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Nano-Mechanical Eukaryotic Cell Behavior by Finite Element Modeling

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***Abstract*—The cell mechanics behavior must be understood by the scientific community. There is two used methods: nanoindentation and atomic force microscopy AFM. The first one gives displacement between 10^{-9} and 10^{-3} meter corresponding to a load from 10^{-7} to 10 Newton. The second one gives displacement between 10^{-11} and 10^{-7} meter corresponding to a load ranging from 10^{-12} to 10^{-5} Newton. This work gives the nanoindentation eukaryotic cell simulation by the use of the commercial software: COMSOL Multiphysics and we give the relation to AFM. The nano-mechanical cell behavior was investigated using the finite element method, especially, we implement on it, the mechanics continuum. First, we created the 2D cell model. This model was constrained vertically at the bottom. We used hyperelastic model for the cytoplasm. Nanoindenter and cell contact was assumed to be a source boundary. In the second part of this work, we incorporated a circular section to the model. This circular section represents the nucleus chosen to be elastic. We then show that nucleus influences the cell mechanical response. After modeling and simulation, we obtain results in good agreements with those obtained experimentally.**

Keywords—Multiphysics, eukaryotic cell, nanoindentation, modeling, COMSOL, finite element method.

I. Introduction

Researches on the mechanical properties of nano particles have attracted increasing interest especially for the biological cell. Our existence depends on cell functions instead of biochemical mechanisms, cell rely on mechanical behavior which is also related to extracellular matrix ECM.

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The mechanical cell behavior gives more details to understand disease and cancer properties [22,27]. Methods used to determine cell mechanical characteristics are AFM which gives the surface soft topology[10-11,14,19,20,22,25-26,30-31,33], and nanoindentation [2,4-5,12,27-28,32]. This later is used to give mechanical cell behavior in experimental try with a rigid indenter and a rigid support. In this work we will model and simulate nanoindentation cell response to predict best conditions which can be used by experimental researcher [23,29,33,34]. First, we will model nanoindentation for a cell without nucleus and then we will give nanoindentation for eukaryotic cell with nucleus as shown in figure 1 and figure 2.

Cells present an hyperelastic behavior [15-16,35] due to cytoskeletal tensegrity filaments [1,3,6-7]. The model used in this work is the hyperelasticity Neo-Hookean model [15,17,35].

Our model was created by the contact finite element method [9,21,24], and the results are simulated by the commercial software COMSOL Multiphysics [13,18,35].

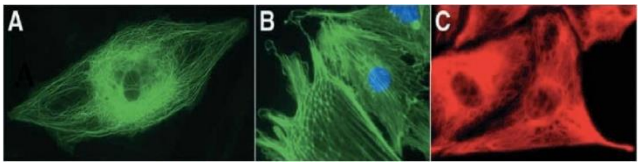

Figure 1. Endothelial cells cytoskeleton. A. microtubules. B.Microfilaments. C. Intermediate filaments [7]

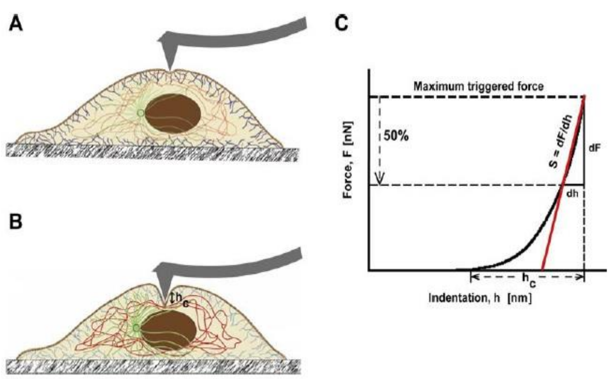

Figure 2. Model of the AFM indentation regime for analyzing Indentation Force nanomechanics in cells. A. AFM tip first encounters the actin cytoskeleton (blue). B. intermediate filament network (red). C. indentation hardness vs force curve [22].

Obtained results are in good agreements with those obtained experimentally [5,22].

