Deconvolution of the Mechanical Effects in Atomic Force Microscopy Material Characterization in Living Cells

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Abstract and Motivation

Abstract

Atomic Force Microscopy (AFM) has been extensively used to determine the mechanical properties of materials ranging from ceramics to soft living tissue. There is an increasing use of AFM for the characterization of biological structures, which have been developed into new diagnostic techniques. However, the effects of cell size, substrate and inclusion presence on AFM measurements have not been exhaustively researched. This study aims to understand these effects through Finite Element Analysis of a size varying cell resting on a glass substrate. The result is a relationship between the height of the cell and the indentation depth necessary for accurate measurements.

Motivation

The proper measurement of a biological tissue's mechanical properties will improve modern diagnostic technics and prosthetic devices.
"Changes in mechanical properties are closely connected to disease and physiological processes."
- Efremov et. al. 2020

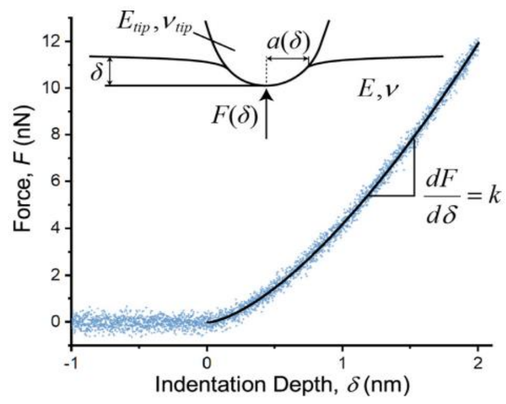

Fig. 1 Force-displacement curve example and geometry of AFM indentation.
- Collinson et. al. 2021

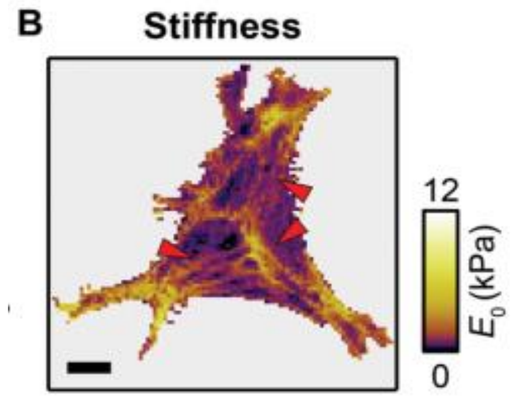

Fig. 2 Stiffness of a cell in different regions. Measured by AFM.
- Schierbaum et. al. 2019

Experimental Setup

We will utilize an isotropic, homogeneous, linear elastic model. The diameter of the cell will be varied as well as the height. A cell has been modeled as a cylinder with elastic modulus $E_{cell} = 4kPa$ and Poisson's ratio $\nu_{cell} = 0.495$. At this stage of research, the material remains linear and isotropic. The probe was modeled as a truncated cone attached to a spring to simulate the real probe stiffness. The specifications of the probe follow Brucker's MLCT-BIO f-AFM probe.
FEA was conducted assuming that the contact between the probe and the cell is frictionless. Displacement control was used, and the reaction force on the tip is used for the analysis.
In the later stages of this investigation, n AFM experiment will be conducted and compared to the FE model for validation.

