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Circular dichroism spectra of α-lactose molecular measured by terahertz time-domain spectroscopy

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Researchers have long studied circular dichroism (CD) for its enormous prospects in life sciences. Many biomolecules have vibration modes in the terahertz region, and terahertz CD spectra are robust to detect biomolecular structures. However, few studies explore the terahertz CD spectra on even natural materials due to technical challenges in both fields. Here, we report a setup of home-built terahertz time-domain spectroscopy to measure the polarization states of terahertz waves. By carefully measuring the transmission Jones matrix, we obtain terahertz CD spectra of α-lactose tablets and D-glucose tablets. Our results show that the terahertz CD spectra are sensitive to vibrational motions in biochemical compounds, which will find wide applications in biosensing and biomedical diagnostics.

Keywords: circular dichroism, terahertz, α-lactose

PACS: 42.25.Ja, 42.62.Be, 87.64.K–

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1. Introduction

Circular dichroism (CD), defined by different absorptions of circularly polarized light with opposite chirality,[1,2] has been an attractive topic for a long time. One origin of this fascinating physical phenomenon is the interaction between light and chiral molecules, which can not be transformed into their images by rotation operations in three-dimensional (3D) space.[1,2] The CD spectroscopy technique is advantageous in studying biomolecules because many of them, such as sugars, DNA, and proteins, are chiral.[2–4] These chiral molecules are building blocks of life. The ability to distinguish the chirality that contributes to the characterization of the secondary structure[2–5] is essential, representing proteins' folding and binding properties and even monitoring the conformational changes of the structures.[2,6,7]

Electronic and vibration transitions lead to CD signals, but the corresponding frequency regions are different: electronic CD is usually in the visible or ultraviolet region, while vibration CD is usually in the infrared or terahertz region. Many biomolecules vibrate at the terahertz frequencies. The terahertz CD spectra related to these vibration modes are excellent to probe biomolecules' soft oscillatory motions.[8–10] Measuring the CD signals requires accurate polarimetry of electromagnetic waves.[11,12] However, in the terahertz region, this kind of technique is still rare because of lacking devices that can modulate the polarization states of terahertz waves. Exceptionally a few works have reported measurement of the terahertz CD spectra of natural material even though it is considered as a prospective tool. Another factor hindering measuring terahertz CD spectra of natural materials is that the CD signal is about three-order weaker at terahertz frequencies than in the invisible or UV region. Some terahertz CD experiments have been conducted on chiral meta-materials to enhance electromagnetic response at resonances.[13–17]

In this paper, we report the experimental study on terahertz CD spectra of α-lactose molecules by carefully measuring the polarization states of the transmitted terahertz waveforms with terahertz time-domain spectroscopy (TDS). While the measured CD signal is weak, it has enough dynamic range compared to a polyethylene (PE) sample. Our work demonstrates a typical application of terahertz CD spectra on biomolecules.

2. Experiment

2.1. Sample preparation

Saccharide is an very important organic compound widely distributed in nature. Sucrose in daily consumption, starch in grain, cellulose in plant body, glucose in human blood and so on all belong to saccharide. It plays an important role in the process of life activities, and it is the main source of energy required by all living things to maintain life activities. Therefore, we choose the α-lactose (0-β-d-galactopyranosyl-(1-4)-α-d-glucopyranose) molecule, which is a disaccharide that has been found in milk of most mammals,[18] to measure terahertz CD spectra. It has a chiral molecular structure. Figure 1 shows the structural formula of α-lactose.[19] The specific rotation of α-lactose solution at 20° is reported to be +89.4° at wavelength 589 nm.[18,19] Moreover, α-lactose molecules have

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many vibration modes in the terahertz region.[20–22] These properties of α-lactose provide conditions for measuring terahertz vibration CD spectra. It is not easy to measure a single molecule because the absorption difference for left-handed circularly and right-handed circularly polarized light is less than 1/1000.[23] Moreover, the absorption of terahertz in an aqueous solution is substantial. Hence, we prepared the samples by pressing the α-lactose polycrystal power into tablets with a pressure of 26 MPa. Table 1 shows that different α-lactose samples with four thicknesses of 0.990 mm, 1.740 mm, 2.305 mm, 2.565 mm are pressed and almost isotropic, but we will show later that they present slightly spatial anisotropy, which will affect the CD signal and need to be considered in data procession. The polyethylene (PE) tablet with a thickness of 2.28 mm is used as the control sample. We also measured the terahertz CD spectra of a D-glucose tablet with thickness of 1.28 mm, which also belongs to saccharide.

