Master's Thesis

Non-invasive Glucose Monitoring with Electrically Separated Sensor Electrode

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Approved by

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Abstract

Still major type of glucose measuring is invasive glucose measuring. Most of Diabetes Mellitus patients use invasive glucose measuring, but it is very painful and expensive. To solve the problem, many researches on various type of non-invasive glucose measuring device are ongoing. Using LED, microwave, impedance spectroscopy etc. Impedance spectroscopy blood glucose monitoring device can measure change of characteristics of skin and underlying tissues due to glucose level change.

But There is a lot of perturbation element on non-invasive glucose monitoring device using Electrical Impedance Spectroscopy (EIC), such as sweat of the skin, thickness of hypodermis layer. To solve the problem, multi electrode sensor is developed to measure perturbation element and skin's stratified model problem. But multi electrode sensor is also affected by cross-talking between electrodes through common ground and conductive materials that want to measure.

For simulation purposes, calculates the dielectric constant of each skin element at the sensor measurement frequency of 150MHz. And making stratified skin model in HFSS program. In order to implement the changes in blood glucose from the HFSS, dielectric constant of E/D layer and blood were mixed in a specific proportion.

The proposed sensor has additional gap between sensor electrodes and via between front and rear plate of the sensor PCB. Additional gap and via are equivalent capacitor between the sensor electrodes. Proposed sensor has 5dB lower S21 than preliminary researched sensor. S21 is power ratio of output power of port 1 to input power of port 2. Unwanted power through sensor electrode is noise. SNR can be increased if the cross-talk level between sensor electrodes at the same input power level is reduced by 5dB.

However, the experimental result doesn't meet the expectation as the analytical predicts. It has less sensitivity and S21 compare to simulation. Further research is needed to meet the gap between experimental result and simulation result.

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Nomenclature

DM	Diabetes Mellitus
SBGM	Self-Blood Glucose Monitoring
FDA	Food and Drug Administration
CGMS	Continuous Glucose Monitoring System
MARD	Mean Absolute Relative Difference
LED	Light Emitting Diode
HFSS	High-Frequency Structure Simulator
PCB	Printed Circuit Board
ISF	InterStitial Fluid

1 Introduction and Backgrounds

In this chapter, preliminary papers are reviewed. And introduce basic of Diabetes Mellitus, Glucose monitoring method, continuous glucose monitoring system.

1.1 About Diabetes Mellitus

Diabetes Mellitus (DM) is one of chronic disease that patients can't secrete insulin properly or have insulin resistance. Patients cannot control their own blood glucose level. So, patients should inject an adequate amount of insulin according to their blood glucose levels.

There are type 1 DM and type 2 DM. Type 1 DM is the inability to produce insulin due to a failure of the pancreas. And type 2 DM begins with insulin resistance that insulin cannot work properly. In worldwide there are 422 million DM patients in 2014 and 90% of patients are type 2 DM. Diabetes caused 1.5 million deaths in 2012. Higher than optimal blood glucose caused an additional 2.2 million deaths, by increasing the risks of cardiovascular and other diabetic complications [1].

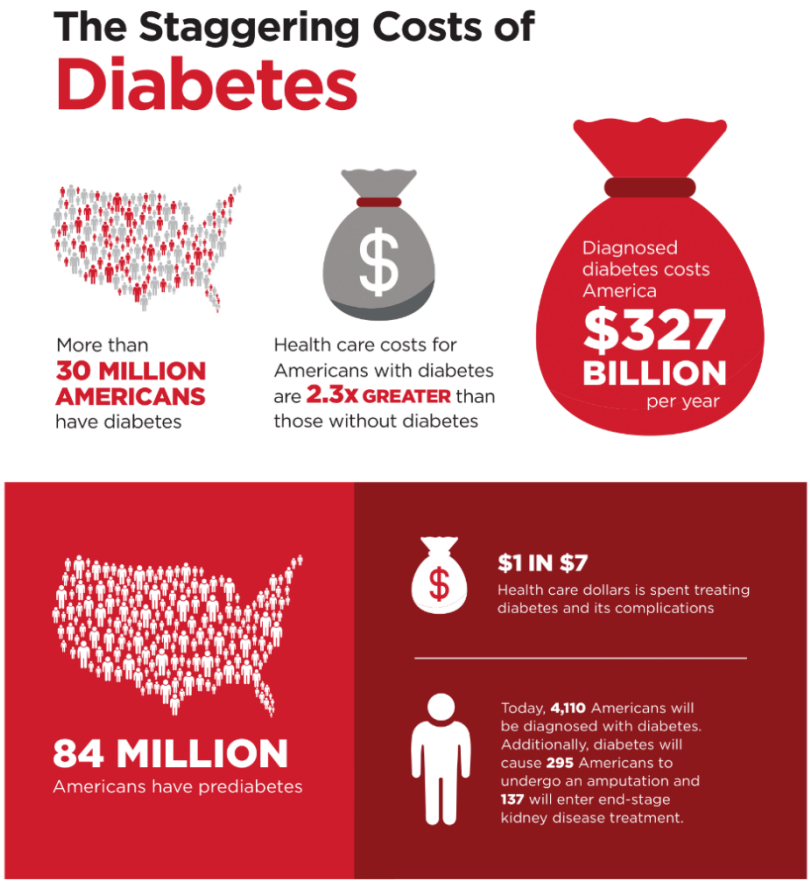


Fig. 1-1. Annual statistics of diabetes in the America [2]

Diabetes and its complications cause substantial economic loss to people with diabetes and their families. Based on cost estimates from recent systematic review, it has been estimated that the direct annual cost of diabetes to the world is more than US$ 827 billion.

Diabetes patients control their blood glucose levels forever. There are several devices which can monitoring glucose levels. Self-blood glucose monitoring (SBGM) is very important to diabetes patients for homeostatic regulation.

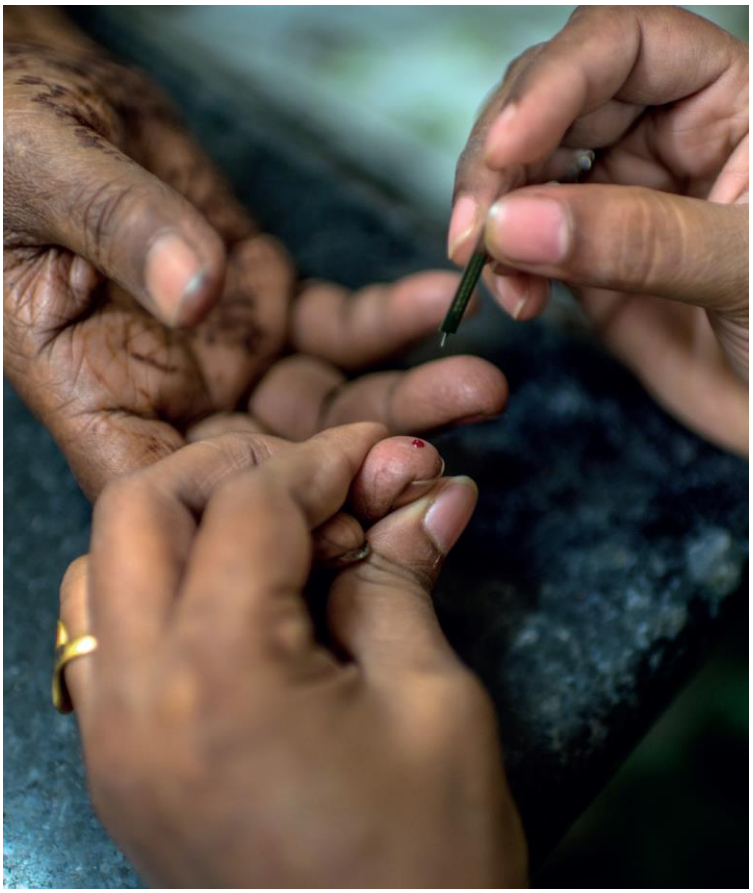


Fig. 1-2. Diabetes mellitus patients pricking their fingers [1]

1.2 Invasive glucose monitoring

Traditional DM patients used the invasive glucose monitoring device, which measures blood glucose by pricking hands. When the enzyme (glucose oxidase) of sensor and glucose in the blood react, the quantity of electrons released according to the amount of glucose. Majority of glucose monitoring device using this enzyme-based sensor method.

In FDA standard, 98% of measured glucose should have accuracy of ±15mg/dl when measured data is less than 75mg/dl and ±15% when measured data is more than 75mg/dl for invasive glucose monitoring device [3].

However, for these invasive glucose monitoring devices, blood must be drawn for each measurement, which is not only painful for patients but also expensive. Usually, patients should measure their own

blood 4 to 10 times per a day. A single-use SBGM strip costs about $1. Especially for type 2 DM patients who are not capable of produce insulin from birth, patients should monitor their blood glucose level continuously to prevent hypoglycemia.

1.2.1 Minimum-invasive glucose monitoring

Continuous Glucose Monitoring System (CGMS) has been studied and commercialized for type 2 DM patients. CGMS uses minimum invasive method that measures glucose level of interstitial fluid. Although CGMS has enabled continuous blood glucose measurement, it also has many disadvantages.

Since this sensor utilizes the chemical properties of glucose so it lacks persistence compared to sensors using electrical properties. The sensor should be replaced every 3-7 days and can cost $30-$50 per week. It is expensive compare to single-use SBGM strip.

Measuring interstitial fluid (ISF) cause time-delay problem. Glucose in blood vessels diffused into ISF.

Also, the calibration must be performed at least twice a day through pricking hands. And CGMS cause skin problems in young children by taping sensors to keep them firmly on their skin [4].

