Analysis of glucose-dependent dielectric properties of aqueous-based solution: A proof of concept

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Abstract
In spite of widespread research and exploration, the status of non-invasive blood glucometer for diabetic people is far from satisfactory. This unlocks the prospect for further significant research in the field of non-invasive blood glucose sensing. An approach towards the research on the development of non-invasive blood glucometer relies on the establishment of correlation, if any, exists between the dielectric properties of blood and the blood glucose level. In this context, the in-vitro study is undertaken as a proof of concept using a standard liquid-dielectric-test-fixture. The research is conducted to analyse the variation in dielectric properties of aqueous-based solution with respect to glucose concentration by utilising test fixture. The employed measurement set-up and the procedure used for the estimation of dielectric properties (complex-relative-permittivity and dissipation factor) of the solution under test are presented. The measurement set-up is validated by determining the dielectric properties of the reference liquid. The evaluation of uncertainty-in-measurement in the complex-relative-permittivity and dissipation factor is also provided in detail. However, the variation in dielectric properties is found to be small under tested conditions, and the in-vitro study conducted out in the perspective of proof of concept has provided an insight that the change in glucose concentration results in quantifiable variation in dielectric properties.

1 | INTRODUCTION

Diabetes Mellitus is one of the most challenging health problems of the 21st century. In 2015, India was second to China in the list of top ten countries in the world, with 69.2 million adults with diabetes [1]. By 2040, this figure will increase to 123.5 million, which is a matter of serious concern for India. Diabetes is a metabolic disorder characterised by the body's inability to maintain blood glucose level within the normal physiological range. The blood glucose level is defined as the quantity of glucose in the blood and is measured usually in milligram per decilitre (mg/dL). The recommended pre-prandial blood glucose level should be less than 110 mg/dL in blood plasma and the post-prandial level should not be higher than 140 mg/dL in blood plasma [2].

The condition of diabetes occurs either when the pancreas is incapable of producing insulin hormone or when the body is unable to utilise the produced insulin effectively. The ‘insulin’ produced by the pancreas helps glucose, present in the blood to move from the blood stream into the body cells. In the absence or lack of normal functioning of this carrier hormone as in the case of diabetes, the level of glucose in the blood increases, resulting in a metabolic disorder called 'diabetes mellitus'. The unattended diabetes can cause life-threatening complications. The complications can be reduced by adopting a correct and efficient diabetic management plan. The important requirement for the right management of diabetes is to have a tight control on the food habits and the regular monitoring of blood glucose level. The monitoring in-turn requires appropriate blood glucose meters.

At present, people with diabetes are bound to use electrochemical-based invasive metre to examine their blood glucose levels. The invasive blood glucometer equipped with a pointing device (called lancet) has occupied place in the life of diabetes people because of several advantages such as; high accuracy and low cost; easy availability and ability to provide blood glucose level quickly. However, the requirement of pricking of finger for the extraction of blood sample makes such
meters uncomfortable and painful for them. Hence, the race for implementing non-invasive technology to develop non-invasive glucometer (pain-free and blood-less) has begun from the last few decades. Pendra based on electrical bioimpedance technique was developed in the form of a wristwatch. It was also brought into the market for commercial use, but due to various limitations associated with it, its manufacturing stopped [3]. Based on reverse iontophoresis technique [4], another non-invasive device named GlucoWatch was developed. Its performance was satisfactorily evaluated in trials conducted at clinics and homes [5]. However, due to some limitations associated with it like inaccuracy in measurement results due to subject’s movement, the requirement of calibration after every use etc., the use of GlucoWatch was stopped in July 2007 [6]. In spite of extensive research, none of the developed non-invasive device is able to substitute conventional invasive glucometer [7, 8]. This opens up a great prospect and challenge for further consequential research and investigation in this field.

It is therefore considered of interest to research and exploration for the implementation of non-invasive technology for blood glucose monitoring using a suitable sensor. The elementary hypothesis in the research is that the change in blood glucose level would result in the variation in dielectric properties of blood and its underlying biological tissues.

