Design for testing SU-8 and PDMS based hybrid glucose sensor

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Abstract— **In this paper, a test method for testing SU-8 and PDMS based hybrid glucose sensor with gold electrodes sandwiched between the two SU-8 layers is presented. Poly dimethylesiloxane (PDMS) and SU-8 is used as a flexible and bio-compatible sensor substrate material. Furthermore, SU-8 and PDMS is optically transparent and haemocompatible which is very important for implantable sensors.**

Different methods for testing glucose sensors are mentioned in a separate section. These test methods are categorized in different sections namely, material related tests, fabrication related tests, electrochemical related test and glucose response tests. And each test section is sub-categorized in appropriate sub-sections.

The bottom PDMS layer of the sensor is ~500 μm thick and both SU-8 layers are ~100 μm. Each sensor chip is 5.5 mm X 10.5 mm in size with 2 mm X 3 mm for the actual sensor area. Resistance of the successfully fabricated gold electrodes is measured between 1 to 5 mΩ. The drift of the sensors are measured using phosphate buffer followed by the linearity test using the glucose solution.

I. Introduction

THE need for regular glucose monitoring was highlighted in a study by the Diabetes Control and Complications Trial Research Group (1993) in the USA [1]. Although early debate centered on whether there was a need for a long-term implantable glucose sensor for diabetics, recent long-term studies have conclusively demonstrated that if glucose levels can be tightly regulated within the normal physiological range, then diabetic complications can be controlled [2].

Many different types of glucose sensors have been developed and can be classified by different aspects of their design. Optical glucose measurement is widely used for portable hand held glucose meters [3]. However, this method gives only rough glucose concentrations instead of the exact measure of blood glucose. Glucose detection using the affinity principle [4] detects a change in the physical properties of a sensitive cantilever, usually a change in the resonant frequency due to mass loading.

The oldest electro-enzymatic detection principle, developed by Clark in the 1960's, is still of interest to many researchers because of its high selectivity to glucose. The stage of proof of concept for such a device has passed, and currently efforts are aimed at improving the performance of electro-enzymatic sensors.

First among the problems with an enzymatic glucose sensor is the unpredictability of the Ag/AgCl electrode fabrication and drift in current. Moreover, platinum is widely used as an active electrode but is quite an expensive material for large scale production of the glucose sensors.

Finally, flexibility and optical transparency is crucial for sensors that may be worn or implanted, such as within contact lenses in the eyes for detecting glucose in tears. However, a fully transparent sensor must be fabricated using optically transparent electrodes (e.g. ITO) and such a transparent sensor should be designed using a flexible material such as PDMS. The only design that is both optically transparent and mechanically flexible has been proposed by Mitsubayashi et. al.[5]. However, this design uses platinum or indium tin oxide (ITO) and silver/silver chloride electrodes.

In order to address some of the problems discussed above, a PDMS based flexible glucose sensor with optically transparent substrate is presented here. Gold as an electrode (both the active and the reference electrodes) material is presented for the first time. A simple fabrication process flow without any manual interaction is also presented. This hybrid polymer fabrication process uses both SU-8 and PDMS as a sensor substrate material.

II. Experimental Tests

For realization of successful glucose sensor, several tests starting from material related tests to the final glucose sensor related tests are required. All the required tests are divided into four main types of tests and each type of test is sub-divided in individual tests if there is more than one type of test. A classification and a very brief description of each test are now discussed:

A. Material related tests

These tests are usually required to check the usability of the chosen materials for the sensor applications. Mainly two types of tests are required.

1) *Bio and haemocompatibility test:* Bio and haemocompatibility test of all the materials used in a sensor are required if the sensor is going be implanted in the body. This test measures toxic effect of the material on our body or the tissue response of our body with the sensor material. Sometimes bio and haemocompatibility of the material is important even if the sensor is not going to be implanted.

2) *Potential drift test for the reference electrode material:* This particular test is important for the sensors designed for long term monitoring of the glucose concentration. In this test, the potential of a reference electrode is measured for an

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extended period of time. Lower potential drift is preferable for the electrodes that are going to be used in a long term monitoring applications.

B. *Fabrication related tests*

Fabrication related tests are usually performed during the fabrication of the glucose sensors. Different test is performed at different stage of the process. These tests are sub-divided in the following three sub-categories.

