

# Glucose-Dependent Dielectric Properties of Blood Plasma

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## Abstract

In this study, we show a correlation between electrical properties (relative permittivity- $\epsilon_r$  and conductivity- $\sigma$ ) of blood plasma and plasma glucose concentration. In order to formulate that correlation, we performed electrical property measurements on blood samples collected from 10 adults between the ages of 18 and 40 at University of Alabama Birmingham (UAB) Children's hospital. The measurements are conducted between 500 MHz and 20 GHz band. Using the data obtained from measurements, we developed a single-pole Cole-Cole model for  $\epsilon_r$  and  $\sigma$  as a function of plasma blood glucose concentration. To provide an application, we designed a microstrip patch antenna that can be used to predict the glucose concentration within a given plasma sample. Simulation results regarding antenna design and its performance are also presented.

## 1. Introduction

The development of a reliable continuous glucose monitoring technology, which would lessen the complications associated with diabetes through optimal glycemic control, is a key to improving the lives of patients living with the disease. In recent years, considerable progress has been made in developing implantable biosensors that can continually monitor glucose levels. These biosensors rely on the interstitial fluid within the dermis to measure the interstitial glucose (IG) levels. However, to be truly beneficial, the implanted sensor must be able to function properly for an extended period of time. The commercial Food and Drug Administration (FDA) approved biosensors can only remain functional up to 72 hours after their implantation in the body [1]. Contributing factors for this loss of functionality include the degradation and fouling of the sensor, and the changes in the tissue surrounding the sensor such as fibrosis and inflammation. While researches explore potential solutions to improve the current implantable biosensors, there is need to investigate other alternative technologies. One alternative way is to explore different sensor technologies that rely on changes in the electrical properties of blood plasma as a function of glucose concentration.

One such application is a microstrip patch antenna sensor. Because the antenna resonances are affected by the electrical property changes in the surrounding medium, microstrip antennas can be used for future continuous glucose monitoring devices. The goal of this study is in two fold. First, to obtain a correlation between electrical properties of blood plasma and glucose concentration levels within the plasma. Second, to design an antenna that can potentially be used to predict glucose concentrations within a given plasma sample. To achieve these goals, as part of a grant from Juvenile Diabetes Research Foundation (JDRF), we performed extensive measurements on blood samples collected from adults at UAB Children's Hospital. Agilent's 85070E dielectric probe kit and an E8362B PNA network analyzer were used for measurements between 500 MHz and 20 GHz. The data at each glucose level was fitted to a sing-pole Cole-Cole model, and a second order polynomial is used to model the glucose concentration dependence for the Cole-Cole parameters. After we formulated the relationship between the electrical properties of the blood plasma and

glucose concentration, we designed a miniaturized antenna sensor for continuous glucose monitoring applications. A parametric study is also conducted to determine the optimum antenna sensor dimensions.

## 2. Electrical Property Measurements of Blood Plasma

In this study, we assume that the changes in other minerals in the blood plasma such as calcium, chloride, potassium, and magnesium will have very minor or no effects on the electrical properties. For instance, the glucose concentration in a diabetic patients' blood may vary between 30 mg/dl and 400 mg/dl while sodium and chloride levels, although they exist in large quantities, only vary from 310 mg/dl to 333 mg/dl and 337 mg/dl to 372 mg/dl, respectively [2]. Other minerals exist in very low quantities in the blood (e.g. magnesium: 1.8-3.4 mg/dl, calcium: 8.5-10.5 mg/dl, potassium: 13.6-21.4 mg/dl) [2]. In our study, the blood glucose concentrations in the collected samples are manipulated *in-vitro*, therefore, the concentrations of other minerals in a specific sample remained unchanged during measurements. This approach guarantees that the changes occurring in electrical properties are only due to glucose manipulation in the sample. Table 1 shows the laboratory tests of 10 different blood samples. As seen, the mineral concentrations do not vary significantly from one individual to another which supports our initial assumption.