TABLE I

CELL MATERIAL PARAMETERS [8]

Name	Value	Unit
Density	1200 kg/m^3	kg/m^3
Lamé parameter λ	144e6 N/m^2	N/m^2
Lamé parameter μ	7.2e6 N/m^2	N/m^2

TABLE II

NANOINDENTER AND RIGID SUPPORT MATERIAL PARAMETERS

Name	Value	Unit
Density	3515 kg/m^3	kg/m^3

II. NUMERICAL EXPERIMENT

The numerical experiment is based on the supposition that system model can be simulated assuming some assumption depending on the studied region. This later is formed by indenter, cell and a support as shown in figure 3 and figure 5.

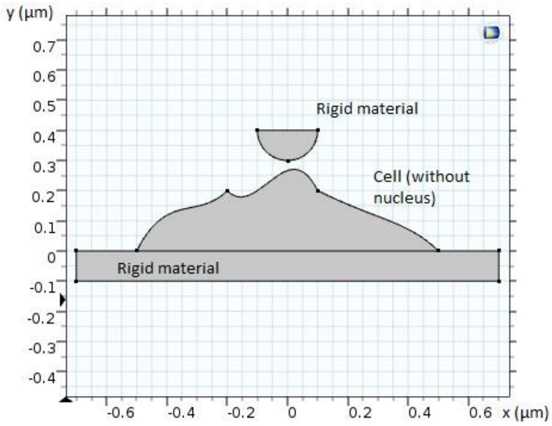

Figure 3: Cell without nucleus and indenter model geometry plus a rigid support designed with Comsol.

TABLE III

MESH GENERATION DETAILS

Triangular elements	280
Edge elements	88
Vertex elements	11
Mesh quality	0.7

A. Nonlinear Structure Material

Elastic Model: For the indenter and rigid support, we used equations for elastic model,

$$-\nabla\sigma = Fv \tag{1}$$

$$\sigma = \left(S\cdot\left(I+\nabla u\right)\right) \tag{2}$$

$$S - S_0 = C:\left(\varepsilon - \alpha\left(T - T_{ref}\right) - \varepsilon_0\right) \tag{3}$$

$$\varepsilon = \frac{1}{2}\left[\left(\nabla u\right)^T + \nabla u + \left(\nabla u\right)^T \nabla u\right] \tag{4}$$

where,

S is the second Pikola-Kirchhoff stress,

∇u is the displacement gradient,

F is the deformation gradient,

v is the left stretch tensor,

σ is the Cauchy stress,

C is the right Cauchy-Green deformation tensor,

ε is the Green strain,

ε_0 is the initial strain,

I is the identity tensor,

T is present temperature,

T_{ref} is the stress free reference temperature,

α is the thermal expansions vector.

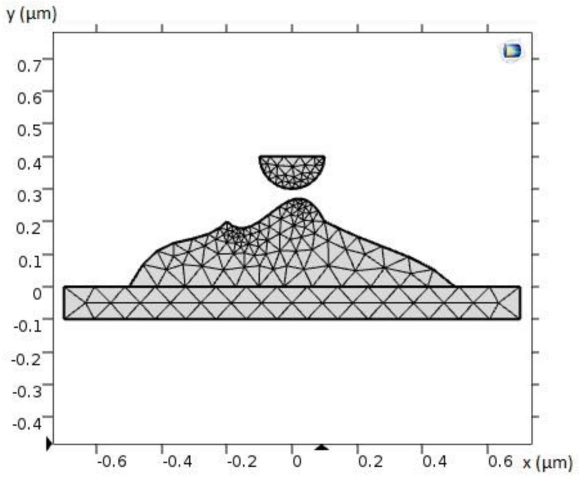

Figure 4: Obtained mesh generation.

