In-vivo and In-vitro Blood Glucose Measurement using Surface Waves

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***Abstract*—In this paper, however, we demonstrate with in-vivo and in-vitro experimental proof that, when a measurement was conducted predominantly in surface modes, a positive association between the glucose concentration and the blood permittivity was noticeably observed. During an in-vivo experiment, a cylindrical volume of meat tissues with a known blood glucose level was first formed with the help of a suction aspirator. The exterior wall of the suction aspirator was then wound with one turn of a gelatine-coated copper wire, which is referred thereafter as Goubau line sensor. The two terminals of the Goubau line sensor were then connected to ports 1 and 2 of a Vector Network Analyzer for measuring the S-parameters. The results of our in-vivo experiment show that, in the absence of any significant leaky wave radiation from the sensor, the measured blood glucose concentration positively correlates with the measured S21 parameters in a highly reproducible manner.**

Keywords: Blood Glucose, Surface Waves, Diabetes, Leaky Waves, Goubau line, Smoking cessation

I. INTRODUCTION

Being able to monitor the fluctuation in blood glucose is highly important for both diabetic and non-diabetic population, particularly for the smokers wishing to quit [1]. Measuring blood glucose levels traditionally requires a finger to be pricked with a lancet to obtain a drop of capillary blood. This drop of blood has to be large enough to produce an accurate reading from a glucose meter. The painful sensation induced by finger-pricking usually renders continuous blood glucose monitoring difficult, if not impossible. Measurement using electromagnetic waves is by far one of the feasible techniques for continuous non-invasive monitoring blood glucose. This technique is based on the assumption that, when the blood glucose level changes, the permittivity of the blood or the muscle tissues change accordingly. However, the results of our investigation reveals that measurement of blood glucose using electromagnetic waves is not unlikely accurate unless the following issues are properly addressed:

1) In microwave frequencies, as pointed out by [2], the permittivity of blood is simply insensitive to any change in the blood glucose concentration within the range between the 85 mg/dl and 500 mg/dl. This insensitivity is due to the measurement being taken in a free space environment.

2) The permittivity of blood is not the only parameter which affects the S-parameters. The body tissues in human are in general elastic. Very often, any physical movement of the body modifies the physical dimensions of the tissues of the body part under test, which in turn induces a far greater change in the S-parameters at microwave frequencies.

3) At some frequencies, a blood glucose sensor based on measurements of S-parameters can turn into an antenna by radiating or absorbing leaky waves. Due to the presence of these leaky modes, the measurements are often erratic, unstable and difficult to reproduce. This problem becomes particularly obvious when the magnitudes of the measured S-parameters fall below the intrinsic noise floor of the network analyzer.

To overcome the above-mentioned problems, our blood glucose measurements were non-invasively conducted in the absence of any significant leaky modes with the help of Goubau-line based sensor in conjunction with a vacuum suction aspirator. Each sample blood glucose level was measured both non-invasively with the proposed technique and compared with the reading obtained invasively with a lancing device.

II. BACKGROUND CONCEPT

Goubau line bends are known to be lossy. The loss at a Goubau line bend is in general caused by the radiation at the bend, of which the mechanism can be explained with the help of Fig. 1a [3]–[5]. In Fig. 1a, the Goubau line is bent to 90 $\deg$ with a radius of curvature. The phase shifts due to the pathway MM' and pathway NN' are respectively $2\pi\frac{L}{\lambda}$ and $2\pi\frac{l}{\lambda}$, where λ is the free space wavelength. L and l are respectively the outer radius and the inner radius. Without the dielectric cylindrical disc, the radiation loss will be a function of $2\pi\frac{L-l}{\lambda}$. However, due to the presence of the cylindrical dielectric disc, the effective wavelength for pathway NN' is $2\pi\frac{l\epsilon^{1/2}}{\lambda}$, where ϵ is the complex permittivity of the cylindrical dielectric disc. In the presence of the cylindrical dielectric disc, the actual radiation loss becomes a function of $2\pi l/\lambda(L - l\epsilon^{1/2})$. The cylindrical dielectric disc with a larger value of ϵ tends to absorb more electromagnetic energy which would otherwise be lost in the form leaky waves. According to [5], the loss is weakly dependent on the thickness of the cylindrical dielectric disc. The electromagnetic energy absorbed will be either stored by the cylindrical dielectric disc or lost as a result of the loss tangent of the cylindrical dielectric disc.

