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Raspberry-Pi based system for propofol monitoring

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A B S T R A C T

Induction of anesthesia with propofol is a largely adopted technique in hospital environments. The correct dosage of this compound is essential to avoid under- or over-anesthesia that may result in serious side-effects. Therefore, in clinical settings, long-term monitoring of propofol is of great importance. To this aim, in this work, we present the design and the validation of a custom-made, low-cost and portable *Point-of-Care* (PoC) system based on electrochemical detection for propofol monitoring. Fouling phenomenon due to phenolic oxidation of propofol has been overcome by adopting a *Pencil Graphite Electrode* (PGE) 3H as sensor. The validation of the system focused on testing the measurement speed through scan-rate analysis, which is important due to the fast clearance of propofol; and interference study with *Paracetamol*(APAP), since it is an analgesic compound frequently administered with propofol in medical practices.

1. Introduction

Intravenous (IV) injections are one of the most common health care procedures in medical applications [1]. Nowadays, general anesthesia is achieved and maintained via *Target Controlled Infusion* (TCI) systems, which enable an appropriate drug-injection procedure to keep the desired depth of sedation in the patient [2,3]. TCI systems help to administer the anesthesia cocktail that consists of three main compounds: (i) an anesthetic, such as propofol, (ii) an analgesic, such as paracetamol or opioids and (iii) a muscle relaxant, such as midazolam [4]. The infusion rate for each compound is evaluated from *Pharma-coKinetic* (PK)/*PharmacoDynamic* (PD) mathematical models implemented in the TCI pump for each infused drug [5]. Nevertheless, these PK/PD models are not able to reproduce the inter-patient variability in metabolism since they are based only on few physical characteristics of the patient, *e.g.* gender, weight and age. Other method to control the level of anesthesia in the patient relies on the monitoring of the *Bispectral Index* (BIS), from *ElectroEncephaloGram* (EEG) signal [6]. However, this value is indirectly evaluated and cannot provide the actual concentration of each compound in the blood [7]. Plus, the clinical measurement of a single parameter that appears relevant for a single drug may not be relevant if the drug is used in a combination, as in case of anesthesia [8]. Therefore, a therapeutic drug monitoring system has a far greater role to ensure safer anesthesia dosage [9].

Up to now, various methods have been used for propofol monitoring [10–14]. However these techniques had some limitations as being bulky, time-consuming and not suitable for fluidics applications. To overcome the limitations stemming from conventional techniques, electrochemical sensors came into play for propofol monitoring ([15–17]). However, due to its electro-polymerization, propofol causes fouling on the sensor surface that leads to a decrease in sensitivity after several measurements [18,19]. Even if some electrochemical sensors are designed to address this issue [20,21], up to now, no continuous or long-term (up to hours) monitoring of propofol has been achieved via a complete and portable system that includes both sensors and electronic platform.

In this work, we aimed to develop a custom-built PoC system for propofol on-line monitoring as follow up of our previous work in Ref. [22]. The system is composed of a portable multi-channel potentiostat based on *Raspberry Pi* (RPi) interfaced with a dedicated three-electrode configuration cell for robust and reliable propofol monitoring. The fouling problem of propofol due to its electro-oxidation was addressed by the usage of PGE as a working electrode with composition of 58% graphite, 36% clay and 5% wax, which guarantees optimum performances [23]. This specific lead composition corresponds to “3H” in the European Letter Scale [24].

Interference studies have been performed for propofol inside its main interference drug; APAP solution that is administered to patients

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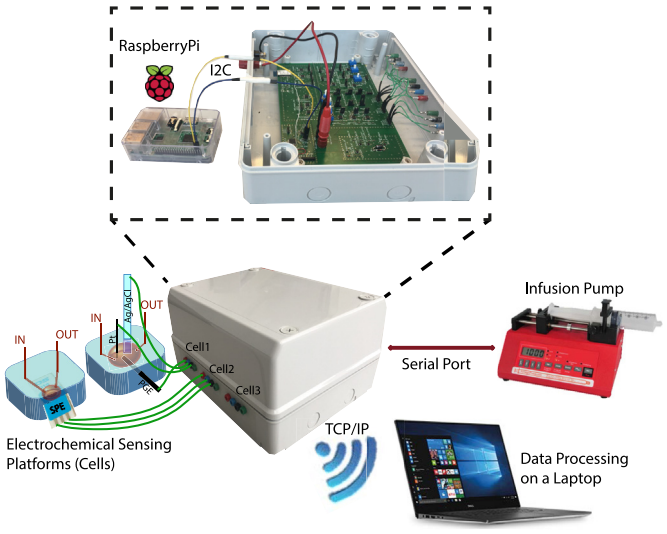

Fig. 1. Sketch of the full system for anesthesia on-line monitoring.

for pain relief inside anesthesia cocktail [25,26]. RPi based sensing platform enables the simultaneous detection of up to three drugs thanks to its three parallel independent channels. In this work, the main focus will be put on the integration of the propofol sensing platform and on the validation of the whole system in successfully detecting this compound with different electrochemical techniques and in presence of interferent drug.

