

Coplanar Waveguide Microwave Sensor for Label-Free Real-Time Glucose Detection

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Abstract. *In this work, a real-time label-free microwave diagnostic approach using Co-Planar Waveguide (CPW) design has been demonstrated for glucose detection. This mechanism has tremendous potential for the biomedical applications. Here, glucose biosensor is implemented with 50Ω CPW transmission line, where the centre localized 3mm diameter of CPW transmission line has been used for the sensing. Glucose sensor is implemented utilizing low cost multilayer PCB and polymer Poly-Di-Methyl-Siloxane (PDMS) fabrication technology. CPW transmission line is fabricated on FR4 microwave laminate board. To confine the Analyte Under Test (AUT) on the sensing area, PDMS polymer cavity is configured in the centre of CPW transmission line. The electromagnetic interaction with the varying dielectric constant of Glucose:DI water solution results shift in S_{11} parameter, which is closely observed to use as the source of sensing. CPW based glucose sensor is experimentally measured for S_{11} parameter using VNA, with varying glucose concentration range from 0 mg/ml (only DI water) to 4 mg/ml with the interval of 1 mg/ml. The measured results showed good sensitivity of 108.4 MHz/mg/ml and high accuracy with good linear regression coefficient of 0.9979.*

Keywords

CPW, polymer, microwave sensing, glucose sensor, label-free, real-time, PDMS

1. Introduction

Diabetes is a chronic disease which may cause life threatening condition. According to WHO, 422 million adults are suffering from diabetes globally and it is increasing haphazardly [1]. The devastating consequences of human life loss created the need of regular glucose monitoring for diabetic patients. There are many glucose level monitoring systems reported by Vashist [2] which are used in hospitals whereas portable kits have been used for patients monitoring at home [3].

Glucose biosensors have been implemented using various sensing techniques such as electrochemical, optical [4], [5], impedance [6] etc. Electrochemical technique is the oldest one and has been regularly upgraded with new materials such as CNT [7–9] and Graphene [10]. All these diagnostic techniques need skilled manpower, well equipped laboratory set-up, mediator chemicals, and also sample preparation and measurement process is cumbersome and time consuming. Seeing the dreadness of diabetes, several research groups are working on real-time sensing and transduction techniques to measure the glucose level. There are commercially available blood sugar testing kits called glucometer, which work in real-time, but these kits are strip based which causes additional usage cost. Microwave sensing approach created the feasibility of strip free reusable device with real-time sensing without usage cost. Microwave sensing technique utilizes the glucose concentration dependent dielectric constant for glucose level measurements. In literature, various microwave glucose sensor designs have been reported, such as intertwined spiral inductor coupled with an interdigital capacitor structure [11], air bridge structure on rectangular meandered line [12] fabricated on GaAs and theoretical modeling of artificial transmission line section implemented in microstrip technology [13] etc. Li [14] reported Distributed MEMS Transmission Line (DMTL) glucose biosensor on silicon. These devices have been fabricated using MEMS micromachining processes which need clean room and sophisticated equipments which cause high device cost. Therefore, there is need to explore the possibilities of low cost fabrication techniques to reduce the device cost e.g. Mason et al. [15] reported a coplanar sensor fabricated on FR4 for glucose detection AUT.

In this paper, a low cost glucose diagnostic microwave sensor fabricated on FR4 integrated with PDMS polymer cavity to hold the AUT is proposed. PDMS polymer is widely used in the area of microfluidics [16] and bioengineering due to its properties of chemical inertness, viscoelasticity, adhesion to metals, easy to process, biocompatibility etc. The major advantages of proposed design are, it is an integrated system-on-chip glucose biosensor fabricated in-house without using cleanroom and microfabrication process. This paper is organized in six sections, where CPW sensor design

is discussed under Sec. 2, CPW sensor fabrication and experimental results are discussed under Sec. 3 and Sec. 4 respectively. Results and discussion under Sec. 5, and conclusion under Sec. 6.

