Development of tip-enhanced single beam coherent anti-stokes Raman scattering microscopy

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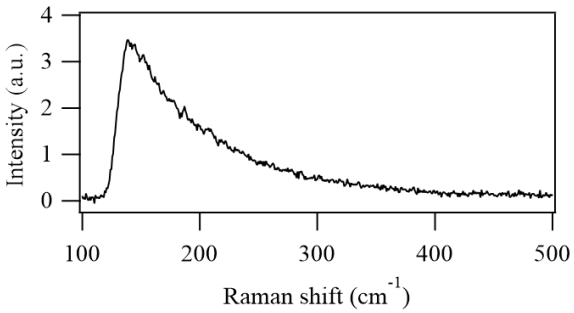
Coherent anti-stokes Raman scattering (CARS) provides rich spectroscopic information on label-free microscopic molecular imaging [1]. Recently, several progress has been reported on CARS microscopy using heterodyne detection [2], Fourier-transform technique [3], multiplex excitation [4] *etc.*, which have achieved significant improvement of data-acquisition time compared with spontaneous Raman microscopy. Especially, single beam multiplex CARS have advantages of measuring low wavenumber and of simple optical system [5]. However, in general, the spatial resolution of CARS microscopy is ~μm limited by the diffraction of light which prevent to study spatial information of molecular species.

Tip-enhanced Raman spectroscopy (TERS), utilizing plasmon-enhanced near-field, enables nano-scale optical imaging beyond the diffraction limit [6]. In this study, we developed a new Raman microscope combining TERS and the single beam multiplex CARS to achieve sensitive, stable and low wavenumber CARS for molecular imaging.

In experiments, we used a mode-locked Ti:S laser with the center wavelength of 800 nm, the spectral width of 50 nm. The beam passed through a narrow band notch filter of $\Delta\lambda$ = 0.4 nm at 785 nm to make a spectral dip on the beam. The beam was focused on samples with an objective of NA = 0.45. The signal was collected by the same objective (epi-detection) and measured by a CCD camera equipped with a spectrometer.

Figure 1 shows a raw spectrum of non-linear signal from doxorubicin, which includes resonant CARS signal and non-resonant background. We succeeded measuring low-frequency CARS signal ranging from 140 cm^{-1} to 400 cm^{-1}. Detailed results of far-field and tip-enhanced CARS will be discussed the conference day.



A raw CARS spectrum from doxorubicin with 1 s exposure.

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