

Electro-Optic Modulator-Enabled Long-Term Stability in Brillouin Microscopy for Cellular Mechanics

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Brillouin Microscopy (BM) is a label-free optical technique for non-invasive, contactless measurement of mechanical properties at sub-micron scales. However, its application to cellular samples—where Brillouin shifts are subtle (e.g., ~150 MHz between nucleoli and cytoplasm)—is limited by long-term spectrometer frequency precision. We address this challenge by integrating an Electro-Optic Modulator (EOM) for real-time calibration and drift compensation. The EOM enables: (i) high-precision, sample-free spectrometer calibration, (ii) in-situ reference generation, and (iii) closed-loop feedback to correct laser frequency drifts. This system achieves stable, automated operation for >48 hours without realignment, with unprecedented precision (5 MHz in shift, 9 MHz in width at 532 nm). We demonstrate the technique's biological relevance by distinguishing solid-like pathological aggregates, which are associated with amyotrophic lateral sclerosis (ALS) from liquid-like physiological structures *in vivo*.

Short Bio:



Li Zhang received her PhD degree in Photonics from *École Polytechnique Fédérale de Lausanne*, Switzerland in 2020. She continued to work in the Group of Fiber Optics (GFO) as a postdoc until 2023. During her stay in GFO, her study was focused on distributed fiber sensing based on Rayleigh and Brillouin scattering. Since 2023, Dr. Li Zhang has been working as a postdoc in the *Center for Life Nano- & Neuro-Science* in *Istituto Italiano di Tecnologia*, Rome, Italy. Her current research interest is on the advancement of the implementation and application of Brillouin microscopy.