

TOWARDS HIGH-THROUGHPUT ALL-OPTICAL BIOMECHANICAL IMAGING VIA BRILLOUIN SCATTERING MICROSCOPY

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Biomechanical properties of cells have been identified as important biomarkers in many biological processes, but traditional techniques to probe them result to be invasive and limited to experimental settings with physical access to the cell.

Confocal Brillouin microscopy has recently emerged as an all-optical, contact- and label-free technique for *in vivo* 3D subcellular mapping of elasticity distribution within cells and tissues, even in settings where physical contact is not possible [1,2]. Current Brillouin technology relies on the spontaneous Brillouin scattering phenomenon, in which photons are inelastically scattered by the acoustic phonons intrinsically propagating in the material, thus acquiring a characteristic frequency shift which can be linked to the local elastic modulus.

Being an extremely weak process, spectrometers with high contrast and resolution are required in order to extract and analyze the Brillouin peaks (typically in the GHz range) from the scattering spectrum, which is dominated by the elastic peak. This translates into long acquisition times which may result incompatible with many bioimaging applications. A two-stage cross-axis VIPA (Virtual Imaged Phased Array) spectrometer was introduced to speed up the acquisition down to 50-100 ms per spectrum, thus allowing *in situ* characterization of biological samples [1]. Moreover, a parallel detection configuration where the Brillouin shift of hundreds of points in a line is measured simultaneously showed the potential to shorten the acquisition time of 2D Brillouin images from hours to ~30 seconds [3].

Here, an additional approach to improve the performances of Brillouin spectroscopy, based on the stimulated version of the Brillouin scattering process, will be investigated. In stimulated Brillouin scattering (SBS) the probed acoustic wave is amplified by the interaction of two counterpropagating laser beams, a pump and a probe, whose frequency difference equals the acoustic one. As a result, the inelastic scattered signal experiences an exponential increase which can be detected as a gain in the probe transmission and extracted employing a fast intensity modulation of the pump and an ultrafast lock-in demodulation of the transmitted probe. Thus, the Brillouin peak can be localized by scanning the probe frequency, without inserting any spectral dispersive element [4].

Here, the main limiting factors and new optimization strategies for SBS will be discussed. Due to the nature of the process and the employed signal read-out scheme, shot-noise-limited Brillouin spectra are expected to be acquired ~1000 time faster than with the spontaneous approach, paving the way for a high-throughput platform for mechanical signature assessment.

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