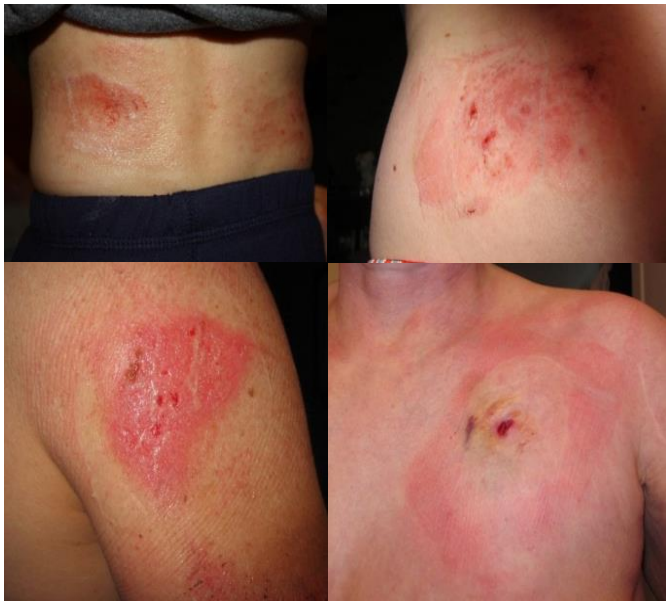


Fig. 1-3. CGMS stick to the skin cause skin rash

1.3 Non-invasive glucose monitoring

Non-invasive blood glucose measurement methods are being studied and developed to solve the problem of minimum-invasive blood glucose measurement methods. Method such as Infrared Spectroscopy, Optical coherence Tomography, Raman Spectroscopy, Polarization change, ultrasound, fluorescence and impedance spectroscopy are widely studied. Since there are various advantages and disadvantages of each, so introduce the most popular optical method and microwave method.

1.3.1 Glucose monitoring using Infrared spectroscopy

In order to measure blood glucose using light, light must first reach the blood or tissue where the glucose is present. Light is then reflected or scattered, passed through tissue, and molecules struck by it emit specific energy. The intensity of the light is equal to $I = I_0 e^{-\mu_{eff} d}$. (I_0 is the initial intensity of the light, μ_{eff} is the attenuation factor, d is the distance light has passed in the tissue) [5] The attenuation factor μ_{eff} is determined by the absorption coefficient and the scattering coefficient of light. Since changes in blood glucose concentrations affect the scattering and absorption of light in tissues, based on these principles, blood glucose concentrations can be measured using light.

However, using light to measure blood glucose in a living body has many difficulties. The layers that make up the skin themselves cause reflections and refraction of light, and the roughness of skin can affect the path of light. Another is the state of the tissue. It is affected by blood pressure, body temperature, humidity of the skin, beat of the arteries and dilation of blood vessels [6].

1.3.2 Glucose monitoring using fluorescence

This method utilizes the properties of the tissue producing fluorescence when it receives light at a certain frequency. UV laser irradiation on a glucose-dissolved solution results in fluorescence at 340, 380 and 400 nm and maximum fluorescence at 380 nm. The intensity of fluorescence is determined by the glucose concentration in the solution. However, when measured through the skin, UV rays can cause strong scattering in addition to fluorescence [7].

1.3.3 Glucose monitoring using electromagnetic sensing

Electromagnetic sensing is a similar principle to impedance spectroscopy and uses dielectric properties in the blood. In the case of impedance spectroscopy, current is used, but electromagnetic sensing uses an electric field between the two inductors. The electromagnetic coupling of the two inductors varies with the dielectric properties of the solution, and since the dielectric properties of the solution are affected by glucose, the concentration of glucose solution can be measure. However, there is a limitation that is highly affected by temperature and that the dielectric properties of the solution can vary by several substances other than glucose [8, 9].

1.3.4 Glucose monitoring using impedance spectroscopy (IS)

The impedance of a tissue can be measured by the current passing through it at a known pressure/intensity. If repeated measurements are made by varying wavelengths and currents, the impedance spectrum of the dielectric is determined. In order to accurately measure the impedance of the skin and underlying tissue, the correct frequency must be selected. Operating frequencies above

200MHz cause beta-dispersion of the cell membrane (the cell membrane that filters low-frequency currents and allows high-frequency currents to pass) and decrease the sensitivity to the direct current conduction of the ions. On the other hand, low frequencies in the KHz band (<100KHz) cannot be used due to the electrode dispersion and alpha dispersion of tissues. Therefore, 1-200MHz frequencies were used that could be studied for the interfacial membrane polarization of erythrocytes and other cell membranes in the dermis.

Very small changes in blood glucose levels lead to a decrease in sodium ions and an increase in potassium ions in red blood cells, leading to a reaction of cell membranes. These special reactions between blood and tissue cells [10] are changed by blood glucose. This changes the electrolyte equilibrium between the cell membranes, resulting in changes in membrane penetrability, conductivity and interfacial membrane polarization (Maxwell-Wagner polarization). In other words, changes in blood glucose change the dielectric properties of the skin and underlying tissue and result in changes in the dielectric spectrum which can be measured by impedance.

Although blood glucose itself does not strongly affect the dielectric spectrum present in the MHz frequency band, it can instead transform the above series of changes into blood glucose levels using impedance spectroscopy. When a small amount of alternating current is input to the sensor, the impedance to the tissue is expressed as a function of frequency. Within the range of the acceptable frequencies(1-200MHz), impedance has a sensitivity of 2.7 ohms per glucose change of 150mg/dl.

There was a study that first discovered the properties of skin and underlying tissue and measure blood glucose using impedance spectroscopy [10, 11].

This study was based on the study of the changes in the electrical properties of skin and underlying tissue according to blood glucose concentration and frequency spectrum [12].

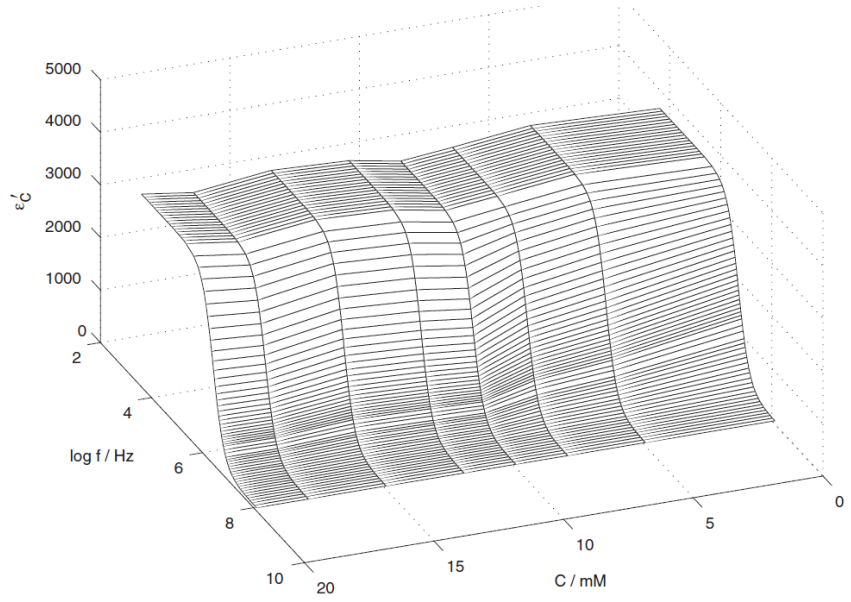


Fig. 1-4. One-cell dielectric spectra of spherical erythrocytes measured at 25°C in the presence of increasing concentrations of L-glucose [12]

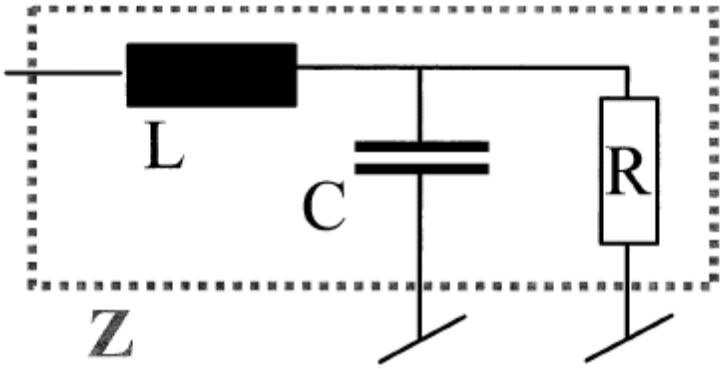


Fig. 1-5. Equivalent model of the sensor attached to the skin

L is the inductance of the external coil, C is the fringing capacitance of the sensor attached to the skin and R is the averaged resistance of the skin and underlying tissue.

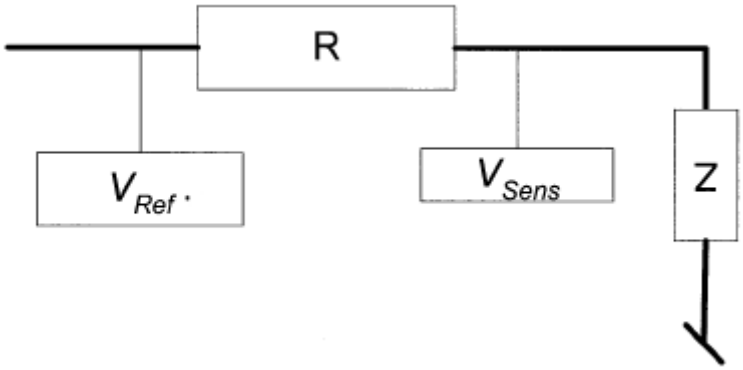


Fig. 1-6. Voltage divider circuit for measuring impedance of sensor

The change in impedance resulting from changes in blood glucose is measured with a simple voltage divider.

$$Z_{Sens} = R_s\left(\frac{V_{Sens}}{V_{Ref} - V_{Sens}}\right)$$

Since the impedance is the smallest at the resonant frequency, the blood glucose is estimated using the magnitude and phase data of the impedance by sweeping the measurement frequency.

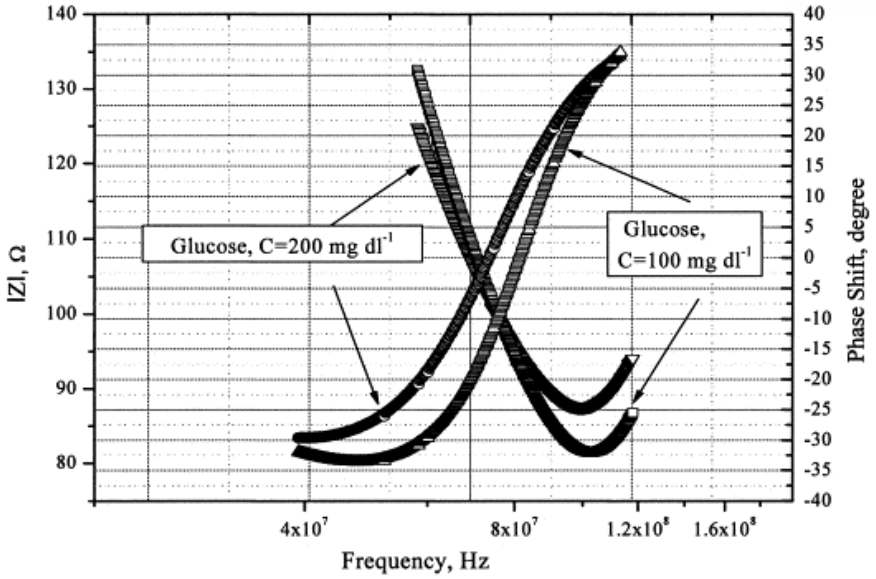


Fig. 1-7. Measurement result of the sensor attached to the skin of a patients at different blood glucose concentrations measured by Vector Network Analyzer

However, there are several issues with such devices. It is difficult to obtain a precise frequency because frequency sweeping is controlled by controlling the voltage of the VCO rather than the PLL. In Addition, since the sensor is attached to the skin, measurement accuracy is decreased by many variables such as temperature, body position, skin humidity, sweat and micro circulation [13].

