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THz Time Domain Spectroscopy of Human Skin Tissue for In-Body Nano-networks

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Abstract—This paper presents experimental study of real human skin material parameter extraction based on Terahertz (THz) Time Domain Spectroscopy in the band 0.1 - 2.5 THz. Results in this paper show that electromagnetic properties of the human skin distinctively affects the pathloss and noise temperature parameters of the communication link, which are vital for channel modeling of in-body nano-networks. Refractive index and absorption coefficient values are evaluated for dermis layer of the human skin. Repeatability and consistency of the data is accounted for in the experimental investigation and the morphology of the skin tissue is verified using a standard optical microscope. Finally the results of this paper are compared with the available work in the literature, which shows the effects of dehydration on the path loss and noise temperature. The measured parameters *i.e.*, the refractive index and absorption coefficient are 2.1 and 18.45 cm^{-1} , respectively at 1 THz for a real human skin, which are vital for developing and optimizing future in-body nano-networks.

Index Terms—Nanonetwork, Channel Modeling, Pathloss (PL), Terahertz Time Domain Spectroscopy, Skin.

I. INTRODUCTION

The gradual expansion from gigahertz (GHz) to the infrared region has remarkably improved the consistency and efficiency of medical devices resulting in better healthcare services. In past human skin dielectric properties have been studied extensively within the MHz to GHz range, however, limited studies are presented on animal and human tissue dielectric properties in the THz domain using Time Domain Spectroscopy (TDS) [1-3]. Earlier characterization techniques reported [4-6] were based on contact probe technique, which calculates the reflection coefficient using network analyzer. For frequencies from around 100 KHz to 100 MHz there are large changes in dielectric properties associated with the resistive nature of cell membranes. At frequencies above 100 MHz, differences between tissue types are largely lost, and at all frequencies the dielectric properties are directly associated with the tissue water content.

In open literatures [7-10], the spectral range of 0.1 – 10 THz is exploited for wide range of applications in biomedical mainly to better understand the water dynamic, security , dental,tissue imaging, protein folding and unfolding. The

strong absorption of terahertz radiation by water shows that terahertz imaging is very sensitive to changes in the water content of materials, and this can therefore be exploited for biomedical applications [11]. The water absorption peak in the atmosphere exists around 1.1 and 1.7 THz. In addition, THz region is considered as safe for such applications as compared to conventional microwave frequencies [13]. Extensive studies have been performed on skin imaging at these frequencies; Pickwell *et al.* [12] conducted an *in vivo* terahertz imaging study from 0.1 - 1.4 THz to investigate the person-to-person variations of terahertz skin properties, and demonstrated how the thickness of the stratum corneum on the palm of the hand could be measured non-invasively. It has been reported in [14], that THz radiation with its non-ionizing and non-invasive innateness, when exposed to cells does not express any changes in DNA repair. Novel materials, like CNT (carbon nano-tubes) and Graphene have unfolded new technologies, working in Terahertz (THz) band [15-17].

In this paper, the authors explicitly focuses on the THz spectroscopic techniques to emphasize the influence of water dynamics of tissue on channel parameters of Nano-networks as the future of health diagnostic technology. The growing need for wireless medical devices stems for remote and continuous monitoring of the patients' health, while delivering informative, interactive, non-invasive and reliable systems [18-19]. The relatively fast data transmission of wireless medical devices enables service providers with timely diagnosis and prior control of any major disease [20]. In body nano-networks and nano-communication are novel domains of the internet of nano-things with applications in healthcare. However, certainly one needs to revise the basic communication theory and establish its understanding at a nano and cellular level. Some studies have been presented on such nano-devices proposing them to be Graphene-based [21]. The transmission schemes have been investigated in the presence of lossy air medium and results in favor of THz communication theoretically studied to have a high physical transmission rates (1Tb/s) and transmission distance of order of few tens of mm [22]. Therefore, it is imperative to understand the fundamental electromagnetic behavior of the tissue samples while achieving repeatability in results. In paper [6], network arrangement is proposed to comprise of nano-nodes, router, interface devices and gateway. Tiny devices such as nodes and routers can be exploited from the

naturally existing biological units at a molecular level to establish hybrid molecular-EM communication. Molecular communication is based on the concepts of diffusion and is a different study altogether. In this paper, the focus is on the EM communication approach.

