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# PROPOSED METHOD FOR LIPOPROTEIN CONCENTRATION IN BLOOD USING MICROWAVE RESONATOR

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## ABSTRACT

This report is used to design a microwave microfluidic sensor to measure the lipoprotein concentration in human blood plasma. Microwave engineering is an important material characterization technology as it is used in many applications. Microwave resonant is one of the sensors used to classify the material and one of the most sensitive sensors for the measurement of dielectric properties. It has been suggested that the resonant approach be used in this project because of its accuracy and sensitivity. A compact sensor based on the Split Ring Resonator is proposed to observe the relative permittivity of various types of blood, enabling the determination of lipoprotein content in human blood. The split ring resonators could be placed on a microfluid to test the protein in the blood. The resonator is proposed at 6 GHz using Rogers. The tool CST software is used to design a split-ring resonator and microwell to decide which design parameters are most important in maintaining resonant behavior. The results show the coupling gap, and the ring radius has the greatest effect on the maintenance of resonant behavior. The predicted outcome of the s-parameter response is based on the dielectric constant and the relative allowability of different blood levels based on the previous research paper.

## 1.0 INTRODUCTION

Stroke is emerging as one major health concern in Malaysia. According to the Malaysian National Burden of Diseases Study. National Stroke Registry is developed in the year 2009 to coordinate and improve stroke care and act as a platform to generate data from different aspects of stroke in Malaysia. Often, stroke is associated with a blockage in the bloodstream caused by cholesterol levels generally. The need for cholesterol detection brings a crucial role to prevent heart diseases. The blood circulation is restricted inside the affected arteries by cholesterol plaques and this condition leads the arteries wall to lose its flexibility (get harden) as time goes by, which is called atherosclerosis. Atherosclerosis is the most important risk factor for stroke and heart attack. Hence, knowing the cholesterol level is essential for a person’s heart health. Total cholesterol level in the bloodstream consists of Low-Density Lipoprotein (LDL), High-Density Lipoprotein (HDL), and triglyceride levels. Elevated LDL levels can lead to coronary heart disease (CHD) and atherosclerosis.

The conventional test to measure cholesterol levels in the bloodstream is using a lipid profile test or lipid panel. The collected blood samples undergo many enzyme reactions to detect cholesterol levels. In the lipid profile test, the total cholesterol and triglyceride levels are directly measured with a help of laboratory instruments. Lipoproteins are complex particles that have a central hydrophobic core of non-polar liquid. The non-polar liquids have molecules that only develop a net electrical polarization when an electric field is applied. When an electric field is applied to the blood, the interaction between the blood and the electric field is described by the blood permittivity. Blood permittivity can be analyzed using complex permittivity from transmission and reflection measurements. Therefore, a two-port microwave microfluidic resonator is proposed for cholesterol concentration detection. Due to growing sensitivity and precision, the most common techniques are the open-ended dielectric probe, closed waveguide device, and coaxial cavity (Resonator et al. 2017). Microwave sensing is a label-free approach based on the difference in capacitance and inductance as a result of electromagnetic sample interaction (Yee et al. 2020).

## 2.0 LITERATURE REVIEW

Many studies have been conducted for biosensing which significantly reduces the measurement time. Biosensing devices have been realized using three key detections which are electrical, optical, and mechanical (Bashir 2004). A Microfluidic system is a potential platform for biochemical processing and analysis with numerous advantages including low sample/reagent consumption, high sample throughput, and total analysis capability. Cholesterol detection using flow injection microfluidic device with functionalized carbon nanotubes-based electrochemical sensor was developed (Wisitsoraat et al. 2010). The sensing scheme is developed based on in-channel amperometric flow injection analysis utilizing a carbon nanotube (CNT) electrode integrated on a PDMS/glass microfluidic chip. The microfluidic chip was designed to have two inlets and one outlet. For two inlets, one was used for buffer carrier stream and the other was used for injection of analyte or enzyme immobilization. The working (CNTs), auxiliary (Pt), and reference (Ag) electrodes were designed as straight stripes across the microchannel and located opposite to the outlet of the microchannel. In the last part, the PDMS and glass chip was treated in 35-W radio-frequency oxygen plasma for the 30s. The inlets and outlet of microchannels were drilled and connected to micro-tubing via pipette tips, which were sealed to PDMS holes by physical attachment. Diagram and photographs of the microchip with in-channel carbon nanotubes based amperometric detector.

