A new open-source toolbox for estimating the electrical properties of biological tissues in the terahertz frequency band

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Abstract **–** The dielectric properties of biological tissues and their substructures at terahertz frequencies are needed for computational dosimetry, radiation safety regulation, and medical imaging, but experimental tissue data are only scarcely available for the terahertz band. Tissue properties can be theoretically predicted at terahertz frequencies if the tissue microstructure and composition, and the dielectric properties of several basic biological materials are known. This paper introduces a new open-source toolbox where a material database and many of the relevant formulas are implemented to facilitate related research. An example has been analyzed and successfully verified with available experimental data.

Keywords – *Dielectric mixing, homogenization, dielectric properties of tissues, terahertz.*

Introduction

As new technologies appear in the terahertz band, it becomes increasingly necessary to study possible health effects and properly revise public radiation safety standards [1]. computational dosimetry has been an important tool at lower frequencies and is now being employed at THz frequencies as well, but electrical properties data are needed to set up computational models of tissues [2, 3]. With the growing interest towards biological and medical applications of THz technology [4], computational electromagnetic models of tissues and physiological solutions are needed also in experimental research for accurate characterization of exposure conditions. Furthermore, THz imaging has been shown to provide high sensitivity to hydration contrasts between tumors and normal tissue background, and seems to be a promising technology for cancer diagnosis [5]. The need for computational tissue models relating hydration to electrical properties is obvious for theoretical investigations of THz imaging [6].

The widely accepted set of experimental tissue data from [2] has its upper frequency at 100 GHz. Although some limited experimental data is available at frequencies up to about 2 THz [7, 8], gaps in the currently available experimental tissue data at terahertz frequencies become more evident if we consider that the wavelength *in tissue* approaches the typical size of certain tissue sub-structures in the terahertz band. Consequently, it might be necessary to model tissue sub-structures explicitly with their specific electrical properties [3]. Obviously, a measurement approach to such properties is quite difficult, if not impossible.

To effectively overcome such difficulties, it has been suggested to employ a mixing approach to estimate the electrical properties of tissues through their often known chemical composition and constituents, and the success of this approach has previously been shown [6, 9-10] and will be further verified in this paper. This paper introduces a new open-source toolbox where many useful mixing formulas have been implemented together with the available required data of electrical properties of basic biological constituents from recent sources in the literature. It shall provide a useful tool for constructing tissue models, and to

facilitate research in THz waves-tissues interactions, computational dosimetry and imaging, especially where little or no experimental data exists regarding the electrical properties of a certain type of biological tissue. To the best of the authors' knowledge, no similar toolbox has been previously reported in the literature.

The open-source MATLAB-based toolbox is available for research use, and modification and improvement at *http://antennalab.ut.ac.ir/en*, from the *Downloads* section. This paper explains the theoretical and practical aspects of tissue modeling, and demonstrates the use of the developed tool through a verifying example. We review the current knowledge of the electrical properties of some basic constituents of biological material at high (esp. terahertz) frequencies in section 2, followed by a brief review of dielectric mixture rules in section 3. We then exemplify the procedures by estimating the high-frequency properties of muscle tissue in section 4.

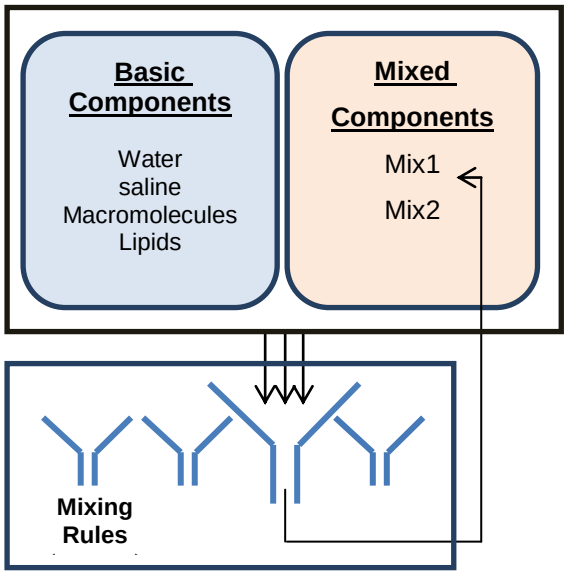


Fig.1. The typical workflow in the toolbox. The input to the mixing formulas are complex, frequency dependent permittivity data of two or more components. The output is the complex permittivity of the mixture, which itself will then be available as a component for subsequent mixing steps.

Basic Components

The mixing approach needs the properties of the basic components to be known. These include water, ions, proteins and lipids. A brief review of the currently available literature data and some physical insights, with focus on terahertz frequencies, are given in this section. The required input parameters for each material model are shown in the title of each entry. In

the following, *f* denotes the frequency vector in units of Hz and *T* denotes temperature in degrees Celsius.

