BROADBAND STIMULATED RAMAN SCATTERING MICROSCOPY FOR BIOMEDICAL APPLICATIONS: A MULTI-CHANNEL LOCK-IN APPROACH

Alejandro De la Cadena[a*], Federico Vernuccio[a], Andrea Ragni[b], Giuseppe Sciortino[b], Renzo Vanna[a], Carlo M. Valensise [a], Marco Sampietro[b], Giorgio Ferrari[b], Giulio Cerullo[a] and Dario Polli[a▪]

[a]IFN-CNR and Physics Department, Politecnico di Milano, P.zza L. da Vinci 32, 20133 Milano (Italy)

[b]Dipartimento di Elettronica, Informazione e Bioingegneria, Politecnico di Milano, P.zza L. da Vinci 32, 20133 Milano (Italy)

*alejandro.delacadena@polimi.it

▪dario.polli@polimi.it

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Stimulated Raman scattering (SRS) microscopy is a powerful non-linear optical technique for label-free identification of biochemical components in cells and tissues. The archetypical SRS microscope delivers images with inherent chemical contrast, as it is sensitive to the molecular vibrations of the scrutinized specimen. Narrowband SRS microscopy is nowadays a well-established imaging technique with high acquisition speed. However, it cannot simultaneously image multiple biomolecules of a complex heterogeneous material, e.g., a biological system, due to its single-frequency operation. To tackle this, we developed a broadband SRS microscope [1] equipped with a home-built differential multichannel lock-in detection board [2]. Our system can record modulation transfers as low as 10 parts per million with an integration time of 40 µs, delivering, in a single shot, SRS spectra with 32 vibrational frequencies. We will discuss the elements of the system as well as its characterization, showing imaging applications of different heterogeneous systems. In particular, we will show how the microscope is capable of distinguishing oleic and palmitic fatty acids in hepatic cells and discern fibrosarcoma tumour from healthy tissue in a mouse model (see Figure 1).

[1] A. De la Cadena, C. M. Valensise, M. Marangoni, G. Cerullo and D. Polli, "Broadband stimulated Raman scattering microscopy with wavelength- scanning detection", *J. Raman Spectrosc.* 51, 1951-1959 (2020)

[2] G. Sciortino *et al.*, "Four-Channel Differential Lock-in Amplifiers With Autobalancing Network for Stimulated Raman Spectroscopy", *IEEE J. Solid-State Circuits* (in press, 2021). doi:10.1109/JSSC.2020.3046484

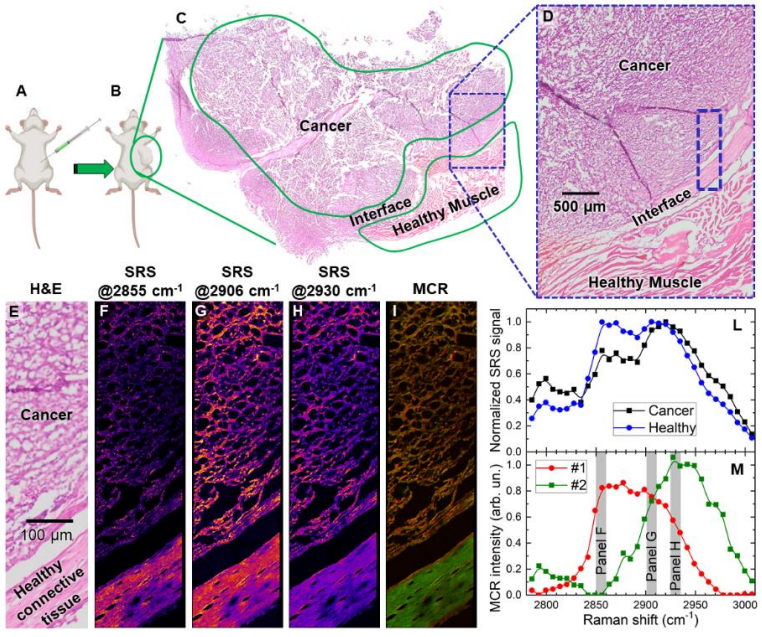

Figure 1: Chemical imaging of mouse fibrosarcoma. (C-E) H&E staining (gold standard). (F-H) SRS imaging at various Raman frequencies. Mean spectra from healthy (blue) and cancerous (black) regions (L), concentration map (I) and spectra (M) retrieved with multivariate curve resolution alternating least squares (MCR-ALS) analysis.