Based on the above study, a non-invasive glucose monitoring device named Pendra was manufacture by Pendragon medical in the European market. However, the results showed that the Mean Absolute Relative Difference (MARD), which represents the accuracy of blood glucose monitoring device, was 35%, which is much higher than the commercialized CGMS [14].

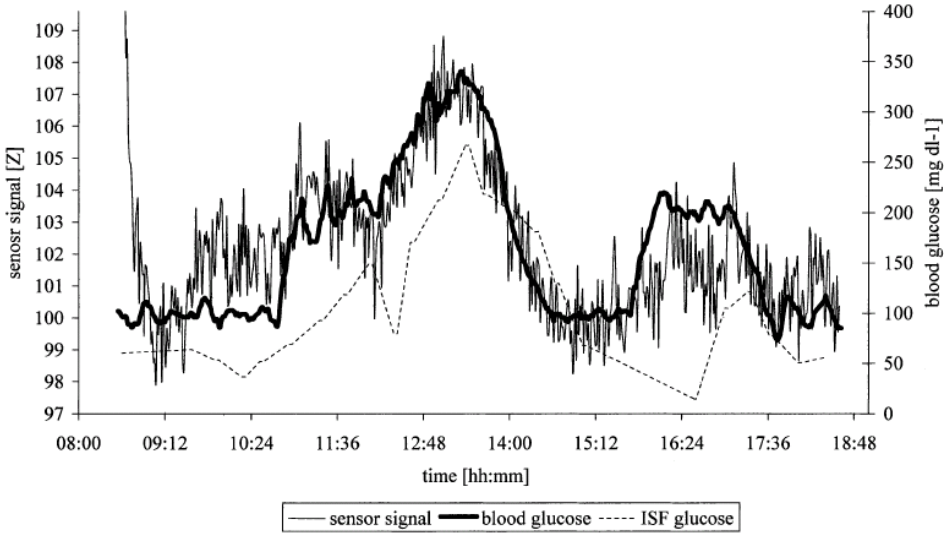


Fig. 1-8. Sensor signal compared to blood glucose and interstitial fluid (ISF) glucose levels during glucose clamps with glucose administered intravenously [10]

However, despite the above problems, the study overcame Time-lag, the biggest problem with ISF methods.

In order to create a more accurate non-invasive glucose monitoring device as a follow-up study, there is the study on multi-sensor monitoring device that has been integrated with humidity sensors, pressure sensors and infrared LEDs to eliminate various perturbation [14].

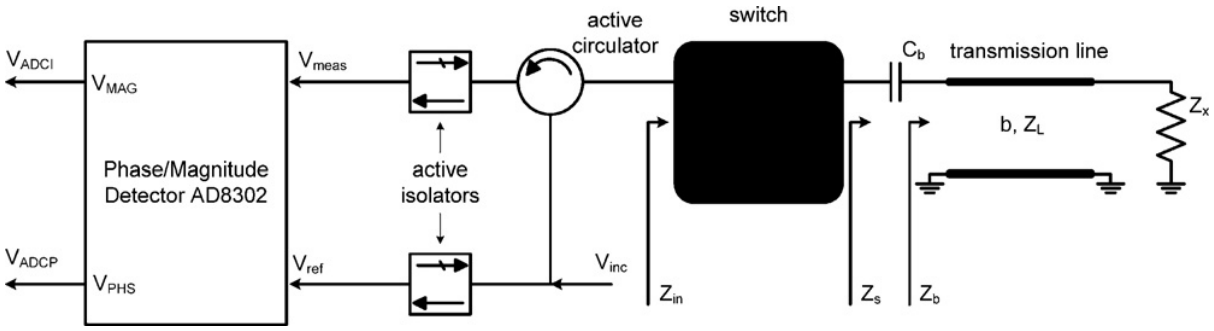


Fig. 1-9. Detail circuit of MHz sensor measurement based on voltage divider having switch to measuring electrode [15]

In subsequent studies, sensors using impedance spectroscopy are similar to the conventional sensors. The difference is that multi-electrodes are used to make sensors with multiple penetration depths.

Skin and underlying tissues are composed of several layers, including stratum corneum, dermis, epidermis and hypodermis. It is impossible to accurately measure the dielectric constant of skin, which is a stratified layer structure, by using a single fringing field sensor. In addition, in the electric field generated from the sensor electrode, blood glucose cannot be measured because electric field is reflected at a boundary which have relatively large dielectric constant differences. Therefore, the multi-electrode sensor can be used to determine the dielectric constant of several layers to measure blood glucose [16].

Measured using the MHz, temp, GHz, optical and KHz sensors in the above study, the MARD is 23.7%

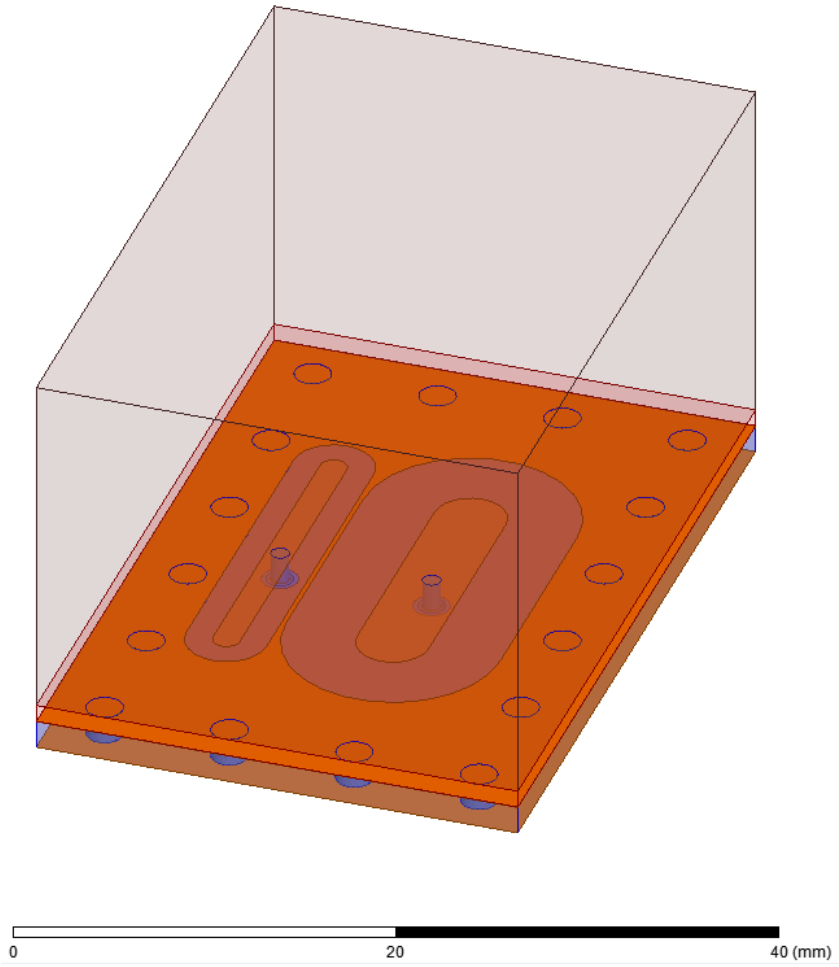


Fig. 1-10. Simulation model of preliminary sensor in HFSS

The interference between electrode can be large because the spacing between electrode is too narrow and the common-ground is shared on a small size PCB, as shown by the shape of the preliminary MHz sensor. It is important to reduce the interference between the electrodes in order to efficiently irradiate the fringing field into the human body. The sensor in the preliminary study was simulated by HFSS, and the S21 measured about -30 dB.

In addition, the direction of the electric field formed by the sensor is tilted to the opposite electrode, so that the measurement range of each sensor overlaps. If the sensing ranges overlap, the measurements range becomes shallow and narrow. Since the changes in blood glucose within the range of the fringing field needs to be measured, the wider the measurement range, the more accurate the measurement can be. Therefore, narrowing the sensing range can reduce accuracy.

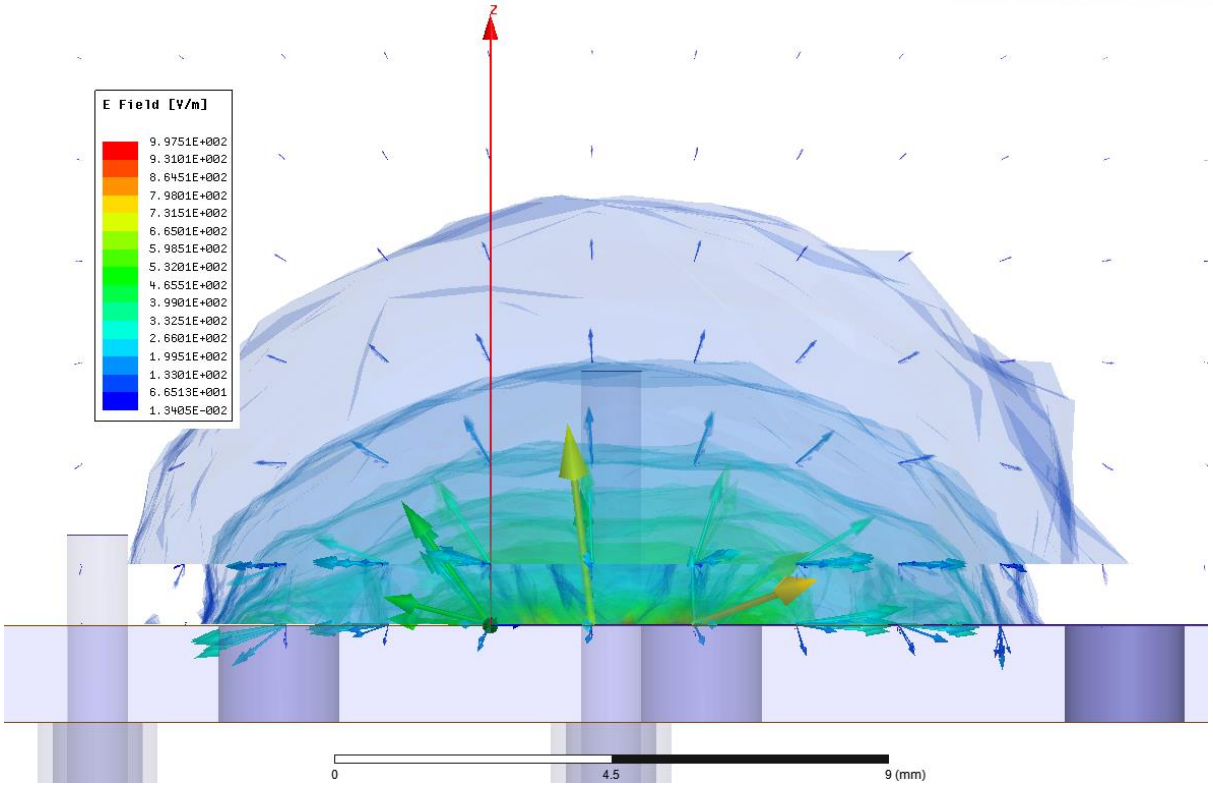


Fig. 1-11. Complex magnitude and vector of electric field of preliminary sensor in HFSS (Long electrode)

