Cole–Cole Model for the Dielectric Characterization of Healthy Skin and Basal Cell Carcinoma at THz Frequencies

Enrico Mattana, Matteo Bruno Lodi, *Member, IEEE*, Marco Simone, *Member, IEEE*, Giuseppe Mazzarella, *Senior Member, IEEE*, and Alessandro Fanti, *Senior Member, IEEE*

***Abstract*—THz radiationeffectively probes biological tissue water content due to its high sensibility to polar molecules. Skin and basal cell carcinoma (BCC), both rich in water, have been extensively studied in the THz range. Typically, the Double Debye model is used to study their dielectric permittivity. This work focuses on the viability of the multipole Cole-Cole model as an alternative dielectric model. To determine the best fit parameters, we used a genetic algorithm-based approach, solving a least squares problem. Compared with the Double Debye model, a maximum reduction of the RMSE value up to more than 50% and maximum relative percentage errors of 2.8% have been measured for both second and third order Cole-Cole models. Since the errors of the second and third order Cole-Cole models are similar, a two-poles model is enough to describe the behaviour both tissues from 0.2 THz to 2 THz.**

***Index Terms*—Basal cell carcinoma (BCC), cole-cole model, double Debye model, dielectric, terahertz.**

***Impact Statement*—The authors employed a third and second order Cole-Cole model to describe with minimal errors the permittivity of healthy skin and basal cell carcinoma in the THz range.**

I. INTRODUCTION

TERAHERTZ (THz) technology is gaining large attention from the scientific community for its potential in healthcare applications. The THz band is usually defined as the region of the electromagnetic spectrum with frequencies ranging from 0.1 to 10 THz, between the microwave and infrared regions [1]. From a biomedical point of view THz radiation exhibits interesting properties, namely its non-invasive and non-ionizing nature allows a safe interaction with the human body [2].

Among a large number of biomedical applications of interest such as sensing, spectroscopy and imaging, significant attention is directed to cancer detection and diagnosis [3]. THz waves are incredibly sensitive to polar molecules, in particular to water, thus strongly limiting the penetration depth in living tissues [4]. It is also possible to detect small and simple biomolecules by exploiting their unique spectral fingerprints, allowing for early detection of cancer biomarkers. The research has focused mainly on the skin tissue and its pathologies, since the THz radiation is able to penetrate through its outer layers without excessive losses and as a result can provide precious information of both water content and tissue structure [5], [6].

Non-melanoma skin cancers (NMSC) are the most widespread malignancy and their incidence is sharply rising globally. Basal cell carcinoma (BCC) is the most common form of NMSC and represents an important economic burden on healthcare services. Both mortality rate and metastatic risk are extremely low, so BCC is usually easily curable [7]. Usually a large number of therapeutic options are available, which includes curettage and electrodesiccation, tangential shave removal, surgical excision and Mohs micrographic surgery (MMS) [8]. Skin tumors usually exhibit a larger concentration of water molecules with respect to healthy tissues [9], indeed this is the major contrast mechanism in the THz range. For this reason both terahertz pulsed spectroscopy (TPS) and terahertz pulsed imaging (TPI) are able to provide insightful information on the histologic subtype of BCC, its size and margins, thereby supporting lesion removal and allowing for early detection [10], [11], [12], [13], [14].

Several research efforts in this field, and so this work, have been directed to the modeling of the frequency-dependent complex dielectric permittivity of both skin and BCC within the frequency range of 0.2 THz to 2 THz. The skin contains a large amount of water that heavily influences its dielectric response in the THz range [15], [16], [17], [18], because of this the prevalent model to approximate the permittivity is the Double Debye (DD), as it accurately represents the complex behavior exhibited by liquid water at these high frequencies [19], [20]. In [19]

Manuscript received 22 April 2024; revised 24 June 2024 and 11 July 2024; accepted 16 July 2024. Date of publication 5 August 2024; date of current version 14 August 2024. This work was supported by the European Union - NextGenerationEU through the Italian Ministry of University and Research under PNRR - M4C2-I1.3 Project PE 00000019 “HEALITALIA” to Enrico Mattana, Matteo Bruno Lodi and Alessandro Fanti CUPF53C22000750006 University of Cagliari. The views and opinions expressed are those of the authors only and do not necessarily reflect those of the European Union or the European Commission. Neither the European Union nor the European Commission can be held responsible for them. The review of this article was arranged by Editor Sergio Fantini. *(Corresponding author: Alessandro Fanti.)*

Enrico Mattana, Matteo Bruno Lodi, Giuseppe Mazzarella, and Alessandro Fanti are with the Department of Electrical and Electronic Engineering, University of Cagliari, 09123 Cagliari, Italy (e-mail: alessandro.fanti@unica.it).

Marco Simone is with the Department of Electrical, Electronics, Computer Engineering (DIEEI), University of Catania, Catania, Italy.

Digital Object Identifier 10.1109/OJEMB.2024.3438562

authors claim that the DD model is able to accurately represent water permittivity up to 1 THz while, for higher frequencies, two Lorentzian resonance terms were incorporated to refine the model. In [16] the DD was employed to simulate THz pulses interaction with both healthy skin and BCC from 0.2 to 2 THz, with the goal to understand the interaction between THz pulses and the skin. The DD model failed to accurately replicate the behavior of tissues below 0.6 THz, exhibiting maximum errors of approximately 17% of the permittivity.