When the Goubau line bend as shown in Fig. 1a radiates leaky waves, it can equally absorb leaky waves from the surrounding. If the both ends of the Goubau line were connected to ports 1 and 2 of a network analyzer, the S11 and S12 parameters should be both low to effect these leaky modes.

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Here, the interaction between this absorption and radiation of leaky modes often makes the measurement of S-parameters unstable and non-reproducible.

To overcome the leaky modes, the original scheme proposed by Chiron [5] for reducing radiation loss at the $90\,\deg$ bend is used to our advantage for measurement of the dielectric permittivity of a blood-filled body tissue (see Fig. 1b). In Fig. 1b, the cylindrical dielectric disc is now replaced with a fixed cylindrical volume of a blood-filled body tissue. To do this, we create a cylindrical volume of a body tissue with the help of a vacuum suction aspirator (See Fig. 1c). The volume of the cylindrical column of blood-filled tissue formed by the suction effect of the aspirator is expected to be the same for all measurements. Since the height of the cylindrical volume of the body tissue is not a strong function of the insertion loss, the S-parameter measurement should be easily replicated at a right frequency range. In this case, the S12 parameter (or the insertion loss between port 1 and port 2) will be a strong function of $2\pi l/\lambda(R - r\epsilon^{1/2})$, where ϵ is the blood permittivity which can change as a result of a change in the blood glucose concentration [2] and [6].

In Fig. 1b, the Goubau line is completely shielded with a layer of thermally cured gelatine and glycerin (where the ratio is 1:1 by volume). Since the permittivity of gelatine is very similar to that of the blood, the electromagnetic energy along the Goubau line will most likely propagate in surface with very little radiation loss and reflection in either directions. This Goubau line bend should have very little interaction with the surrounding environment. The blood-permittivity induced change in the S-parameters should remain stable and reproducible even after a few round measurements.

Fig. 1c shows the photo the proposed blood glucose sensor used in in-vitro experiment, whilst Fig. 1d shows how the proposed blood glucose sensor has been used in in-vivo experiment.

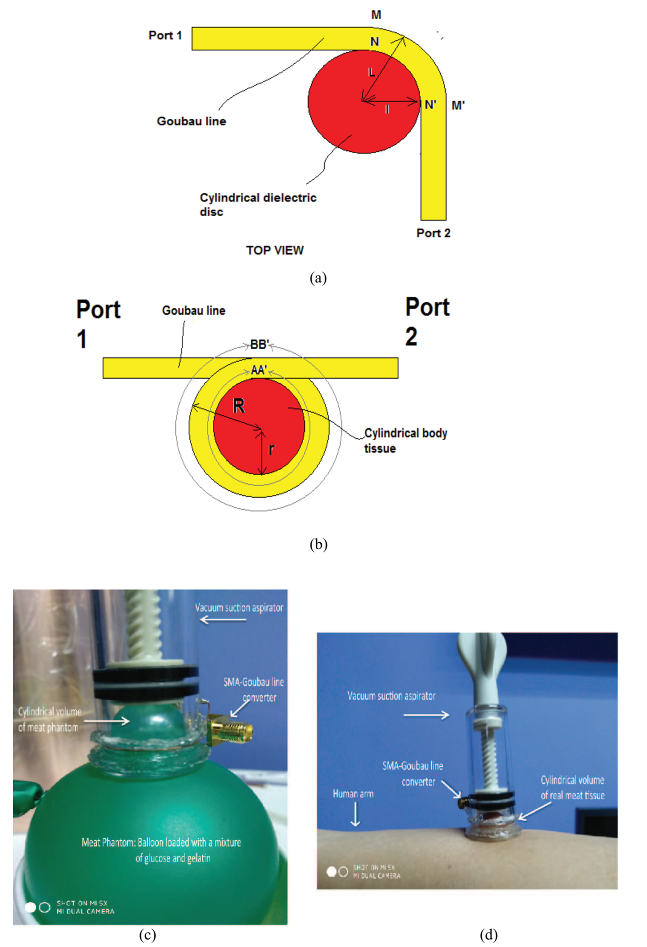


Fig. 1. Use of the dielectric cylinder for absorbing electromagnetic radiation. a) Original scheme proposed by Chiron for reducing radiation loss caused by the $90\deg$ bend [7]; b) Extension of Chiron's scheme for measuring the dielectric constant; c) Suction aspirator for forming a fixed cylindrical volume of a meat phantom; d) Suction aspirator for forming a fixed cylindrical volume of a blood-filled human tissue.

