31st Annual International Conference of the IEEE EMBS
Minneapolis, Minnesota, USA, September 2-6, 2009

Validation of human skin models in the MHz region.

Sonja Huclova [1], *Student Member, IEEE*, Jürg Fröhlich [1], Lisa Falco [2], François Dewarrat [2], Mark S. Talary [2] and Rüdiger Vahldieck [1], *Fellow, IEEE*

***Abstract*— The human skin consists of several layers with distinct dielectric properties. Resolving the impact of changes in dielectric parameters of skin layers and predicting them allows for non-invasive sensing in medical diagnosis. So far no complete skin and underlying tissue model is available for this purpose in the MHz range. Focusing on this dispersion-dominated frequency region multilayer skin models are investigated: First, containing homogeneous non-dispersive sublayers and second, with sublayers obtained from a three-phase Maxwell-Garnett mixture of shelled cell-like ellipsoids. Both models are numerically simulated using the Finite Element Method, a fringing field sensor on the top of the multilayer system serving as a probe. Furthermore, measurements with the sensor probing skin *in vivo* are performed. In order to validate the models the uppermost skin layer, the stratum corneum was i) included and ii) removed in models and measurements. It is found that only the Maxwell-Garnett mixture model can qualitatively reproduce the measured dispersion which still occurs without the stratum corneum and consequently, structural features of tissue have to be part of the model.**

I. INTRODUCTION

In order to reduce the infection risk or to increase patient comfort there is a strong trend towards non-invasive diagnosis. In particular for the analysis of blood parameters the measurement of physiological changes via a detectable difference in dielectric properties seems to be feasible. But these measurements also face the same challenges experienced when applying electrodes on the skin in other medical applications such as EMG, EEG, etc. These challenges include the interface between the electrodes and the skin as well as other variations causing changes in the impedance. Moreover, in order to be able to reconstruct any wanted parameters from measured data a correct solution of the forward problem is indispensable.

When measuring dielectric parameters of layered structures including very thin layers as in skin, the bulk parameters are a combination of the dielectric properties of the sublayers. The skin is composed of stratum corneum (SC), epidermis, dermis (E/D) and followed by subcutaneous fat (SCF). Although the SC belongs to the epidermis, it is often treated separately due to its very different properties compared to the remaining epidermal cell layers. Epidermis (without SC) and dermis together are also entitled as viable skin and are considered as one layer. The underlying SCF is also dielectrically distinct from E/D.

[1]Laboratory for Electromagnetic Fields and Microwave Electronics, ETH Zurich, Gloriastrasse 35, 8092 Zurich, Switzerland sonja.huclova@ifh.ee.ethz.ch

[2]Solianis Monitoring AG, Leutschenbachstrasse 46, 8050 Zurich, Switzerland

A. Motivation

To date no complete (continuous) set of the dielectric properties of skin layers (SC, E/D and SCF) is available in the range between 1 and 100 MHz. In [1] and [2] the dielectric properties of the uppermost layer, the SC have been assessed by measurements of skin *in vivo* with and without this top layer. Coaxial probes of different sizes were employed in order to distinguish the SC, E/D and SCF, providing permittivity estimations for these layers, however, only at single frequencies [2]. Native and treated SC was also measured with a coaxial probe using the time domain reflectometry (TDR) method by [3] including an identification and quantification of two relaxation processes in the microwave frequency range. *In vivo* skin measurements as well as measurements of blood, infiltrated and non-infiltrated fat were performed by [4] also providing Cole-Cole relaxation models for all measured materials. [5] also measured human skin *in vivo* and included a Cole-Cole fit.

In order to establish a dielectric profile in this work planar electrodes with different distances to ground are employed as the electric field penetrates the deeper into the probed material the wider the distance from the driven to ground electrode. According to the mentioned measurements the presence of the relatively thin SC strongly influences the measured values and measurement of pure fat also differ significantly from skin measurements (without SC) it can be concluded that the SC, E/D and SCF are not dielectrically significantly distinct. Therefore the thickness of each layer is a relevant quantity directly relating to the detected signal. An electrode with a gap width s can resolve a layer with a (electrical) layer thickness in the range of s.