In [21] a global optimization approach based on the branch and bounding method was developed to improve the accuracy of the DD model, demonstrating that it is able to model both healthy skin and BCC across the full [0.2, 2] THz range. Moreover, in [22], it has been demonstrated that the improved fitting algorithm allows to use the static permittivity at low frequencies of the DD model to discriminate between cancerous and healthy skin tissue. Despite this, using the parameters extracted thanks to the least squares approach of [21], there are still errors as high as 4%–4.5% especially near the extremes of the interval of interest.

BCC is not the only skin tumour investigated and characterized at THz frequencies. In [23], [24] THz TPS has been successfully employed to study the dielectric properties of in vivo healthy skin, non-dysplastic and dysplastic skin nevi. THz dielectric dispersion allows to differentiate between non dysplastic and dysplastic skin nevi, with the latter known as a precursor to melanoma. In [25], a THz TDS system was utilized to study a mouse skin sample containing melanoma. The tumor was correctly identified since it has a higher absorption coefficient and refractive index than normal tissue. Finally, the dielectric permittivity of artificial healthy skin and melanoma was examined across the 0.4 THz to 1.6 THz range in [26]. The particle swarm optimization (PSO) algorithm was utilized to extract the best fit parameters. The study demonstrated that these parameters were influenced not only by the water content in both tissues but also by cell type and density. Moreover, they can be used to effectively differentiate between healthy and tumoral tissue.

In recent studies [27], a DD model extracted with a combinational optimization algorithm has been employed to investigate the impact of anticancer drugs on the dielectric permittivity of a 3-D organotypic model of BCC in a narrower frequency range, from 0.4 THz to 1.6 THz. Since THz science and technology is looking forward to tissue phantoms, for device prototyping and testing, that can mimick both healthy and pathologic skin tissues, a deeper understanding of their THz dielectric response is needed. From the above discussion, it must be critically recognized that there is still room for improvement when it comes to dielectric models employed to interpret and approximate the permittivity of both healthy skin and BCC. Dielectric models able to describe with minimal errors the tissues' permittivity are essential, also to obtain reliable results in numerical simulations, reduce their computational workload and providing deeper insights on the tissues relaxation mechanisms, as well as physio-pathological state. Therefore, as alternative to DD models, multipoles Cole-Cole models can be considered as valid physical frameworks for the THz dielectric spectra of healthy and pathologic skin tissues.

Since the integration of THz technologies in healthcare is an ongoing challenge, to facilitate this process it is of crucial importance the development of models capable of analytically describing the dielectric properties of skin cancer cells at THz. This work will deal with demonstrating the feasibility of employing the second and third order Cole-Cole model to accurately approximate the permittivity of both skin and BCC and then we will critically compare the results with the DD models available in the literature.

II. MATERIALS AND METHODS

In this section a brief description of the Cole-Cole dielectric model, the formulation of the non linear least-squares problem and the settings of the employed genetic algorithm are presented.

A. The Cole-Cole Model

Based on the first order Cole-Cole model, the complex relative permittivity $\epsilon_r^{CC}(\omega)$ can be expressed as [28]

$$\epsilon_r^{CC}(\omega) = \epsilon_\infty + \frac{\epsilon_s - \epsilon_\infty}{1 + (j\omega\tau)^n}, \tag{1}$$

where ϵ_s and ϵ_∞ are respectively the static and the high frequency limit of permittivity, and τ is the generalized relaxation time constant. The shape of the spectral profile depends on the distribution parameter n, for $n = 1$ the equation simplifies to a Debye model, while smaller n corresponds to a broader dispersion curve and distribution of relaxation times [29]. The generalization to the Nth order is defined as [30]

$$\epsilon_r^{CC}(\omega) = \epsilon_\infty + \sum_{i=1}^{N} \frac{\Delta\epsilon_i}{1 + (j\omega\tau_i)^{n_i}}, \tag{2}$$

where N corresponds to the number of poles and $\Delta\epsilon_i$ is the difference between the ith static permittivity and ϵ_∞ and represents the magnitude of the ith dispersion. Relaxation is a reactive process involving translational and rotational diffusion, hydrogen bond rearrangement, and structural changes. These processes are time-scale dependent and have specific activation energies, leading to significant temperature dependence [15], [31]. Liquid water organizes in a hydrogen-bond network of tetrahedral cages. When excited by THz radiation, this structure is disrupted and four hydrogen bonds must break in order for the molecules to reorient, this is a slow process described by the time constant τ_1. Subsequently, the single water molecules reorient and move to a new tetrahedral site, this is a fast process described by τ_2. This is the reason why the Double Debye model ($N = 2$, $n_1 = n_2 = 1$) is used to describe the permittivity of liquid water, as it can effectively model these two relaxation processes. The skin, however, is a complex biological and chemical environment and its dielectric properties do not exclusively depend on water content [26]. Therefore, given that in the tumor microenvironemnt several macromolecules and proteins are synthesized and concentrates, the water dynamics and THz-response is altered, leading to a continuum of relaxation processes and times. Therefore, Cole-Cole models, with their non-resonant and broad response, are suitable for framing and understanding these dielectric features. Furthermore, as N increases, the multipole Cole-Cole becomes capable of describing complex relaxation laws manifested by biological tissues [29]. This is because the superposition of the Cole-Cole dispersion curves in the frequency domain can account for dipole-dipole interactions and distribution of relaxation times, which may vary in terms of broadness.

