Progress in Cell Identification Using Raman Spectroscopy in Combination with Optical Trapping and Microfluidics

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The progress of the research initiative "Jena Cell Identification Group" (JenZIG) is presented. Scope is the combination of Raman spectroscopy with optical trapping and microfluidic chips for cell identification and sorting. A model system consists of cells that can be found in peripheral blood of tumor patients. Lymphocytes and erythrocytes were extracted from blood samples. Breast carcinoma derived tumor cells (MCF-7, BT-20) and acute myeloid leukemia cells (OCI-AML3) were grown in cell cultures.

Three important technical innovations were reported towards Raman activated cell sorting[1]. First, a microfluidic chip made of quartz is introduced which integrates injection of single cells, trapping by laser fibers and sorting of cells. Second, a chip holder was designed to provide simple, accurate and stable adjustment of chips, microfluidic connections and the trapping laser fibers. The new setup enables to collect Raman spectra of single cells at 785 nm excitation with 10 seconds exposure time. Lastly, a new type of modeling the various background contributions is described, improving Raman-based cell identification by the classification algorithm linear discriminant analysis.

A Raman-on-chip device integrating detection fibers with fiber Bragg gratings was introduced for analysis of solutions and particles[2]. Such a compact all-fiber based setup enables to collect Raman spectra without microscopes or objectives. The limit of quantitation is 7.5 mM for urea and 2.5 mM for nicotine with linear Raman spectroscopy. This is an improvement of more than two orders of magnitude compared with previous fiber based microfluidic Raman detection schemes.

Wavelength modulated Raman spectroscopy has been applied to suppress fluorescence background in Raman spectra of single cells in aqueous buffer [3]. The laser excitation wavelength of 785 nm was modulated with a frequency of 40 mHz by 0.6 nm. The classification behavior of wavelength modulated Raman spectra was studied in comparison to a common background correction method in chemometrics. The stability of the classification was tested by performing training and validation 200 times with randomly selected data sets. The results are displayed in box whisker plots. Cell identification based on wavelength modulated Raman spectra gives similar classification rates than classical and averaged Raman spectra with a tendency of reduced accuracies and increased modeling variations.

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