Invited Paper

Detection of aqueous α-lactose based on THz spectroscopy with parallel plate waveguide

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(Received December 2023)

Abstract: Rapid and accurate identification of the types and level of early pathological markers by THz technology is of great importance for clinical prevention and treatment of major diseases. However, these markers are usually severely attenuated by the strong absorption signal of water, resulting in a low signal-to-noise ratio (SNR), making identification and quantitative analysis difficult. In this paper, a THz - TDS system based on a high-power terahertz (THz) source radiated by $LiNbO_3$, coupled with parallel plate waveguide detection platform, is used to achieve quantitative THz detection of α-lactose monohydrate solutions with an accuracy of 1.0 *mg/μL*. Both its solid and solution have fixed absorption peak at 0.53 *THz*, while the corresponding absorption baseline increases with decreasing concentration. The high-power radiation source combined with the parallel plate waveguide directly detects water-containing samples, which fundamentally solves the difficulty of capturing the effective signal of aqueous biological samples due to the attenuation of the sample THz signal by water. This method not only avoids the destruction of the biological sample activity, but also has the characteristics of high-cost performance, high detection accuracy and wide application.

Keywords: Terahertz spectroscopy, α-lactose, Parallel plate waveguide

Doi:

1. Introduction

Vibrational dynamics of biomolecules on picosecond time scales is key to the study of biological and chemical functions of biomolecules, cells and tissues [1-3]. Molecular structure and conformational information closely related to biological functions can be obtained by THz spectroscopy [4-6]. In many diseases, especially cancer, the blood supply to the affected tissues increases, resulting in changes in physiological parameters such as the structure, density, and water content of the diseased tissue [7-9]. Therefore, it is possible to determine whether cancerous lesions have occurred by the differences in THz absorption and refractive index between the cancerous and normal tissues due to changes in physiological parameters [10-16].

However, conventional terahertz time-domain spectroscopy (THz-TDS) systems propagating in free space cannot meet the demand for rapid detection of trace water-containing biomolecules and cells [17-20], which severely limits its application in the medical field. The main technical bottlenecks are: (1) the serious influence of water absorption in biological samples; (2) the inability to realize transient detection; and (3) the inability to fine-tune the detection of tiny amounts of biological samples due to the diffraction limit of THz waves. Therefore, it is crucial to further explore THz spectroscopic detection techniques for measuring biomolecules in aqueous solutions.

In this paper, THz waves in free space are coupled to the parallel plate part of the waveguide by means of a parallel plate waveguide, so as to realize the local field enhancement effect of THz electromagnetic field. Combined with the local field enhancement effect of the parallel flat waveguide, the intensity and sensitivity of THz detection of water-containing samples can be maximized, thus realizing the THz detection of α-lactose monohydrate solution with a minimum detection concentration of 1 *mg/μL*.

2. Sample preparation and experiment

The α-lactose monohydrate used is purchased from Aladdin Reagent (Shanghai) Co. The purity of the samples used in the experiments is analytically pure. An electronic analytical balance with an accuracy of 0.001 *mg* is used to weigh the sample powder, and a pipette gun with a range of 10-100 *μL* and an accuracy of 1 *μL* is used to quantitatively add water. In order to detect the characteristic absorption spectrum of α-lactose monohydrate aqueous solution in the THz band, 0.01*g* of α-lactose monohydrate is used in this experiment to prepare different concentrations of aqueous solutions for testing, and the configured mass concentrations are shown in Table 1. Since α-lactose monohydrate is not completely dissolved and belongs to the suspension, we still use the mass concentration to express it.

