

T-ray spectroscopy of biomolecules

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Abstract—In the past few years it has been shown that the THz spectra of many polycrystalline biomolecules show very distinct, characteristic features. The fact that these specific signatures can be used to identify many samples such as pharmaceuticals, illicit drugs, and explosives through a wide range of common packaging materials has spurred an increased commercial interest in THz-TDS and imaging. However, most of these signatures that occur in the spectra of polycrystalline samples originate from phonon-like vibrations of the well-ordered intermolecular structure. The spectra of larger biomolecules, due to the lack of such a long-range order, quite often show only a broad, featureless absorption. Furthermore, the sample preparation becomes more and more important, as many of these sample are only available in very small quantities or in liquid solutions. These hurdles constrict many biomedical applications of THz spectroscopy. In this presentation, we will show, based on a wide range of examples, the potential that THz-TDS and imaging hold for biomedical applications and discuss possibilities for overcoming the hurdles that currently obstruct their application.

I. INTRODUCTION

The characteristic signatures that dominate the THz (or T-ray) spectra of most polycrystalline biomolecules are very sensitive to the molecular and crystalline structure. Therefore it is possible to differentiate and identify molecules of similar structure [1] and even their isomeric [2], [3] and crystalline configuration [4], [5]. This fingerprint ability and the low, featureless absorption of most typical packaging materials at THz frequencies are the basis for many biosensing applications. However, if the spectra lack such distinct signatures—as it is for example the case for amorphous samples [6], solutions, and most complex biomolecules even in the solid phase [7], [8]—an identification of the sample based on recognition of sharp, specific spectroscopic features is often not possible. Yet, a differentiation between for example a test sample and a known reference sample is still feasible, and for many biomedical applications such differentiations are sufficient.

II. EXPERIMENTAL

The spectra that will be shown in this presentation have been recorded using a custom built THz-TDS spectrometer in transmission and reflection mode (see for example [9]) and a commercially available fibre coupled system (Picometrix T-ray 2000) that can be used either in transmission or reflection mode.

III. RESULTS

In order to demonstrate the high sensitivity of THz spectra to small differences in the molecular structure we show

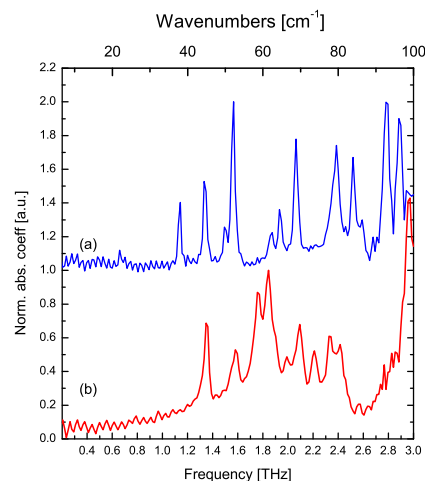


Fig. 1. Normalized Absorption of polycrystalline (a) estrone and (b) estriol (shifted vertically for better visibility). Both spectra show several sharp, distinct spectral features. These features differ clearly for both samples, despite the pronounced similarity in the molecular structure. These characteristic signatures can then be used to identify the sample even through many typical unpolar packaging materials.

in Figure 1 the THz spectra of two hormones, estrone and estriol, recorded at 10 K. Despite the pronounced similarity of the molecular structure, the spectra differ significantly from each other. As most of the the low-frequency vibrations that give rise to the characteristic features in the THz range are of intermolecular rather than intramolecular character, THz-TDS can also be used to distinguish and identify different crystalline configurations [5]. This ability of THz-TDS for chemical recognition [7] has spurred the increased interest in THz-TDS for applications such as pharmaceutical quality control and detection of explosives and illicit drugs.

However, the spectra of most amorphous samples, liquids [10] and solutions, and also of many complex biomolecules in the solid state [8], [11] lack such pronounced characteristic features. Therefore, spectral identification based on the recognition of the characteristic spectral fingerprints is often impossible for such samples. As example, we show in Figure 2 a typical absorption spectrum of a polypeptide, recorded at ambient temperature. Compared for example to the richly structured spectra of the polycrystalline hormone

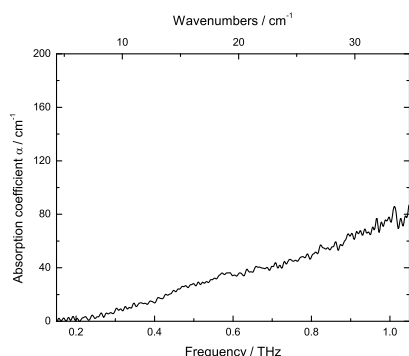


Fig. 2. Absorption spectrum of a polypeptide. Compared to the richly structured spectra of most polycrystalline samples, only a broad, featureless slope is observed.

samples shown in Figure 1 only a broad, featureless absorption is observed. Yet, by applying a careful sample preparation in order to avoid any artifacts arising from uncertainties in thickness, water content, density, and changes in the conformational state induced by inappropriate sample handling, the slope and absolute value of the absorption coefficient can still be used to differentiate between different samples such as for example a test substance and a reference sample. For example, we have recently shown that it is possible to differentiate between two different artificial RNA strands, Poly-A and Poly-C [11]. In this presentation, we will discuss the potential of THz-TDS for detecting structural differences in complex biomolecules such as for example polypeptides. By applying careful sample preparation, increasing the SNR [12] and applying advanced signal processing techniques [13], we can demonstrate that despite the lack of distinct signatures in the spectra of complex biomolecules THz spectroscopy and imaging are still versatile tools for biosensing and biomedical applications.

IV. CONCLUSION

The THz spectra of small, polycrystalline biomolecules show very characteristic features. These THz signatures are the basis for many recent applications of T-ray spectroscopy and imaging. For larger molecules, due to the lack of such characteristic signatures, these fingerprinting techniques are in many cases not applicable. However, a comparison of the absolute value and slope of the absorption spectra can still lead to valuable information about structural and conformational properties of the samples.

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