Development of Novel Gold/PDMS Sensors for Medical Applications

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Abstract—The paper presents the design and fabrication of novel gold/PDMS sensors using the sputtering method to use them for biomedical applications. The electrodes on the sensor patches were formed by placing a masked template containing the design over the PDMS. The sensor patches were flexible in nature with interdigitated electrodes formed on them. CTx-I, being one of the significant bone turnover biomarkers to determine the condition of the bones was tested at different concentrations to validate the functionality of the patches for this purpose. The results look promising to upgrade this idea into a fully-functionalized system for medical applications.

Keywords— *Gold; PDMS; CTx-I; Flexible; Sputtering.*

I. INTRODUCTION

The advancement in the sensing field has brought a big revolution in the quality of life of human beings [1]. In today's world, sensors are used in almost every field like domestic [2, 3], environmental [4, 5] and industrial sectors [6-8]. There has been a continuous demand to improve the quality and efficiency of the sensors since its intervention. Initially, the semi-conductive sensors [9] were a very popular choice due to their favorable operating conditions like the low cost of fabrication, linear response, high longevity and low input power. But still, there were some disadvantages like the limited range of operation, brittle nature and temperature dependence of the output which caused the researchers to opt for alternative approaches. With the innovation of sensors with flexible substrates [10, 11], a lot of problems related to the intransigence of the sensors were resolved, which increased their range of applications.

When the researchers were able to develop Microelectromechanical Systems (MEMS) based sensors [12], the cost of fabrication was reduced to a great extent. The problem of cost and ease of production of sensors were still into the picture, especially for the sensors which are used for day to day applications. Moreover, there are some sensors which have high efficiency in terms of sensitivity but are complex in nature and tough to fabricate, especially for unskilled workers. Thus, it is a state-of-art to develop sensors which have a low cost of fabrication and are simple in operation. This paper presents the design and fabrication of novel gold/PDMS sensors which were subsequently implemented for medical applications.

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With the flexible sensors in the picture, there are different materials, differing in terms of their electrical, mechanical and thermal properties are used for fabrication purposes. Some of the common materials used to develop the substrate part of the sensors are Polydimethylsiloxane (PDMS) [13], Polyethylene terephthalate (PET) [14], Polyethylene Naphthalate (PEN) [15] and Polyimide (PI) [16]. The selection of these materials mainly depends on the final dimension of the sensor patch and the applications they are being employed for. Among these, PDMS is the most advantages polymer due to its low-cost, non-toxicity and hydrophobicity. These advantages make it a popular choice to use to develop sensors for biomedical applications. Some of the common types of materials used to develop flexible sensors are Carbon Nanotubes (CNTs) [17], graphene [18], gold [19] and silver [20]. There have been prominent use [21-23] of gold nanoparticles compared to other materials due to their distinct advantages like high electrical conductivity, narrow size distribution, high aspect ratio and consistent size and shape. Another major advantage of using gold nanoparticles is their biocompatibility that includes non-toxicity and non-immunogenicity which increases the dynamicity in its applications [24]. The use of gold nanoparticles for sensing purposes is considered to be one of the standard applications.

For the electrode part of the sensor, there are different designs which have been used employed in the sensor structure for monitoring purposes. The operating principle differs as a result of the structural differences of the electrode parts. Interdigitated electrodes are one of the common types of electrodes which are largely exploited due to the advantages like minimized resonant frequency, increased effective capacitance and non-invasive nature. The interdigitated electrodes serve a great purpose for dielectric materials due to the ionic and faradic currents generated as a result of the interaction at the electrode-electrolyte interface leading to a highly sensitive response [25]. In this paper, we demonstrate the use of gold nanoparticles to develop interdigitated electrodes on the sensor patches.

Bio-medical sensing has been one of the major sectors for the applications of sensors in recent years [26-28]. Different kinds of sensors have been employed using wearable and non-wearable systems for ubiquitous monitoring of different parameters related to human health. Bio-medical biomarkers have been a significant part in this field of application, where the output of many chronic diseases can be monitored and cured at early stages by analyzing the information provided by them. This paper showcases the monitoring of one of the C-terminal Telopeptides which has been used to determine the risk of osteoporotic fractures [29]. Even though the current methodologies like Enzyme-linked Immunosorbent Assay

(ELISA) [30] and Dual-energy X-ray Absorptiometry (DEXA) [31] serve as gold standards for diagnosing the possibility of osteoporotic fractures by determining the bone densities, these processes have certain limitations like high equipment cost, highly time consuming method because of the high sample preparation time, and several steps need to complete the process of antibody binding, incubatory and spectrophotometric measurements [32]. So, a technique needs to be presented where the above-mentioned drawbacks can be addressed and rectified, keeping the efficiency and sensitivity of the working system constant. This paper highlights the proposal of a new system where the fabricated interdigitated sensors have been used to analyze the capability of the sensor to detect one of the C-Terminal biomarkers (CTx-I) at different concentrations.