2. CPW Sensor Design

2.1 Working Principle

CPW transmission line is formed on a dielectric substrate with finite ground conductor on both sides of the central signal conductor. CPW supports Quasi-TEM (Transverse Electromagnetic) mode of propagation [17] in which electromagnetic wave (EM) propagates through substrate on the backside and air on the topside. The EM wave propagates on the surface of the centre conductor along the transmission line. In this, localized central part of CPW transmission line is being used as the sensing area. Sensing area is confined in the centre of the 50Ω CPW transmission line using PDMS polymer film cavity, as shown in Fig. 1. The AUT is placed on the sensing area of the CPW transmission line. Therefore, EM field interacts with localized air/AUT and PDMS polymer film on the topside and PCB dielectric materials on the backside. Here, AUT is varying concentration of glucose. Therefore EM waves interacts with AUT varying glucose concentration, and dielectric constant decreases on increasing the glucose concentration [18], resulting to peak shift to the higher frequency side [11].

2.2 Sensor Design

The 50Ω CPW transmission line is modeled in MATLAB version 7.10 (R2010a) using the CPW characteristic impedance (Z_0) standard formulae, as given below [17].

$$Z_0 = \frac{30\pi K(k'_0)}{\sqrt{\epsilon_{\text{eff}}} K(k_0)}, \quad (1)$$

$$\epsilon_{\text{eff}} = 1 + \frac{(\epsilon_r - 1)K(k_1)K(k_0)}{2K(k'_1)K(k'_0)} \quad (2)$$

where

$$k_0 = \frac{S}{S + 2G}, \quad (3)$$

$$k_1 = \frac{\sinh\left(\frac{\pi S}{4h}\right)}{\sinh\left(\frac{\pi(S+2G)}{4h}\right)}, \quad (4)$$

$$k'_0 = \sqrt{1 - k_0^2}, \quad (5)$$

$$k'_1 = \sqrt{1 - k_1^2}. \quad (6)$$

In this, equation (1) is for the CPW transmission line in which the effective dielectric constant can be calculated using (2). In (2), ϵ_r is the relative permittivity of the backside

substrate, h is the substrate height, S is the CPW centre signal conductor width, G is the gap between signal and the ground conductor. Equation (2) is applicable only when there is air on the top side and substrate on the back side of the CPW conductor lines. In our design, CPW conductor lines are partially occupied by air, PDMS and AUT on the top side whereas on the backside there is substrate. Under these circumstances, when top side air has been replaced with other materials, equation (2) has been modified as below equation [17]:

$$\epsilon_{\text{eff}} = 1 + q_1(\epsilon_r - 1) + q_2(\epsilon_{r1} - 1), \quad (7)$$

$$q_1 = \frac{1K(k_1)K(k_0)}{2K(k'_1)K(k'_0)}, \quad (8)$$

$$q_2 = \frac{1K(k_2)K(k_0)}{2K(k'_2)K(k'_0)}, \quad (9)$$

$$k_1 = \frac{\sinh\left(\frac{\pi S}{4h_1}\right)}{\sinh\left(\frac{\pi(S+2G)}{4h_1}\right)}, \quad (10)$$

$$k'_2 = \sqrt{1 - k_2^2}. \quad (11)$$

Equation (2) is having only one dielectric constant term which is for the backside substrate considering air on the top side, whereas equation (7) includes two dielectric constant terms for both top side and backside dielectric materials of the CPW conductor lines. At the sensing area, ϵ_r is the dielectric constant of the backside substrate, and topside films dielectric constant is $\epsilon_{r1} = (\epsilon_1 h_1 + \epsilon_2 h_2)/(h_1 + h_2)$ where ϵ_1 is the dielectric constant of the respective material in the cavity, Air/AUT (as shown in Fig. 1) which is localized, h_1 is the cavity height, ϵ_2 is the dielectric constant of the PDMS polymer, h_2 is the thin PDMS polymer film. Dielectric constant of the PDMS layer is constant whereas the dielectric constant of the AUT will vary depending on the glucose concentration in the solution. The variation in AUT dielectric constant ϵ_{r1} w.r.t. the glucose concentration will cause the change in the characteristic impedance, consequently CPW S-parameters which are being used for the sensing mechanism. The analytically modelled CPW glucose sensor design parameters are listed in Tab. 1, fabrication details are discussed under next section.

