FE Simulation of Cell Indentation by AFM

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Abstract

The realization of promising potential of stem cells for engineering bone, cartilage, muscle and other connective tissues requires a proper characterization of their unique biological, biochemical, proteomic, and biomechanical properties that are yet to be fully elucidated. The mechanical properties such as elasticity, membrane tension, cell shape, and adhesion strength may play an important role in the cell fate and differentiation. The mechanical properties of biological cells have been studied with different techniques; the most popular ones are optical tweezers, magnetic beads, and micropipette aspiration. However, those methods cannot compete with the precision that can be attained with atomic force microscopy (AFM) method. AFM has been widely used in the study of micro and nanostructures including living cells. As the interpretation of atomic force microscopy-based indentation tests is highly dependent on the use of an appropriate theoretical model of the testing configuration, in this paper various contact models were presented to predict the mechanical behavior of individual stem cells. Due to special conditions assumed, the most proper one was chosen. A comparison study with finite element simulations (FEM) of spherical tip indentation demonstrates the effectiveness of our computational model to predict the cell deformation during indentation tasks.

Key words: Cell indentation, Hertz theory, FE simulation

1. Introduction

The mechanical properties of many “soft” materials are of interest for biomedical applications, including natural tissues, hydrogels and cells for tissue engineering applications. In the last 15 years, nanoindentation techniques have gained prominence in the mechanical testing community for three reasons: first, the fine resolution in load and displacement transducers, second the fine spatial resolution for mapping local mechanical properties, and finally the relative ease of performing mechanical testing. Atomic force microscopy (AFM) indentation has become an important technique for quantifying the mechanical properties of live cells at nanoscale. Through various biochemical and biomechanical mechanisms, cells are able to respond to their three-dimensional mechanical environments and alter their mechanical properties such as Young’s Modulus or stiffness during subjecting to an external force. AFM techniques allow solving a number of problems of cell biomechanics by simultaneous evaluation of the local mechanical properties and the topography of the living cells, at the high spatial resolution and force sensitivity. In these experiments AFM cantilever serves as a micro-indenter to probe the cell. In addition, AFM indentation technique can be used to characterize the viscoelasstic behavior of the cell cytoskeleton. As the interpretation of AFM-based indentation test is highly dependent on the use of an appropriate theoretical model of the testing configuration, our results demonstrate the applicability of the Hertz contact model as the most appropriate model in this condition compared to other theories. We have used Hertzian contact model for the spherical tip indenter to compute cell stiffness and provide load-indentation depth curve. A numerical validation study of the Hertzian contact model has been conducted through a realistic two dimensional finite element modeling (FEM).

2. Research Methodology

In this paper different contact mechanics models were studied and the Hertz theory was the most appropriate one. Since the cell dimensions are about micrometer, adhesion forces can be omitted so models which do not consider adhesion forces can be used. To have small deformation, indentation depth is limited to 0.34 micrometer so Hertz contact model is applicable because it is a small deformation model and does not consider adhesion forces.

Hertz theory model

The Hertz theory model does not consider the surface forces and adhesion in contact. If surface forces present, this model does not appropriate for low loads. However, for the condition considered here this model with all its shortages can be used. The relationship between applied load and indentation depth (d) on the tip–particle and particle–substrate is given by the following equations:

$$F = Ka\delta \tag{1}$$

$$\delta = \frac{a^2}{\tilde{R}} \tag{2}$$

Contact-radius (a) and adhesion force (Fad) are obtained as follows:

$$a^3 = \frac{\tilde{\mathrm{R}}}{\mathrm{K}}\mathrm{F} \tag{3}$$

$$\mathrm{F}_{ad}=0 \tag{4}$$

FE simulation

In this part a two dimensional FE model with some considerations was provided. These considerations were as follows:

a- The mechanical problem is axisymmetric
b- The cell is supposed to have homogenous, isotropic and elastic material properties with the average young module of about 17.8 Kpa.
The mechanical and geometrical properties are related to mouse embryonic stem cell obtained from published papers (Table-1).

Diameter of the cell(μm)	12
Height of the cell(μm)	8
Elastic modulus(Kpa)	17.8
Poisson ratio	0.49
Indentation range(μm)	0.34

Tabel.1: Mechanical and geometrical properties used in FEM

The ABAQUS 6.9 was used for this numerical analysis. The specimen used in numerical analysis was divided in to 380 elements (3 node element).

3. Results and Analysis

As mentioned before a 2D FE model was provided and results were obtained in force-indentation depth curve form to compare with the results from Hertz model (fig-1 and 2).

