CELL MECHANICS

CTU CZECH TECHNICAL UNIVERSITY IN PRAGUE

AUTHOR
Ing. Katarína Mendová*

STUDY FIELD
Biomechanics

SUPERVISOR
prof. RNDr. Matej Daniel, Ph.D.

MOTIVATION

The cell is affected not only by chemical processes but also by mechanical forces. The mechanical properties of cells are intimately related to biological processes occurring in a living organism, such as adhesion, migration, and so forth. These changes are associated with various pathological phenomena and diseases. External forces acting on the cell result in alterations to its shape, internal structure, and in some instances, its degradation.

METHODS

1. Production of liposomes using a microfluidic device

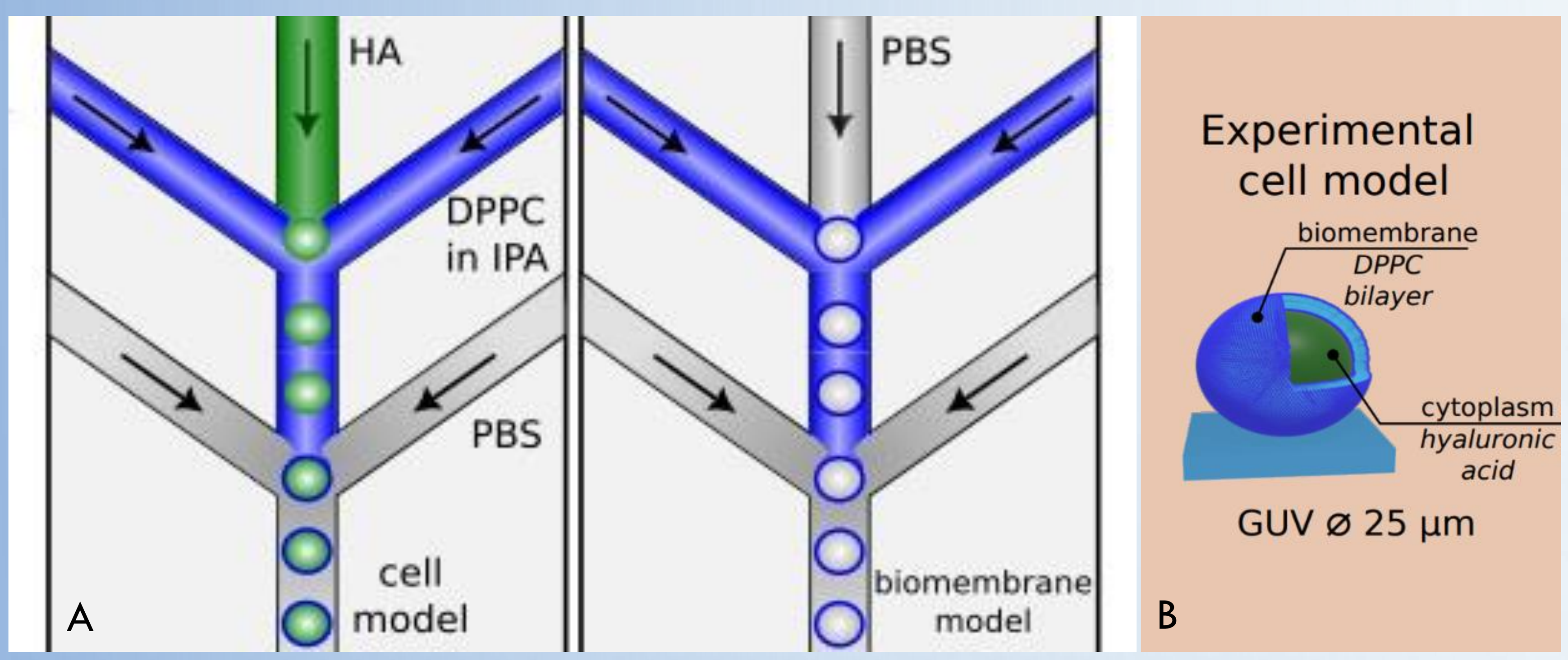

Figure 1: (A) Fabrication of a Model Cell using a Double-Drop Microfluidic Device, (B) Experimental cell model