2.1 CORRELATION BETWEEN DIELECTRIC PROPERTIES AND GLUCOSE CONCENTRATION

The dielectric properties such as the complex-relative-permittivity ($\varepsilon_r$), dissipation factor, or loss tangent ($\tan \delta$) and electrical impedance play a vital role in assessing the physiological state of the biological tissue [9, 10]. In the material possessing dielectric properties, the majority of the charge carriers are bound, due to which they cannot contribute to the conduction of current. However, when the external electric field is applied across such material, the positively charged carriers are forced to align in the direction of an applied electric field and the negatively charged carriers are forced to align in the opposite direction. Because of this dislocation of the carriers, the electric dipoles build up that produce their internal electrical field, which opposes the externally applied electric field. The process of building up of electric dipoles is known as dielectric polarisation. It can be thus stated that the dielectric material polarises under the influence of an externally applied electrical field. The ability of the dielectric material to be polarised under the influence of an applied electrical field is defined by the complex-relative-permittivity ($\varepsilon_r$) [11], given by (1).

$$\varepsilon_r = \varepsilon_r' - j\varepsilon_r''$$  \hspace{1cm} (1)

where $\varepsilon_r'$, the real component of $\varepsilon_r$, represents electrical energy storage capability of material in the presence of an external electric field and is defined by the term dielectric constant while the imaginary part, $\varepsilon_r''$, represents loss factor which accounts for the loss in the dielectric material.

The dissipation factor or loss tangent ($\tan \delta$) [11] can be defined as the ratio of imaginary and real components of complex-relative-permittivity and can be represented by (2).

$$\tan \delta = \frac{\varepsilon_r''}{\varepsilon_r'}$$  \hspace{1cm} (2)

The variation in the permittivity with respect to change in blood glucose concentration was observed at a frequency below 10 MHz [12]. The work reported in [13] claimed that change in glucose concentration in blood indirectly produces variation in the dielectric properties of the subject’s blood and its underlying tissues over a frequency range from 1 to 200 MHz. Hayashi et al. [14] reported the results of their in-vitro study on erythrocytes that were exposed to varying glucose concentrations. Another research group attempted to demonstrate the correlation between complex permittivity and glucose concentration in the kHz frequency range [15]. Based on the literature survey, it appears that change in glucose concentration in blood would produce change in its dielectric properties [16–18]. However, to determine the most appropriate frequency range for the estimation of variation in dielectric properties due to the change in glucose concentration, it is planned to undertake the proof of concept study to demonstrate the correlation, if any existed between the dielectric properties of blood and blood glucose level. In this context, a series of in-vitro experiments are performed on different types of aqueous-based solutions having different Dextrose-glucose (D-glucose) concentrations using different types of measuring systems over a wide range of frequencies varying from audio to microwave spectrum. The first experiment based on the open-ended coaxial method was conducted to observe the effect of D-glucose concentration on the dielectric properties of ringer lactate (RL) solution from 100 MHz to 2.5 GHz as reported in previous published work [19, 20]. The RL was chosen in the experiment as its chemical composition is similar to interstitial fluids [21]. The variation was observed in the dielectric properties (dielectric constant and loss factor) of RL solution with respect to D-glucose concentration. Another experiment was performed to estimate the glucose-dependent electrical impedance parameters (capacitance and conductance) of aqueous-based solution using a customised four-terminal-pair (4TP) configuration in a frequency range varying from 1 to 100 kHz [22]. The experiment established that there was a considerable dependence of glucose concentration on impedance parameters of solution under test.

The third experiment conducted to analyse the glucose-dependent dielectric properties of aqueous-based solution using standard liquid-dielectric-test-fixture (LDTF) (Model: Keysight 16452A) is highlighted in the present manuscript. The dielectric properties include complex-relative-permittivity (comprising dielectric constant and dielectric loss) and dissipation factor. The in-vitro experiment is performed on solutions prepared using de-ionised (DI) water (Make: Millipore MilliQ...
Element System) with different concentrations varying from 50 to 400 mg/dL. The LDTF is compliant as per the ASTM-150 standard. It employs a parallel-plate capacitive technique in which the solution is sandwiched between high and low electrodes of the fixture resulting in the development of equivalent parallel-plate capacitance ($C_p$) and resistance ($R_p$) parameters, which are measured using precision LCR meter (Model: Agilent E4980A). These parameters are thereafter used to determine complex-relative-permittivity and dissipation factor of solution under test. Before proceeding with the experiment procedure, the measurement set-up is validated by determining the dielectric properties of the reference liquid. In the present research work, DI water is used as a reference liquid. The equivalent parameters: $C_p$ and $R_p$ of DI water are measured at 1 MHz using LCR meter. After carrying out the validation process, $C_s$ and $R_s$ of aqueous-based solutions with different D-glucose concentrations are measured. The evaluation of uncertainty in measurement in the complex-relative-permittivity and dissipation factor is performed using uncertainty budgets that provides in detail all the sources of uncertainty taken into account.

