A FINITE ELEMENT STUDY OF MICROPIPETTE ASPIRATION OF SINGLE CELLS: EFFECT OF COMPRESSIBILITY

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SUMMARY

Micropipette aspiration (MA) technique has been widely used to measure the elastic and viscoelastic properties of different cell types. An analytical solution presented by Sato et al. [1] is usually employed to interpret these parameters from the aspiration test data. However, the intrinsic strain-hardening and large deformation behaviors are not incorporated into this analytical solution. Further, that solution and other models in the literature do not account for the cell compressibility and bulk relaxation behaviors. In the current work, the influence of different material parameters and specifically the compressibility on passive response of the cells during microaspiration were investigated.

Neo-Hookean and Arruda-Boyce viscohyperelastic (NHVH and ABVH) incompressible and compressible material models were used to simulate microaspiration of cells. In order to find optimum set of material constants, the models were fitted to the experimental data using a particle swarm optimization between MATLAB and ABAQUS based on MA experiment data on stem cells [2].

The incompressible NHVH model could not capture the early creep data points. A similar behavior was observed from the ABVH incompressible model. Instead, the compressible NHVH model with the Poisson's ratio of approximately 0.42 and bulk relaxation behavior was able to successfully mimic the experimental creep points.

It is suggested that cell compressibility and bulk relaxation behavior should to be considered in determination of viscoelastic properties of the cell from MA test. Considering the low permeability of the cell membrane and short duration of the MA experiment, the observed compressibility is not likely to be a result of fluid exudation from the cell. Further studies are required to investigate the underlying mechanism of the cell compressibility.

INTRODUCTION

The results from different experimental techniques used in the cell mechanics literature tend to vary greatly depending on the induced forces, time, and strain types and scales. Besides the heterogeneity of the cells and their active adaptation to environmental stimuli, the mechanical models used to interpret the results of different techniques also contribute to discrepancies between the outcomes of different techniques. Evaluating the capability of material models to mimic the cell behavior in different experimental conditions facilitates a better understanding of the mechanical behavior of cells and a convergence of the results between different techniques.

Micropipette aspiration (MA) technique has been widely used to measure the mechanical properties of different cell types. In this experiment, a cell is aspirated into a micropipette by exerting a negative pressure gradient, and the projection length of the cell inside the micropipette is recorded as a function of time. An analytical solution presented by Sato et al. [1] has been commonly employed to interpret the elastic and viscoelastic parameters of the cells from experimental data. In this model, the cell is assumed as an infinite, homogenous, incompressible half-space considering small strain tensors. The semi-infinite space assumption for the cell is only accurate when the cell to micropipette radii is considerably large. Further, in practice the cell undergoes very large strains and living cells exhibit a strain-hardening behaviour owing to the mechanical contributions of intracellular elements. Besides, the incompressible assumption for the cell should be scrutinized.

Zhou et al. [3] have studied the influence of cell-pipette geometries in MA test. In this study, we focused on the influence of different material parameters and specifically the compressibility on the deformation of a single cell during the microaspiration.

METHODS

The NHVH and ABVH material models were used to particularly account for the compressibility and hardening phenomenon under large strain. Specifically, compressibility was allowed in the models by a value of Poisson's ratio ($\nu < 0.5$). In the finite element (FE) model of the MA, axisymmetric geometries were created for the micropipette and cell. The cell was considered as a homogenous continuum discretized with four-node bilinear quadratic hybrid axisymmetric elements. ABAQUS 6.8.1 FEA package was used for pre and post-processings.

In order to find optimum sets of material constants, models were fitted to the experimental data using a particle swarm optimization between MATLAB and ABAQUS. The cost function was defined as a weighted sum of squared errors between the FE results and experimental data of MA of stem cells [2].

