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# Multi-layer Intrabody Terahertz Wave Propagation Model for Nanobiosensing Applications



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#### ABSTRACT

Enabling wireless communication between intrabody nanosensors and wearable devices can transform the field of nanobiosensing and, ultimately, lead to revolutionary healthcare systems. Recently, it has been demonstrated that such communication can occur at Terahertz (THz) band frequencies (0.1–10 THz). For the time being, existing studies are focused on characterizing the propagation of THz waves in a uniform medium. However, in a practical system, the THz waves will traverse different body tissues as they go in/out of the body. In this paper, the propagation of THz waves across human tissues is analytically modeled and numerically analyzed. More specifically, an impedance model that accounts for the discrepancies and the thicknesses of the human tissue layers is developed to allow us to predict the loss encountered as the wave propagates through the human body at THz band frequencies. The results show the necessity of accounting for the lost power due to multi-layer reflection in order to formulate a complete intrabody communication model. At the same time, the viability of utilizing the THz band for developing a feasible intrabody communication link is demonstrated.

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# 1. Introduction

Advancements in electronics, photonics, electro-mechanical systems and wireless communications have resulted in smart wearable systems able to continuously monitor human activities [1]. Besides conventional applications of wearable technology, Intra Body Communication (IBC) between wearable devices and implantable nanosensors will enable a myriad of transformative applications, such as in-vivo health monitoring and drug delivery systems, as well as minimally invasive surgery through (autonomous) nanorobots. In all these applications, wireless communication between intrabody nanodevices and body-worn surface nodes is required [2].

While several wireless technologies can be considered to permit IBCs, major recent progress in the field of nanoeletronics and nanophotonics is facilitating the development of miniature signal sources, antennas and detectors that operate in the Terahertz (THz) band (0.1–10 THz) [3,4]. Moreover, the rapid development of ultrafast lasers contributed to the establishment of modern THztime domain spectroscopy, used to probe and characterize various

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http://dx.doi.org/10.1016/j.nancom.2017.08.005 1878-7789/© 2017 Elsevier B.V. All rights reserved. biomaterials since most low-frequency biomolecular motions, including vibration and rotation of the molecular skeleton, lie in the same frequency range as THz radiation [5]. Hence, this traditionally under-utilized spectral band is expected to significantly contribute to potential future medical technologies as its non-ionization characteristic is considered advantageous for biological tissues as well as its scattering losses are negligible [6]. To date, initial THz channel characterization studies have focused on analyzing the electromagnetic propagation effects in a single human tissue [7–9], such as skin [10] or fat [11]. Nevertheless, the aforementioned medical applications require communication between the nanosensors and the wearable device. This implies the need to investigate the effect of electromagnetic wave propagation across *multiple* tissue layers rather than a single layer especially that the present literature lacks a full wave intrabody communication model that predicts the degradation a signal will encounter as it traverses multi-layer biological samples at the THz band.

In this paper, we bridge this gap by analytically modeling the propagation of THz waves across layers of different tissues. More specifically, we derive the equivalent impedance of the tissue layers and utilize tools from electromagnetic theory to compute the power loss as the signal propagates from the transmitter to the receiver taking into account the dispersive electrical properties and thicknesses of the human tissues. Such cascaded multi-layer approach is applied to both scenarios involving propagation from the nanosensor to the wearable device, as well as from the wearable device to the nanosensor. The results presented emphasize the importance of accounting for the lost power due to cross-layer reflection in order to formulate a complete intrabody communication model. Concurrently, the viability of utilizing the THz frequency band for developing a feasible intrabody communication link is demonstrated. It is to be noted that the presented model complements the model presented in [12], which takes into account the spreading, molecular absorption as well as the scattering of the intrabody THz propagating wave.

The rest of the paper is organized as follows. In Section 2, we discuss medical applications of THz intrabody propagation. In Section 3, the cascaded multi-layer intrabody model is demonstrated in which both analysis based on the scattering matrix and the transmission matrix are presented. In Section 4, electrical properties of human tissues at the THz band are characterized using the double Debye model. In Section 5, the numerical results are illustrated and validated via electromagnetic wave propagation simulation. Finally, we draw our conclusions in Section 6.