1) *Dimension measurement:* The thickness measurement of thin films is usually carried out using the profilometer. This profilometer can be optical or mechanical. The thick film thickness can be measured either using a vernier calipers or a micrometer screw.

The width and the length of the micro structures are measured using an optical microscope with cross-bars and measuring equipment.

2) *Cracks and voids check:* The micro cracks and voids are sometimes present in the sensors. To improve the fabrication process yield of the sensors, micro-cracks and voids should be avoided. Usually, micro-cracks and voids are checked using the optical microscope with high magnification factor. For very small size features, scanning electron microscope (SEM) can also be used to identify the micro-cracks and voids.

3) *Electrode continuity check:* After the active and the reference electrodes are successfully patterned during fabrication, the electrical continuity of the electrodes is measured. Furthermore, the resistivity of the electrodes is also an important factor for reliable response of all the sensors.

C. *Electrochemical related test*

In the electrochemical response test, the sensor response without immobilizing the glucose oxidase (enzyme) is measured. Hydrogen peroxide (H_2O_2) is used as an electrolyte solution to measure the electrochemical behavior of the sensors. The electrochemical test helps to identify the required voltage for the electrochemical measurement of the electrolyte concentration. This test is the primary check of the sensor before using it as an actual glucose sensor.

D. *Glucose response tests*

After satisfactory results of all the tests mentioned above, the final glucose response tests are carried out after immobilizing the enzyme (glucose oxidase) on the actual sensors. The glucose response tests are divided into the following sub-sections:

1) *Linearity test:* The linearity test of the sensors is performed using by increasing the glucose concentration in the phosphate buffer solution. The change in current based on the glucose concentration is plotted. To use the glucose sensor for reliable measurements, the current generated should increase linearly with the glucose concentration.

2) *Long term stability test:* Long term stability of the sensor is very important if the sensor is going to be used for a long term monitoring applications. The sensors are kept in constant glucose concentration for an extended period of time and the current response is logged in a computer. The lower current drift is desirable for a long term application of the glucose sensor.

III. Design

The flexible electro-enzymatic sensor is fabricated using PDMS and SU-8 as a sensor material. PDMS is widely used for microfluidic and biomedical applications because of its ease of fabrication and biocompatibility [6]. PDMS is used as a sensor substrate which is optically transparent and flexible.

In addition, both the active and the reference electrodes of the flexible sensor are fabricated using only gold. Gold, similar to platinum, is also a biocompatible material [7] [8]. The motivation for further characterization of gold electrodes for the flexible sensors comes from the primary results obtained on a glass substrate [9].

The fabrication process can be used for batch fabrication of many sensors at once, which is crucial for commercialization of any glucose sensor. The sensor design avoids any manual assembly or alignment steps. The presented sensors are cost effective, simple to fabricate, and easy to release after complete fabrication.

In order to test and characterize different properties of the flexible electro-enzymatic glucose sensor, we designed a flexible sensor with sandwiched gold electrodes between two SU-8 layers on a PDMS layer (Fig. 1). The bottom layer of the sensor is a 500µm thick rectangular PDMS layer. This bottom layer is little larger than the area occupied by the electrodes. There is also a thin layer (100 µm) of SU-8 on PDMS layer. These two layers are tightly bonded which can not be separated.

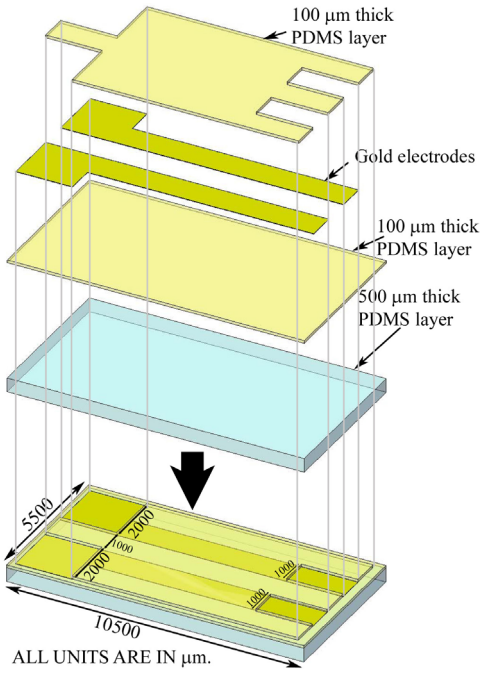

Fig. 1: Design of the flexible polymer based electro-enzymatic glucose sensor

The top sensor layer is designed using a 100 µm thick SU-8 layer with contact pad openings and electrode openings (Fig. 1). The electrode opening is provided only in the sensing area. Two separate openings are designed so that any of the gold electrodes can be used as an active electrode by immobilizing the enzyme on them. And, as mentioned previously, both gold electrodes are sandwiched between the two SU-8 layers.

