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Design and construction of a low cost single-supply embedded telemetry system for amperometric biosensor applications

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Abstract

A new embedded telemetry system for amperometric biosensor application is presented. The device consists of a single-supply miniature potentiostat-*I*/*V* converter, a microcontroller unit (MCU), a signal transmitter, and a stabilized power supply. The sensor current is converted to a digital value using a peripheral interface controller (PIC) MCU with an integrated analog-to-digital converter (ADC). The PIC firmware is developed in assembly and transferred to the MCU through an in-circuit-serial-programmer (ICSP). The digital data are sent to a personal computer using a miniaturized 433.92 MHz amplitude modulation (AM) transmitter with a linear range up to 30 m. The radio receiver is connected to a PC via a Universal Serial Bus (USB). Custom developed software, written in C and Basic, allows the PC to record, plot and handle the received data. The design, construction and operation of the hardware and software are described. The system performance was evaluated in vitro using a dummy cell and a platinum (Pt) amperometric glucose biosensor. This device serves as a basic model to realize an in vivo, low-cost, miniaturized telemetry system built with standard hardware components readily available.

Keywords: Potentiostat; Amperometry; Microcontroller; Biosensor; Telemetry

1. Introduction

A biosensor is defined as a device that combines a transducer with a biologically sensitive and selective component [1]. Many biologically oxidable molecules can be directly detected using amperometric sensors connected to an electronic device called a potentiostat [2]. When direct electrochemical oxidation is not possible under standard experimental conditions, a biosensor may then be used instead [3]. Glucose is oxidized by the enzyme glucose oxidase (GOx), an oxidoreductase with a covalently linked flavin adenine dinucleotide (FAD) cofactor [4]:

$$\beta\text{-d-glucose} + \text{FAD-oxidase} \rightarrow \text{d-glucono-}\delta\text{-lactone} + \text{FADH}_2\text{-oxidase}$$

The reconversion of $FADH_2$ to FAD produces H_2O_2 in the presence of O_2, as follows:

$$\text{FADH}_2\text{-oxidase} + \text{O}_2 \rightarrow \text{FAD-oxidase} + \text{H}_2\text{O}_2$$

The application of a potential of +700 mV to the Pt working electrode, relative to a reference electrode (e.g. Ag/AgCl), causes the following reaction:

$$\text{H}_2\text{O}_2 \rightarrow \text{O}_2 + 2\text{H}^+ + 2\text{e}^-$$

generating a measurable current that is proportional to the rate of the H_2O_2. The high specificity and stability of GOx makes this enzyme suitable for biosensor construction [5] when immobilized on the surface of platinum electrodes with poly-*o*-phenylenediamine [6].

Biomedical telemetry is a well established technique which allows real-time reading of glucose levels [7,8] reducing distress in patients [9]. In recent years sophisticated telemetry systems have been developed to analyse neurochemical data, such as brain variations of dopamine, in freely moving animals [10,11].

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In this paper we describe a MCU-based telemetry system, which can be used with biosensors for the measurement of brain glucose and other molecules in vitro and in vivo.

2. Materials and methods

2.1. Reagents and solutions

All chemicals were of analytical grade and used as supplied; MilliQ water was used throughout. The glucose oxidase (GOx) from Aspergillus Niger (EC 1.1.3.4.), *o*-phenylenediamine (*o*-PD) and D(+)-glucose were obtained from Sigma Chemicals (Milano, Italy). The stock solution of glucose (1 M) was prepared in water and stored at room temperature for 24 h to allow the equilibration of the two anomers then used for calibration. The phosphate-buffer saline (PBS) solution was made using NaCl (137 mM), KCl (2.7 mM), NaH_2PO_4 (1.4 mM) and Na_2HPO_4 (4.3 mM) from Sigma, then adjusted to pH 7.4. The GOx solution was prepared dissolving 895 units (5 mg) of enzyme in 50 μl of PBS and then stored at 4 °C. The *o*-PD monomer was dissolved in deoxygenated PBS immediately before the potentiostatic electrosynthesis of the polymer (poly-*o*-PD, PPD) on the Pt surface. The 3 M NaOH solution for the development of the positive photoresist was made in 1 l of water dissolving 120 g of NaOH tablets (Sigma). The ferric chloride etching solution (2 M) was prepared dissolving 162.2 g of $FeCl_3$ (Sigma) in 500 ml of water.

2.2. Materials and electronic parts

Electronic parts were from RS Components Spa (Milano, Italy); the radio modules were from Telecontrolli spa (TC, Casoria, Italy), and the USB components preassembled by Elettronicamente (ELT, Milano, Italy). The power section of the transmitter unit was stabilized using a National LP2950-05 voltage regulator. The amperometric module of the transmitter unit was built using the National-LMC6064. The ADC was an integral part of the MCU used in this system (Microchip-PIC12F683). The 433.92 MHz AM transmitter with integrated antenna was a RT2-433.92 (TC). We selected a RR3-433.92 (TC) as AM receiver with external antenna. The serial-to-USB converter was a FTDI-FT232BM module (ELT) with a 6 MHz quartz and a 93C46 E^2PROM. All resistors were precision metal oxide thick film (250 mW, 0.1% tolerance, Ohmite, Rolling Meadows, IL). All capacitors were NP0-type multilayer ceramic (low pass filter, decoupling) or electrolytic (decoupling). The components were soldered on a single side PCB board (eurocard size −160 mm × 100 mm). Emilac®, Positiv® and Plastic® technical sprays were from Cramolin (Mühlacker, Germany).