The paper has been sub-divided into five sections. Followed by the introduction given in section one, the fabrication and working principle of the sensor patches are explained in sections two and three respectively. Then, the experimental set-up and results of the sensor patches for different CTx-I concentrations are shown in section four. The conclusion is given in the final section of the paper.

II. FABRICATION OF THE SENSOR PATCHES

The whole fabrication process was carried out in the laboratory at fixed temperature and humidity conditions. Figures 1(a) – 1(c) shows the schematic diagram of the fabrication process. PDMS (SYLGARD® 184, Silicon Elastomer Base) was formed by mixing the prepolymer and a curing agent at a ratio of 10:1 and cast on a petri dish as shown in Figure 1(a). The height of the cast PDMS was adjusted to around 1000 microns with a casting knife (SHEEN, 1117/1000 mm). This was followed by its desiccation for two hours to remove any trapped air bubbles in it. Then the PDMS was cured in the oven at 70°C for 2 hours to solidify the substrate. Then the sample was taken for sputtering of gold nanoparticles over it to form the electrodes. The sputtering was done using an EMITECH K550 machine with a pressure and current of 3×10^{-2} mbar and 25 mA respectively.

Figure 1: Schematic diagram of the fabrication process of the sensor patches. A layer of PDMS of fixed thickness was cast on a Petri dish (a). A template of the designed electrodes of specific dimensions was placed (b) top of the PDMS layer, followed by the sputtering of gold on it. The template was then removed to obtain the final product (c).

A mask was placed firmly over the PDMS substrate. The mask was made up of steel with the hollow part in it in the shape of the electrodes of the sensor patches. Steel was used as the mask due to its good adhesive nature with the PDMS. CREO Parametric 2.0 was used to design the electrodes for the mask with specified dimensions. The mask was placed properly over the PDMS substrate to nullify any gap between the former and the later, thus nullifying the shadow effect. The thickness of the sputtered gold was 100 nanometers. Followed by the sputtering of gold nanoparticles, the mask was taken off the substrate, leaving behind the electrode on the sensor. Figure 2 shows the final product of the fabrication process. It is seen that there was no shadow effect of the sputtering and the electrodes came off clean and perpendicular to the surface. Three pairs of interdigitated fingers were present each with a length and width of 10 mm and 2 mm respectively. The interdigital distance (d) between two consecutive electrodes is 100 microns. The total surface area of the sensing area is around 100 cm² with an area of 400 cm² of the total sensor.

Figure 2: Final view of the fabricated sensor patch.

III. WORKING PRINCIPLE OF THE ELECTRODES

The electrodes of the developed sensor patches operate on capacitive principle as a result of their interdigitated shape. Figure 3 shows the schematic diagram of the working principle of these sensors. An electric field produced as a result of it a potential difference is applied to the two electrodes of the sensor. This field bulges from one electrode to another of opposite polarity due to its planar structure. When any material is kept in the proximity to the sensing area of the sensors, the electric fields penetrate the material while traveling from one electrode to another. This changes the characteristics of the field which is studied to analyze the attributes of the material. This technique has been largely used to study the properties of many dielectric materials in domestic [33, 34] and industrial [35, 36] applications. Out of the different methods used to study this field, Electrochemical Impedance Spectroscopy (EIS) [37] is one of the primary techniques employed to study the applications of interdigital sensors. Frequency Response Analysis (FRA) [38] is one common phenomenon in EIS where a frequency sweep over a fixed range is done to analyze the difference between the input

and the output signal. This output is monitored in terms of the effective impedance (Z) of the material.

Figure 3: Schematic diagram of the working principle of the electrodes.