B. Problem Modeling

From [16] and [17], we extracted the data of the real part of the refractive index $n(\omega)$ and the absorption coefficient $\alpha(\omega)$ of both healthy skin and BCC in the frequency range [0.2, 2] THz, with a total of $N_{s1} = 29$ samples for the first dataset and $N_{s2} = 57$. The complex relative permittivity can be easily obtained since [16]

$$\epsilon_r(\omega) = \epsilon' - j\epsilon'' = \left(n(\omega) - j\frac{c\alpha(\omega)}{2\omega} \right)^2, \tag{3}$$

where c is the speed of light in vacuum, ϵ' and ϵ'' are respectively the real and imaginary part of the complex dielectric permittivity.

To estimate the parameters of the second and third order Cole-Cole model a nonlinear least squares problem has been resolved. For every discrete circular frequency ω_k, we defined the kth residual r_k as the squared module of the difference between the actual value of the complex permittivity, $\epsilon_r(\omega)$, and the value predicted by the second and third order Cole-Cole models, denoted as $\epsilon_r^{CC}(\omega)$

$$r_k = \left| \epsilon_r(\omega_k) - \epsilon_r^{CC}(\omega_k) \right|^2. \tag{4}$$

The objective function to minimize is the total square error function, defined as

$$\min_{\mathbf{x}} \frac{1}{N_s} \left(\sum_{k=1}^{N_s} r_k \right), \tag{5}$$

where N_s is the number of samples and $\mathbf{x}$ is the vector containing the $3N + 1$ unknown parameters of the Nth order Cole-Cole model (see (2)). The search for the optimal Cole-Cole parameters is subject to the following boundaries

$$\epsilon_\infty > 0, \tag{6}$$

$$\tau_i > 10\tau_{i+1} \qquad i = 1, \ldots, N-1, \tag{7}$$

$$\Delta\epsilon_j > 0, \quad 0 \leq n_j \leq 1, \qquad j = 1, \ldots, N. \tag{8}$$

To analytically estimate the fit goodness the percentage relative errors and the root-mean-square error (RMSE), i.e., the square root of the minimized total error function, were considered.

C. Algorithm

The minimization of (5) was performed employing the genetic algorithm (GA) of Matlab v2021b (The MathWorks Inc., MA USA) global optimization toolbox. In this study, a stochastic uniform selection method was considered with a starting population size of 250 individuals and a crossover probability of 0.8. This selection method ensures that parents are selected with a probability linked to their scaled fitness value, which is inversely proportional to the value of the total square error function (5). The optimization problem has bounds and a linear inequality (see (6)–(8)), the crossover function creates children as the weighted average of the parents in order to avoid poorly distributed populations. Moreover, since the bounds and inequality are strictly linked to the physics of the problem, an adaptive mutation function ensuring that directions and step lengths are compatible with these constraints has been employed. The GA solver iteratively refines the selection vector $\mathbf{x}$ through operations of crossover and mutation until it meets a termination criteria, which is either a maximum number of iterates equals to 20000 or an average relative change in the best fitness function value less than 10^{-7}. The optimization problem was solved 15 times, and in the next section the models that best fit the experimental data will be presented.

TABLE I
THIRD ORDER COLE-COLE PARAMETERS

	$[\varepsilon_\infty,\ \Delta\varepsilon_1,\ \Delta\varepsilon_2,\ \Delta\varepsilon_3]$	$[\tau_1,\ \tau_2,\ \tau_3]$ (ps)	$[n_1,\ n_2,\ n_3]$
HS [16]	[1.33, 231.36, 2.41, 2.87]	[63.40, 0.70, 0.025]	[1, 0.86, 0.72]
BCC [16]	[0.52, 243.89, 3.5, 3.05]	[53.65, 0.61, 0.012]	[1, 0.76, 0.86]
HS [17]	[2.34, 208.14, 2.41, 1.71]	[6.33, 0.64, 0.044]	[1, 0.84, 0.85]
BCC [17]	[0.50, 65.53, 3.79, 2.42]	[11.16, 0.32, 0.009]	[1, 0.66, 1.00]

