Investigation on Dielectric Properties of Glucose Aqueous Solutions at 500 KHz-5MHz for Noninvasive Blood Glucose Monitoring

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Investigation on Dielectric Properties of Glucose Aqueous Solutions at 500 KHz-5MHz for Noninvasive Blood Glucose Monitoring

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***Abstract*—Noninvasive blood glucose monitoring (NBGM) provides patient with diabetes a prospective approach with the characteristics of painless and sustainable monitoring. In this study, the dielectric properties of glucose aqueous solutions, namely, deionized water solutions and saline solutions were studied. Specifically, the conductivity and the dielectric constant were measured by using impedance analyzer in the frequencies range of 500 KHz to 5MHz at 25℃. The results showed that both the dielectric constant and the conductivity for the two types of glucose aqueous solutions decreased with the increase of glucose concentration in the above frequency band. By comparing the two solutions with human blood, it was found that the dielectric properties of physiological saline are closer to that of human blood. In the study, saline solution was adopted as research object. In order to formulate the relationship between the dielectric properties of saline solutions and glucose concentration, the third-order Cole-Cole model for each glucose concentration was developed and the coefficient of determination R^2 was as higher as 0.99. In addition, a second-order polynomial is used to model the glucose concentration dependence for the Cole–Cole parameters. The result indicates that the NBGM at low frequencies has potentials in practical applications.**

Keywords- Noninvasive blood glucose monitoring; dielectric properties; glucose concentration; Cole-Cole parameters

I. INTRODUCTION

Diabetes, one of the most commonly seen metabolic diseases, is a well-known disease affecting over 300 million people worldwide[1, 2]. According to predictions by the Diabetes Alliance, the number of diabetes will reach 693 million by 2045[3]. For effective diabetic management, the diabetic patients have to detect the blood glucose concentration continuously[4]. Therefore, the research for noninvasive blood glucose monitoring (NBGM) technology is of great significance.

Numerous researches attempt to achieve NBGM by researching the effects of blood glucose concentration on electrical signals[5]. In[6], blood plasma was collected from 10 volunteers. Dielectric constant and conductivity of the blood plasma by adding different proportions of glucose were measured with a network analyzer at 500MHz-20GHz. The single-pole Cole-Cole model was used to fit the dielectric constant and the conductivity. In the Cole-Cole model, a quadratic polynomial was used to fit the glucose concentration and related parameters. A similar work was performed at 1GHz-10GHz, and it was concluded that as the blood concentration increases, the resonance frequency also increases[7]. In addition, the effect of temperature on the dielectric properties at 915MHz was explored in[8]. The result showed that dielectric constant increases with temperature, but decreases with increasing concentration of glucose aqueous solutions. The loss factor decreases with increasing temperature, but increases with the increasing concentration of glucose aqueous solutions. Nonetheless, a single-pole Debye model was used to fit the dielectric constant of glucose aqueous solutions at different glucose concentrations at 1GHz-8GHz by using an artificial neural network algorithm[9]. Furthermore, reference [10-14]studied the resonant frequency and impedance of aqueous solutions with different glucose concentrations in 1GHz-40GHz. Besides, the effect of electrode polarization on the dielectric properties of deionized water and physiological saline was considered at 40Hz-110MHz[15]. In summary, above 500 MHz, there are many related investigations on the electrical signals of different glucose concentrations, but little in lower frequency range. Some research discussed about the polarization effect of the electrode with different glucose concentration. However the relationship between dielectric properties and blood glucose concentration at low frequencies remains blurred and the dielectric properties may be sensitive to glucose concentration at low frequencies. Therefore, it is necessary to study the dielectric properties of glucose aqueous solutions with different glucose concentrations at lower frequencies.

This research aims to study the influence of blood glucose concentration on dielectric properties. For this purpose, two types of glucose aqueous solutions are fabricated, deionized water solutions and saline solutions with different glucose concentrations. In section Ⅱ, we briefly illustrate the measurement of dielectric constant and conductivity. Furthermore, the results from the measurement are compared. Section Ⅲ present the methodology for the relationship between the dielectric properties of saline solutions and glucose concentration with a three-order Cole-Cole model and *a second-order polynomial*. Discussion of the result of the experiment is done in section IV and the conclusion in section V.