Table 1. Materials.

Sample	Thickness (mm)	Mass (g)
α-lactose1	0.990	0.4045
α-lactose2	1.740	0.2990
α-lactose3	2.305	0.3987
α-lactose4	2.565	0.4765
PE	2.275	0.2331
D-glucose	1.280	0.1908

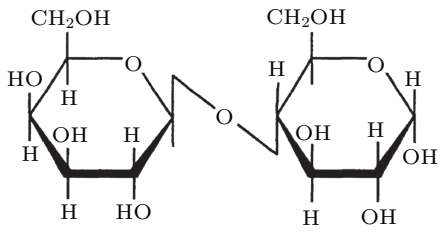


Fig. 1. The structural formula of α-lactose.[19]

2.2. Experimental setup

To measure terahertz CD spectra, one critical thing is to track the variation of the polarization states when the terahertz waves transmit through the sample. Our home-built terahertz TDS has the ability to characterize the polarization state of terahertz waves. The experimental setup is shown in Fig. 2. A ZnTe crystal generates terahertz pulses under the excitation of femtosecond laser pulses (repetition frequency 80 MHz, central wavelength 800 nm, duration 70 fs) delivered from a commercial Ti:sapphire oscillator. The terahertz polarization detection system consists of three terahertz wire-grid polarizers (P1, P2 and P3). The first polarizer P1 is used to ensure the incident wave ($\boldsymbol{E}_0$) to be vertically polarized. Behind the sample, the polarizer P2 is mounted on a precise and electrically controlled rotation stage (newport), allowing polarization projections of the transmitted terahertz electric fields to be $+45°$ (p^+) or $-45°$ (p^-) with respect to the incident terahertz pulse. The two projected components are written as E_1 and E_2.

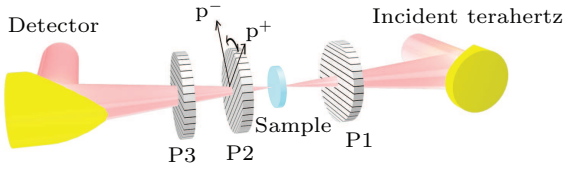


Fig. 2. Schematic of the experimental setup for polarization-sensitive terahertz TDS.

The polarizer P3 projects E_1 and E_2 into vertical polarization to maintain the same response function of electric-optic sampling detector. All the terahertz optics are sealed in a vacuum chamber to prevent vapor absorption of terahertz waves. The experiments are conducted at room temperature. The signal-to-noise ratio of our Terahertz TDS system is 1000:1.

The transmittance of anistropic or chiral media can be fully described by the Jones matrix

$$\boldsymbol{T}^M = \begin{pmatrix} t_{xx} & t_{yx} \\ t_{xy} & t_{yy} \end{pmatrix}. \tag{1}$$

Here, the coordinate system xyz is defined on the sample and terahertz wave propagates along the z-axis. To measure t_{xx} and t_{yx}, we rotate the sample so that the incident electric field E_0 is parallel with the x-axis. Then, $t_{xx} = (E_1 + E_2)/E_0$ and $t_{yx} = (E_1 - E_2)/E_0$. Rotate the sample around the z axis by $90°$ so that $\boldsymbol{E}_0$ is parallel with the y axis, t_{yy} and t_{xy} can be obtained in the same way. The Jones matrix between 0.3 THz and 2.5 THz can be obtained with enough dynamic range with our home-made THz-TDS. We will show in the next section how to extract CD signals from the measured Jones matrix.