2. Mechanical testing – AFM measurements

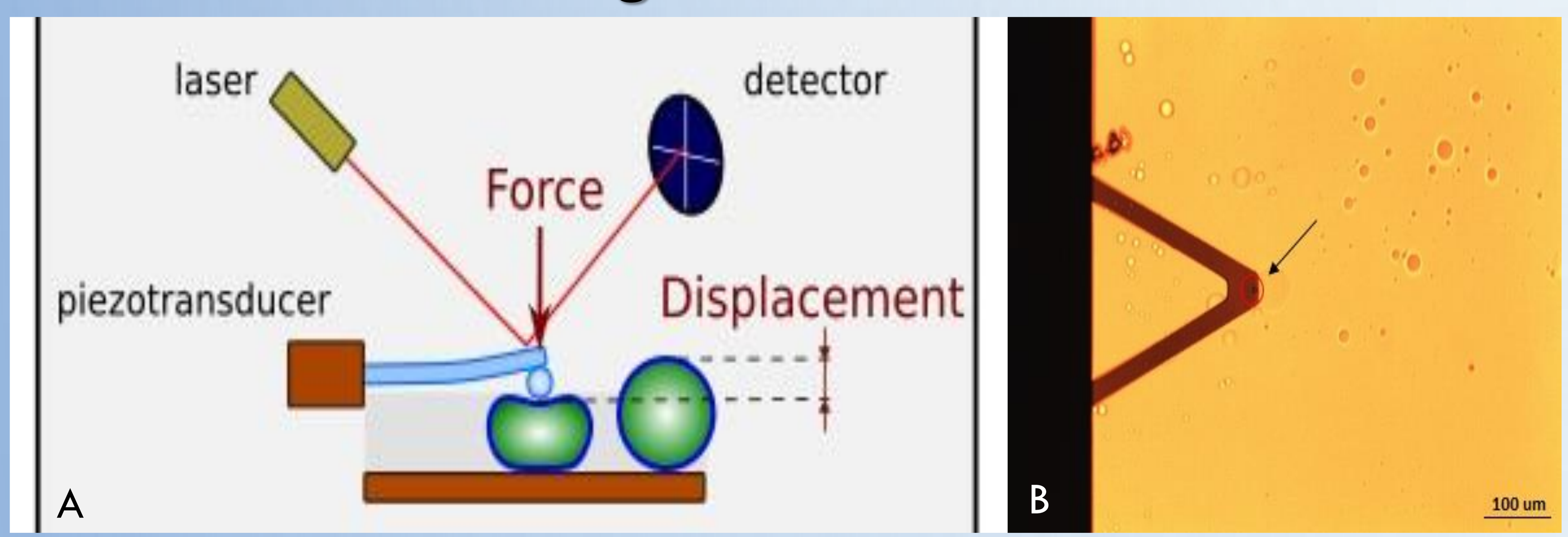

Figure 2: (A) Force - Displacement Measurements using AFM with a Colloidal Probe, (B) AFM tip with measured liposome

