Graphene-enabled stimulated Raman microscope for oncology

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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 [1]. However, despite its promise as a disruptive label-free imaging and diagnostic tool, SRS microscopy still suffers from several limitations, which prevent its massive uptake in the biomedical arena and confine it to applications in specialized optics laboratories. The laser sources required for generation of the synchronized pump/Stokes pulses are exceedingly complex, bulky and expensive. Furthermore, SRS microscopes typically work at one or a few vibrational frequencies, providing limited biochemical information. In this work, exploiting the unique optical properties of graphene and other 2D materials [2], we drastically simplify the architecture of the laser system used for SRS microscopy, reducing its footprint and cost and enhancing its reliability. Furthermore, we implement broadband SRS microscopy [3], measuring the SRS signal over a wide spectrum of frequencies simultaneously and thus combining the molecular information of spontaneous Raman microscopy with the imaging speed of a coherent process. Our broadband SRS microscope has the following unique characteristics, which cannot be found in any other commercial instrument: i) label-free imaging; ii) living cell imaging; iii) high (μs pixel dwell time) acquisition speed, enabling the observation of cellular dynamics by time-lapse imaging or fast scanning of human biopsies. All this is achieved in a compact, low-cost, hands-free product design. Our broadband SRS microscope thus combines information on the morphology and on the biomolecular composition of cells, without altering their natural state with exogenous molecules or invasive interventions. As such, it is expected to revolutionize the study of the cellular origin of diseases and of cancer immunotherapy. Furthermore, our microscope allows high resolution, high speed measurement of the vibrational spectra of large areas of unstained tissue samples, providing at the same time morphological and biomolecular data and allowing label-free histopathology and accurate tumour diagnosis (Figure 1).

References

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[2] D. Brida *et al.* Nat. Commun. **4**, 1 (2013).
[3] D. Polli *et al.* Laser Photonics Rev. **12**, 1800020 (2018).

Figures

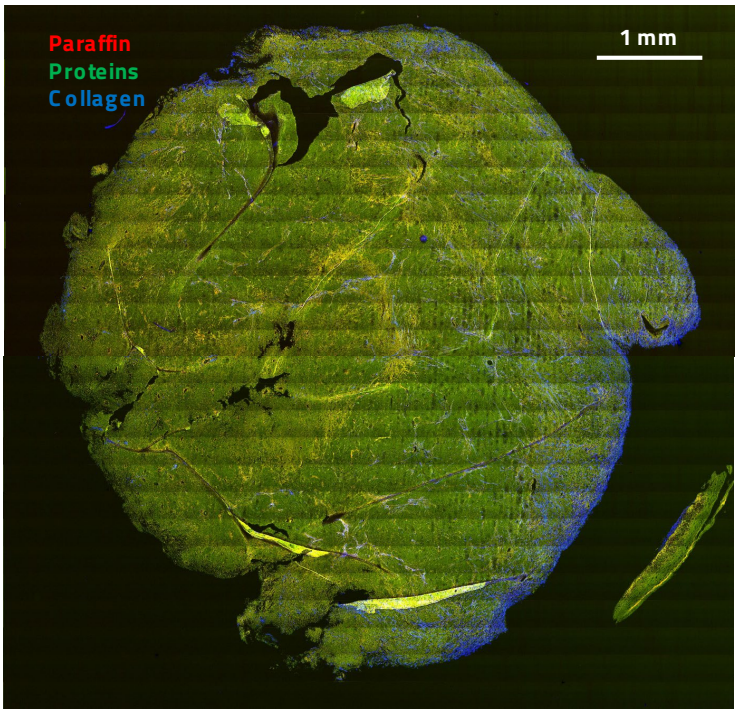

Figure 1: SRS image of a 10-μm-thick human tumor tissue sample (size: 6650 x 6910 μm) following formalin fixing/paraffin embedding and dewaxing.