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On the influence of water on THz vibrational spectral features of molecular crystals

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***Abstract*—The collective vibrations in molecular crystals can be probed using terahertz spectroscopy, providing unique characteristic spectral fingerprints. However, the association of the spectral features to the crystal conformation, crystal phase and its environment is a difficult task. We present a combined computational-experimental study on the incorporation of water in lactose molecular crystals, and show how simulations can be used to associate spectral features in the THz region to crystal conformations and phases. Furthermore, we also show that water does not play only a perturbative role but fully participates in the emergence of the THz vibrations**

I. Introduction

The nanoscale structure of molecular assemblies plays a major role in many (µ)-biological mechanisms. Molecular crystals are one of the most simple of these assemblies and are widely used in a variety of applications ranging from pharmaceuticals and agrochemicals, to nutraceuticals and cosmetics. Water molecules play an essential role in their structural and functional properties.

THz spectra include information of both water of crystallization and the host crystal structure making THz-TDS very sensitive to dehydration. During dehydration, THz spectroscopy will precisely monitor both the loss of water of crystallization and the eventual molecular rearrangement. This could then be further extended to study systems where multiple solid-state forms appear as a result of dehydration.

The purpose of this communication is to go a step further in understanding the role of water in molecular crystals; we present a detailed study of the THz spectrum of one of the most used and thought-to-be-simple materials by the THz community, namely alpha-lactose monohydrate because it is the golden standard in the community [5, 2].

II. Results

To deepen our understanding of the role of water and to validate the simulation results, an experimental setup was developed. It allows the heating and temperature control of the samples, and thus provides the possibility for the dehydration. In our experiments, our samples go through two phase-transitions. We observed the spectral signatures of three different "metastable" crystal phases (stable in N_2 atmosphere, namely, the α-lactose monohydrate (α-LM or phase 1), and two other phases, hereafter called phase 2 and 3) in agreement with the predictions by calculations and mass-spectroscopy tests. We analysed our spectrum by fitting our time traces thanks to a software fit@tds and a method explained elsewhere [7, 6, 8]. The spectra are shown in fig 1.

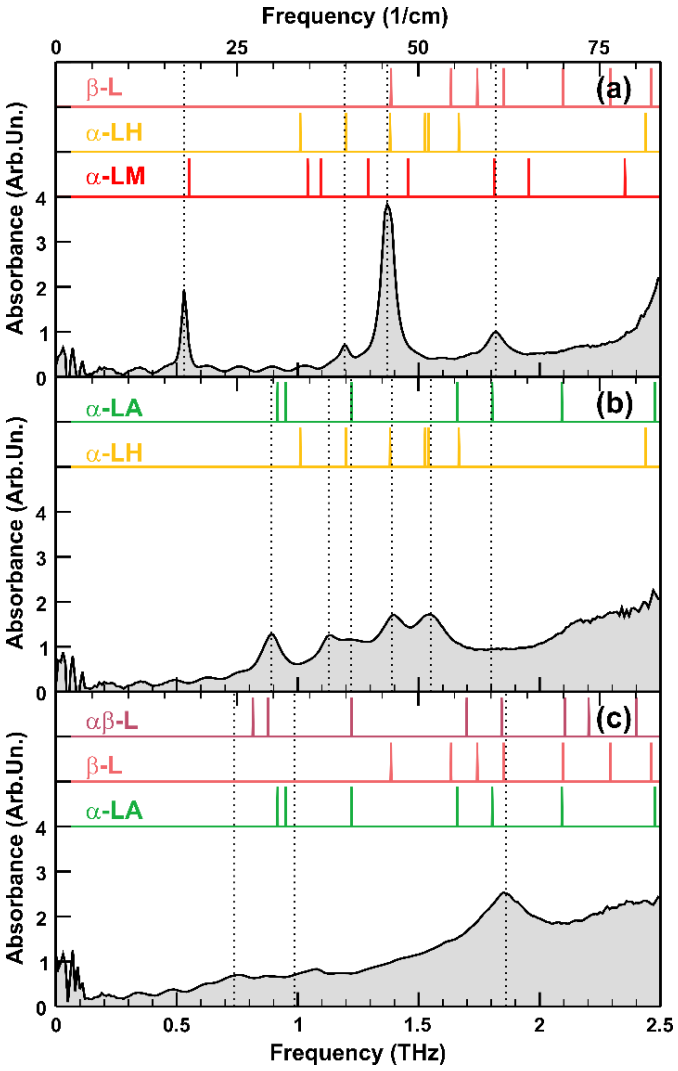

Figure 1: Comparison of calculated low THz vibrational modes at the Γ-point (colour vertical lines) to spectra of the three experimentally obtained morphologies (black curves), (a)-(c) – phases 1-3, correspondingly. The vertical dotted lines indicate the position of the experimentally fitted modes.

For a better interpretation of these spectra we performed DFT calculations. The gas phase single molecule approach for spectral modelling is insufficient for the THz range, as this concerns long ranged vibrational modes. We consequently pursued periodic boundaries DFT calculations. The frequency of the modes found in these calculations are given in fig 1 without further scaling.

Here, one can see that the phase identification is far from obvious and that the simple: $X \rightarrow Y \rightarrow Z$ phase transformation picture, is hard to maintain. It appears the seemingly distinct phases and transformations in reality involve mixtures and/or additional intermediate phases. For example, the alpha-lactose monohydrate sample – widely used in the community for test purposes – cannot be explained by only one single crystal phase.

Secondly, our spectra show drastic changes with decreasing water content. From experimental work [3], these spectral changes could be attributed to the appearance/disappearance of the absorption peaks upon hydration. Thanks to the DFT calculations, we show that although the water molecules have a larger freedom of motion than the carbohydrates, one cannot separate the vibrations of the carbohydrate lattice from the vibrations of the water molecules. Consequently, these water molecules and associated hydrogen bonds do not only play a perturbative role, but also participate in the formation of the vibration. More importantly, the water molecules' impact is not related to their donor-acceptor role, instead their presence loosens the hydrogen bridges between the lactose molecules allowing long ranged collective modes to emerge. They can be seen as having a lubricating role, allowing the motion of several rigid pieces together.

Conclusion

In this work [4], we provide a first step by proposing a credible explanation for the well-known lactose spectrum. Using periodic DFT simulations of lactose molecular crystals, the role of water in the observed lactose THz spectrum is clarified, presenting both direct and indirect contributions. By integrating our results, we come to the clear conclusion that the alpha-lactose monohydrate system is more complex than generally thought.

In addition, this work aims to further stress the importance of good and accurate periodic DFT calculations. In contrast to the mid infrared spectroscopic range where the vibrations are localized around one or several molecular bonds, in the THz range, the vibrational modes are delocalized among several molecules. They form what one can call "phonons of the molecular crystal", making the use of periodic calculations inevitable, as was also pointed out by Banks *et al.* [1]. The clear corollary of this conclusion is that different crystal structures will give rise to different THz spectra. One can exploit this property experimentally and use THz spectroscopy to probe and discriminate the crystalline structure of a molecular crystal sample.

Even though THz spectroscopy exists already more than two decades, we believe that we are still experiencing its infancy. Further work and combination with other experimental and theoretical techniques will be needed to bring it to its full potential and to allow for its straightforward application on more complex structures such as protein crystals or even protein structures like amyloids or viral capsids.

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