RESULTS

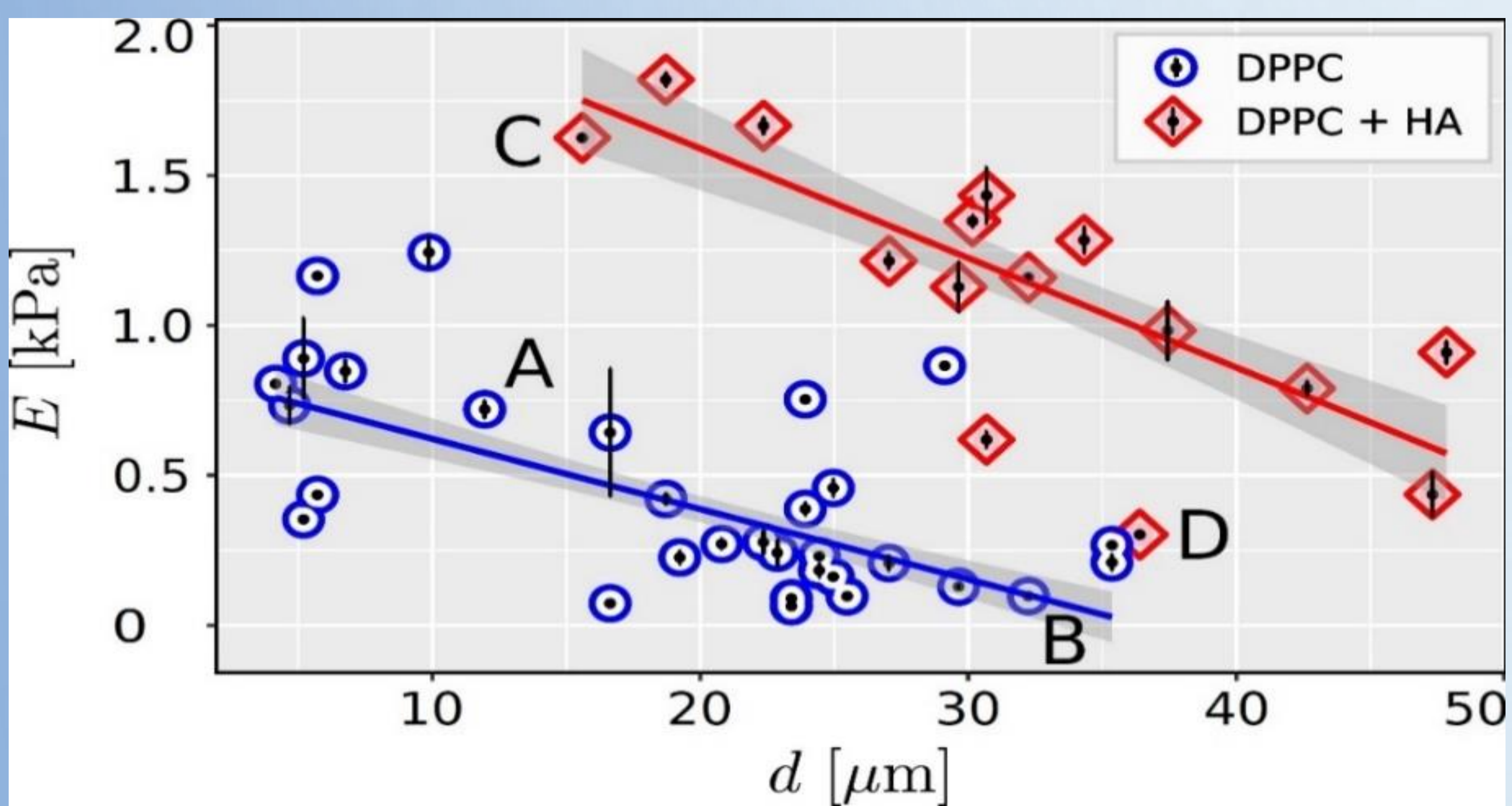

Figure 8: Linear regression plot with 95 % confidence intervals (shaded areas) showing measured dependence between the size of DPPC liposomes and Young's modulus estimated from Hertz model measured data along with the range of measured values are shown for liposomes filled with PBS and HA solution, denoted as DPPC and DPPC+HA, respectively

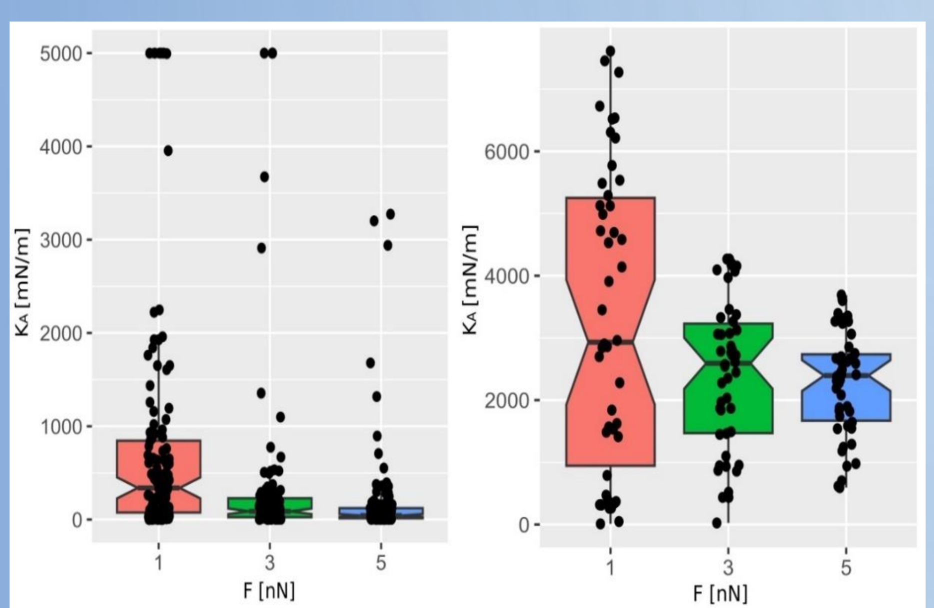

Figure 9: Boxplot of measured area compressibility modulus estimated by prescribed shape model for (left) liposomes filled with PBS and (right) liposomes with HA at indentation forces of 1 nN, 3 nN and 5 nN