III. SUGGESTED SETUP FOR MEASUREMENT OF BLOOD GLUCOSE USING ELECTROMAGNETIC WAVES

In this work, the blood glucose levels were monitored using electromagnetic waves in a setup as illustrated in Fig. 2. In Fig. 2, the network analyzer was used to measure the scattering parameters (S11, S12, S21 and S22 parameters) over the 1 kHz-67 GHz range. The Goubau line sensor, which was used to support propagation of a surface electromagnetic wave along the surface of the meat tissue [5], has both ends terminated with a Goubau line to SMA converter [7]. The signals from port 1 and port2 were originally in the form of a transverse electromagnetic mode (i.e. TEM modes) but the Goubau line to SMA converter converts this TEM mode into a surface electromagnetic wave (i.e. TM mode) The device under test (DUT) was cylindrical volume of either a real blood-filled meat tissue or a meat phantom. The meat phantom was a balloon filled with a mixture of glucose solution of a certain concentration and gelatin. A near-cylindrical volume was then formed with the help of a vacuum suction aspirator. The exterior surface of the suction aspirator was further coiled by a looped Goubau line [5]. During the S-parameter measurement, the Goubau line was expected to radiate a limited extent of fringing electric field in close vicinity of the surface of the Goubau line. Due to the dielectric nature of the human meat tissue, a large portion of the fringing electric on the surface of the Goubau line will be absorbed inwards by the meat tissues, ending up with less energy radiating in the outwards direction. During the measurement, a portion of the electromagnetic wave from port 1 of the network analyzer was incident onto the device under test (DUT) and reflected back to port 1. The measured S11 parameters can be used to determine how much electromagnetic energy was reflected. The remaining portion of the electromagnetic wave from the network analyzer was either transmitted through Goubau line loop surrounding the DUT or dissipated by the DUT as heat. The S21 parameters in conjunction with the S11 parameters can determine how much electromagnetic energy is transmitted from port 1 to port 2. At a stop band, how much electromagnetic energy is dissipated as heat by the DUT is a function of permittivity of the cylindrical volume of either a real blood-filled tissues

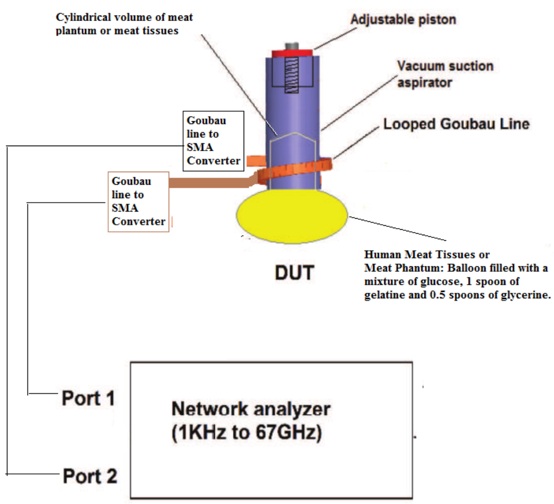
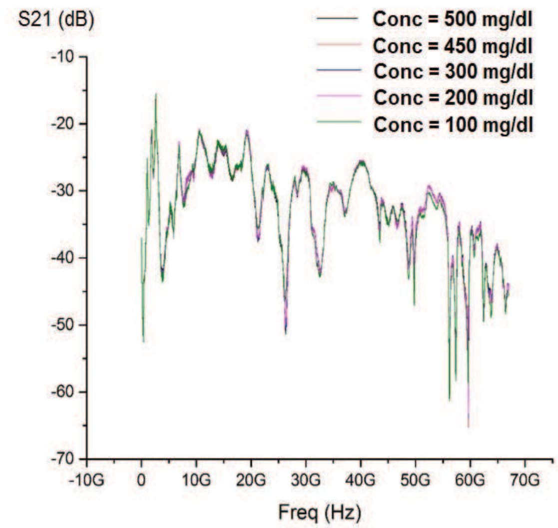
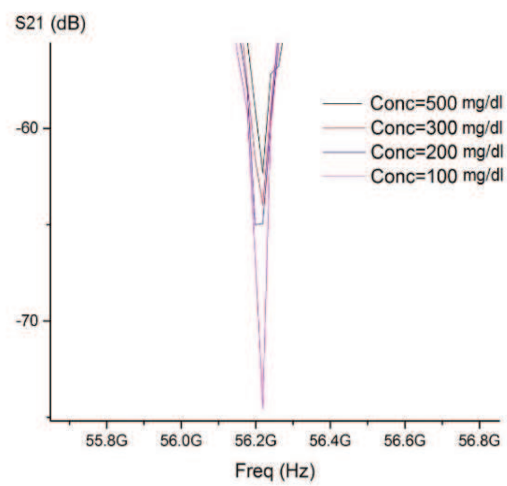