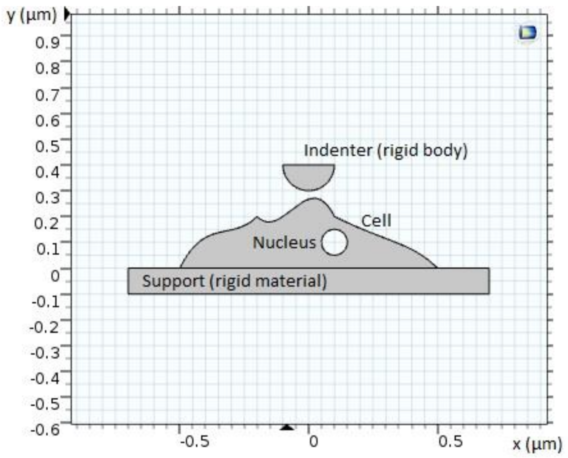

Figure 5: Cell with nucleus and indenter model geometry plus rigid support designed with comsol.

TABLE IV

MESH GENARATION DETAILS

Triangular elements	557
Edge elements	125
Vertex elements	15
Mesh quality	0.8

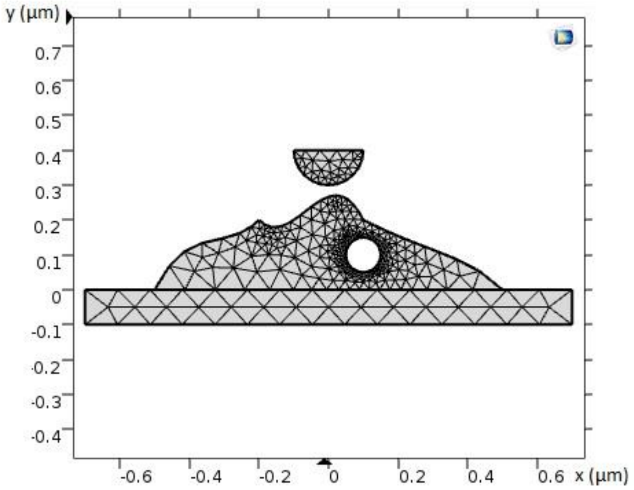

Figure 6. Obtained mesh generation.

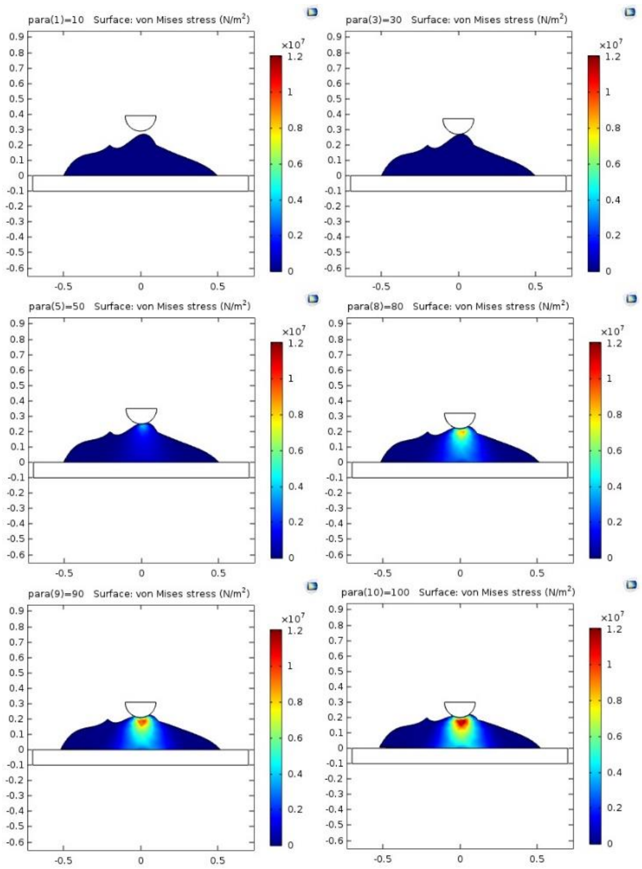

Figure 7: Von Mises indentation steps N/m².

