Dynamic SERS imaging of intracellular molecules

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1. Introduction

Surface-enhanced Raman scattering (SERS) spectroscopy has been attracting researcher for the capability of detecting and analyzing samples with high sensitivity. However, since the enhancement factor and SERS spectra are highly sensitive to the local environment in the sample, SERS spectroscopy typically requires the temporal or spatial averaging of SERS spectra to obtain data for reproducible and quantitative measurement. This sometimes hinders the benefit of the high sensitivity of SERS spectroscopy in applications that require microscopic observation. To tackle this issue, we developed a technique of dynamic SERS imaging, with which SERS spectra are obtained with high temporal and spatial resolution. We expected that the temporally and spatially resolved measurements help us to extract the information from the complicated behavior of SERS spectra. We have developed two types of SERS imaging technique with laser tracking [1-3] and line-illumination [3,4] and applied the technique to measure intracellular molecules in living cells.

2. Dynamic SERS imaging with laser tracking

We introduced gold nanoparticles into living HeLa cells to enhance Raman scattering from the intracellular molecules. Light from a Ti:Sapphire laser oscillating at 667 nm was focused into one of the nanoparticles in the cells to induce SERS. The position of the nanoparticle was monitored by dark-filed microscopy continuously so that the excitation laser keeps irradiating the same nanoparticle that moved in the cell. The position of the nanoparticles and SERS spectra from the nanoparticle was simultaneously recorded to analyze the temporal and spatial behavior of SERS spectra form the cell. Fig. 1 shows the result of SERS intensity map obtained by the measurement of a gold nanoparticle in the cell with a temporal resolution of 250 ms. The position of the nanoparticle moved in the cell by the intracellular transportation function and the intensity of the Raman peaks were plotted at the positions where the spectra were detected. The SERS map shows the clear dependence of SERS spectra on the intracellular environment in the cell.

3. Dynamic SERS imaging with line illumination

In order to track the chemical change in different positions in a living cell, we have utilized line-illumination Raman microscopy. A sample was irradiated by a line-shaped focus with which SERS spectra from different points in a sample can be measured simultaneously. Repeating SERS measurement with scanning the line illumination to the direction vertical to the line provides a 2D map of SERS spectra from the sample. Fig.2 shows a frame from time-lapse SERS imaging of a living HeLa cell. The 2D map was measured in 2 s and the individual SERS spectrum provides the chemical information in the local positions. We applied this technique to monitor the drug intake into living cells.

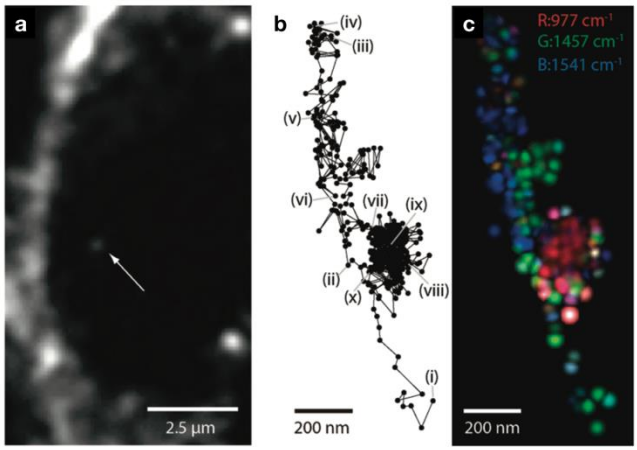

Fig.1 a) a dark-field image of a gold nanoparticle (ø:50nm) in a living HeLa cell. b) a trajectory of nanoparticle movement. c) a SERS map obtained by plotting SERS intensities at the positions where they are detected.

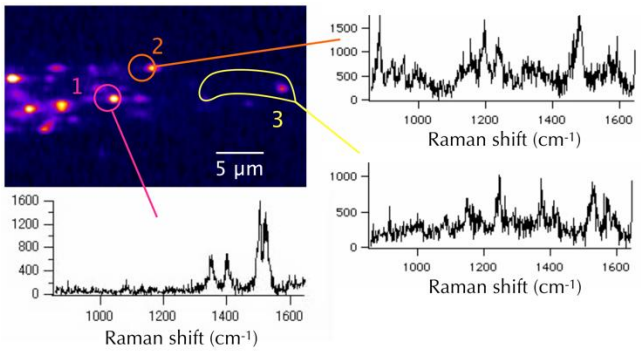

Fig.2 A frame from time-lapse SERS imaging of a HeLa cell with gold nanoparticles (ø:50nm). The image was reconstructed with the average intensity of Raman spectrum between 900-1600 cm^{-1}.

Reference

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[4] Fujita et al., J. Boomed. Opt., **14**, 024038 (2009).
[5] Palonpon et al., Nat. Protoc., **4**, 677 (2013).