Table I  
Laboratory tests showing the minerals in the blood plasma

Na (mmol/L)	138	137	138	139	138	137	139	136	139	140
K (mmol/L)	6.8	9.0	5.9	7.8	9.8	9.7	6.4	7.1	7.2	4.7
Cl (mmol/L)	101	101	101	103	101	102	102	100	101	102
Ca (mg/dL)	9.1	8.8	9.2	9.0	8.8	8.7	9.1	8.2	8.9	9.2

The glucose levels on each sample are reset to zero before measurements. Each sample is then measured at eight different glucose concentrations (0 mg/dl, 250 mg/dl, 500 mg/dl, 1000 mg/dl, 2000 mg/dl, 4000 mg/dl, 8000 mg/dl, and 16000 mg/dl). Measurements are repeated three times for each sample to ensure data reliability. The blood plasma samples and the measurement setup are shown in Fig. 1a and Fig. 1b, respectively. After measuring each sample, averages for 10 samples are calculated for each glucose concentration. The dielectric constant and conductivity results are shown in Fig. 2a and Fig. 2b, respectively. As seen from the figures, the dielectric constant and the conductivity decrease when the glucose concentration in the sample increases. The difference is more apparent in the higher frequency range.

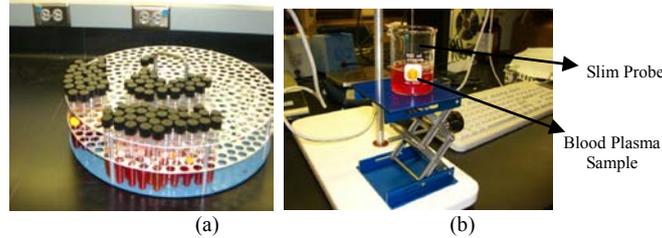


Fig. 1. a) The blood plasma samples and b) the measurement setup.

## 3. Methodology

Following the measurements, the wideband dielectric properties at each glucose concentration are fitted to the single-pole Cole-Cole Model. The Cole-Cole Model offers an efficient and accurate representation of biological tissues over very wide frequencies and has been recently used to reduce the complexity of the experimental data obtained for various human tissues (brain, fat, breast, skin, bone, liver etc.) [3]-[8]. The expression is defined as:

$$\hat{\epsilon}(\omega) = \epsilon'_c(\omega) - j\epsilon''_c(\omega) = \epsilon_\infty + \sum_n \frac{\Delta\epsilon_n}{1 + (j\omega\tau_n)^{(1-\alpha_n)}} + \frac{\sigma_i}{j\omega\epsilon_0} \quad (1)$$

where  $\omega$  is the angular frequency,  $\epsilon'_c(\omega)$  is the frequency dependent dielectric constant,  $\epsilon''_c(\omega)$  is the frequency dependent dielectric loss,  $n$  is the order of the Cole-Cole model,  $\epsilon_\infty$  is the high frequency

permittivity,  $\Delta\epsilon_n$  is the magnitude of the dispersion,  $\tau_n$  is the relaxation time constant,  $\alpha_n$  is the parameter that allows for the broadening of the dispersion, and  $\sigma_i$  is the static ionic conductivity. All calculations are carried out using particle swarm optimization. The pole broadening parameter,  $\alpha_n$ , is fixed at 0.1. A comparison of dielectric constant and the conductivity of the measured data and the fitted models at three distinct glucose levels are shown in Fig. 3a and Fig. 3b at 500 MHz - 20 GHz band. The calculated parameters for each glucose concentration are also given in Table II.