IV. EXPERIMENTAL RESULTS

The experiments for the different CTx-I concentrations were conducted as per the experimental setup is shown in figure 4. The sensing area of the sensor was dipped inside the solution carefully to avoid any effect of the solution on the bonding pads of the sensor. The other end of the sensor was connected with IM 3536 HIOKI High tester via Kelvin probes to determine the response of the sensor for different concentrations. The High Tester was connected to a computer via a USB cable to collect the data in Microsoft Office Suite via automatic data acquisition system. An input of 1 V RMS with a frequency sweep of 500 Hz - 10 kHz was provided from the tester to the sensor. The frequency was considered from 500 Hz as the sensor patch did not respond properly for the preceding frequencies for the different solutions. An average of three readings from the tester was taken to ensure repeatability of the responses.

Figure 4: Experimental set-up depicting the placement of the sensing area of the sensor patch inside the solution. The bonding pads of the sensor are connected to the impedance analyzer via Kelvin probes to monitor the changes occurring as a result of the different concentrations of CTx-I.

The solutions were prepared by using CTx-I peptide as the solute and de-ionized water (Resistance: 18.2 M Ω) as the solvent. A series of dilution solutions were prepared to perform the experiments. Initially, a stock solution of 1000 ppm was prepared by mixing 1 gm of CTx-I to 1 L of de-

ionized water. This was used to prepare different concentrated solutions of 100 ppm, 50 ppm, 10 ppm, 1 ppm and 0.1 ppm for experimental purposes. Figures 5 and 6 show the response of the sensor patches for the CTx-I concentrations in terms of impedance (Z) and conductivity (S) with respect to the swept frequency range. It is seen from Figure 5 that the sensor was capable differentiating the CTx-I concentrations. The impedance values remain pretty much constant and do not change much with the variation in frequency.

Figure 5: Response of the sensor patch for different CTx-I concentrations in terms of impedance vs. frequency.

The difference between the values took place due to the solution resistance occurring due to the ionic charge transfer between the solution and the electrodes of the sensor. The change in conductivity as a result of the CTx-I solutions are shown in Figure 6. It is seen that the conductivity values change symmetrically with the different concentrations. The decrease in conductivity values with different concentrations is evident from the increase in the impedance values from Figure 5.

Figure 6: Response of the sensor patch for different CTx-I concentrations in terms of conductivity vs. frequency.

The sensitivity of the sensor patches was also obtained by determining the change in the conductivity values with respect to the control value at different concentrations. The control

value was obtained by measuring the conductivity of the de-ionized water. The change in sensitivity for different concentrations as shown in Figure 7 is obtained from the following equation:

$$\text{Sensitivity} = \frac{S_{\text{control}} - S_{\text{measured}}}{S_{\text{control}}} \quad (i)$$

where,

S_{control} is the conductivity value of the control solution (de-ionized water).

S_{measured} is the conductivity of different solutions.

Figure 7: Sensitivity of the sensor patches for the tested CTx-I concentrations.

It is seen from Figure 7 that the sensitivity obtained from the sensor was 0.013, as evident from the slope of the graph. The linear fit plotted in the graph is very close to the experimental values as evident from the high coefficient of determination (R^2). The limit of detection (LOD) for these experimental solutions has been 0.1 ppm.

V. CONCLUSION

The paper showcases the fabrication and implementation of low-cost, novel gold/PDMS sensors. The sensors were developed using the sputtering technique having a mask containing the electrode design was placed over the substrate. The advantages of these sensors are its low-cost and easy fabrication process. The conductivity of the electrodes is also very high ($\sim 4 \times 10^6$ S/m). The sensor patches were also very flexible due to the nature of the substrate. The sensor patches were experimented with different CTx-I concentrations to employ them for osteoporotic applications. However, there are some issues that need to be addressed to optimize the use of these sensors for medical applications. The sensitivity of these sensors for any medical applications needs to be high. This can be achieved by two ways. The design, technique of fabrication or processed materials have to be altered to optimize the net electric field created between the electrodes of opposite polarity. The thickness of the electrodes can be changed to optimize the sensitivity. The individual passive elements of the sensor patch should also be determined to have a better understanding of the working circuitry. The

authors would address and rectify the above-mentioned points performing further experiments and report in the future work.