A. Pure water and salts: Water (f(Hz),T(°C), σ_{DC} (S/m))

The electrical properties of pure water have been widely studied experimentally, and a useful overview can be found in [11]. General models for the complex permittivity of pure water have been obtained based on a meta-analysis of available data [12, 13]. It is known that the double-Debye equation can model the frequency-dependent dielectric behavior of water up to at least 1 THz [12]. The more recent and comprehensive investigation of [13] has made use of a comprehensive set of available data to express this behavior in terms of three relaxations (around 18.56 GHz, 167.3 GHz, and 1.944 THz) and two resonances (around 4.03 and 14.48 THz) from very low frequencies up to 25 THz and in the temperature range from 0-100 °C. The function Water is based on the properties of pure water provided by the latter reference [13].

The behavior of salt solutions (esp. NaCl) at RF and microwave frequencies have been extensively investigated, examples of which can be found in [14-17]. For the frequency range from DC up to at least the region of millimeter waves, the effects of salts on the complex permittivity can be described through experimental coefficients [18, 19]. However, at physiological *concentrations (typically 0.1 moles.lit^{-1} or less) and temperatures*, the salt content affects primarily the total conductivity and its effect on *real permittivity* is usually negligible when compared to that of macromolecular content or temperature variations [18, 20]. In this sense, modeling the electrolytes is done by the addition of an ionic conductivity term $\sigma / j\omega\varepsilon_0$ to the complex permittivity of the pure water model [14]. This can be adjusted through the user-provided parameter σ_{DC} . $\sigma_{DC} = 1S/m$ is a good first assumption for many biological backgrounds [9]. Providing $\sigma_{DC} = 0$ corresponds to choosing free, pure water.

B.Proteins and other macromolecules: UserDefined (f, ε_M)

Most studies of proteins up to several THz relate to dry powders in form of pressed pellets or their hydrated forms [21]. Available experimental data suggest negligible loss factor as compared to water below 2 THz for most macromolecules [6]. Moreover, the fact that water content is the dominant factor for dielectric behavior up to 2 THz lowers the sensitivity of the

mixture properties to the exact choice of a permittivity model for macromolecular inclusions. It is therefore common practice in the literature at microwaves [22] and also up to 2 THz [6] to model the effect of macromolecular content on water by assuming a mixture with inclusions of constant, real ε_M . This value is usually chosen in the range 2-3 [6]. The exact value can be adjusted in the relevant dialog box of the provided toolbox. The function User-Defined outputs a vector of the same length as the frequency vector, with all elements equal to ε_M .

C. Lipids: Lipid (f); Bilip (f)

Lipids are mostly observed in form of cellular and intra-cellular bi-lipid membranes. Relatively large fat droplets can be seen in adipose tissue, where the cells are responsible for accumulating fat. The terahertz properties of oils and lipids have been studied in [23, 24] and have been implemented through the Lipid (f) model. The bi-lipid membranes have been independently studied experimentally and modeled in [25] for a lower frequency range (0.1-2 GHz) and are provided for completeness through the function Bilip (f).

Mixture rules

Let us consider a mixture of generally lossy, dispersive dielectric material as composed of a *background* with one or several types of *inclusions*. Whenever the condition $\left|k_0.n.d\right| \ll 1$; with $n = \sqrt{\varepsilon' - j\,\varepsilon''}$, is satisfied for all the inclusions of the heterogeneous material, and the inclusions form a repetitive arrangement with sufficiently high number of repetitions, one can employ dielectric mixing (or effective medium theory) to construct an "overall" homogeneous model for the material [26]. The electrical properties of the background and inclusions and their volume fractions have to be known. Various mixing rules have been described for cases of spherical, ellipsoidal, and cylindrical, and layered inclusions. Each of these cases can suitably approximate certain biological material arrangements or tissue substructures. In table 1, we briefly describe the mixing rules that have been implemented in the tool provided, specify their input structure and show their recommended usage. In all cases, the notation ε_n implies a vector of complex permittivity values, which are samples of the frequency-dependent complex permittivity of the constituent *n*. The subscripts *b* and *i*

refer to “background” and “inclusion”, respectively, and v_n denotes the volume fraction of the inclusion from the total mixture.

