



Terahertz Time-Domain Spectroscopy of Glucose and Uric Acid

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Abstract. We report the use of terahertz time-domain spectroscopy for the study of two therapeutic bio-molecules: glucose and uric acid. Terahertz transmission spectra of crystalline samples of both molecules were measured between 0.1–3.0 THz using an evacuated spectroscopy system. We propose that the stereo-isomers of glucose show spectral features originating from intermolecular vibrational modes, as do uric acid and its derivative molecule, allantoin. In addition, we present a full temperature dependence of the terahertz absorption of L-glucose.

Key words: Glucose, intermolecular, temperature dependent absorption, terahertz, time-domain spectroscopy, uric acid

1. Introduction

Terahertz time-domain spectroscopy is an extremely promising technique for biomedical applications since rotational and vibrational transitions of molecules lie across the far- and mid-infrared spectral ranges [1]. Specifically, at low frequencies, transitions originate from intra- and/or inter-molecular collective vibrations. Terahertz time-domain spectroscopy thus enables the direct quantitative detection and conformational analysis of bio-molecules. To date, there have only been a few terahertz investigations on large molecules of biological relevance owing to the dearth of technologies to access this spectral range and a lack of theoretical models to interpret the observed features. However, Walther et al. [2] measured the far-infrared spectrum of retinal chromophores and could distinguish between different isomeric configurations. Markelz et al. [3] discussed low frequency collective vibrational modes of DNA, bovine serum albumin, and collagen. Furthermore, far-infrared spectra of benzoic acid and its derivatives [4], and of nucleobases of DNA [5] have been reported.

In this article we present the absorption spectra of D- and L-glucose, two stereo isomers of glucose, together with the absorption spectra of sucrose, uric acid and allantoin. We also report the temperature dependent absorption of L-glucose.

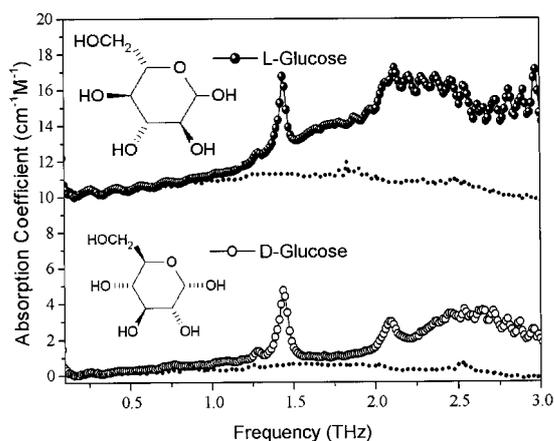


Figure 1. Far-infrared absorption of pure D- and L-glucose at room temperature in pellets of 0.5mm thickness. Dotted curves show the absorption for 1.7 M solutions of these samples. The curves for L-glucose have been vertically offset for clarity.

2. Experimental

All samples were purchased from Sigma-Aldrich Co. and used without further purification. For low temperature measurements, each was mixed with polyethylene (PET) powder in a mass ratio of 8:1 (PET: sample) minimising the quantity of material needed. Since PET is nearly transparent in the terahertz range, it is an ideal matrix material. Pellets were generally made with thicknesses between 1.2 and 1.4 mm. However, for room temperature measurements, the observed spectral features were less distinct and so samples were prepared as pure pellets with thicknesses between 0.3 and 0.7 mm. This resulted in clearer absorption features. In both cases, the crystals were crushed well before making the pellets in order that the particles were of sub-micron size, ensuring that the observed spectral features were not a result of Mie scattering [6]. Indeed, some of the particles have sizes of a few tens of nanometers, as confirmed by environmental SEM measurements.

A vacuum-capable terahertz time domain spectroscopy system [7] was used for the room temperature measurements, and typical vacuum levels of 0.3 mbar were obtained. The spectrometer had a useful bandwidth of 0.1–3.0 THz and a spectral resolution better than 30 GHz. The spectroscopic information was obtained by comparing the terahertz electric field recorded with and without a sample in the beam path. For the low temperature measurements, samples were mounted in a cryostat equipped with mylar windows. The terahertz beam path was purged with dry nitrogen to eliminate absorption by water vapour.