2.3. Transmitter unit circuit description

The transmitter unit (Fig. 1) comprised four different modules. The amperometric module was built around the integrated circuit (IC) LMC6064, a quad single-supply operational amplifier (OPA). National Semiconductors designed this CMOS family of OPA for micropower applications with low input bias current (10 fA) and high input resistance (>10 TΩ). The LMC6064 can operate from a single-supply voltage with "rail-to-rail" inputs and outputs. One OPA (Fig. 1a) serves as voltage follower connected to the wiper of 1 MΩ multiturn trimmer potentiometer. This circuit produces the voltage necessary to polarize the working electrode (WE) between 0 and +1.25 V while the single OPA potentiostat (Fig. 1b) controls the reference (RE) and the auxiliary (AE) electrodes. The current-to-voltage (*I*/*V*) converter (Fig. 1c) is a single-supply adaptation of a classic transimpedance amplifier [12] with a three-position adjustable gain varied by a rotary switch. The transfer function of the *I*/*V* converter is:

$$V_{out1} = -(i_{ox} R_f) + V_{app} \quad (1)$$

where i_{ox} is the oxidation current flowing through the WE, R_f is the feedback resistor and V_{App} is the potential applied to the WE. The resistors have capacitors in parallel to complete a low pass filter with a cut-off frequency ($F_{cut\text{-}off}$) of 10 Hz for each range. The capacitor values (C_F) were calculated in Farads according to the equation:

$$C_F = 1/(F_{cut\text{-}off} 2\pi R_f) \quad (2)$$

in which R_f is the resistor value for each range. The values of C_F are shown in Fig. 1c.

The difference amplifier circuit (Fig. 1d) has the dual role of subtracting the potential applied to the WE [12] while amplifying ten times the resulting signal. The transfer function of the differentiator is:

$$V_{out2} = (V_{out1} - V_{app})(R_2/R_1) + V_{ref}(R_2/R_1) \quad (3)$$

where: V_{out1} and V_{app} are the signals applied to the inputs and the values of R_1 and R_2 are respectively 1 and 10 MΩ. V_{ref} is equal to 0 V because the 10 MΩ resistor is grounded, then:

$$V_{out2} = 10\,(V_{out1} - V_{app}) \quad (4)$$

The combination of the two stages of amplification (Fig. 1c and d) provides three different full scales, ranging from 1 nA/V (100 MΩ) up to 100 nA/V (1 MΩ), with the global transfer function:

$$V_{out} = -10\,(i_{ox} R_f) \quad (5)$$

The low tolerance resistors (0.1%) reduce the error in the *I*/*V* and differentiator circuits. With a power supply of +5 V the maximum input current is almost 500 nA (494 nA in the observed "rail-to-rail" output). In this range of amplifications it is possible to calibrate accurately a glucose biosensor (Pt disk, 125 μm diameter) in vitro.

The power supply module (Fig. 1e) was constructed using a LP2950-5.0, +5 V voltage regulator, and two decoupling capacitors. This IC has very low quiescent current (75 μA), low drop-out voltage (40–100 mV) and excellent linear regulation (0.05%).

The PIC12F683 is the heart of the digital module (Fig. 1f). This is a 8-bit CMOS IC with low power features equipped with an internal variable clock (31 KHz–8 MHz, software selectable) and a 10 bit ADC with four multiplexed channels. The MCU, working at 4 MHz, performed the ratiometric A/D conversion