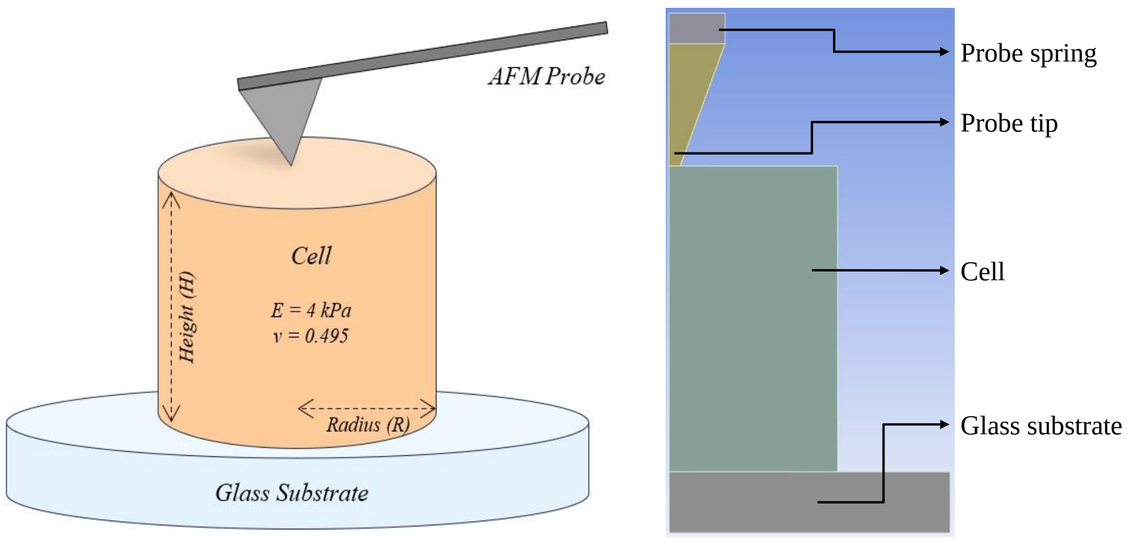

Fig. 3 Experimental setup (right) and FEA setup for cell with height of 500 nm (left).

The images below show the FEA setup in the Ansys software. It is possible to appreciate the triangular quadratic mesh that becomes fines closer to the indentation area.

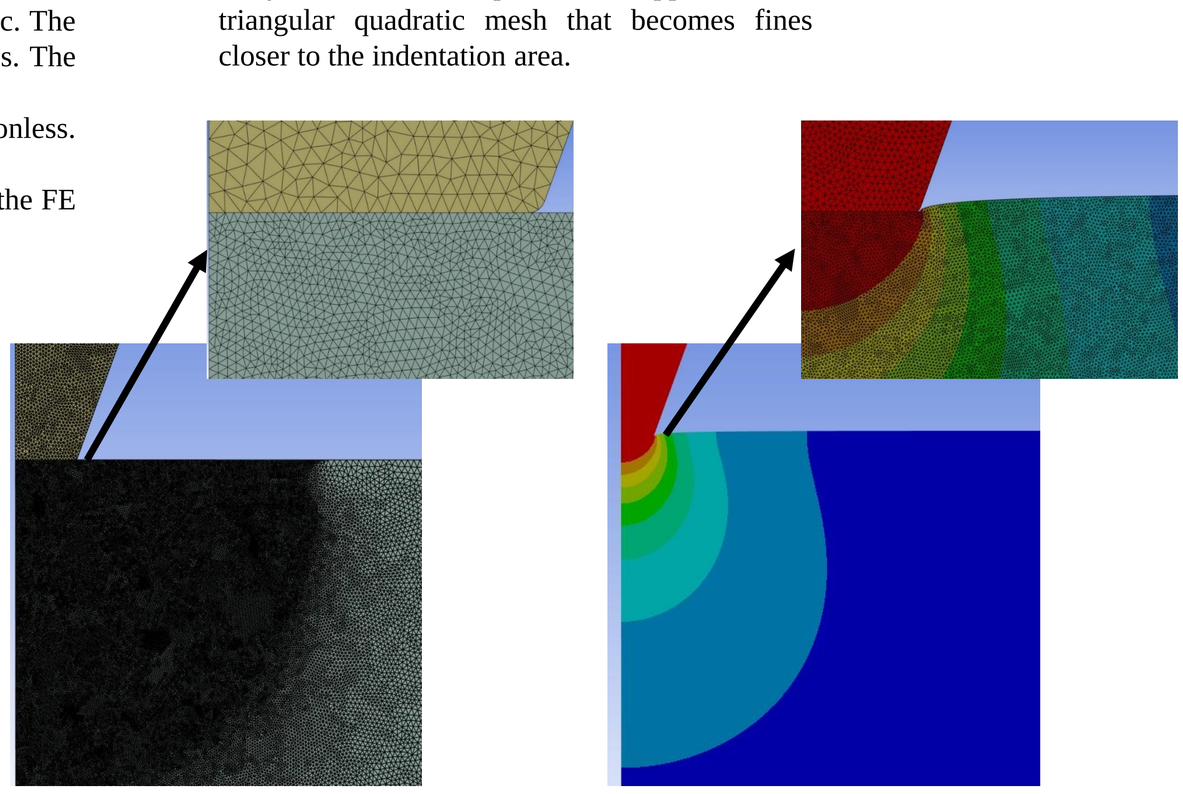

Fig. 4 FEA setup and mesh (left). Deformation contours in force control test (right).

Results

Contact mechanics

Through the equations presented below, the reaction force measured at the top of the probe tip, and the indentation depth, yield information about the contact modulus. Using the DMT contact mechanics model, it is possible to obtain the Youngs modulus of the cell.

$$\frac{1}{E^*} = \frac{1-\nu_{cell}^2}{E_{cell}} + \frac{1-\nu_{tip}^2}{E_{tip}}$$

$$d = a\tan\theta \arccos\left(\frac{b}{a}\right)$$

$$F = E^* \tan\theta\, a^2 \left[\arccos\left(\frac{b}{a}\right) + \frac{b}{a}\sqrt{1-\frac{b^2}{a^2}}\right]$$

Where 'E*' is the effective modulus of the contact, 'b' the tip radius, 'Θ' the angle between the tip and horizontal and 'a' the contact radius.