All the sensor designs consist of three sections: a sensing area, a connecting conductor, and a contact pad. Each sensor die is 5.5 mm x 10.5 mm in size and is fabricated with gold electrodes sandwiched between the two SU-8 layers on a PDMS layer (Fig. 1). In a single step metal patterning process, the active and the reference electrodes, the connecting conductors, and the contact pads were fabricated using only gold. It should also be noted that the sensor dimensions, including bond pad dimensions, were chosen for easy handling and testing; the batch fabrication process could be utilized for both larger and much smaller sensors.

The actual sensing area, in all the designs, is 2 mm x 3 mm (Fig. 1). However, the active and reference electrode areas are 2mm x 2mm in size.

Large contact pads are designed for each electrode to make wire connections easier. Each 2mm x 2mm contact pad is connected with a 6mm long gold conductor. The openings in the top SU-8 layer for the contact pads and the sensing electrode (Fig. 1) are made for the physical connection with wires and for contact with the enzyme respectively. The gold conducting wire is covered with SU-8 to avoid direct external contact (Fig. 1).

IV. FABRICATION

The hybrid polymer fabrication process of the flexible electro-enzymatic glucose sensor is carried out using PDMS and SU-8 as the sensor substrate. Moreover, a thin layer of SU-8 is used for the metallization on the PDMS surface.

A hybrid polymer fabrication flow for the gold electrodes sandwiched between the two SU-8 layers (Fig. 2). Each step of the hybrid polymer fabrication flow is explained below.

- First of all, a cleaned glass substrate is spun with SU-8 2005 to make uniform coating on the glass substrate. This SU-8 layer behaves as a low adhesion material between the glass substrate and the bottom PDMS layer. The SU-8 2005 layer is soft baked, flood exposed and hard baked (Fig. 2(a)).
- To fabricate the bottom PDMS layer, Sylgard® 184 elastomer with 10% curing agent is mixed and is poured on the substrate. The mixture is cured at 85° C for 2 hours and 30 minutes (Fig. 2(b)).
- 100µm thick SU-8 2035 is spun on the treated PDMS layer and is soft baked by ramping the temperature. The SU-8 layer is exposed with the first mask to realize the bottom SU-8 layer. The 365nm (i-line) UV source is used to expose the SU-8 layer. The SU-8 is baked again for a post exposure bake (to cross-link the polymer) by ramping the temperature. Finally, the unexposed SU-8 layer is developed using SU-8 developer until the unexposed SU-8 is completely dissolved (Fig. 2(c)).
- To make gold electrode patterns, 50nm chrome and