REFERENCES

- [1] A. Nag, and S. C. Mukhopadhyay, "Smart Home: Recognition of activities of elderly for 24/7; Coverage issues." pp. 480-489.
- [2] M. S. A. Rahman, S. C. Mukhopadhyay, and P.-L. Yu, "Novel Planar Interdigital Sensors," *Novel Sensors for Food Inspection: Modelling, Fabrication and Experimentation*, pp. 11-35: Springer, 2014.
- [3] M. S. A. Rahman, S. C. Mukhopadhyay, P.-L. Yu *et al.*, "Detection of bacterial endotoxin in food: New planar interdigital sensors based approach," *Journal of Food Engineering*, vol. 114, no. 3, pp. 346-360, 2013.
- [4] M. A. M. Yunus, S. Mukhopadhyay, and A. Punchihewa, "Application of independent component analysis for estimating nitrate contamination in natural water sources using planar electromagnetic sensor." pp. 538-543.
- [5] M. A. M. Yunus, G. R. Mendez, and S. C. Mukhopadhyay, "Development of a low cost system for nitrate and contamination detections in natural water supply based on a planar electromagnetic sensor." pp. 1-6.
- [6] A. I. Zia, S. Mukhopadhyay, I. Al-Bahadly *et al.*, "Introducing molecular selectivity in rapid impedimetric sensing of phthalates." pp. 838-843.
- [7] A. I. Zia, A. M. Syaifudin, S. Mukhopadhyay *et al.*, "Electrochemical impedance spectroscopy based MEMS sensors for phthalates detection in water and juices." p. 012026.
- [8] A. I. Zia, A. Mohd Syaifudin, S. Mukhopadhyay *et al.*, "Development of Electrochemical Impedance Spectroscopy based sensing system for DEHP detection." pp. 666-674.
- [9] S. M. Sze, *Semiconductor sensors*: Wiley New York, 1994.
- [10] A. Nag, S. C. Mukhopadhyay, and J. Kosel, "Wearable Flexible Sensors: A Review," *IEEE Sensors Journal*, 2017.
- [11] D. Vilela, A. Romeo, and S. Sánchez, "Flexible sensors for biomedical technology," *Lab on a Chip*, vol. 16, no. 3, pp. 402-408, 2016.
- [12] A. Wisitsoraat, V. Patthanasetakul, T. Lomas *et al.*, "Low cost thin film based piezoresistive MEMS tactile sensor," *Sensors and Actuators A: Physical*, vol. 139, no. 1, pp. 17-22, 2007.
- [13] S. Khan, L. Lorenzelli, and R. Dahiya, "Bendable piezoresistive sensors by screen printing MWCNT/PDMS composites on flexible substrates." pp. 1-4.
- [14] A. Nag, S. C. Mukhopadhyay, and J. Kosel, "Tactile Sensing From Laser-Ablated Metallized PET Films," *IEEE Sensors Journal*, vol. 17, no. 1, pp. 7-13, 2016.
- [15] R. Shabannia, and H. Abu-Hassan, "Vertically aligned ZnO nanorods synthesized using chemical bath deposition method on seed-layer ZnO/polyethylene naphthalate (PEN) substrates," *Materials Letters*, vol. 90, pp. 156-158, 2013.
- [16] A. Nag, S. C. Mukhopadhyay, and J. Kosel, "Sensing System for Salinity Testing Using Laser-induced Graphene Sensors," *Sensors and Actuators A: Physical*, 2017.
- [17] A. Nag, S. C. Mukhopadhyay, and J. Kosel, "Flexible carbon nanotube nanocomposite sensor for multiple physiological parameter monitoring," *Sensors and Actuators A: Physical*, vol. 251, pp. 148-155, 2016.
- [18] M. E. E. Alahi, A. Nag, S. C. Mukhopadhyay *et al.*, "A temperature-compensated graphene sensor for nitrate monitoring in real-time application," *Sensors and Actuators A: Physical*, vol. 269, pp. 79-90, 2018.
- [19] S. Gong, W. Schwalb, Y. Wang *et al.*, "A wearable and highly sensitive pressure sensor with ultrathin gold nanowires," *Nature Communications*, vol. 5, 2014.
- [20] J. Wang, J. Jiu, M. Nogi *et al.*, "A highly sensitive and flexible pressure sensor with electrodes and elastomeric interlayer containing silver nanowires," *Nanoscale*, vol. 7, no. 7, pp. 2926-2932, 2015.
- [21] A. Shiohara, J. Langer, L. Polavarapu *et al.*, "Solution processed polydimethylsiloxane/gold nanostar flexible substrates for

