BIOLOGICAL APPLICATIONS OF A TECHNIQUE FOR BROADBAND COMPLEX PERMITTIVITY MEASUREMENTS

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Abstract: A broadband coax technique developed by us for the measurement of dielectric properties of biological substances upto at least 20 GHz, is discussed. For water-based materials such as blood or muscle substitute phantoms, a 0.047 inch size probe is essential to minimize errors due to radiation. The data indicate the importance of the dielectric volume of the constituents, and enable tailoring of phantoms and substitutes for use in biomedical applications.

I. INTRODUCTION

Accurate measurements of dielectric properties of biological substances are essential for both fundamental studies and biomedical applications, such as microwave hyperthermia. We have developed a coaxial line technique[1,2] for accurate measurements of dielectric spectra from 45 MHz to 20 GHz and possibly upto 50 GHz. An open-ended coax line is used as a non-invasive probe[3,4] and we have developed procedures for minimization of the principal difficulties which are: (1) accurate determination of the frequency-dependent probe-end impedance, (2) elimination of spurious impedances such as those due to connector mismatch, and (3) accurate modeling of the probe-liquid interface. The experimental procedure and the data processing computer program, used with a frequency domain automatic network analyzer, enable rapid measurement of the permittivity of samples, and yield plots and fits to spectral forms such as Debye, Cole-Cole and Cole-Davidson functions.

We have utilized the technique to study a wide range of samples, such as ionic solutions[5,6], polymer solutions, liquid mixtures and solids. We have also studied liquid solutions of importance in biophysics and biomedical technology. In aqueous protein solutions we have obtained the hydration shell of the protein molecule in solution, and also studied conformational dynamics as functions of pH of the solution. Here we discuss our results and analysis on a muscle phantom and human blood.

II. MEASUREMENT TECHNIQUE

The method utilizes three calibrations: open, short and a standard liquid, all at the probe end, and employs bilinear transformations to extract the probe-end impedance. For low ϵ' liquids, such as methanol, a simple capacitive approximation for the terminating impedance is adequate. For high ϵ' liquids such as water, more terms need to be added to the complex capacitive impedance due to the radiation from the coax aperture, which plays an important role. Samples and the calibration standard are kept at a constant temperature utilizing a temperature stabilizer.

The calibrations and the bilinear transformations eliminate the frequency-dependent complex capacitance at the probe end and the spurious impedances such as those due

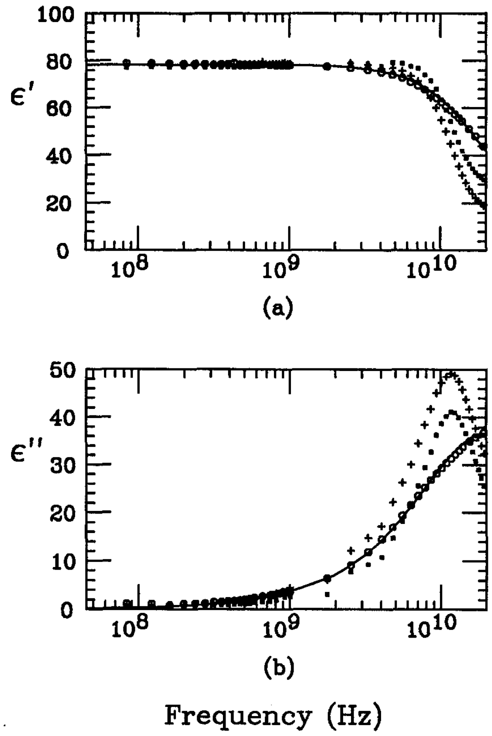

Fig. 1. Results for water illustrating probe size and radiation correction effects. 0.047 in. flanged probe with radiation correction (o's), Debye fit (ϵ_0=78.2, ϵ_∞= 5.1, τ = 7.9 ps) to the 0.047 probe data (solid line), 0.141 in. probe with radiation correction (+'s) and 0.141 in. probe without the correction (solid squares).

to connector mismatch, as demonstrated by the four curves for water shown in Fig. 1. Marcuvitz's expressions for the conductance and reactance of a flanged, vacuum-filled coaxial line open to half free space, and Dechamps theorem are used to approximate[2] the probe-end impedance of a flat-end, teflon-filled coaxial line. We find that the size of the coaxial line is crucial for the water based solutions, because of the large deviation caused by the high dielectric constant. The radiation correction model is adequate for the 0.047 in. probe[2] as a result of the small correction required, in contrast to the large errors introduced by the 0.141 in. probe, as shown by measurements on water in Fig. 1. It is apparent from Fig.1 that a narrow probe is essential for accurate measurements, particularly at high frequencies. The correction causes some improvement for the 0.141 in. only at frequencies lower than 8 GHz, since the deviation due to a simple capacitance approximation is small at low frequencies. The superiority of the 0.047 in. probe at high frequencies is apparent. The 0.047 probe data for water shown in Fig. 1 were taken with a flanged coax. There are no significant differences from a simple flat-ended coax measurement, but the flange does seem to decrease small wiggles due to a "container effect". The 0.047 in. probe without a flange has the added convenience of measuring sample liquid size as small as 0.5ml.

