Dynamic Light Scattering Microrheology for Soft and Living Materials

Pamela C. Cai,[a] Brad A. Krajina,[a] Michael J. Kratochvil,[bc] Lei Zou,[d] Audrey Zhu,[a] Elizabeth B. Burgener,[e] Paul L. Bollyky,[c] Carlos E. Milla,[e] Matthew J. Webber,[d] Andrew J. Spakowitz,[abfg] and Sarah Heilshorn.[b]

[a] Department of Chemical Engineering, Stanford University

[b] Department of Materials Science and Engineering, Stanford University

[c] Stanford Immunology, Stanford University

[d] Department of Chemical & Biomolecular Engineering, University of Notre Dame

[e] Center for Excellence in Pulmonary Biology, Department of Pediatrics, Stanford University

[f] Department of Applied Physics, Stanford University

[g] Biophysics Program, Stanford University.

Statement of Purpose: Using biomaterials to study biophysical factors that regulate cellular behavior requires the development of techniques that can quantify biophysical observations occurring in cellular environments. Many of the current techniques that can quantify biophysical forces and changes are invasive or work on such large scales as to be impractical for many precious biological materials. Here we present the development of a microrheology method to characterize the mechanical properties of biological materials, both those with and without living cells, that is noninvasive for time-lapse measurements and requires only small volumes (~12µL) of sample.

Materials and Methods: Polystyrene microparticles of varying sizes (500nm to 2µm in diameter) were used as probe particles during dynamic light scattering (**DLS**) experiments. DLS was performed using a Malvern Zetasizer Nano ZS instrument. The samples probed here to demonstrate the broad range of biophysical characterization that Dynamic Light Scattering Microrheology (**DLSµR**) is capable of include: cystic fibrosis sputum (obtained from patients at the Stanford Cystic Fibrosis Clinic), MCF10A breast cancer cells encapsulated in rat tail collagen I, PEG-based gels formed via Diels-Alder chemistry, and hyaluronic acid-based polymer networks chemically modified with cucurbit[7]uril guest-host chemistries. The technique presented, DLSµR, begins by embedding tracer particles at a concentration of 0.1 wt% into the fluid to be measured. Next, DLS is performed on the sample. The scattering correlation from the DLS instrument is extracted, and the mean-squared displacement of the tracer particles is derived using our custom Python script. Lastly, the mean-squared displacement of the particles is used to derive the rheological behavior of the measured fluid with the generalized Stokes-Einstein equation. This method is described visually in Figure 1.

Results: We present a method that leverages DLS to probe the physical properties of biomaterials in a non-invasive manner, capturing dynamics in the materials from very short to very long lengthscales and timescales. DLSµR only requires a small sample volume of 12 µL to measure up to six decades in time of rheological behavior from 10 Hz to 10^6 Hz and can be used to study a variety of soft materials with stiffnesses in the range of 10^{-1} to 10^4 Pa, including dilute polymer solutions, covalently-crosslinked polymer gels, and active, biological fluids. Compared to other microrheology techniques, this method requires less sample volume, can measure a higher range of stiffnesses, does not require samples to be transparent, and involves more easily implementable technology. We detail the steps for applying DLSµR and demonstrate how it can be used not just to characterize biopolymeric materials, but also how it can reveal biophysics in complex biologically relevant systems: breast cancer cells encapsulated in collagen and cystic fibrosis sputum.

Conclusions: Overall, we show that DLSµR is an easy, efficient, and economical rheological technique that can guide the design of new biomaterials and facilitate the understanding of the underlying biophysical cues present within cellular microenvironments.

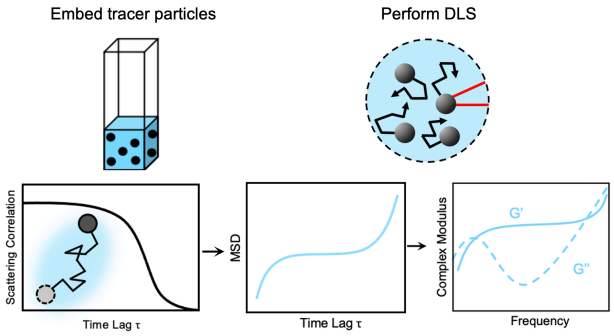

Figure 1. Visual description of Dynamic Light Scattering Microrheology (DLSµR) workflow.

References:
(Krajina BA. ACS Cent. Sci. 2017;3:1294-1303.)
(Cai PC. Soft Matter. 2021;17:1929-1939.)