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Microwave based resonant biosensors for multiple molecular concentrations quantification

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***Abstract*—This paper presents several microwave based resonant biosensors realized with a microfluidic and thin film microstrip technology. Due to the use of multiple stubs terminated by an interdigitated capacitor, this paper demonstrates that this circuit topology is suitable for multiple and simultaneous molecule concentration measurements. The accuracy study of the measurement is conducted depending on the concentration of glucose and the frequency stub loaded with an aqueous-based glucose solution.**

Keywords—Microwave, interdigitated capacitor, biosensors, molecules.

I. Introduction

The rapid and non-destructive quantification of molecules in liquid solution present a high interest in many applicative domains, chemistry, biology, medicine and in the food processing industry notably. Among the possible sensing techniques, one under development is related to the microwave dielectric spectroscopy due to its non-invasivity and non-alteration of the tested samples. Broadband and narrowband circuits have been investigated. In general, resonant-based configurations are preferred to obtain high sensitivity. Various circuits configurations realized with different technologies and suitable for diverse liquid quantities, liters down to nanoliters, have been developed so far. Some are based on cavities, others on metamaterial devices, split-ring or quarter-wavelength resonators configurations [1]-[4]. Moreover, enabling the characterization of single liquids may not be sufficient in many applications. Processing and quantifying several liquids in the same time constitutes an important leitmotiv in sensing system development in order to get a better efficiency as well as time saving.

This paper consequently focuses on the presentation and the characterization of three biosensors based on an interdigitated capacitor-terminated stub configuration. Their design enables the molecular concentration quantification of one or several liquid solutions performed with a single measurement. Up to four different liquids may be characterized. The first section of the paper consequently provides a presentation of the different investigated biosensors. Next section is dedicated to the fabrication process, which has been developed to realize these sensors, whereas section IV presents the microwave characterization of these sensors in the case of glucose measurements in aqueous solutions.

II. Biosensors Presentation

Figure 1 presents a photography of each investigated sensors. The first sensor includes a single quarter-wavelength stub, terminated by a grounded interdigitated capacitor, whereas the second and third devices exhibit two and four stubs respectively. A microfluidic channel is placed on top of each ending capacitor. These channels are all independent, enabling the loading of distinctive liquids in each channel.

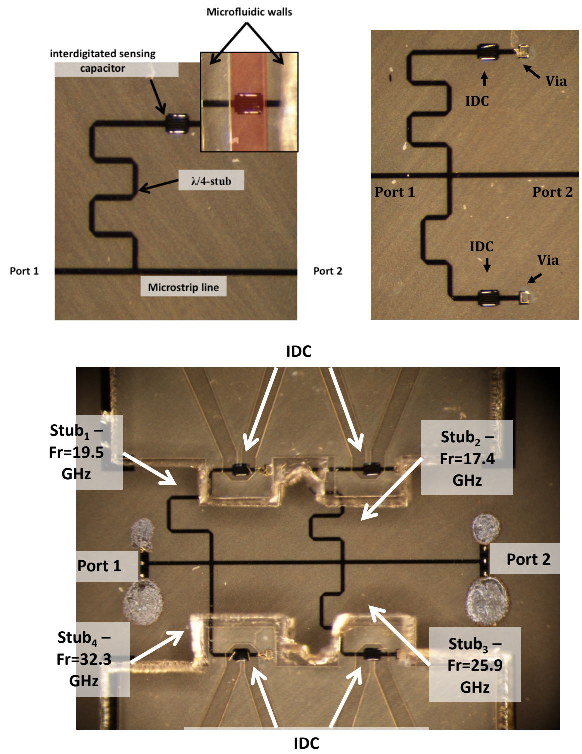

Fig. 1. Photographies of the single, double and quadruple interdigitated capacitor-based microwave biosensors.

In order to discriminate the different stubs, each of them presents a different resonant frequency. Finally, coplanar accesses are preferred for microwave measurements, as shown in Fig. 1 with the 4 stubs configuration.

III. Fabrication of the Biosensors

These biosensors are fabricated with a compact microfluidic and thin film microstrip technology, which is compatible with the characterization of low liquid volumes, in the order of less than a microliter.

The microwave devices are realized on a silicon substrate. To elaborate the thin film configuration, a first metal layer is evaporated on the substrate as the ground plane. The dielectric layer of the microstrip configuration is then obtained with a 20 µm thick polymer layer. To decrease dielectric losses, benzocyclobuten (BCB) is chosen as the polymer layer due to its low loss tangent in the GHz range. In order to enable the grounding of the stubs, the photosensitive BCB layer is patterned.

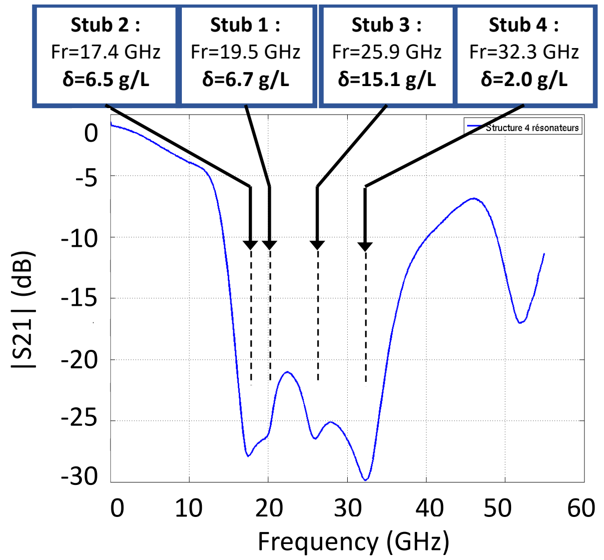

Fig. 2. Transmission coefficient of the quadruple stub sensor while empty.