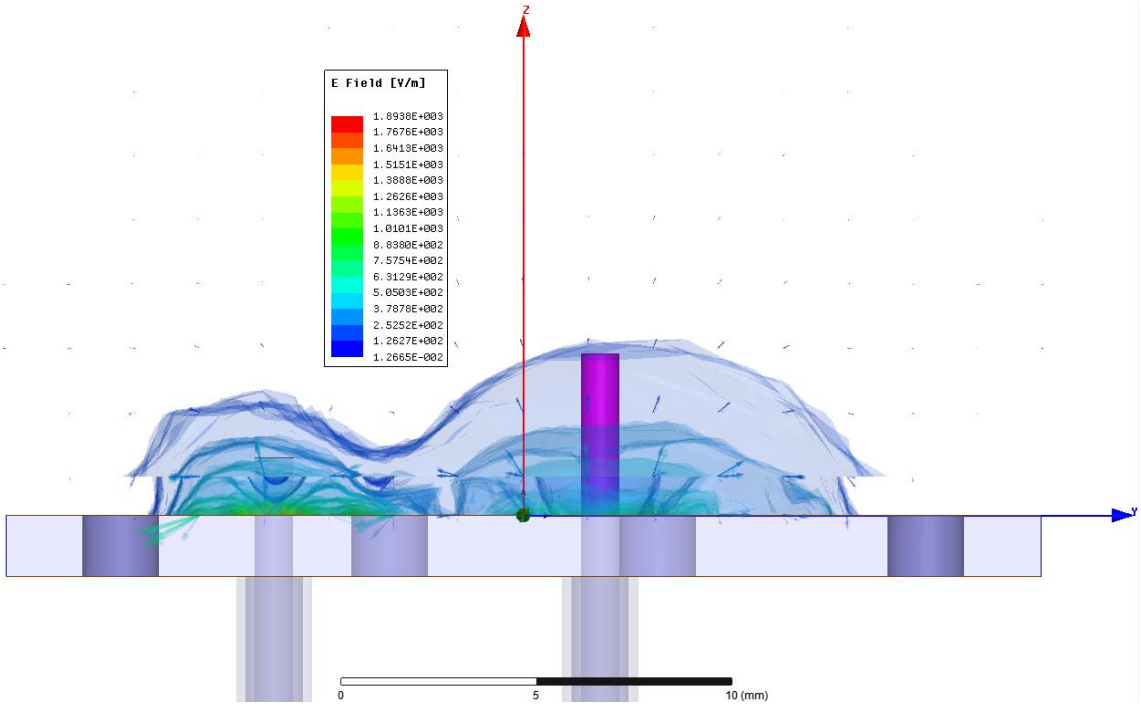
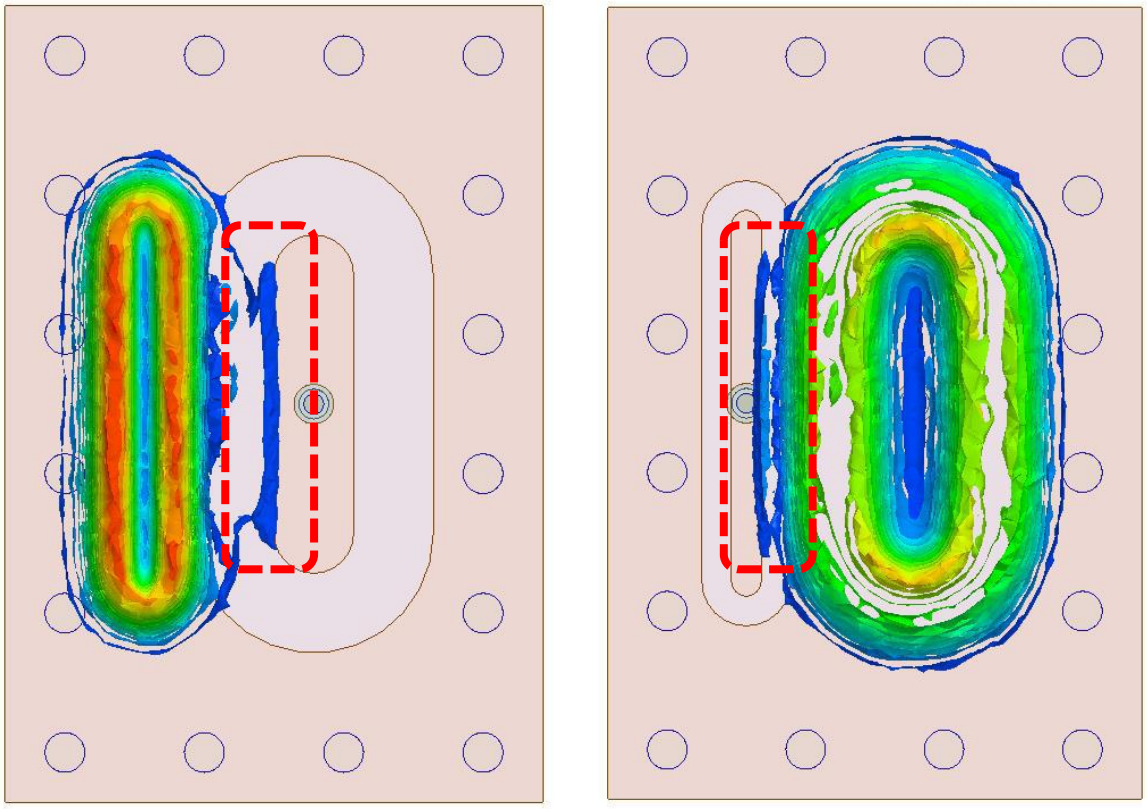


Fig. 1-12. Complex magnitude and vector of electric field of preliminary sensor in HFSS (Both sensors activated)



(a) (b)

Fig. 1-13. (a) E-field invade when short electrode turns on (dotted line), (b) E-field invade when long electrode turns on (dotted line)

1.4 Dielectric properties of materials

All materials have a unique property, electric permittivity. Permittivity is a measure of the strength of the internal electric field that is generated by the polarization of charges when an electric field is applied to an object. Dielectric constant is a unit for measuring the dielectric constant based on vacuum and is often used in real life.

The permittivity is not a constant and its value varies greatly with frequency. There are several ways to model the dielectric constant according to the frequency of an object, but Cole-Cole modeling is mainly used to model body organs and cells.

1.4.1 Dielectric dispersions

Cole-Cole Modeling is dielectric relaxation in polymers. Dielectric relaxation is time delay of the dielectric constant when dielectric medium is in changing electric field. Cause of the molecular polarization. Dielectric relaxation is often described in terms of permittivity as a function of frequency. In ideal systems, there is only molecular polarization and system is described as debye equation. [17]

$$\hat{\varepsilon}(\omega) = \varepsilon_\infty + \frac{\varepsilon_s - \varepsilon_2}{1 + j\omega\tau_1} + \frac{\varepsilon_2 - \varepsilon_\infty}{1 + j\omega\tau_2}$$

But in real life, there are distortion from ionic and electronic polarization shows behavior of the resonance or oscillator type. With these polarizations, system is described with Cole-Cole equation. [18]

$$\varepsilon^*(\omega) = \varepsilon_\infty + \frac{\varepsilon_s - \varepsilon_\infty}{1 + (i\omega\tau)^{1-\alpha}}$$

ε^* is the complex dielectric constant, ε_s and ε_∞ are the static and infinite frequency dielectric constants. ω is the angular frequency and τ is the time constant.

2 Proposed non-invasive glucose monitoring sensor using IS

The proposed sensor uses the Z-parameter response, which detects changes in the dielectric constant due to changes in blood glucose and inference blood glucose by measuring the change of Z-parameter.

Noise reduction is important because changes in electrical characteristics to be measured by sensors is very small. By reducing the noise of unwanted signals between electrodes in sensors with high isolation, higher SNR can be achieved than with conventional sensors.

Therefore, this study was conducted on the multi-electrode glucose monitoring sensor, which can measure small changes in blood glucose more accurately by reducing interference between electrode.

2.1 Main consideration in simulation environment

The simulation was conducted with HFSS. The measured frequency band is 20 MHz to 200 MHz. After implementing the sensor and simulation environment, the measured frequency is set by 50MHz which is previous work's frequency.

2.1.1 Design of proposed sensor

The sensor is 40 mm x 40 mm in size, small enough to fit a hand-held blood glucose meter but with enough distance between the electrodes. Two sensors are made by adjusting the distance between the electrode and the common-ground to have various penetration depths in order to measure the body with three layers. Sensors with short penetration depth are called short electrodes and sensors with long penetration depth are called long electrodes. The penetration depth of the fringing field is proportional to the distance between the electrode and the ground [19]. Also make the via evenly around the electrode and connect the front and rear ground.

Single electrode capacitive fringing field sensor coupled to the skin and underlying tissue is simplified to a parallel circuit with C [16].