From the information obtained from various kind of fits, we are able to tell if the dielectric spectra has simple Debye or two Debye behavior or a distribution of relaxation times. For water we find a good fit to a Debye spectrum with ϵ_0=78.2, ϵ_∞= 5.1, τ = 7.9 ps at 25C. In solutions we are able to extract the dielectric excluded volume, which is the volume that is unable to respond at microwave frequencies, and the amount of free water in aqueous solutions.

The dielectric excluded volume R_V is estimated from the Maxwell-Wagner formula

$$R_V = \frac{(\epsilon_{0s} - \epsilon_{0w})(\epsilon_u + 2\epsilon_{0w})}{(\epsilon_{0s} + 2\epsilon_{0w})(\epsilon_u - \epsilon_{0w})} \qquad (1)$$

where ϵ_{0s} is the static dielectric constant of the solution obtained from the fit, ϵ_{0w} is the static dielectric constants of water, and ϵ_u the "high" frequency dielectric constant of the "dielectric void". R_V gives the total dielectric excluded volume in 1 liter of the solution. Therefore, the volume of the free water is

$$V_{fw} = 1 - R_V \qquad (2)$$

If the water concentration c_w of the solution is known in Molar, and there is only one species of molecule in the solution with concentration c, the number of bound water molecules can be figured out as

$$N = [c_w - V_{fw}/(0.018 d_{fw})]/c \qquad (3)$$

III. RESULTS AND ANALYSIS ON THE PHANTOM AND HUMAN BLOOD

The dielectric spectra of blood, 11g/l of NaCl/H_2O and the phantom are shown in Fig.2.

The fit for the muscle phantom[7] ϵ_0 = 73.6, ϵ_∞= 4.6 and τ = 8.3 ps, gives the dielectric excluded volume as 0.05 liter in 1 liter of solution which indicates there is 96.wt.% of free water. By comparing to the known water content given by the recipe in Ref. [7], about 1.5% of water appears to be bound to other ingredients.

Fig. 2 shows that the 11g/l NaCl solution, which is often used to imitate the conductivity of the human blood, is a very poor dielectric substitute for blood at microwave frequecies.

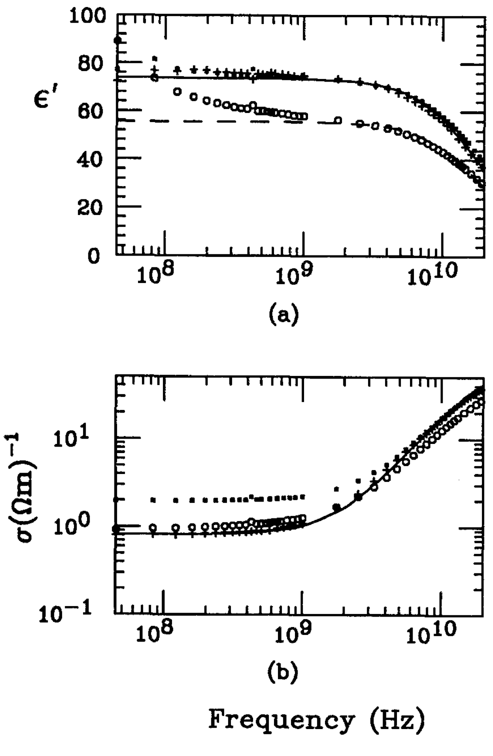

Fig. 2. Dielectric spectra of human blood (o's) at 25C, and fit for high frequencies (ϵ_0=55.6, ϵ_∞= 4.5, τ = 8.4 ps, dashed line), muscle phantom (+'s) and fit (ϵ_0=73.6, ϵ_∞= 4.6, τ = 8.3 ps, *solid line*), *11g/l* NaCl/H_2O solution (solid squares).

The dielectric spectrum of human blood[8] seems more complicated. It can not be fitted to a single Debye behavior, Cole-Cole expression or the form with two Debye relaxation time, due to the complexity of the ingredients and the high viscosity. Human blood contains[9] about 45% of red cells, 1% of platelets and white cells, and the rest is the plasma which has 90% of water content.

The reduced dielectric constant of blood is caused by (i) the dipole moments of big biological molecules have reduced response at microwave frequencies; (ii) water molecules bound to proteins, etc. should have about one order of magnitude longer relaxation times due to stronger interaction, hence they become "dielectric voids". At frequencies above about 8 GHz, the dielectric spectrum is entirely due to free water molecules. This is confirmed by analyzing the data from about 8 GHz to 20 GHz which fits well to a Debye form with ϵ_0 = 55.6, ϵ_∞= 4.5 and τ=8.4 ps, as shown as the dashed line in Fig.2.

We suggest that from our analysis on the blood microwave dielectric data, the non-aqueous ingredients for blood substitues, if they are hydrophobic and have low ϵ', their total volume should be approximately 1/3 of that of water. Alternatively, large molecules with strong polarizability may be used at smaller volumes for the composition of such materials. Of course an appropriate ionic content is also required to match the conductivity.

IV. CONCLUSIONS

Our microwave dielectric measurements on a muscle phantom and human blood suggest that besides the conductivity, the dielectric excluded volume, which is not the real volume of ingredients, play an important role in determining the dielectric properties of blood sustitutes and phantoms for microwave hyperthermia[10].

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