3 | EXPERIMENTAL SET-UP

The experimental setup employed to analyse the dielectric properties of aqueous-based solution with respect to D-glucose concentration using LDTF is illustrated in Figure 1. The solution under test is poured through inlet smoothly up to the mark shown in the setup to avoid any bubble creation. The LCR meter supports 4TP measurement, which minimises the prevalent secondary effects due to stray capacitances and mutual or self-inductances of connecting leads. In addition, it is metrologically traceable to the National Standard of Impedance maintained at the "National Measurement Institute" of India, the CSIR-National Physical Laboratory (CSIR-NPL) [23–26]. The LDTF is fitted with 4TP Sub-Miniature versions A (SMA) connectors to support 4TP measurement as shown in Figure 1.

There is one shorting plate, four spacers with thickness varying from 1.3 to 3.0 mm, four SMA to Bayonet Neill–Concelman (BNC) adapters, and a fixture stand provided with LDTF. The spacers are available to vary the space or gap between high and low electrodes of the fixture and a stand is provided to keep the fixture in a stable position. The test lead set (Model: Agilent 16048A) is used to establish the connection between LDTF and LCR meter. The tip of the lead is equipped with BNC (m) type connector and is provided with a board having four BNC (f) type connectors. The LDTF is placed inside the temperature air-bath (Model: Guildline 5032) which provides a uniform temperature ($25^\circ$C) with stability of less than 0.02 $^\circ$C over 24 h, thereby reducing the uncertainty contribution from temperature effects. The temperature sensor of the air-bath is metrological traceable to the National Standard of Temperature maintained at CSIR-NPL India. The LCR meter and air-bath are connected to a workstation through IEEE 488.2 (also known as General Purpose Interface Bus (GPIB)) interface. The experiment is supported by a measurement automation program module developed in National Instrument’s Laboratory Virtual Instrument Engineering Workbench (also known as LabVIEW). The module is developed by utilising Standard Commands for Programmable Instruments using Virtual-Instrument-Software-Architecture. The module is responsible for controlling and configuring LCR meter and air-bath. It also represents and exports, the observations to a specified file for post-measurement analysis.

4 | EXPERIMENTAL PROCEDURE

The experimental procedure to determine the dielectric properties of aqueous-based solution using LDTF is preceded with the three-step compensation process utilising SHORT standard, OPEN standard, and a reference liquid (De-ionised water). The compensation is performed in order to reduce the parasitic capacitances and inductances that may affect the accuracy of the measurement. The SHORT compensation is performed by positioning a shorting plate between the two electrodes of LDTF. After that, using a short compensation function of the LCR meter, errors caused by the residual components of LDTF are reduced. For the OPEN compensation, the shorting plate is removed and the reference capacitance ($C_0$) is measured using LCR meter over a frequency range varying from 100 kHz to 1 MHz. The 3 mm spacer provides 5.5 pF of the reference capacitance with an accuracy of $\leq$ 10% at 1 MHz. The spacer having a thickness of 3 mm provides the gap of 2.0 mm $\pm$ 12 $\mu$m between the electrodes [27].

After performing SHORT and OPEN compensations, the DI water is used as a reference liquid. The parallel-plate capacitance and resistance of DI water are measured at 1 MHz using LCR meter, which are thereafter used to compute its dielectric properties ($\varepsilon_r$ and $\tan \delta$). After carrying out a three-step compensation process, $C_p$ and $R_p$ of aqueous-based solutions with different D-glucose concentrations (varying from 50 to 300 mg/dL) are measured using the experimental setup described earlier.
5 | COMPUTATION OF DIELECTRIC PROPERTIES OF LIQUID SOLUTION UNDER TEST