By this work for the first time in literature, a complete RPi-driven portable system for propofol monitoring has been developed as a big step into "reliable feedback loop system for IV anesthesia monitoring".

2. System architecture

Fig. 1 depicts the architecture of the entire system for the continuous monitoring during anesthesia practices. It includes four different main blocks: (i) sensing platform in direct contact with the analyzed solution (patient's blood), (ii) central RPi-based electronic system to drive measurements, (iii) TCI pump to infuse the anesthetic drugs, and (iv) a laptop for data processing and for calculation of the concentration of drugs. In this paper we concentrate on the full integration of the sensing platform with the custom *Printed Circuit Board* (PCB) by validating the resulting system with propofol, taken as benchmark anesthetic drug. The drug concentration is evaluated by electrochemical tools on laptop and this value will be used as future work to drive the infusion pump, which we have already connected to the RPi through serial communication and validated in our previous work [27]. Our next goal is also to include an automatic electrochemical data analysis in the RPi software to make the process even more portable.

The sensing platforms are electrochemical cells, each of them consisting of a *Reference*, a *Counter* and a *Working Electrodes* (RE, CE and WE) and able to detect a compound. In this case, as shown in Fig. 2.b, we adopt as WE a PGE with lead composition of graphite, wax and clay that corresponds to 3H as international classification [28], a platinum (Pt) wire as CE and a silver/silver-chloride (Ag/AgCl) RE to sense propofol.

The electronic system has been already presented and described in detail previously [22]. Briefly, it consists of a RPi directly connected with a custom-made PCB. The schematic of the PCB, shown in Fig. 2, comprises a *Direct Digital Synthesizer* (DDS) and a read-out-circuit. The DDS is comprised of a microcontroller, which drives the *Digital-to-Analog* (DAC) to apply a stable potential to the electrochemical cell through a *Control Amplifier*. The read-out-circuit collects the signal from the electrochemical cell due to RedOx reaction, amplifies it with two stages of amplification (one with fixed gain *Trans-Impedance Amplifier* (TIA) and one with programmable gain *Programmable Gain Amplifier* (PGA)) and finally adjusts the signal offset before the *Analog-to-Digital Conversion* (ADC).

The RPi plays a central role in the architecture by performing and enabling different tasks. It receives the set-up parameters chosen by the user and it configures the PCB according to these values (exciting waveform to be generated and PGA gain) for different electrochemical experiments. It drives the electrochemical measurements through the PCB circuitry, it gathers the measured current from the front-end PCB and it sends the data to the laptop for post-processing analysis. Finally, RPi is connected with the infusion pump through serial communication so that it can control its injection.

All in all, the system is able to measure up to three drug in parallel thanks to its three independent and parallel channels.

In our previous work, we have successfully integrated the sensors and pump with PCB [27]. The data processing running on the laptop for the automatic evaluation of drug concentration and the subsequent calculation of the amount of propofol to be injected to maintain the level of sedation [29,30], has not been integrated in the loop yet. After

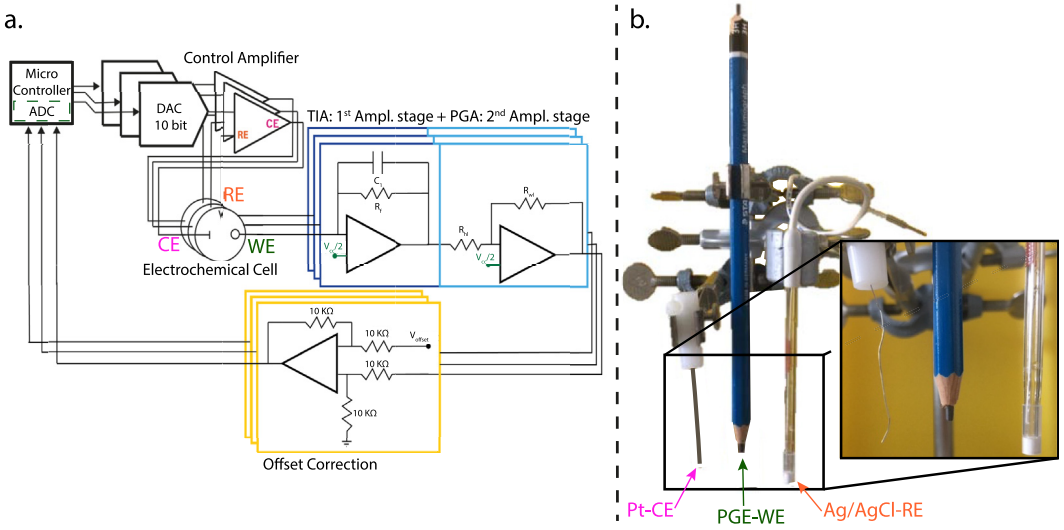

Fig. 2. a.) Schematic of our custom-built PCB (as in Ref. [22]). It consists of three parallel channels, each of them has a control amplifier, a two-stage amplification as read-out and an offset correction. b.) Electrochemical cell: Pt-wire as CE, *Pencil Graphite Electrode* (PGE) as WE and Ag/AgCl ad RE.