#### 2. Medical Applications of THz Intrabody Propagation

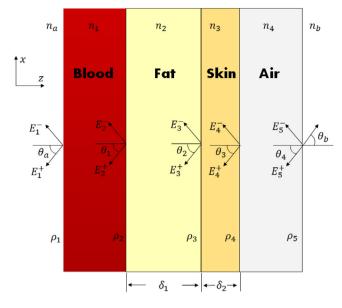
The significance of multi-layer propagation lies in identifying the capability of THz waves to be utilized in various medical applications. Indeed, since the feasibility of THz wave propagation through human tissue layers will be proven in this paper, applications that fall under the umbrella of nanomedicine will be enabled including nanobiosensing and drug delivery. In the former, communication occurs from the nanosensor to the wearable device, while in the latter, communication takes place from the wearable device to the nanosensor.

## 2.1. Nanobiosensing

The capability of recognizing and analyzing target molecules using minuscule, often integrated and multiplexed, nano-sized devices to attain both selective and sensitive detection limits is referred to as nanobiosensing [13]. Analysis at such wavelengths does not only permit measuring human physiological and behavioral data, but also allows a comprehensive insight into dynamic, cellular metabolic events which lead to a complete understanding of the metabolism of human biology [14]. Therefore, the ultimate goal of nanobiosensors is to detect any biochemical and biophysical signal associated with a specific disease at the level of a single molecule or cell. For instance, monitoring the concentration of certain antigens found in the blood stream or other bodily fluids allows both early cancer detection and diabetes screening [15,16]. It is to be noted that nanobiosensing will be allowed through the synthesis and utilization of materials whose morphological features on a nanoscale both confer a unique set of electrical and optical properties as well as achieve the desired detection sensitivity [17].

## 2.2. Drug-Delivery

Nanotechnology has provided the possibility of delivering drugs to specific cells using nanoparticles [18]. A distributed network of nanosensors and nanoactuators can work cooperatively to deliver drugs invasively without external interference [19]. In fact, nanoparticles are ideal carriers that deliver therapeutic drugs at the target site with optimum proficiency and minimum collateral damage to neighboring healthy tissues [20]. For example, smart



**Fig. 1.** Multi-layer dielectric structure in the transverse plane for an intrabody propagation scenario from blood to air going through a fat layer ( $\delta_1 = 5 \text{ mm}$ ) [25] and a skin layer ( $\delta_2 = 1.5 \text{ mm}$ ) [26].

insulin nanoactuators can constantly monitor the blood sugar level and inject pre-calculated amounts of insulin upon determination of insulin deficiency. Other examples of drug delivery usages include the treatment of cancerous cells using cellular-level chemotherapy [21]. Consequently, to achieve efficient drug delivery it is important to understand the interactions of nanomaterials with the biological environment, targeting cell-surface receptors, drug release, multiple drug administration, stability of therapeutic agents and molecular mechanisms of cell signaling involved in pathobiology of the disease under consideration [22].

Drug delivery is considered a fundamental part of drug development in which a wide range of drug delivery systems have been designed due to the developments of this technology. Ideally, all these systems would result in improving the stability, absorption, and therapeutic concentration of the drug within the target tissue [23].

#### 3. Cascaded Multi-layer Intrabody Model

To mimic an intrabody environment, we first consider an innermost blood layer, followed by fat, skin, and finally air. We assume that a nanosensor operating at the THz frequency band is located in the blood to sense vital body parameters and is sending data to an on-body sensor, which communicates with an external health infrastructure (for example, a wearable device connected to the user's smartphone). From the analysis of layered media [24], the adopted human tissue model relates the various field quantities, such as the electric fields and reflection coefficients, at the boundary of each interface. This topology is illustrated in Fig. 1, where  $n_i$ denotes the refractive index of the *i*<sup>th</sup> layer needed to calculate the refraction angle  $\theta_i$ , through each interface, by using Snell's law.

We define the phase thickness parameter  $\delta_i$  as

$$\delta_i = \frac{2\pi}{\lambda} l_i n_i \mathbf{cos} \theta_i, \quad i = 1, 2, \dots, M+1,$$
(1)

where  $\lambda$  is the wavelength, and  $l_i$  is the thickness of the *i*<sup>th</sup> layer. Moreover, we define the effective refractive index of each layer for both types of plane wave polarization, Transverse Electric (TE) and Transverse Magnetic (TM), respectively as

$$\hat{n}_{i} = \begin{cases} n_{i} \mathbf{cos} \theta_{i}, & \text{TE Polarization} \\ \frac{n_{i}}{\mathbf{cos} \theta_{i}}, & \text{TM Polarization.} \end{cases}$$
(2)

Thus, the transverse reflection coefficients at the M + 1 interfaces are defined as

$$\rho_i = \frac{\hat{n}_{i-1} - \hat{n}_i}{\hat{n}_{i-1} + \hat{n}_i}, \quad i = 1, 2, \dots, M + 1,$$
(3)

in which we set  $n_0 = n_a$ , and  $n_{M+1} = n_b$ .