After performing a hardcure of the BCB layer at 250°C for polymerization, a plasma treatment is realized to enhance the adhesion of the next metal deposition. The strip line is obtained with the sputtering of titanium and gold layers.

The microfluidic part is realized with PolyDiMethylSiloxane (PDMS), an elastomer, which is obtained while using a silicon mold previously defined by Deep Reactive Ion Etching. To facilitate the accuracy of the channels' placement on the microstrip stubs, the channels are made 2 by 2.

IV. Microwave Characterization of the Sensors

Each sensor is characterized from 40 MHz to 57 GHz. The evaluation of the single stub and double stub sensors is already published in [5] and [6] respectively. As far as the quadruple stub is concerned, the measured transmission coefficient while the structure is empty is given in Fig. 2.

The measurement protocol includes two steps, a calibration previously to random measurements. The first step therefore consists in measuring four times the sensor while each channel is loaded with a known glucose solution of 80g/l whereas others are filled with de-ionized water. Based on these four calibration measurements, other glucose concentrations are evaluated. Fig. 3 presents the measured and extracted glucose concentrations compare to the real one for two different channels, number 1 and number 4 respectively. The dashed lines delimitate the first zone of the Clarke abacus, which permits to determine the accuracy of glucose concentration. This particular area corresponds to an acceptable concentration error.

Table 1 summarizes the mean error performed on the glucose concentration for the different sensor configurations.

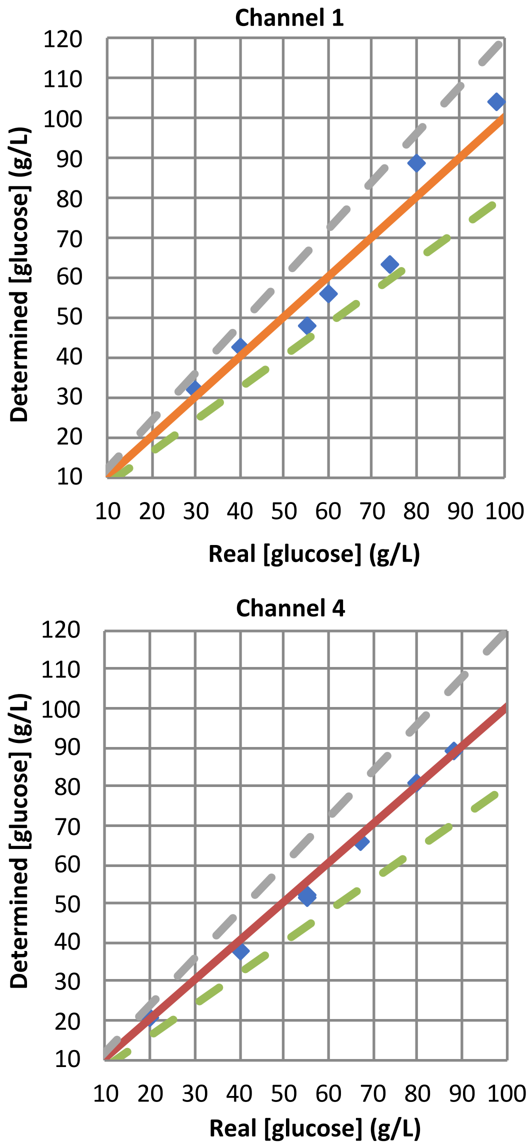

Fig. 3. Accuracy evaluation of glucose concentration in the Clark chart for channels 1 and 4.

TABLE I. Mean error of glucose concentration depending on the sensor configuration, in g/l

1 stub	*2-stubs*	*4 stubs*
0.3	3.2	2 (channel 4) 6.5 (channels 1,2) 15 (channel 3)

One may first notice that the single stub presents the lowest error, where this one increases progressively as the number of stubs rises. The single liquid-based sensor indeed exhibits an accuracy of 0.3 g/l of glucose in aqueous solution, whereas the 2-liquids based sensor presents an accuracy of 3.2 g/l. In the case of the 4-liquids based sensor, an accuracy of 2 g/l is obtained, whereas 6.5 g/l may be reached in the channels 1 and 2, and a 15 g/l accuracy in channel 3. The important error performed in channel 3 is not clarified yet. However, these results already demonstrate the possible measurement of 4 different glucose solutions in one measurement with a microwave-based sensor.

V. CONCLUSION

Different microwave and microfluidic sensors are presented and described. The double and quadruple stub topologies are consequently suitable for multiple and simultaneous molecule concentration measurements. This demonstration reinforces the possible use of microwave sensing of multiple molecules solutions in aqueous solution through a single measurement.

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