Cole-Cole Model for Glucose-Dependent Dielectric Properties of Blood Plasma for Continuous Glucose Monitoring

***Tutku Karacolak*[1], *Elaine C. Moreland*[2], *Erdem Topsakal*[1]**

[1]Department of Electrical and Computer Engineering
Mississippi State University
Mississippi State, MS 39762, USA
tk57@msstate.edu, topsakal@ece.msstate.edu

[2]Department of Pediatrics
University of Alabama at Birmingham
Children's Hospital, Pediatric Endocrinology, Birmingham, AL 35294, USA
emoreland@peds.uab.edu

Abstract

Next generation continuous glucose monitoring systems depends on the accurate relationship between the glucose concentration and the dielectric properties of the blood plasma. In this study, the dielectric properties of 10 blood plasma samples were measured for various glucose levels in the frequency range of 500 MHz to 20 GHz. To relate the glucose concentration with the dielectric properties, first an accurate Cole-Cole model is used to fit the dielectric properties as a function of frequency and then the Cole-Cole parameters are defined as a function of glucose using a polynomial fitting. Computational efficiency, accuracy, and stability will also be considered in terms of different optimization techniques.

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 biosensors developed so far can only remain functional up to 10 days after their implantation in the body. 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 would be to determine the dependence between the glucose concentration and the electrical properties of the blood plasma.

The goal of this study is to develop an accurate parametric model to describe the change of dielectric properties (ε_r and σ) of blood plasma as a function of both glucose concentration and frequency. The measurements were performed on 10 blood plasma samples collected from healthy individuals between the ages of 18 and 40 at UAB Children's Hospital of Alabama. Agilent's 85070E dielectric probe kit and an E8362B PNA network analyzer was used for measurements between 500 MHz and 20 GHz. The data at each glucose level is fitted to a Cole-Cole model, and a polynomial is used to model the glucose concentration dependence of the Cole-Cole parameters. In this way, it will be possible to calculate the dielectric properties of the blood plasma at each glucose concentration.

2. Methodology

The Cole-Cole Model offers an efficient and accurate representation of many types of biological tissues over a very wide frequency band 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.) [1-5]. For our measurements, we collected blood plasma samples from 10 healthy individuals and each sample is then reduced to 0 mg/dl glucose level which was our starting point. Each sample is measured between 500 MHz and 20 GHz for 1800 frequency

points at 8 different glucose concentrations. Later, the wideband dielectric properties at each glucose concentration are fitted to the below Cole-Cole expression:

$$\hat{\varepsilon}(\omega) = \varepsilon_c'(\omega) - j\varepsilon_c''(\omega) = \varepsilon_\infty + \sum_n \frac{\Delta\varepsilon_n}{1 + (j\omega\tau_n)^{(1-\alpha_n)}} + \frac{\sigma_i}{j\omega\varepsilon_0} \tag{1}$$

where ω is the angular frequency, $\varepsilon_c'(\omega)$ is the frequency dependent dielectric constant, $\varepsilon_c''(\omega)$ is the frequency dependent dielectric loss, n is the order of the Cole-Cole model, ε_∞ is the high frequency permittivity, $\Delta\varepsilon_n$ is the magnitude of the dispersion, τ_n is the relaxation time constant, α_n is the parameter that allows for the broadening of the dispersion, and σ_i is the static ionic conductivity. Finally, the calculated Cole-Cole parameters are fitted to a second-order polynomial as the following:

$$\varepsilon_\infty(g) = a_1 g^2 + b_1 g + c_1 \tag{2}$$
$$\Delta\varepsilon(g) = a_2 g^2 + b_2 g + c_2 \tag{3}$$
$$\tau(g) = a_3 g^2 + b_3 g + c_3 \tag{4}$$
$$\alpha(g) = a_4 g^2 + b_4 g + c_4 \tag{5}$$
$$\sigma_i(g) = a_5 g^2 + b_5 g + c_5 \tag{6}$$

3. Results

To show the applicability of the method, the dielectric properties of a blood plasma sample with a glucose concentration of 500 mg/dl are fitted to single-pole, two-pole, and three-pole Cole-Cole models, respectively. All calculations are carried out using particle swarm optimization. The pole broadening parameter, α_n, is fixed at 0.1 in all three models. The dielectric constant and the conductivity of the sample and the fitted models are shown in Fig. 1 and Fig. 2, respectively. As seen, the single-pole model is sufficient to represent this data with less number of parameters and computational time. The calculated parameters are also given in Table I.