Fig. 2. Experimental setup for measuring blood glucose using a surface wave (frequency up to 67GHz).



(a)



(c)

or a meat phantom, which theoretically depends on the blood glucose levels. In the in-vitro test, in order to check if our proposed can generate results comparable to those from other research groups, the S-parameters were measured at 60 GHz for 6 different concentrations of blood glucose in the meat phantom, namely 100 mg/dl, 200 mg/dl, 300 mg/dl, 450 mg/dl, 500 mg/dl and 2000 mg/dl [7]–[11].

IV. EXPERIMENTAL RESULTS

Fig. 3a shows the S-parameters over the frequencies from 1 kHz to 67 GHz. Upon careful examination, we found that 50GHz-60GHz was the only frequency range in which the positive correlation between the blood glucose concentration the S21 parameters can be clearly observed. This range was also the only frequency range without any overlapping of S21 parameters. In this frequency range, the circuit in our experimental configuration was found to resonate at 56.2 GHz.

Fig. 3b shows a significantly enlarged plot of S21 parameter against frequency with focus on frequencies in the neighbourhood of 56.2 GHz. At 56.2 GHz, there exists a positive correlation between the S21 parameter and the blood glucose concentration. The S21 parameter has noticeably changed even though the glucose concentration has changed very little. The S21 parameter was found to be most sensitive to the blood glucose change at 100 mg/dl, which was within the normal blood glucose concentration of a healthy human.

Fig. 3c shows a plot of the S21 parameters against the blood glucose concentration right at the resonant frequency (56.2 GHz). The measured results obviously suggest that, at 56.2 GHz, there exists a near linear relationship between the blood glucose concentration and the S21 parameters.

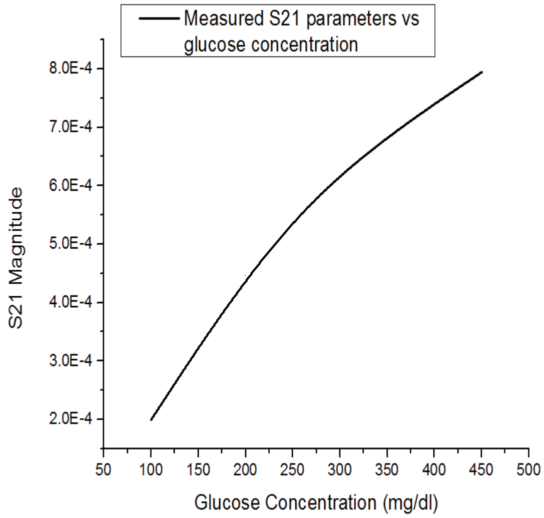
We have also used the proposed suction aspirator as shown in Fig. 1c to conduct in-vivo S-parameter measurements as shown in Fig. 2a under the direction of a health care professional in Vietnamese-German University. The measurements were conducted on the surface of the human arms of 6 students at around 4 GHz on different days. The measured S-parameters for different blood samples are shown in Fig. 4a. It can be seen from Fig. 4a that there exists a positive correlation between the S21 parameter and the blood glucose levels.

Fig. 4b shows a plot of S22 and S12 parameters on a student's arm whose blood glucose level was at that 109 mg/dl. The magnitudes of the S22 and S12 parameters have decreased together at frequencies 4 GHz or higher. At this frequency, the surface modes were changed to leaky modes.

