DEVELOPMENT OF MICROMACHINED ELECTROCHEMICAL SENSOR AND PORTABLE METER SYSTEM

Chii-Wann Lin*, Chien-Yu Jan**, Oscal T.-C. Chen***, Sandy Wang***, T. Kao**
* Center for Biomedical Engineering, College. Medical, National, Taiwan University
** Institute of Biomedical Engineering, National Yang-Ming University
***EE Department, National Chung Cheng University
**E-mail: cwlin@cbme.mc.ntu.edu.tw

Abstract

An integrated microsensor has been designed and developed by using standard semiconductor technology and post-processing by micromachined procedures. The microsensor is implemented by using the UMC 0.5μ CMOS technology with a die size of 1.0 mm × 1.0 mm. The microsensor consists of a two-electrode electrochemical cell, current-to-voltage converter and operational amplifier. The electrode area is 600μ × 800μ. The complete system contains a microsensor strip, a single chip microprocessor (80C196KC) and a LCD for portable instrument prototype. The system is capable of both amperometric and cyclic voltametric measurement for continuous monitoring and detail analysis of electrode response.

Introduction

The use of semiconductor technologies for microstructure fabrication has been given the name of micro electromechanical system (MEMS) or micro system technology (MST). Microsensors for medical applications are part of the major interests in this active research area [1,2]. Among those principles for chemical sensing, electrochemical sensor has widely used for its sensitivity, selectivity, and simplicity. Incorporated with bio-sensing materials, such as enzymes, receptors, and gene fragments, it can work as a biosensor to provide quantitative information of bio-chemical substances within biological substances [3]. The monitoring of blood glucose level has always been on the priority list for the research and development of biosensors. It is extremely important for the treatment of mellitus diabetes. The issues of electrochemical sensor for this purpose include surface conditions for reproducibility, better interface design for smart performance, and possible mass production for cost reduction. The potential small size, low cost, high precision and good reproducibility can significantly contribute to the quality of health care with smart design for better performance. The same technologies can also meet the increasing demands in food industries, environmental monitoring and process control [4, 5]. In this paper, we report the development of an integrated microsensor, which has microelectrode for amperometric measurement and an on board amplifier for signal transduction. The portable meter system includes the microsensor chip, A/D and D/A converters, a LCD screen, microprocessor, memories and simple keypad. The system is capable of both amperometric and cyclic voltametric measurement for continuous monitoring and detail analysis of electrode responses.

Methods

Amperometric sensors are based on heterogeneous electron transfer reactions, i.e., the oxidation and reduction of electroactive substances. The enzyme catalyses the following reaction in the membrane.

$$glu\cos e + O_2 \xrightarrow{GOD} gluconic\ acid + H_2O_2$$

This approach is to monitoring production of hydrogen peroxide or the oxygen consumed in the enzymatic reaction [6]. The resulting current is a function of glucose concentration and working electrode area. A current-to-voltage amplifier is integrated on the microsensor chip to provide on board signal amplification for analog-to-digital converter (ADC). Provided that electrode area is small enough, a two-electrode system with an additional GOD or mediator membrane can measure level of glucose concentration in samples with little over-potential effect. This configuration has been implemented with platinum (Pt) working electrode and a silver/silver chloride (Ag/AgCl) reference electrode. The two-electrode cell is shown as in figure 1. The design of the feedback voltage controlled resistor allows a flexible dynamic range for linear conversion of the induced current in various applications.

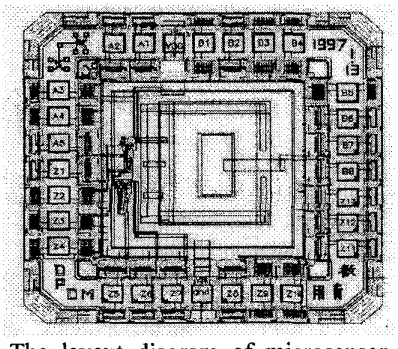

Figure 1. The layout diagram of microsensor. It has a working electrode in the center and a reference electrode. The on board amplifier provides the necessary current to voltage conversion and amplification.

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The portable meter system includes the microsensor chip, A/D and D/A converters, a LCD display, a microprocessor, memories, serial transmission and keypad. The system is capable of both amperometric and cyclic voltametric measurement for continuous monitoring and detail analysis of electrode responses. Figure 2 shows the block diagram of this system. The D/A converter can provide pulse width modulation (PWM) output for either fixed or scanning potential to the working electrode for effective sensing operations of the microsensor. The single chip controller (80C196KC) contains a 10 bits ADC for signal conversion.

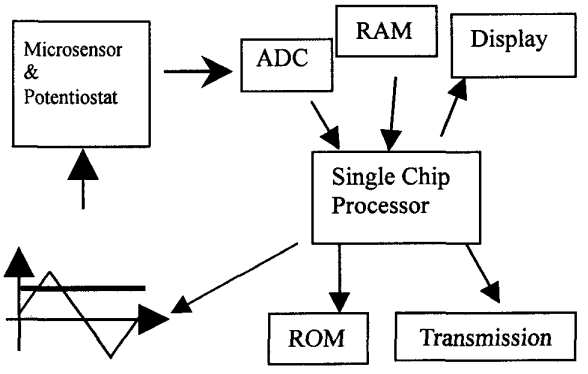

Figure 2. The system block diagram of portable meter for microsensor.

A variety of materials are available for the reaction of amperometric sensor. In this study, we tried several methods.

