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Predictions of Liver Dielectric Properties using Bruggemann Mixture Equation for Microwave Medical Applications

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Abstract

This paper discusses a numerical method to predict the dielectric properties of mixture solutions that can mimic the properties of ex-vivo and in-vivo liver tissue between 500 MHz and 10 GHz. In this study, the Bruggemann mixture equation (BE) was used. This equation treats the liver tissue as being comprised of two phases, the inclusion phase which refers to solid spherical insertions (dry tissue) and the host phase which refers to the biological fluid content. The predicted mimicking solution consisted of dried liver tissue as the inclusion phase and a phosphate-buffered saline (PBS) solution with a concentration of Triton X-100 (TX-100) as the host phase. Dielectric parameters for the host phase and inclusion phase were measured as a function of frequency using a slim form open-ended coaxial probe at a constant room temperature of circa 25 °C. These results indicate that these solutions can be used to model the human body phantoms for microwave medical applications. The mimicking solution being proposed in this study provides a liquid environment whose dielectric response is similar to that of bovine liver. Therefore, it can be used for electromagnetic (EM) experiments and simulations related to the liver, without the need of obtaining any animal organs.

1. Introduction

With the rapid expansion of electromagnetic (EM) applications in biology and medicine, there has been a growing interest in studying the interactions of EM waves with biological tissues, particularly at microwave frequencies. Therefore, the need for anatomical phantoms that simulate the EM properties of tissues at the microwave frequencies has dramatically increased. The key to EM medical technologies is related to the contrast in dielectric properties response of biological tissues to EM waves. Accurate simulation of dielectric properties of biological tissues is invaluable to evaluate clinical imaging, therapeutic device performance and medical procedures in a test environment avoiding risk to animal or human subjects [1]. Hence, it is crucial for advancements in EM therapeutic technologies [2].

In general, mixing equations are mathematical models that describe the macroscopic dielectric properties of materials based on the dielectric properties of its constituent components. In this case, components of interest are the extracellular fluid, cells and extracellular macro-molecules (proteins). In previous studies, it has been shown that the Bruggemann formulae [3] (consisting of an inclusion and host phase) can be used to estimate the complex permittivity of biological tissues in different dehydration states [4]. However, this requires accurate information in relation to the total volume fraction of fluid content in a tissue.

This can be determined using a loss on drying process during which the tissue is dried in a sophisticated oven (Genlab Drying Cabinet), such that the temperature inside remains constant. As the excised liver samples are heated, biological fluid is excreted from the tissue and thus liver samples are dried during this process. In this study, apart from predicting the fraction of the tissue's constituent contents to mimic the respective tissue, Bruggemann's model was adopted to estimate the complex permittivity of ex-vivo bovine liver tissue. The mixing model considers a two-component mixture comprised of a host liquid medium with solid spherical inclusions. The two components which make up the theoretical representation of the medium are usually referred to as host phase and inclusion phase respectively [3].

The rest of the paper consists of the Methodology section, where the measurement of the fluid content of liver is discussed alongside the use of Bruggemann's mixture equation (BE). The Results section follows, representing the result obtained by substituting the measured biological fluid volume fraction v_f and the measured dielectric properties of the host and inclusion phases inside the mixture equation. Finally a conclusion is made in order to summarize this study.

2. Methodology

In order to characterize the volume fraction in the BE a measurement campaign to determine fluid content of different biological tissues was conducted by Di Mio et. al. [4] on 191 different animal and human samples from liver and kidney cortex (bovine, ovine and porcine animals and one human cadaver). Tissues were obtained post-mortem from a public abattoir operations MESDC in Marsa, Malta, and the organs were preserved in sterile plastic bags and presented in the laboratory within an hour of death. The biological fluid content of the samples was determined using the loss-on-drying method. For controlled dehydration, the samples were placed in a professional oven (Genlab Drying Cabinet, temperature range 30 to ambient + 50ºC) at a controlled temperature of 40 °C, and on a regular time interval their weight and dielectric properties were recorded by taking out samples from the oven.

