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Impact of Fibroblast Cell Density on the Material Parameters of Thin Artificial Human Skin in the Terahertz Band

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***Abstract*—This paper presents the material parameters of collagen gel and dermal equivalents with different fibroblast cell densities in a Terahertz (THz) band from 0.2 THz to 1.5 THz. It is shown that collagen gel without cells has much higher refractive index and absorption coefficient than dermal equivalents, while the parameters of dermal equivalents slightly decrease with cell density. It denotes that the material parameters at the THz band is not only dependent on the water concentration but also their intrinsic biological features. The obtained results help understand the interaction of the THz wave with biological tissues and the diversity of material parameters of real human skin.**

***Index Terms*—Terahertz, dermal equivalent, fibroblast cell density**

I. INTRODUCTION

The THz wave is highly sensitive to water content in biological tissues, which enables the THz wave to distinguish healthy tissues from malignant ones. Skin is a promising candidate because it is the most abundant tissue and offers dynamic analysis due to its various hydration levels throughout the human body. There are several papers providing the electromagnetic parameters of human skin in [1], [2]. However, the presented parameters differ from each other, which could be caused by the difference in the type, state, complexity of the human skin, and etc. It motivates us to study the intricate biological feature and its effect on the optical behaviours of human skin at the THz frequencies. However, it is carefully regulated to conduct experiments on real human skin tissues; thus, artificial human skin samples are used instead for experimental investigation.

Skin can be divided into three main layers: epidermis, dermis and subcutaneous fat. Among them, dermis is the thickest layer comprised of extracellular matrix (ECM), fibroblasts, vascular endothelial cells and skin appendages as shown in Fig.1. Collagen is the most abundant fibrous protein within the ECM. Starting from collagen gel and then the dermal equivalents (constructed by seeding dermal fibroblast cells in a collagen gel to progressively reorganise the lattice[3]), we comparatively study the effect of the fibroblast cell density on the material parameters.

A preliminary study of collagen with different cell numbers have been presented in [4]. But the limited number of samples and measurements brought many uncertainties to the results. Moreover, the traditional sandwich technique could bring unnecessary press to the sample, which could negatively affect its biological features. Therefore, instead of sandwiching samples, we mounted the sample on one TPX (poly-4-methyl pentene-1) plate. TPX is chosen to be the plate because it is transparent to the THz wave with low absorption ($\leq 1cm^{-1}$) and almost constant refractive index (1.46) over the band of interest. Besides, collagen gels without cells were made as a control group in our experiment. Meanwhile, the dermal equivalents with three different cell densities were cultured. For each scenario three samples were cultured. THz-TDS system operating in transmission mode is utilised to characterise the materials. Frequency domain analysis methods were used to extract the refractive index and absorption coefficient for each dermal equivalent sample over the frequency range 0.2-1.5 THz. The obtained results help understand the interactions between THz radiation and human tissues and provide fundamentals for its application in health diagnosis.

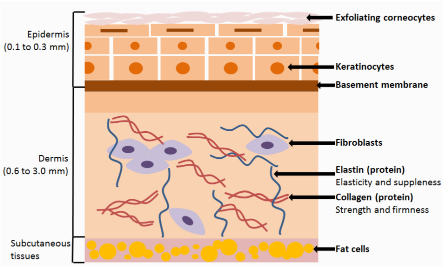


Fig. 1. Schematic of skin histology

II. MATERIALS

Collagen gel was cultured with a concentration of $2.5mg/ml$. Dermal equivalents were constructed by casting fibroblasts with three different densities, $0.1M(Million)/ml$, $0.5M/ml$ and $1M/ml$ into rat tail collagen solution and allowing the solution to solidify and contract. The dermal equivalent floating in the medium is shown in Fig.2. The initial volumes of the solution for all collagen gels and dermal equivalents are the same. Due to the extremely high molecular absorption of biological tissues as shown in [1], [5], thick sample cannot allow THz wave transmit through the sample. Thus, we made the initial thickness of collagen sample and dermal equivalents

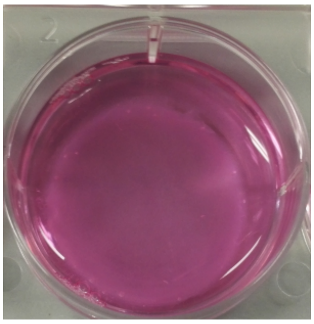


Fig. 2. Artificial dermal equivalent

to about $100\mu m$, which enables THz signal transmits the sample without significant attenuation.

III. METHODS

Terahertz Time Domain Spectroscopy in transmission mode is utilised to characterise the material, the details of the system can be found in [6]. The sample is enclosed in a dry-air purged chamber for removing the water vapor influence during the experiment. For each sample, we repeated measurement three times, and THz-TDS data were collected at various time intervals. The original measurement data from THz-TDS system is the received electric field in time domain. Optical parameters extraction requires the amplitude and phase information of signal, thus Fast Fourier Transform(FFT) is evaluated of the time-domain measurements of sample and reference, E_{sample} and E_{ref}, respectively.