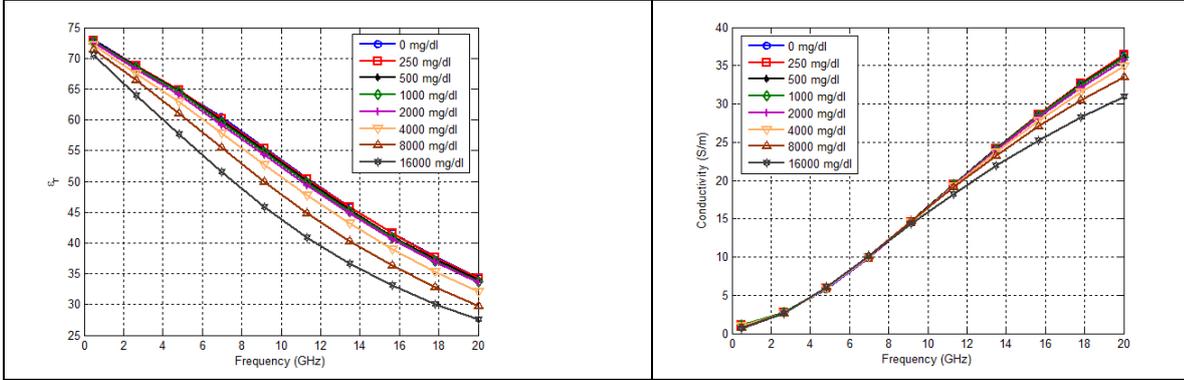


Fig. 2. The measured a) dielectric constant b) conductivity from 500 MHz to 20 GHz for various glucose levels.

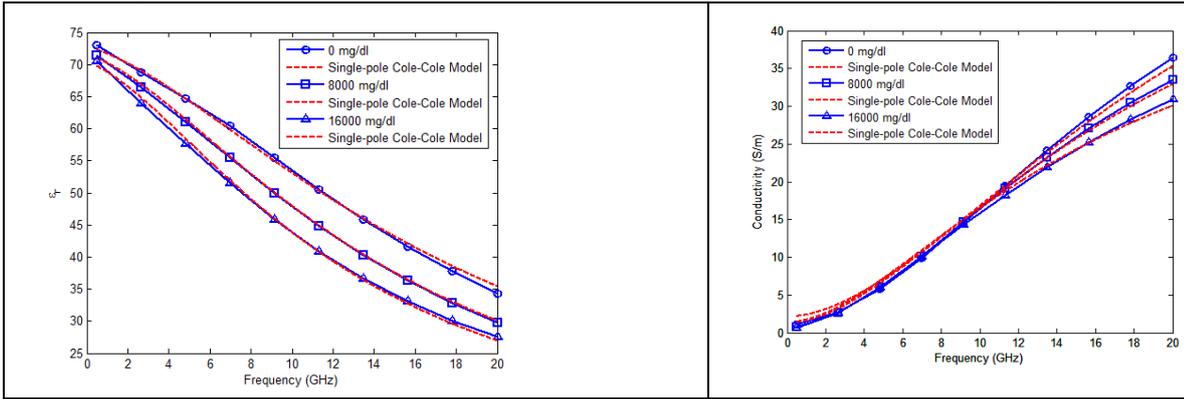


Fig. 3. The a) dielectric constant and b) conductivity of the measured data and the fitted models at three distinct glucose levels at 500 MHz-20 GHz band.

In order to validate the fitting of the dielectric properties of the blood plasma, the difference between the measured data and the single-pole Cole-Cole fit are calculated at each frequency and glucose concentration:

$$\delta\epsilon_{r,fit} = \epsilon_{r,measured} - \epsilon_{r,fit} \quad (2)$$

$$\delta\sigma_{fit} = \sigma_{measured} - \sigma_{fit} \quad (3)$$

Fig. 4 shows the calculated differences for 500 MHz - 20 GHz. As seen, the maximum difference for 500 MHz - 20 GHz band is less than one unit.