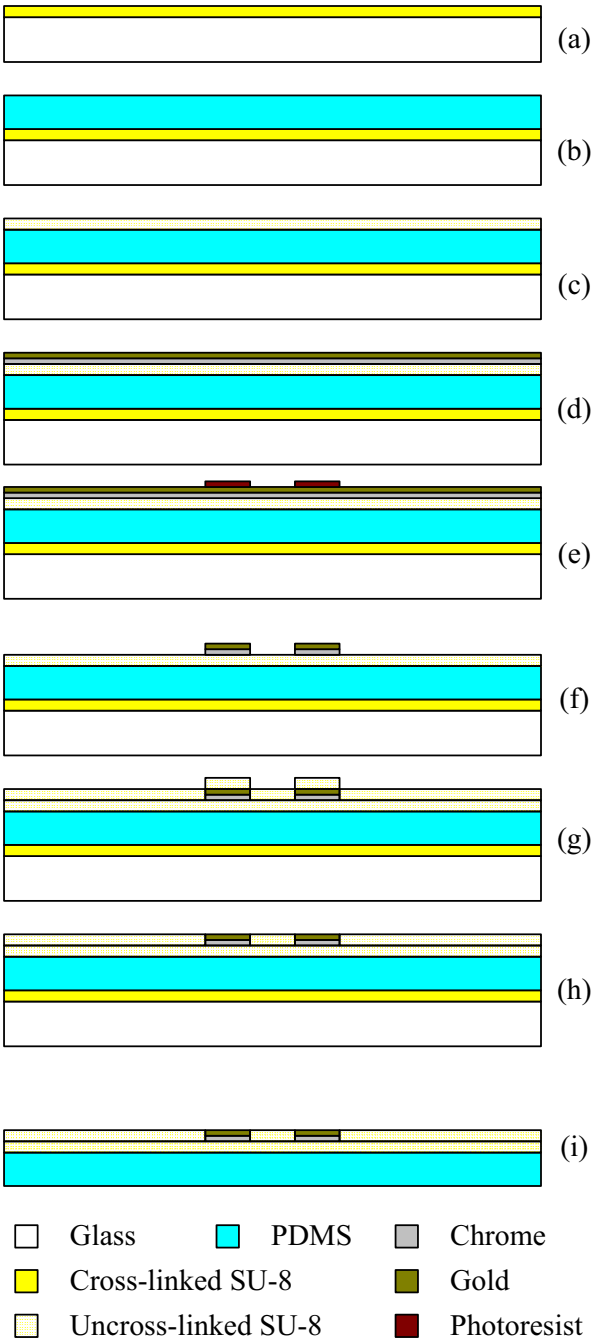

Fig. 2: Hybrid polymer fabrication process for the sandwiched gold electrodes between the two SU-8 layers on a PDMS layer: (a) clean glass substrate and thin SU-8 2005 layer; (b) pour PDMS on the substrate and cure; (c) treat PDMS surface and pattern bottom SU-8 layer; (d) sputter chrome and gold; (e) spin and pattern positive photoresist; (f) pattern gold and chromium layer using Transene® gold and chrome etchant; (g) spin SU-8 2035 layer for the top SU-8 layer, (h) pattern top SU-8 layer with active area openings and contact pad openings and (i) peel off PDMS and SU-8 based glucose sensors from

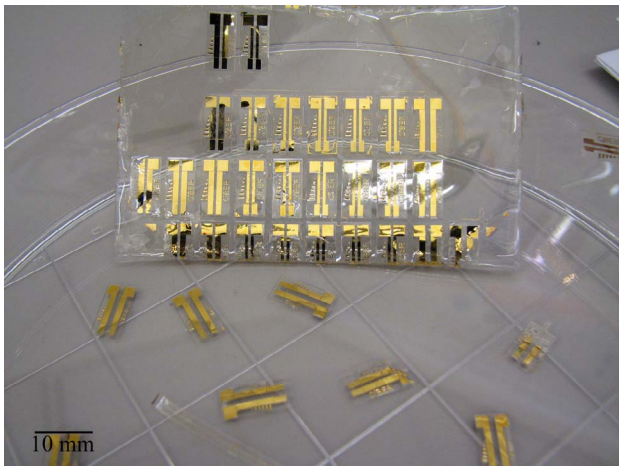

Fig. 3: Successfully peeled SU-8 and PDMS based sensors

Fig. 4: Single glucose sensor with sandwiched gold electrodes between two SU-8 layers

100nm gold layer are sputtered using the Corona sputtering system (Fig. 2(d)).

- Spin positive photoresist S1827 and pattern using the gold electrode mask (Fig. 2(e)).
- Pattern gold and chrome layer using Transene® gold and chrome etchant respectively (Fig. 2(f)).
- Now, spin 100 µm thick SU-8 2035 layer. This layer is used to make the top SU-8 layer. Soft bake the SU-8 layer with ramping up the hot plate followed by the UV exposure of the layer. The development of the thick layer is done after post exposure bake on the hot plates Fig. 2(g).
- The unexposed top layer of the SU-8 layer is removed using the SU-8 developer (Fig. 2(h)).
- Finally, the sandwiched SU-8 and PDMS based sensors are peeled off from the glass substrate and separated out using a knife (Fig. 2(i)).

Sensors are connected with wires using a conductive silver epoxy for testing. At this point, after optical verification, each sensor is ready for the electrical test.

V. Results and Discussion

The substrate with sensors was optically checked several times during the hybrid polymer fabrication process. After the electrodes were patterned on the first layer of SU-8, electrical conductivity of all the electrodes were satisfactorily checked. The results obtained from each test during the fabrication process and after the fabrication are discussed below.

