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Original Research Article

A miniature and low-cost glucose measurement system

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ABSTRACT

One of the bottlenecks in widespread adoption of biosensors is the large and sophisticated bioanalytical system that is required to perform signal transduction and analysis. A miniaturized bioanalytical system facilitates biosensing techniques that are portable, easy to handle and inexpensive for fast and reliable measurements of biochemical species. Thus, downscaling the bioanalytical system has become a highly active research area, significantly assisted by recent advances in the microelectronics technology. In this work, a miniaturized system is designed and implemented for amperometric detection, and subsequently tested with a glucose biosensor based on the one-step approach utilizing water soluble poly(o-aminophenol). Several experiments are conducted to assess the viability of this system including calibration, interference and application tests. The results are compared with the previously published work performed using the same biosensor tested with a commercial potentiostat in order to verify the applicability of the designed system.

1. Introduction

The quantitative determination of biochemical and biological processes is of great importance in medicine, biology and biotechnology. However, one of the significant challenges is the conversion of this biological information into a quantitative signal [1]. A common biological measurement is the determination of blood glucose levels which is carried out multiple times a day by the millions of people affected by *Diabetes mellitus* (DM) globally [2]. This disorder is characterised by high or low concentrations of blood glucose over an

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extended time period. All those affected are required to closely monitor their glucose levels in order to manage the disorder [3]. Accordingly, continuous in vivo monitoring of blood glucose level has become a major objective for researchers, and several techniques, such as chemiluminescence [4], fluorescence [5], colorimetry [6], and liquid chromatography [7], have been investigated for their efficacy in glucose detection. The key limitations of such techniques are the difficulty of their miniaturization, and the high cost of their production [8]. Moreover, these methods require skilled personnel and complicated sample preparation prior to the analysis [9]. Due to these disadvantages, the research has shifted to the development of glucose biosensors. The majority of glucose biosensors are of the electrochemical type since they provide reproducibility, high sensitivity and easy maintenance [10,11].

Electrochemical biosensors are based on the generation or consumption of electrochemical species producing an electrochemical signal that is measurable by an electrochemical detector. They can be operated in turbid media and are more amenable to miniaturization [12]. Electrochemical sensing systems can consist of either two or three electrode systems. A typical three electrode electrochemical cell, consisting of a working electrode, a reference electrode and a counter electrode, is more advantageous since the produced current from the reaction passes through the counter electrode instead of the reference electrode which provides the protection of the reference electrode from any change in its half-cell potential [13]. Between electrochemical biosensor types, amperometric biosensors possess additional selectivity and are based on the measurement of the current produced as a result of oxidation or reduction of the electroactive species in the medium while a constant potential is maintained at the working electrode [14]. Advantageously, since the potential during the measurement is fixed, amperometric biosensors have a negligible charging current, that is the current required to apply the potential to the system. As a result, the background signal affecting the detection limit is minimized [15]. Since biosensors are easy to fabricate, fast and low-cost devices, designing an amperometric biosensor that is specific to glucose and sensitive enough to detect glucose precisely is a significant advancement in the treatment of diabetes [16]. Such a sensor system can provide glucose level data collection, development of an insulin delivery system and glycemia research [17].

The most important step in the preparation of biosensors is the surface design. The biomolecules must be attached on the biosensor surface in a proper and reproducible way in order to prevent any loss of activity. For this purpose, different kind of materials can be employed for the fabrication such as conjugated polymers (CPs) that are organic polymers with extended π-conjugated system which consist of alternating single and double bonds along the polymer chain providing delocalization of electrons along the polymer backbone that results in charge mobility [18]. Due to their unusual electrochemical properties, CPs have attracted great attention and become as potential material candidates for biosensor applications especially due to their processability, low cost, conductivity and ease of preparation. They provide enhanced stability, sensitivity and fast response for the biosensors [19–23]. Among these materials, PANI derivatives have attracted great attention due to their controllable conductivity [24], promising electrochromic characteristics [25] and stability [26].

One of the key barriers to biosensor technology achieving widespread adoption is the relatively high resource requirement needed to perform the measurements. Despite fixed-potential amperometry being one of the cornerstones of electrochemistry research, it is still predominantly restricted to the laboratory setting where sophisticated equipment and highly trained personnel are required in order to perform the assay. Even in a lab-on-a-chip setting, many studies are still constrained to the laboratory due to the necessity of a benchtop device to perform the amperometric measurement [27–29].

In the literature, a number of studies have investigated the development of generic low-cost potentiostatic devices, including the popular CheapStat device developed by Rowe et al. [30]. This device is a low-cost open-source potentiostat which utilizes a microcontroller circuit in order to perform amperometry and voltammetry experiments. However, this device is what we would describe as "medium form-factor" which is suitable for handheld use but not integration into a microsystem. This circuit was improved by Dryden and Wheeler who developed a device called the DStat which performed more accurate measurements in a smaller form factor, however, this device was still "medium form-factor" and was designed for handheld use [31]. In addition to these works, several other researchers have reported on development of this type of systems [32–35]. All the devices reviewed were designed as general use devices for multiple test types and applications, and are thus larger, and include significantly more components than a device designed for a single specific application. In addition, these devices are designed as standalone systems, making them difficult to fully integrate into a lab-on-a-chip system. A device that is capable of performing sufficiently precise amperometric measurements, in a form-factor that is suited for integration into a lab-on-a-chip system, can be considered a significant leap forward in biosensing applications.

Herein, with these motivations we designed a miniaturized amperometry device and tested it with a glucose biosensor which was fabricated in consideration of the previously published works utilizing the water-soluble poly(o-aminophenol) (POAP) polymer that provided a proper immobilization of glucose oxidase (GOx) resulting in excellent analytical parameters [36]. GOx is the standard enzyme for glucose biosensor applications having a high glucose selectivity, and it can work under extreme temperature, pH and ionic strength conditions, and it is also cheap and easy to obtain. The working principle of the glucose biosensor is based on the oxidation of β-D-glucose by molecular oxygen which is catalyzed by GOx and results in the production of gluconic acid and hydrogen peroxide [10]. The biosensor was prepared by the same simple one-step approach as reported in a previous study [36]. Electrochemical measurements were made with the designed miniaturized amperometry device by the amperometric detection technique through monitoring the level of the oxygen consumption at -0.7 Ag wire reference electrode.

Most of the existing commercial glucose sensors are only designed for use with fixed parameters, and their circuit