To the best of the authors' knowledge, the human skin/tissue material properties in the THz range remain sparse and lack consistency. For the purpose of establishing EM communication in the THz range for in-body (in-vivo) nano-networks, the focus of this paper is to construct a comprehensive database on human skin dielectric properties in the THz band. In addition to dielectric properties, we aim to provide channel model parameters for skin tissues by characterizing different layers. This is achieved by extracting the refractive index and absorption coefficient of the dermis layer from the THz time domain spectroscopy measurements on the real human skin and these parameters are further used to calculate the pathloss and noise temperature. Also the results of this paper are compared with the available literature [35], which shows the improvement in path loss and absorption coefficient measurement for dehydrated tissue.

The rest of the paper is organized as follows: Section II presents the experimental settings with a detailed description of the biological sample, human skin, and subsequently THz-TDS. Data processing methods and techniques are described in Section III. Section IV, discuss about the channel performance based on numerical studies and Finally, conclusions are drawn in Section V.

II. EXPERIMENTAL METHODOLOGY AND MEASURED SKIN TISSUE SAMPLES

A. Principles of THz-Time Domain Spectroscopy

The exposition of THz spectroscopy is the Time Domain measurement where pulsed THz wave is mixed with sampling optical pulses in a detector [23]. Thus, this coherent detection scheme used to analyze THz spectral waveform provides information on both phase and amplitude. The tool utilizes similar concepts of pump-probe techniques [24], where the optical beam is split into two parts, one of which goes through a translational stage to provide a relative time delay. In THz – TDS, not only the absorption, but also the dispersion of the sample can be obtained by analyzing the Fourier transform of the waveforms. The aim is to utilize this technique to study the dielectric properties of skin layer, which is dermis in this work. THz-TDS at Queen Mary University of London (QMUL) [25] has a typical range of 0.1- 4 THz, which provides access to broader spectral analysis. The TDS system is a carefully designed assembly of the following components - Ti:Sapphire is the femtosecond pulsed laser with adjustable wavelength range of 750 - 850 nm; pulse repetition rate of 80 MHz and peak power is about 1 W. The delay stage has maximum travel distance of 15 cm. THz emitter is LT-GaAs photoconductive antenna with a biased voltage of 200 V and a gap size of approximately 0.5 mm, which makes the laser beam positioning relatively easier. A ZnTe crystal is employed as an electro-optic detector with thickness of 2 mm, which

allows enough interaction length of probe beam and THz wave in the crystal.

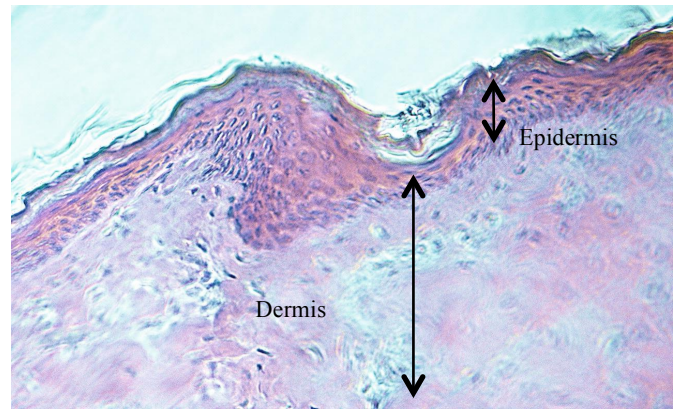


Fig.1 Microscopic image of real human skin presenting the two defined layers: Epidermis and Dermis. The sample sections were stained using Haematoxylin (purple/blue stain) and Eosin (red/pink stain), used for identifying nuclei and cytoplasm respectively. Stratum Corneum (SC) traces were visible in the microscopy, however the thickness is not quantifiable.