B. Objectives

The objective of this study was to assess the following issues concerning dielectric modeling of the skin in the MHz region: i) The setup of various numerical models for skin including analytical expressions related to microscopic structure properties for the complex permittivity of each layer and ii) validating the models by comparing them to measurements with and without SC.

II. EXPERIMENTAL

A. Measurements

Dielectric measurements were performed with the sensor shown in Fig. 1 connected to a HP8753ES vector network analyzer between 1 and 100 MHz. The voltage between driven electrode and ground was 1V; the other two electrodes were set on ground, repeating the procedure for all three

electrodes (denoted as E1, E2 and E3 in Fig. 1). The setup was calibrated with air and deionized water ($\sigma_{DC} = 5 \cdot 10^{-8}$ S/m). The left upper arm was chosen as measurement site because of its accessibility, relative "homogeneity" compared to other body parts (e.g. wrist) and ability to tightly attach the sensor on the skin. After measuring untreated, dry skin the SC was removed by consecutive stripping with adhesive tape [2] and [1]. After each stripping the admittance was measured. The stripping was terminated after 11 strippings.

III. NUMERICAL MODELING

A. Model Setup

The numerical modeling was performed using the commercial Finite Element software COMSOL™ Multiphysics 3.4. As the dimensions of the geometry are much smaller than the wavelength of the electromagnetic field and the skin depth is much larger than the geometry the quasi-static approximation applies, i.e. the Laplace equation has to be solved. A sketch of the numerical model is given in Fig. 1. The 2D model is supposed to be a good approximation for electrodes E2 and E3 while for electrode E1 the error will be more significant due to the large curvatures compared to the electrode length.

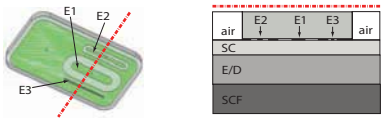


Fig. 1. 3D view (left) and 2D-cross-section used in the numerical model (right) of the fringing field sensor. Please note that the SC, E/D and SCF dimensions are not to scale. Layer thicknesses: $d_{SC} = 40\mu$m, $d_{E/D} =$ 1.1mm and $d_{SCF} = 1.5$cm(∞). Electrode/gap width dimensions: E1: 4mm, E2: 1.5mm, E3: 0.3mm.

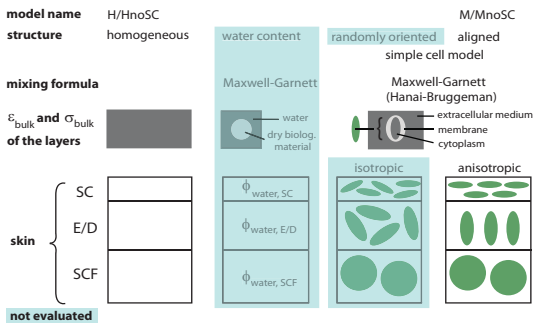


Fig. 2. Schematical overview of potential skin models. For geometrical and dielectric parameters of the single layers and their structure see text (H/HnoSC) and Table I (M/MnoSC).

Modeling of thin layers due to large aspect ratios (here electrodes and SC) is a known problem in numerical modeling. Scaling of the dielectric length of the SC has only limited application in the case of fringing field sensors due to the highly inhomogeneous electric field. Preliminary tests in a two-layer test case ($\varepsilon_1 = 10$, $\sigma_1 = 10^{-4}$, $d_1 = 4 \cdot 10^{-5}$, $\varepsilon_2 = 100$, $\sigma_2 = 2 \cdot 10^{-1}$) showed a deviation in ε_{bulk} of only 1.5% for the big electrode but 13.7% for the small electrode after doubling the first layer thickness and adjusting ε_1 and σ_1. For comparison, discretization effects assessed with an extremely fine mesh in the critical layers only caused an error of max. 0.5% over the entire frequency interval.