The complex-relative-permitivity can be represented as $\varepsilon_{rs}$ in terms of three measured parameters [28]: the reference capacitance ($C_0$), the equivalent parallel-plate capacitance, ($C_p$) and resistance ($R_p$) and is expressed as (3).

$$\varepsilon_{rs} = \varepsilon_{rs}^' - j\varepsilon_{rs}^"$$

(3)

where $\varepsilon_{rs}^'$ and $\varepsilon_{rs}^"$ are real and imaginary components of $\varepsilon_{rs}$ and can be represented by (4) and (5), respectively

$$\varepsilon_{rs}^' = \frac{dC_p}{\omega R_pC_0} = \frac{C_p}{C_0}$$

(4)

$$\varepsilon_{rs}^" = \frac{d}{\omega R_pC_0} = \frac{1}{\omega R_pC_0}$$

(5)

In (4) and (5), $d$ is the distance between two electrodes of LDTF, $A$ is the area of an electrode, $\omega$ is the angular frequency (rad/s) and $\varepsilon_0$ is absolute permittivity equal to 8.854 187 817 $\times 10^{-12}$ $F/m$.

Using (4) and (5), the $\tan\delta$ can be expressed by (6)

$$\tan\delta = \frac{\varepsilon_{rs}^"}{\varepsilon_{rs}^'} = \frac{1}{\omega R_pC_p}$$

(6)

The magnitude of $\varepsilon_{rs}$ and $\tan\delta$ can be written by (7) and (8), respectively.

$$|\varepsilon_{rs}| = \sqrt{\frac{C_p^2}{C_0^2} + \frac{1}{(\omega R_pC_0)^2}}$$

(7)

$$\tan\delta = \frac{1}{\omega R_pC_p}$$

(8)

The measured results of $C_0$ and $C_p$ include measurement error due to the formation of fringe capacitance on the edges of the electrodes. This effect of fringe capacitance (also called stray capacitance) is minimised by using the correction coefficient $\alpha$ (as defined by (9)) [28] in the computation of dielectric properties of L-SUT.

$$\alpha = \frac{100|\varepsilon_{rs}|}{97.0442|\varepsilon_{rs}| + 2.9558}$$

(9)

The expression for $\varepsilon_r$ can be rewritten as follows by (10), taking into account the correction coefficient.

$$\varepsilon_r = \alpha\varepsilon_{rs}^' - j\alpha\varepsilon_{rs}^" = \frac{C_p}{C_0} - j\frac{\alpha}{\omega R_pC_0}$$

(10)

6 | OBSERVATIONS

The measured values of $C_0, C_p$, and $R_p$ for the DI water along with the associated expanded uncertainty ($u_e$) in every parameter is illustrated in Table 1 which are measured at 1 MHz using the setup defined earlier. The uncertainty-in-measurement has been evaluated as per the 'ISO Guide to the expression of uncertainty-in-measurement' (GUM) document [29].

Table 2 summarises the computed values of $\varepsilon_r^'$, $\varepsilon_r^"$, and $\tan\delta$ along with an associated $u_e$ for reference liquid. The values of $\varepsilon_r^'$, $\varepsilon_r^"$, and $\tan\delta$ are found to be comparable with the results reported in [30]. Table 3 summarises the glucose-dependent measured parameters ($C_p$ and $R_p$) and computed

| TABLE 1 | Measured $C_0$, $C_p$, and $R_p$ for DI water @ 1 MHz |
|----------------------------------|-----------------|-----------------|
| Parameters | Value            | \(\pm\) Value   |
| $C_0 \pm u_e(C_0), pF$ | 5.27 $\pm$ 0.45  |
| $C_p \pm u_e(C_p), pF$ | 401.20 $\pm$ 1.21 |
| $R_p \pm u_e(R_p), \Omega$ | 4487.29 $\pm$ 8.39 |

| TABLE 2 | $\varepsilon_r^'$, $\varepsilon_r^"$, and $\tan\delta$ for reference liquid |
|----------------------------------|------------------|------------------|
| Parameter | Value             | \(\pm\) Value   |
| $\varepsilon_r^' \pm u_e(\varepsilon_r^')$ | 78.41 $\pm$ 6.66  |
| $\varepsilon_r^" \pm u_e(\varepsilon_r^" )$ | 6.93 $\pm$ 0.59  |
| $\tan\delta \pm u_e(\tan\delta)$ | 0.09 $\pm$ 0.02  |

