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Characterization of cell and nucleus stiffness by coupling Scanning Ion Conductance Microscopy (SICM) and finite element modeling

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1. Introduction

One of the reasons for the survival of cancer cells is their ability to adapt their mechanical properties in response to changes in environmental pressure (Runel.G, et al. 2021). Understanding the biomechanical and biological mechanisms involved is therefore important to consider for cancer therapy. Developing reliable methods to measure the stiffness of these cells is the first step. A non-contact experimental technique, such as Scanning Ion Conductance Microscopy (SICM), has been used to assess cell properties (Rheinlaender.J, et al. 2013). This method measures the stiffness of a surface by applying local pressure, but it does not take into account the heterogeneity of the material beneath the surface. This study aims to distinguish and characterize the stiffness of the nucleus from that of the rest of the cell using a combination of experiments and numerical finite element simulations based on confocal microscopy images.

2. Methods

2.1 Experimental stiffness measure by SICM

This study was performed with LN229 human glioblastoma cells. The cells were grown on a Matrigel substrate cultured in DMEM medium supplemented with 10% fetal calf serum and 1% antibiotics. SICM works by measuring ion currents between a sensor in a probe and another in the cell medium. The current decreases as the probe approaches a surface. Applying a constant pressure to the probe as it moves closer to the membrane allows to measure the decrease in current as a function of the relative position of the probe. Comparing this slope with that on a rigid substrate (plastic) gives the local Young's modulus (Kalinin.S, et al. 2011). The nucleus was fluorescently labelled. This allowed measurements to be taken on the cell surface at locations with and without the underlying nucleus.

2.2 Numerical simulation

The cytoplasm of the cells was fluorescently labelled and volume images (1400 x 1400 x 130 voxels) of the cells were acquired using confocal microscopy (Olympus FV3000). This labelling allowed the nucleus of each cell to be seen as a negative in the images. Segmentation techniques were used to extract the geometries of the cells and their nuclei. Using the SICM data and knowing the ratio of nucleus to cytoplasm, experimental heterogeneity of Young's moduli was performed. To improve these results, a finite element model of the cell was constructed. This model distinguishes between the cytoplasm and the nucleus. Experimental Young's moduli and Poisson's ratio ν=0.3 were used as material properties in the model. Finite element simulation techniques can be used to replicate SICM experiments. Boundary conditions corresponding to SICM environment measurements were considered by applying pressure provided by the probe. Vertical displacements

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were imposed to 0 on the basal surface of the cell. The stress and strain fields were calculated. The local strains obtained numerically (Ansys) and experimentally were compared to update the heterogenous numerical model by varying the cell and nucleus volumes.

3. Results and discussion

The experimental results obtained by SICM are shown in Table 1. It can be seen that the Young's modulus of the cell with nucleus underneath is higher than the cell alone.

Table 1. Experimental Young's modulus from SICM.

E cell	E cell+nucleus
2kPa	6kPa

The mesh of a cell in blue and a nucleus in red are shown in Figure 1. This triangular mesh has been generated by segmentation of a volume image from confocal microscopy.
Finite element analysis performed on this model provided the mechanical fields in the whole volume of the cell. Simulation and SICM results are compared. Gaps between simulated and experimental fields were analyzed and reduced by optimization of the values of Young's modulus in the cytoplasm and the nucleus.

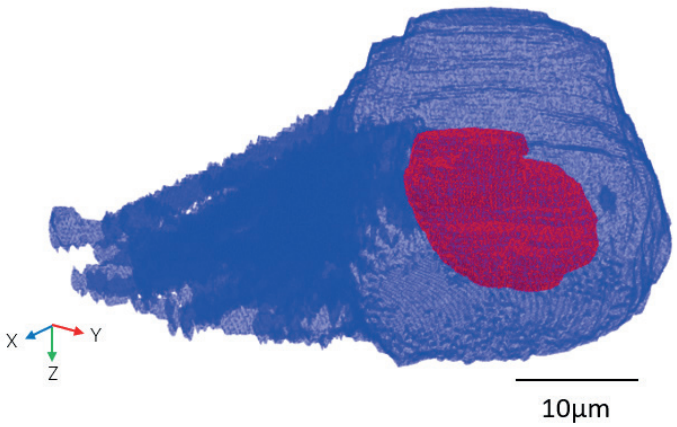

Figure 1. Mesh of a cell in blue with its nucleus in red.

Experimental Young's modulus obtained are in agreement with previous studies using SICM (Pellegrino.M, et al. 2012) or AFM on LN229 (Pogoda.K, et al. 2017). It confirms that cell stiffness is influenced by its internal organization and nucleus plays a significant role on this rigidity.

This approach by mechanical couplings between modeling and SICM experiments allowed the identification of mechanical parameters by identifying various structures in glioblastoma cells. In the present work, we considered two parts, nucleus and cytoplasm, as homogeneous components. In future studies, we could analyze potential variations in stiffness at different points within the cell and decompose the cytoplasm into other subcomponents such as actin filaments.

4. Conclusions

The possibility of characterizing mechanical properties between the cytoplasm and the nucleus is demonstrated in this study. The differences in stiffness between the nucleus and the cytoplasm have been quantified experimentally using a combination of SICM measurements and images obtained by volume confocal microscopy. The results were coupled with finite element simulations to improve these values and account for information that is difficult to measure, such as the pressure drop in the pipette. This is the first step towards the development of a cell model that can reproduce how cell stiffness changes under external pressure.

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Conflict of Interest Statement

The authors declare that they have no conflicts of interest.

References

Runel, G., Lopez-Ramirez, N., Chlasta, J., & Masse, I. (2021). Biomechanical Properties of Cancer Cells. *Cells*, 10(4), 887. https://doi.org/10.3390/cells10040887

Rheinlaender, J., & Schäffer, T. E. (2013). Mapping the mechanical stiffness of live cells with the scanning ion conductance microscope. *Soft Matter*, 9(12), 3230. https://doi.org/10.1039/c2sm27412d

Kalinin, S. V., & Gruverman, A. (Éds.). (2011). *Scanning Probe Microscopy of Functional Materials : Nanoscale Imaging and Spectroscopy*. Springer New York. https://doi.org/10.1007/978-1-4419-7167-8

Pellegrino, M., Pellegrini, M., Orsini, P., Tognoni, E., Ascoli, C., Baschieri, P., & Dinelli, F. (2012). Measuring the elastic properties of living cells through the analysis of current–displacement curves in scanning ion conductance microscopy. *Pflügers Archiv - European Journal of Physiology*, 464(3), 307-316. https://doi.org/10.1007/s00424-012-1127-6

Pogoda, K., Chin, L., Georges, P. C., Byfield, F. J., Bucki, R., Kim, R., Weaver, M., Wells, R. G., Marcinkiewicz, C., & Janmey, P. A. (2014). Compression stiffening of brain and its effect on mechanosensing by glioma cells. *New Journal of Physics*, 16(7), 075002. https://doi.org/10.1088/1367-2630/16/7/075002