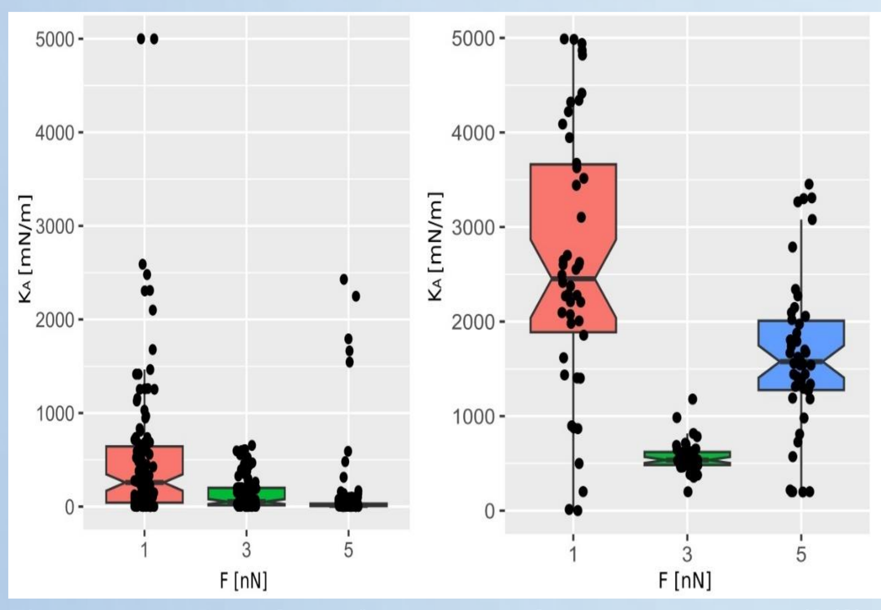

Figure: 10 Boxplot of measured area compressibility modulus estimated by fluid shell model for (left) liposomes filled with PBS and (right) liposomes with HA at indentation forces of 1 nN, 3 nN, and 5 nN

AIM OF STUDY

The aim of this work is to establish a standardized cell model (liposome) using a microfluidic device to evaluate cell mechanics and verify testing methods. Cell's mechanical properties indicate their condition and function, which is important in processes like cancer metastasis and leukocyte activation. However, most studies oversimplify cells as elastic homogeneous materials, ignoring factors like cytoskeleton properties, cell size, shape, and environmental effects. These cell models will facilitate comparison of mechanical properties across experimental techniques and validate assumptions in mathematical models, such as size effects.