| TABLE 3 | $\varepsilon_r^'$, $\varepsilon_r^"$, and $\tan\delta$ for DI water solutions |
|----------------------------------|------------------|---------------|------------------|------------------|
| D-glucose concentration (mg/dL) | $C_p$, pF | $R_p$, $\Omega$ | $\varepsilon_r^'$ | $\varepsilon_r^"$ | $\tan\delta$ |
| 0 | 1801.8 | 772.75 | 59.70 | 68.24 | 1.143 |
| 50 | 1744.8 | 1051.62 | 58.86 | 30.38 | 0.516 |
| 100 | 1781.7 | 1444.27 | 59.03 | 36.51 | 0.619 |
| 150 | 1771.0 | 1615.76 | 59.03 | 32.63 | 0.556 |
| 200 | 1776.1 | 1682.83 | 58.84 | 31.33 | 0.532 |
| 250 | 1776.6 | 1735.79 | 58.86 | 30.38 | 0.516 |
| 300 | 1775.0 | 1766.63 | 58.80 | 29.85 | 0.507 |
DISCUSSION AND SUMMARY

The in-vitro study is undertaken as a proof of concept by conducting the series of experiments on different types of aqueous-based solutions over different frequency to investigate the variation in dielectric properties of solutions with respect to D-glucose concentration. In the present manuscript, the in-vitro experiment performed to analyse the glucose-dependent dielectric properties of aqueous-based solution using LDTF is presented. The experimental set-up employed is validated by determining the dielectric properties of the reference liquid. The uncertainty-in-measurement in the complex-relative-permittivity of DI water is also evaluated for different DI water solutions at 100 kHz. The detailed analysis of uncertainty-in-measurement is provided in the following section of the manuscript.

It is observed that $\varepsilon_r''$ and $\tan\delta$ decreased significantly while $R_p$ increased with D-glucose concentration. However, $\varepsilon_r'$ did not show a significant dependence on the change in glucose concentration because of the various residual and parasitic components associated with LDTF.

The uncertainty analysis for dielectric constant, dielectric loss, and $\tan\delta$ is performed for the reference liquid. The sources of uncertainty taken into account are the uncertainty-in-measurement in $C_0$, $C_p$, and $R_p$. For the evaluation of uncertainty-in-measurement in $C_0$, $C_p$, and $R_p$, various sources of uncertainty are taken into account such as repeatability in measurement, also termed as Type A uncertainty, temperature coefficient of solution under test, uncertainty of LCR meter. For instance, Table 4 presents the uncertainty budget for $C_p$ measured for the reference liquid at 1 MHz.

Table 5 and Table 6 illustrated the uncertainty budgets for computed $\varepsilon_r'$ and $\varepsilon_r''$ for the reference liquid, respectively.

### Table 4 Uncertainty budget for $C_p$

| Parameter | Estimates | $\pm$ Limits | Probability distribution | Relative standard uncertainty | Sensitivity coefficient | Uncertainty contribution |
|-----------|-----------|--------------|--------------------------|-----------------------------|-------------------------|--------------------------|
| Repeatability | $-$ | $-$ | Normal, A | 0.066 pF | 1 | 4.33E-27 F² |
| Temperature coefficient | $-$ | $-$ | Normal, B | 0.115 pF/°C | 0.1°C | 1.33E-28 F² |
| Uncertainty of Standard | 400 pF | 1.20 pF | Rectangular | 0.60 pF | 1 | 3.60E-25 F² |
| $C_p$ | 401.20 pF | Expanded uncertainty ($k = 2$) | | | | |

### Table 5 Uncertainty budget for $\varepsilon_r'$

| Parameter | Estimates | $\pm$ Limits | Probability distribution | Relative standard uncertainty | Sensitivity coefficient | Uncertainty contribution |
|-----------|-----------|--------------|--------------------------|-----------------------------|-------------------------|--------------------------|
| $\alpha$ | 1.03 | 3.48E-05 | Gaussian | 1.74E-05 | 76.1 | 1.76E-06 |
| $C_p$ | 401 pF | 1.22 pF | Gaussian | 0.612 pF | 1.95E+11 F⁻¹ | 0.0143 |
| $C_0$ | 5.27 pF | 0.447 pF | Gaussian | 0.224 pF | 1.33E-28 F⁻² | 11.1 |
| $\varepsilon_r'$ | 78.41 | Expanded uncertainty ($k = 2$) | | | | 6.66 |

parameters ($\varepsilon_r'$ and $\varepsilon_r''$) for different DI water solutions at 100 kHz. The detailed analysis of uncertainty-in-measurement is provided in the following section of the manuscript.