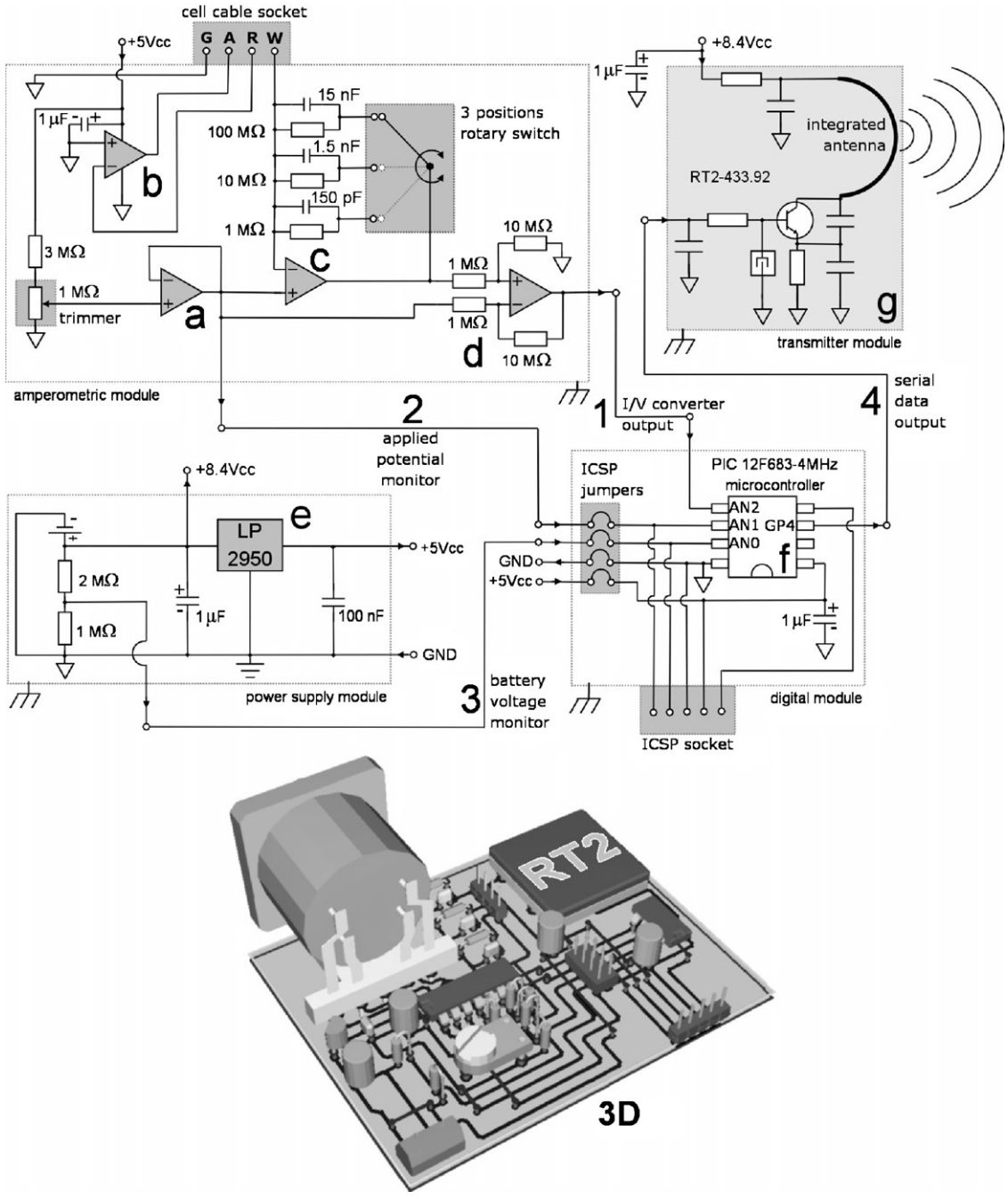

Fig. 1. Circuit diagram and three dimensional representation (3D) of the transmitter unit. The amperometric module comprised a buffered voltage follower (a), a single OPA potentiostat (b), a current-to-voltage converter (c) and a single supply differentiator/amplifier (d). The +5 V_{cc} voltage was stabilized by the power supply module equipped with a low drop out voltage regulator (e). The in-circuit programmable digital module (f) was equipped with a PIC-12F683 MCU connected to three analog lines: *I/V* converter output (1), applied voltage monitor (2) and battery voltage monitor (3). The serial data output (4) from the MCU was directly connected to the input pin of the transmitter module (g).

of V_{out} (Fig. 1 1–3), V_{app} and battery voltage (V_{batt}). After the digital signal processing (DSP) of acquired raw data, a serial data packet was generated and sent to the transmitter (Fig. 1 4). The in-circuit-serial-programming (ICSP) bus provides the possibility of programming the IC "on-board" in a few seconds.

The miniaturized transmitter (17.8 mm × 10.16 mm; Fig. 1g) is a thick film AM module, with SAW controlled oscillator and integrated antenna, running at the frequency of 433.92 MHz. In conjunction with the MCU, this hybrid component allows the realization of a serial data transmitter working at the maximum speed of 2400 baud.

A rechargeable 8.4 V Nickel–Metal hydride (Ni–Mh) Battery pack (3300 mA/h) provided the power to the transmitter unit.

2.4. Receiver unit circuit description

The receiver unit (Fig. 2) comprises two parts: the receiver module (Fig. 2a) and the serial-to-USB converter (Fig. 2b). The