- plasmonic sensing," *Nanoscale*, vol. 6, no. 16, pp. 9817-9823, 2014.
- [22] C. Tasaltin, and F. Basarir, "Preparation of flexible VOC sensor based on carbon nanotubes and gold nanoparticles," *Sensors and Actuators B: Chemical*, vol. 194, pp. 173-179, 2014.
- [23] M. Segev-Bar, and H. Haick, "Flexible sensors based on nanoparticles," 2013.
- [24] R. Shukla, V. Bansal, M. Chaudhary *et al.*, "Biocompatibility of gold nanoparticles and their endocytotic fate inside the cellular compartment: a microscopic overview," *Langmuir*, vol. 21, no. 23, pp. 10644-10654, 2005.
- [25] R. Igreja, and C. Dias, "Analytical evaluation of the interdigital electrodes capacitance for a multi-layered structure," *Sensors and Actuators A: Physical*, vol. 112, no. 2, pp. 291-301, 2004.
- [26] S. Kruss, A. J. Hilmer, J. Zhang *et al.*, "Carbon nanotubes as optical biomedical sensors," *Advanced drug delivery reviews*, vol. 65, no. 15, pp. 1933-1950, 2013.
- [27] A. Chen, and S. Chatterjee, "Nanomaterials based electrochemical sensors for biomedical applications," *Chemical Society Reviews*, vol. 42, no. 12, pp. 5425-5438, 2013.
- [28] P. Roriz, O. Frazão, A. B. Lobo-Ribeiro *et al.*, "Review of fiber-optic pressure sensors for biomedical and biomechanical applications," *Journal of biomedical optics*, vol. 18, no. 5, pp. 050903-050903, 2013.
- [29] C. M. R. Barco, S. M. Arija, and M. R. Pérez, "Biochemical markers in osteoporosis: usefulness in clinical practice," *Reumatología Clínica (English Edition)*, vol. 8, no. 3, pp. 149-152, 2012.
- [30] S. Jabbar, J. Drury, J. N. Fordham *et al.*, "Osteoprotegerin, RANKL and bone turnover in postmenopausal osteoporosis," *Journal of clinical pathology*, vol. 64, no. 4, pp. 354-357, 2011.
- [31] C. Heiss, P. Govindarajan, G. Schlewitz *et al.*, "Induction of osteoporosis with its influence on osteoporotic determinants and their interrelationships in rats by DEXA," *Medical science monitor: international medical journal of experimental and clinical research*, vol. 18, no. 6, pp. BR199, 2012.
- [32] N. Afsarimanesh, S. C. Mukhopadhyay, and M. Kruger, "Molecularly Imprinted Polymer-Based Electrochemical Biosensor for Bone Loss Detection," *IEEE Transactions on Biomedical Engineering*, 2017.
- [33] A. Nag, A. I. Zia, X. Li *et al.*, "Novel Sensing Approach for LPG Leakage Detection: Part I—Operating Mechanism and Preliminary Results," *IEEE Sensors Journal*, vol. 16, no. 4, pp. 996-1003, 2016.
- [34] A. Nag, A. I. Zia, X. Li *et al.*, "Novel Sensing Approach for LPG Leakage Detection—Part II: Effects of Particle Size, Composition, and Coating Layer Thickness," *IEEE Sensors Journal*, vol. 16, no. 4, pp. 1088-1094, 2016.
- [35] M. S. A. Rahman, S. C. Mukhopadhyay, and P.-L. Yu, *Novel sensors for food inspection: Modelling, fabrication and experimentation*: Springer, 2014.
- [36] A. I. Zia, M. S. A. Rahman, S. C. Mukhopadhyay *et al.*, "Technique for rapid detection of phthalates in water and beverages," *Journal of Food Engineering*, vol. 116, no. 2, pp. 515-523, 2013.
- [37] E. Azzarello, E. Masi, and S. Mancuso, "Electrochemical impedance spectroscopy," *Plant Electrophysiology*, pp. 205-223: Springer, 2012.
- [38] M. Bagheri, M. S. Naderi, T. Blackburn *et al.*, "Frequency response analysis and short-circuit impedance measurement in detection of winding deformation within power transformers," *IEEE Electrical Insulation Magazine*, vol. 29, no. 3, pp. 33-40, 2013.