# COMPUTATIONAL CELL BIOMECHANICS

**Sofia Pettenuzzo[a]*, Alessandro Arduino[a] , Alice Berardo[a,b,c],Carmelo Majorana[a], Emanuele Luigi Carniel[c]**

[a] Department of Civil, Environmental and Architectural Engineering, University of Padova, Italy
[b] Department of Biomedical Sciences, University of Padova, Italy
[c] Department of Industrial Engineering, University of Padova, Italy

## Aim

Tumour is nowadays one the most concerning worldwide disease that causes millions of deaths each year. Furthermore, the intrinsic inter and intra tumour variability make it difficult to investigate the mechanical properties of cancerous cells. The aim of the research activity is the development of a computational model of the cell biomechanics. The use of Finite Element Models (FEMs) would provide major advantageous capabilities such as: (i) observing the mechanical contributions of the cell subcomponents, (ii) controlling the variables involved in the overall response and (iii) providing reproducibility to the mechanical results.

## Materials and Methods

The virtual solid model has been realized with the FE software Abaqus CAE 2019 (Dassault Systèmes Simulia Corp., Providence, RI).

**FE model of the cell**
The cell is a complex biological structure, for this reason the model has been reduced to its main subcomponents (fig. 1):

- Cytoplasm
- Plasma membrane
- Nucleus
- Cytoskeleton

The model has been discretized by means of linear hexahedral elements and truss elements (fig. 2).

**Continuum-tensegrity structure**
Both continuous and discrete structures have been used to describe the subcomponents. In particular, the cytoskeleton was modelled by means of a network of truss elements, building a tensegrity structure that provides a prestress to the overall structure.

**Material Formulation**
Viscohyperelastic material properties were assigned to each subcomponents using a Neo-Hookean formulation. Special attention was given to the cytoplasm and to the cytoskeleton.
Prestress was described by means of thermal expansion and predefined fields.

$$\varepsilon^{th} = \alpha(\vartheta, f_\beta)(\theta - 0^0) - \alpha(\theta^I, f_\beta^I)(\vartheta^I - \theta^0)$$

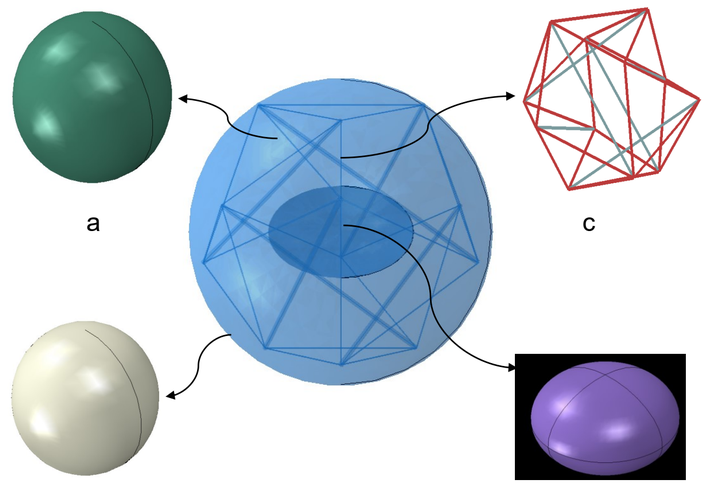


***Fig.1**: Finite Element Model of the cell with its subcomponents: (a) cytoplasm, (b) plasma membrane, (c) cytoskeleton and (d) nucleus.*

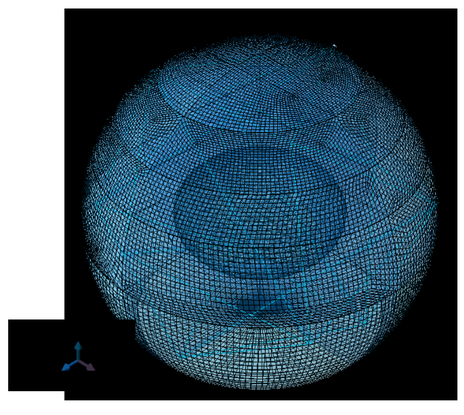

***Fig.2**: Finite Element Finite element discretization of the cell and its subcomponents.*

## Results

**Strain hardening due to prestress**.

- Strain hardening is a phenomenon observed in cells due to the tensegrity structure of the cytoskeleton [1].
- Most of the stress is concentred along the cytoskeleton trusses. This highlights the role of the cytoskeleton in the cell mechanical response.
- Applying a thermal expansion (to simulate prestress) to the cytoskeleton, causes a non linear increase in the cell stiffness (fig. 3).