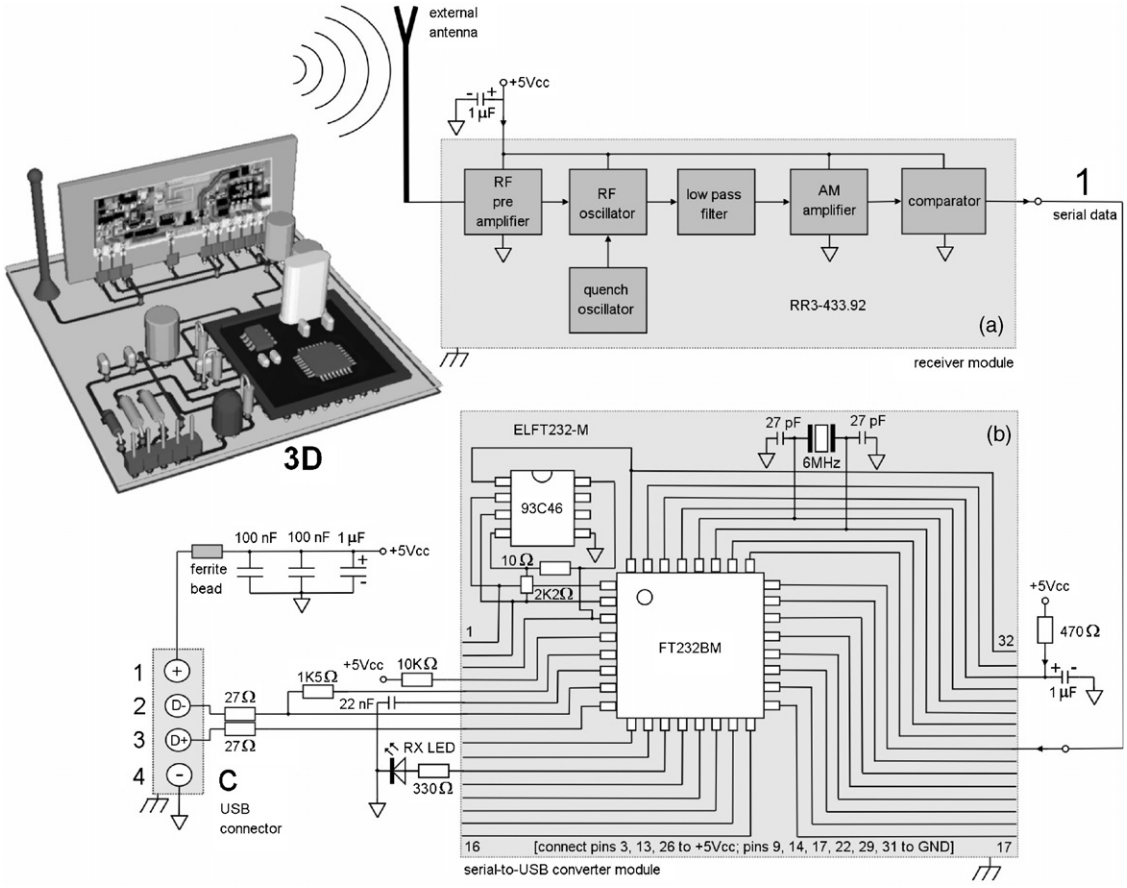

Fig. 2. Receiver unit: three dimensional representation (3D) and circuit diagram. The AM signal was decoded by the receiver unit (a) connected to a 17.28 cm "whip" antenna. The serial data (1) was sent to the serial-to-USB converter (b) and transmitted to the personal computer (c). The unit was powered by the USB bus without the necessity of using an external power supply.

RR3-433.92 receiver (RX) is a super regenerative data receiver with a high frequency accuracy conferred by virtue of a laser trimmed inductor. An external "whip" antenna, consisting of one quarter of wavelength (λ/4) straight wire, was connected directly to the antenna pin of the RX. The length of the wire was calculated in centimetres from the following formula:

$$L_{\mathrm{cm}} = 7500/\ \mathrm{frequency}_{\mathrm{MHz}} \quad (6)$$

At 433.92 MHz, L_{cm} is equal to 17.28. The RX module sent the digital serial data (Fig. 2 1) to the Serial-to-USB converter. This module was built around the FT232BM, clocked at 6 MHz and connected to an external 93C46 E^2PROM (used to store USB ID parameters, resource configuration, etc.). A LED provided direct visualization of received packets. A few resistors and decoupling capacitors completed the USB interface and the +5 V power supply, derived from the USB.

2.5. PCB design and construction

The components placement was simulated using a graphic software (KiCAD). The three-dimensional (3D) reconstructions of the transmitter and receiver units are illustrated in Fig. 1, 3D and Fig. 2, 3D.

The printed circuit board (PCB) tracks were designed with a freely available software (KBan 2.0) and printed on a transparency using a HP Laserjet 1200. The PCB board was cleaned with sandpaper (3 M, Microfine-1500 grit) and rinsed with water and acetone before applying a coating of positive photoresist (Positiv®). After 45 min the board was coupled with the printed transparency, using removable tape, and exposed to direct UV light for 5 min. The PCB was then immersed in the development solution for a few minutes and etched in a $FeCl_3$ bath for 15 min at 40 °C. After inspection, and photoresist cleaning using sandpaper and acetone, the through-holes (ø = 0.6 mm) were drilled and the two units were separated using a snap-off knife. The electronic components were soldered with a low power solder iron (12 W, Weller, Germany) and an insulating coating (Plastic®) was applied to the copper side of the boards. The final size of the transmitter and the receiver boards was 60 mm × 80 mm and 160 mm × 80 mm, respectively. At the end, the units were put in small plastic envelopes pre-treated with copper-based antistatic spray (Emilac®) to minimize electromagnetic interferences (EMI).