3. Mechanical properties – mathematical models

A) Hertz contact model

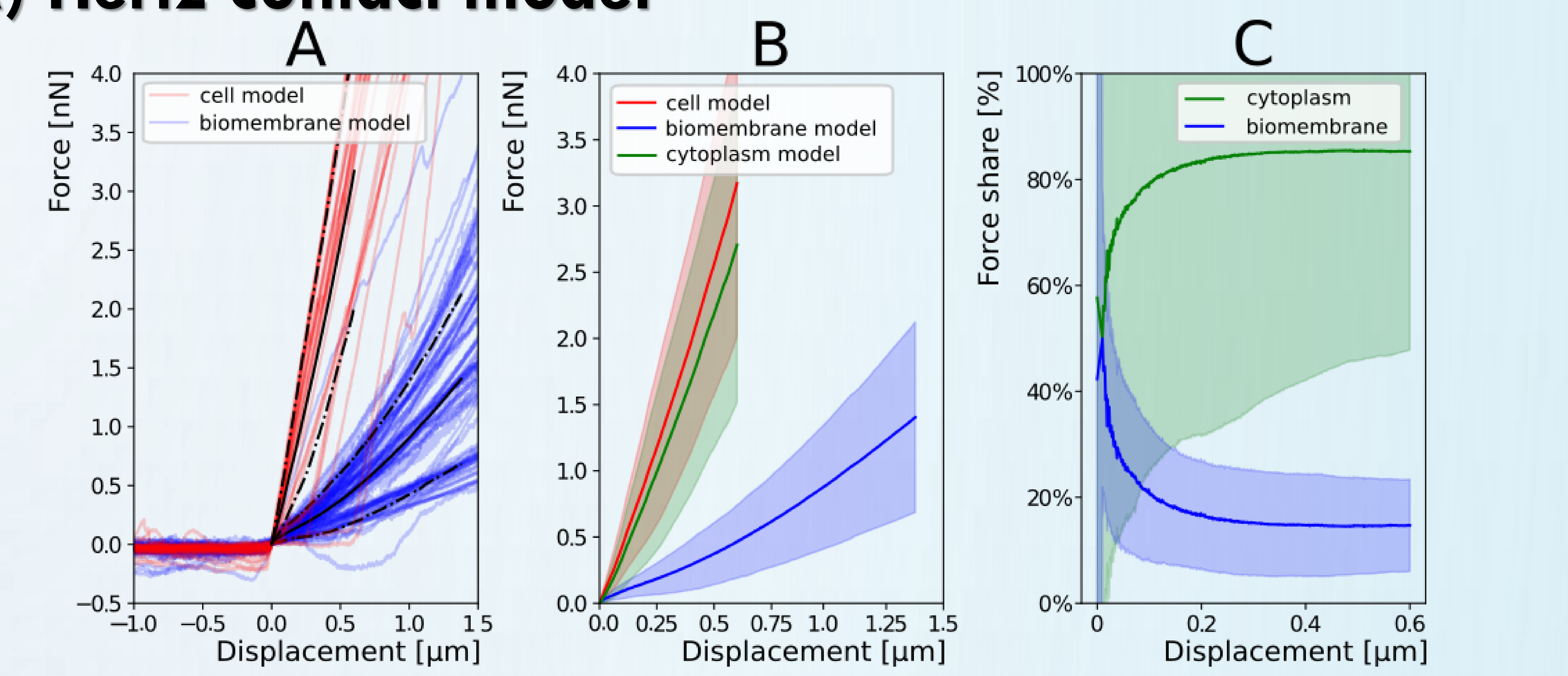

Figure 3: (A) Force deformation curves of whole cell model (biomembrane + viscous cytoplasm) and empty liposome (biomembrane model), (B) average force curves and estimation of load transmitted through cytoplasm, (C) relative contribution of cytoplasm and biomembrane to the load bearing capacity