However, higher costs and complicated fabrication processes limit the scope of these biosensors (Chen, Li, and Sun 2012). Another study using an optical fiber sensor was conducted (Budiyanto, Suhariningsih, and Yasin 2017). The study was to determine the cholesterol level by the character of the laser beam to the material through an optical fiber sensor by using a laser beam intensity modulation. The beam of light entering the optical fiber receiver and processed by an optical detector into electrical signals to be displayed on the computer. It obtained a linear relationship between the peak voltage output of the sensor as a function of variations in the concentration of cholesterol and measured parameters and sensor performance include sensitivity, linear range, and linearity.

Another method to realize biosensor is using a microwave device. Many types of research focus on liquid characterization such as blood, saliva, chemical, etc (Artis et al. 2013). A sensor of the planar structure has attracted attention because of its simple structure, easy fabrication, and low cost (Staszek et al. 2017). Many planar microwave sensors have been proposed for detecting solutes in biological and chemical (Sharma, Lao, and Falcone 2018) samples. By using microwave signal analysis, it is possible to identify the liquid concentration by measuring the S-parameter (Zarifi et al. 2018). Glucose concentration detection using a microwave dielectric resonator has been studied (Wiwatwithaya et al. 2011). The change of the glucose concentration is directly related to the change of the reflection coefficient, S11 due to the glucose solution. To improve the previous technique, a cavity sensor was introduced by S. Kim et al (S. Kim et al. 2014). To increase the sensitivity and selectivity of the sensor the microwave source size and position in the resonator are modified according to the computer analysis of the Q-factor of the resonant cavity.

Liquid concentration can also be analyzed using S21. A microwave LC resonator on the integrated passive design was proposed to detect glucose levels. The size of the sensor is small, however, the fabrication process is complicated (E. S. Kim et al. 2018). Therefore, a split ring resonator is designed to determine the dielectric properties of liquid and solid materials based on resonance frequency shifting (Rahman et al. 2018).

In 2013 microwave and microfluidic were introduced by T. Chretiennot et al (Chretiennot, Dubuc, and Grenier 2013). The two-port resonator consists of a planar folded quarter wavelength- type resonator etched in the central conductor of a coplanar waveguide. A microfluidic channel is bonded on the top face of the structure, perpendicularly to the central conductor. A one-port microwave microfluidic was introduced by A. Salim et al (Salim et al. 2018) by introducing gold vias around the structure. Gold vias were introduced to contain electric field energy in the center of the SIW cavity. The sensor was fabricated on Rogers substrate using a rectangular patch antenna on top of the substrate with a microwell in the middle of the rectangular.

## 3.0 METHODOLOGY

The method used in this project will be explained through several techniques about the development of the resonator model which is used to investigate the interaction between the lipoprotein in blood with permittivity using microwave microfluidic. The model was done in CST simulation which provides insight on how to properly alter the structure of the split-ring resonator based on the parameter changes and permittivity of the substrate.

### *3.1 Software development*

This project used CST software version 2018 as the main software development medium where the design will be developed. A split-ring resonator was designed that could hold the material under tests such as solid and liquid. The system starts with designing the frequency and substrate parameters in CST software simulation and will be designed with 50 ohms of impedance. The basic design of the split-ring resonator is starting by choosing a suitable template in CST software. The suitable dimension and scaling parameter for the split ring resonator were used based on the previous research article. Microwell will be designed after the resonance of the split ring shows reasonable performance. The microwell position must be at the maximum electric field magnitude to maximize the electric field perturbation. Then, the proposed resonator will be fabricated on Rogers/Duroid substrate using conventional photolithography. A hole is drilled in the patch and substrate. The hole diameter is the same as the PDMS size. The cup-shaped micro container will be fabricated using PDMS.