RESULTS AND DISCUSSION

A set of optimized material parameters for the compressible NHVH model, the incompressible NHVH model with optimized material parameters and the incompressible NHVH model with the material parameters obtained from the experiment [2] by using the Sato et al. [1] equation are shown in Table 1. The suggested Poisson's ratio (0.42) is interestingly close to the findings of previous studies on chondrocytes [4] and THP-1 cells [5]. With material parameters derived from the experiment by using the Sato et al. solution as inputs for NHVS FE model, results showed a significant divergence from the experimental curve (Figure 1). This mainly arises from strain-hardening, finite cell to pipette diameters and finite deformation that are not taken into account in the analytical solution. The optimized material parameters for an incompressible NHVS are in accordance with an equation provided by Zhou et al. [3]. However, the curve could not capture the early creep data points (Figure1). By permitting the compressibility and bulk relaxation behavior in the optimization procedure, the compressible NHVH model could capture the short-term as well as the equilibrium data points (Figure 1).

Consequently, it is suggested that the creep behavior of the cell can be attributed to both shear and bulk relaxation behaviors, the latter of which is absent in incompressible assumption of the continuum cell. By assuming the cell as an incompressible medium, there is only the shear behavior to enable the deformation of the cell and hence a lower value for this parameter is estimated. This also leads to a lower value for dimensionless shear modulus. Hence, the stiffness parameters (i.e. shear moduli) of the cell measured with the MA technique are expected to be lower compared to their equivalents from the AFM indentation tests where the effect of compressibility has been considered to be negligible [6].

Since the permeability of the cell membrane is assumed to be very low and given the short time span of MA test, fluid exudation is not likely the main contributor to the cell compressibility. Hence, another mechanism must be responsible for the compressibility of the cell.

CONCLUSIONS

It is suggested that compressibility and bulk relaxation behavior are two important factors in the deformation behavior of cells in MA technique that should be considered to obtain more realistic mechanical parameters of cells.

More sophisticated numerical models are required to study the effect of fluid and evaluating the contribution of intracellular elements in cell deformation behavior, and thus to get deeper insight into the observed bulk relaxation and compressibility in MA.

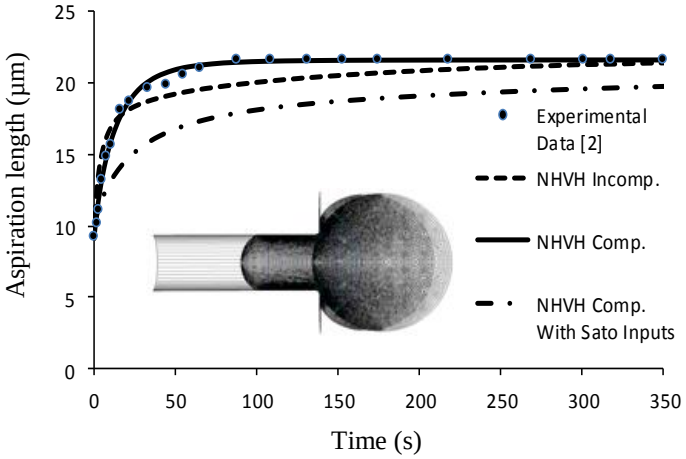

Figure 1: Comparison between optimized incompressible and compressible NHVH, as well as NHVH with inputs from the MA experiment [2] interpreted by Sato et al. [1] analytical solution.

ACKNOWLEDGEMENTS

Financial support from the Academy of Finland (projects 125415 and 218038) and Sigrid Juselius Foundation, Finland is acknowledged.

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Table 1: Optimized material parameters for incompressible and compressible NHVH models and incompressible NHVH model with the material parameters obtained from MA of stem cells [2] based on the analytical solution by Sato et al. [1].

Model	ν	τ [s]	k_p	g_p	G_0 [Pa]
Incompressible NHVH with inputs from [2]	0.5	7.8	0	0.58	296
Incompressible NHVH	0.5	1.2	0	0.60	319
Compressible NHVH	0.42	3.6	0.7	0.51	414