In general, the results of our repeated experiments on different days and on different subjects suggest that the in-vivo measurements were highly reproducible.

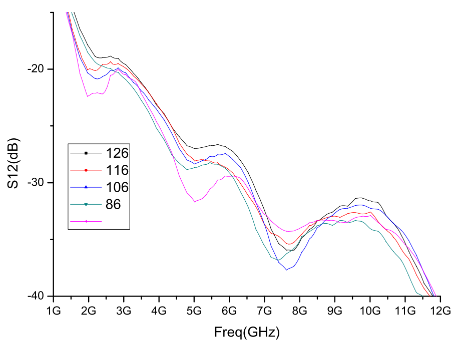
V. DISCUSSION

The in-vitro measurements as shown in Fig. 3 have proven the fact that, at 56.2 GHz, there exists a near-linear relationship between the S21 parameters and the blood glucose concentration. These findings consistently agree with the conclusion drawn by some other research groups who have successfully



(d)

Fig. 3. S-parameters measured using Keysight Signal Analyzer N9030A: a) S21 parameters for frequencies from 1Hz to 67GHz; b) S21 parameters focused in the neighbourhood of 56 GHz; c) Measured S21 parameters as a function of Glucose Concentration.



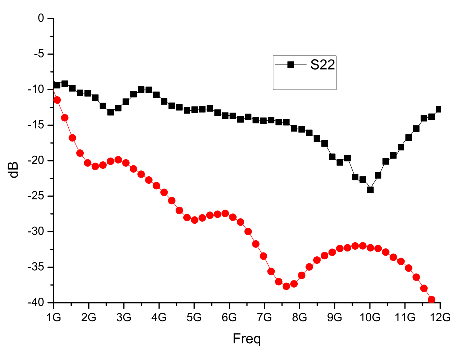


Fig. 4. S-parameters measured using Keysight Signal Analyzer N9030A: a) S12 parameters for different concentrations of blood glucose; b) S22/S12 parameters for blood glucose concentration at 109 mg/dl.

measured blood glucose concentrations at around the frequency range from 55GHz to 65GHz [7]–[11].

The in-vivo measurements as shown in Fig. 4a have proven the fact that, below 4 GHz, there exists a positive correlation between the S12 parameters and the blood glucose concentration. According to Fig. 4b, 4 GHz is the frequency where the surface modes were turned into leaky modes. This was the reason why the correlation between the S12 parameters and the blood glucose concentration were no longer positive at frequencies higher than 4 GHz.

As suggested in Section II, when the blood glucose sensor turns into an antenna, where the electromagnetic waves propagating along the Goubau line were predominantly leaky modes, the measurement became unstable and non-reproducible. There was the reason why we choose the conduct the in-vivo experiment at 4 GHz rather than 56 GHz.

The presence of skeletal tissues in the body tissue tends to decrease the overall accuracy of measurement because of the unwanted electromagnetic reflection. This reflection would have been unavoidable if space waves were used in our S-parameter measurement instead of surface electromagnetic waves. However, with the vacuum suction aspirator as shown in Fig. 1c, a fixed cylindrical volume of tissue can be formed in the absence of any skeletal tissues. The results of this investigation, though preliminary, at least prove the fact that the suction aspirator allows a cylindrical volume of blood-filled tissues or meat phantom to be formed non-invasively and measured using the surface wave set-up as shown in Fig. 2a with reproducible results.

Despite having promising preliminary results, measurement of blood glucose using millimetre waves is still in its infancy. More research is needed before clinical use of electromagnetic wave for monitoring blood glucose can become a reality. Our next step is to conduct in-vivo characterization on the surface of a body part using the setup with the help of a commercially available glucose sensor.

VI. Conclusions

In this work, we have successfully used a surface electromagnetic wave to conduct an S-parameter in-vitro and in-vivo experiments. Consistent with the conclusions drawn by some other research groups, the results of the in-vitro investigation suggest that, at 56.2 GHz, there exists a near-linear relationship between the S21 parameters and the blood glucose concentration. In addition, the results of the in-vivo investigation suggests that below 4 GHz, there exists a positive correlation between blood glucose concentrations and the magnitudes of the S12 parameters. Overall speaking, the findings of the work strongly suggest that the proposed technique can be used to conduct in-vivo measurement with predictable and reproducible results.

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