# 3.1. Analysis Based on Scattering Matrix

The scattering matrix approach is applied in order to calculate the input reflection coefficient using the cascaded effective medium model. We demonstrate the scattering matrix approach by assuming TE polarization as follows

$$\begin{bmatrix} E_{i+} \\ E_{i-} \end{bmatrix} = \frac{1}{\tau_i} \begin{bmatrix} 1 & \rho_i \\ \rho_i & 1 \end{bmatrix} \begin{bmatrix} e^{j\delta_i} & 0 \\ 0 & e^{-j\delta_i} \end{bmatrix} \begin{bmatrix} E_{i+1,+} \\ E_{i+1,-} \end{bmatrix},$$
(4)

where the transmission coefficient,  $\tau_i$  is given by  $1+\rho_i$ . Multiplying the matrix factors, we obtain

$$\begin{bmatrix} E_{i+} \\ E_{i-} \end{bmatrix} = \frac{1}{\tau_i} \begin{bmatrix} e^{j\delta_i} & \rho_i e^{-j\delta_i} \\ \rho_i e^{j\delta_i} & e^{-j\delta_i} \end{bmatrix} \begin{bmatrix} E_{i+1,+} \\ E_{i+1,-} \end{bmatrix},$$
(5)

for i = M, M - 1, ..., 1. The recursion is initialized at the left of the  $(M + 1)^{\text{th}}$  interface by performing an additional matching to the right of that interface

$$\begin{bmatrix} E_{M+1,+} \\ E_{M+1,-} \end{bmatrix} = \frac{1}{\tau_{M+1}} \begin{bmatrix} 1 & \rho_{M+1} \\ \rho_{M+1} & 1 \end{bmatrix} \begin{bmatrix} E'_{M+1,+} \\ 0 \end{bmatrix}.$$
 (6)

It follows from the recursions in (5) and (6) that the overall reflection responses are combined to compute the overall scattering matrix as

$$\begin{bmatrix} S_{11} & S_{12} \\ S_{21} & S_{22} \end{bmatrix} = \prod_{i=1}^{M-1} \frac{1}{\tau_i} \begin{bmatrix} 1 & \rho_{i+1} \\ \rho_{i+1} & 1 \end{bmatrix}.$$
 (7)

The overall reflection coefficient can be expressed as

$$\Gamma_{i} = \frac{\rho_{i} + \Gamma_{i+1} e^{-2j\delta_{i}}}{1 + \rho_{i}\Gamma_{i+1} e^{-2j\delta_{i}}}, \quad i = M, M - 1, \dots, 1,$$
(8)

which is initialized at  $\Gamma_{M+1} = \rho_{M+1}$ . It is to be noted that the input reflection coefficient is obtained by setting i = 1 in (8), which corresponds to the  $S_{11}$  parameter. Further, the recursive formula (8) can be used to compute the overall reflection coefficient for both TE and TM polarization, using the appropriate effective refractive index defined in (2).

# 3.2. Analysis Based on Transmission Matrix

Beside the cascaded scattering matrix approach used to find the total reflection coefficient, we can also model the cross-layer wave propagation using the cascaded transmission matrix approach in order to compute both the electric and magnetic field patterns at the input port for both TE and TM polarizations

$$\begin{bmatrix} E_i \\ H_i \end{bmatrix} = \begin{bmatrix} \cos \delta_i & j\eta_i \sin \delta_i \\ j\eta_i^{-1} \sin \delta_i & \cos \delta_i \end{bmatrix} \begin{bmatrix} E_{i+1} \\ H_{i+1} \end{bmatrix}, \quad i = M, M - 1, \dots, 1,$$
(9)

where  $\eta_i$  is the transverse characteristic impedance related to the

refractive index by  $\eta_i = \eta_0/n_i$ , in which  $\eta_0 = 377 \ \Omega$ . The matrices can then be cascaded to calculate the total transmission matrix representing the entire inhomogeneous medium [27].