The samples were allowed to dry out until no change in mass was observed, and at this point all the biological fluid has evaporated and the material remaining is purely dry mass. The difference in mass between this final weight and the first is then assumed to be the mass of biological fluid lost, giving the biological fluid mass fraction of the samples. The sample database is summarized in Table 1.

Table 1. Summary of biological fluid content range and average for ovine and porcine liver samples [5].

Fluid Content Rang and Average	
Sheep Liver	68 – 72 % (avg 70%)
Pig Liver	64 – 72 % (avg 70%)

In this study, the weight of each sample exactly after excision was measured using a precise Adam Nimbus scale. Nine porcine liver samples (S1 – S9) from the same liver (obtained from public abattoir operations MESDC) were used to make liver hydration measurements. These samples were left for 7 days inside the oven and their weight was measured on days 2,3,4 and 7, where day 1 refers to the day of excision when the samples first entered the oven. The change in weight was monitored during the drying procedure and the respective complex permittivity was calculated for each day. On day 7, the liver tissue almost completely dried out and each sample resembled a solid, more than a semisolid.

For this reason, it was not possible to measure the dielectric properties on day 7 because the probe need to have good contact with the material under test (MUT) at the reference plane at which the measurement is made. In addition, no air gaps should be present within the sensing volume around the probe tip. These conditions are satisfied within a semisolid or liquid (provided no air bubbles are present). However, the same does not apply for solids in most cases, especially solid with a rugged surface such as dried liver tissue. Therefore, data obtained from dry liver on day 4 was used as the inclusion phase when using the BE. On day 4, liver tissue samples still resembled a semisolid and therefore reliable measurements could be carried out. In addition, the samples were significantly dry when compared to completely dry liver on day 7 (see Table 2) and thus it seemed adequate to use this data for the inclusion phase.

Table 2. Summary for Biological fluid content and mass for porcine liver samples (S1-S9). Percentage loss on day 1 can be considered to be 0 % since it corresponds to freshly excised liver.

Sample no.	**Day 1** (Fresh)	**Day 4**		**Day 7**	
	Mass / g	Mass / g	% loss	Mass / g	% loss
S1	31.295	11.630	62.8	9.308	70.3
S2	59.372	25.219	57.5	18.946	68.1
S3	29.413	11.362	61.4	9.199	68.7
S4	34.717	15.739	54.7	11.229	67.7
S5	45.614	19.089	58.2	14.367	68.5
S6	69.403	31.391	54.8	22.565	67.5
S7	34.638	13.108	62.2	10.281	70.3
S8	36.522	13.786	62.3	10.877	70.2
S9	60.978	26.375	56.8	19.331	68.3

The host phases used were 0P, 4P, 5P, 7P, 12P, PBS with 1.5 ml TX-100 (motivated from another measurement campaign), pig blood with heparin and without heparin. The dielectric properties of these host phases were determined using the open-ended coax technique [4] and plugged in the BE. In the Results section, Bruggemann predictions when varying the host phase are presented graphically for an averaged value over all the samples for the inclusion phase. The volume fraction for the host phase used for fresh liver corresponds to the average percentage of biological fluid lost by the samples when completely dried out, i.e., 70 %. The Bruggemann mixture equation is given in terms of ε_{eff} by equation (1), simplified from [3]:

$$\varepsilon_{eff} = \frac{1}{4}\left(3v_f\varepsilon_h - 3v_f\varepsilon_i + 2\varepsilon_i - \varepsilon_h + \sqrt{\left(3v_f\varepsilon_h - 3v_f\varepsilon_i + 2\varepsilon_i - \varepsilon_h\right)^2 + 8\varepsilon_i\varepsilon_h}\right), \quad (1)$$

where ε_h is the permittivity of the host environment, ε_i is the permittivity of the inclusion phase, ε_{eff} is the effective permittivity of the material and v_f is the volume fraction. For any particular biological tissue, the host medium is considered to be the biological fluid within the tissue and thus v_f is the volume fraction of this component, whilst

$(1 - v_f)$ is the volume fraction of the inclusion phase made up of the dry biological component. All dielectric properties substituted in equation (1) are complex numbers and all the operations are acting on complex numbers in this case. This was achieved by making use of Python's Numpy library.