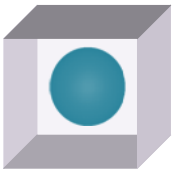
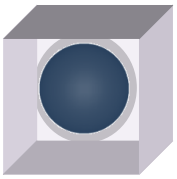
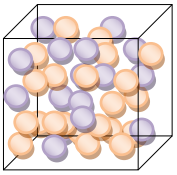
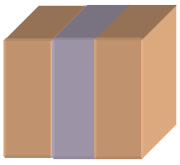
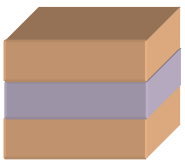
Case Study: Muscle Tissue

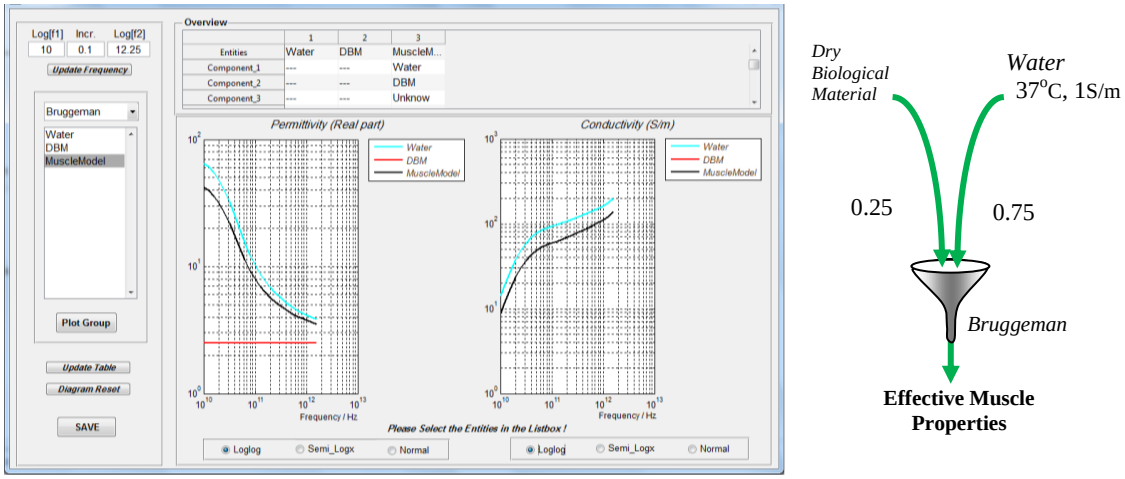
The dielectric properties of muscle have been reported for 10 Hz-100 GHz [28]. At terahertz frequencies, measurements for muscle have been reported in [29] for the frequency range 0.5-1.5 THz. Below, we use the introduced toolbox to estimate theoretically the dielectric properties of muscle tissue from 10 GHz to 2 THz. The Muscle tissue has been chosen because it has been widely studied and characterized. We then compare our results with those from the literature.

In accordance with experimental conditions [28], we take pure water at 37°C (for the terahertz dataset [29] the temperature has been set to 20°C). The contribution of ionic conductivity is included through assuming an ionic conductivity of 1 S/m, close to the value $\sigma_i = 1.2\,\mathrm{S/m}$ assumed for the aqueous phases of biological tissues in [9]. The total volume fraction of water for muscle has been given in [6] as v_w=0.75, and we model the rest of the constituents as *dry biological material* (abbreviated as DBM) with a user-defined constant, low permittivity of $\varepsilon_{DBM} = 2.5$. We assume water to be uniformly distributed in the tissue, and we choose the Bruggeman mixing model since it is more exact for relatively high volume fractions. This procedure is graphically shown in figure 2. The results are shown in figure 3 together with two sets of experimental data from [28] and [29].

A very good agreement between the theoretical and experimental values to within approximately $\pm 10\%$ is obtained in figure 2. Such successful reproduction of the electrical behavior can be partly attributed to the absence of interfacial charge accumulation and its localization phenomena at terahertz frequencies [14], which might suggest that the electrical properties are less sensitive to the structure and arrangement, and depend dominantly on tissue composition. Additional details are needed when attempting to model biological material at lower frequencies, e.g. below 100 MHz, including contributions arising from macromolecule rotation [14] and exact knowledge and modeling of cell shapes [31].

