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Broadband RF Impedance Spectroscopy in Micromachined Microfluidic Channels

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Abstract— **Impedance spectroscopy in the radio frequency range from 100 MHz to 20 GHz can reveal the dielectric relaxations of biological and chemical solutions. S-parameters for a coplanar waveguide are derived. To perform these measurements, a coplanar waveguide device was fabricated on a conventional FR-4 substrate for fluid interrogation. The microfluidic channel was formed by milling conventional waveguides and laser-cutting channels in the dielectric substrate. Measurements using this device were performed on standards: deionized water, isopropyl alcohol, and air. These measurements were compared to those taken with a conventional dielectric probe. The results demonstrate the ability of the fabricated device to extract varying transmission parameters due to changing sample properties.**

I. Introduction

Impedance spectroscopy has been used for many years to probe the electrical properties of materials and, in particular, liquids of biological relevance [1]. The charge structure of proteins, size, and overall shape can be extracted from dielectric relaxation data [2]. Impedance measurements are attractive for biomedical sensors because the transduction of electrical signals is relatively straightforward for integrated devices. Thus, they are used in various configurations for monitoring bacteria or counting cells [3], [4].

Impedance measurements can be performed over many decades of frequency, from sub-Hz to THz. Various physical mechanisms are probed on different timescales and thus choice of frequency depends on the phenomena that will be analyzed. Radio frequency (RF) impedance spectroscopy, examining the dielectric relaxation of proteins in solution, is a low-resolution experiment when compared to techniques such as nuclear magnetic resonance (NMR) [5]. However, its advantage lies in its simplicity, low cost, and speed at which experiments can be performed. The technique also has the potential to be implemented in highly-parallelized assays.

Most dielectric spectroscopy experiments must be performed in solutions of low ionic strength because high conductivity reduces the phase angle between the real and imaginary parts of the impedance and the series impedance of the electrodes becomes a serious difficulty [6]. This is most problematic in the kHz-low MHz range. However, in the RF range the influence of polarization is much less pronounced [7]. Thus, higher ionic strength fluids can be used.

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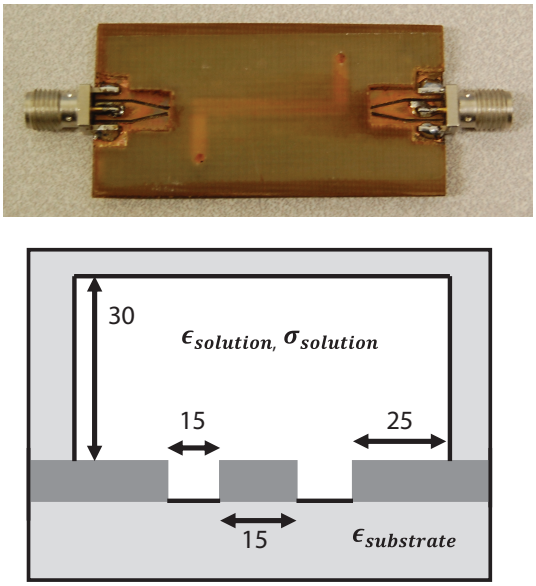

Fig. 1. Photograph (top) and cross-section schematic (bottom) of the RF impedance spectrometer. Dimensions are in mil. The spectrometer is made out of FR-4 with a 1 ounce copper layer, which translates to an effective thickness of 1.4 mil.

Recently, microfluidic RF impedance measurements have been demonstrated using devices fabricated using conventional photolithography to form metal waveguides on glass substrates with microfluidic channels made of cast polydimethylsiloxane (PDMS) [8], [9], [10] or a combination of fused silica capillary tubing and conventional waveguides [11]. In this paper, we aim to demonstrate low-cost fabrication of a RF liquid impedance measurement device (shown in Fig. 1) using conventional materials and traditional milling and laser-cutting methods.

II. Theory

The device geometry was designed so that the electric field between transmission line conductors passes through the solution under test, thereby making the impedance characteristics of the waveguide sensitive to changing sample electrical properties. To allow close contact between a small solution volume over a relatively large signal propagation length, the sensor was fabricated using coplanar waveguide (CPW). Such a geometry naturally lends itself to sub-milliliter volume requirements, in contrast to coaxial termination probes [12]. Similar to an optical path length, the sensitivity to the liquid conditions can increase with the interrogation length.

