COMPUTATIONAL INVESTIGATION OF POWER-LAW BEHAVIOUR OF CELLS UNDER AFM CONDITIONS

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Introduction

A mechanical behaviour called power-law (PL) rheology is an intrinsic feature of cell structure when responding to mechanical stimuli. Several models have been proposed to describe spatial and temporal aspects of cell responses. However, they treat cells as spring-dashpot viscoelastic materials while experiments show that PL rheology has been associated to the cytoskeleton (CSK) dynamics. Cell rheology studies provided insight into localised cell relaxation but did not investigate how a whole cell spatially equilibrates in response to stress [Rosenbluth, 2008]. Here, we evaluate the applicability of power-law rheology with a finite element multi-structural model in the context of atomic force microscopy (AFM) in adherent cells for stress propagation phenomena.

Methods

A biomechanical model of the cell, composed of a nucleus, cytoplasm, cortex, microtubules, and actin bundles [Barreto, 2012] was integrated with the material law associated with PL rheology using the finite element method for time-domain viscoelasticity defined in Abaqus:

$$G(t) = G(1)t^{-\alpha} \qquad (1)$$

where t is time in seconds, α is the PL exponent ($0 < \alpha < 1$) and $G(t)$ is the shear modulus. Prony-series coefficients were used to fit the PL relationship defined in Eq. (1) considering $G(1)=100Pa$ [Zhou, 2012] and therefore, extending the time domain. Prestress defined in the actin bundles of our model, is linked to both cell stiffness and PL exponent [Kollmannsberger, 2010]. The viscoelastic behaviour defined in Eq. (1) was used for the cytoplasm of the cell and the remaining elastic properties of the CSK were used as in Barreto, 2012. A bead was modelled to apply a displacement of 0.5µm in compression and was held constant for 15sec after which the bead was retracted to its original position.

Results

Upon indentation, high values of minimum principal strains are located under the bead affecting the nucleus, and at the end nodes of the CSK due to actin contractility. When holding the indentation for 15sec, the force decreased ~25% with the bead on the top of nucleus, showing that we measured force–relaxation (Fig. 1). The equilibration time of the cell increases with the instantaneous elastic modulus and the applied displacement. Whole cell force and relaxation times depend on the position of the indenter on the top of the cell (Fig. 1). The results suggest that the physical mechanism for the different relaxation times in different positions in the cell is related to the spatial heterogeneity of the CSK and not with the position of the nucleus.

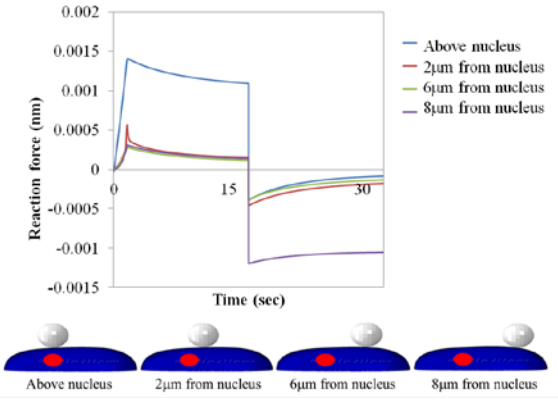

Figure 1: Force and relaxation times of whole cell for different indentation points using α=0.1

Discussion

We investigated the usefulness of this model for cell incorporating the material behaviour associated with power-law under AFM. The results suggest that the origin of different relaxation times is due to the structural presence of interconnected CSK fibres. We were capable to predict whole stress propagation in cells and gain insight into CSK dynamics. This way we can have future indication of remodelling processes.

References

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