1. Place 20μl of GOD (500 units/ml) solution on top of cellulose acetate and then place PU membrane over the electrode and secure with a rubber 'O'-ring. Stretch the membrane tight [7].
2. Pyrrole was purified just before use by vacuum distillation at 70℃. Polypyrrole enzyme electrodes (Pt/PPy/GOD) were prepared at +0.7 V vs. Ag/AgCl in a 0.1 M KCl solution containing 0.4 M of pyrrole and 1 mg/ml of GOD. Pt/PPy/GOD electrodes were overoxidized at + 0.7 V vs. Ag/AgCl in a phosphate buffer (I=0.1 M, pH 7.2) [8-10].
3. BSA solution (50 mg/dl) in the phosphate buffer saline solution (0.1 M phosphate, 0.15M NaCl, pH 7.2). Then mixed 20 μl of each of the protein solution. After 2 minutes added 10 μl of 2.5% glutaraldehyde solution and after one hour we fit the outer membrane as described in Method 1 [11,12].
4. Test strip from commercial brand which use mediator instead of GOD.

Results

The integrated microsensor has been fabricated with UMC 0.5μ CMOS technology with a die size of 1.0 mm × 1.0 mm. The microsensor consists of a two-electrode electrochemical cell, a current-to-voltage converter and an operational amplifier. The electrode area is 600μ × 800μ. The DIP packaged sensor with bonding wires is shown as in figure 3. Our current effort is post-processing by lithograph and sputtering of Pt and Ag.

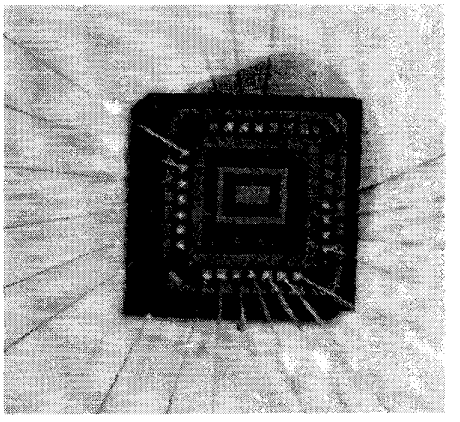

Figure 3. The fabricated microsensor with wire bonds for testing.

In this study, we have used several methods to immobilization enzyme. To show the functions of our portable meter, we will use the results from a commercial test strip. Figure 4 shows the resultant graph of a time response after adding a drop of glucose solution to the test strip. It has a transient overshooting response, which are possible for he hydration process, and a slow decay to the final steady state. The typical response time is around 20-25 seconds. We normally allow 30 seconds before the value was taken for either calibration or evaluation. Figure 5 shows the calibration curve obtained from a set of standard glucose solutions. The linearity of the calibration curve is up to 400 mg/dl (Y = 0.0497X + 1.7413, R= 0.9967, where y is the electrode response (uA) and x is the glucose concentration (mg/dl).

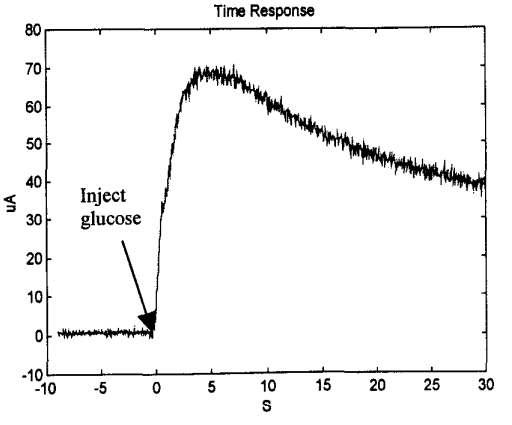

Figure 4. The time response measurement of the test strip after adding a drop of glucose solution.

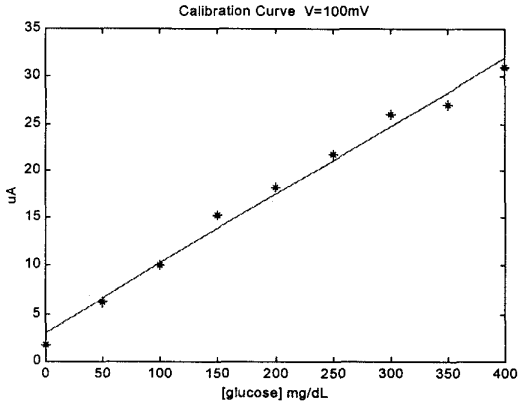

Figure 5. The calibration curve of test strip measured with developed meter system. The slope and intercept is 0.0497 and 1.7413 the correlation coefficient is 0.9967. The linear response can be up to 400 mg/dl.

Discussion

The semiconductor technology has been applied to design and fabricated an integrated microsensor, which has two electrodes for electrochemical measurement and an amplifier circuit for signal amplification. The standard double poly double metal (2D2M) processes result in a metal2 layer with Al/Ti alloy currently. We have tried to measure glucose solution with this surface material. The results indicate that the peak current can still change with glucose concentrations. However, the measurement of CV curve shows that this metal participates in the redox cycles. To improve the performance, we are currently working on the post-processing procedures to modify the electrode area with Pt and Ag. The meter system is able to perform both amperometric and cycle voltametric measurement. The serial transmission capability will allow the remote attending of physicians for better health care quality.

Conclusions

The proposed microsensor with an amplifier circuitry, had been implemented by using the UMC 0.5μ CMOS technology. The portable meter system contains a microsensor strip, a single chip microprocessor (80C196KC) and a LCD for portable instrument prototype. The system is capable of both amperometric and cyclic voltametric measurement for continuous monitoring and detail analysis of electrode response.

Acknowledgment

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