

MICROFLUIDIC CHIP DESIGNS FOR SHEAR AND EXTENSIONAL MANIPULATION OF ISOLATED BIOLOGICAL CELLS

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INTRODUCTION

In order to understand diseases such as osteoarthritis and the biomechanical factors which stimulate regenerative processes, a more complete knowledge of cellular biomechanics must be realized. The first steps toward this goal have been made with our development of an integrated micro-particle image velocimetry and optical tweezer (μ PIVOT) system for chondrocyte and osteoblast biomechanics. The integrated device quantifies multiaxial biomechanical properties from a single living cell. In order to enhance the capabilities of the μ PIVOT, a microfluidic chip was designed and fabricated for control of the local microenvironment. The microfluidic chip is a testbed tailored to facilitate mechanical test sequences including the shear and extensional manipulation of individual biological cells.

METHODS

Mechanical stresses will be applied either through direct laser manipulation from the dual OT or through fluid induced stresses from external flow fields. An apparent limiting factor in induced hydrodynamics stresses is the potential for overheating the cell due to an increase in laser power associated with trapping. A solution is to trap the cell at stagnation points within the flow (Figure 1) [1,2]. The cell experiences zero net force at a stagnation point/plane regardless of the magnitude of the shear or extension rate. In practice, the OT will be present to apply small restoring forces since the stagnation point represents a saddle point, unstable to perturbations in particle position. The first design iteration of our microfluidic chip included cross-junction channel geometry to create a stagnation point.

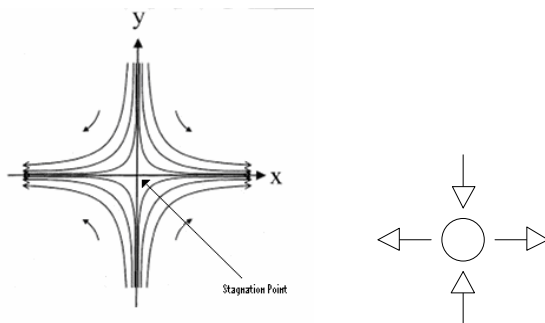


Figure 1: Left: Streamlines producing a stagnation point at the center of the cross junction. Right: Compressive and extensional forces on a biologic cell at a stagnation point.

Utilizing the OT and translation of the microscope stage, an individual cell may be retrieved from a culture reservoir and positioned in one of two testing regions (Figure 2). This procedure can be repeated to perform sequential measurements of cells in nearly identical conditions for statistical comparison of larger sample sizes.

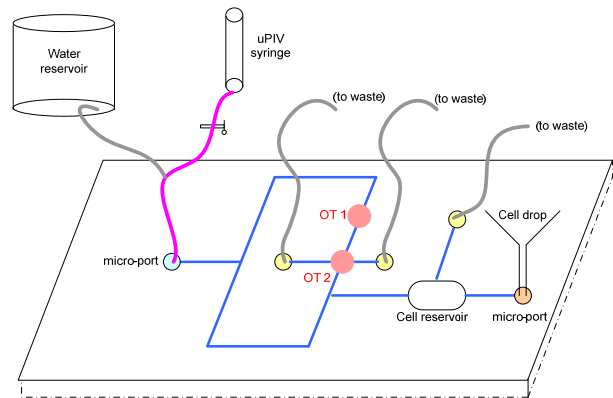


Figure 2: Schematic of the microfluidic chip. Nano-particles are inserted into the system via the gravity driven flow tube. Cells are positioned within the cell reservoir through capillary flow from the cell drop port. Two testing regions subject the cell to either shear forces (OT1) or extensional forces (OT2).

The microfluidic chip was fabricated from a master mold of a silicon substrate created using photolithography. Flexible polydimethylsiloxane (PDMS, Sylgard 184) was then cured over the master. The PDMS was peeled off of the mold, microport access holes were made, and the PDMS was bonded to a glass coverslip. Replica chips can then be fabricated using the master mold. Ongoing flow velocity fields are being characterized throughout the channels (2.4 mm/s flow application).

RESULTS AND DISCUSSION

The resulting microfluidic chip creates a microenvironment in which the same individual cell can be subjected to a wide range of dynamic and static mechanical stresses. These include variations in hydrostatic pressure, tensile, compressive, and torsional loading with a dual OT, imposing shear stresses by holding a cell in a flow with one OT, and/or imposing extensional stresses by holding a cell at a stagnation point. The applied fluid stresses will be calculated with μ PIV analysis while elastic and plastic deformations will be measured directly with high resolution images. Future work will modify the chip design allowing application of shear forces present in a stagnation plane separating two adjacent opposing flows while examining normal and pathologic cellular states.

REFERENCES

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ACKNOWLEDGMENTS

Support was provided by the NSF (MRI grant BES-0521637) and the Stanford Microfluidics Foundry.