Intracellular applications of surface-enhanced Raman scattering

J. Kneipp[1,2], H. Kneipp[2], M. McLaughlin[3], D. Brown[3], B. Wittig[4] and K. Kneipp[2]

[1] Federal Institute for Materials Research and Testing, I.42, janina.kneipp@bam.de
[2] Wellman Center for Photomedicine, MGH /Harvard Medical School, WEL-224, 55 Fruit Street, Boston, MA 02114, USA
[3] Renal Unit, Massachusetts General Hospital, Harvard Medical School, Boston, MA 02114, USA
[4] Institute for Molecular Biology and BioInformatics, Charité, Arnimallee 22, 14195 Berlin

Raman spectroscopy delivers a high content of molecular structural information from cultured cells. However, Raman studies using laser powers low enough for living cells to withstand usually require accumulation times on the order of minutes or even longer, which prevents observation of a number of cellular processes that take place on a faster time scale. Surface enhanced Raman scattering (SERS) provides a means to overcome this problem. We have shown that SERS enables the collection of excellent signal-to-noise Raman spectra in very short times (≤1 sec per spectrum) and low laser power (≤2 mW/1 µm spot) at selected positions in individual living cells [1]. The SERS effect has its origin in the favourable optical properties of metal nanostructures, and benefits from the enhanced local optical fields in their proximity. As these local fields are highly confined, we obtain strong and specific spectroscopic SERS signatures from the molecules contained in nanometer-scaled volumes. In the reported experiments, SERS signatures were measured from single living cells at different times after the uptake of gold nanoparticles. They were indicative of molecular changes in the environment of the nanostructures over time. The increase of the SERS signal strength and parallel TEM studies indicate the formation of nanoaggregates providing optimum SERS enhancement for ultrasensitive probing inside the endosomal compartment [2]. The endosomal compartment of many cell types is characterized by a so-called maturation process, which is accompanied by a drastic decrease in pH. We have constructed an optical, SERS-based pH nanosensor consisting of 4-mercaptobenzoic acid on gold nanoaggregates and demonstrate spatially resolved probing and imaging of pH inside the endosomal compartment of live cells [3]. Since the sensor infers information from pairs of spectrally narrow Raman bands in the same spectrum, quantitative measurements are possible without corrections regarding cellular background absorption and emission signals.

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