Hyperelastic model (Neo-Hookean) - For the cell model, we use the Neo-Hookean hyperelastic model,

$$-\nabla\sigma = Fv$$

$$\sigma = \left(S \cdot \left(I + \nabla u\right)\right)$$

$$S = \frac{\partial W_s}{\partial \varepsilon} \tag{5}$$

$$W_s = \frac{1}{2}\mu\left(\overline{I}_1 - 3\right) - \mu \ln\left(J_{el}\right) + \frac{1}{2}\lambda\left[\ln\left(J_{el}\right)\right]^2 \qquad (6)$$

$$\varepsilon = \frac{1}{2}\left[\left(\nabla u\right)^T + \nabla u + \left(\nabla u\right)^T \nabla u\right]$$

where,

W_s is the strain energy function,

μ and λ are Lame elastic constants,

J_{el} is the elastic deformation gradient,

I_1 is the scalar invariant of C.

TABLE V

COMPUTATION INFORMATION

Computation time	42 s
CPU	Intel(R) Core (TM) i3-3217U CPU @ 1.80GHz, 2 cores
Operating system	Windows 8

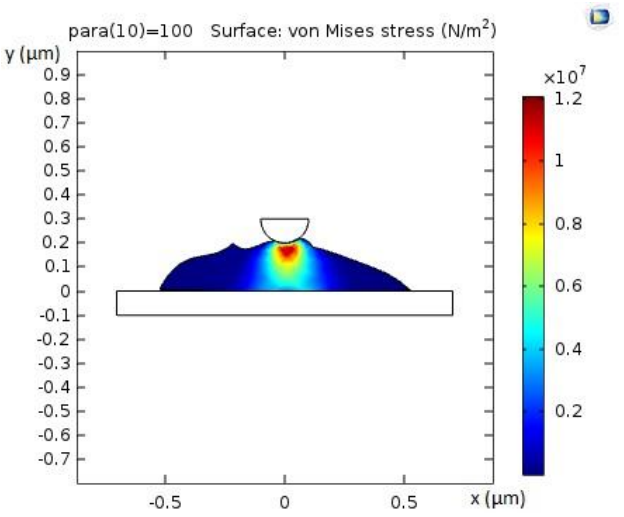

Figure 8: Von Mises stress in N/m²

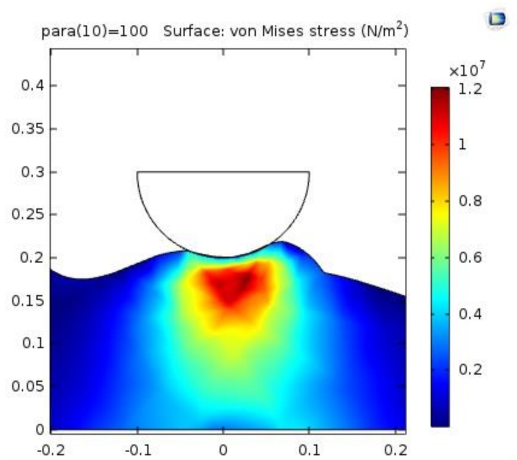

Figure 9: Indenter effect on cell interface.

Materials: For cell material parameters we used data given in table 1. For rigid indentor and support which are in carbon-diamond, we used data given in table 2.

B. Cell Model without Nucleus

The numerical simulation was performed by the finite element method implemented in COMSOL multiphysics 5.2 software [13,15,35].

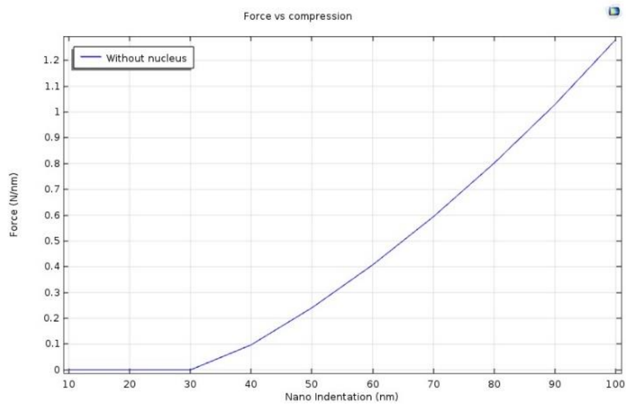

Figure 10: Force vs compression curve for cell without nucleus.