B) Prescribed shape model

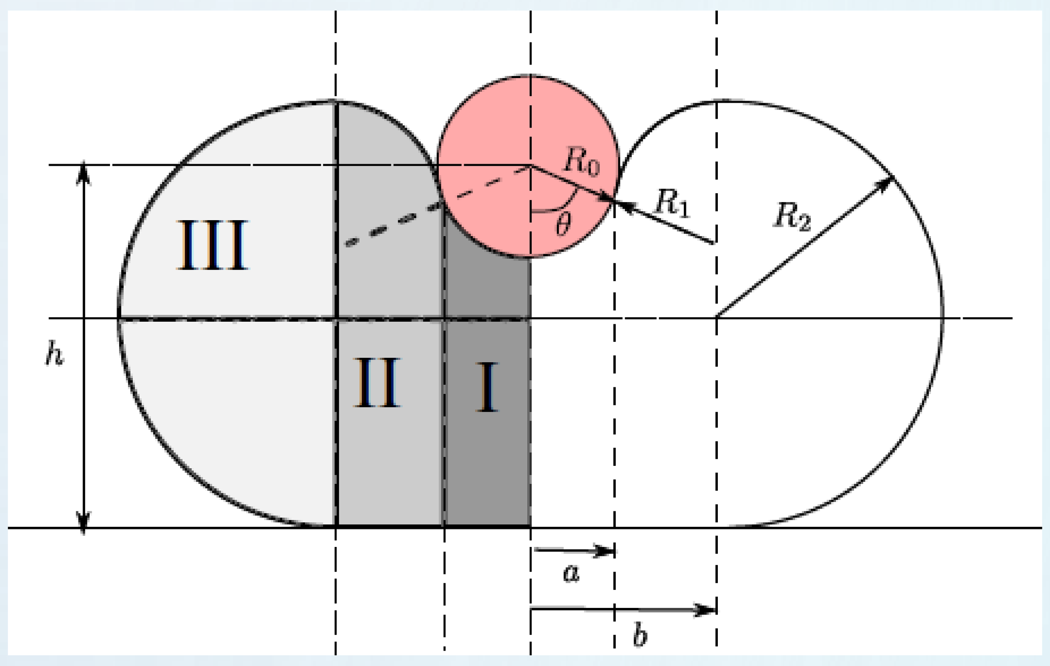

Figure 4: Geometry of spherical AFM tip and membrane interaction

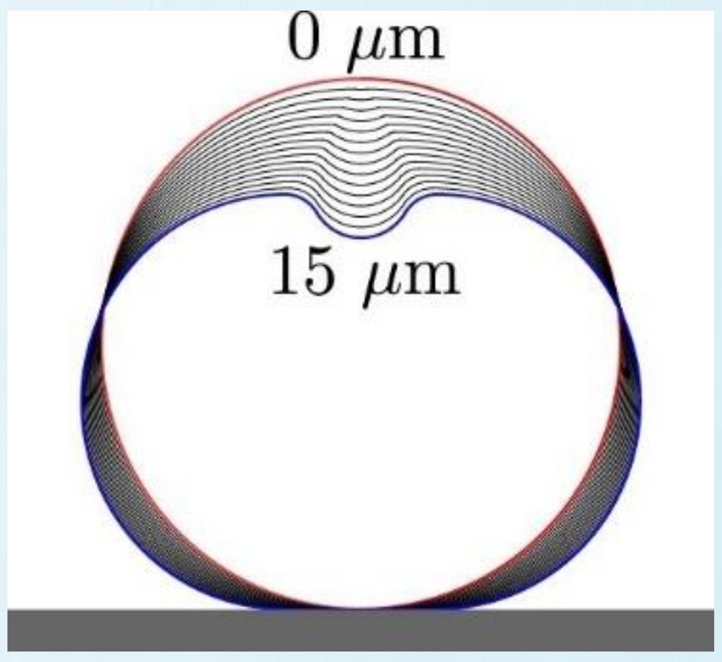

Figure 5: Contours of liposomal shape during mechanical testing. Each contour corresponds to a 1 µm increment in displacement, ranging from 0 to 15 µm