Here, a simple method is employed to study the sensi-

tivity of the impedance spectrometer to changes in solution electrical properties. CPW propagation is governed by an effective permittivity which depends on the transmission line geometry, dielectric substrate, and dielectric constant of the material above the transmission line [13]. We will parameterize the effect of sample on the effective permittivity according to

$$\epsilon_{\text{eff}} = \alpha \epsilon_{\text{eff},0} \tag{1}$$

where $\epsilon_{\text{eff},0}$ is the effective permittivity of the unloaded CPW line, ϵ_{eff} is the effective permittivity when loaded with sample, and α is a function of the CPW geometry and sample dielectric constant. Tedious analytical approximations for ϵ_{eff} exist, but for the purposes of this simple sensitivity analysis, it suffices to represent the dependence of effective permittivity on sample properties through the factor α. For the unloaded device, $\alpha = 1$, and $\alpha \neq 1$ when sample is loaded. If the sample is lossy, then α becomes complex.

The estimated unloaded CPW characteristic impedance is $Z_0 = 50\,\Omega$. The characteristic impedance with sample present is

$$Z_1 = Z_0 \frac{v_{\text{p}}}{v_{\text{p},0}} = Z_0 \sqrt{\frac{\epsilon_{\text{eff}}}{\epsilon_{\text{eff},0}}} \tag{2}$$

where v_{p} is the transmission line phase velocity. The input impedance looking into the device with load impedance Z_0 is given by

$$Z_{\text{in}} = Z_1 \frac{Z_0 + jZ_1 \tan \beta l}{Z_1 + jZ_0 \tan \beta l} \tag{3}$$

where l is the length of the transmission line and β is the wave number given by $2\pi f / v_p$ with f the measurement frequency.

This results in S-parameters that are given by

$$S_{11} = \frac{Z_{\text{in}} - Z_0}{Z_{\text{in}} + Z_0} \tag{4}$$

and

$$S_{21} = \frac{1}{1 + S_{11}} \frac{e^{j\beta l} + \Gamma_2 e^{-j\beta l}}{1 + \Gamma_2} \tag{5}$$

where

$$\Gamma_2 = \frac{Z_1 - Z_0}{Z_1 + Z_0}. \tag{6}$$

These expressions characterize the effect of dielectric material properties and other parameters on the observed device S-parameters.

For our device, the S-parameter sensitivity to different solution permittivities is shown in Fig. 2. At higher frequencies, resonance conditions cause oscillations in the predicted parameters.

The liquid electrical properties are expected to vary greatly with temperature and frequency [14], [15]. In this RF frequency range, the interrogated dipoles will not be able to keep rotating with the applied alternating field and effectively this reduces the permittivity of the solution as the frequency is increased. These frequency-dependent variations are important for predicting the expected characteristics of our measurement device. To establish baseline data, a calibrated Agilent 85070E-020 High Temperature Dielectric Probe was

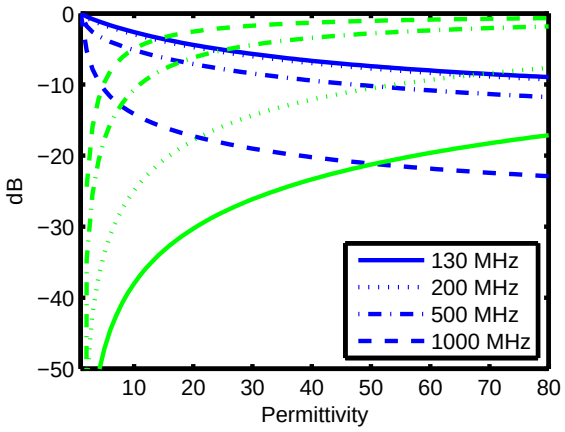

Fig. 2. Predicted S_{21} (blue) and S_{11} (green) as a function of permittivity and frequency. The S_{21} transmission parameters decrease with increasing permittivity and frequency and the S_{11} reflection parameters increase with increasing permittivity and frequency as computed from Eqs. 4 and 5.