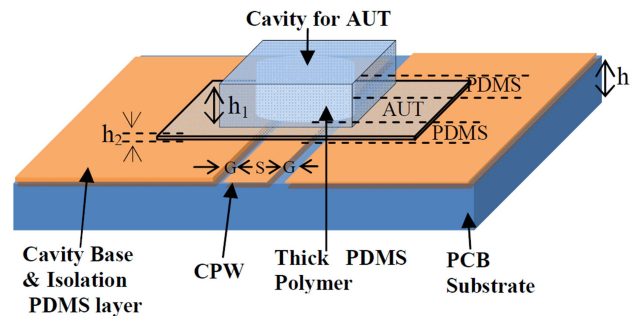


Fig. 1. 3D view of CPW glucose sensor.

Design Parameters	Dimensions (mm)
Substrate Height (h)	1.576
CPW Length	20
CPW $G-S-G$	0.34 - 2 - 0.34
Cavity Diameter	3
Cavity Height	4

Tab. 1. CPW sensor design parameters.

3. CPW Sensor Fabrication

Micromachined glucose sensor with design parameters listed in Tab. 1, is fabricated using PCB and PDMS polymer multilayer fabrication processes. 50Ω CPW transmission line is fabricated on FR4 substrate, whereas cavity to confine the AUT to the sensing area is fabricated using PDMS polymer as discussed below:

CPW transmission line fabrication– Commercially available FR4 board with both side copper clad of $35\mu\text{m}$ thickness is used as the substrate. CPW transmission line Ground-Signal-Ground (GSG) conductors with dimensions listed in Tab. 1, are patterned on one side and copper is completely etched away from the backside of PCB. The CPW design parameters G-S-G 0.34 mm-2 mm-0.34 mm has been used to fabricate 50Ω transmission line.

Formation of the Cavity to hold AUT– The cavity is formed of PDMS polymer layers using Dow Corning Sylgard 184 kit. In Dow Corning Sylgard 184 kit, PDMS base and curing agent are taken in the ratio of 10 : 1 by weight. Then whisked thoroughly with a stirrer for 10 minutes, to mix the curing agent uniformly. PDMS polymer layers are cured by keeping still for 48 hours at room temperature. Through hole of diameter 3 mm is formed in the thick PDMS layer using surgical biopsy punch.

Device Assembling: Device is assembled by configuring the cavity on the CPW transmission line. Cavity is formed by fixing the through hole thick PDMS layer with underneath thin layer PDMS on the CPW transmission line. The fabricated device is measured for the RF performance, experimental set-up details are discussed next.

4. Experimental Setup

The fabricated CPW Glucose sensor is measured for RF performance using Rohde & Schwarz ZNB20 Vector Network Analyzer (VNA). Experimental set-up of the CPW glucose sensor is shown in Fig. 2(a), whereas close-up view of DUT is shown in Fig. 2(b). D-glucose ($C_6H_{12}O_6$):DI water solution of concentrations 0 mg/ml, 1 mg/ml, 2 mg/ml, 3 mg/ml and 4 mg/ml had been prepared. AUT of $20\mu\text{l}$ volume was dropped using micropipette in the cavity. RF measurements are carried out with all these glucose concentrations are measured in sequence. The cavity is thoroughly cleaned with water after each measurement and gets it completely dry before reuse. Measurements are carried out under 20.3°C temperature and 52% humidity. Measured result has been presented in the next section.