II. DIELECTRIC PROPERTIES MEASUREMENT AND COMPARISION

A. Measurement of dielectric properties

We prepared deionized water solutions and saline solutions with six different concentrations respectively. As displayed in Fig.1, an impedance analyzer (E4990A) was used to measure dielectric constant and conductivity in the frequency range of 500 KHz to 5MHz at a constant temperature of 25°C. The measurement results are shown in Fig. 2 and Fig .3

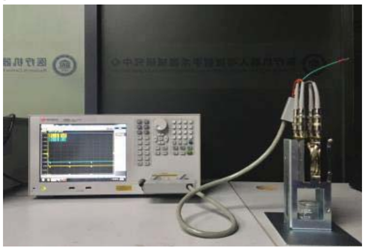
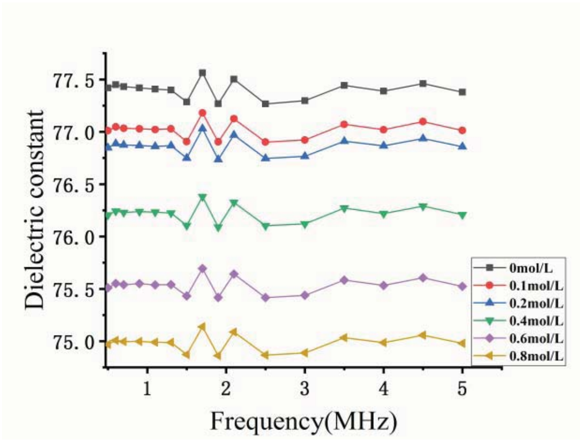


Figure 1.Measurement of dielectric properties



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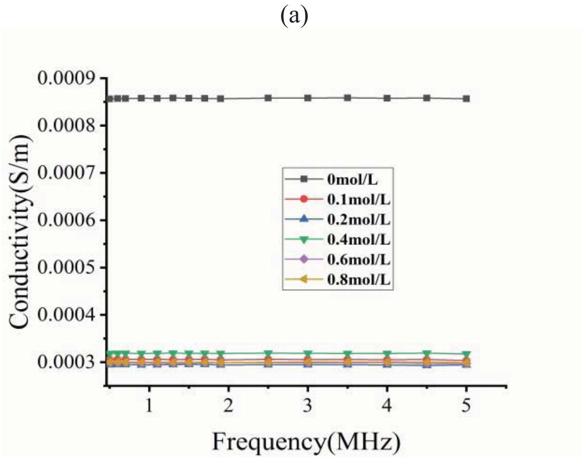
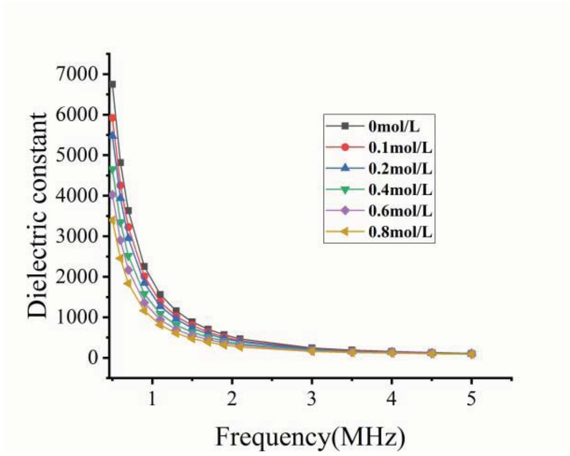
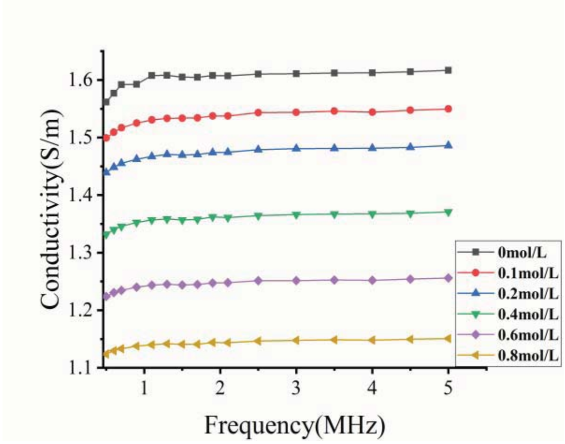


(b)

Figure 2. Measured dielectric constant (a); Conductivity (b) of deionized water solutions



(a)



(b)