2.3. Data analysis

The α-lactose tablet may process some spatial anisotropy caused by the polycrystal structure. The birefringence induced by spatial anisotropy should be eliminated from the measured Jones matrix to extract the CD signal. Every Jones matrix can be decomposed into a symmetric matrix:

$$\boldsymbol{T}^{\mathrm{S}} = \frac{1}{2}\begin{pmatrix} t_{xx} & t_{yx}+t_{xy} \\ t_{xy}+t_{yx} & t_{yy} \end{pmatrix}, \tag{2}$$

and an anti-symmetric matrix:

$$\boldsymbol{T}^{\mathrm{A}} = \frac{1}{2}\begin{pmatrix} t_{xx} & t_{yx}-t_{xy} \\ t_{xy}-t_{yx} & t_{yy} \end{pmatrix}. \tag{3}$$

We can obtain two electromagnetic eigenmodes by diagonalizing the Jones matrix. As shown in Fig. 3, the two eigenmodes are generally elliptically polarized. The two eigenmode ellipses of both $\boldsymbol{T}^{\mathrm{S}}$ and $\boldsymbol{T}^{\mathrm{A}}$ have the same ellipticity, and their principal axes are orthogonal with each other. However, the two eigenmodes of $\boldsymbol{T}^{\mathrm{S}}$ have the same chirality while those of $\boldsymbol{T}^{\mathrm{A}}$ have opposite chirality. These properties indicate that the transmission resulting from the chirality is represented by $\boldsymbol{T}^{\mathrm{A}}$ and that resulting from spatial anisotropy is represented by $\boldsymbol{T}^{\mathrm{S}}$.

To gain further insight, we perform coordinate transformations on $\boldsymbol{T}^{\mathrm{A}}$ and $\boldsymbol{T}^{\mathrm{S}}$ from the linear base $(\hat{x},\hat{y})$ to circular base $(\hat{e}_+ = \frac{\hat{x}+\mathrm{i}\hat{y}}{\sqrt{2}}, \hat{e}_- = \frac{\hat{x}-\mathrm{i}\hat{y}}{\sqrt{2}})$. The transformation matrix $\boldsymbol{A}$ is denoted by

$$\boldsymbol{A} = \frac{1}{\sqrt{2}}\begin{pmatrix} 1 & 1 \\ \mathrm{i} & -\mathrm{i} \end{pmatrix}. \tag{4}$$

The x and y axes are defined in arbitrary orthogonal directions. Hence, before transformation to a circular base, we rotate the sample by an arbitrary angle θ. The rotation matrix is

$$\boldsymbol{R}(\theta) = \begin{pmatrix} \cos\theta & \sin\theta \\ -\sin\theta & \cos\theta \end{pmatrix}. \tag{5}$$

Then, in a circular base, the symmetric Jones matrix can be calculated by $\boldsymbol{T}_{\mathrm{C}}^{\mathrm{S}} = \boldsymbol{A}^{-1}\boldsymbol{R}(\theta)^{-1}\boldsymbol{T}^{\mathrm{S}}\boldsymbol{R}(\theta)\boldsymbol{A}$ and the anti-symmetric one is calculated by $\boldsymbol{T}_{\mathrm{C}}^{\mathrm{A}} = \boldsymbol{A}^{-1}\boldsymbol{R}(\theta)^{-1}\boldsymbol{T}^{\mathrm{A}}\boldsymbol{R}(\theta)\boldsymbol{A}$. The results are

$$\boldsymbol{T}_{\mathrm{C}}^{\mathrm{S}} = \frac{1}{2}\begin{pmatrix} \frac{t_{xx}+t_{yy}}{2} & -\mathrm{e}^{-2\mathrm{i}\theta}\left[\frac{t_{yy}-t_{xx}}{2} + (t_{yx}+t_{xy})\,\mathrm{i}\right] \\ \mathrm{e}^{2\mathrm{i}\theta}\left[\frac{t_{xx}-t_{yy}}{2} + (t_{yx}+t_{xy})\,\mathrm{i}\right] & \frac{t_{xx}+t_{yy}}{2} \end{pmatrix}, \tag{6}$$

$$\boldsymbol{T}_{\mathrm{C}}^{\mathrm{A}} = \frac{1}{2}\begin{pmatrix} \frac{t_{xx}+t_{yy}}{2} - (t_{xy}-t_{yx})\,\mathrm{i} & \mathrm{e}^{-2\mathrm{i}\theta}\frac{t_{xx}-t_{yy}}{2} \\ \mathrm{e}^{2\mathrm{i}\theta}\frac{t_{xx}-t_{yy}}{2} & \frac{t_{xx}+t_{yy}}{2} + (t_{xy}-t_{yx})\,\mathrm{i} \end{pmatrix}. \tag{7}$$