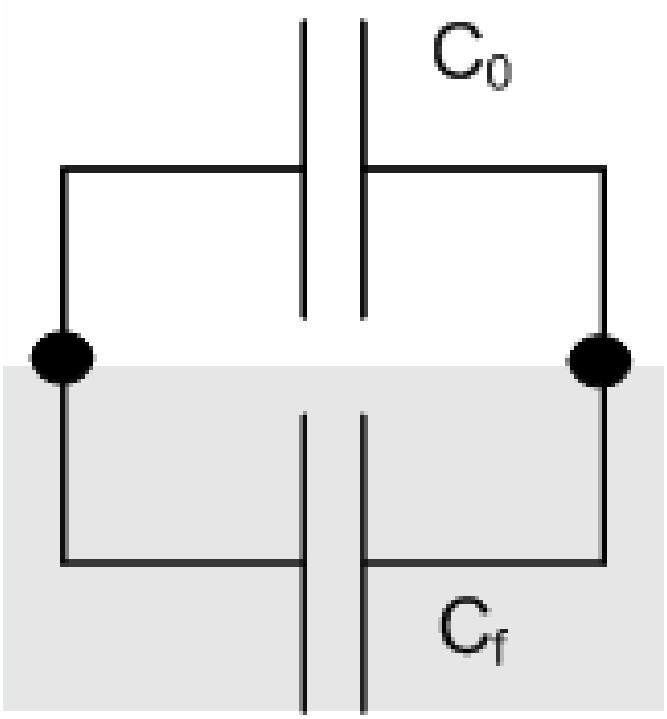


Fig. 2-1. RLC modeling of the single capacitive fringing field sensor

And RLC modeling of two-electrode fringing field sensor which shares sensing electrode is following figures.

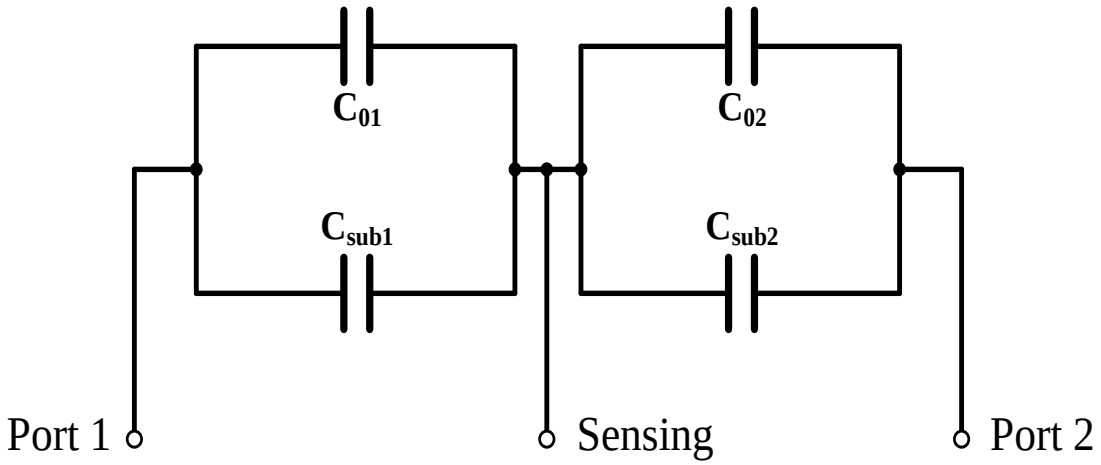


Fig. 2-2. RLC modeling of the previous work's sensor. C_0 is capacitance of air. C_{sub} is capacitance of substrate

Each electrode's admittance is following equation. Y-parameter from HFSS simulation is used to acquire equivalent modeling capacitance.

$$Y = \sigma_{dc}\frac{C_0}{\varepsilon_0} + i\omega\left(\varepsilon' C_0 + C_f\right)$$

Previous sensor's equivalent modeling capacitances C_{01} is 0.2567 pF, C_{02} is 0.2567 pF, C_{sub1} = 1.997 pF, C_{sub2} = 1.36 pF.

And Y_{12} and Y_{21} of the previous sensor are following equations.

$$Y_{12} = \frac{C_{01} + C_{sub1} + C_{02} + C_{sub2} + C_{sens}}{\omega^2 \cdot (C_{01} + C_{sub1} + C_{sens})^2 \cdot (C_{02} + C_{sub2})}$$

$$Y_{21} = \frac{C_{01} + C_{sub1} + C_{02} + C_{sub2} + C_{sens}}{\omega^2 \cdot (C_{02} + C_{sub2} + C_{sens})^2 \cdot (C_{01} + C_{sub1})}$$

The Modeling of proposed sensors is shown in the following figure.

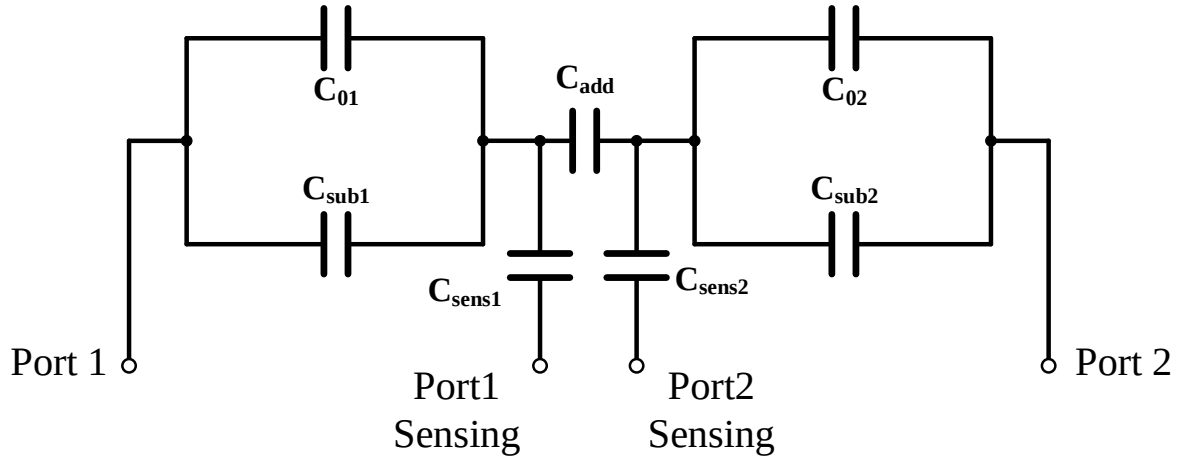


Fig. 2-3. RLC modeling of the proposed sensor. C_0 is capacitance of air. C_{sub} is capacitance of substrate. C_{add} is capacitance of additional gap. C_{sens} is sensing capacitance

Compared to previous sensor's equivalent circuit, C_{add} and C_{sens2} is added. C_{add} is additional capacitance. Proposed sensor's Y_{12} and Y_{21} are following equations.

$$Y_{12} = \frac{C_{02} + C_{sub2} + C_{sens2} \cdot (C_{01} + C_{sub1} + C_{sens1} + C_{add}) + (C_{01} + C_{sub1} + C_{sens1}) \cdot C_{add}}{\omega^2 \cdot (C_{01} + C_{sub1} + C_{sens1}) \cdot (C_{02} + C_{sub2}) \cdot \{C_{sens2} * (C_{01} + C_{sub1} + C_{sens1} + C_{add}) + (C_{01} + C_{sub1} + C_{sens1}) \cdot C_{add}\}}$$

$$Y_{21} = \frac{C_{01} + C_{sub1} + C_{sens1} \cdot (C_{02} + C_{sub2} + C_{sens2} + C_{add}) + (C_{02} + C_{sub2} + C_{sens2}) \cdot C_{add}}{\omega^2 \cdot (C_{02} + C_{sub2} + C_{sens2}) \cdot (C_{01} + C_{sub1}) \cdot \{C_{sens1} * (C_{02} + C_{sub2} + C_{sens2} + C_{add}) + (C_{02} + C_{sub2} + C_{sens2}) \cdot C_{add}\}}$$

Smaller additional capacitance, the smaller Y_{12} and Y_{21}. And S_{21} is proportional to Y_{21}, so additional capacitance can make S_{21} smaller. When C_{add} is about 100uF, S21 is negligible. So additional gap between electrodes which has 2mm width, have about 100uF. So proposed sensor has 2mm additional gap and lower the interference between electrodes.

Due to the characteristic of the sensor attached to the upper arm, the volume can be quite large when the SMA connector is attached to the side of the sensor. So, it is printed to back-feed through via in the center of the electrode.

2.1.2 Stratified model of skin and underlying tissue

Physical thickness and dielectric constant should be known in order to implement skin and underlying tissue in HFSS. The position to be measured by the sensor is usually the upper arm with a large area without much movement. Since epidermis and dermis layers have similar moisture content and are similar in composition, they can be composed of one E/D layer to simplify the simulation and reduce

the time taken. In the upper arm, the stratum corneum is 20um, the E/D layer is 1mm and the hypodermis is about 5mm. However, the hypodermis was thick enough (2cm) in HFSS so that no electric field was transmitted [20].

The Cole-Cole dispersion parameters of each human tissue used in this simulation are shown in the following table [21, 22].

	STRATUM CORNEUM	**BLOOD**	**HYPODERMIS**
$\boldsymbol{\varepsilon_\infty}$	4.4093	4	2.5
$\boldsymbol{\sigma_{DC}(Sm^{-1})}$	0.188	0.7	0.035
$\boldsymbol{\Delta\varepsilon_1}$	40.6	56	9
$\boldsymbol{\tau_1}$ **(PS)**	35	8.38	7.96
$\boldsymbol{\alpha_1}$	0	0.1	0.2
$\boldsymbol{\Delta\varepsilon_2}$	195	5200	35
$\boldsymbol{\tau_2}$ **(NS)**	2.58	132.6	15.92
$\boldsymbol{\alpha_2}$	0	0.1	0.1
$\boldsymbol{\Delta\varepsilon_3}$	-	-	33000
$\boldsymbol{\tau_3}$ **(US)**	-	-	159.15
$\boldsymbol{\alpha_3}$	-	-	0.05
$\boldsymbol{\Delta\varepsilon_4}$	-	-	10^7
$\boldsymbol{\tau_4}$ **(MS)**	-	-	15.915
$\boldsymbol{\alpha_4}$	-	-	0.01

Table. 1. Cole-Cole parameters of Stratum corneum, Blood, Hypodermis layer [21, 22]

	EPIDERMIS/DERMIS
$\boldsymbol{\varepsilon_\infty}$	3
$\boldsymbol{\varepsilon_s}$	58
$\boldsymbol{\tau_1(ps)}$	9.4
$\boldsymbol{\varepsilon_2}$	3.6
$\boldsymbol{\tau_2}$**(ns)**	180

Table. 2. Debye parameters of the epidermis/dermis layer [17]

Each layer's dielectric constants at 50MHz are shown in the following table.