Figure 3. Measured dielectric constant (a); Conductivity (b) of saline solutions

B. Comparison of measurement

From the measurement results, it can be seen that the dielectric constant and the conductivity reveal a certain variation with the increase in the concentration. As demonstrated in Fig. 2(a) and Fig. 3(a), the dielectric constant decreases as the glucose concentration increases. Compared with Fig. 2(a), the dielectric constant value of Fig. 3(a) is more similar to the dielectric constant value of human blood[16], which decreases rapidly with increasing frequency. As shown in Fig. 2(b) and Fig. 3(b), the conductivity basically decreases with the increase of the glucose concentration. In Fig. 2(b), when the concentration increased from 0 mol/L to 0.1 mol/L, the conductivity decreased from 0.00085 S/m to 0.0003 S/m. However, when the concentration continues to increase, the conductivity remains at around 0.0003 S/m. The value of conductivity which is too small compared with human blood. Fig. 3(b) illustrates that as the glucose concentration increases, the conductivity decreases uniformly. In the frequency range of 500 KHz to 5MHz, the conductivity of human blood increase from 0.74816 to 1.04[16].

In general, both the dielectric constant and the conductivity of the glucose aqueous solutions decrease as the concentration increases. This is obviously different from the results at high frequencies. At high frequencies, the dielectric constant decreases with increasing glucose concentration, but the conductivity increases with increasing glucose concentration[8]. Between both solutions, as the frequency increases, the value of the dielectric constant of the saline solutions changes closely to human blood[16]. In addition, the conductivity value of deionized water is as low as 0.0003 S/m; the value of conductivity is not obvious with the change of glucose concentration. The conductivity of the saline solution is slightly larger than the dielectric constant of the human blood; its conductivity changes significantly with the glucose concentration. Therefore, in the next section, the saline solution will be selected as the research object. .

III. METHODOLOGY

A. COLE-COLE Model

From comparison of dielectric properties measurement result, saline solutions are more suitable for research. Here, dielectric properties of different saline solutions are computed with third-order Cole- Cole model for each glucose concentration[17]. The Cole–Cole model offers an efficient representation of biological tissues over a wide frequencies and is used to reduce the complexity of the experimental data obtained for various human tissues [17]. The model is given as:

$$\varepsilon^* = \varepsilon'(\omega) - j\varepsilon''(\omega) = \varepsilon_\infty + \sum_{n=1}^{3} \frac{\Delta\varepsilon_n}{1+(jw\tau_n)^{(1-\alpha_n)}} + \frac{\sigma_0}{j\omega\varepsilon_0} \quad (1)$$

Where ω is the angular frequency, ε^* is the complex permittivity to describe the dielectric properties. $\varepsilon'(\omega)$ is the frequency dependent dielectric constant, $\varepsilon''(\omega)$ is the frequency-dependent dielectric loss, n is the order of the Cole–Cole model, ε_∞ is the high frequency dielectric constant, $\Delta\varepsilon_n$ 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_0 is the static ionic conductivity. For computation purpose, the pole broadening parameter α_n is fixed at 0.

B. Quadratic Polynomial Implementation

In order to express the relationship between the dielectric properties of the saline solutions and the glucose concentration, we use MATLAB to perform quadratic polynomial implementation for the parameters from the Cole-Cole model .The quadratic polynomial is given as:

$$\varepsilon_p = a_n x^2 + b_n x + c_n \quad (2)$$

$$\tau_m = a_n x^2 + b_n x + c_n \quad (3)$$

$$\sigma_0 = a_n x^2 + b_n x + c_n \quad (4)$$

Where p = ∞, 1, 2, 3 and m=1, 2, 3. x is the concentration of the glucose in mol/L.a_n,b_n, c_n are the coefficients of the quadratic polynomial. Calculating the parameters for third-order Cole-Cole model of the saline solutions with different glucose concentration is feasible by the fitting equations, that didn't be measured in the experiment.

IV. EXPERIMENTAL RESULTS AND DISCUSSION

Parameters of Cole-Cole model and quadratic polynomial were successfully implemented. The calculated parameters for fitting at each glucose concentration are given in Table I. 0, 0.1, 0.2, 0.4, 0.6, 0.8 are glucose concentrations in mol/L used in experiment. $\varepsilon_\infty, \Delta\varepsilon_1, \tau_1, \Delta\varepsilon_2, \tau_2, \Delta\varepsilon_3, \tau_3, \sigma_0$ are parameters of Cole-Cole model. Obviously, fitted parameter value ε_∞ , τ_1 , τ_2 and τ_3 increases with increasing glucose concentration, but $\Delta\varepsilon_1, \Delta\varepsilon_2, \Delta\varepsilon_3$ and σ_0 decrease with decreasing concentration. The fitting parameters and the coefficients of the quadratic polynomial are shown in Table II. $\varepsilon_\infty, \Delta\varepsilon_1, \tau_1, \Delta\varepsilon_2, \tau_2, \Delta\varepsilon_3, \tau_3, \sigma_0$ are parameters from Cole-Cole model. Therefore, by substituting the value in Table I into (1) and coefficients of the quadratic polynomial in Table II into (2) to (4), the connection between the dielectric properties of saline solutions and glucose concentration can be observed. When glucose concentration is 0 mol/L, the fitting effect is shown in Fig. 4. As the frequency increases, the better the fitting effect as displayed in Fig. 4(a). Fig. 4(b) demonstrates a good fitting result from 500 KHz to 5MHz. Also, the fitting results for parameter ε_∞ and σ_0 with glucose concentration are given in Fig. 5 respectively. As mentioned above, parameter ε_∞among with τ_1, $\tau_2$and τ_3 increase with increasing concentration, parameter σ_0 among with $\Delta\varepsilon_1, \Delta\varepsilon_2, \Delta\varepsilon_3$ decrease with increasing glucose concentration.