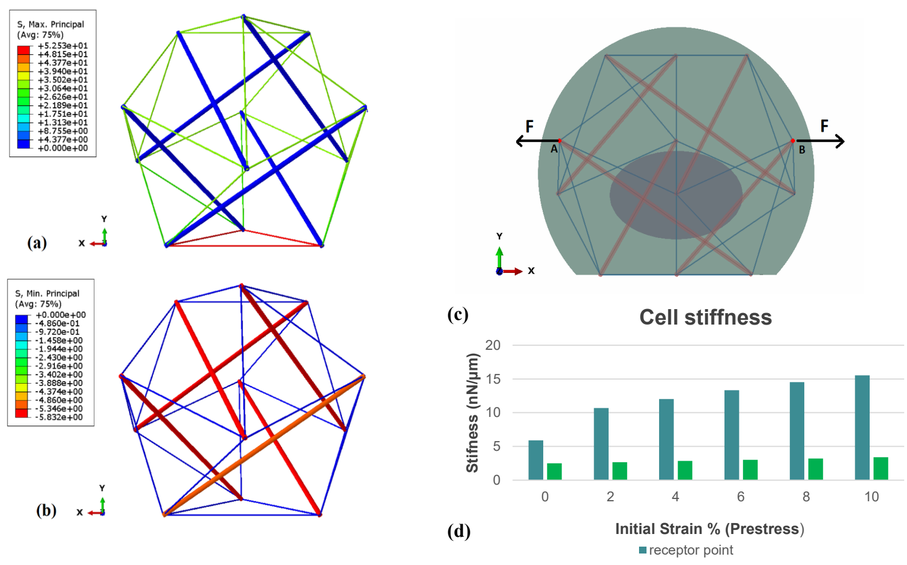


***Fig. 3:** Effects of the prestress on the mechanical response of the cell. (a) and (b), distribution of the stresses along the truss elements of the cytoskeleton. (b) Schematics of the forces applied to the cell during the simulation. (d) non-linear increase of the cell stiffness due to the prestress.*

## Discussion

- The differences between the homogeneous and the continuum-tensegrity models were assessed when referring to cell subcomponents.
- The model can mimic the behaviour of an average human cell.
- Role of prestress: structural stability to the cell.
- Cytoskeleton: tensile behaviour, Cytoplasm: compression behaviour.
- Different ratios of cell and pipette ($D_c/D_p$) diameters strongly influence the global response of the cell during MPA.

FE models can be applied to deepen the knowledge about cell biomechanics.

## Acknowledgments
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## Simulation of experimental setups

- The cell model provided good fit to the usual mechanical experimental setups used to assess the cell biomechanics.
- Both Atomic Force Microscopy indentation technique (fig. 4) and micropipette aspiration (fig. 5) were used to validate and test the model [2,3].

### AFM indentation tests

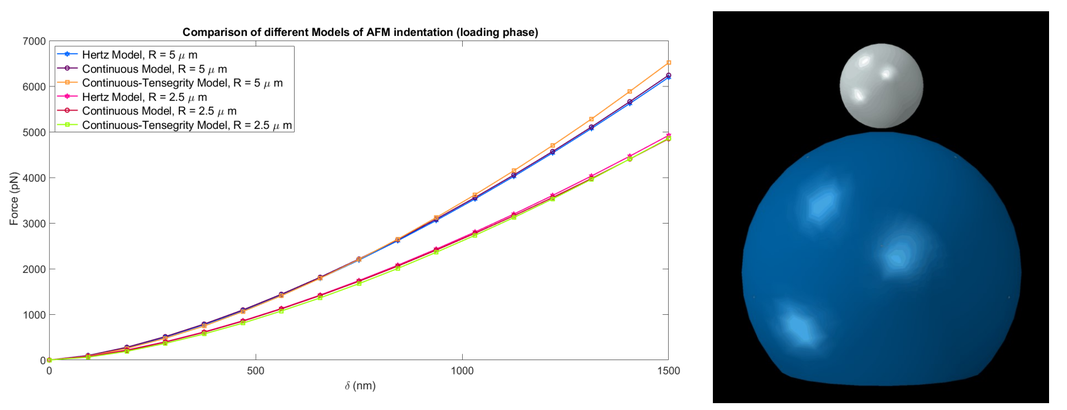


***Fig. 4:** Simulations of the AFM indentation experiments to observe the behaviour of the continuous model against the continuous-tensegrity model.*

### Micropipette aspiration tests

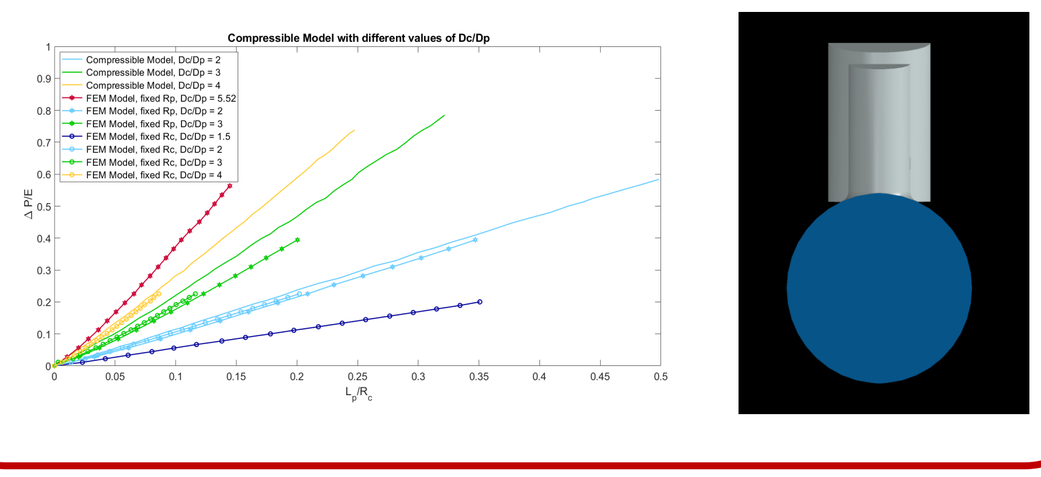


***Fig. 5**: Simulations of the micropipette aspiration experiments to analyze the effect of varying the ratio between the micropipette radius and the cell radius.*

## References
1. J.G. McGarry et al., “A three-dimensional finite element model of an adherent eukaryotic cell”, 2004.
2. E.M. Darling et al., “Viscoelastic properties of human mesenchymally-derived stem cells and primary osteoblasts, chondrocytes, and adipocytes”, 2008.
3. R.M. Hochmuth et al., “Micropipette aspiration of living cells”, 2000.

***Corresponding author: sofia.pettenuzzo@unipd.it**