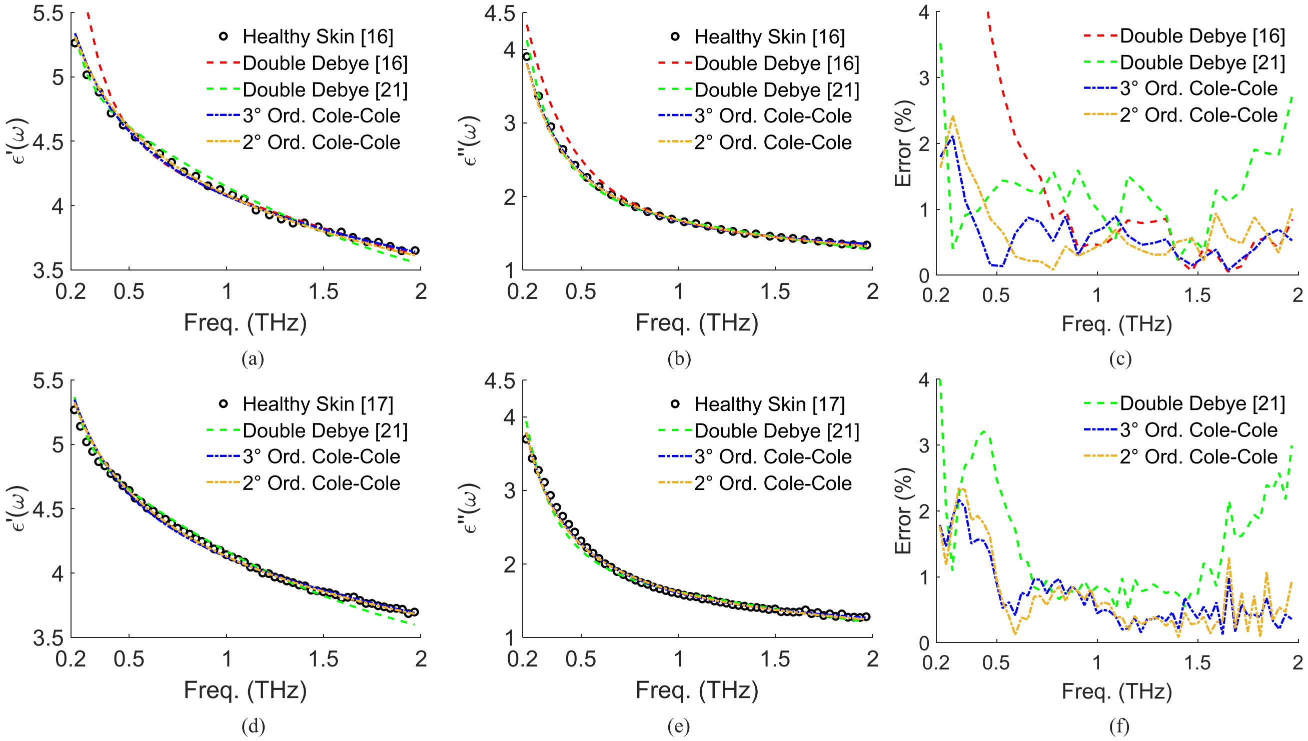
TABLE II
SECOND ORDER COLE-COLE PARAMETERS

	$[\varepsilon_\infty,\ \Delta\varepsilon_1,\ \Delta\varepsilon_2]$	$[\tau_1,\ \tau_2]$	$[n_1,\ n_2]$
HS [16]	[0.69,280.57,6.54]	[100.1,0.15]	[0.92,0.36]
BCC [16]	[0.9, 300.51, 6.84]	[82.47,0.23]	[0.93,0.37]
HS [17]	[1.54,205.89,5.52]	[67.32,0.23]	[0.94,0.41]
BCC [17]	[1.14,114.84,5.69]	[22.78,0.12]	[0.94,0.44]

III. RESULTS

The second and third order Cole-Cole parameters for both healthy skin (HS) and BCC are listed in Tables I and II, respectively. For both models and both dataset of dielectric data, it can be noticed from Tables I and II that, since $n_1 \approx 1$, the first pole of the models behaves like a quasi-Debye term and its center is within the range [1.59, 25] GHz. The second dispersion curve is much broader with $n_2 < 1$ and is centered inside the frequency band of interest [0.2, 2] THz. Finally, for the third order Cole-Cole model the last poles are centered at frequencies higher than 3.5 THz.

Fig. 1 shows the real (ϵ') and imaginary (ϵ'') part of the dielectric permittivity of healthy skin extracted from [16] and [17] and the relative percentage error for the fittings with different models. The dielectric data from the two different datasets [16], [17] are very similar. From Fig. 1(c) The DD model proposed in [16], available only for the first dataset, is able to approximate the permittivity of healthy skin with errors with respect to the module lower than 1% for frequencies higher than 0.85 THz, while unable to do the same for lower ones, reaching errors as high as 15% around 0.2 THz. The DD model proposed in [21] exhibits better tracking capabilities, trading off the accuracy in the higher end of the frequency range for errors on the module of



(a) (b) (c) (d) (e) (f)

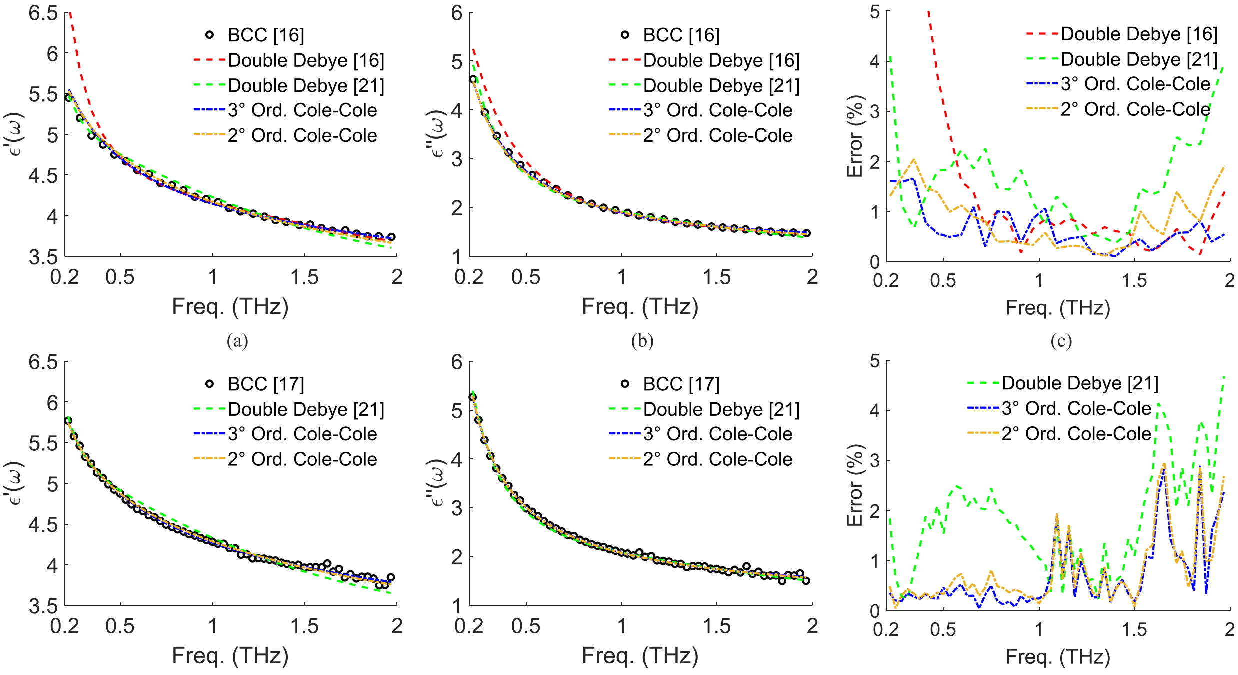
Fig. 1. Approximations of healthy skin permittivity in the THz range, data extracted from [16] (a), (b), (c) and [17] (d), (e), (f). Comparison between the fitting of the second and third order cole-cole models and (a), (b) the double debye models from [16], [21] and (c), (d) the double debye model from [21]. Percentage relative error computed on the module of the relative permittivity $|\epsilon_r(\omega)|$ (c), (f) for the different dielectric models.

