Viscoelastic characterization of chondrocytes with a 3D-printed variable-height fluidic device

Doctoral Defense

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Mechanical characterization of cells supports advancements in tissue engineering, drug development, and diagnostics, making it an essential tool in basic research and clinical applications. Conventional methods, such as atomic force microscopy (AFM) and micropipette aspiration (MPA), are currently limited by a low throughput of roughly 10 cells/h. To address this challenge, this work aims to develop a measurement platform with increased throughput to characterize chondrocyte cells responsible for maintaining the articular cartilage, which lines bones in joints and is associated with a prevalent disease, osteoarthritis (OA).

A 3D-printed variable-height fluidic channel was fabricated on a glass substrate to apply mechanical deformation to chondrocyte cells suspended in a buffer solution. Chondrocytes were compressed between two pieces of glass integrated into the 3D-printed fluidic channel and then recovered to their original shape after removing the applied strain. The cells' cytoplasm was fluorescently stained and imaged with confocal laser scanning microscopy (CLSM) during deformation and recovery. The projected area of chondrocytes was converted to linear strain and fit to a Burgers viscoelastic mechanical model. The viscoelastic recovery time of bovine chondrocytes was found to be 39 s with a std of 18 s, which was consistent with previously reported values from MPA and AFM measurements.

It has been shown that chondrocytes harvested from cartilage and grown in 2D monolayer cultures do not mimic the *in vivo* phenotype, preventing the translation of research to practical applications. The developed measurement platform was used to compare chondrocytes from the typical 2D monolayer cultures to a recently developed 3D alginate-encapsulation culture, which produces chondrocytes visually resembling the *in vivo* phenotype. Chondrocytes from monolayer and alginate cultures were distinct, with 31 s and 14 s recovery times, respectively, for bovine chondrocytes. This difference was also observed for primary OA chondrocytes, with a recovery time of 34 s and 12 s for monolayer and alginate cultures, respectively.

This work demonstrates a novel measurement platform capable of a throughput of 50 cells/h. Given this system's throughput scales with FOV, it shows great potential for the mechanical characterization of cells.

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