2.6. Electrochemical cell

The three electrode cell for biosensor electropolymerisation and calibration was home made and the schematic is shown

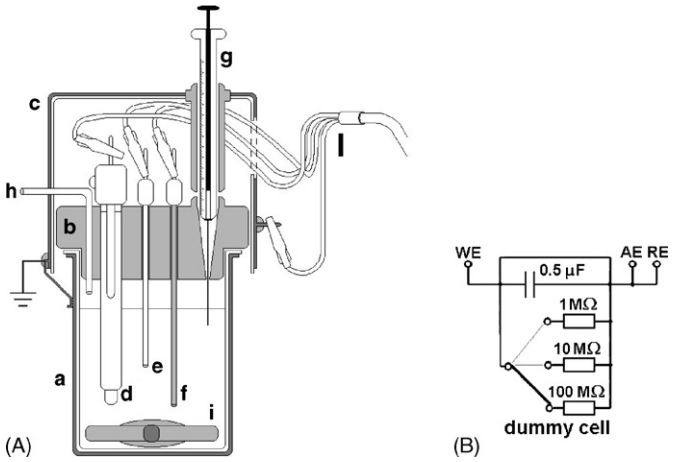

Fig. 3. Schematic representation (A) of the electrochemical cell used for electropolymerisation and for testing the telemetry system with a glucose biosensor; (a) 25 ml PTFE beaker externally coated with antistatic spray (see text); (b) drilled Teflon© top; (c) antistatic cup enclosing the various electrode connectors (see text); (d) Ag/AgCl reference electrode; (e) working electrode/glucose biosensor; (f) platinum auxiliary electrode; (g) Hamilton injection syringe used for glucose calibration; (h) nitrogen/air inlet tube; (i) magnetic stirrer bar; (l) cell cable. A dummy cell (B) was used for testing the amperometric module of the transmitter unit before the biosensor calibration.

in Fig. 3 (panel A). It comprises a 25 ml PTFE beaker (H: 45 mm × diam.: 33 mm, Plastibrand, Milano, Italy) sealed with a Teflon© lid (ø = 32 mm) with five holes drilled into it to insert the electrodes, the nitrogen/air tube and the syringe needle. The external surface of the beaker was treated with antistatic spray (Emilac©) and connected to the ground of the transmitter unit and to the earth ground. An antistatic cup, enclosing the various electrode connectors (crocodile clips), was constructed by cutting a 50 ml PTFE beaker (H: 30 mm × diam.: 45 mm, Plastibrand) externally sprayed with Emilac©. Electrical continuity between the cup and the beaker was consistently achieved through a small copper plaque glued to the cup with epoxy before the antistatic treatment. The conducting surface formed a Faraday cage to reduce EMI. For the duration of the electrosynthesis, nitrogen was introduced into the cell to prevent oxygen interference. During the calibration procedure with glucose the cell was placed on the stirrer and a 32 mm diameter magnetic bar was used to mix the solution after each addition of glucose. A dummy cell was made as shown in Fig. 3 (panel B) for testing the amperometric module of the transmitter unit before the biosensor calibration.

2.7. Glucose biosensor preparation and calibration

Poly-*o*-PD-based glucose biosensors were prepared modifying a protocol described by Lowry and co-workers [6]. This biosensor design has been successfully used to quantify ECF striatal brain glucose (∼400 μM) in freely moving rats [13]. In brief 40 mm length Teflon©-coated platinum/iridium (90%/10%) wire (5T-125 μm diameter, Advent Research Materials, Suffolk, UK) was soldered to a gold pin (RS Components) after carefully cutting 2 mm of the Teflon© insulation. The other end of the wire was cut with a scalpel blade to expose the 1 mm platinum cylinder and rinsed with bidistilled water. The sensor was immersed in the GOx solution for 5 min to ensure adequate enzyme adsorption. After 10 min drying at room temperature the biosensor was placed in the cell filled with 5 ml of nitrogenated PBS containing the *o*-phenylenediamine monomer in nitrogen atmosphere. The reference and auxiliary electrodes were respectively an Ag/AgCl electrode and a 50 mm platinum wire (BAS-Bioanalytical Systems Inc., West Lafayette, US). The cell was connected to a CV37 voltammograph (BAS) and the electropolymerisation process started by applying a +700 mV potential to the WE versus RE. The gain of the CV37 was fixed to 500 nA/V to prevent the saturation of the input stage. After 20 min the potential was disconnected and the glucose biosensor was rinsed with bidistilled water and stored at 4 °C overnight. The in vitro calibration was carried out the following day at room temperature. The glucose biosensor was placed in the cell containing 15 ml of air-bubbled PBS (Fig. 3). A +700 mV potential was applied and the current recorded until a stable baseline was obtained. Ten successive injections of glucose (1 M stock solution) were performed and a calibration curve in the range of concentrations between 0.2 and 140 mM was obtained (Fig. 5).