	STRATUM CORNEUM	**EPIDERMIS/DERMIS**	**BLOOD**	**HYPODERMIS**
DIELECTRIC CONSTANT	162.6897	57.3997	94.2051	14.4520

Table. 3 Dielectric constants of skin and underlying tissue at 50MHz

In the E/D layer, capillaries are randomly distributed in about 30% of the total volume. Therefore, the dielectric constant of the E/D layer containing blood was used as 68.44 sum of multiplying the dielectric constant of blood by 0.3 and the dielectric constant of E/D layer by 0.7. The dielectric constant of the solution according to the exact change of glucose concentration in the used band was not known, the simulation was conducted by sweeping the permittivity in small units arbitrarily.

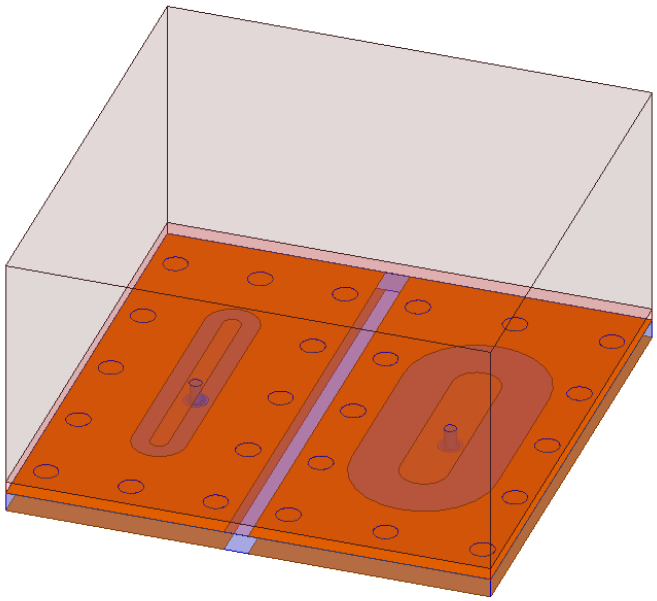
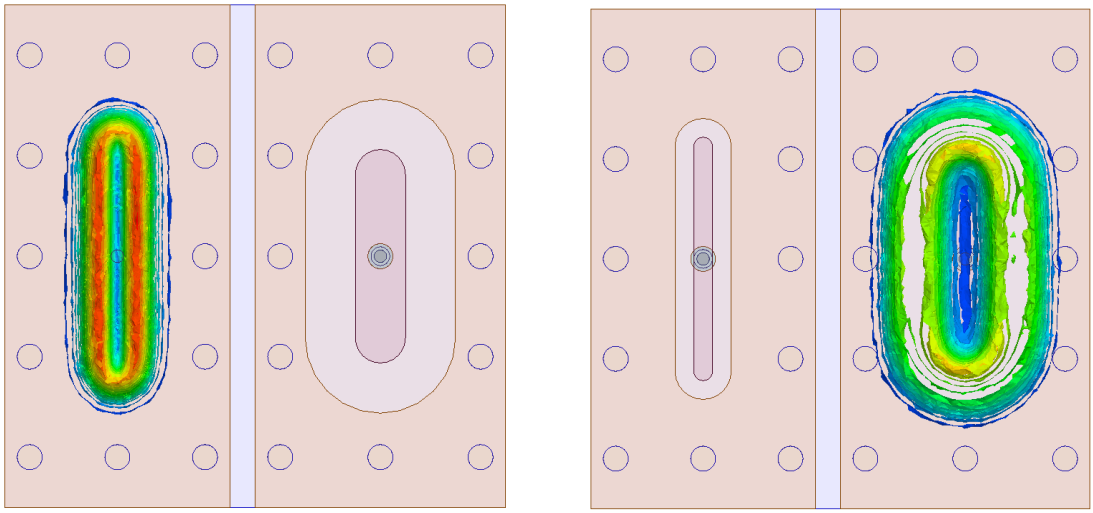


Fig. 2-4. Simulation setup in HFSS sensor attached to skin and underlying tissue

2.2 Simulation result

The simulation results showed that the following figures.



(a) (b)

Fig. 2-5. No E-field invade to each other electrodes

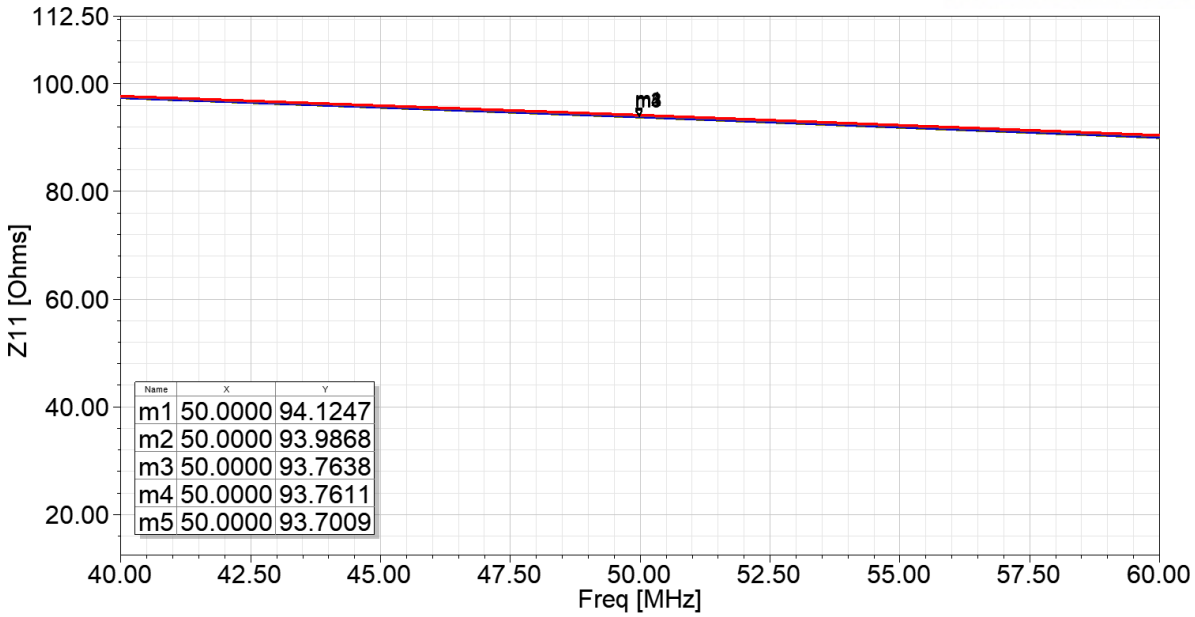


Fig. 2-6. Z-parameter response of long electrode

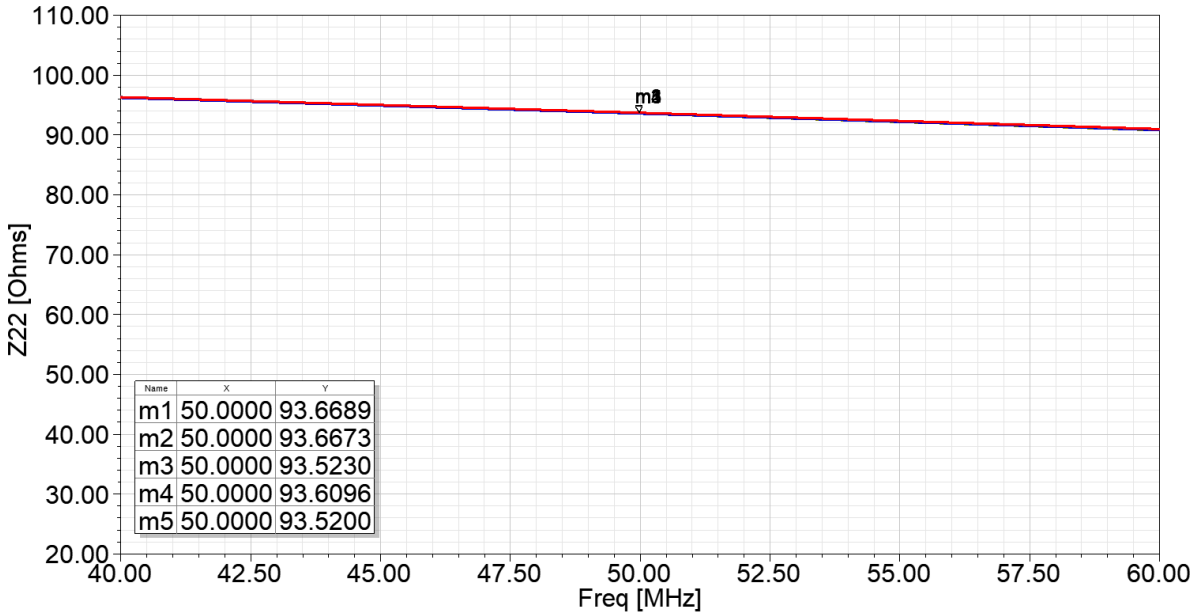


Fig. 2-7. Z-parameter response of Short electrode

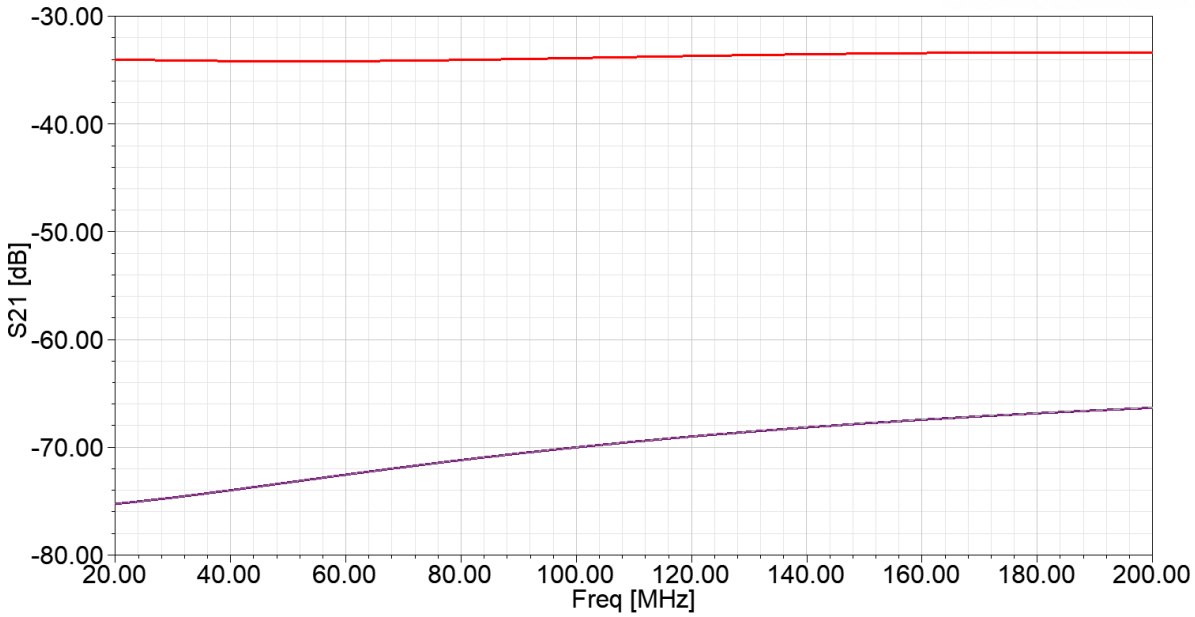


Fig. 2-8. S21-parameter decreased -40dB from -34dB(previous work – red line) to -75dB(proposed work – purple line)

