical analytes, impedimetric circuitry for evaluation of sea water conductivity and low noise high impedance voltage repeater for measurement of ORP. Multiparametric sensing device was implemented onto a single micro fabricated silicon chip with 20×30 mm^2 dimensions. The chip contained two platinum counter electrodes electrically-connected in parallel, three rectangular Pt microdisc arrays and a rectangular Ag microdisc array, which played a part of the working sensing electrodes, a circular silver-based reference electrode, which was common for all working electrodes, a Pt interdigitated electrodes for impedimetric measurement and an ORP electrode. For improving sensor sensitivity the working electrodes were realized as a microdics array. Sixty four discs of 30 µm diameter and separated each other by 300 µm were arranged in a hexagonal structure [14]. The impedimetric sensor for conductivity measurements was made of two interdigitated electrodes. Number of electrode pairs was 40, the electrode width and length was 20 µm and 1500 µm correspondingly, inter electrode distance was 40 µm. Selection platinum rather than gold as material for working electrodes was related to the better stability of Pt to the impact from seawater. The control computer was Gumstix. The system was of 152×52×26 mm^3 dimensions and provided for the autonomous measurements of all parameters in real time with pollution detection limit of 0.2 µM for cupper and 11.2 µM for phenol.

Comprehensive multichannel scalable instrumentation for toxicity assessment is a main part of the smart non-animal high throughput platform for screening the impact of nanomaterials on human and environment. The sensors are based on biological objects including DNA, miRNA, membrane lipids, single cells and lung, intestine, liver, kidney and placenta cells. Each channel includes a wafer-based sensor located inside of a flow chamber of the microfluidic module shown in Figure 4.

Fluidic hardware of the module comprises of 13 solenoid pinch valves, peristaltic and vacuum pumps providing capability of implementation different fluidic protocols including: System filling, Cells cultivation, Exchange („harvesting“). The design of the fluidic system allows for combination of fluidic modules in a complex system to simulate bio interaction between different organs. Instrumentation provides full automated multichannel fluidic flow control synchronized with electrochemical examination of the cell-based sensors. The channel hardware consists of Microfluidic Control Unit (MCU) and Electrochemical Sensing Unit (ESU) each of 60 x 105 x 165 mm^3 dimensions. MCU and ESU units are equipped with corresponding user-friendly software (Figure 5) with in-built signal processing to automate toxicity assessment and simplify its protocol development.

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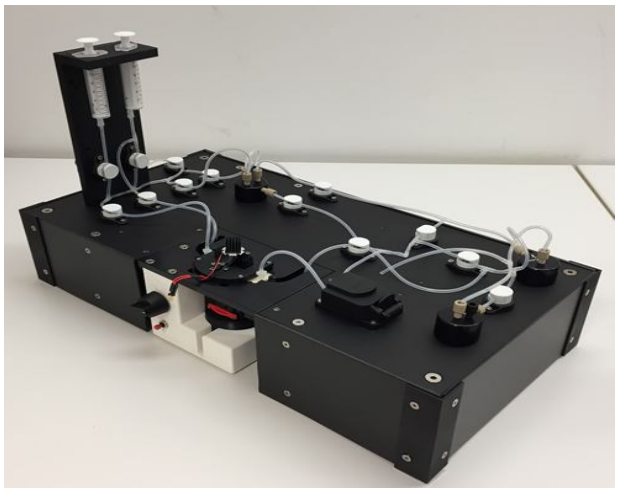

Figure 4. Microfluidic module with fluidic hardware.

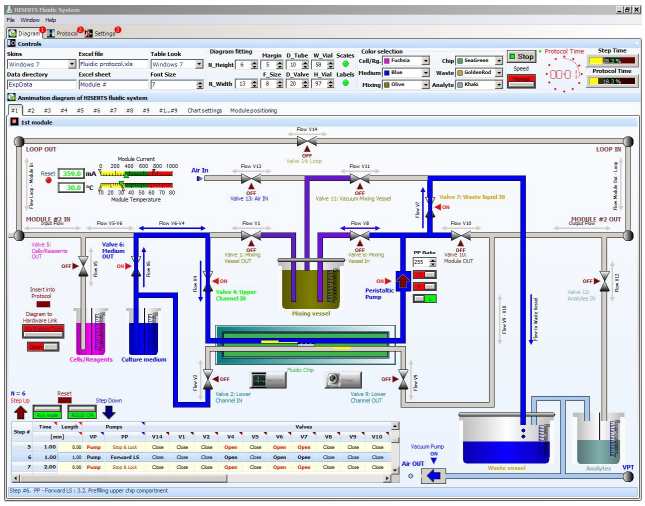

Figure 5. User-friendly software by an example of fluidic diagram tab of MCU module