2.8. Firmware and software

The firmware to drive the PIC12F683 was realized in assembly language using MPLab, the Microchip integrated development environment, freely available from http://www.microchip.com. The program, which runs on the MCU, consists of a main routine that is divided in two portions of code. The first portion initializes the communications port and all the other modules of the PIC (ADC and timers in particular). The second portion is an infinite loop that performs the ADC conversions, calculates the 8 Bit Cyclic Redundancy Check (CRC) and sends data through the serial port. The analogue signals V_{out}, V_{app} and V_{bat} are multiplexed, digitized with a sample period of 2 μs, and sent to the transmitter module. Only for the V_{out} signal, the hardware ADC resolution (10 bit) was improved following the oversampling and averaging method [14]:

$$F_{os} = 4^{w} F_{s} \tag{7}$$

where w is the number of additional bits of resolution (4), F_s is the sampling frequency (20 Hz) and F_{os} is the oversampling frequency (5120 Hz). In accordance with the Nyquist's theorem F_s was calculated as follows:

$$F_{s} = 2F_{max} \tag{8}$$

where F_{max} is equal to 10 Hz, the highest frequency of the input signal. To do that, the PIC acquired and accumulated 256 consecutive samples in 50 ms then right-shifted the sum by one bit (divided by 2). This technique increased the ADC resolution from 10 to 14 bits. The seven byte packets (20 per second), sent by the MCU, were composed as follows: the "head" byte (synchronization), the value of V_{out} (2 bytes), the 8-lower-significant-bits (8-LSB) of the V_{app} and V_{batt} (8-LSB). The CRC

value of the previous four bytes and the "tail" synchronization byte completed the sequence.

The compiled file was downloaded to the MCU using the Microchip USB programmer (PICkit®) connected to the ICSP bus.

The software, running on the PC under Windows XP Professional, was interfaced to the USB receiver unit by using the low-level driver freely available from http://www.ftdichip.com. The graphic user interface was developed in RealBasic 2006 while the dynamic link library (DLL) serial-data-parser was programmed in C (Dev-C^{++} 4.9). The application is capable of plotting, storing and retrieving data. A software alarm was generated when the calculated CRC differed from the transmitted value, a data reception time-out occurred or the battery level in the transmitter unit was too low (<7.2 V).

3. Results

3.1. Electronics test and calibration

The dummy cell previously described (Fig. 3B) was used as a Thevenin current source connected to the amperometric module. The voltage applied to the dummy cell was generated between the WE and the AE/RE electrodes and is equal to the voltage applied to the WE:

$$i_{\text{dummy}} = V_{\text{app}} / R_{\text{dummy}} \quad (9)$$

The resulting anodic current (i_{dummy}) was read by the WE and converted in the resulting voltage (Eq. (5), V_{out}) by the amperometric module.

The calibration was made indoors with a linear distance between the TX RX units of ~10 m. The baseline was recorded for six consecutive days of continuous operation and a 10-point calibration was performed daily ($n = 6$) for each amplification range. The logarithmic plot in Fig. 4 (panel A) represents the calibration currents for each amplification decade: 100 MΩ (slope = 0.00991 ± 0.00007 nA mV^{-1}; $r^2 = 0.9996$), 10 MΩ (slope = 0.09931 ± 0.00046 nA mV^{-1}; $r^2 = 0.9998$) and 1 MΩ (slope = 0.9931 ± 0.0048 nA mV^{-1}; $r^2 = 0.9998$). From the same plot it is possible to extrapolate the values of R_{dummy} and V_{app} used for calibrating. A second calibration was made under the same conditions, connecting the V_{out} of the amperometric module to a Fluke 45 Voltmeter. No significant statistical differences were observed between the two calibrations (data not shown). After the operations described above, a 2.5 nA current was generated though the dummy cell, setting the R_{dummy} and the *I/V* resistors to 100 MΩ and fixing V_{app} to + 250 mV. The system was left under these conditions up to the next calibration, which was made the following day. A maximum V_{app} shift of 10 mV was observed overnight while the current of the baseline noise was around 10 pA (Fig. 4, panel B).

At the end of the calibrations, all the values of the recorded current were plotted versus the expected current values, producing a 30-point graph (slope = 0.9954 ± 0.0022 nA nA^{-1}; $r^2 = 0.9999$; $n = 6$) comprehensive of the full amplification range (Fig. 4, panel C).