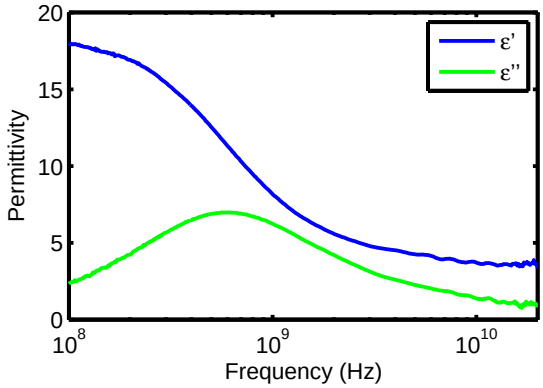

Fig. 3. Measured complex permittivity from 100 MHz to 20 GHz for isopropyl alcohol at room temperature using an Agilent N5230C PNA-L Network Analyzer with an Agilent 85070E-020 High Temperature Dielectric Probe.

used with an Agilent N5230C PNA-L Network Analyzer to record complex permittivity data for air, isopropyl alcohol, and deionized water. A representative trace obtained from this probe is shown in Fig. 3. The frequency-dependent, measured permittivity data is then used directly in the formulas to calculate the impedance.

To predict how the material properties will affect the expected transmission characteristics for our device, the S_{21} and S_{11} parameters are plotted in Fig. 4 for isopropyl alcohol. It is evident that the higher-frequency resonances will be heavily dependent on the actual geometry of the fabricated device. Some general trends do emerge. Simulations of air show much less attenuation in S_{21} over the entire spectra and simulations of water show much greater attenuation in the S_{21} parameters, particularly at frequencies below 2 GHz.

The theory and simulations predict that the coplanar waveguide should be sensitive to varying liquid electrical parameters over the range from 100 MHz to 20 GHz.

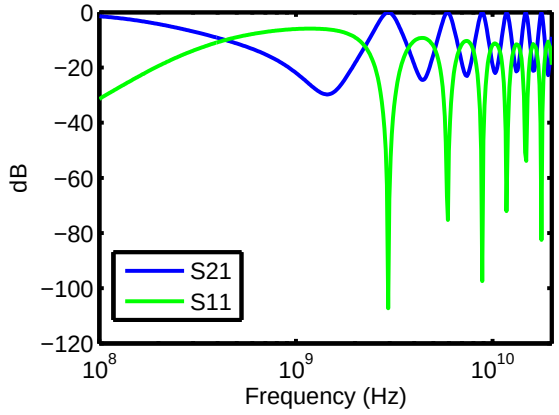

Fig. 4. Simulated S-parameters for the waveguide containing isopropyl alcohol in the channel. Low-frequency loss is expected to increase with increasing permittivity. The frequency-dependent nature of the S-parameters is evident.

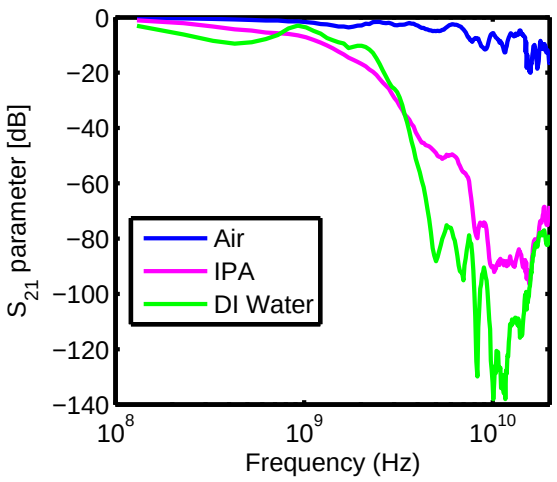

Fig. 5. Measured S-parameters for the waveguide containing air, water, and isopropyl alcohol. At low frequencies, the loss in S_{21} parameters decreases with increasing permittivity. At high frequencies, much higher losses are measured than predicted.

III. Materials and Methods

A. Device Fabrication

Two identical rectangles 1 inch x 2 inch are cut from double-sided 1-ounce copper, FR-4 circuit board stock. These rectangles will form the microfluidic channel and the substrate with the coplanar waveguide.