The detection platform used in this experiment is the high-power static detection mode of THz-TDS system, as shown in Fig. 1, which mainly consists of a MaiTai femtosecond laser, a $LiNbO_3$ radiation source, a horn shaped tapered parallel plate waveguide and a THz detector. A horn shaped tapered parallel plate waveguide is placed at the THz focus position to detect the THz spectral information of the sample through the local field enhancement effect of the waveguide on the THz wave. In order to make the THz wave enter the horn of the waveguide completely, and make sure that the energy of the THz center spot passes through the sample in the waveguide to the maximum extent, i.e., the THz transmittance is highest when the THz focal point is just in the parallel plate part of the waveguide. First, the parallel plate waveguide is placed on a 3D translation stage and the periphery of the waveguide is covered with a copper sheet to prevent THz wave loss; in addition, the waveguide position is adjusted up and down, left and right, and forward and backward on the 3D translation stage to maximize the transmitted THz wave amplitude. Maximizing the amplitude ensures that the beam enters the waveguide completely, thus ensuring that the intensity of the THz wave interacting with the sample is maximized.

Finally, in order to avoid the influence of water vapor in the air, we place the whole system in a closed box and fill it with dry air so that the relative humidity of the working environment is less than 3%, and the temperature of the working environment is kept at 24 ℃. When the waveguide is used without sample, the spectral width is 0.1 *THz* - 1.5 *THz*, and the signal-to-noise ratio of the system is more than 50 *dB*. In the actual sample detection, the spectral width is generally only 0.1 *THz* - 1.0 *THz*, and the signal-to-noise ratio of the THz spectrum of the sample will be reduced to between 30*dB* - 40*dB*.

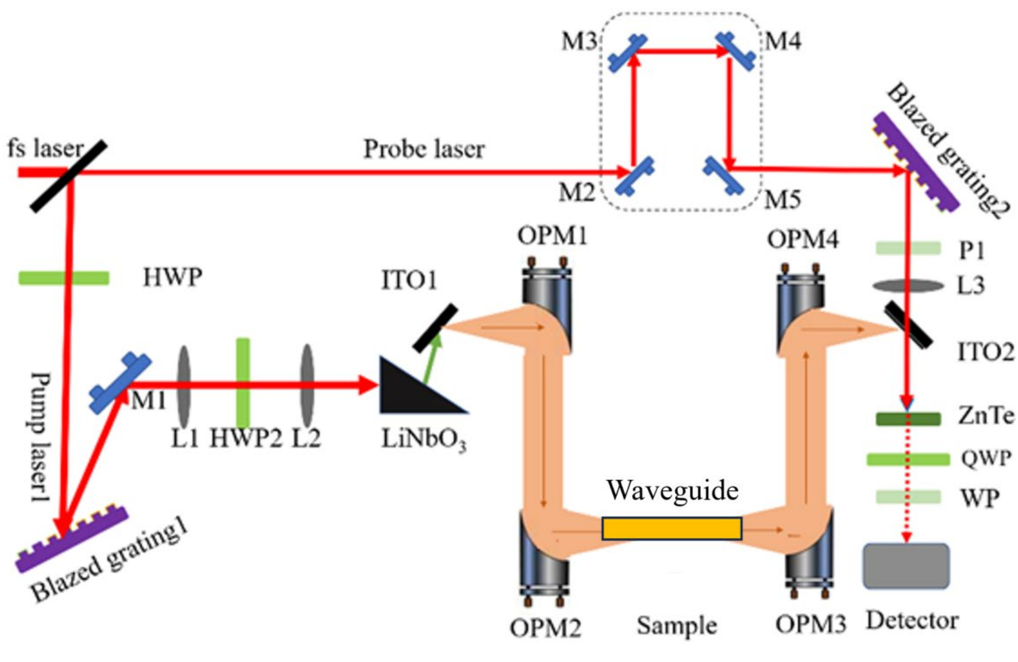

Fig. 1 High power static detection mode optical path diagram of THz-TDS system based on parallel planar waveguide.

3. Design and preparation of waveguides

3.1 Design details and parameters

Metallic parallel plate waveguides have received much attention for their use at THz frequencies, where they provide transverse electromagnetic (TEM) mode propagation without dispersion, with losses determined by the conductivity of the metal plate, and thus have very low group velocity dispersion. Since parallel plate waveguide and free-space THz radiation can be well coupled, they are ideal devices for the distortion-free transmission of sub-picosecond THz pulses.