3 Experiment

The change of Z-parameter according to the concentration of glucose solution is observed by printed PCB sensor. Glucose solution was made by mixing d-glucose and DI-water to have a concentration from 50mg/dl to 300mg/dl with 50mg/dl steps. The top of the sensor was taped to prevent leakage of the solution into the via gap in the sensor. In order to perform the function of the sample holder, a transparent acrylic plate was cut and attached to the outside of the sensor. The measurement range of the sensor was defined just above the sensor electrode, so there was no influence of the acrylic plate on the measurement. Sensor was also sealed with silicon to prevent liquid from leaking between the gap between the acrylic plate and the sensor. There was no change in the measurement result of the sensor before and after silicon application.

The progress of the experiment is as follows. First, prepare 100ml of each concentration solution. The temperature of each solution is measured before the experiment. Because permittivity is very sensitive to temperature. Put 10ml of solution on the sensor using a syringe and observe Z parameter through VNA(Rhode-Schwarz ZNL3). Repeated for average measurements, the solution of each concentration was tested 10 times. In addition, two experiments were conducted, -10 dBm and 0dBm to measure the change in the power from the signal from the VNA. The experiment was conducted by connecting the long electrode of the sensor to port1 and the short electrode to port2.

Experimental environment configuration is as follows.

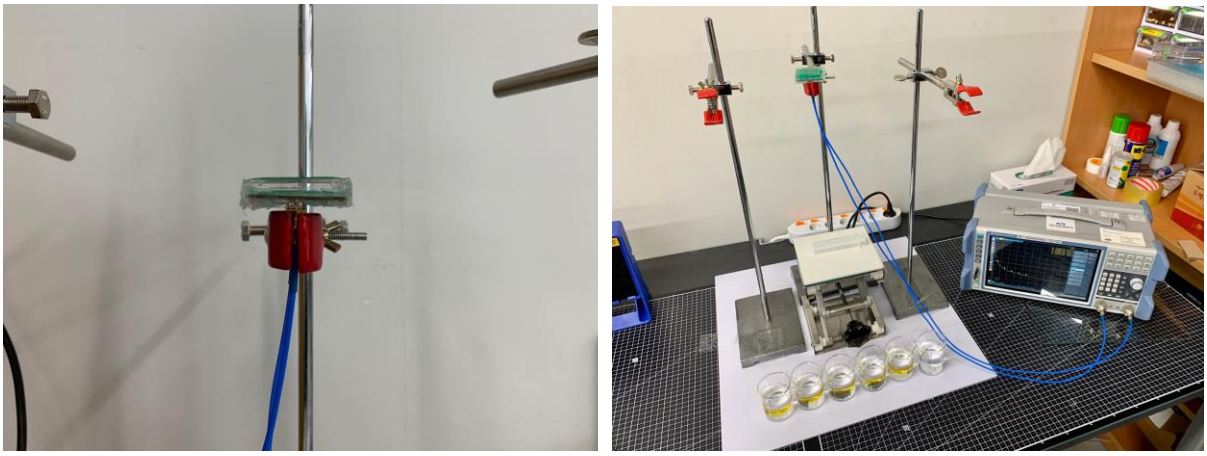


Fig. 2-9. Experimental setup

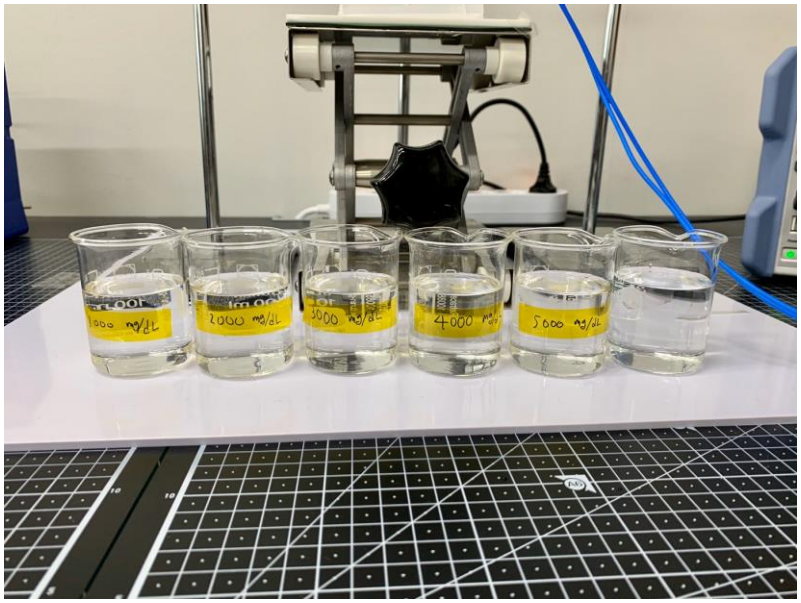


Fig. 2-10. Glucose, DI water solution from 50 to 300 mg/dl concentration

3.1 Experiment result

The experimental results measured Z11 and Z22 at 50MHz to 300MHz with 50MHz step, respectively. The measurement results are shown in the following graph. Red point on graph is infinite average of measure value.

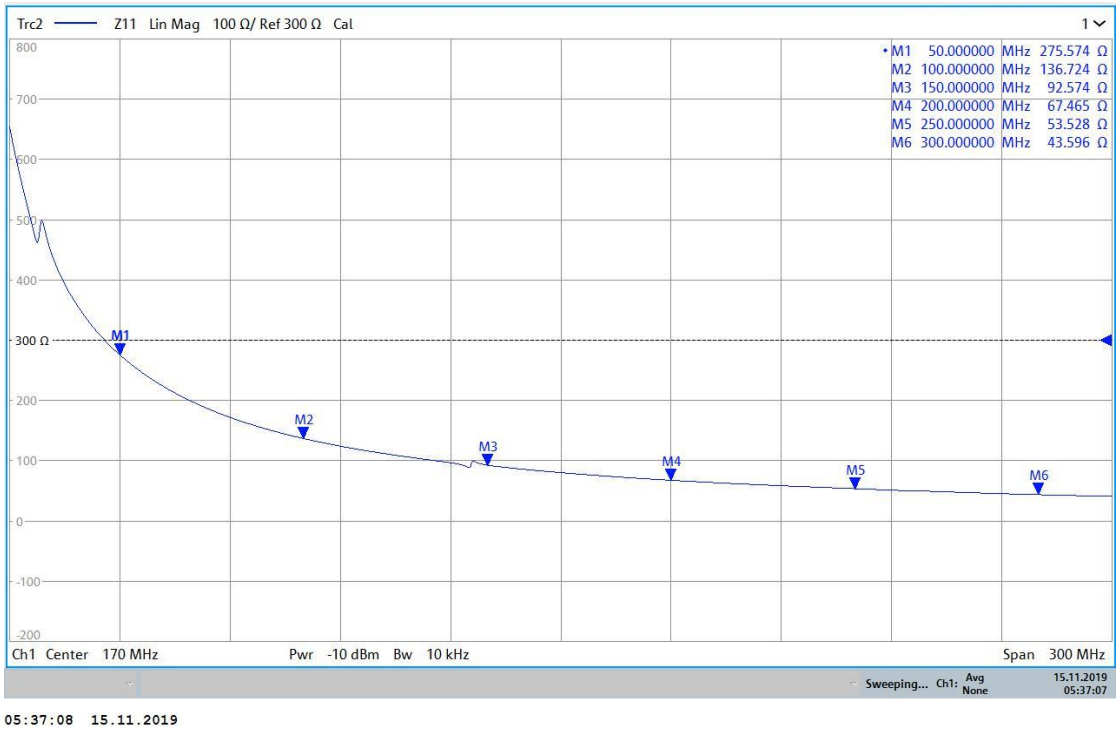


Fig. 2-11. Z11 of glucose-DI water solution (50mg/dl concentration) with -10dBm power input