TABLE I
PARAMETERS FOR THIRD-ORDER COLE-COLE MODEL FOR EACH GLUCOSE CONCENTRATION

	0	0.1	0.2	0.4	0.6	0.8
ε_∞	2.5	3	3.6	4.2	4.8	6
$\Delta\varepsilon_1$	960	890	850	789	600	520
τ_1 (ns)	272.089	282.921	285.186	308.504	331.856	338.027
$\Delta\varepsilon_2$	1491	1400	1345	1298	1200	1086
τ_2 (ns)	272.119	282.975	285.314	308.564	331.989	338.117
$\Delta\varepsilon_3$	4340	4200	3853	3789	3600	3545
τ_3 (ns)	272.169	282.996	285.295	308.481	331.932	338.132
σ_0 (S/m)	1.4	1.34	1.29	1.19	1.1	1.0

The efficiency of the model is performed using coefficient of determination which measures the ratio of the fitted value to measured value, it is defined as:

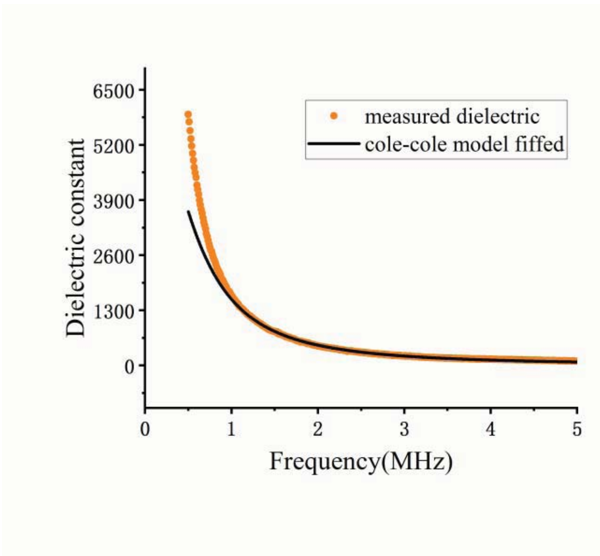
$$R^2 = \frac{\sum_{i=1}^{n}\left(Y_i - y_i^{'}\right)^2}{\sum_{i=1}^{n}\left(y_i - y_i^{'}\right)^2} \tag{5}$$

Where n is the number of samples, Y_i is fitted value, y'_i is average value, y_i is the measured value. R^2 is the coefficient of determination. R^2 should vary between 0 and 1. A value close to 1 indicates a good fit.

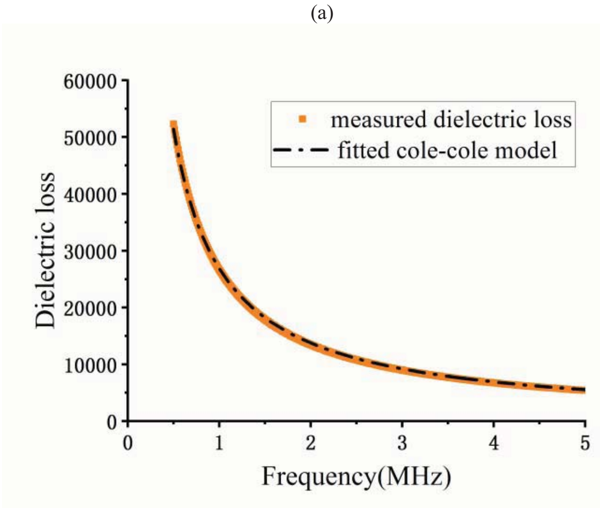
The coefficient of determination for the Cole-Cole model for each glucose concentration from 0 to 0.8 in mol/L is 0.99876, 0.99909, 0.99916, 0.99939, 0.99941, and 0.99964 respectively. Table III shows the coefficient of determination for each quadratic polynomial.