The model will be created in the simulation to get the accurate verification of the resonant frequency shift of the system. When the verification is achieved, the analysis and a relationship will be drawn for resonant frequency as a function of the system's loss. This method will be observing how the parameter of the split-ring resonator can be altered to maintain a resonant frequency within the lossy system. The parameter for this design includes the parameter width w, the height h, radius outer ring r1, and radius inner ring r2.

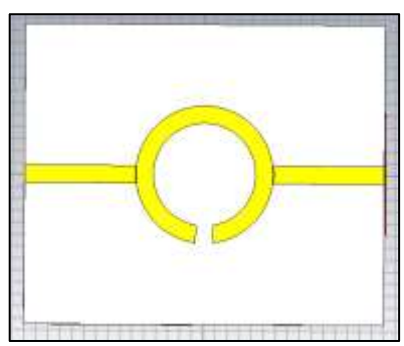

**Figure 1.** Split ring resonator

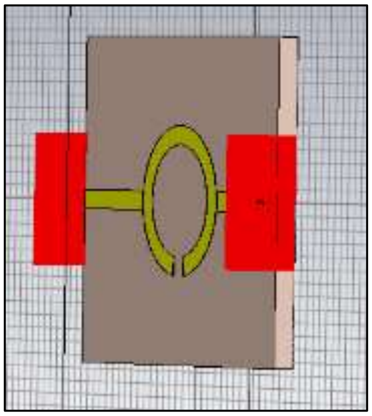

**Figure 2.** Design for split ring resonator

The arrangement of the split-ring resonator consists of circular rings consisting of a complete electric conductor. The structure is excited perpendicular to the split ring plane by a time-varying electric field. The current is flowing along with the rings and produced the solenoid. A resonator with a split ring is a resonant magnetic dipole. The ring content was copper, and the ring resonator substratum is loss FR-4. The analysis that has been done in CST software based on the parameter below:

**Table 1: Parameter of a split ring resonator**

| Parameter | Dimension |
|---|---|
| Feedline length | 15mm |
| Width of the feedline | 1.4549mm |
| Coupling gap | 0.07mm |
| The total length of the substrate | 30mm |
| The total width of the substrate | 25mm |
| The radius of the ring | 5.7275mm |

### *3.2 Analyze the dielectric constant and the conductivity*

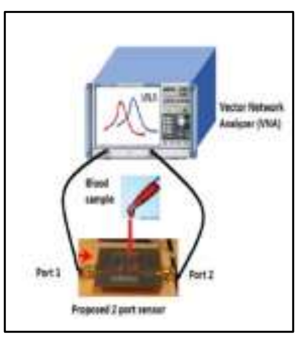


**Figure 3.** Proposed measurement setup

The dielectric constant and the conductivity of the blood samples will be analyzed using complex permittivity. The analysis will be conducted using MATLAB software.

## 4.0 EXPECTED RESULT AND DISCUSSION

### *4.1 Simulation of the split ring resonator (without MUT)*

In numerical simulations run by CST Microwave Studio, the characteristics and potential of the proposed sensor were first analyzed. The results showed that the designed system is feasible and has a perfect resonant frequency. In general, the simulation is presented the scattering coefficient in software to show the characteristic of reflection and transmission in the frequency domain with the change of parameter in the radius of the ring and the coupling gap.

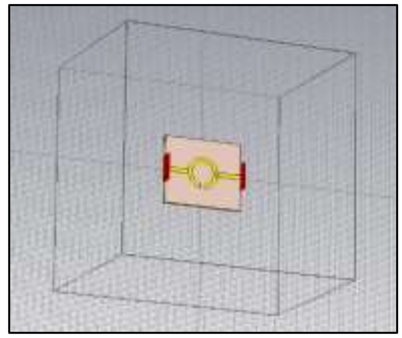

**Figure 4.** Split ring resonator using CST Software

The ring resonator was enclosed in a box because the resonator was not to be put in a perfect electric conductor. The airbox needed to surround the structure so that the reception and transmission of the electromagnetic waves could occur in free space.