B. Anatomy of Human Skin

Skin layer can be divided into three major sections; epidermis, dermis and fat with definitive thicknesses and functionality. However, the structure is far more complex and random. In this study, the skin for in-body network is investigated for three fold reasons: firstly, most of the in-body functioning or dis-functioning affects the skin (and water concentration). Secondly, skin is rich in biological entities and structures such as blood vessels, sweat ducts, capillaries, proteins etc. and finally it's easily accessible for measurement making it a versatile subject of THz-TDS.

Skin in the human body is a protective layer, sensor of multiple parameters such as pressure, temperature, *etc.* Epidermis is the thin outer layer (as shown in Fig.1), which can be further divided as: Stratum Corneum (SC), Keratinocytes and Basal membrane. SC consist of mature keratinocytes, which contains fibrous protein namely keratin. The layer just beneath is keratinocytes containing live cells that mature and forms SC. The deepest layer of epidermis is Basal membrane responsible for preparing new keratinocytes and replacing the old ones [26-27]. The thickest (~3 mm) of all is the dermis (Fig.2 C) lying just beneath epidermis (Fig. 1), which houses vital entities such as sweat glands, hair follicles (as shown in Fig. 2 A & B), and nerve endings. This layer is rich in proteins such as elastin, fibrin, fibrogen and collagen. Collagen forms an extra cellular matrix, acting as scaffolding for the dermis. The last layer of the skin is a network of collagen and fat cells, known as subcutaneous layer. The subsequent section in this paper aims to characterize real human skin via THz-TDS, while evaluating material properties and comparing the measured results to numerical data. The sample consists of two layers: epidermis and dermis, however, epidermis is very thin in comparison to

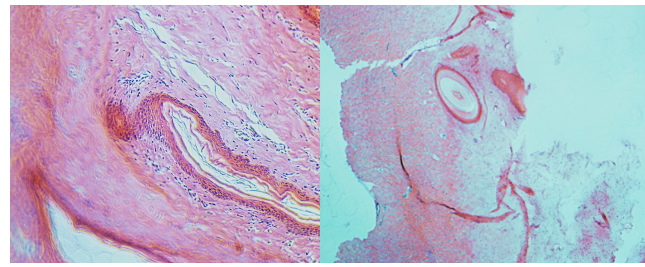
dermis. In this work, the material properties of dermis part of the skin are investigated. The epidermis mainly consists of keratinocytes and dermis is a result of many protein structures and fibroblast cells. Although epidermis is an amalgamation of many different layers as explained before but this is challenging to identify at a microscopic level. However a layer of stratum corneum is slightly visible.

C. THz Time Domain Spectroscopy of The Human Skin

Human skin is mainly composed of water [28], which leads to high absorption of THz radiation during the measurement. Hence, in this paper the material properties of dry skin samples are investigated, which have been stored in glycerol over the past 10 years aiding in preserving the structural integrity of the tissue. This is mainly for controlled experimental purposes and also provides the cornerstone for measuring the effects of sample dehydration at THz frequencies. Moreover, freshly excised skin samples are measured to account for parallel studies. Glycerol treated samples; specifically the dermal layer remains unperturbed, when examined in standard light microscopy. When comparing to a freshly excised skin the only change one would expect is the hydration level. Since, these samples have been preserved for over a span of 10 years, their hydration level is expected to be low. Hence one would only observe shrinkage of some keratinocytes [29]. The biological studies are performed in collaboration with the Subcutaneous Group of the Blizzard Institute at QMUL. The sample initially consisted of the following layers: epidermis, dermis and fat. From the measurement perspective, main focus is investigating the different layers of the skin; for the same reason dermis layer was sliced and separated from fat, since this layer is the thickest and adobe of many biological entities.

