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Broadband stimulated Raman scattering microscopy

Stimulated Raman scattering (SRS) microscopy is a powerful nonlinear optical technique for chemical identification of (bio)-molecules based on their intrinsic vibrational spectrum, which allows high-speed label-free imaging of cells and tissues. It is based on the combination of two narrowband laser pulses, the pump and the Stokes, whose frequency difference matches a vibrational frequency, and the measurement of the Stokes beam amplification (stimulated Raman gain, SRG). Single-frequency SRS microscopy allows the detection of molecules with a specific Raman response but is not sufficient to distinguish different components within complex heterogeneous systems in which chemical species display spectrally overlapped resonances. For this reason, there is ongoing research aimed at extending SRS to broadband detection, combining the speed of coherent Raman spectroscopy with the information content of spontaneous Raman [1]. Broadband SRS is however technically challenging, as it requires simultaneous detection of the tiny SRG signal at multiple wavelengths simultaneously. In this talk we present a broadband SRS system specifically designed for deployment in a biomedical environment, for both research and clinical applications. The system starts with an intrinsically synchronized all-fiber laser, generating a narrowband pump and a broadband Stokes, with frequency detuning covering the CH stretching region (2800-3100 cm^{-1}). A home-built high-frequency multichannel lock-in amplifier is then used to simultaneously measure the SRS signal over 38 frequencies simultaneously [2], covering the CH stretching band with 10-20 µs pixel dwell time and allowing for detailed, high spatial resolution mapping of spectrally congested samples [5]. We demonstrate the performance of our SRS microscope by high-speed, label-free, non-destructive imaging of senescent cancer cells and liver tissues of mice subject to non-alcoholic steatohepathitis (NASH, Figure 1).

References

[1] Polli, D. *et al.*, Laser Photonics Rev. (2018); 12, 1800020.
[2] De la Cadena, A. *et al.*, APL Photonics (2022); 7, 076104.

Figures

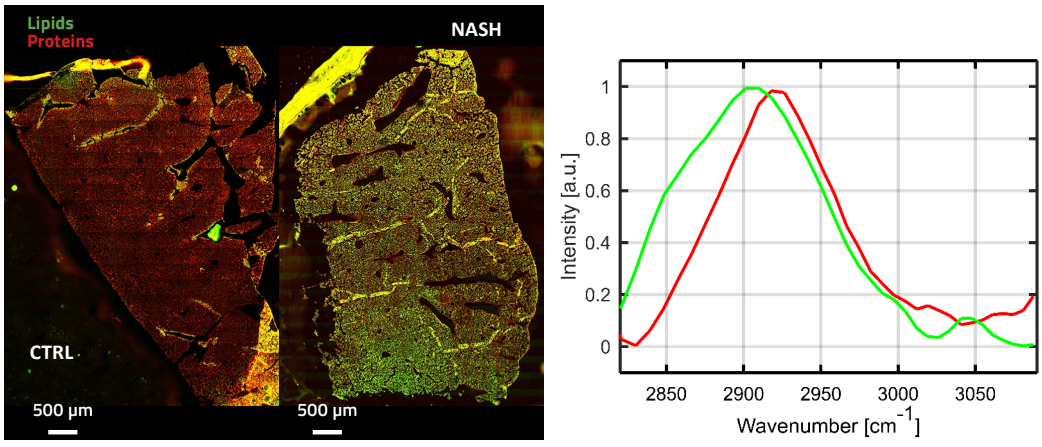

Figure 1: Left panel: SRS images of tissue samples from the liver of a mouse affected by the NASH disease (right) as compared to a control sample (left). Pixel dwell time: 20 µs. Right panel: SRS spectra of lipids (green) and proteins (red).