The number of channels corresponds to the number of the microfluidic modules; channel measurements are synchronised with operation of corresponding microfluidic flow module. Extension of the channels is performed by cable connection of the modules to the common SPI bus.The key features of electronic instrumentation are easy channel extensions, independent or synchronised work MCU with the sensing instrumentation, intelligence, possibility to work under main PC operational systems and in different environments (i.e., NET, LabVIEW, MATLAB). The microfluidic control unit besides of providing full pumping and valve switching control is allowed for decreasing power consumption, smart control of the fluidic hardware command fulfilment, overheating, overcurrent and short circuit protections, module current and temperature monitoring.

Electrochemical sensing unit is realized as a multichannel mix signal scalable system. It is implemented with the following key off-the-shelf electronic components: microcontroller Atxmega128A1U and 16 bit DAC LTC2641 (the digital part), ADA4807 and AD8622 (potentiostat) and ADA4350 and AD8253 (TIA) OP AMPs for the analog front-end of the channel hardware. The potentiostat is capable of provided stimulus signal with scan rate up to 100V/s in the in -3V – +3V range; transimpedance amplifier secured the frequency bandwidth of 41.28 kHz with WE capacitance CS = 10nF with RF = 1M and CF = 4pF (expected bandwidth calculated according recommendation [17] was 40 kHz). Each ESU channel/module acts as a low noise, analog front-end highly sensitive measurement unit under microcontroller control capable of simultaneous and independent from other channels operation. The ESU module provides voltammetric or impedance measurements in three or two electrode configurations correspondingly. Example of voltammetric measurements obtained with the developed ESU for a three electrode electrochemical cell (CE - Pt wire, RE - Silver/Silver chloride, WE - 40 um microdisk gold electrode array) in solution of 0.1M Ferrocyanide in 0.1M KCl at scan rate of 100 mV/s is shown in Figure 6.

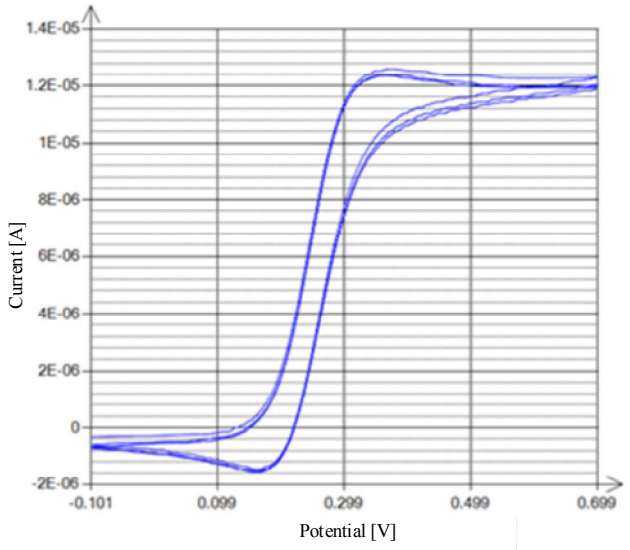

Figure 6. Voltammogram obtained by developed electrochemical sensing module with 40 um gold disk array in 0.1M Ferrocyanide in 0.1M KCl at scan rate of 100 mV/s.

As one can see the voltammogramm has a sigmoidal shape as expected in case of microdisc electrodes. Comparison of the results obtained with the developed sensing system and with a commercial electrochemical station CH 620a showed their good agreement.

IV. CONCLUSION

Nowadays, electrochemical sensing systems are rapidly transforming from the research laboratory based bulky equipment in autonomous portable systems capable of working at point of needs in an automatic mode with no-live operator. Such platforms are key of importance for environmental and bio applications as they often require real

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time continuous monitoring and detection different targets in complex media in field conditions. The combination of emerging silicon based sensing microfabricated platforms, state of art electronic instrumentation, microcontroller and signal processing technologies promise to address main challenges of such systems such as sensitivity, portability and intelligence to enable the whole systems to provide required multiparametric real time sensing. The presented in the study examples of custom-designed systems including a swallowable capsule with wireless communication link for in-vivo gastrointestinal track investigation, an automatic chemical sensing system operating on-board of a robotic fish for detection pollution and monitoring of the water quality in seaport areas and multichannel electrochemical sensing instrumentation with fluidic control of flow-through system for screening the impact of nanomaterial on human health and the environment demonstrate possible directions for implementing of these system in practical environmental and bio applications.

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