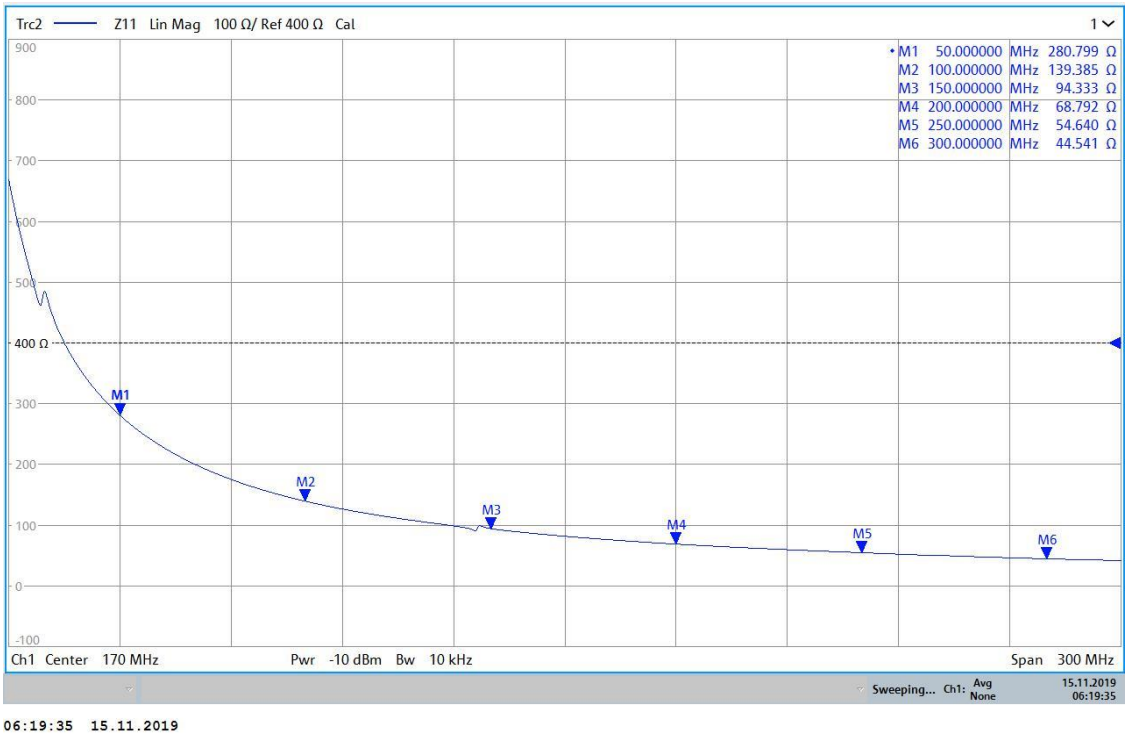


Fig. 2-12. Z11 of glucose-DI water solution (300mg/dl concentration) with -10dBm power input

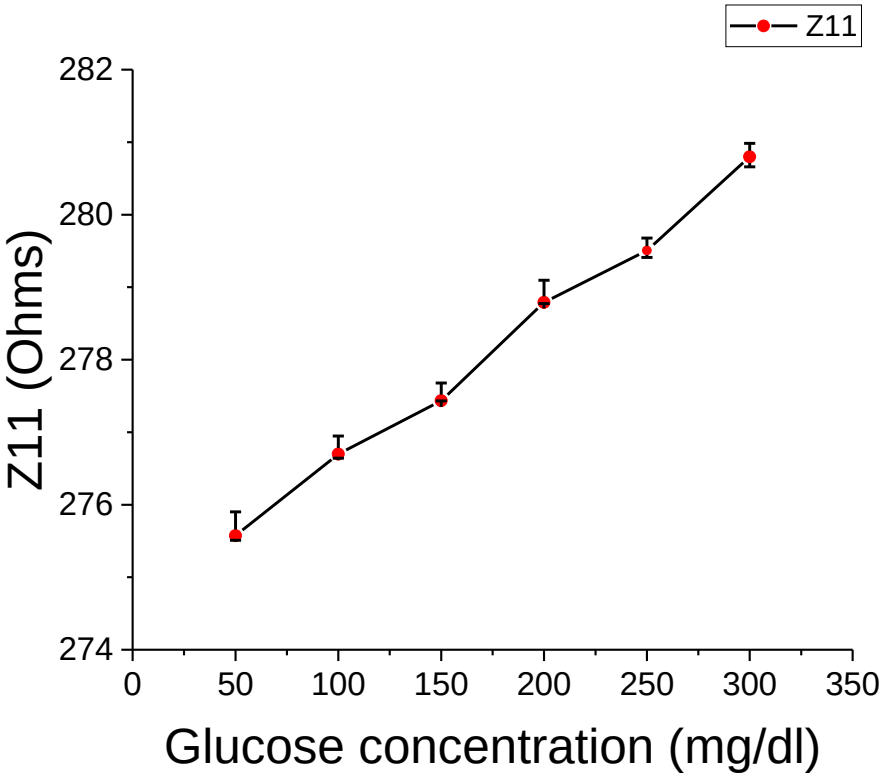


Fig. 2-13. Z11 change from glucose concentration 50mg/dl to 300mg/dl at 50MHz with -10dBm power input

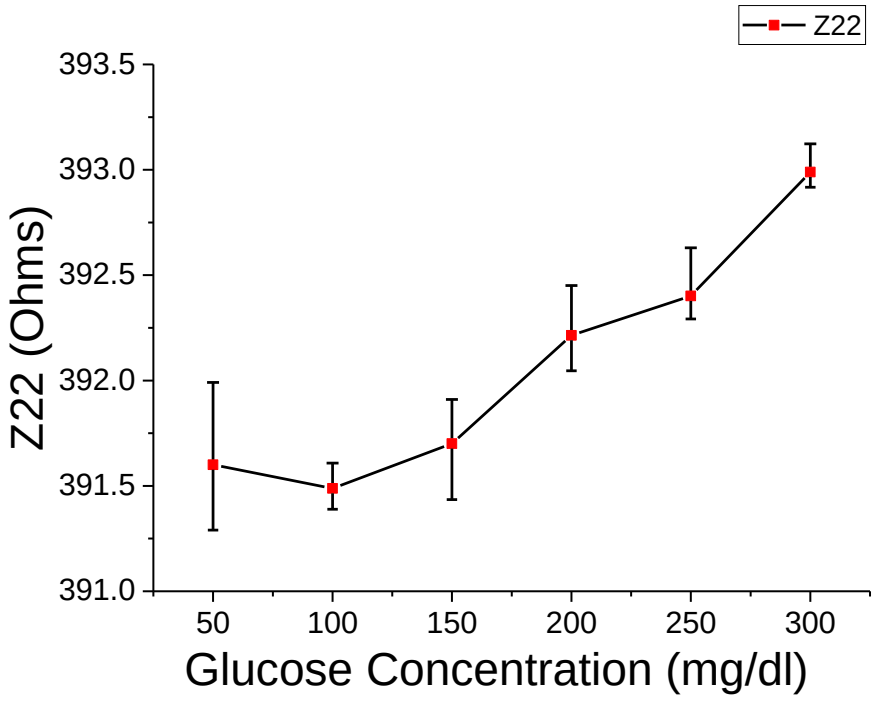


Fig. 2-14. Z22 change from glucose concentration 50mg/dl to 300mg/dl at 50MHz with -10dBm power input

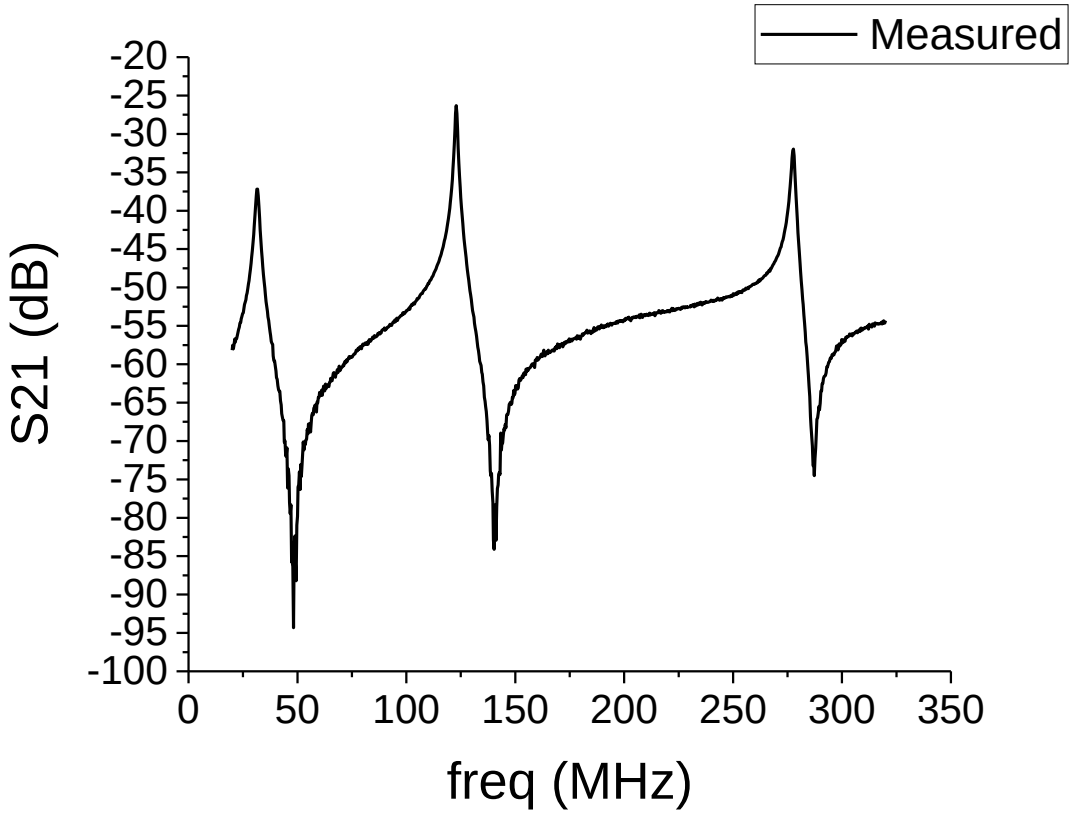


Fig. 2-15. Measured S21 with solution on the sensor

When the measurement frequency is 50MHz, the proposed sensor has sensitivity of 0.0208Ω.

Experimental results of inputting -10dBm to the sensor showed that the lower the frequency, the higher the sensitivity, and the lower the accuracy of the short electrode with the smaller sensing range.

At 50MHz, S21 decreased -90dB. But not like simulation result, there are multiple resonance points. Multiple resonance points are occurred by SMA connector which is attached to the sensor for signal input.

4 Conclusions and future work

In conclusion, this study has made following contributions to non-invasive glucose monitoring sensor using impedance spectroscopy. The study was conducted using glucose and DI-water solutions for changes in blood glucose concentration.

The existing multi-electrode sensor was not modeled as the RLC circuit. This study was conducted to investigate how the new capacitance parameters represent the real-world problems.

The experimental results supporting these simulation results have improved the accuracy by reducing interference between sensor electrodes and influence of noise. Different concentrations of glucose solution were measured with the sensor. As the glucose concentration increased, the measured impedance increased. Proposed sensor has shown promising results which agrees to simulation results.

For the future work, further experiments need to be carried out by attaching the sensor to the human body.

Research on sensor read-out IC, not VNA, is required for portable blood glucose measurement devices.

In addition, the study of the blood's dielectric properties, skin and underlying tissue at the measuring frequency is necessary for more accurate blood glucose measurement.

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