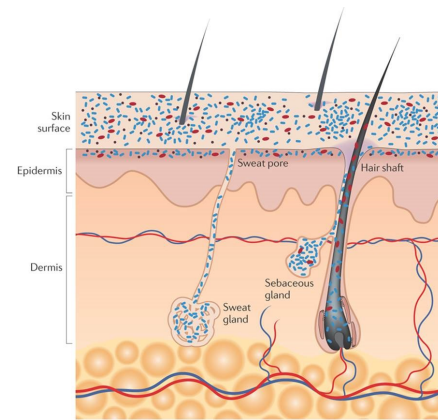
The samples are wedged between two TPX (Polymethylpentene) slabs with a spacer of known thickness. TPX is used as a sample holder, since it is transparent to THz radiation; the light is mostly transmitted through the sample with minimal absorption in TPX [30]. These measurements are performed applying the aforementioned THz TDS system and therefore phase and amplitude information are collected and post processed using transfer equation based algorithm [31]. The TDS pulses are generated and detected via mode locked laser. The lock-in amplifier locks and records the detected THz data for all three samples – air, TPX and skin and is aided by a computer-generated program written in LabView®.

In this study, the incoming THz signal consists of total 1024 consecutive samples, which are recorded at each position of the delay stage. THz-time domain data takes the form of a single pulse, with a period of 1 picosecond, followed by a series of attenuated pulses arising either from reflections at the interface of components within the TDS system, or from etalon reflections within the sample itself.



(A) Sweat Duct

(B) Hair Follicle



(C) Schematic of human skin with layered structure [38]

Fig.2 Cross-section of skin sample (A): Longitudinal section of the hair follicle attached to a sweat duct in the dermis layer, (B). Cross-section of oval shaped hair follicle structure. The hair follicles are mainly present in dermis layer acting as sensory receptors. (C) Illustration of different layers of human skin.

III. SKIN TISSUE ELECTRIC PROPERTIES EXTRACTION

To quantify the interaction of THz wave with given samples, at least two basic material parameters needs to be determined *i.e.*, refractive index and absorption coefficient. The measured time domain data is converted to frequency domain by using Fast Fourier Transform (FFT) to acquire amplitude and phase information. The measured time domain signal for the sample, air and TPX are shown in Fig. 3 and it can be seen from the figure that the biological sample is highly attenuated and the second peak is almost diminished for the sample. The transmission through TPX is used as a reference data with its main peak at 15.7 ps and attenuated satellite peak at 27.6 ps. In order to extract the material properties, it is essential to have a time delay between the reference and sample data. Fig. 3 shows that that the sample is shifted with respect to TPX with it main peak at 20 ps and satellite peak at 31.9 ps. The oscillations and attenuation in the data is due to presence of water vapors in the atmosphere.

The refractive index is calculated using the following equation [32]:

$$n(\omega) = 1 + \frac{c[\varphi_{samp}(\omega) - \varphi_{ref}(\omega)]}{\omega * d_{samp}} \quad (1)$$

where $\varphi_{samp}(\omega) - \varphi_{ref}(\omega)$ is the phase difference between the sample and reference, corresponding to the shift in time domain. The thickness of the sample is given by d_{samp} , which is fixed to 1 mm with the help of a spacer in this study. The absorption coefficient is calculated using equation [32]:

$$\alpha(\omega) = -\frac{2}{d_{samp}} + \ln \left[\frac{|E_{samp}(\omega)|}{|T(\omega) * |E_{ref}(\omega)|} \right] \quad (2)$$