As shown in Fig. 2, we use oxygen-free copper as the processing material, which approximates a perfect electrical conductor in the THz band, to fabricate a flared tapering parallel flat plate waveguide with a spacing of $d = 100\ \mu m$ at the parallel flat plate positions.

The THz wave generated by the femtosecond laser incidence is coupled to the center of a parallel plate waveguide through a horn-shaped tapering waveguide, and the THz wave propagates in a transverse electromagnetic wave mode in the parallel flat plate. The smaller spacing d between the parallel-plate waveguide plates can realize the local enhancement effect of the THz electric field, which makes the interaction of the THz wave with the biological samples to be detected more adequate, thus realizing the THz detection of trace water-containing samples.

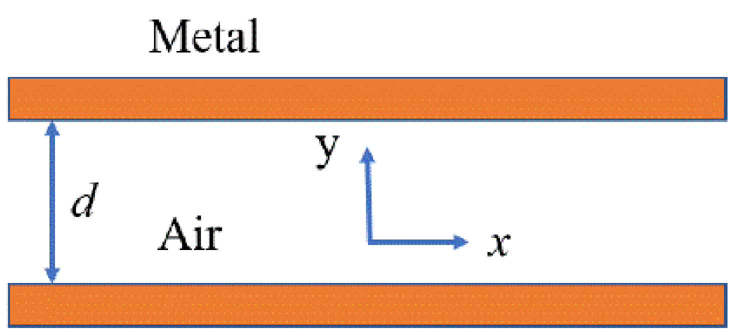

Fig. 2 Schematic diagram of a parallel plate waveguide

3.2 Performance test

The THz transmission performance of the ultra-precision machined and polished parallel plate waveguide are tested, and the test results show that the burr excess, knife pattern, roughness and flatness of the waveguide surface have serious loss on the THz transmission efficiency. The above problem is mainly caused by the diffuse reflection on the waveguide surface resulting in THz wave loss, which leads to the waveguide transmission rate not meeting the detection requirements. In order to improve the transmission rate of the waveguide, we refine the surface of the waveguide (surface roughness <10 *nm* after finishing), and the transmission rate of the metal waveguide is greatly improved after finishing, and the transmission rate in the low-frequency region (0.1 - 2 *THz*) can reach up to 70%, and its THz transmission rate detection results are shown in Fig. 3.

3.3 THz spectral detection of α-lactose solution

In this paper, $LiNbO_3$ crystal photo rectification is used to radiate strong-field THz waves, on the one hand, the radiated power of THz waves is increased from the source, and on the other hand, the flared gradient parallel plate waveguide enhances the local electric field of incident THz waves. As a result, the detection sensitivity of terahertz spectra of water-containing samples is greatly improved, and the study of trace water-containing biomolecules is finally realized. We firstly detect different concentrations of α-lactose solutions.

Fig. 4 (a) THz time-domain spectra of α-lactose solid and aqueous solutions of α-lactose at different concentrations are detected by a parallel plate waveguide. From the figure we observe that as the lactose concentration decreases, both the time delay effect and the decrease in amplitude of the sample signal prove that the detection spectrum carries the sample information. From the spectrum in Fig. 4(b), we can clearly observe that the whole detection spectrum is very smooth and the effect of noise on the sample signal can be completely ignored. At 0.53 *THz* of the spectrum, it can be clearly seen that the spectrum has a decreasing point of absorption peaks, and at 0.53 *THz*, both the α-lactose solid and the α-lactose solutions with different concentrations have decreasing points, and we further analyze the above phenomenon in combination with the characteristic absorption spectra.