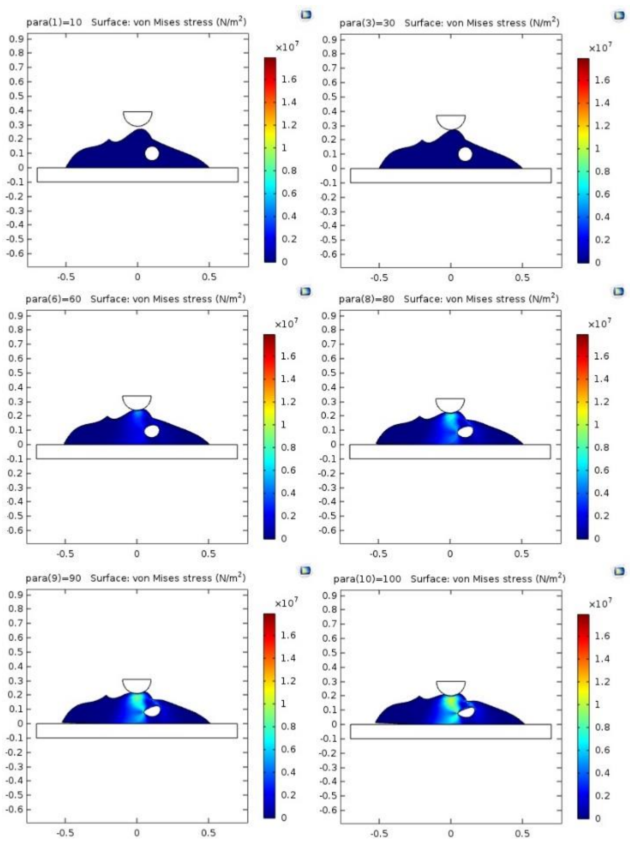

Figure 11: Von Mises indentation steps N/m².

Geometry: The 2D geometry model gives an approximation to the real cell with the assumption that cell out of plane thickness is equal to 10nm. In the plane strain approximation this setting only affects total force computations. The cell total length is chosen equal to 1000nm and the height is equal to 255nm. The cell shape presents a tensegrity form [1,3,6,7]. The circular indenter diameter is equal to 200nm. The support is modeled at the bottom part of cell, as shown in figure 3.

Mesh Generation: The mesh generation was chosen to be *normal* triangular elements, and it was physics controlled which means that COMSOL refines mesh in the critical regions. The mesh detail obtained is given in the table 3.

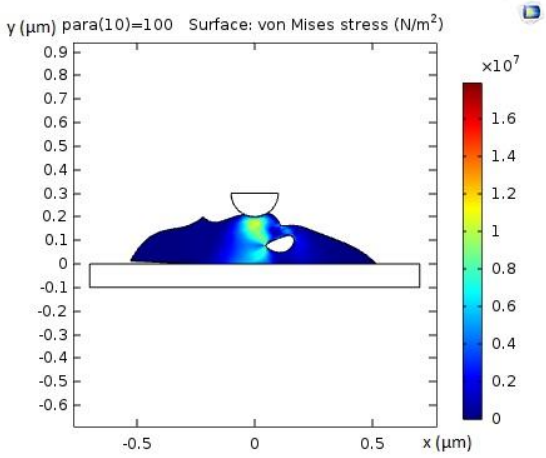

Figure 12: Von Mises stress in N/m².

TABLE VI
COMPUTATION INFORMATION

Computation time	50 s
CPU	Intel(R) Core(TM) i3-3217U CPU @ 1.80GHz, 2 cores
Operating system	Windows 8

Once the mesh obtained figure 4, we launch the computational operations which were described in section III. A. i.e. mechanics cell behavior without nucleus.

C. Cell Model with Nucleus

Geometry: For the cell model with nucleus geometry, we used the same data from model without nucleus, with the nucleus geometry adding. We choose the nucleus diameter equal to 100nm as shown in figure 5.

Mesh Generation: The mesh generation was chosen to be normal triangular elements, and it was physics controlled which means that COMSOL refines mesh in the critical regions. The mesh detail obtained is given in the table 4.