Where $T(\omega) = \frac{4n(\omega)}{(n(\omega)+1)^2}$ is the transmission coefficient and $|E_{samp}(\omega)|$ and $|E_{ref}(\omega)|$ represents the magnitude of sample and reference in the frequency domain. The transfer function $H(\omega)$, is the ratio of the two defined as:

$$H(\omega) = T(\omega) * \exp \left[-\alpha(\omega) \frac{\omega * d_{samp}}{c} \right] * \exp \left[-j(n(\omega) - 1) \frac{\omega * d_{samp}}{c} \right] \quad (3)$$

The results for refractive index and absorption coefficient are illustrated in Fig. 4 and 5 respectively. Results show that refractive index values decreases and absorption coefficient increases with frequency, which can be explained using Kramer-Kronig relation given for dispersive materials. It is a special Hilbert transform pair and yields a comprehensive dispersion curve spanning entire frequency spectrum [33]. Table 1 shows the extracted parameters at certain chosen frequencies. The measured refractive index results are compared with [18, 20, 34] and are in good agreement; however it's still a challenge to predict the nature and biological details of the samples. The samples used in these papers, were either sliced porcine, in-vivo human skin or frozen samples. For in-vivo skin, the measurements were done directly on the volunteers. It is important to note that skin structure is layered and intricate; therefore it is essential to comprehend material properties of different layers of the skin. In this paper, we deliberately measured dermis layer of the skin and found out that at 1 THz the refractive index value is 2.1, which decreases to 1.8 at 1.2 THz. The absorption coefficient (calculated using eq. 2) values are considerably low (Fig. 5) due to uniform dehydration of the sample. This amounts to the fact that water in these tissues plays a significant role when interacted with THz radiation. Repeatability of experimental techniques and hence stability of obtained parameters value is investigated by repeating each measurement 4 times on the same sample with the thickness intact resulting in consistent refractive index value.

TABLE I
MEASURED REFRACTIVE INDEX AND ABSORPTION COEFFICIENT

| Frequency (THz) | Measured Refractive Index (n) | Absorption Coefficient (α , cm^{-1}) |
|-----------------|-------------------------------|--|
| 0.8 | 2.33 | 8.96 |
| 1 | 2.10 | 18.450 |
| 1.2 | 1.81 | 27.55 |

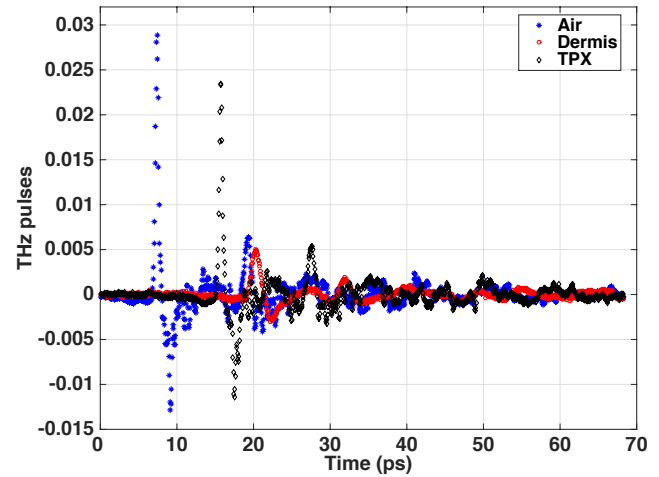


Fig. 3 Measured THz pulses through air, TPX and tissue. As expected the biological sample is highly attenuated and second peak is almost lost due to absorption with maximum peak value of 2.2mV in comparison to air with second peak value of 6.7mV .