permittivity $\leq 2\%$ in a broader band, approximately [0.5, 1.65] THz for both datasets. The second and third order Cole-Cole models have comparable errors and follow similar trends. The highest error registered for the third order Cole-Cole model on the real part of $\epsilon_r(\omega)$ is 0.97% on the first dataset and for ϵ'' is 3.31% on the second dataset. The second order Cole-Cole model is characterized by maximum errors of 1.02% of ϵ' on the first dataset and 3.8% of ϵ'' on both datasets. In general the third order Cole-Cole model is able to approximate better the imaginary part of the permittivity of healthy skin. To compare the Cole-Cole models with the Debye it is possible to consider the RMSE as a figure of merit. The third order Cole-Cole model presents RMSEs of 0.0417 and 0.0465 while the second order one 0.0461, 0.0487, for the first and second dataset respectively. Both are an order of magnitude smaller than the RMSE of the DD proposed in [16]. Moreover, there's an approximate mean 38% reduction in the RMSEs compared to the DD model from [21].

Fig. 2 shows the dielectric data relative to the BCC samples from the two datasets, with the comparison between the simulations of the DD and Cole-Cole models. From an analysis of Fig. 2 it is possible to notice similar trends with respect to the healthy skin approximations. The DD model proposed in [16] is not able to track the permittivity of BCC with degrees of accuracy comparable to the other models under 0.5 THz (see Fig. 2(a) and (c)) and reaches errors on the module of approximately 17% around 2 THz. The DD presented in [21] manifests errors of roughly 3.5% of $|\epsilon_r(\omega)|$ near 0.2 THz and 2 THz. In this case, it appears that the DD model struggles to accurately track the BCC dielectric data, in particular near the extremes of the interval of interest. On the other hand, the Cole-Cole models exhibit good tracking, as it can be seen from Fig. 2(f) especially. For both Cole-Cole models, low errors has been registered on the real part with a maximum of 2.8% for the second order Cole-Cole model on the second dataset. The fitting of the imaginary part for the second dataset was the most critical one for frequencies higher than 1.5 THz, where the second and third order Cole-Cole model are characterized by errors up to 6.72% and 6.92%, mainly because the experimental data from [17] data shows considerable fluctuations. The third order Cole-Cole model presents RMSEs of 0.0438 and 0.0425 while the second order one 0.0527, 0.0461, for the first and second dataset respectively [16]. It is relevant to note that the error in the second dataset is averaged over nearly twice the number of samples compared to the first one. The RMSE values of the second order Cole-Cole model are approximately 44% and 53% smaller compared with the DD model proposed [21].

IV. DISCUSSION

From the presented results it can be evinced that the third order and second order Cole-Cole model are able to track the permittivity of both skin and BCC in the THz range, with errors always lower than 3% of $|\epsilon_r(\omega)|$. For this reason, the numerical condition (7) is fundamental to ensure a good result of the fitting



(a) (b) (c)

(d) (e) (f)

Fig. 2. Approximations of BCC permittivity in the THz range, data extracted from [16] (a), (b), (c) and [17] (d), (e), (f). Comparison between the fitting of the second and third order cole-cole models and (a), (b) the double debye models from [16], [21] and (c), (d) the double debye model from [21]. Percentage relative error computed on the module of the relative permittivity $|\epsilon_r(\omega)|$ (c), (f) for the different dielectric models.

procedure. Since the multipole Cole-Cole model is used to model materials that exhibits multiple distribution of relaxation times with varying degrees of broadness, it is completely reasonable to expect the resonant frequencies of the poles to be sufficiently distant in the frequency domain. Since the two poles Cole-Cole approximation is definitely comparable to the third order one, while having 3 less unknown parameters, the most relevant poles are the first two. The first poles are characterized by the largest magnitude, $n_1 = 1$ and are centered at frequencies <25 GHz, meaning that, in the frequency range of interest, they contribute mainly to the shape of the imaginary part of the permittivity while they almost acts as an offset for the real part. On the contrary, the second poles, with smaller magnitude and centered in the frequency band [0.2, 2] THz, contribute generally to the shape of both the real and imaginary part. Having a Cole-Cole pole inside the band [0.2, 2] THz, with limited slopes ($n_2 < 1$) ensures a good tracking where the DD model falls short, since $\epsilon_r(\omega)$ doesn't vary sharply with frequency. The third pole, if present, contributes slightly to both ϵ' and ϵ''. Essentially, while the first two poles provide the general shape with good precision, the third pole further enhances the approximation where possible. From the above analysis, while the third order Cole-Cole model reaches numerical errors smaller than the second order one, the improvement of the fitting is not enough to justify the increased computational complexity of the fitting.

