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Terahertz optical properties of the cornea

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ABSTRACT

We present a study aimed at developing a terahertz time domain spectroscopy (THz-TDS) system for detection of the optical properties of ex vivo rabbit corneal tissues with different water content at terahertz frequencies (0.1–0.3 THz). The refractive index decreased with frequency while the absorption coefficient increased with frequency. Our experimental results matched the theoretical calculation very well revealing that both the absorption coefficient and the refractive index of a hydrated cornea were much larger than that of a dehydrated cornea and the terahertz properties depended on the hydrate conditions of the biosamples.

1. Introduction

The cornea is the principal transmission and refracting (focusing) eye component and the water content is about 75–80% [1]. The water content of the cornea is regulated by both passive and active mechanisms to preserve its transmission and focusing properties. A key indicator of corneal health is its ability to properly regulate its water content [2]. Therefore, the accurate measurement of corneal hydration is essential for diseases effective diagnosis and corneal treatment. The contemporary corneal hydration is usually detected by ultrasound or optical coherent tomography (OCT) based pachymetry. Because the mapping from thickness to hydration is extremely inaccurate [3], the utility of this technique is severely limited.

Sandwiched between microwaves and the infrared, the terahertz (THz) region of the electromagnetic spectrum hosts a wealth of intriguing and highly complex THz-matter interactions in physical chemical and biological systems [4]. Recently, THz spectroscopy has emerged as a promising technique for biomedical studies [5–18]. Due to the extremely high sensitivity of THz radiation to water content in tissues, THz spectroscopy may be ideally suited to directly measure the corneal tissue for diagnosis. Nonetheless, it is important to know the THz optical properties (e.g. refractive index and absorption coefficient) of corneal tissue for the understanding of the interaction between THz radiation and cornea. However, THz spectroscopy of biological systems is still a burgeoning research area with no formalized standard. To date, only a few paper demonstrated the THz sensing of corneal hydration [2,3,18,19], there is less literature reported the optical properties of corneal tissue at THz frequencies.

In this paper, we report the experimental study on the optical properties at the low frequency (0.1–0.3 THz) of ex vivo rabbit corneal tissue using a developed terahertz time domain spectroscopy (THz-TDS) system with fast scanning. By comparing our experiment results with data calculated by four term Cole-Cole expressions, we found these measured optical properties agreed well with the theoretical model. In addition, we concerned how ex vivo rabbit corneal tissues dehydration over an extended time interval affects the frequency responses of samples at THz frequencies. It is clearly observed that dehydrating the sample reduced both the absorption coefficients and the refractive indices of the samples.

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2. Theoretical calculation

The relative complex permittivity of corneal tissue in the THz frequency has been theoretically calculated and simulated. So far, a suitable permittivity model for cornea in THz regime is yet to be achieved in the literature. The Debye theory has been used to understand the interaction of THz radiation with biological tissues [20,21]. However, the Debye model may fail in accurately simulating the biological tissue [22]. It is likely that the complexity of both the structure and composition of biological material is such that each dispersions region may be broadened by multiple contributions to it. The Cole–Cole model offers an alternative approach which can describe many types of biological tissues accurately over a very wide frequency band [23]. Therefore, we consider the cornea as the Cole–Cole media with the frequency dependent relative complex permittivity $\hat{\varepsilon}_r(\omega)$ given by:

$$\hat{\varepsilon}_r(\omega) = \varepsilon_\infty + \sum_{n=1}^{N} \frac{\Delta\varepsilon_n}{1 + (j\omega\tau_n)^{1-\alpha_n}} + \frac{\sigma_i}{j\omega\varepsilon_0} \tag{1}$$

where ω is the angular frequency, N is the order of the Cole-Cole model, ε_∞ is the high frequency permittivity, τ_n is the relaxation time, $\Delta\varepsilon_n(\Delta\varepsilon_n = \varepsilon_n - \varepsilon_{n+1})$ is the pole amplitude, $\alpha_n(0 \le \alpha_n \le 1)$ is a measure of the broadening of dispersion,$\sigma_i$is the static ionic conductivity, ε_0 is the permittivity of free space (vacuum), and $j^2 = -1$.

To predict optical properties of the cornea, the following equations are applied to convert to refractive index $n(\omega)$ and absorption coefficient $\alpha(\omega)$:

$$n(\omega) = \sqrt{\frac{\varepsilon'(\omega) + \sqrt{\varepsilon'^2(\omega) + \varepsilon''^2(\omega)}}{2}} \tag{2}$$

$$\alpha(\omega) = \frac{2\omega}{c}\sqrt{\frac{-\varepsilon'(\omega) + \sqrt{\varepsilon'^2(\omega) + \varepsilon''^2(\omega)}}{2}} \tag{3}$$

where ω is the angular frequency, $\varepsilon'(\omega)$ is the real part of $\hat{\varepsilon}_r(\omega)$,$\varepsilon''(\omega)$ is the imaginary part of $\hat{\varepsilon}_r(\omega)$, c is the velocity of light in free space.