3. Uncertainty Calculation

Accuracy of the measurement system was inspected following the standard technique described in [6] on a standard solution with known dielectric properties (0.1 M NaCl). For an estimation of the total uncertainty of the measurement system, repeated measurements were performed on 0.1 M NaCl to assess random and systematic errors. The error was calculated for each discrete frequency point in the measurement and averaged over the measurement frequency band. The accuracy of the measurement system was calculated as deviation from the reference data obtained from the Cole-Cole model presented in Peyman et al. [7]. Table 3 lists the random and systematic errors in the system, evaluated over 0.1 M NaCl solution at 22 °C. These values confirm that the measurement system is capable of conducting dielectric measurements with high accuracy and high repeatability.

Table 3. Measurement uncertainty of the system evaluated on 0.1 M NaCl solution.

Uncertainty	Dielectric Constant	Conductivity
Repeatability	1.08	0.63
Accuracy	3.42	1.92
Drift	0.05	0.05
Combined	1.7	1

Figure 1 shows a comparison between the dielectric properties of 0.1 M NaCl solution measured in this study for three different validation tests and the reference data obtained from Cole-Cole model in [7]. Measured data is found to be in agreement with the reference data with average error less than 2%.

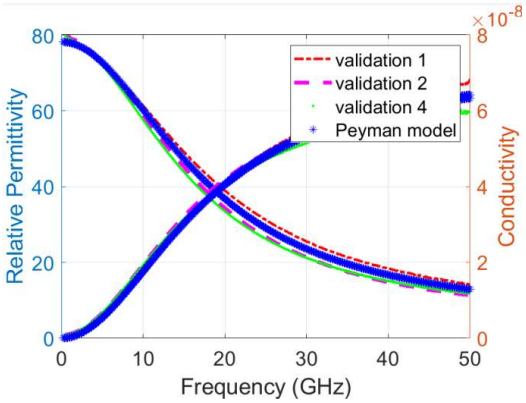

Figure 1. Measured relative permittivity of system validation measurements using 0.1 M NaCl, and standard model from Peyman model.

4. Results

The Bruggemann equation (BE) predictions discussed in the previous section were plotted alongside fresh liver (averaged over the 9 samples) against frequency (500 MHz – 10 GHz) as shown in Figures 2 and 3. Figure 2 shows the behavior of the relative permittivity (real part) and Figure 3 shows the loss factor (imaginary part).

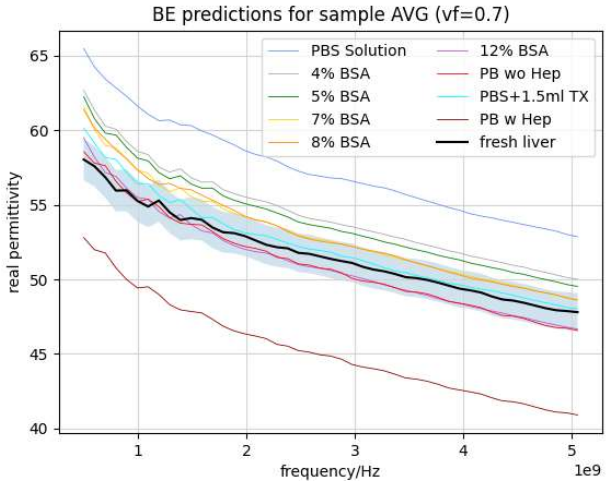

Figure 2. A plot showing the relative permittivity of averaged fresh liver alongside BE predictions for different host phases.