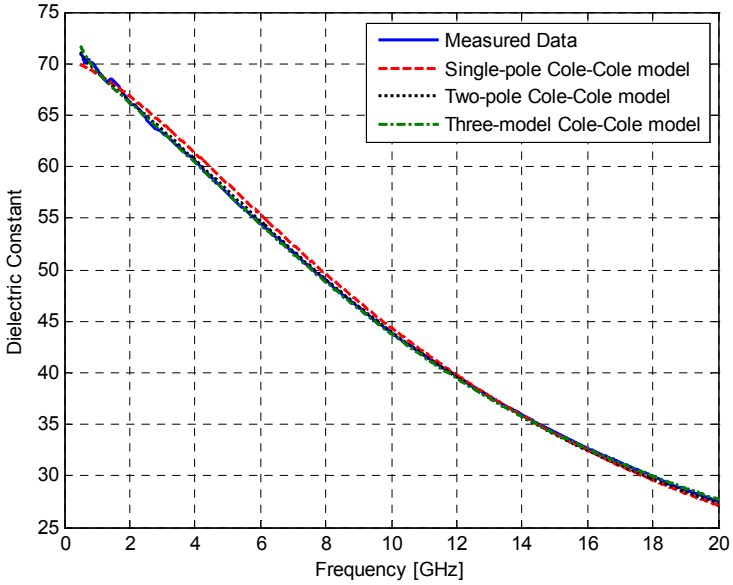

Fig. 1. The dielectric constant of the measured data and the fitted models.

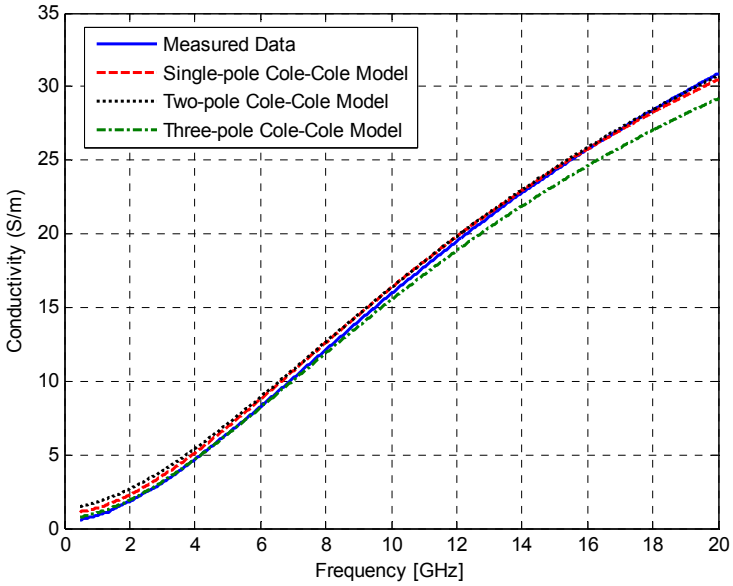

Fig. 2. The conductivity of the measured data and the fitted models.

TABLE I
PARAMETERS FOR THE SINGLE-, TWO-, AND THREE-POLE COLE-COLE MODELS

	Single-pole	Two-pole	Three-pole
ε_∞	4.72	3.58	7.15
$\Delta\varepsilon_1$	65.95	64.14	63.33
τ_1 (ps)	12.2	11.55	12.12
$\Delta\varepsilon_2$		4913.82	3632.97
τ_2 (ns)		143.99	172.98
$\Delta\varepsilon_3$			256744
τ_3 (μs)			156.74
σ_i (S/m)	1.02	0.88	0.28

4. Conclusion

The dielectric properties of the human blood plasma are measured for various glucose concentrations from 0.5 to 20 GHz. A two-step model is applied to obtain a very compact data representation. The data is first fitted to a Cole-Cole model as a function of frequency and the glucose concentration dependence of the calculated Cole-Cole parameters are modeled using a second order polynomial.

5. References

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