Cell identification based on Raman spectroscopy in combination with optical trapping

C. Krafft[1], M. Hedegaard[2], U. Neugebauer[1], S. Dochow[1], J. Popp[1,3]

1. Institute of Photonic Technology, Jena, Germany
2. Institute of Sensors, Signals and Electrotechnics (SENSE), Technical Faculty University of Southern Denmark, Odense, Denmark
3. Institute of Physical Chemistry, University Jena, Jena, Germany

Raman spectroscopy is well known for its prospects in biomedical applications. The advantages to identify single cells include that vibrational spectroscopy provides a sensitive fingerprint of their biochemical composition and molecular structure, the method is label-free and non-destructive. So far Raman spectroscopy was coupled with microscopes to study subcellular features. Within the research initiative “Jena Cell Identification Group” (JenZIG) this method is combined with optical micromanipulation to exploit it as an innovative tool for cell sorting. The first step is to develop algorithms to distinguish single cells. The second step is to adapt optical traps and microfluidic devices for use with Raman spectrometers. The third step is to combine both approaches. The presentation gives an overview to discriminate highly similar cancer cell lines, to differentiate cells from peripheral blood and to collect Raman spectra from single cells in capillaries trapped by optical tweezers.

A first example of cell identification is to distinguish the two highly similar cancer cell lines M-4A4 and NM-2C5 originating from the parent cell line MDA-MB-435. Both cell lines show equal tumorigenity. But M-4A4 cells establish easily detectable metastases whereas NM-2C5 cells disseminated to distal organs, remained dormant and did not establish metastases. Partial-least-squares discriminant analysis (PLS-DA) was used for classification. The Raman spectra of both classes reveal differences in unsaturated fatty acids.

A second example is the identification of different cells that can be found in peripheral blood. Breast carcinoma derived tumor cells (MCF-7, BT-474) and lymphoblasts (OCI) were grown in cell culture. Leukozytes were isolated from healthy donors. Differentiation of these cells could be achieved by a combination of multivariate algorithms including principal component analysis and support vector machines.

Optical traps and optical stretchers have been integrated in microfluidic devices to sort cells according to biophysical properties like elasticity [1]. However, most microfluidic chips are made of materials such as PMMA or glass which are not compatible with Raman spectroscopy using 785 nm excitation lasers. Quartz capillaries have recently been used to collect Raman spectra of trapped cells [2].

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