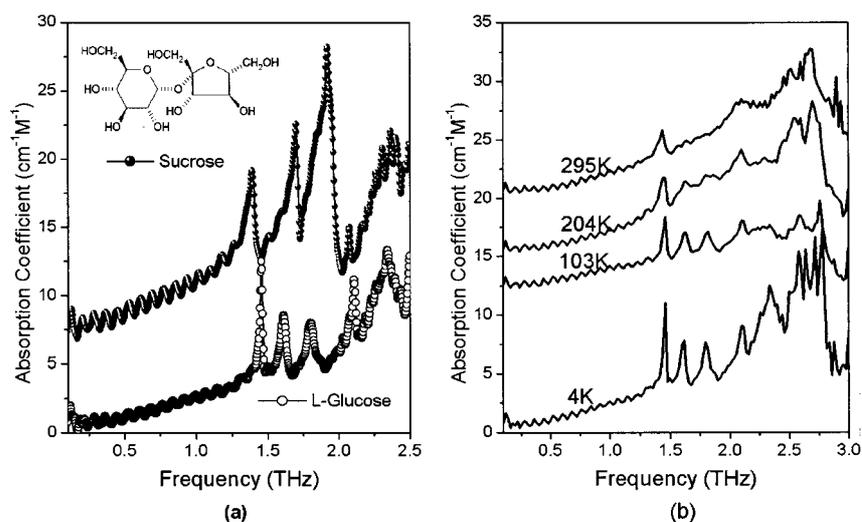


Figure 2. Comparison of terahertz absorption in (a) L-glucose and sucrose at 4K, and (b) L-glucose at different temperatures. The curves have been vertically offset for clarity.

3. Results and Discussion

Room temperature terahertz absorption spectra for glucose isomers are shown in Figure 1 in the frequency range 0.1–3.0 THz. The small oscillations in the spectra at low frequencies are caused by etalon effects resulting from terahertz reflections at the pellet sample surfaces.

D-glucose has sharp absorption peaks at 1.45 THz and 2.1 THz, and a minor peak at 1.26 THz whereas L-glucose has a sharp peak at 1.45 THz and a broad feature at 2.12 THz. In contrast, 1.7 M aqueous solutions of these glucose samples showed no sharp spectral absorption features in this spectral range. In the terahertz beam path, the amount of glucose in the solution sample is about half of that in poly-crystalline sample. It is thus likely that the observed absorption features are a result of intermolecular vibrational modes rather than intramolecular modes, the latter being expected to be independent of the degree of crystallinity of the sample.

In Figure 2a we show a comparison between the absorption spectra of L-glucose and sucrose. Although the sucrose molecule incorporates the glucose molecular structure, the spectral features of sucrose and glucose are found to be different, with no common spectral features. This is consistent with the observed modes originating from intermolecular vibrations.

The temperature dependence of absorption in L-glucose is illustrated in Figure 2b. The absorption line profiles shift to lower frequencies and broaden as the temperature is increased. In addition, more distinct absorption peaks are observed at low temperatures.

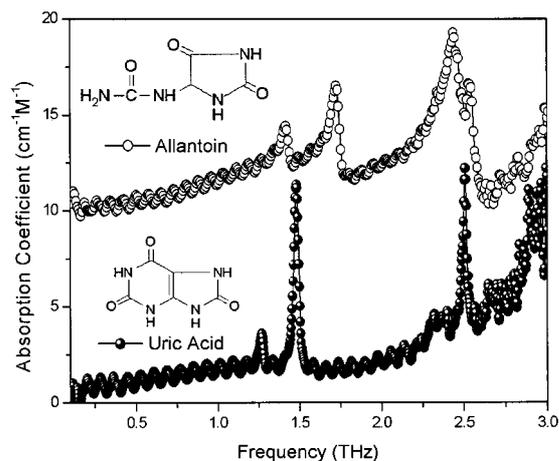


Figure 3. Terahertz absorption in uric acid and allantoin at 4K. The curves have been vertically offset for clarity.

The structural dependence of far-infrared absorption is further suggested by Figure 3 in which absorption spectra of uric acid and allantoin, a derivative compound of uric acid, are compared. Uric acid with two aromatic rings and allantoin, with an aliphatic chain attached to the aromatic ring, have isolated, but different, spectral features in the 0.1–3.0 THz range. Once again, no common features are observed. Moreover, allantoin has a much stronger temperature dependent absorption than uric acid.

4. Conclusion

We have demonstrated the use of terahertz time-domain spectroscopy for measuring absorption spectra in D- and L-glucose, sucrose, uric acid and allantoin. We suggest that intermolecular vibrational modes may contribute to the observed spectra of these molecules in the THz frequency range.

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