The layer thicknesses were set for all models to $d_{SC} =$ 40μm and $d_{E/D} =$ 1.1mm, although these values are only approximations due to the large intra- and inter-individual variations [6], [7].The fat layer was supposed to be the lowest detected layer (several mm) with a thickness of 1.5cm in the numerical model.

B. Modeling of the Dielectric Parameters of Single Sublayers

The simplest model of skin and SCF is established with homogeneous dielectric parameters assigned to each layer (see Fig. 2, model H/HnoSC). The values used in this study were taken from [3] (SC) and [4] (E/D, SCF) at 10 MHz. Since [4] provides values for skin *in vivo* and therefore not only contains information on E/D as well as from the SC and SCF, the values for blood were taken in order to approximate E/D. SCF was represented by infiltrated fat. The corresponding dielectric parameters (model H/HnoSC) are the following: $\varepsilon_{SC} = 34.05$, $\sigma_{SC} = 0.0193$ [S/m], $\varepsilon_{E/D} = 280.03$, $\sigma_{E/D} = 1.097$ [S/m] and $\varepsilon_{SCF} = 29.58$, $\sigma_{SCF} = 0.053$ [S/m].

Another possibility to calculate ε_{bulk} and σ_{bulk} is to use a mixture formula, e.g. the Maxwell-Garnett equation [8], for each layer with the water volume fraction as the layer's characteristic parameter. However, the formula is applicable with reliability only at frequencies above 400 MHz according to [4] which makes sense because in the lower MHz range β-dispersion dominates and masks the influence of free water. Therefore the two-phase water mixture is not considered in this work.

The Maxwell-Garnett mixture formula is not limited to homogeneous spherical inclusions but can be extended for n-shelled spherical and even ellipsoidal particles [8]. An extension of the two-phase mixture is the representation of tissue cells by shelled ellipsoids. The idea is that the external electric field of the sensor is approximately homogeneous for each cell, accounting for the basic constitution of cell membrane and cytoplasm. Additionally, the cell shape can be adjusted by varying the ellipsoid semi-axes. The analytical expression provides exact values only for confocal shells, but as the cell membrane thickness is much smaller than the outer cell dimensions [8] the approximation is considered as justified. A suspension of randomly aligned ellipsoids provides an averaged isotropic ε_{bulk} and σ_{bulk}. By aligning particles specific tissue structure (e.g. flat SC cells, spherical fat cells) can be taken into account, providing a diagonal anisotropy tensor with respect to the ellipsoid axes (see Fig. 2, model M/MnoSC). As the Maxwell-Garnett formula neglects mutual interactions between particles they are only valid for small volume fractions of the inclusion ($\phi < 0.1$) [8]. The Hanai-Bruggeman formula is an extension of the Maxwell-Garnett formula for higher volume fractions and is referred to model colloidal suspensions accurately up to

TABLE I

THE M/MNOSC MODEL PARAMETERS. THE CYTOPLASMS OF SC AND SCF ($\varepsilon_{x_{SC}}$, $\sigma_{x_{SC}}$ AND $\varepsilon_{x_{SCF}}$, $\sigma_{x_{SCF}}$) ARE REPRESENTED BY TWO-PHASE MAXWELL-GARNETT MIXUTRES OF AND DRY BIOLOGICAL MATERIAL AS HOST ($\varepsilon_h = 2.5$, $\sigma_{DC,h} = 0$) AND GOOD-CONDUCTING WATER AS INCLUSION ($\varepsilon_i = 80$, $\sigma_{DC,i} = 1.25$) IN ORDER TO ACCOUNT FOR THEIR LOW WATER AND HIGH LIPID CONTENTS. WATER VOLUME FRACTIONS: ϕ_h, x_{SC} = 0.2 AND ϕ_h, x_{SCF} = 0.1.

