Trends and Perspectives in Molecular Spectroscopy: An Introduction

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Over the past 20 years, detailed information on structural and functional properties of biological molecules, biopolymers, membranes and cells has been deduced from molecular spectroscopy, i.e. from Raman and infrared spectroscopy. The tremendous progress in this field was possible because of the development and availability of Fourier transform infrared (FT-IR) spectrophotometers, which cover the entire mid-infrared range (MIR, approx $2000 - 500 \text{ cm}^{-1}$) with very high sensitivity, and can be extended into the near infrared (NIR) and far infrared (FIR) range using appropriate sources and detectors. Mid-infrared spectroscopy has opened numerous applications in biochemistry: Protein secondary structure analysis, the investigation of enzyme reaction mechanisms, the characterization of protein stability and dynamics, or the study of protein folding and misfolding are just a few key examples. With this scope, IR spectroscopy has become a strongly supporting technique in proteomics. Beyond biochemistry, the analysis of clinical parameters using the potential of MIR spectroscopy has been demonstrated and will find wide application.

It would be highly desirable to use the FIR and THz range as a useful extension of the MIR to have access to the manifold of structural information contributed from all constituents of a biological system. However, the sensitivity in the FIR is inherently low due to the low photon flux from thermal sources and mercury arcs. With the advent of coherent sources for this range and with the development of time-domain spectroscopy, the FIR range and THz range becomes increasingly interesting for the analysis of low frequency modes from biomolecules. In line with these technical developments, suitable sample forms for FIR and THz spectroscopy have been developed, which represent a compromise between water background absorbance and the necessary water content required for structural and functional integrity of the samples.

Little is known about the modes that DNA, proteins, lipids and other cell constituents exhibit in the FIR and THz range, and pioneering spectroscopic work is required. Moreover, the rather straightforward bond-to-band correlation which represents one of the strengths of MIR spectroscopy, is partially or fully lost at

longer wavelengths. In line with this, simulations of spectra from normal mode and molecular dynamics calculations which have reached a remarkable level in the MIR will often fail in this spectral region. Delocalized modes, out-of-plane modes, torsional modes, weak molecular interactions, H-bond interactions and networks, as well as the movements of entire protein domains can be expected to represent the main causes of the absorbance. It will require tedious work on model compounds of increasing complexity, isotope labeling, and chemical modification to obtain a library of FIR and THz absorbance of biological matter. Support could come from careful calculations for limited structural units. For the THz-BRIDGE consortium, these are some of the defined tasks.

Thus, the goals are defined and most of the prerequisites are available. Coherent FIR and THz sources provide sufficient intensity to study biopolymers at high sensitivity. Suitable sample cells and sample forms have been developed which ensure structural and functional integrity of the biological matter investigated. Experiments are on the way to obtain and to understand spectra, at least of simple compounds present in biological structures.

The first part of these proceedings 'IR and THz spectroscopy of biological samples' provides a first approach to this field. Absorption properties of relevant molecules, blood cells, and different tissues provide at least some qualitative information on the wavelength-selective attenuation of IR-, FIR-, and THz-radiation, and can provide a feedback to exposure and imaging studies using 'T-rays'.