Further, cross-layer intrabody wave propagation phenomenon can be interpreted by replacing the cascaded layers with an effective medium having an equivalent impedance that accounts for the discrepancies between the layers. This approach is analogous to the one applied in transmission line theory [28]. Basically, the wave impedances,  $Z_i = E_i/H_i$ , satisfy the following recursions initialized by  $Z_{M+1} = \eta_b$ 

$$Z_i = R_i + jX_i = \eta_i \frac{Z_i + j\eta_i \mathbf{tan} \delta_i}{\eta_i + jZ_{i+1} \mathbf{tan} \delta_i}, \quad i = M, M - 1, \dots, 1,$$
(10)

where  $R_i$  and  $X_i$  are the equivalent input resistance and input reactance, respectively. The significance of (10) is that it allows us to calculate the equivalent impedance at both the skin–fat and the fat–blood interfaces, which is important for computing the individual cross-layer reflectances,  $(|\Gamma_i^2|)$ , that enable us to predict the percentage of the transmitted power through each interface of the human tissue model.

## 4. Electrical Properties of Human Tissues in the THz Band

In order to be capable of developing the multi-layer propagation model, electrical properties of tissues at the THz frequency must be accounted for. The scale that we are operating at is referred to as the "mesoscopic" length scale, which is intermediate between the molecular and macroscopic [29]. At the THz frequency, the disordered nature and microstructure of biological matter as well as the supracellular organization in such materials, often taking the form of fractal structures, trigger different polarization mechanisms which include multiple relaxation times and non-symmetric time-domain responses [30]. In particular, the dielectric response in the frequency domain of tissues having high water content can be characterized by the Debye Relaxation Model [31], which describes the reorientation of molecules that could involve translational and rotational diffusion as well as structural rearrangement. It is worth noting that we adopted the Debye model for computing the dispersive electrical properties of the tissue layers since it has proven to produce values that are in very good agreement with those obtained from experimental THz spectroscopy [32]. For a pure material, multiple Debye processes are possible in which the complex permittivity is described by [33]

$$\epsilon = \epsilon_{\infty} + \sum_{j=1}^{n} \frac{\Delta \epsilon}{1 + j w \tau_j},\tag{11}$$

where  $\epsilon_{\infty}$  is the permittivity at the high frequency limit,  $\Delta \epsilon = \epsilon_j - \epsilon_{j+1}$ ,  $\epsilon_j$  are intermediate values, occurring at different times of the permittivity,  $\tau_j$  is the relaxation time relating to the  $j^{\text{th}}$  Debye type relaxation process, and w is the angular frequency given as  $2\pi f$ .

To provide the best approximation of complex permittivity for polar liquids at frequencies up to 1 THz, the double Debye equations are used [34]

$$\epsilon = \epsilon_{\infty} + \frac{\epsilon_1 - \epsilon_2}{1 + jw\tau_1} + \frac{\epsilon_2 - \epsilon_{\infty}}{1 + jw\tau_2}.$$
(12)

Eq. (12) is rationalized and the real and imaginary parts of the complex permittivity are separated as follows

 Table 1

 Permittivity and relaxation time values.

Model	$\epsilon_{\infty}$	$\epsilon_1$	$\epsilon_2$	$\tau_1$ (ps)	$\tau_2$ (ps)
Water [31]	3.3	78.8	4.5	8.4	0.1
Whole Blood [32]	2.1	130	3.8	14.4	0.1
Skin [31]	3.0	60.0	3.6	10.6	0.2
Fat [35]	1.63	500	100	17.7	3.64

$$\epsilon' = \epsilon_{\infty} + \frac{\epsilon_1 - \epsilon_2}{1 + (w\tau_1)^2} + \frac{\epsilon_2 - \epsilon_{\infty}}{1 + (w\tau_2)^2},\tag{13}$$

$$\epsilon'' = \frac{(\epsilon_1 - \epsilon_2)(w\tau_1)}{1 + (w\tau_1)^2} + \frac{(\epsilon_2 - \epsilon_\infty)(w\tau_2)}{1 + (w\tau_2)^2}.$$
(14)

Using the values in Table 1,  $\epsilon'$  and  $\epsilon''$  are computed. These values are then used to calculate the effective index of refraction. *n*.

$$n = \sqrt{\frac{\sqrt{\epsilon^{\prime 2} + {\epsilon^{\prime}}^{\prime 2}} + \epsilon^{\prime}}{2}}.$$
(15)

## 5. Numerical Results

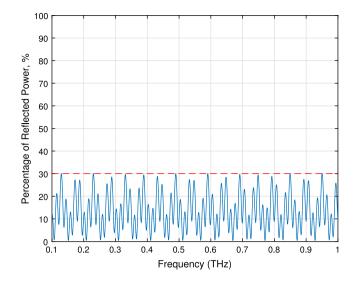
In this section, we numerically evaluate the analytical model based on the cascaded tissue layers by taking into account actual electrical parameters of the intrabody properties (summarized in Table 1).