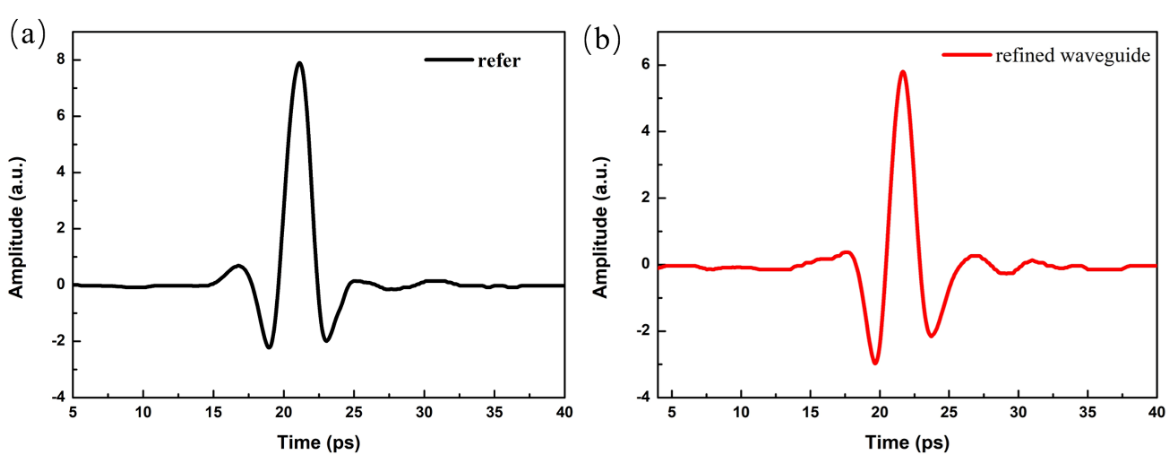

Fig. 3 Detection of the transmittance of refined waveguide. (a) THz reference signal of the system and (b) THz signal of the waveguide.

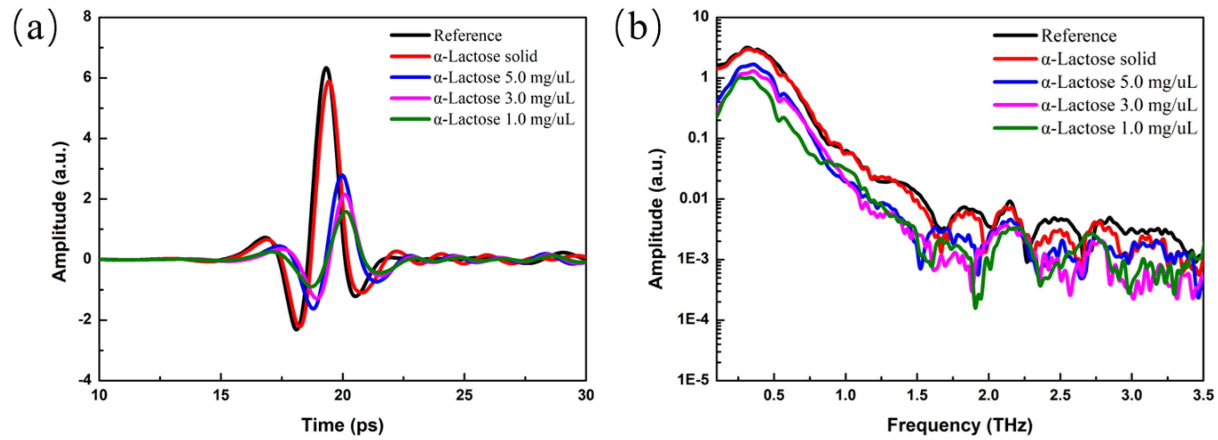

Fig. 4 High-power THz spectra of α-lactose samples with different concentrations based on parallel plate waveguide detection, (a)Time-domain waveforms; (b) the corresponding frequency-domain waveforms.

Combined with the absorption spectra in Fig. 5(a), we can observe that the point at which the spectrum of the sample drops at 0.53 *THz* with respect to the reference signal is the absorption peak for both the α-lactose solid and the solution. Moreover, as the concentration decreases, the absorption baseline of the absorption spectrum also increases with water content increment.