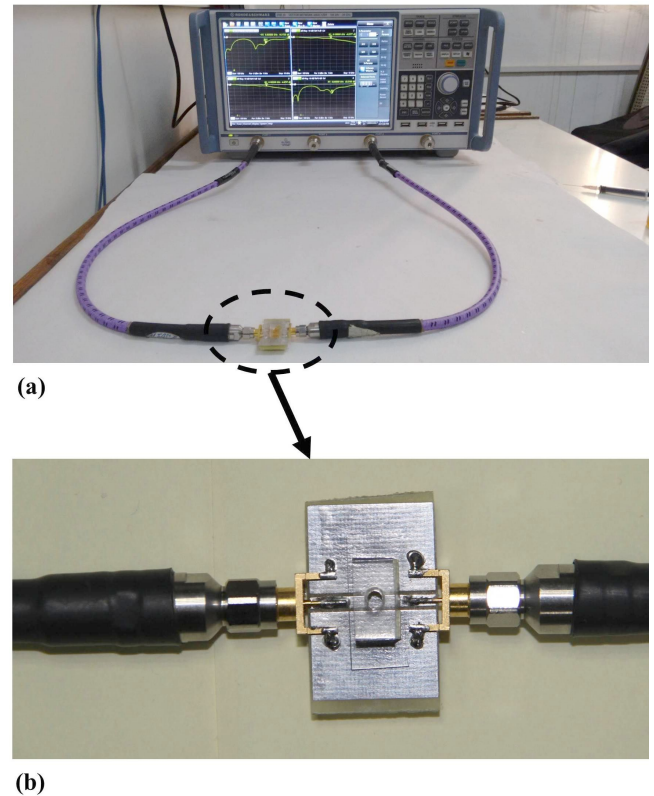


Fig. 2. (a) Experimental set-up of glucose sensor, (b) close-up view of the device under test.

5. Experimental Results and Discussion

5.1 Experimental Results

CPW glucose sensor is experimentally measured for the reflection coefficient S_{11} parameters with varying glucose concentration. The measured S_{11} parameter of CPW, microwave biosensor with air cavity and for glucose concentration ranging from 0 mg/ml to 4 mg/ml with the interval of 1 mg/ml as listed in Tab. 2. RF Measurements carried out for CPW (without any PDMS layers) showed peak frequency 3.6 GHz, which shifted to 3.236 GHz for assembled device (air cavity). The shift is due to high dielectric constant 2.8 of PDMS polymer compared to the air dielectric constant 1. The shifted peak frequency for air cavity, 0 mg/ml, 1 mg/ml, 2 mg/ml, 3 mg/ml and 4 mg/ml is 3.236, 2.519, 2.636, 2.753, 2.856 and 2.951 GHz respectively listed in Tab. 2. The measured peak frequency shifts toward high frequency as the glucose concentration is increased (as shown in Fig. 3), which is due to decrease in the dielectric constant on increasing the glucose concentration. The experimentally measured plot Fig. 3 showed S_{11} peak gets sharper on decreasing the glucose concentration which is because of decrease in loss factor with decrease in the glucose concentration in the solution [11]. The RF measurements are carried out in < 10 s time span to avoid any substantial temperature

variation of the solution during the measurements. The regression analysis presents the glucose concentration w.r.t. peak frequency, which is linear with curve fitting (as shown in Fig. 4), and actual values are exactly in the linear curve a good linear correlation ($R^2 = 0.9979$) between glucose concentration and shift in centre frequency with a linear regression equation expressed as follows. Hence, measured device sensitivity is 108.4 MHz/mg/ml with good linear correlation of 0.9979.

$$y = 0.108x + 2.526,$$

$$R^2 = 0.997.$$

Glucose concentration (mg/ml)	Peak Frequency f (GHz)
CPW (without PDMS layer)	3.6
CPW with cavity on the top	3.236
0	2.519
1	2.636
2	2.753
3	2.856
4	2.951

Tab. 2. Measured peak frequency w.r.t. the glucose concentration.