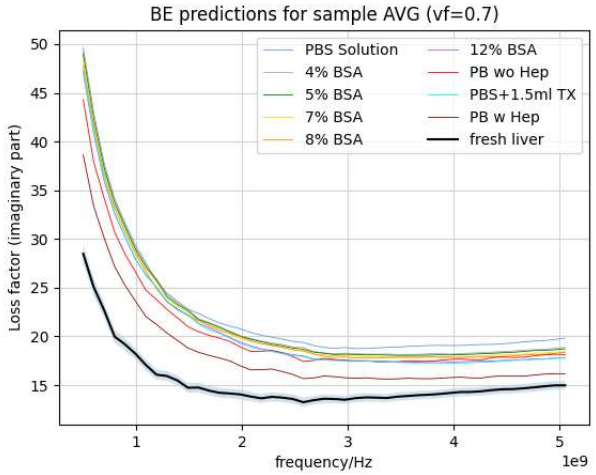

Figure 3. A plot showing the loss factor of averaged fresh liver alongside BE predictions for different host phases.

Averaging over all the samples is reliable in this case because the volume fraction of fluid content is very similar between one sample and another, as shown in Table 2. In order to make the selection process of choosing the best host phase easier, another plot (see Figure 4) was made whereby the percentage difference between the relative permittivity of fresh liver and each BE prediction is plotted as a function of frequency. Such a plot was not made for the loss factor because neither prediction is even close to the uncertainty range of fresh liver.

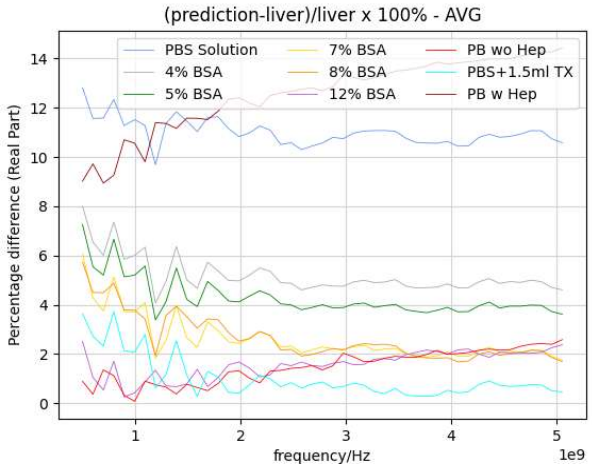

Figure 4. A plot showing the percentage difference between the relative permittivity of fresh liver and each BE prediction for different host phases.

The numerical method on its own produced a satisfactory result but not a conclusive one, because at frequencies lower than ~2 GHz pig blood without heparin and the 12 % BSA solution are similarly the best host phases (see Figures 2, 3 and 4). However at higher frequencies, 40ml PBS + 1.5ml TX-100 is clearly the best host. Even though this numerical prediction did not produce a conclusive result on its own, it did reinforce an experimental result obtained in a separate measurement campaign within the Electromagnetic Research Group (EMRG) at the University of Malta that the 40P + 1.5ml TX-100 solution is an excellent mimic for the relative permittivity of fresh porcine liver tissue.

5. Conclusion

The fact that the Bruggemann two-phase mixture equation produced similar results to what was found experimentally is very promising for future dielectric spectroscopy studies on liver and possibly other organs such as kidneys. Although the numerical method is not conclusive on its own, it reinforces a result that was obtained experimentally, which concluded that a 40P + 1.5ml TX-100 (40 ml) solution mimics the relative permittivity of fresh liver precisely.

One of the main advantages of such liquid solutions is that they are relatively cheap to produce and can be easily prepared within a few minutes, given that the necessary apparatus and chemicals are made available. There also exists the possibility of using the liquid solution as a culture medium to grow cancerous cells inside it. Micro/Radio frequency medical imaging techniques such as Magnetic Resonance Imaging (MRI) can then be tested inside the solution itself. It is essential to remark that microwave heating applications should not be tested in such a mimicking solution since the loss factor (which depends on the conductivity) is not properly mimicked.

Having the possibility of synthesizing a solution within minutes in a lab that mimics the dielectric properties of biological tissues is extremely convenient and useful since no organs and tissues are required for initial testing phases, making it easier to carry out testing procedures since no ethical procedures are required. In addition animals would not be used as experimental subjects. This makes the development and research of dielectric spectroscopy mimicking solutions a very useful and an active growing field of study.

References

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