To verify the validity of the split-ring resonator model created in CST software, it must be tested against other collected simulation data sets with different changes in the parameter. The results are shown in Table 5.1 below. The starting split-ring resonator parameters are:

**Table 2: Parameter of a split ring resonator**

| Parameter | Dimension |
|---|---|
| Feedline length | 15mm |
| Width of the feedline | 1.4549mm |
| Coupling gap | 0.09mm |
| The total length of the substrate | 50mm |
| The total width of the substrate | 30mm |
| The radius of the ring | 8.6307mm |

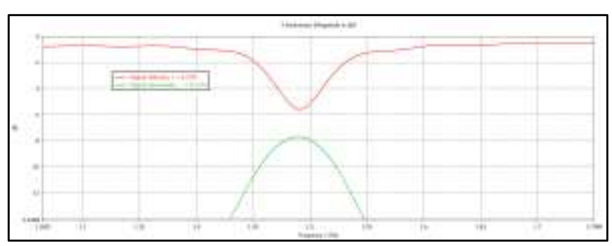

**Figure 5.** S-parameter vs frequency (GHz)

Based on the result in figure 12, notice that the fundamental resonant frequency is close to the design frequency. Thus, the tuning process is needed. Either to tune the coupling gap, radius, and feedline width to work out within 3GHz. To get resonant at the frequency to which it is tuned, the split ring resonator is attached to substrate FR-4 loosy.

***4.2 Result for changing the radius and coupling gap distance of split-ring resonator (without MUT)***

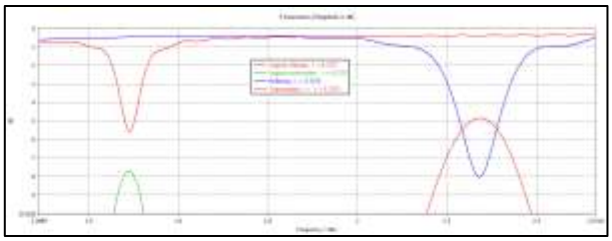

**Figure 6.** S-parameter vs frequency (GHz)

The resonant frequency first matched can be seen from the simulation result above. The original parameter of coefficient relation is in red and the modified parameter of coefficient relation is blue. The dips in relation and transmission indicate the points for resonant frequencies. Relation needed only one port while transmission needed two ports. The measurement and simulation were done in between frequency range from 0Hz to 3GHz because from the analysis result, as shown in the figure above, the first resonant frequency falls is between these frequencies. Moreover, this frequency has the perfect frequency shifts as it fits well into achieving the aim to measure the dielectric constant. The reflected and transmitted signals for the split ring resonator design is placed with a substrate of increasing the permittivity. The reflected signal is observed above and centered on the split ring resonator structure, while the transmitted signal is observed directly below and centered on the design of the split ring resonator.

## 5.0 CONCLUSION

This research paper proposed a low cost, less complexity, and small biosensor to measure the concentration of lipoprotein in blood by using microwave microfluidic. Cholesterol test has drawbacks such as its requirement of a lab environment to collect and store the blood samples and the time-consuming enzyme reactions with many procedures for cholesterol level measurements. Cholesterol can be detect using nanotubes based electrochemical sensor and optical technologies. However, the higher cost and complicated fabrication process of these two sensors limit the scope of these biosensors. Lipoproteins are complex particles that have a central hydrophobic core of non-polar liquid. The non-polar liquids have molecules that only develop a net electrical polarization when an electric field is applied. When an electric field is applied to the blood, the interaction between the blood and the electric field is described by the blood permittivity. Blood permittivity can be analyzed using complex permittivity from transmission and reflection measurements. Therefore, a two-port microwave microfluidic resonator is proposed for cholesterol concentration detection.

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