Table II

Parameters for the single-pole Cole-Cole model at 500 MHz-20 GHz band for 8 different glucose concentrations

	0 mg/dl	250 mg/dl	500 mg/dl	1000 mg/dl	2000 mg/dl	4000 mg/dl	8000 mg/dl	16000 mg/dl
$\epsilon_r$	2.8	2.04	2.67	2	2.11	3.1	3.29	5.63
$\Delta\epsilon$	70.02	70.72	70.41	70.85	70.81	69.08	68.37	64.87
$\tau$ (ps)	8.68	8.62	8.88	8.86	9.32	9.51	10.57	12.6
$\sigma_i$ (S/m)	2.13	1.96	1.93	1.73	1.46	1.66	1.31	1.38

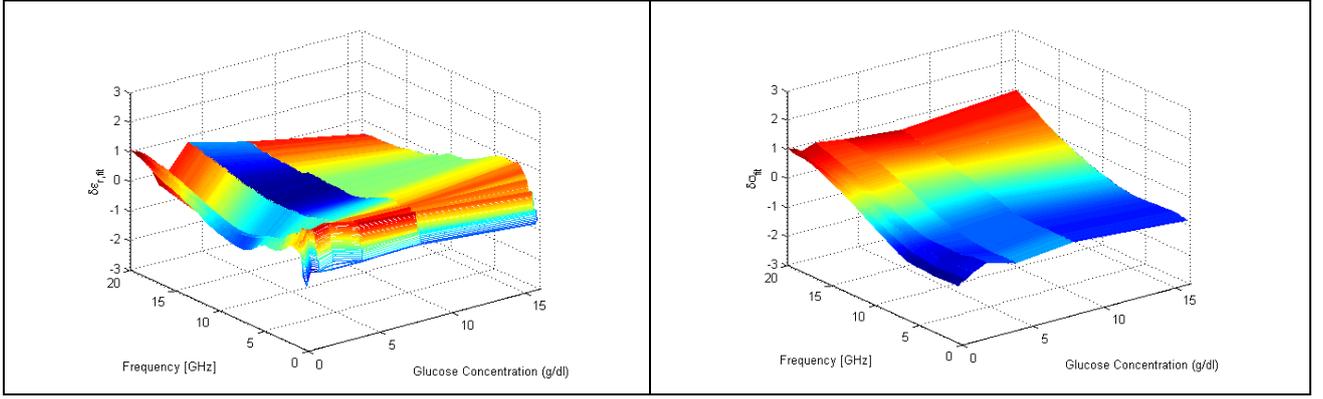


Fig. 4. The difference between the measured a) dielectric constant and b) conductivity and the single-pole Cole-Cole fit at 500 MHz – 20 GHz.

Finally, to investigate the reliability of the method, the quadratic coefficients are used to reconstruct the Cole-Cole parameters at various glucose concentrations, and the reconstructed Cole-Cole parameters are used to calculate the dielectric properties as a function of frequency. The difference between the reconstructed and measured data is defined as follows:

$$\delta\epsilon_{r, recon} = \epsilon_{r, measured} - \epsilon_{r, reconstructed} \quad (8)$$

$$\delta\sigma_{recon} = \sigma_{measured} - \sigma_{reconstructed} \quad (9)$$

Table III  
Coefficients of the quadratic fits to the glucose-dependent Cole-Cole parameters for 500 MHz and 20 GHz

	$a_n$	$b_n$	$c_n$
$\epsilon_\infty$	0.0099	0.047	2.3
$\Delta\epsilon$	-0.0093	-0.21	71
$\tau$ (ps)	0.0012	0.23	8.7
$\sigma_i$ (S/m)	0.0063	-0.14	2

Finally, when the coefficients in Table III are used in the equations (4)-(7) along with equation (1), we arrive at the glucose dependent electrical properties of the blood plasma. Resulting equations can be used to derive dielectric properties of any plasma sample for a given glucose concentration. This is critical for designing electromagnetic sensors to detect plasma glucose concentration.

## 4. References

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