TABLE II
COEFFICIENTS OF THE QUADRATIC POLYNOMIAL FOR THE GLUCOSE-DEPENDENT COLE-COLE PARAMETERS

	a_n	b_n	c_n
ε_∞	0.3592	3.8093	2.6110
$\Delta\varepsilon_1$	-128.3260	-450.7514	951.8087
τ_1(ns)	-23.795	106.8310	270.5050
$\Delta\varepsilon_2$	146	-474.8	146.66
τ_2(ns)	-24.0510	107.1049	270.5432
$\Delta\varepsilon_3$	134.62	-204.30	433.14
τ_3(ns)	-23.3814	106.5064	270.6055
σ_0(S/m)	0.0520	-0.5340	1.3964

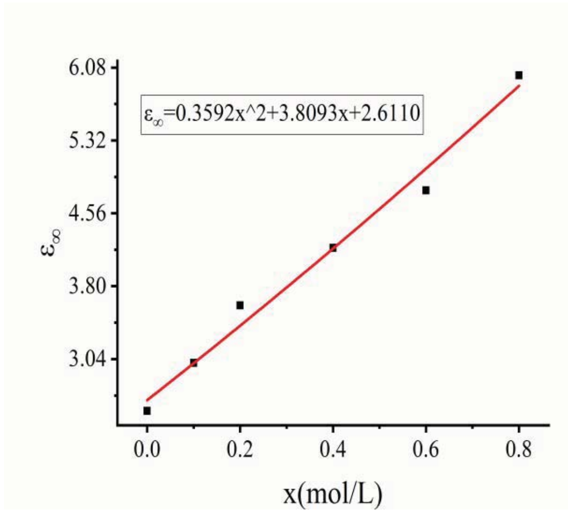


(a)



(b)

Figure 4 Dielectric properties of saline solutions without glucose fitted by a third-model Cole-Cole model at 500 KHz-5MHz



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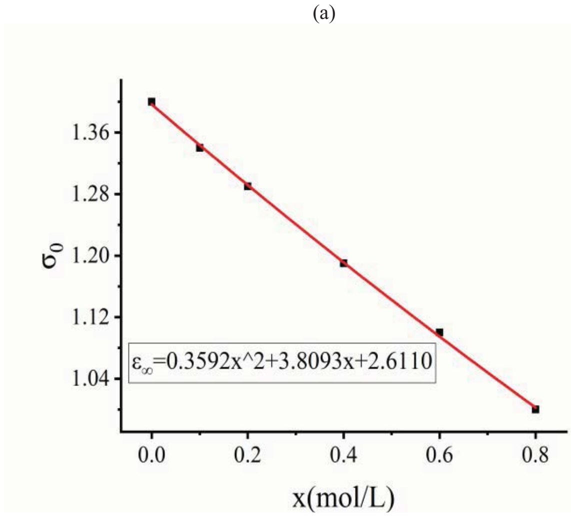

(b)

Figure 5 the parameters of Cole-Cole model: (a) ε_∞; (b) σ_0 fitted at 500 KHz-5MHz

TABLE III
THE COEFFICIENT OF DETERMINATION FOR EACH QUADRATIC POLYNOMIAL

	ε_∞	$\Delta\varepsilon_1$	τ_1	$\Delta\varepsilon_2$	τ_2	$\Delta\varepsilon_3$	τ_3	σ_0
R^2	0.98	0.97	0.97	0.97	0.97	0.87	0.97	0.99

V. CONCLUSION

In this paper, we presented the effect of glucose concentration on the dielectric properties of saline solutions and deionized water solutions with different glucose concentrations at 500 KHz-5MHz. The result showed that both the dielectric constant and the conductivity of two types of glucose aqueous solutions decrease with the increase of glucose concentration in this frequency band which is different from the result in the high frequency band. By comparing the two solutions with human blood, it was found that the dielectric properties of physiological saline are closer to that of human blood. In the study, saline solution was adopted as research object. Therefore, we performed a third-order Cole-Cole model for the dielectric properties of saline solutions with different glucose concentrations, and the coefficient of determination R^2 was as higher as 0.99. In addition, we also implemented quadratic polynomial for the parameters in the Cole-Cole model. Finally, the result from this experiment successfully proves the relationship between dielectric properties and the change in glucose concentration of saline solution. The result indicates that the NBGM at low frequencies has potentials in practical applications.

ACKNOWLEDGMENT

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