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Short communication

Microchip based electrochemical-piezoelectric integrated multi-mode sensing system for continuous glucose monitoring

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ABSTRACT

We presented a MEMS multi-mode sensing system by integrating electrochemical working electrode and solid-mounted thin-film piezoelectric resonator (SMR) on a single micro-sized chip, which is capable of detecting three sensing modes of electrochemistry, gravimetry and viscometry. As a model test sample, glucose concentration was successfully monitored using this integrated sensor. The electrochemical sensor amperometrically detected glucose concentration change, and SMR tracked the concentration variation through impedance response to viscosity. Optimized number of single-walled carbon nanotubes (SWCNTs) – poly (dimethyldiallylammonium chloride) (PDDA) / glucose oxidase (GOD) modification layers was also determined with the help of SMR by monitoring the mass-sensitive frequency shift. SMR proved to be a suitable support for chip-integrated electrochemical sensor for glucose detection. This integrated chip sensor can be conveniently fabricated with high throughput, shows significant potential for chemical and biological sensing applications.

1. Introduction

Biological and chemical sensors based on fluorescence labelling [1,2], surface plasmon resonance (SPR) [3,4], field effect transistor (FET) [5], electrochemistry [6,7], acoustic wave resonator such as quartz crystal microbalance (QCM) [8] and thin-film piezoelectric resonator [9,10], have been realized successfully. Although each of these techniques has its own advantages, detection based on single method can only provide limited information. For example, optical method of fluorescence labelling enables us to visually monitor the biomolecular interaction, but fails to quantify the interaction from more aspects, such as the change of mass or viscoelasticity which is detectable using QCM and thin-film piezoelectric resonator and the change of electric charge which can be acquired from FET and electrochemical sensor. To solve the problem, several research groups have tried to integrate two or more sensors in one system. Graneli and his co-workers investigated the formation of multilayers of DNA-modified lipid vesicles using QCM coupling with SPR [11]. Sakata et al. combined QCM and FET for real-time monitoring of the cell death [12]. However, none of these sensors can be used for multi-mode sensing in a small sized array form, resulting in time-consuming, sample-wasting and high-cost detection platforms. The development of micro-fabrication technology has opened new opportunities for miniaturization of device and integrating multi-functional sensor on a single chip.

With the aim of developing a micro-fabrication based multi-mode sensor array, in this letter, for the first time, we reported a novel CMOS-compatible micro-electromechanical sensing system, which integrates 4 pairs of electrochemical working electrode and solid-mounted type thin-film piezoelectric resonator (SMR) on a single chip. The integrated system enables detection of analytes with three sensing modes of electrochemistry, gravimetry and viscometry. The sharing of the same electrode facilitates the surface modifications and characterizations of the sensing electrode by different sensing mode. As a verification of the device performance, a classical glucose concentration monitoring experiment was carried out. The abilities of electrochemical sensor for detecting the redox reaction of glucose and SMR for monitoring viscosity changes induced by glucose concentration variation and modification of functional materials were thoroughly investigated.

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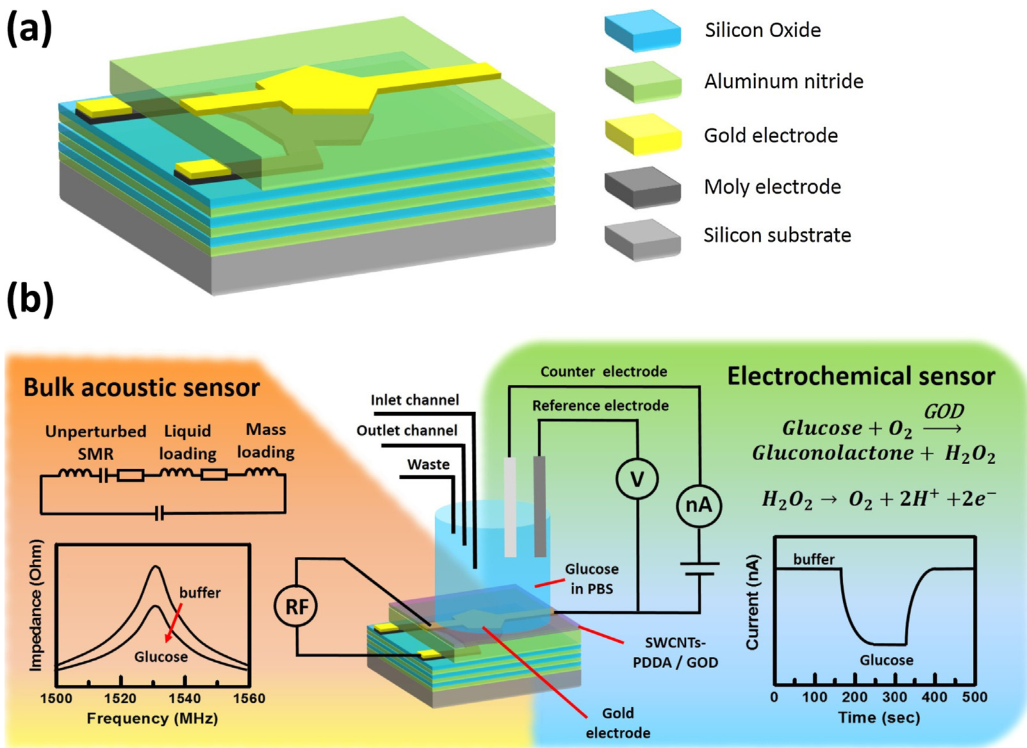