Table 1. Mixing Rules

Mixing Rule	Usage		Equation /Reference
Maxwell-Garnett (Spherical inclusions)		MG3d(ε_b , ε_i , v_i) • Assumes spherical inclusions. • Most exact for relatively low volume fractions [9] of inclusions, i.e. $v_i < 0.1$.	[27]
Maxwell-Garnett (Cylindrical inclusions)		MG2d(ε_b , ε_i , v_i) • Most exact for low volume fractions of aligned cylinders, which have no geometrical variations along the cylinder axis.	[30]
Maxwell-Garnett (layered inclusions)		MGShell(ε_b , ε_c , ε_l , v_i, w) • A typical usage consists of a suspension of cells in a *background medium* ε_b , with the cytoplasm represrented by ε_c (*core*), and the cytoplasmic membrane by ε_l (*layer*). The parameter w represents the volume fraction of the core from the whole inclusion.	[27]
Bruggeman		Bruggeman(ε_1 , v_1, ε_2 , v_2, …, ε_N , v_N) • Symmetrical, i.e. Bru(ε_1 , v_1, ε_2 , v_2) = Bru(ε_2 , v_2, ε_1 , v_1) • applicable to higher volume fractions, • Up to N=5 components can be mixed in the current implementation.	[6]
Linear		ParCap(ε_1 , v_1, ε_2 , v_2, …, ε_N , v_N) • applicable to all cases where the electric field polarization is parallel to all material interfaces, (implying uniform electric field intensity). • The formula can be derived from the well-known combination of parallel capacitors.	$\varepsilon = \sum_{n=1}^{N} v_n \varepsilon_n .$
Inverse-Linear		SerCap(ε_1 , v_1, ε_2 , v_2, …, ε_N , v_N) • Applicable to parallel layers with perpendicular electric field polarization. • The formula can be derived from the combination of series capacitors [30].	$\frac{1}{\varepsilon} = \sum_{n=1}^{N} \frac{v_n}{\varepsilon_n}.$



(a) (b)

Fig. 2 (a) Snapshot from the graphical user-interface of the toolbox for the current case study (b) The modeling procedure for the muscle tissue

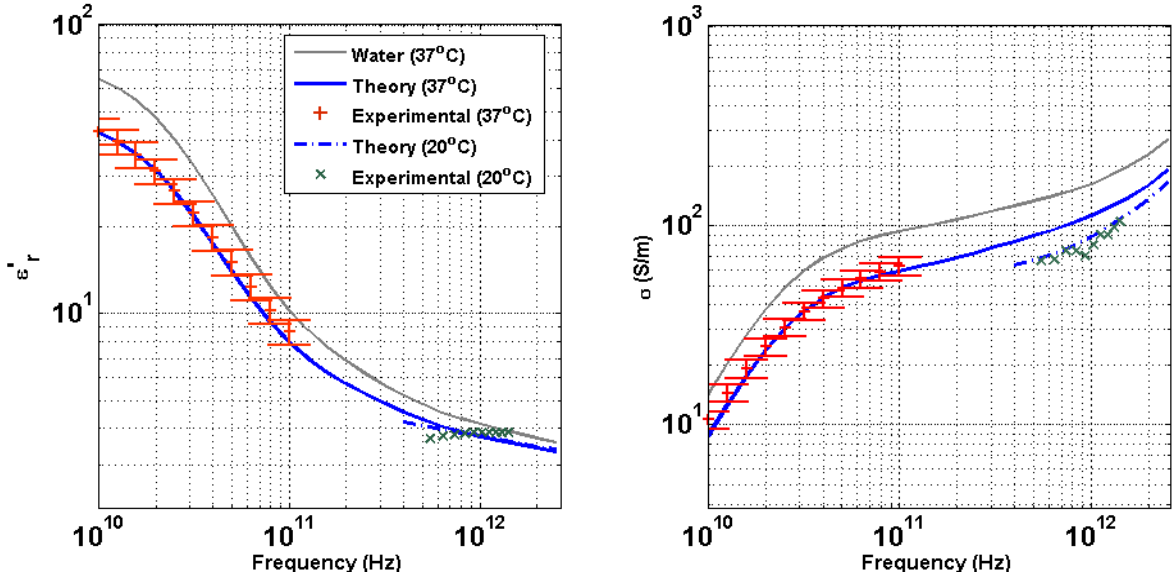


Fig. 3 Theoretical mixture-based estimations for the effective real permittivity and conductivity of muscle for 10 GHz - 2 THz. Theoretical curves are given for two temperatures in accordance with the experimental temperatures (37°C dataset from [28] with 10% error bars and 20 °C from [29]). Properties of pure water at 37 °C are also given for comparison

Conclusion

We have reported on the success of a tissue modeling approach to estimate the electrical properties of tissues at high (esp. terahertz) frequencies, and a flexible toolbox with user-friendly graphical interface for theoretical estimation of terahertz tissue properties. The properties of basic constituents of biological tissues at terahertz frequencies have been reviewed, and the implemented mixing rules and their usage have been discussed. These include three types of the Maxwell-Garnett mixing rule, a general Bruggeman mixing model, and the linear and inverse-linear mixing rules. The capabilities and limitations of the approach have been addressed. To demonstrate the capabilities of the approach, the properties of muscle have been theoretically estimated and verified with experimental data from the literature to within $\pm 10\%$.

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