A. Results related to fabrication process

SU-8 and PDMS based hybrid fabrication process is first time used to fabricate glucose sensors. The peeled SU-8 and PDMS based sensors are shown in Fig. 3. The electrical resistance of each electrode is between 1 and 5 mΩ which is very low.

After successful fabrication of each sensor, all the sensors are easily peeled from the SU-8 coated glass substrate. The electrical conductivity of each sensor is checked and the sensors with lost conductivity are discarded. A dual layer sandwiched SU-8 and PDMS based sensors are shown in Fig. 4. The conductivity measurement indicates uniform and defect-free gold electrodes, SU-8 layers and PDMS layer.

B. Results for the current response

After successful fabrication, the current response of the glucose sensor is measured. The current response is measured by submerging the sensors in appropriate solution. First of all, the current generated in the phosphate buffer solution using the gold only electrodes is measured. The current response (Fig. 5 and Fig. 6) is measured and logged using a potentiostat. The current drift in the phosphate buffer is plotted in Fig. 5 and the linearity response of the sensor with increasing glucose concentrations is shown in Fig. 6.

The current generated in phosphate buffer (drift) is less than ±6 pA which clearly indicates no drift in the sensor current (Fig. 5). The linearity test (Fig. 6) with increasing glucose concentration also indicates that the sensor current also increases with increasing glucose concentration.

VI. Conclusion

A polymer based electro-enzymatic glucose sensor using a new hybrid fabrication process, SU-8 and PDMS as a sensor substrate layer and gold electrodes is presented for the first time. The new fabrication process for hybrid SU-8 and PDMS based sensors with transparent hybrid polymer fabrication technique is successfully demonstrated. The total thickness of the fabricated sensors is measured 700 µm. The actual sensor size in all the designs is 2mm x 3mm. Both active and reference gold electrodes are successfully tested. The SU-8 and PDMS polymer based glucose sensor is economical to fabricate, with the use of gold electrodes making the fabrication process very simple to perform in any basic micro-fabrication facility.

Post fabrication tests such as electrical conductivity, profilometry, and glucose concentration response are utilized to characterize the process and working sensors. Optical imaging and electrical conductivity tests show for the first

time successful fabrication of the electro-enzymatic sensor using the novel materials in the multi layer SU-8 and PDMS process with sandwiched gold electrodes. A linearity measurement is successfully done on working sensors, showing a linear response for sensors.

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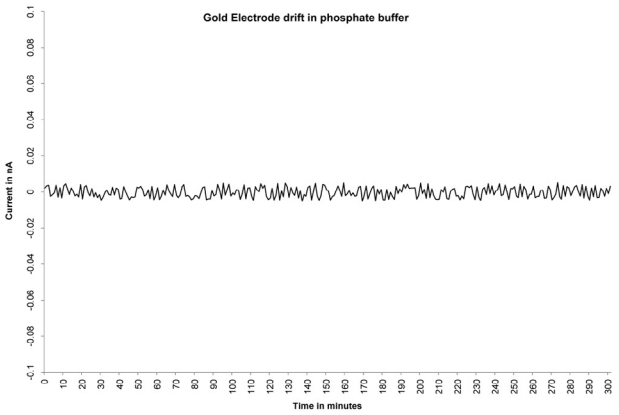

Fig. 5: Gold electrode current drift in phosphate buffer

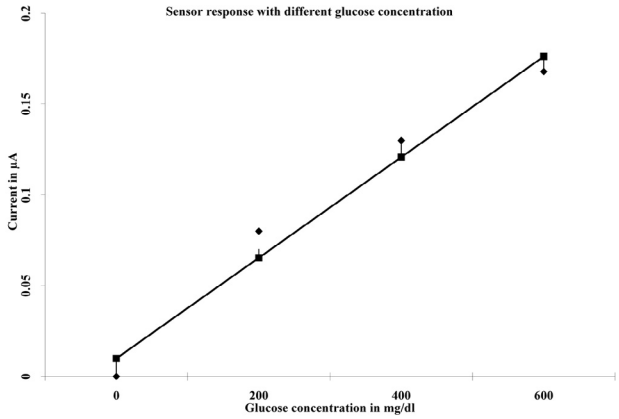

Fig. 6: Linearity response of the sensor with respect to glucose concentration in phosphate buffer