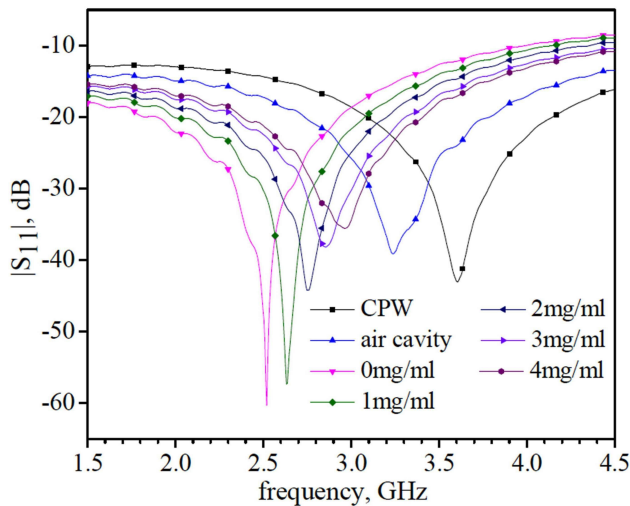


Fig. 3. Shift in the peak frequency and the variations in S_{11} magnitude for the glucose samples of varying concentrations.

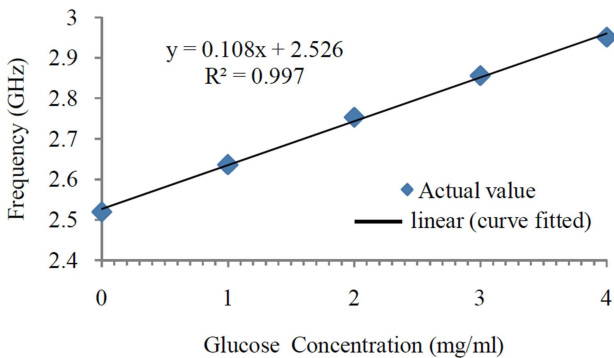


Fig. 4. Comparison in linearly curve fitted peak frequencies with the actual peak frequencies.

5.2 Discussions

A comparison of our proposed CPW planar glucose sensor with the ring resonator based glucose sensor reported by Camli et al. [19] on the basis of various aspects, such as performance, design, fabrication, and measurements as listed in Tab. 3, which shows our proposed glucose sensor is with very high sensitivity of 108.4 MHz/mg/ml compared to 0.107 MHz/mg/ml [19], very high linear correlation 0.9979 compared to 0.79 [19]. Sample requirement in this proposed work is only 20 μ l compared to 90 μ l [19] in the literature. The device reported in literature [19] needs a laser cutter to make the cavity to confine the AUT, whereas the proposed CPW glucose sensor is easy to design and is fabricated in-house.

Parameters	Ref [19]	Our Work
Sensitivity (MHz/mg/mL)	0.107	108.4
Linear correlation (R^2)	0.79	0.9979
Sample value (μ l)	90	20
Substrate used	FR4	FR4
Fabrication Technique	PCB AUT holder: Reservoir formed by Laser Cutter	PCB technology AUT Holder: PDMS Polymer Process, Surgical Biopsy Punch was used to create cavity
Design	Spilt ring Resonator Based	CPW Planar
Fabrication Complexity	Medium	Low
Design Complexity	High	Low
Measurement Process Complexity	High	Low
Overall Device Cost	Medium	Very Low

Tab. 3. Proposed device compared with the reported [19].

6. Conclusion

In this paper, a portable real-time and label-free glucose diagnostic approach based on microwave sensing technique is demonstrated using a low cost PCB and PDMS Polymer fabrication technology. The demonstrated device is fabricated without using any cleanroom processes. Proposed microwave sensing device is a strip free reusable sensor. The proposed device is with high sensitivity, good accuracy and easy to fabricate compared to the reported in literature.

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