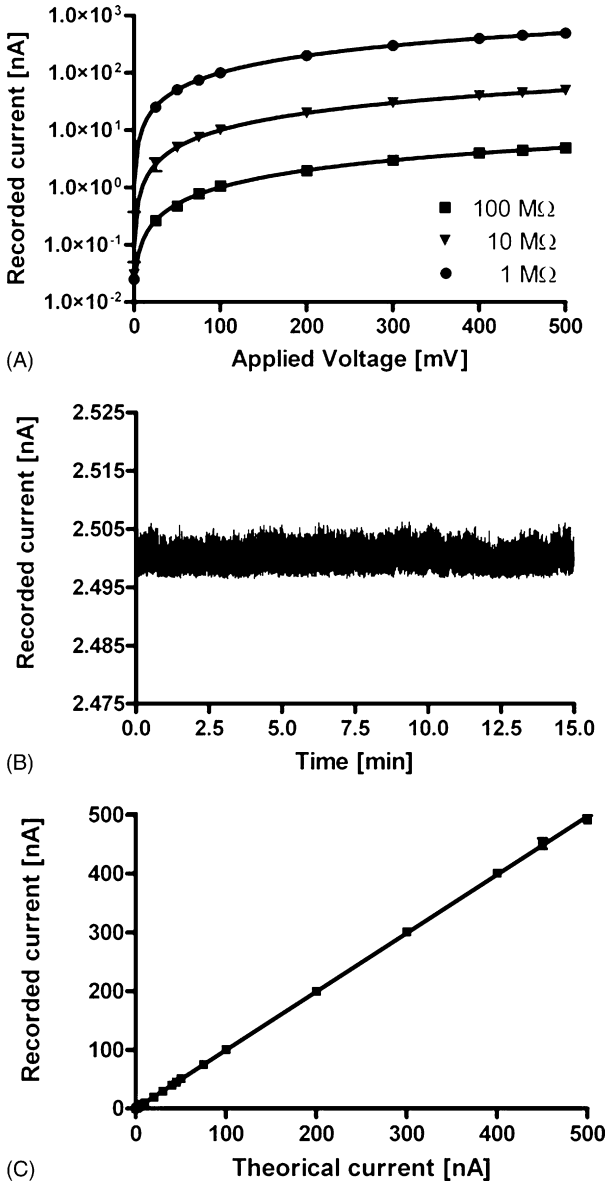

Fig. 4. Calibration of the transmitter unit by connecting the dummy cell and using it as a Thevenin current source (see text). The baseline was recorded for six consecutive days of continuous operation and a 10 points calibration was performed daily ($n = 6$) for each amplification range. The logarithmic plot in panel A represents the calibration currents: 100 Ω (slope = 0.00991 ± 0.00007 nA mV^{-1}; $r^2 = 0.9996$), 10 MΩ (slope = 0.09931 ± 0.00046 nA mV^{-1}; $r^2 = 0.9998$) and 1 MΩ (slope = 0.9931 ± 0.0048 nA mV^{-1}; $r^2 = 0.9998$). The noise was quantified around 10 pA (panel B) setting the dummy cell and the *I/V* resistors to 100 MΩ and applying +250 mV to the WE. The values of the recorded current were then plotted vs. the expected current values generating a 30 points calibration graph (slope = 0.9954 ± 0.0022 nA nA^{-1}; $r^2 = 0.9999$; panel C) comprehensive of the full amplification range.

3.2. Power consumption

The total current necessary to drive the transmitter unit, powered with a + 8.4 V Ni–Mh battery, was experimentally determined [15] as 8.5 mA. The calculated power consumption was 71.4 mW. After the insulation of the modules we tested the partial power consumptions determining the subcircuit currents using an external power supply (TP3005D-3, TekPower®,

US) and a precision microammeter (Fluke 45, Fluke, US). The power supply module without load had a quiescent current of 78 μA (655 μW). The amperometric + digital modules (+5 V) consumed 27 mW, and the transmitter module 25 mW (+8.4 V). In order to reduce the power consumption we decreased the supply voltage of the transmitter module down to +5 V without effects on the transmitter performance. Because the power consumption of the receiver unit is less critical, we checked only the total current necessary to drive the unit (45 mA, 225 mW).

3.3. Biosensor response to glucose

The in vitro response to glucose (Fig. 5) of PPD-based biosensors ($n = 4$) in the range between 0 and 140 mM showed classical Michaelis–Menten kinetics ($r^2 = 0.989$). The values of V_{max} and K_m, expressed as mean ± SEM, were respectively 82 ± 2 nA and 4.2 ± 0.4 mM. The response to low concentrations of glucose (0–2 mM) revealed a good linearity ($r^2 = 0.991$) with a slope of 13.5 ± 0.8 nA mM^{-1}. After the calibration of each biosensor connected to the telemetry system, the calibration (of the same sensor) was repeated using a BAS CV-37 potentiostat. No statistical differences were observed between the two calibrations (data not shown).