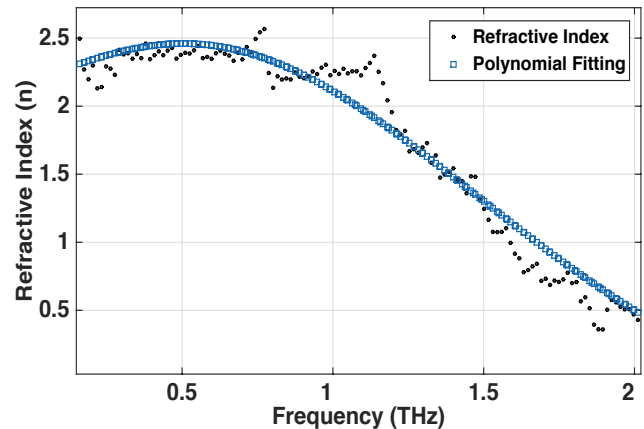


Fig.4 Measured Refractive index as a function of frequency. The refractive index decreases with the increasing frequency from 0.8 THz to 1.2 THz.

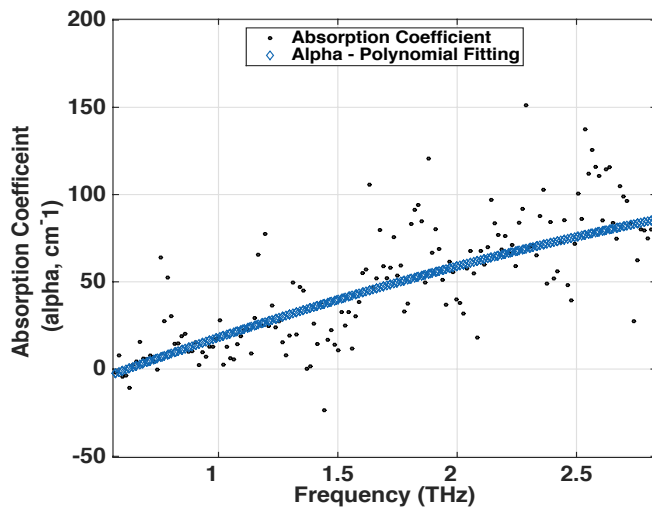


Fig.5 Measured absorption coefficient using THz-TDS. The alpha value is significantly low due to the dehydration and the main absorption of THz radiation is as a result of atmospheric water vapors.

IV. NUMERICAL ANALYSIS

The presented experimental results on refractive index and absorption are utilized to evaluate the path loss and molecular absorption noise temperature of the THz channel in human tissues. These are based on modified Friis equation [37] and can be divided as: the spreading path loss and the absorption path loss as explained in reference [35,36]. To highlight the usability of these equations and for readers' convenience, the equations are [36] :

$$PL[dB] = PL_{spr}[dB] + PL_{abs}[dB] = 20 \log \frac{4\pi d}{\lambda_g} + 10\alpha d \log e$$

where, d is the propagation distance of the wave; α is the absorption coefficient. Also, the noise temperature can be obtained [36]:

$$T_{mol} = T_o (1 - e^{-4\pi f d K/c}) \quad (3)$$

where T_{mol} is the equivalent noise temperature due to molecular absorption;

T_o is the reference temperature, which is 310 K which is the normal human body temperature.

The absorption pathloss (PL_{abs}) is as a result of material dynamics, sample's composition and molecular behavior, on the other hand spreading pathloss (PL_{spr}) is introduced by the expansion of the wave in the medium. The two-channel modeling features (*i.e.*, path loss and noise temperature) are illustrated in Fig. 6 and 7 accentuating the premise of this experimental study. Total pathloss as shown in Fig. 6 is a sum of spreading and absorption pathloss and vary as a function of frequency and distance. At 1 THz and at the distance of 1 mm, the pathloss is around 52.12 dB, which gradually increases with distance and frequency. The results presented in this paper are for dehydrated sample; hence the absorption due to

water is relatively low. In [22], the numerically modeled skin pathloss is around 150 dB at 1 THz, which is higher as compared to the results presented in this paper hence illustrates that water present in the dermis is the main source of attenuation and need further research. The sample has no traces of stratum corneum but thin layer of epidermis and hair follicles are still present. Thus, these results encompass attenuation due to microscopically visible biological entities present in the tissue.

