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Emerging technologies in Single Cell Research

Numerical analysis of effective pressure on microfluidic aspiration of a single cell before constriction

Aldo Abarca-Ortega[1,2], Blanca González-Bermúdez[1], Miguel Corcoles Lucas[1], Gustavo R. Plaza[1]

1. Center for Biomedical Technology, Technical University of Madrid, Madrid, Spain ; 2. Departamento de Ingeniería Mecánica, Universidad de Santiago, Santiago, Chile

Introduction

The importance of measuring mechanical properties in cells its translated into two topics: movement and functionality or cell state. In terms of movement, there are studies that analyse differentiation, wound healing and division or cell migration. In terms of functionality, **mechanical properties have been linked to common human diseases**, such as cancer, asthma, malaria, cardiovascular disorders and lymphocyte activation, among others. Generally, if a cell group presents significantly high stiffness compared to a control group, it is because there are alterations in their biological behaviour, as happens with studies related to deformability and cancer.

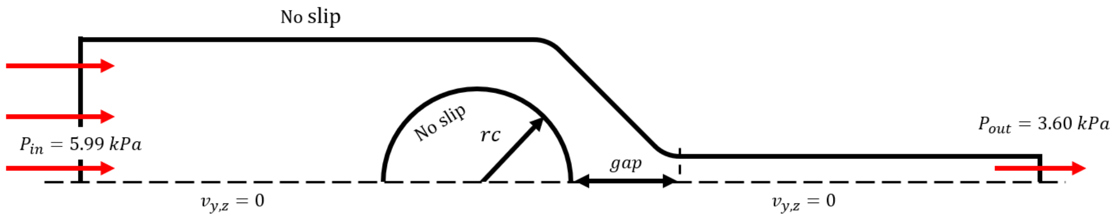
Several techniques exist to evaluate the cell behavior under mechanical stresses, mainly analyzing its stiffness and deformability, properties related to the internal structure and biomarkers. A commonly used procedure to test deformability of cells is to **study their flow through constrictions.** However, **no detailed stress analysis** has been performed on the cell during its deformation using numerical simulations for this case and is postulated could reduce the variability of results. High throughput devices, like Microfluidic devices, once manufactured and put into operation, do not require long training and the equipment is relatively cheap compared to others. **However several authors have reported great variability in the results of cell deformability and stiffness.**

In this study, and in consideration of the previous mentioned, it is proposed an **analysis of standardized pressures in a cell while it is being aspirated by a rectangular channel of a microfluidic device** through time using numerical CFD simulations and not considering viscoelastic effects that can make the mechanical behavior of the cell vary.

Materials and Methods

The objective of the study involves steady state flow, for which a totally implicit method (backward-Euler) is used for the development of the governing equations. On the other hand, the present problem is developed in a decoupled way, focusing on the pressure-velocity development of the fluid and leaving the structural analysis of the cell for a future work, so in each time step proposed, or distance traveled by the cell as it enters the duct, it is calculated independently from the previous one.

When each simulation is finished, the tensions, in the direction of flow, on each surface element of the cell will be analysed and multiplied by its area to obtain the complete force on the simulated geometry quarter, which will be divided by its transversal area, being equal to the nominal tension $\sigma_{nom} = F_{nom}/A$. This nominal stress will finally be divided by the difference of pressures applied as a boundary condition, a quotient that **indicates how much the pressure of the flow on the cell surface is manifested.**



Navier – Stokes Eq. $$\rho\left(\frac{\delta v}{\delta t} + v\cdot\nabla v\right) = -\nabla p + \mu\nabla^2 v + \rho g$$

$$\mu\nabla^2 v \gg v\cdot\nabla v$$

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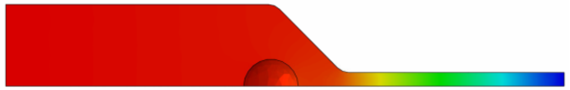
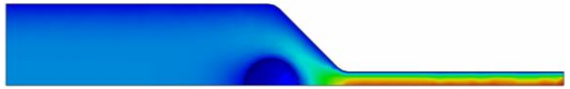
Results and discussion