For the spectra in different concentrations of α-lactose solution, the relationship between the amplitude of the absorption peaks and the concentration are extracted in the concentration range of 1.0–5.0 *mg/μL*. We extract the amplitude of 0.53 *THz* for the linear fitting [see Fig. 5 (b)], and the corresponding expression of the corresponding linear fitting function is

$$y = -10.65x + 83.75, R^2 = 0.911$$

The high-power THz waves and the local field enhancement effect of the THz waves by the parallel flat plate waveguide increase the sample transmission intensity with a maximum transmission thickness of 300 *μm*. This detection is much larger than the limit value of 175 *μm* thickness that can be detected by conventional free-space THz-TDS systems, which prove that the parallel plate waveguide has a local field enhancement effect on the THz wave carrying the sample at the parallel plate site, which realizes the THz transmission detection of water-containing samples with large thickness by enhancing the THz field strength of the water-containing samples. However, at the same time, as the thickness of the sample increases, the strong absorption of water leads to the attenuation of the THz signal of the sample, which affects the actual detection of the minimum concentration of water-containing samples. This new detection method provides an experimental basis for qualitative research on biological samples with larger thickness, such as cells and tissues.

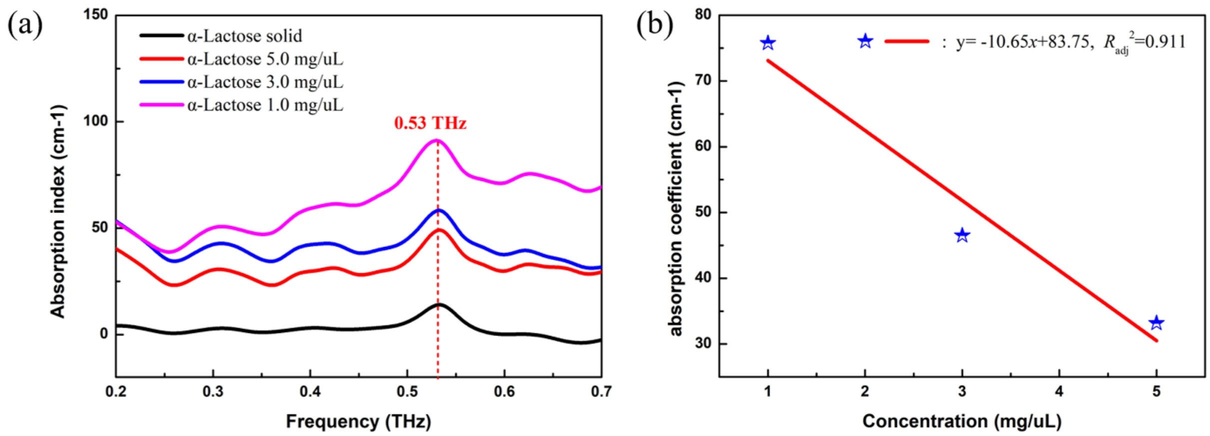

Fig. 5 (a)Characteristic absorption spectra of α -lactose samples with different concentrations and (b) position changes of absorption peaks of α -lactose solutions with different concentrations.

4. Conclusions

In this paper, we have presented the design and construction of a set of THz - TDS system based on a high-power terahertz (THz) source radiated by $LiNbO_3$, and coupled with parallel plate waveguide detection platform, for highly sensitive detection of liquid biological samples. We have achieved qualitative identification and quantitative detection of low-concentration lactose solutions with a maximum thickness of 300 μm and a minimum detection concentration of 1 $mg/\mu L$. Moreover, we have also observed that the absorption peak position changes linearly with the decrease of sample concentration. Overall, our work contributes to the advancement of THz spectroscopy and its potential applications in the field of biomedical research.

Acknowledgments

This work was supported by the National Natural Science Foundation of China (62371391); the Key Project of Baoji College of Arts and Sciences (209010928).

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