3. THz time domain spectroscopy system and cornea detection

Fig. 1 schematic illustrates the set up of a terahertz time-domain spectroscopy system with fast scanning. A mode-locked Ti:Sapphire laser is used to generate THz pulses with the central wavelength of 800 nm, average power of 800 mW, and pulse width < 100 fs, and the repetition rate of 80 MHz. The laser beam has been split by the prism beam slitter (PBS) into the pump beam and the probe beam where they are launched into the emitter for generating the THz pulse and to the detector for real time monitoring, respectively. The pump beam is passed through a mechanical stage based slow delay line which is used to adjust the pump and probe beams temporally. The probe beam is incident to a novel motor based fast delay line which is used to acquire the signal in real time. In this work, the fast delay line developed ourselves could provide a fast delay range over 130 ps. Such a delay line could reach the scanning rate of up to 100 Hz with effective cost. The transmitted THz electric field both in amplitude and phase is monitored by varying the time delay between the probe beam and the THz pulse. The THz beam is focused onto the corneal samples by a pair of gold coated off-axis mirrors with one common focal point.

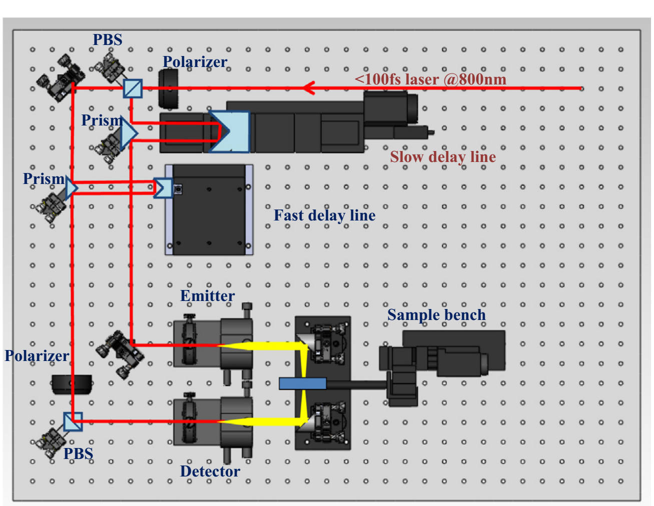

Fig. 1. Schematic of experimental setup for terahertz time domain spectroscopy system used to measure the properties of the cornea. (PBS: prism beam splitter).

The fresh rabbit corneal samples were obtained from the Peking University Shenzhen Hospital. Dissected samples in saline buffer are packed in a cold box together with ice packs and transported for about 30 min to the THz laboratory. Prior to the measurement, the cornea were stored in saline. After we started the measurement, the cornea was not stored in saline. The cornea samples are dehydrated by storage in drying oven to remove their water content. The special sample holders have been designed as the corneal tissues may be moist and supple. We used a solution sample cell for mounting the cornea in each measurement. This sample cell consists of two homogeneous parallel plates (polymer window) sandwiched together where the polymer window was well cleaned. During dehydration the samples are placed in the cell in order to keep them flat during the process. The samples were then placed in the THz spectroscopy system to carry out the test every 24 h for the subsequent measurement period. The cornea placed in the sample cell was dehydrated in drying oven for over 144 hours to remove its water and the corneal thickness decreased as water was lost. A brief description of the corneal thickness throughout the follow up scans on subsequent days is display in the Table 1.The corneal thickness was likely to be unchanged since 120-h-dehydration because water was lost completely. Note that refractive index (RI) of the polymer widow has been determined firstly, a nearly constant RI of 1.48 and nearly zero absorption coefficient of the polymer widow were obtained which are consistent with those of the literature reported [24]. A reference pulse in the absence of cornea was also recorded. The THz transmission spectra could be obtained by the fast scanning THz-TDS technique with an acquisition time of 1 s for each spectrum. Additionally, the measurements for system calibration and validation were made from distilled water.

As shown in Fig. 2, THz radiation E propagating through the polymer window cell to produce $\boldsymbol{E_{ref}}$ and through the sample to produce $\boldsymbol{E_{sam}}$, respectively, should be recorded by THz time-domain spectroscopy system. A fast Fourier transform algorithm is used to obtain their amplitude and phase spectra as the function of frequency. A complex transmission coefficient, as detailed in reference [25], is then defined by the deconvolution of the measured THz pulse with sample and the reference pulse in the frequency domain, which can be used for the extraction of the complex

Table 1
The thickness of the cornea throughout the measurement period.

Time (Hrs)	0	24	48	72	96	120	144	168
Thickness (mm)	0.65	0.57	0.44	0.41	0.39	0.37	0.37	0.37