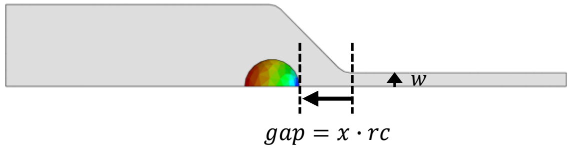
Flow pressure

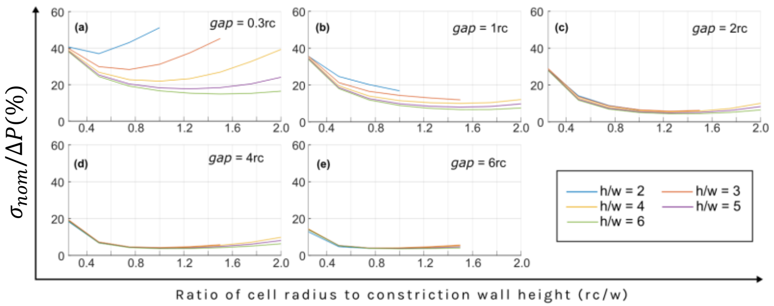


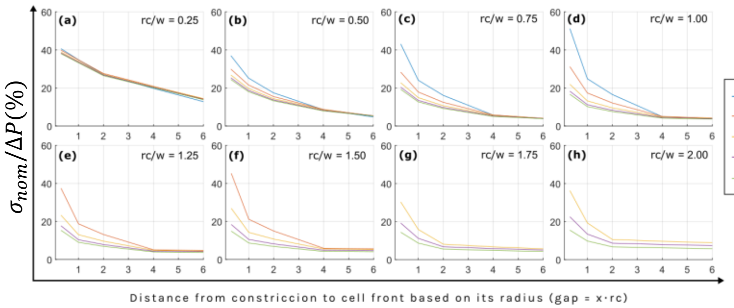
Flow velocity, magnitude

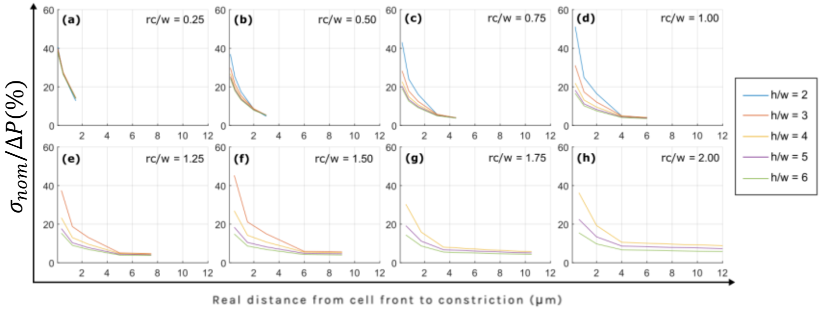


Tensile stress, magnitude









The analysis shows that the effective pressure increases inversely with the ratio of cell radius over width of the constriction, effect that is manifested when this is less than 1. **Just over half of the aspiration pressure is exerted on the cell effectively**, the rest of the pressure drop is mainly due to the movement of the fluid in the areas surrounding the cell in the rectangular cross section of the device, which will never be covered entirely by the cell as it happens in other techniques for measuring mechanical properties

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Conclussions

- The present work approaches the problem, of the **mechanical characterization of cells using a high performance microfluidic device**, utilizing numerical CFD simulations under different geometric configurations. Our model allows understanding the relationship between the deformation parameters and the deformability of the cell for a given aspiration pressure, which will be used in future analysis of deformability tests.
- The results indicate an increase in the effective pressure as it approaches the constriction. Pressure on the cell increases as the rc/w ratio is higher, that is, while it takes up more space in the duct. In all the cases studied, **the effective pressure is not much higher than 50%.**
- We need to obtain **new mathematical formulations** that consider the geometric configuration of both the device and the size of the cell under study.

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Upcoming work

- The response of the cell to the aspiration must be analyzed in conjunction with what happens with the fluid, which can be faced through a **numerical analysis of fluid-structure interaction in a coupled way**, which would allow to obtain representative curves of pressure applied in each instant even while contact between cell and device walls is produced, inducing deformation in the cell, constituting a model closer to the real physical problem.
- Currently, **hyperviscoelastic models** are being implemented in FSI simulation in order to measure the aspiration times in the device.
- We are working on an implementation for the automatic analysis of images obtained by microfluidics based on open source **artificial intelligence**. This will allow optimizing the analysis time as well as making it independent of the operator's abilities.