# Raman- Opto-Fluidics for high resolution cell imaging

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Microfluidics devices are usually fabricated from materials such as glass or organic polymers. The use of these materials significantly lowers the quality of Raman images due to the strong contribution of Raman scattering and/or fluorescence emission from these materials to the spectra. This dramatically lowers the signal-to-noise ratio of the Raman signal from objects in the microfluidics device. Some desirable design aspects compromise further the quality of Raman optical signals, such as 1) small channel height and 2) small overall height of the device, and 3) the ability to prepare a tight seal between an optical window thickness and the device, together with 4) the implementation of high NA objectives for confocal Raman microscopy.

We present our new developments in integration of microfluidic devices and Raman spectroscopy for high resolution Raman imaging inside a microfluidic channel without (surface) enhancement of the signal or labeling. High resolution Raman images of individual cells are shown to exemplify the quality of imaging in Raman- Opto- Fluidics (Figure 1).

The microfluidic chip has been made from polydimethylsiloxane (PDMS) and the channels were successfully sealed with calcium fluoride or quartz windows. Raman z-scans were acquired through the chip to determine the optical signal contribution of each component of the chip at any height. The z- scan was performed also with cells in the channel. The results show that the contributions of material components of the microfluidic device is sufficiently low to obtain high signal to noise ratio Raman spectra of cells. The Raman images of cells were acquired in raster scan with a step size of 270 nm in less than 7 minutes. The Raman spectra, for instance obtained with multivariate analysis of the Raman datasets, present aspects of the chemical composition of voxels in the cell. Moreover, Raman images of different confocal planes in the cell, every 2µm along the z–direction, were acquired to show 3D images of the chemical distribution in the cell.

This new development in dedicated engineering of Raman-Opto-Fluidics is promising for time-lapse high resolution imaging of dynamic changes in cells.

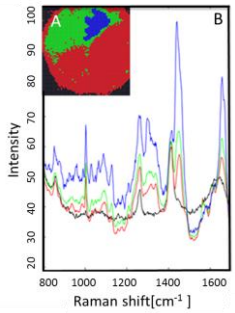


*Figure 1. (A) 4 cluster image of a cell in microfluidic. The image size of 15µm X 15µm was acquired with the a step size of 270 nm, time 0.1 second per pixel and a laser power of 35 mW, (B) Color coded Raman cluster spectra in correspondence with colors in the image.*