# *TERS for label free cell diagnostic*

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In order to investigate cell-cell interactions or interactions between drugs and cell surfaces, information on the cell membrane composition is essential. It is known that cell surface glycoproteins are acting as cell specific identifiers for cell-cell interactions. Those macromolecules are often important integral membrane proteins, where they play a role as a receptor for active ingredients and second messengers.

A common method to identify membrane proteins is antibody labeling. Depending on the nature of the markers it is possible to use fluorescence or Raman spectroscopy as an analytical method. Especially silver and gold-labeled antibodies turned out to be very interesting as they can be used to increase the sensitivity of Raman labels via a plasmon enhancement[1]. However, the lateral resolution capability with respect to the location of specific protein arrangements of this method is limited. A limitation of labeling with antibodies is the selectivity of the marker. Different and specific markers must be chosen for each protein of interest.

To provide spectroscopic information with high spatial resolution tip-enhanced Raman scattering (TERS) was chosen[2]. The combination of an atomic force microscope (AFM) with a Raman microscope simultaneously provides information on the topography and the molecular structure of a sample with high sensitivity.

We present TERS measurements on colon cancer cells (cell line HT29, fixed with 2% formaldehyd) and demonstrate the distinction of different membrane proteins. In particular, an area of 90x90 nm was analyzed. Within this area spectra were recorded on a square grid with a spacing of 10 nm. The TER spectra were processed using multivariate data analysis like principle component analysis and cluster analysis.

Based on the clustering, a band assignment of the mean spectrum of each cluster was done. As expected all the TERS bands can be attributed to proteins or lipids, the known components of the cell membrane. By correlating the band assignment and the cluster analysis the location of distinct cell membrane components can be shown.

We demonstrate that he combination of high lateral resolution and specificity of TERS potentially allows a direct characterization of single membrane proteins.

**References:**

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