#### 5.1. Wave Propagation from Inside to Outside the Human Body

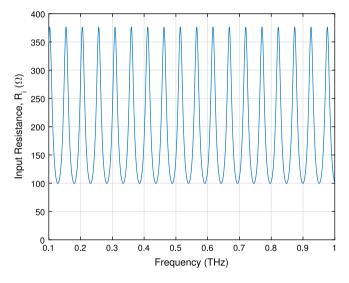
To assess the feasibility of operating at the THz frequency, the scenario in which a nanosensor embedded within the inner tissues of the human body sends information to a wearable device is considered. Fig. 2 illustrates the variations of the THz wave reflectance as a function of frequency, at the blood-fat interface, by representing the fat-skin-air in terms of equivalent impedance as per (10). It is evident from Fig. 2 that the reflectivity at the bloodfat interface is limited to 30% of the incident power. The results obtained indicate the need to account for the lost power due to cross-laver propagation encountered between the communication links of the nanosensor and the on-body device. Despite the impact of multi-layer reflection, the THz band is still an efficient tool to achieve intrabody communication. It is worth noting that the pattern in Fig. 2 is periodic since the variation of the frequency changes the effective thickness of the skin and fat layers. In addition, the results have been obtained assuming normal incidence since the objective is to study the effect of the cross-layer discontinuity.

Figs. 3 and 4 present the equivalent input resistance and input reactance of the impedance at the fat–skin–air interface, respectively. By examining the results of the reactance in Fig. 4 and their associated resistive values in Fig. 3, it is concluded that the equivalent medium has a relatively small reactance compared to its equivalent resistance. As an example, our results at 1 THz indicate that the ratio of the reactance to the resistance ( $\frac{X}{R}$ ) is only 0.2%, which implies that the THz wave electric and magnetic fields are in phase.

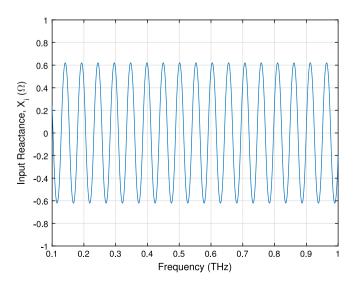
These findings confirm that the equivalent impedance of the cascaded layers is almost perfectly resistive giving rise to an effective dielectric medium where THz waves can penetrate without significant losses. This indicates that the signal degradation for THz intrabody propagation occurs mainly due to the cross-layer discontinuities rather than the medium absorption when considering the multi-layer human tissue scenario.



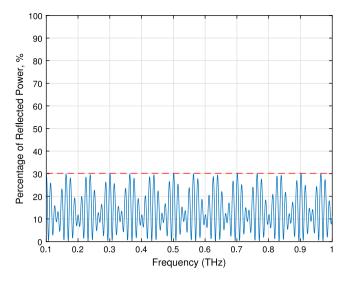
**Fig. 2.** Percentage of reflected power at the interface from inside to outside the human body when operating at the THz frequency.



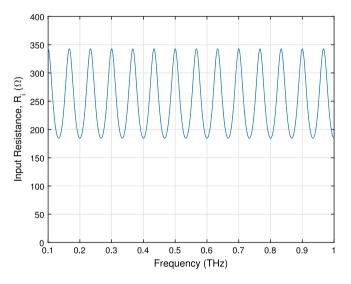
**Fig. 3.** Spectral response of the equivalent input resistance,  $R_i$ , as a function of the THz frequency when operating from inside to outside the human body.



**Fig. 4.** Spectral response of the equivalent input reactance,  $X_i$ , as a function of the THz frequency when operating from inside to outside the human body.



**Fig. 5.** Percentage of reflected power at the interface from outside to inside the human body when operating at the THz frequency.



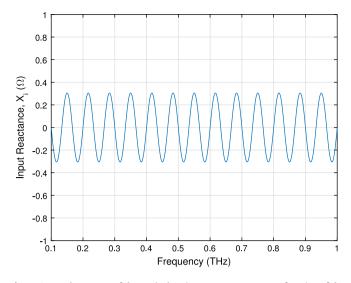
**Fig. 6.** Spectral response of the equivalent input resistance,  $R_i$ , as a function of the THz frequency when operating from outside to inside the human body.