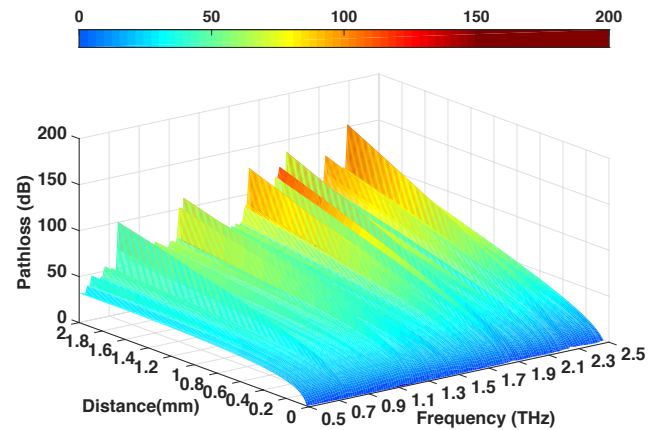


Fig.6 Total pathloss as a function of distance and frequency for human skin. The pathloss is as a result of absorption and spreading pathloss. These parameters significantly influence the propagation schemes. It is illustrated that the value is significantly low due to absence of water in the tissue.

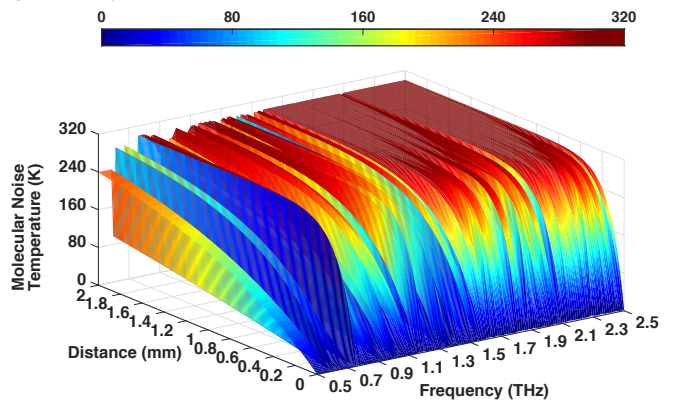


Fig.7 The figure illustrated the Molecular noise temperature as a function of frequency. The noise tends to increase with the increase in frequency; however this is rather fluctuating and not gradual owing to the fact that noise spectral density is influenced by molecular absorption.

In reference [35], the author highlights the effects of noise power spectral density, obtained from equation 3 and 4. The molecular noise temperature for real skin is shown in Fig.7. It can be seen that the noise temperature increases with the increase in frequency and distance, which will lead to the rise of the noise power. Theoretical results illustrated in paper [35,22], highlights that at a millimeter level, the noise

temperature is not very high (300 K). Experimental results validates that up to 1 mm, the noise level is permissible for a communication link to exist inside the dermis layer. However, further research is needed to investigate these parameters for different layers of skin and from different parts of the body. Results in this paper highlight that the path loss is not only the function of distance and frequency but also related to the dielectric loss of human tissues.

V. CONCLUSION

Nano-networks aim to offer comprehensive and unambiguous healthcare solutions for medical diagnostic systems. The study of material properties via THz TDS contributes to intricate and vital human body information. The results presented in this paper sustain consistency of the biological sample. The characterization of dehydrated sample attributes to a low absorption coefficient value as compared to fresh tissue. This study suggests that water plays a vital role even when optimizing channel models. The noise temperature results, up to 1 mm proves to be substantial for establishing communication links in the skin dermis layer. The results of this study are significant for optimizing future in-body Nano-networks inside the human body. These results aid to applications in medical sensor technologies for tumors and breast cancer owing to the sensitivity of THz-TDS to water dynamics. The next steps aim to encompass fresh tissues while considering tissues from various parts of the body in addition to different layers of the skin to outline complete understanding of the skin properties in the THz range.

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