PASSIVE AND ACTIVE MICRORHEOLOGY OF CELLULAR MICROENVIRONMENTS

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Microrheology is an extension of conventional bulk rheology, as it probes a medium of interest at a microscopic level, revealing the local mechanical properties and microstructure. Microrheological techniques have been increasingly used to investigate biological systems, for their advantages over conventional bulk rheology, such as the ability to perform targeted measurements, small sample requirement, non-invasiveness, and a wide frequency range. Video particle tracking microrheology is a passive technique that can also assess spatiotemporal information of local microenvironments and describe the heterogeneity of structured complex fluids. However, passive techniques are limited to very soft materials. Active techniques, such as optical tweezers, manipulate probe particles by the external optical force. This manipulation allows active methods to probe materials with higher mechanical properties and a wider frequency range. Here, video particle tracking and optical tweezers are integrated with other techniques, such as confocal imaging, bulk rheology, and RNA sequencing, to characterize the mechanical development of biological systems. The microenvironments investigated here include bacterial biofilms, pancreatic acinar to ductal metaplasia (ADM), and pancreatic ductal adenocarcinoma (PDAC) models. In the passive microrheological investigation of delicate early-stage *Pseudomonas aeruginosa* (PA) and *Staphylococcus aureus* (SA) biofilms, it is observed that cultures initially seeded with equal populations of each species have the most development over the course of 24 hours. In the pancreas, ADM has been identified as the precursor of pancreatic ductal adenocarcinoma (PDAC). Our evaluations of mouse models using video particle tracking showed that ADM is accompanied by extracellular matrix (ECM) stiffening; however, the stiffening can be reduced by histone deacetylase inhibitors and histone methyltransferase inhibitors. Lastly, PDAC is characterized by dense stroma enriched with ECM. Optical tweezers are employed here to investigate the ECM remodeling by PDAC.