V. CONCLUSION

The main objective of this work was to identify an alternative to the Double Debye model for better approximating the permittivity of both skin and BCC in the THz range. Additionally, the study aimed to investigate the feasibility of describing them using a second and third order Cole-Cole model. To achieve this result, starting from dielectric data extracted from the literature, the Cole-Cole parameters of the best fit were obtained solving a nonlinear least squares problem employing a genetic algorithm routine. Then, the different dielectric models approximations have been quantitatively compared, considering the relative errors as a function of frequency and the RMSE. The results of the numerical analysis indicate that the errors of both Cole-Cole models are similar, while with respect to the DD, the first ones are able to better track the permittivity of both healthy skin and BCC, reaching maximum reductions of the RMSE values of more than 50%. An accurate approximation of the tissues permittivity over the entire frequency band is essential to understand how THz pulses interact and propagate through biological systems, thus allowing for the development of THz technologies for biomedical applications and imaging.

REFERENCES

[1] M. Gezimati and G. Singh, "Terahertz imaging and sensing for healthcare: Current status and future perspectives," *IEEE Access*, vol. 11, pp. 18590–18619, 2023.

[2] X. Chen et al., "Terahertz (THz) biophotonics technology: Instrumentation, techniques, and biomedical applications," *Chem. Phys. Rev.*, vol. 3, no. 1, 2022, Art. no. 011311, doi: 10.1063/5.0068979.

[3] Y. Peng, C. Shi, X. Wu, Y. Zhu, and S. Zhuang, "Terahertz imaging and spectroscopy in cancer diagnostics: A technical review," *BME Front.*, vol. 2020, 2020, Art. no. 2547609, doi: 10.34133/2020/2547609.

[4] Z. D. Taylor et al., "THz medical imaging: In vivo hydration sensing," *IEEE Trans. Terahertz Sci. Technol.*, vol. 1, no. 1, pp. 201–219, Sep. 2011.

[5] J. Wang, H. Lindley-Hatcher, X. Chen, and E. Pickwell-MacPherson, “Thz sensing of human skin: A review of skin modeling approaches,” *Sensors*, vol. 21, 2021, Art. no. 3624.

[6] D. B. Bennett, W. Li, Z. D. Taylor, W. S. Grundfest, and E. R. Brown, “Stratified media model for terahertz reflectometry of the skin,” *IEEE Sensors J.*, vol. 11, no. 5, pp. 1253–1262, May 2011.

[7] A. Lomas, J. Leonardi-Bee, and F. Bath-Hextall, “A systematic review of worldwide incidence of nonmelanoma skin cancer,” *Brit. J. Dermatol.*, vol. 166, no. 5, pp. 1069–1080, 2012, doi: 10.1111/j.1365-2133.2012.10830.x.

[8] A. Fahradyan, A. C. Howell, E. M. Wolfswinkel, M. Tsuha, P. Sheth, and A. K. Wong, “Updates on the management of non-melanoma skin cancer (NMSC),” *Healthcare*, vol. 5, no. 4, Nov. 2017, Art. no. 82.

[9] M. Mertens, M. Chavoshi, O. Peytral-Rieu, K. Grenier, and D. Schreurs, “Dielectric spectroscopy: Revealing the true colors of biological matter,” *IEEE Microw. Mag.*, vol. 24, no. 4, pp. 49–62, Apr. 2023.

[10] P. Siegel, “Terahertz technology in biology and medicine,” *IEEE Trans. Microw. Theory Techn.*, vol. 52, no. 10, pp. 2438–2447, Oct. 2004.

[11] R. M. Woodward et al., “Terahertz pulse imaging in reflection geometry of human skin cancer and skin tissue,” *Phys. Med. Biol.*, vol. 47, no. 21, Oct. 2002, Art. no. 3853, doi: 10.1088/0031-9155/47/21/325.

[12] R. M. Woodward et al., “Terahertz pulse imaging of ex vivo basal cell carcinoma,” *J. Invest. Dermatol.*, vol. 120, pp. 72–78, 2003, doi: 10.1046/j.1523-1747.2003.12013.x.

[13] V. P. Wallace et al., “Terahertz pulsed imaging and spectroscopy for biomedical and pharmaceutical applications,” *Faraday Discuss.*, vol. 126, pp. 255–263, 2004, doi: 10.1039/B309357N.

[14] A. Sadeghi, S. M. H. Naghavi, M. Mozafari, and E. Afshari, “Nanoscale biomaterials for terahertz imaging: A non-invasive approach for early cancer detection,” *Transl. Oncol.*, vol. 27, 2023, Art. no. 101565. [Online]. Available: https://www.sciencedirect.com/science/article/pii/S1936523322002248

[15] E. Pickwell, B. E. Cole, A. J. Fitzgerald, V. P. Wallace, and M. Pepper, “Simulation of terahertz pulse propagation in biological systems,” *Appl. Phys. Lett.*, vol. 84, no. 12, pp. 2190–2192, 2004, doi: 10.1063/1.1688448.