In the case of thin film materials, the THz pulse transmission is strongly affected by multiple reflections. In order to disentangle the FP effect (Fabry-Perot effect due to the multiple reflections inside the sample) and measure the material parameters with high accuracy, an iterative fitting process based on a polynomial fit of the transmission parameters is utilised in the signal processing. It enables a confident extraction of the refractive indexes and absorption coefficients.

The complex transfer function of the sample in the frequency domain is calculated by normalising the sample spectrum by the reference as [7],

$$
\begin{aligned}
H(f) &= \frac{E_{sample}(f)}{E_{ref}(f)} \\
&= \hat{\tau}(f) e^{-j(n_s(f)-n_0)\frac{2\pi f d}{c}} e^{-\kappa_s(f)\frac{2\pi f d}{c}} FP(f)
\end{aligned}
\tag{1}
$$

$$
FP(f) = \left(1 - \frac{\hat{n}_s(f)-n_0}{\hat{n}_s(f)+n_0}\frac{\hat{n}_s(f)-n_T}{\hat{n}_s(f)+n_T} e^{-4j\hat{n}_s(f)\pi f d/c}\right)^{-1} \tag{2}
$$

where c is the speed of light in vacuum, $n0$, n_T and $\hat{n}_s$ are the complex refractive index of air, TPX and the biological sample, respectively. $FP(f)$ presents the Fabry-Perot effect, and $\hat{\tau}(f)$ refers to the transmission coefficient.

In this measurement orientation, the incident THz signal encounters the sample first and then the TPX as shown in Fig.3. Therefore, the reference signal is the transmission through a blank TPX alone. The propagation of signal through both the sample and reference points is calculated using well-established impedance and reflection interactions for multiple layers. The transmission coefficients is given by,

$$
\hat{\tau}(f) = \frac{2\hat{n}_s(f)(n_0+n_T)}{(\hat{n}_s(f)+n_T)(\hat{n}_s(f)+n_0)} \tag{3}
$$

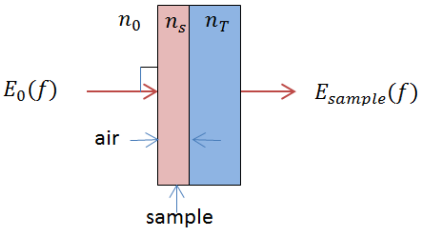
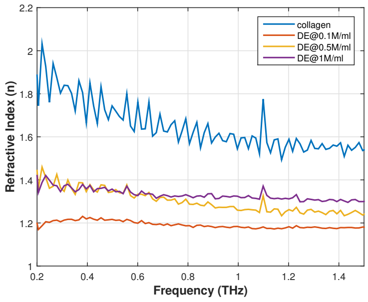
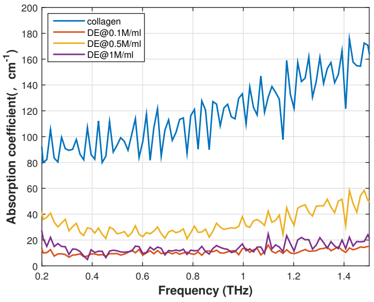


Fig. 3. Geometry of sample measurement



(a) Refractive index



(b) Absorption coefficient

Fig. 4. Extracted refractive indexes and absorption coefficients ranging from 0.2 THz to 1.5 THz for collagen gel, and dermal equivalents with cell densities, $0.1M(million)/ml$, $0.5M/ml$ and $1M/ml$.

IV. RESULTS AND DISCUSSIONS

The extracted refractive index and absorption coefficient of the collagen gel, and dermal equivalents with different cell densities are illustrated in Fig. 4.

It can be seen that the refractive indexes of collagen gel ranging from 2 to 1.6, while the refractive indexes of the dermal equivalents have slight drop from 1.4 to 1.2 in the frequency band of interest. Specifically, refractive indexes of dermal equivalent with $0.5M/ml$ and $1M/ml$ cells have a similar trend which goes down from 1.4 to 1.2, while the $0.1M/ml$ sample have the lowest and almost constant values of 1.2. Furthermore, the absorption coefficients of collagen gel are the biggest and increase sharply in the band of interest from around $80cm^{-1}$ to $180cm^{-1}$, while the values of dermal equivalents are much smaller. The absorption coefficients of dermal equivalent with $0.5M/ml$ cell density experience a small rise from about $20cm^{-1}$ to $60cm^{-1}$, while the other two types present similar numbers at about $10cm^{-1}$.

V. SUMMARY

The material parameters of artificially synthesised collagen gel and dermal equivalent in the frequency band 0.2 THz to 1.5 THz has been provided, and the effect of the fibroblast cell density on the optical properties of the artificial human skin has been comparatively studied. When conducting the experiment, it is noticed that the precise thickness information is difficult to be measured which causes some uncertainties to our results. In order to avoid the negative effect caused by the thickness, an advanced algorithm to extract both the complex refractive index and sample thickness will be considered in our further work.

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