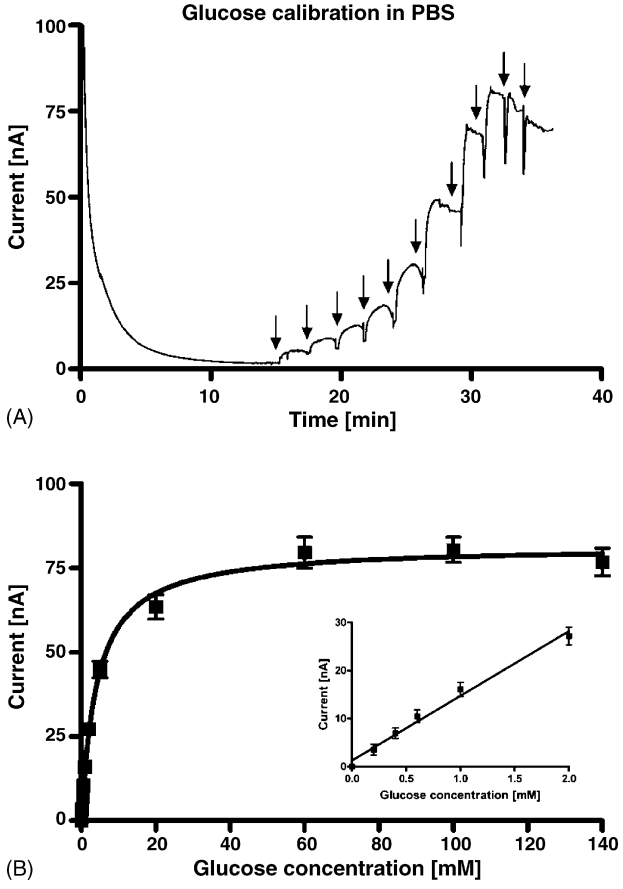

Fig. 5. In vitro response to glucose (0–140 mM) of PPD-based glucose biosensors ($n = 4$) connected to the transmitter unit. Ten successive injections of glucose (panel A) were made, using the three electrode cell illustrated in Fig. 3, after the stabilization in PBS at room temperature (25 °C). The calibration (0.2, 0.4, 0.6, 1, 2, 10, 20, 60, 100, 140 mM) showed classical Michaelis-Menten kinetics ($r^2 = 0.9885$) with a V_{max} of 81.65 ± 1.61 nA and a K_m of 4.193 ± 0.383 mM (panel B). The response to low concentrations of glucose (0–2 mM; panel B, small graph) revealed good linearity ($r^2 = 0.9913$) with a slope of 13.48 ± 0.76 nA mM^{-1}.

4. Discussion

4.1. Principles of operation and performance of the amperometric module

The amperometric module circuit was optimized for single-supply, low-voltage operation, through the distributing of the gain between the *I*/*V* converter and the differentiator. In this way a maximum voltage output of 500 mV from the first stage of amplification, with a theorical V_{app} span from 0 to 4.5 V, was achieved without the saturation of the second stage. The "rail-to-rail" output of the differentiator circuit (V_{out}) corresponds to 10 times the V_{app}-subtracted current signal. V_{out} is comprised between 0 and +4.94 V. The limitations of this design are related to variations of the resistor values, mainly in the difference circuit. The choice of low tolerance (0.1%) components minimized such limitations. In fact, the module is characterized by high stability, low noise (Fig. 4A) and good linear response (Fig. 4B and C). The system can operate only in oxidation mode and it is particularly suited to work in conjunction with oxidase-based biosensors and direct H_2O_2 detection [6] as illustrated in Fig. 5. An alternative oxidation/reduction configuration is possible connecting the differentiator V_{ref} (Eq. (3)) to 2.5 V and substituting the 10 MΩ with 1 MΩ resistors (R_2). In this case V_{app} becomes 2.5 $V \pm V_{app}$ but the system loses all the advantages previously described.

4.2. Digital module and data transmission

The MCU, present in the transmitter unit, serves as ADC, DSP and serial transmitter. In conjunction with the AM module, a complete digital wireless system has been implemented and the CRC calculation guarantees an optimal error check. The low pin number, internal ADC and the built-in oscillator make this component ideal for embedded applications.

All experiments were made indoors and no communication problems were observed modifying the transmission distance in a linear range between 0 and 15 m.

The low transmission speed may prove to be a disadvantage for real-time applications. However, the 20 Hz sample rate is sufficient to detect sub-second variations of oxidation current compared with previous studies [9–11]. In addition, the MCU DSP improves the system performance. Experiments are in progress using frequency modulation (FM) modules to obtain an increase in the serial data stream up to 9600 bps.

The receiver unit was interfaced to the software via USB with the possibility of high-level access to the received packets. This means simple data capture and handling with popular software packages such as LabView® or Dasylab®.

4.3. Miniaturization and future applications

The system developed in this paper is similar to that previously described by Yun and colleagues (2004) [16]. Yun illus-

trated a miniaturized wireless device for amperometric environmental monitoring with a built-in FM transmitter. In the present study we propose a system based on discrete components and pre-built critical modules (TX, RX, USB-transceiver), available at low cost, so no complex hardware calibrations are needed. The CMOS technology allows one to decrease the operating voltage and the power consumption. Studies are in progress to develop a miniaturized TX unit using surface mount (SM) components and a single +3 V lithium cell. The reduction of the size and the weight of the transmitter unit should permit its use in in vivo applications as a lightweight portable/implantable device. The in vitro characteristics of the proposed system justifies further studies in order to monitor glucose levels in the brain of freely moving animals, but also other molecules present in the extracellular brain compartment such as lactate, ascorbic acid and nitric oxide.

5. Conclusion

In this paper we have described a new complete telemetry system for biosensor applications. Although based on simple and inexpensive components, the transmitter and the receiver devices can be used for accurate transduction of the anodic oxidation current generated on the surface of a biosensor. At this stage of the development process the system exhibits high stability, low noise and good linear response in the nanoampere current range. The choice of low power CMOS technology makes the project suitable of further improvements such as the reduction of the operating voltage and the power consumption. The use of SM components and careful PCB design will make it possible to miniaturize the circuitry and to assemble a transmitter unit suitable for in vivo applications with freely moving animals.

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Biographies

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