## 5.2. Wave Propagation from Outside to Inside the Human Body

Considering the opposite case in which a wearable device conveys information to a nanosensor embedded in the human blood, the same metrics as those discussed in the preceding section are again analyzed for this scenario. Fig. 5 plots the variations of the wave reflectivity at the air–skin interface, by representing the skin–fat–blood interface with an effective medium having an equivalent impedance. It can be seen that the reflectivity at the skin–air interface also reaches 30%, signifying the symmetry of the human body. Moreover, Figs. 6 and 7 illustrate the equivalent input resistance and input reactance for skin–fat–blood, respectively. The results reaffirm our previous finding indicating that the effective medium at the THz frequency is almost purely resistive with a negligible conductivity.

# 5.3. Model Validation using COMSOL Multiphysics

To validate the results obtained using the theoretical model of Section 2, COMSOL Multiphysics software has been utilized to



**Fig. 7.** Spectral response of the equivalent input reactance, *X<sub>i</sub>*, as a function of the THz frequency when operating from outside to inside the human body.

simulate intrabody propagation. In fact, one of the critical features that distinguishes this software is that it provides a deeper physical insight into the problem in which electric fields are all coupled within the same simulation environment.

The scenario where a plane wave propagating through the blood, fat, skin, and air layers has been considered as an example to investigate the losses encountered as we move from inside to outside the body. Such analysis mimics the scenario of a nanosensor sending information to a wearable device where the interest lies in the attenuation the THz signal will encounter as it traverses through the human tissues. A geometry of a block (3D unit cell) has been considered to resemble the propagating environment in which the frequency of operation is 1 THz and the electrical properties of the human tissues analogous to those presented in the analysis above are utilized. Boundary conditions are applied on the top and bottom unit cell boundaries as the solution is periodic across the interface. The angle of incidence ranges from 0° to 90° for both TE and TM polarizations.

Fig. 8 illustrates the field amplitude distribution and the direction of the power flow (Poynting vector) as the wave propagates through the human tissue layers for the example of the electric field intensity of a TE wave. The propagation pattern is periodic and the power flow changes from one media to the other as indicated by the arrows. Further, the reflectance of the power through the multi-layered tissue structure has been computed using COMSOL for the example of both a TE and a TM polarized wave at 1 THz. Fig. 9 shows minimal reflectance at most angles of incidence as the wave propagates.

#### 6. Conclusion

This paper analyzed multi-layer electromagnetic THz wave propagation through a cascaded human tissue model. Two scenarios were considered in which the nanosensor either communicates with a wearable device for the purpose of sensing signals and monitoring the human vital parameters, or the wearable device interacts with the nanosensor to deliver drugs or detect cancer. It was found that the discrepancies between the human tissues result in a periodic type of spectral response for the wave reflectance, which can reach up to 30% of the incident power. This confirms the need to account for cross-layer reflection for an accurate characterization of the communication link between the nanosensors and the on-body device in the THz band. Extension of this paper involves

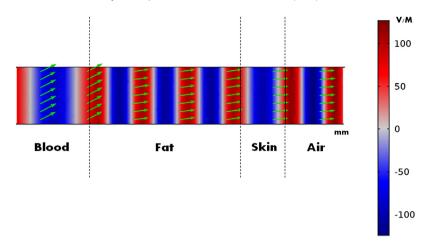
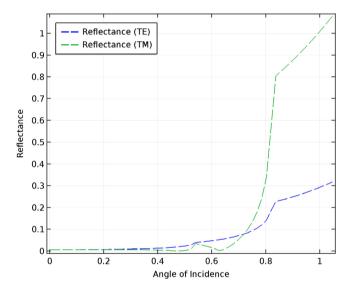


Fig. 8. COMSOL Multiphysics results for the field amplitude distribution as the EM wave propagates through the human tissues at an incident angle of 25° for electric field intensity (V/M) of TE wave.



**Fig. 9.** The reflectance versus angle of incidence of both TE and TM waves propagating through multi-layered human tissue using COMSOL Multiphysics.

combining the results obtained for cross-layer propagation with the intrabody communication model presented in [7]. The nanobio thermal effect due to the lost power caused by the multiple layer discrepancies will also be further investigated.

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