Parameters			**SC**			**E/D**			**SCF**		
ϕ	$d_m x$		0.7	$7 \cdot 10^{-9}$		0.7	$7 \cdot 10^{-9}$		0.7	$7 \cdot 10^{-9}$	
a_x [m]	a_y [m]	a_z [m]	$2 \cdot 10^{-6}$	$2 \cdot 10^{-6}$	$5 \cdot 10^{-7}$	$5 \cdot 10^{-7}$	$2 \cdot 10^{-6}$	$5 \cdot 10^{-7}$	$2 \cdot 10^{-6}$	$2 \cdot 10^{-6}$	$2 \cdot 10^{-6}$
ε_{em}	σ_{em} [S/m]		80	0.75		80	0.75		80	0.75	
ε_m	σ_m [S/m]		10	0		10	0		10	0	
ε_c	σ_c [S/m]		$\varepsilon_{x_{SC}}$	$\sigma_{x_{SC}}$		80	0.5		$\varepsilon_{x_{SCF}}$	$\sigma_{x_{SCF}}$	

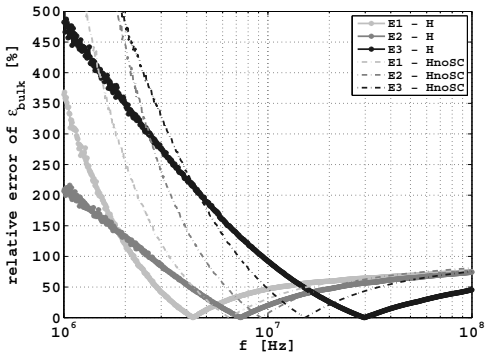
$\phi < 0.8$ [8]. Shelled ellipsoids in an environment have already been employed as a model for e.g. red blood cells [9] or rat liver tissue [10]. In this work the Maxwell-Garnett formula is employed as a first attempt, the Hanai-Bruggeman formula will be implemented in a next step. The approximate cell dimensions were on the same scale as [8] and the volume fractions were set according to [10], initial dielectric parameters for extracellular medium, cell membrane and cytoplasm according to e.g. [8], [9]. All geometrical and dielectric parameters for this model (M/MnoSC) are listed in Table I.

C. Extraction of the Dielectric Parameters

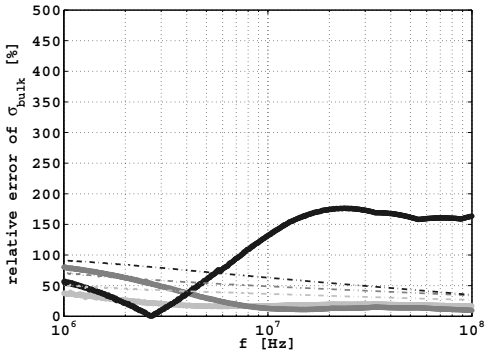
The dielectric parameters were extracted using the same standard procedure in both, measurements and simulations via determination of the cell constants [11]. The plotted quantities, bulk permittivity ε_{bulk} and conductivity σ_{bulk} are defined as follows: The complex permittivity is $\varepsilon^* = \varepsilon_0\varepsilon_r = \varepsilon^{'} - j\varepsilon^{''}$. Consequently $\varepsilon_{bulk} = \mathrm{Re}(\varepsilon^*) = \varepsilon^{'}$ and $\sigma_{bulk} = \mathrm{Re}(\sigma^*) = \sigma_{DC} + \omega\varepsilon_0\varepsilon^{''}$ where σ_{DC} denotes the static conductivity, f is the frequency of the applied external field ($\omega = 2\pi f$) and ε_0 the permittivity of free space.

IV. RESULTS

The relative errors (measured data is taken as reference) of ε_{bulk} and σ_{bulk} calculated using model H/HnoSC are given in Fig. 3, while those for the model M/MnoSC, Maxwell-Garnett mixture of aligned ellipsoids in Fig. 4. The measured data lies in the same range and exhibits very similar characteristic as literature values obtained from measurements of dry skin with open-ended coaxial probes [4], [5].