One can find that for $\boldsymbol{T}_{\mathrm{C}}^{\mathrm{S}}$, we have $t_{++}-t_{--}=0$, but for $\boldsymbol{T}_{\mathrm{C}}^{\mathrm{A}}$, $t_{++}-t_{--}=t_{yx}-t_{xy}$, which are related to the CD spectra. Here, $+$ and $-$ denote two opposite rotating circular lights. The foregoing subscript of t_{++} represents the polarization state of the outgoing beam, and the posterior one represents the incident polarization state. Note that the value of $t_{++}-t_{--}$ is independent of the sample azimuth angle. These results indicate that performing a coordinate transformation on the measured Jones matrix TM (Eq. (1)) to the circular base, the CD signal from the chiral molecules can be defined as

$$\text{CD signal} = |t_{++}| - |t_{--}|. \tag{8}$$

This CD signal eliminates the effects caused by the spatial anisotropy of the sample and is independent of the sample azimuth angle.

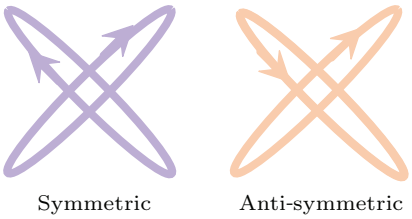


Fig. 3. Eigenmodes of symmetric Jones matrix (left) and anti-symmetric Jones matrix (right). The ellipses represent the trajectories of electric fields.

3. Results and discussion

First, we measure the Jones matrix $\boldsymbol{T}^{M}$ [Eq. (1)] of the same α-lactose2 tablet at an azimuth of 0°, 10°, 20°, 30°, 40°, 50°, 60°. Transforming the $\boldsymbol{T}^{M}$ to circular base with the equation $\boldsymbol{T}_{\mathrm{C}}^{M} = \boldsymbol{A}^{-1}\boldsymbol{T}^{M}\boldsymbol{A}$, we can obtain CD signal [Eq. (8)] at the seven sample azimuth angles, as shown in Fig. 4. We can find that both the shapes and values of the CD signal almost remain unchanged when rotating the sample, which is consistent with the theoretical prediction given by Eq. (8) and confirms the validity of the CD signal measurement.

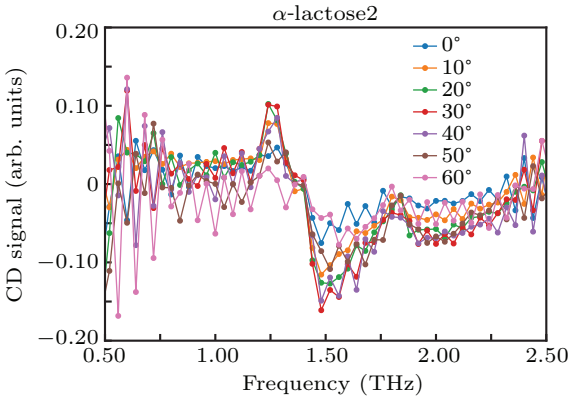


Fig. 4. CD signals at different sample azimuths with the thickness of α-lactose tablet being 1.74 mm.

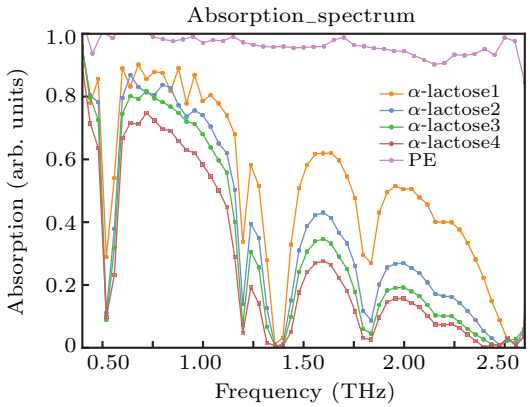


Fig. 5. Transmittance of the lactose tablets with different thicknesses.