% confidence level. It may be concluded there is an effect of glucose concentration on the dielectric properties of DI water solution at low frequencies. Although the variation in dielectric properties is small under the tested conditions, the findings of the series of in-vitro experiments carried out in the perspective of proof of concept have provided an insight that the change in glucose concentration results in quantifiable variation in dielectric properties of solution under test over a different range of frequencies. Concisely, the three sets of experiments have given an insight into the measurements of glucose concentration can be performed more accurately either in the low-frequency range (1 kHz - 100 kHz) or in microwave range (1.0 GHz - 2.5 GHz). One may therefore concentrate on designing and developing sensor in these frequency ranges.

The results of experiments served as a proof of concept and motivated us to design and develop a suitable microwave sensor that would be employed for non-invasive blood glucose monitoring. It will be utilised for determining variations in dielectric properties of biological tissue under test due to the change in blood glucose level. After an in-depth analysis of the findings of in-vitro study, it is observed that the precision of measurement is better in a frequency range varying from 1.0 to 2.5 GHz.

Therefore, microwave spectrum having a frequency ranging from 300 X 10⁶ Hz to 300 X 10⁹ Hz with equivalent-electrical-wavelength, varying from 1000 to 1 mm will be selected for the design and development of the suitable microwave sensor in the future. The ability of electromagnetic field to penetrate deeper into the biological tissues and its non-ionising effect on them is providing the basis of microwave sensors in medical applications [31]. The microwave sensor does not require a physical contact with the biological tissue under test as the signals are coupled with it through electromagnetic waves. Thus, such a sensor is likely to provide a better solution to non-invasive blood glucose sensing. The details of the sensor including its modelling, designing, simulation, and characterisation will be provided in the follow-up paper.
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APPENDIX
The expressions for the standard combined uncertainty [29] in the real and imaginary components of ε′, of reference liquid can be written by (13) and (14), respectively:

\[ u(\varepsilon'') = \sqrt{\left(\varepsilon''_{c_{p}, C_p}\right)^2 + \left(\varepsilon''_{c_{0}, C_0}\right)^2} \]

(\text{A.1})
\[
\frac{\partial u}{\partial (\varepsilon_r^\prime)} = \sqrt{(c_{\varepsilon_r^\prime-C_0}^2) \cdot u(C_0)^2 + (c_{\varepsilon_r^\prime-R_p}^2) \cdot u(R_p)^2 + (c_{\varepsilon_r^\prime-R_p}^2) \cdot u(C_0)^2}
\]
\[(A.2)\]

where \(u(C_0), u(R_p), u(C_0)\): Standard uncertainty \((k = 1)\) in \(C_p, R_p\) and \(C_0\), respectively.

\(u(\alpha)\): Standard uncertainty in \(\alpha\) and can be expressed by (15):
\[
u(\alpha) = \sqrt{(c_{\alpha-[\varepsilon_r]})^2 \cdot u([\varepsilon_r])^2}
\]
\[(A.3)\]

where \(c_{\alpha-[\varepsilon_r]}\) represents sensitivity coefficient [29] obtained by partial differentiation of (9) with respect to \([\varepsilon_r]\) and is expressed by (16)
\[
c_{\alpha-[\varepsilon_r]} = \frac{\partial \alpha}{\partial [\varepsilon_r]} = \frac{100}{97.0442 [\varepsilon_r] + 2.9558} - \frac{970.442 [\varepsilon_r]}{(97.0442 [\varepsilon_r] + 2.9558)^2}
\]
\[(A.4)\]