(a)

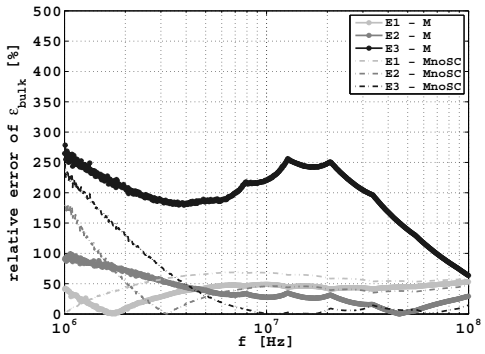


(b)

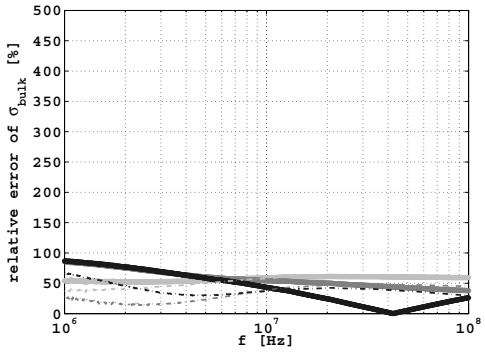
Fig. 3. Model **H/HnoSC**. Relative error for ε_{bulk} **(a)** and σ_{bulk} **(b)** using sublayers with homogeneous non-dispersive dielectric parameters (parameters see text). Simulation data is compared to measurements (reference) with and without SC. Data is shown for planar electrodes with gap widths (driven to ground) of 4mm (E1), 1.5mm (E2) and 0.3mm (E3).

V. DISCUSSION

The dielectric and physical thickness parameters of SC, viable skin and SCF are in a such relation that a layered model with homogeneous dielectrics (model H) generates a relaxation in the MHz region due to the thin (compared to the inter-electrode distance) poorly conductive SC between electrode and viable skin. On the other hand measurements on skin also exhibit a strong dispersion in this region, the mentioned β-dispersion [4] caused by interfacial polarization at the cell membranes or in other words by shorting them out. In order to test the suitability of the models the SC was removed (model HnoSC, MnoSC). Measurements show a prominent increase in both ε_{bulk} and σ_{bulk} for the E3 and E2 electrode and a decrease of ε_{bulk}/increase of σ_{bulk} for the E1 electrode after removal of the SC. As expected the HnoSC model could not reproduce this behaviour. The contrast between viable skin and subcutaneous fat is too poor as the E/D is about 2 orders of magnitude thicker than the SC. Therefore the observed values will not be reconstructed by the model and the contribution of the layering to the dispersion is very small. These results also indicate that the theory SC strongly contributing at lower frequencies and E/D dominating at higher frequencies (> 100 MHz) [2] might be wrong. The contribution can be equal but caused by other parameters (water content!) for whose the contrast between layers decreased. This will be further assessed by evaluating



(a)



(b)

Fig. 4. Model **M/MnoSC**. Relative error for ε_{bulk} **(a)** and σ_{bulk} **(b)** using the Maxwell-Garnett formula for a mixture containing aligned shelled ellipsoids I. Simulation data is compared to measurements (reference) with and without SC. Data is shown for planar electrodes with gap widths (driven to ground) of 4mm (E1), 1.5mm (E2) and 0.3mm (E3).

the electric energy and resistive heating in the layers. An additional argument against a significant contribution drop of the SC is also provided in [12]. The MnoSC model qualitatively reproduces the observations in the measurements after removal of the SC (rise of ε_{bulk} and σ_{bulk}), at least for the E2 and E3 electrodes. For E1, the decrease of ε_{bulk} could not be reproduced. But it has to be noted that the penetration depths of E2 and E3 are smaller and therefore the accumulated uncertainty due to assumptions on layer properties as well. Modeling the ε and σ of each layer as shelled particles embedded in a host medium is a good initial approach in order to reproduce trends based on morphological parameters and material composition on the cellular level, even though the initial presented model is not accurate yet. Initial studies (results not shown) indicated that the oriented ellipsoidal particles resulting in anisotropic dielectric parameters (especially for SC) provide a better reproduction of the trends than randomly oriented particles. Several aspects such as the constitution, anisotropic bound water shells [9] or the inclusion of organelles [8] can be accounted for already using an analytical or semi-analytical mixing rule.