After several experiments, a pattern arose: the precise measurement of elastic modulus seems to depend on the indentation depth and cell height. Through linear interpolation I obtained the cell height values where the elastic modulus reached 4000 Pa (the expected value.) As a result, a plot was created with the relationship between the height of the cell and the indentation depth necessary for accurate measurement.

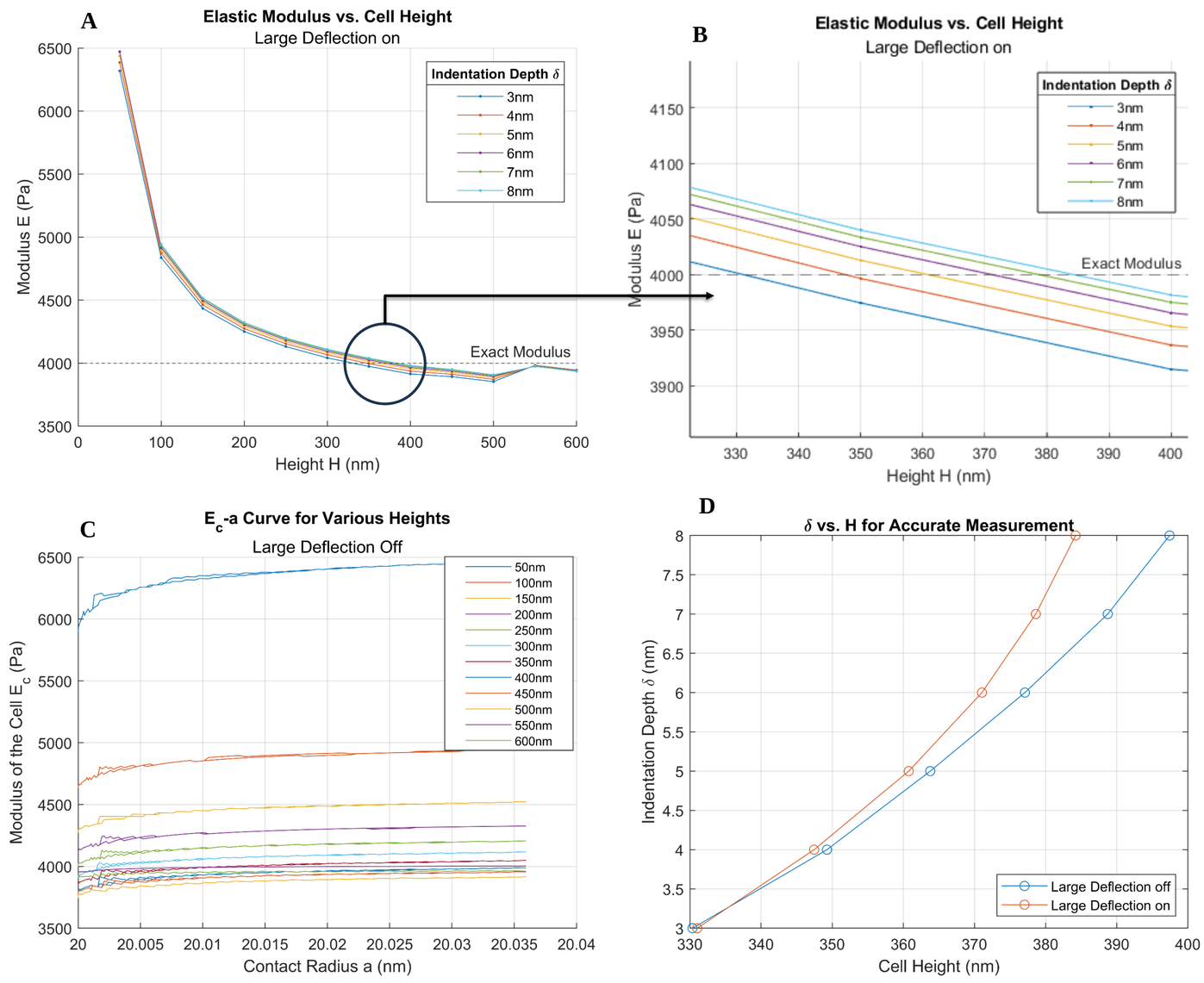

Fig. 5 A) Average measured elastic modulus as a function of cell height. B) Intersection point with expected elastic modulus (from image 5A.) C) Elastic modulus for several cell heights as a function of contact radius. D) Cell height and indentation depth for accurate measurement of original modulus.

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