The CD signal scales linearly with the sample thickness. To show this property, we measure the Jones matrix of α-lactose tables with different thicknesses from 0.990 mm to 2.565 mm, as given in Table 1. The average transmittances $(|t_{++}|+|t_{--}|)/2$ are shown in Fig. 5. The absorption dips by vibration modes at 0.54 THz, 1.20 THz, 1.36 THz, and 1.82 THz are observed, consistent with other reports.[20–22] According to Eq. (8), we can obtain the CD signals of the

four samples, as shown in Fig. 6. One can see that all samples have obvious CD signals compared to the reference sample PE. These CD signals increase with the sample thickness, which is in agreement with the signature of the CD signal. Moreover, the CD signals are prominent near 1.4 THz, where a vibration mode locates. This result indicates that the CD signals measured originate from the chiral vibration mode. However, the reason why the vibration modes at 0.54 THz present no obvious CD signal needs further investigation.

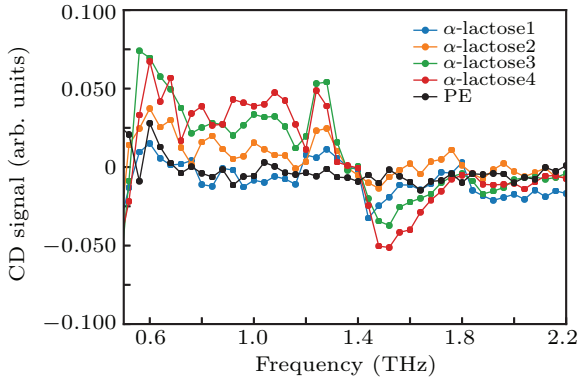


Fig. 6. CD signals of the lactose tablets with different thicknesses.

Other sugar molecules such as D-glucose also have chiral structures. To demonstrate that our method can be used in glucose molecules, we measured the Jones matrix of D-glucose tablet at an azimuth of 0°, 10°, 20°, 30°. The CD signals are shown in Fig. 7. Similar to the CD signal of the α-lactose molecules, the shapes and values of the CD signal almost remain unchanged at all the azimuth angles.

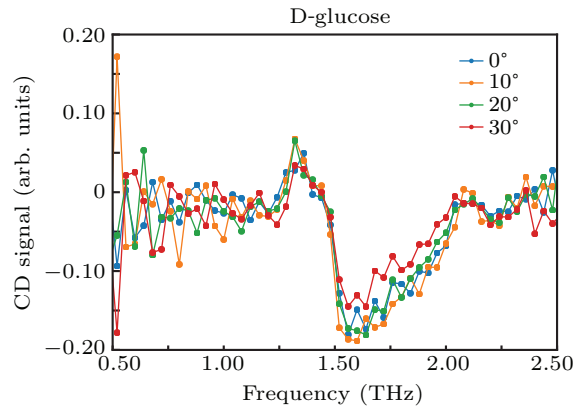


Fig. 7. CD signals at different sample azimuths with the thickness of D-glucose tablet being 1.280 mm.

4. Conclusion and perspectives

We have demonstrated an experimental observation on the terahertz CD spectra of α-lactose. A polarization-sensitive terahertz TDS is built to measure the transmission Jones matrix, from which the CD signal defined by Eq. (8) is obtained. The CD signal of lactose has enough dynamic range compared to PE. We have shown that the obtained CD signal does not contain the birefringence caused by spatial anisotropy. Although we have captured the terahertz CD signal, the intensity is not strong enough to directly extract the difference of the refractive index of two circular modes with opposite chirality from the experimental data. Nevertheless, our terahertz CD spectra demonstrate the related advances in terahertz CD techniques and typical applying scenarios in investigating vibrational motion in biochemical compounds that are instructive to biosensing in the terahertz frequency region.

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