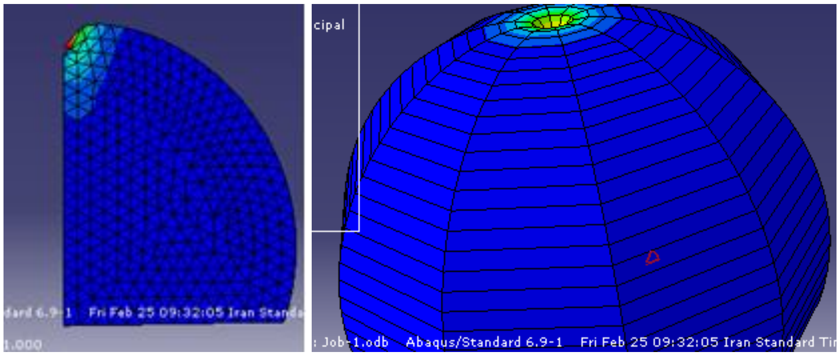

Figure.1: Analysis of the axisymmetric cell from a numerical analysis

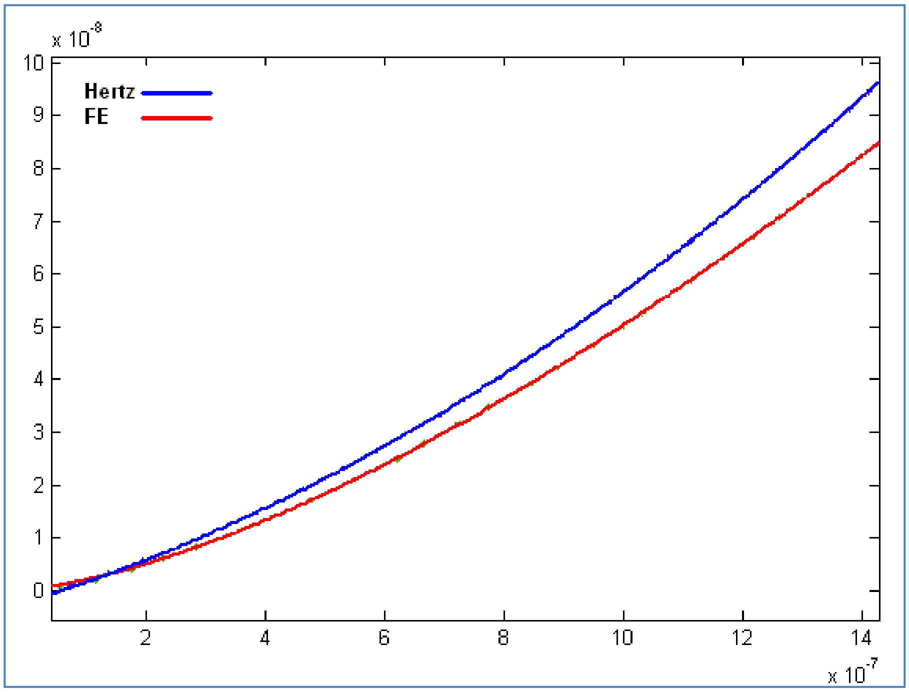

Figure.2: Force-indentation depth curve of cell obtained from Hertz theory and FE simulation

As shown in fig-2 Hertz model and FE simulation curves are approximately the same in small deformations. As deformations become larger, the slope of the curves differs. This shows that these analytical and numerical models can be conveniently used in small deformation. Results were compared with experimental data from other studies which shows that these models have a good agreement with small deformation data and for the large deformation analysis they are not applicable. Further analysis was done considering the cell as a spring with the stiffness of k which can be obtained from force- displacement curve due to following equation:

$$F = k_{cell}\delta_{cell} \qquad (5)$$

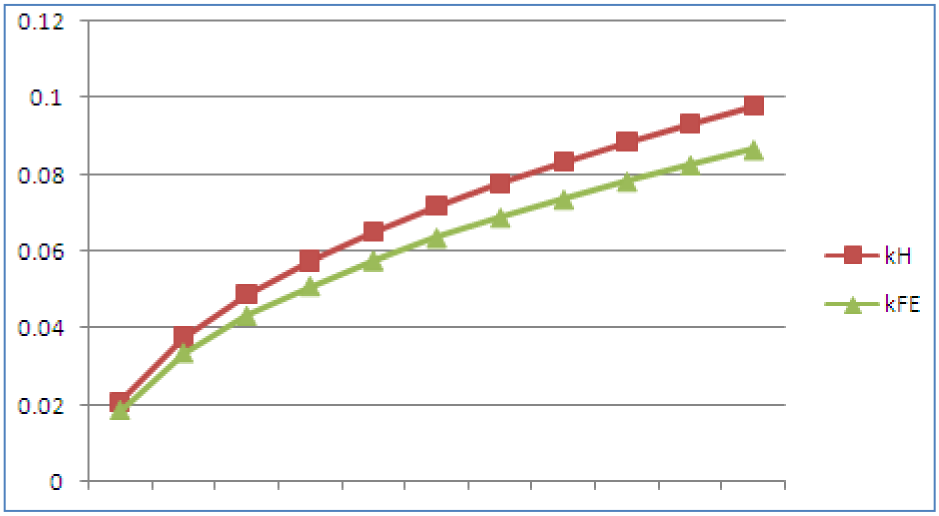

Figure.3: Cell stiffness obtained from Hertz theory and FE simulation

As demonstrated in fig-3, cell stiffness curves have good agreement at small deformations. As the force increased indentation depth increases which result in different stiffness in each point.

4. Conclusions

As an overall conclusion, based on results from 2D finite element numerical analysis and Hertz theory compared with experimental data from other studies, Hertz theory can be used for small deformations and its results are the same with FE analysis in this range. But this theory is not applicable for large deformations, because in these deformations its results are not compatible with FE and Experimental data. In this study for more simplification, cell was considered as an elastic particle but the real cells present visco- or hyper-elastic behavior which have more reliable results in FE simulations.

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