C) Fluid shell model

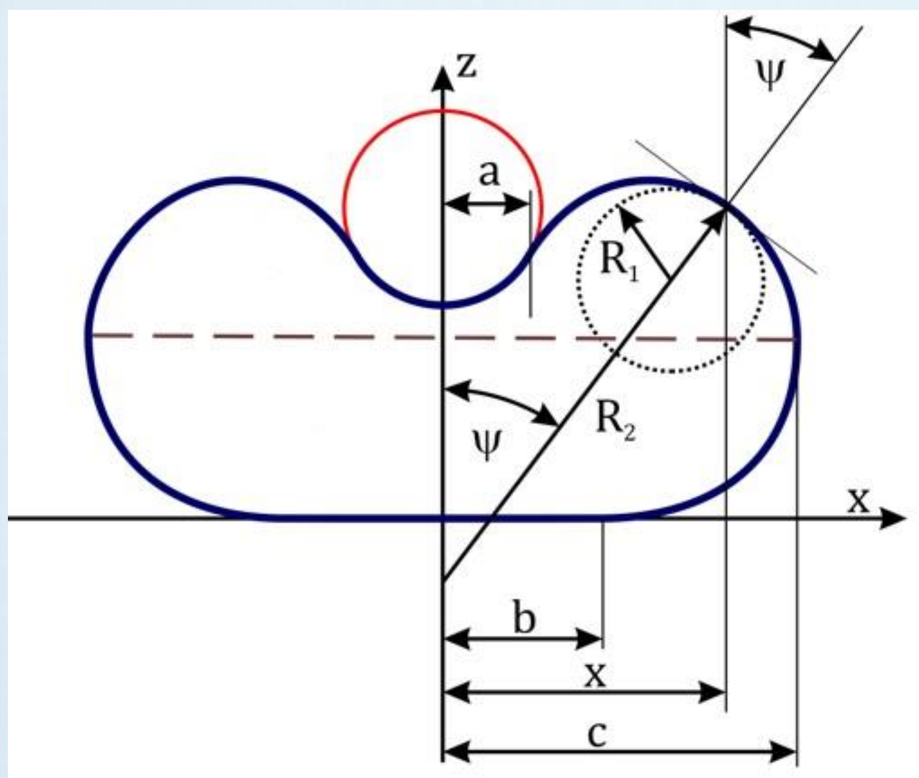

Figure 6: Schema of the fluid shell model during indentation

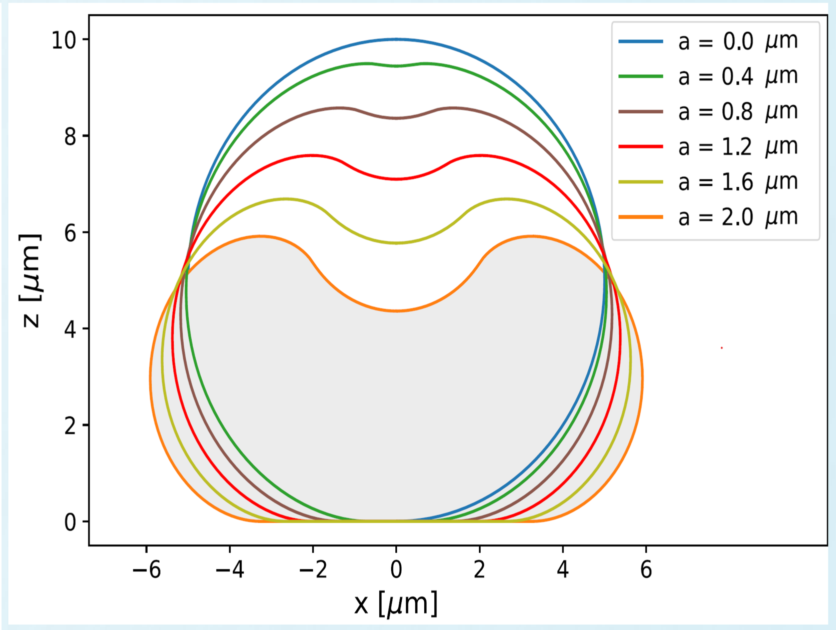

Figure 7: Cell change shape during the indentation

CONCLUSION

Using our designed microfluidic device, we created liposomes filled with (PBS) and (HA) as artificial cell models to investigate their mechanical properties. AFM measurements provided force-deformation curves and confirmed high reproducibility. Analysis showed that cell size had a significant effect on the measured stiffness and Young's modulus. We observed that the load bearing ratio between cytoplasm and biomembrane shifts from 1:1 at minimal indentation depths to 4:1 at greater depths. This supports the continuum approach for large deformations and highlights the importance of including the cell membrane in minimal deformation analyses. We therefore proposed two models - the prescribed shape model and the fluid shell model. The fluid shell model accurately reflects the size-dependent relationship between liposome indentation force and agrees with literature values. Our results demonstrate the potential of experimental models in the study of cell mechanics. Future research should develop models that represent specific living cells with complex internal structures.

SELECTED PUBLICATIONS

- MENDOVÁ, K., M. DANIEL, and M. OTÁHAL. Nonlinear cell deformation model. Journal of Mechanical Engineering. 2023 ISSN 2450-5471. DOI 10.2478/scjme-2023-0026
- MENDOVÁ, K., et al. Rethinking Hertz Model Interpretation for Cell Mechanics Using AFM. International Journal of Molecular Sciences. Manucsript number: ijms-3036525, Under Review., doi:10.20944/preprints202405.1183.v1
- M. OTÁHAL., MENDOVÁ, K, and M. DANIEL. AFM cell indentation: fluid shell model. In: Proceedings of 2023 EHealth and Bioengineering Conference (EHB). IEEE International Conference on e-Health and Bioengineering EHB 2023 - 11-th edition, Bucuresti, 2023-11-09/2023-11-10. Iasi: Gr. T. Popa University of Medicine and Pharmacy, 2023. ISBN 979-8-3503-2887-5

*Katarina.Mendova@fs.cvut.cz