Once the mesh obtained figure 6, we launch the computational operations described in section III. B. i.e. mechanics cell behavior with nucleus.

III. RESULTS AND DISCUSSIONS

The contact between the rigid base and cell is chosen to be prescribed displacement. We obtain results after the indenter vertical displacement along the y direction. We perform a displacement equal to 100nm in which an indentation equal to 55nm. The CPU time is equal to 42s.

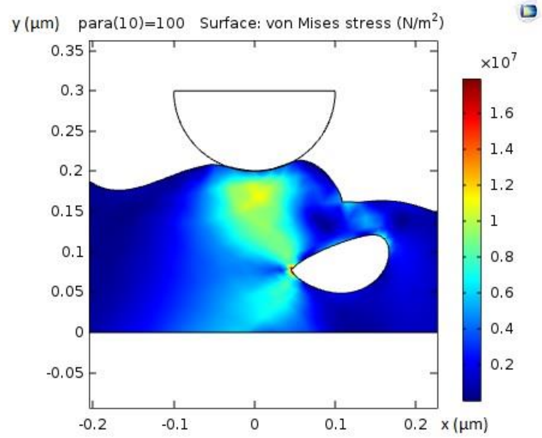

Figure 13: Indenter effect on cell interface.

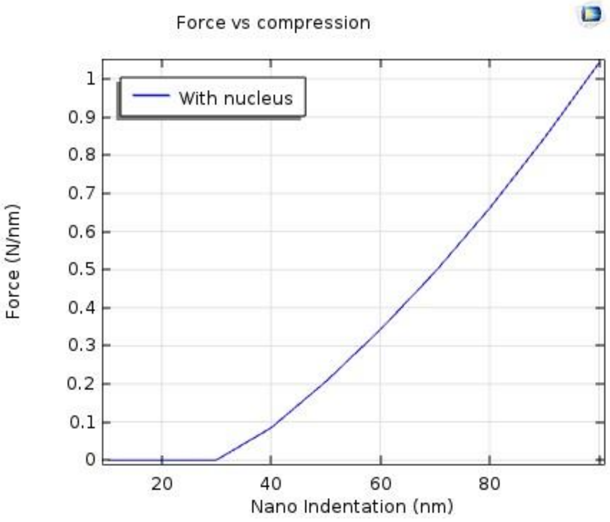

Figure 14: Force vs compression curve for cell with nucleus.

A. Mechanics Cell Behavior without Nucleus

For the cell without nucleus the obtained CPU time is equal to 42s, the computational data are given in table 5.

The different nanoindentation steps following y axis are given in Fig. 7 in which the von Mises stress in N/m^2 is the main result. We observe that the maximum stress is equal to

1.2 x 10^7N/m2 and is concentrated in the region below the indenter.

Figures 7, 8 and 9 shows the von mises stress repartition in the cell without nucleus compressed by a rigid carbon nanoindenter.

These results are in good agreements with those obtained with experiments [5,22].

B. Mechanics Cell Behavior with Nucleus

For the cell with nucleus, the obtained CPU time is equal to 50s, the computational data are given in table 6.

The different nanoindentation steps following y axis are given in figure 11 in which the von mises stress in N/m^2 is the main result. We observe that the maximum stress is equal to 1.7 x 10^7 N/m^2 and is concentrated in the corner near compressed nucleus.

Figures 11, 12 and 13 shows the von Mises stress repartition in the cell with nucleus compressed by a rigid carbon nanoindenter.

These results in figure 10 and figure 14 are in good agreements with those obtained with experiments [5,22].

III. Conclusions

This work shows the nanoindentation cell mechanical characteristics. We investigated the cases in which the main assumptions was first to chose a mathematical model for the rigid part and hyperelastic part, the second assumption was to chose the numerical method which can resolve the mathematical model and to give numerical results in adequation with theoretical and experimentals ones . The models used are cell without nucleus and cell with nucleus. The main result is the observation of a von Mises stress increse for the cell in which a nucleus is incorporated.

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