As mentioned this work contains preliminary measurements and simulation results. A setup for maximizing the reproducibility and quality of the measurements as well as optimization of the numerical model, such as the application of the Hanai-Bruggeman formula, incorporation of bound water shells and organelles or the development of irregularly shaped cell models are part of ongoing work. The validity of approximations (volume fraction, non-constant thickness of the cell membrane, idealized shape, rough and general approximation of the input dielectric parameters) will also be investigated. Additionally, acquisition of various chemical, physiological and geometric properties (input parameters for the model) of each skin layer is required. In order to account for the sensor geometry a 3D model will be realized. Finally, the removal of the SC as a successful validation criterium for skin models will be kept.

VI. CONCLUSION

The presented results indicate that a skin model consisting of homogeneous layers is not suitable in the frequency range between 1 and 100 MHz. At least the basic microstructure of tissue (cells) has to be taken into account in order to indicate trends in the spectra correctly. The model containing shelled ellipsoids providing anisotropic bulk dielectric properties for each skin layer provides promising preliminary results. The concept can be extended to include e.g. thermodynamics and kinetics on protein/molecular level.

REFERENCES

[1] Ø. G. Martinsen, S. Grimnes, and O. Sveen, "Dielectric properties of some keratinised tissues. part 1: Stratum corneum and nail in situ," *Medical & Biological Engineering & Computing*, vol. 35, pp. 172–176, 1997.

[2] E. Alanen, T. Lahtinen, and J. Nuutinen, "Penetration of electromagnetic fields of an open-ended coaxial probe between 1 MHz and 1 GHz in dielectric skin measurements," *Phys. Med. Biol.*, vol. 44, pp. N169–N176, 1999.

[3] S. Naito, M. Hoshi, and S. Yagihara, "Microwave dielectric analysis of human stratum corneum in vivo," *Biochimica et Biophysica Acta*, vol. 1381, pp. 293–304, 1998.

[4] S. Gabriel, R. W. Lau, and C. Gabriel, "The dielectric properties of biological tissues: III. Parametric models for the dielectric spectrum of tissues," *Phys. Med. Biol.*, vol. 41, pp. 2271–2293, 1996.

[5] V. Raicu, N. Kitagawa, and A. Irimajiri, "A quantitative approach to the dielectric properties of the skin," *Phys. Med. Biol.*, vol. 45, pp. L1–L4, 2000.

[6] M. Egawa, T. Hirao, and M. Takahashi, "*In vivo* estimation of stratum corneum thickness from water concentration profiles obtained with raman spectroscopy," *Acta Dermato-Venerologica*, vol. 87, pp. 4–8, 2007.

[7] T. L. Moore, M. Lunt, B. McManus, M. E. Anderson, and A. L. Herrick, "Seventeen-point dermal ultrasound scoring system - a reliable measure of skin thickness in patients with systemic sclerosis," *Rheumatology*, vol. 42, pp. 1559–1563, 2003.

[8] K. Asami, "Characterization of heterogeneous systems by dielectric spectroscopy," *Prog. Polym. Sci.*, vol. 27, pp. 1617–1659, 2002.

[9] J. L. Sebastián, S. Muñoz, M. Sancho, G. Álvarez, and J. M. Miranda, "Electric field distribution and energy absorption in anisotropic and dispersive red blood cells," *Phys. Med. Biol.*, vol. 52, pp. 6831–6847, 2007.

[10] V. Raicu, T. Saibara, and A. Irimaijiri, "Dielectric properties of rat liver in vivo: a nonivasive approach using an open-ended coaxial probe at audio/radio frequencies," *Bioelectrochemistry and Bioenergetics*, vol. 47, pp. 325–332, 1998.

[11] B. R. Midmore, R. J. Hunter, and R. W. O'Brien, "The Dielectric Response of Concentrated Lattices," *Journal of Colloid and Interface Science*, vol. 120(1), pp. 210–217, 1987.

[12] C. Gabriel, *Handbook of Biological Effects of Electromagnetic Fields*. Taylor & Francis, 2006, ch. Dielectric Properties of Biological Materials, pp. 52–94.