Fig. 1. (a) Schematic of the chip from oblique view, electrochemical sensor and SMR shares the same film stack with good compatibility; (b) schematic of the electrochemical-piezoelectric integrated sensing system.

2. Materials and methods

2.1. Device structure

Fig. 1(a) shows the schematic of the sensing element on chip. The SMR consists of a piezoelectric aluminum nitride (AlN) film sandwiched between a gold electrode and a bottom moly electrode. The sandwich structure is isolated from silicon substrate with an acoustic reflector array, which consists of alternative layers of SiO_2 and AlN. The overlapping region of the two electrodes defines the active area of SMR (0.02 mm^2). The electrochemical working electrode shares the gold electrode layer with the SMR, with an active area of 0.5 mm^2 for electrons transduction. Piezoelectric AlN film of SMR also works as dielectric film underneath the electrochemical working electrode, and isolates the bottom electrode of SMR and electrochemical working electrode with a thickness of 1 μm. Compared with air cavity, the acoustic reflector is a much more rigid structure and can prevent liquid penetration which may cause failure of SMR, and, meanwhile, it also serves as a dielectric layer to further isolate DC crosstalk between electrodes of electrochemical working electrodes. By taking advantages of the compatibility of material and structure, the two devices share the same electrode and the film underneath, which facilities the integration of two sensors on a single chip. Fabrication process information is provided in supplementary information (Fig. S1). The fabricated chip is shown in Fig. 2. A sensing array consisting of 4 pairs of sensing elements is demonstrated in Fig. 2(a), and a close view of one sensing element is provided in Fig. 2(b).

2.2. Measurement and setup

The chip was designed for direct-current (DC) and radio-frequency (RF) measurements, as illustrated in Fig. 1(b). For this purpose, a 150 μl plastic cap was mounted onto center of the chip as the reaction chamber, SMR pads were touched by an RF probe connected to a vector network analyzer, and electrochemical working electrode was clamped by an alligator clip for DC measurement. Electrochemical measurements were carried out with an electrochemical workstation. A Pt wire was employed as counter electrode, and a customized Ag/AgCl electrode (saturated 3 M KCl) as reference electrode. Compared with on-chip counter and reference electrodes, external electrodes are more stable in performance and is unaffected when working electrode under goes modification, which is a standard and reliable way of testing the sensing system. The two external electrodes and the input–output tubules were all inserted into the plastic chamber and sealed by epoxy. Solution was driven by a syringe pump.

2.3. Layer-by-layer assembly of SWCNTs-PDDA/GOD functional materials

The intrinsic principle of amperometric sensing lies on the immobilization of glucose oxidase (GOD) on electrode surface to detect the redox current produced by the enzymatic product H_2O_2 [13]. To specifically detect glucose, the electrode surface was functionalized with multiple layers of single-walled carbon nanotubes – poly (dimethyldiallylammonium chloride)/glucose oxidase (SWCNTs-PDDA/GOD) composite film. SWCNTs were homogenously dispersed and positively charged with the help of PDDA, and then the positively charged SWCNTs-PDDA grabbed the negatively charged GOD proteins by electrostatic force. Repeating this process several times, one can get multi-layers of SWCNTs-PDDA/GOD in layer-by-layer format [14], which is detailed in supplementary information. Here, SWCNTs were utilized due to their large surface-to-volume ratio for accumulating more GODs, as well as high electro catalytic effect and fast electron-transfer rate, which help improve electrochemical response [15].