For the channel, the copper is chemically etched off (Ferric chloride) of both sides of one rectangle. To form the microfluidic channel in a single pass, the MITS Electronics FP-21T milling machine with a 15 mil bit is used to cut out the channel to the specified depth. For liquid input/output ports, two 125 mil diameter holes are formed at each end of the channel using a standard drill press. Two indents are also cut with a sheet metal nibbler on either side of the board to make room for SMA connectors that will be attached to the substrate boards.

For the substrate board, the copper is chemically removed from one side of the board. Two lines are milled into the copper layer to create a coplanar waveguide as shown in Fig. 1. Tapering the waveguide edges to the SMA connector is also performed for better impedance matching.

The substrate and channel boards then must be bonded together to form a liquid-tight seal. Taconic low-flow prepreg (fastRise-27) is used as an adhesive layer between the boards. The prepreg is placed onto the channel board. A Rayjet laser engraver (Trotec) is used to cut the channel pattern and access holes out of the prepreg to match the original milled features. The substrate board is then aligned and placed on the prepreg layer and the board-prepreg-board sandwich is clamped between aluminum blocks. The device is placed in an oven. The temperature is gradually ramped up to a maximum temperature of 210° C, where the temperature is held stable for 45 minutes, and then the oven is allowed to cool. The entire bonding process takes about two hours.

When the device is cool, the clamps and aluminum blocks are removed. The device is tested for proper sealing using water-based dyes to ensure that there is no leaking. This is particularly important to check in the troughs between the copper signal and ground lines. SMA connectors are then soldered to each end of the waveguide. The completed device appears as in Fig. 1.

B. Experimental Protocol

Deionized water was obtained from our local cleanroom facility. Isopropyl alcohol was also used as a reference liquid because it has a permittivity intermediate that of air and water. Solutions were loaded into syringes for injection into the formed reservoirs.

The device was attached through the SMA connectors to the Agilent N5230C PNA-L Network Analyzer. The entire device was mounted so that it would not move during a round of experiments. All materials and liquids were brought to room temperature. Air, isopropyl alcohol, and water were injected sequentially and network parameters were measured as a function of frequency from 200 MHz to 20 GHz. Liquids were extracted from the device by placing a paper towel in a reservoir and absorbing the liquid. To avoid cross-contamination, the device was repeatedly flushed with the next liquid to be measured when liquids were changed.

IV. Results and Discussion

The measured data for the fabricated impedance device is displayed in Fig. 5 The data clearly show that there are strong differences in the measured signals for the different liquids and air. The result that the isopropyl alcohol, around 1 GHz, has less attenuation than water demonstates the non-linear character of this device and the complicated relationship of geometry, materials, and solution properties.

As expected from simulation, the low-frequency attentuation is correlated with increased permittivity. The waveguide is apparently much more lossy at higher frequencies than the simulations predicted. FR-4 is not a high-performance

microwave material so, to some degree, this behavior is expected. However, it is also evident that the simple models fail to predict the measured behavior over the entire frequency range. Other sources of error in the modeling arise from the connections from the SMA connectors to the waveguide as well as the trace tapering used to go from the SMA connector profile to the slimmer coplanar waveguide.

After a considerable amount of testing, a board was disassembled and the copper surface was examined. No signs of rusting or other deteriorating effects were visible on the surface. Surface changes will be examined in further experiments.

V. Conclusion

A low-cost microfluidic measurement device made from traditional printed circuit board materials has been described in this paper. Over the RF frequency range of interest, it is evident that the electrical properties of water and isopropyl alcohol change significantly as measured by a commercial probe and the microfluidic coplanar waveguide structure.

Further improvements to the device will include temperature stabilization of the substrate and better waveguide-to-connector transitions. Traditional fabrication of the waveguide using photolithography and chemical etching should also improve the waveguide characteristics.

Numerical modeling of the entire device will also improve the accuracy of the models. It is hoped that using a differential measurements against a fluid similar to the fluid of interest will then allow extraction of complex permittivity differences more accurately. It is evident from the analysis presented here that this extraction will be highly dependent on the exact geometry of the device as well as the interrogated fluid. This will be used to then monitor changes in permittivity based on biological objects dissolved in water.

This device will be used as a platform for dielectric spectroscopy work on proteins and their interactions, particularly for substances that can only be found in minute quantities. It can also be used to monitor liquid processes in conjunction with other separation and characterization techniques.

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