\(u([\varepsilon_r])\): standard uncertainty \((k = 1)\) in \([\varepsilon_r]\) and is defined by (17)
\[
u([\varepsilon_r]) = \sqrt{(c_{[\varepsilon_r]-C_0})^2 \cdot u(C_0)^2 + (c_{[\varepsilon_r]-R_p}^2) \cdot u(R_p)^2 + (c_{[\varepsilon_r]-R_p}^2) \cdot u(C_0)^2}
\]
\[(A.5)\]

where \(c_{[\varepsilon_r]-C_0}, c_{[\varepsilon_r]-C_0}, c_{[\varepsilon_r]-R_p}, c_{[\varepsilon_r]-R_p}\): Sensitivity coefficients obtained by partial differentiation of (7) with respect to \(C_0, C_p, \) and \(R_p\) respectively, and are given as follows by (18), (19) and (20)
\[
c_{[\varepsilon_r]-C_0} = \frac{\partial [\varepsilon_r]}{\partial C_0} = -\left(\frac{C_p^2}{C_0^3} + \frac{1}{\omega R_p C_0} \right)
\]
\[(A.6)\]

\[
c_{[\varepsilon_r]-C_0} = \frac{\partial [\varepsilon_r]}{\partial C_0} = \frac{C_p}{C_0^2 \sqrt{\left(\frac{C_p}{C_0} \right)^2 + \frac{1}{\omega R_p C_0}^2}}
\]
\[(A.7)\]

\[
c_{[\varepsilon_r]-R_p} = \frac{\partial [\varepsilon_r]}{\partial R_p} = \frac{1}{\omega R_p C_0^2}
\]
\[(A.8)\]

\[
c_{[\varepsilon_r]-\alpha} = \frac{\partial [\varepsilon_r]}{\partial \alpha} = \frac{C_p}{C_0}
\]
\[(A.9)\]

\[
c_{[\varepsilon_r]-R_p} = \frac{\partial [\varepsilon_r]}{\partial R_p} = \frac{C_p}{C_0}
\]
\[(A.10)\]

\[
c_{[\varepsilon_r]-\alpha} = \frac{\partial [\varepsilon_r]}{\partial \alpha} = -\frac{\alpha C_p}{C_0^2}
\]
\[(A.11)\]

\(c_{[\varepsilon_r]-\alpha}, c_{[\varepsilon_r]-R_p}, c_{[\varepsilon_r]-C_0}\) are the sensitivity coefficients obtained by partial differentiation of (12) with respect to \(\alpha, R_p\), and \(C_0\) and can be expressed by (21), (22) and (23), respectively.

\[
c_{[\varepsilon_r]-\alpha} = \frac{\partial [\varepsilon_r]}{\partial \alpha} = \frac{1}{\omega R_p C_0}
\]
\[(A.12)\]

\[
c_{[\varepsilon_r]-R_p} = \frac{\partial [\varepsilon_r]}{\partial R_p} = -\frac{\alpha}{\omega C_0 (R_p)^2}
\]
\[(A.13)\]

\[
c_{[\varepsilon_r]-C_0} = \frac{\partial [\varepsilon_r]}{\partial C_0} = -\frac{\alpha}{\omega R_p C_0 (R_p)^2}
\]
\[(A.14)\]

For the evaluation of uncertainty in \(\tan \delta\) for DI water tested in LDTF, its combined standard uncertainty can be expressed by (27)
\[
u(\tan \delta) = \sqrt{(c_{\tan \delta, \varepsilon_r^\prime})^2 \cdot u(\varepsilon_r^\prime)^2 + (c_{\tan \delta, \varepsilon_r^\prime})^2 \cdot u(\varepsilon_r^\prime)^2}
\]
\[(A.15)\]

where \(c_{\tan \delta, \varepsilon_r^\prime}\) and \(c_{\tan \delta, \varepsilon_r^\prime}\) are sensitivity coefficients obtained by partial differentiation of (2) with respect to \(\varepsilon_r^\prime\) and \(\varepsilon_r^\prime\), respectively, and can be expressed by (28) and (29), respectively.

\[
c_{\tan \delta, \varepsilon_r^\prime} = \frac{\partial \tan \delta}{\partial \varepsilon_r^\prime} = \frac{1}{\varepsilon_r^\prime}
\]
\[(A.16)\]

\[
c_{\tan \delta, \varepsilon_r^\prime} = \frac{\partial \tan \delta}{\partial \varepsilon_r^\prime} = \frac{-\varepsilon_r^\prime}{(\varepsilon_r^\prime)^2}
\]
\[(A.17)\]