THz Spectroscopy of protein complexses

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Abstract—**We present our preliminary results on the detection of antigen-antibody complexes using terahertz spectroscopy. Our study indicates that a difference between the absortption spectra of pure antibody/antigen and the antibody-antigen complex may be useful for biomedical applications. Furthermore, we introduce a new carrier material, which has several advantages over previously used materials, such as high binding capacity along with high THz transparency.**

I. Introduction And Background

Terahertz (THz) spectroscopy has recently become more and more popular for the investigation of polypeptide and protein structures and dynamics [1-4].

Most molecules have dense and distinctive absorption spectra in the terahertz (THz) range (0-4 THz or 1-130 cm^{-1}), which has led to much interest in THz spectroscopy [5, 6]. Those low frequency vibrational modes are related to hydrogen bonds and other weak interactions; hence they may provide unique information that is relevant to the structure of specific molecules. Vibrational modes in the THz range have been shown to provide information on the conformational state of a protein [5] and are known to play an im-portant part in biochemical reactions such as protein-ligand binding [7].

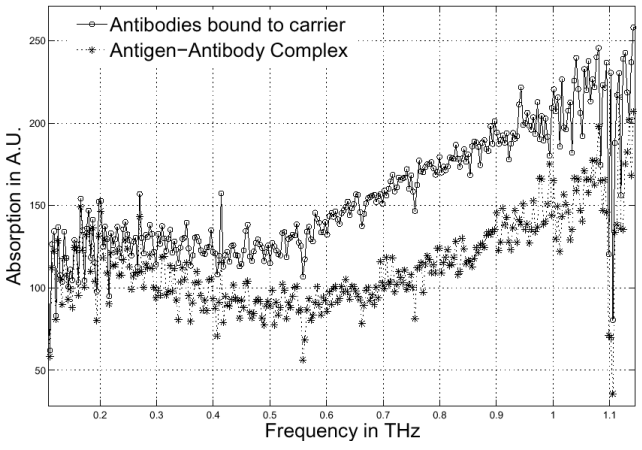
However, wheras the spectra of small, polycrystalline biomolecules are often very richly structured and thus can be used to identify individual molecules and even isomers of a particular molecule [6], larger molecules often lack such characteristic absorption features. THz spectroscopy can in such cases still be useful to differentiate between different biomolecular samples by comparing the exact value of the absorption coeffcient [6]. Due to the fact that that the difference of the absolute value or the difference of the overall frequency dependence of the absorption coefficient can often be quite small, a very careful sample preparation – for example in order to avoid differences and thus uncertainties in the thickness – becomes crucial. If two different complex biomolecules or different configuratios of the same biomolecule are prepared individually on a carrier and then their spectra are compared, errors induced by differences in the background spectrum of the carrier material can often be stronger than the difference in the spectra of the samples under investigation themselves.

A very interesting field with potential biomedical application is the use of THz spectroscopy for label-free detection of protein complexes, protein-ligand complexes and as well as in genetic diagnostics. Mickan *et al* [8] showed that it is possible to use THz spectroscopy for bioaffinity sensing by observing the absorption spectra of biotin-avidin complexes. The label-free detection of the hybridization states of DNA has been shown in various studies [9-11].

II. Results

Based on the previous studies on bioaffinity of proteins and binding interactions mentioned above we carried out experiments on antigen-antibody complexes using THz spectroscopy. Several different antibody/antigen complexes were investigated for this study. Each sample first consists of pure isolated antibody immobilized on the carrier. After recording the spectrum of this pure sample the complex-binding is performed, using standard techniques to ensure that only those antigens that have bound to an antibody remain on the sample. Our preliminary results are very promising, showing that a difference in the absorption spectra for isolated antibodies versus antigen-antibody complexes can be ob-served (see figure).

This may suggest a possible use of THz spectroscopy in biomedical applications. Further extended studies will be carried out and the results shown in this presentation. We also introduce a carrier material which shows several advantages over previously used materials, such as a high binding capacity along with a high transparency to THz radiation. Furthermore, this carrier is already typically being used for antigen-antibody sample preparation and will therefore most likely be widely accepted by biomedical users. We will compare this carrier material to others that have recently been used for spectroscopic investigations of complex biomolecules in the THz region, like for example cyclic olefin coplymers[12].



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