[16] E. Pickwell et al., “Simulating the response of terahertz radiation to basal cell carcinoma using ex vivo spectroscopy measurements,” *J. Biomed. Opt.*, vol. 10, no. 6, 2005, Art. no. 064021, doi: 10.1117/1.2137667.

[17] V. P. Wallace et al., “Terahertz pulsed spectroscopy of human basal cell carcinoma,” *Appl. Spectrosc.*, vol. 60, no. 10, pp. 1127–1133, 2006, pMID: 17059664, doi: 10.1366/000370206778664635.

[18] E. Pickwell, B. E. Cole, A. J. Fitzgerald, M. Pepper, and V. P. Wallace, “In vivo study of human skin using pulsed terahertz radiation,” *Phys. Med. Biol.*, vol. 49, no. 9, Apr. 2004, Art. no. 1595.

[19] H. J. Liebe, G. A. Hufford, and T. Manabe, “A model for the complex permittivity of water at frequencies below 1 THz,” *Int. J. Infrared Millimeter Waves*, vol. 12, pp. 659–675, 1991, doi: 10.1007/BF01008897.

[20] J. T. Kindt and C. A. Schmuttenmaer, “Far-infrared dielectric properties of polar liquids probed by femtosecond terahertz pulse spectroscopy,” *J. Phys. Chem.*, vol. 100, pp. 10373–10379, 1996, doi: 10.1021/jp960141g.

[21] B. C. Q. Truong, H. D. Tuan, H. H. Kha, and H. T. Nguyen, “Debye parameter extraction for characterizing interaction of terahertz radiation with human skin tissue,” *IEEE Trans. Biomed. Eng.*, vol. 60, no. 6, pp. 1528–1537, Jun. 2013.

[22] B. C. Q. Truong, H. D. Tuan, V. P. Wallace, A. J. Fitzgerald, and H. T. Nguyen, “The potential of the double Debye parameters to discriminate between basal cell carcinoma and normal skin,” *IEEE Trans. Terahertz Sci. Technol.*, vol. 5, no. 6, pp. 990–998, Nov. 2015.

[23] K. I. Zaitsev, N. V. Chernomyrdin, K. G. Kudrin, I. V. Reshetov, and S. O. Yurchenko, “Terahertz spectroscopy of pigmentary skin nevi in vivo,” *Opt. Spectrosc.*, vol. 119, no. 3, pp. 404–410, Sep. 2015, doi: 10.1134/S0030400X1509026X.

[24] K. I. Zaytsev et al., “In vivo terahertz pulsed spectroscopy of dysplastic and non-dysplastic skin nevi,” *J. Phys., Conf. Ser.*, vol. 735, no. 1, Aug. 2016, Art. no. 012076, doi: 10.1088/1742-6596/735/1/012076.

[25] D. Li et al., “Detecting melanoma with a terahertz spectroscopy imaging technique,” *Spectrochimica Acta Part A, Mol. Biomol. Spectrosc.*, vol. 234, 2020, Art. no. 118229. [Online]. Available: https://www.sciencedirect.com/science/article/pii/S1386142520302079

[26] R. Zhang et al., “Dielectric and double Debye parameters of artificial normal skin and melanoma,” *J. Infrared, Millimeter, Terahertz Waves*, vol. 40, no. 6, pp. 657–672, Jun. 2019, doi: 10.1007/s10762-019-00597-x.

[27] S. Nourinovin, M. M. Rahman, S. J. Park, H. Hamid, M. P. Philpott, and A. Alomainy, “Terahertz dielectric characterization of three-dimensional organotypic treated basal cell carcinoma and corresponding double Debye model,” *IEEE Trans. Terahertz Sci. Technol.*, vol. 13, no. 3, pp. 246–253, May 2023.

[28] K. S. Cole and R. H. Cole, “Dispersion and absorption in dielectrics I. Alternating current characteristics,” *J. Chem. Phys.*, vol. 9, no. 4, pp. 341–351, 1941, doi: 10.1063/1.1750906.

[29] A. Khamzin, R. Nigmatullin, and I. Popov, “Microscopic model of a non-Debye dielectric relaxation: The cole-cole law and its generalization,” *Theor. Math. Phys.*, vol. 173, pp. 1604–1619, 2012.

[30] K. Sasaki, K. Wake, and S. Watanabe, “Development of best fit cole-cole parameters for measurement data from biological tissues and organs between 1 MHz and 20 GHz,” *Radio Sci.*, vol. 49, no. 7, pp. 459–472, 2014, doi: 10.1002/2013RS005345.

[31] C. Ro/nne, L. Thrane, P.-O. Åstrand, A. Wallqvist, K. V. Mikkelsen, and S. R. Keiding, “Investigation of the temperature dependence of dielectric relaxation in liquid water by THz reflection spectroscopy and molecular dynamics simulation,” *J. Chem. Phys.*, vol. 107, no. 14, pp. 5319–5331, 1997, doi: 10.1063/1.474242.

Enrico Mattana received the bachelor’s degree in biomedical engineering in 2023, from the University of Cagliari, Cagliari, Italy, where he is currently working toward the master’s degree in electronic engineering. His research interests include the modeling of bio-electromagnetic phenomena and food engineering.

