The many facets of Raman spectroscopy in Biophotonics

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Within the last years a rapid increase of applications of Raman spectroscopy to address biomedical questions has been observed. New concepts of cancer diagnostics as well as a rapid identification of sepsis pathogens were among the most important questions answered by innovative Raman approaches. Here we describe briefly some of our latest results concerning the application of linear and nonlinear Raman microspectroscopy for biophotonics.

We will start with highlighting the potential of Raman microspectroscopy for an online / on-site identification of microorganisms [1] that is of great relevance for an efficient medical diagnosis (e.g. rapid identification of pathogens in urine samples [2]) or water-[3], air- and soil monitoring (e.g. identification of anthrax endospores embedded in complex matrices [4]). In addition, the application of this Raman microbial analysis approach for food analysis that is for the detection of pathogens in milk [5, 6] and meat [7] is highlighted.

The main focus within the second part of this presentation is concerned with Raman studies on eukaryotic cells for biomedical applications. Overall, we will report about the great potential of Raman spectroscopy for a label-free discrimination between normal and tumor cells based on their biochemical composition [8, 9] or towards establishing a Raman spectroscopic hemogram i.e. characterizing leukozytes [10]. Thereby cellular Raman spectra were recorded after drying, in laser tweezers or trapped in a microfluidic environment. In particular we will report about recent progress we made towards Raman activated cell sorting (RACS) by coupling Raman spectroscopy with microfluidics and micromanipulation approaches [11-14].

Besides single cells whole tissue sections like biopsy specimens can be characterized by means of Raman-microspectroscopy. The processing of the specific Raman-maps via mathematical approaches enables an objective evaluation of the tissue samples for an early disease diagnosis like e.g. cancer [15-18].

Besides these ex-vivo tissues Raman studies first steps towards in-vivo Raman spectroscopy that is Raman endospectroscopy will be introduced [19]. By doing so novel Raman fiber probes for an intravascular monitoring of the artheriosclerotic plaque in living rabbits will be presented [20].

The low Raman scattering cross section results in long acquisition times. However, the acquisition times can be reduced by utilizing non-linear Raman approaches like CARS (coherent anti-Stokes Raman scattering) and allows recording Raman images of single characteristic Raman bands in real time. In order to further improve the diagnostic result CARS microscopy can be easily extended by the two other non-linear contrast phenomena second harmonic generation (SHG) and two-photon fluorescence (TPF). Overall we will present the development of a compact CARS/SHG/TPF multimodal nonlinear microscope in combination with novel fiber laser sources for use in clinics [21]. The diagnostics potential of this compact multimodal microscope as compared to conventional histopathological images has been demonstrated for the examples of atherosclerosis and cancer [22-27].

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