Matteo Bruno Lodi (Member, IEEE) received the bachelor’s degree in biomedical engineering from the University of Cagliari, Cagliari, Italy, in 2016, the master’s degree in biomedical engineering from Politecnico di Torino, Turin, Italy, in 2018, and the Ph.D. (Hons.) degree in electronic engineering and computer science from the University of Cagliari, in 2022. From 2022 to 2023, he was a Technologist with Electromagnetic Group, University of Cagliari, where he is currently an Assistant Professor (Italian type-A, fixed-term). His research interests include the modeling of bioelectromagnetic phenomena, especially RF and MW hyperthermia treatment, the study, manufacturing, and synthesis of magnetic biomaterials for tissue engineering applications, and the use of microwaves for biotechnology and environmental applications while working in the design and characterization of antennas for space and wearable applications. Dr. Lodi was the recipient of the Roberto Sorrentino Young Scientist award at the 2022 Italian URSI Assembly, Young Scientists Award at the General Assembly and Scientific Symposium of URSI in 2020 and 2021, co-author of the “2021 IEEE IST Best Student Paper Award” at the IEEE International Conference on Imaging Systems and Techniques, Grant from the European Microwave Association for the attendance of the ESoA course titled “Diagnostic and Therapeutic Applications of Electromagnetics,” and COST Action CA17115 for the attendance of the IX International School of Bioelectromagnetism Alessandro Chiabrera, where, in 2019, he was the recipient of the Best Poster Award. He has been a Member of the WG2: “Better thermal-based EM therapeutics” of the COST Action 17115 “MyWave.” In 2022, he was appointed as the Representative of the IEEE Nanotechnology Council Young Professionals. He is part of the NTC technical committee (TC2) Nanobiomedicine. He is a Member of the Editorial Board of the IEEE Future Directions Technology Policy and Ethics Newsletter and of the *International Journal of RF and Microwave Computer-Aided Engineering*.

Marco Simone (Member, IEEE) received the master's degree in electronic engineering and the Ph.D. degree in electronic and computer engineering from the University of Cagliari, Cagliari, Italy, in 2011 and 2016, respectively. He was a visiting Ph.D. student with the Queen Mary University of London (QMUL), London, U.K., in 2015, and Postdoctoral Research Assistant in 2016–2017 with the Antennas & Electromagnetics Research Group, QMUL. From 2017 to 2022, he was an Associate Researcher with the Laboratory of Applied Electromagnetics, University of Cagliari. Since 2023, he has been an Assistant Professor of electromagnetic fields with the University of Catania, Catania, Italy. His research interests include optimization techniques applied to electromagnetics problems, microwave components design for radioastronomy applications, and antennas design for 5G, satellite and mm-wave applications.

Giuseppe Mazzarella (Senior Member, IEEE) received the graduation (*summa with laude*) degree in electronic engineering from the Università Federico II of Naples, Naples, Italy, in 1984, and the Ph.D. degree in electronic engineering and computer science in 1989. In 1990, he became an Assistant Professor with the Dipartimento di Ingegneria Elettronica, Università Federico II of Naples. Since 1992, he has been with the Dipartimento di Ingegneria Elettrica ed Elettronica, Università di Cagliari, Cagliari, Italy, first as Associate Professor and then, since 2000, as Full Professor, teaching courses in electromagnetics, microwave, antennas and remote sensing. He has authored or coauthored more than 100 papers in international journals. His research interests mainly include efficient design of large arrays of slots, power synthesis of array factor, with emphasis on inclusion of constraints, microwave holography techniques for the diagnosis of large reflector antennas, use of evolutionary programming for the solution of inverse problems, in particular problems of synthesis of antennas and periodic structures. He is a reviewer for many EM journals

Alessandro Fanti (Senior Member, IEEE) received the Laurea degree in electronic engineering and the Ph.D. degree in electronic engineering and computer science from the University of Cagliari, Cagliari, Italy, in 2006 and 2012, respectively. From 2013 to 2016, he was a Postdoctoral Fellow with the Electromagnetic Group, University of Cagliari. From 2017 to 2024, he was an Assistant Professor of electromagnetic with the Department of Electrical and Electronic Engineering, University of Cagliari, where he is currently an Associate Professor. From 2020 to 2023, he was the Principal Investigator of the IAPC Project, which was funded with five million euros by the Italian Ministry of Economic Development (MISE), within the AGRIFOOD PON I&C (2014–2020). Since 2024, he has been the Principal Investigator of the AISAC Project, funded with 15 million euros by the Italian Ministry of Enterprises and Made in Italy (MIMIT), within the "ACCORDI PER L'INNOVAZIONE" (2021–2026). He has authored or coauthored 71 papers in international journals. His research interests include the use of numerical techniques for modes computation of guiding structures, optimization techniques, analysis and design of waveguide slot arrays, analysis and design of patch antennas, radio propagation in urban environment, modeling of bioelectromagnetic phenomena, and microwave exposure systems for biotechnology and bioagriculture. He is a Member of the IEEE Antennas and Propagation Society, Italian Society of Electromagnetism, National InterUniversity Consortium for Telecommunications, and Interuniversity Center for the Interaction Between Electromagnetic Fields and Biosystems. He is an Associate Editor for IEEE JOURNAL OF ELECTROMAGNETICS, RF AND MICROWAVES IN MEDICINE AND BIOLOGY.

Open Access provided by 'Università degli Studi di Cagliari' within the CRUI CARE Agreement