JOURNAL OF THE MECHANICAL BEHAVIOR OF BIOMEDICAL MATERIALS ▮ (▮▮▮▮) ▮▮▮–▮▮▮

Available online at www.sciencedirect.com

ScienceDirect

www.elsevier.com/locate/jmbbm

Research Paper

Structural finite element analysis to explain cell mechanics variability

*Sara Barreto, Cecile M. Perrault, Damien Lacroix**

INSIGNEO Institute for In Silico Medicine, Department of Mechanical Engineering, University of Sheffield, Mappin Street, Sheffield S1 3JD, United Kingdom

ARTICLE INFO

Article history:
Received 5 July 2013
Received in revised form
22 November 2013
Accepted 26 November 2013

Keywords:
Finite element analysis
Cell model
Phenotype
Actin cortex
Cytoskeleton
Material properties

ABSTRACT

The ability to model the mechanical responses of different cell types presents many opportunities to tissue engineering research to further identify changes from physiological conditions to disease.

Using a previously validated finite element cell model we aim to show how variation of the material properties of the intracellular components affects cell response after compression and shearing. A parametric study was performed to understand the key mechanical features from different cell types, focussing on specific cytoskeleton components and prestress.

Results show that actin cortex does not have a mechanical role in resisting shearing loading conditions. The sensitivity analysis predicted that cell force to compression and shearing is highly affected by changes in cortex thickness, cortex Young's modulus and rigidity of the remaining cytoplasm. Variation of prestress affects mainly the response of cells under shear loads and the model defines a relationship between cell force and prestress depending on the specific loading conditions, which is in good agreement with in vitro experiments.

The results are used to make predictions that can relate mechanical properties with cell phenotype to be used as guidelines for individual cytoskeletal structures for future modelling efforts of the structure–function relationships of living cells.

© 2014 Published by Elsevier Ltd.

1. Introduction

Theoretical models can be used to predict how the contributions of deformable intracellular components are integrated to determine the overall balance of mechanical forces within the cell (Barreto et al., 2013; Ohayon and Tracqui, 2005).

Mechanical response of cells is dependent on its type, physiological conditions, and mechanical environment. Distinct mechanical properties have been measured for different cell types, which can be related to their specific role in a tissue (Wood et al., 2012; Slomka et al., 2011; Huang et al., 2005). These mechanical differences happen either in different parts of the cell (Bausch et al., 1998) or during distinct cellular processes in the same cell type. Such differences are normally associated with the arrangement of the cytoskeleton (CSK) components in certain locations (Wood et al., 2012; Huang et al., 2005). Typically, actin is enriched in the edges of cells and comprises the cell cortex, whereas microtubules, intermediate filaments and deep actin fibres are predominantly located in the middle of the cell around the nucleus (Deguchi et al., 2006).

*Corresponding author. Tel.: +44 114 2220 156.
E-mail address: d.lacroix@sheffield.ac.uk (D. Lacroix).

1751-6161/$ - see front matter © 2014 Published by Elsevier Ltd.
http://dx.doi.org/10.1016/j.jmbbm.2013.11.022

Please cite this article as: Barreto, S., et al., Structural finite element analysis to explain cell mechanics variability. Journal of the Mechanical Behavior of Biomedical Materials (2014), http://dx.doi.org/10.1016/j.jmbbm.2013.11.022

Concentration, organisation, and type of cytoskeletal polymers, that define the mechanical properties of a whole cell, are expected to vary widely among cell types and dictate not only phenotypic but also physiological conditions of cells. In terms of cell rigidity for different phenotypes, mechanical characteristics of cells are dependent on the physical properties of the tissue of origin, and therefore associated with a cell function. Examples include different ranges of Young's modulus found for different cell types: Young's modulus in the range of 0.2–1.4 kPa measured for leukemia myeloid cells (HL60), a type of leukocytes (Rosenbluth et al., 2006); 1.3–7.2 kPa for human umbilical vein endothelial cells (HUVECs) (Mathur et al., 2004); 3–12 kPa for 3T3 fibroblasts found by Rotsch et al. (1999) with AFM mechanical testing; 14–21 kPa for chondrocytes (Nguyen et al., 2010); 0.4–20 kPa for osteoblasts (HBMSC), measured by Simon et al. (2003); and cardiocytes 90–110 kPa (Mathur et al., 2001).

For example, in terms of the distribution of CSK components found in different cells, nerve cells have single actin filaments without stress fibres, whereas myocytes and osteoblasts have actin bundles organised into stress fibres with different thickness (Gardel et al., 2004). Differences in the mechanical behaviour of alveolar cells could be due to phenotypic differences in biomechanical properties of their microstructure. The observed localised variation of alveolar deformation suggests that mechanical heterogeneity might play a central role in mechanotransduction and intercellular signalling (Azeloglu et al., 2008). Lymphocytes are known to change their rigidity from rigid spheres, that resist shear stress and protect from damage in circulation, into a highly deformable state for extravasation through the endothelial cells to the injury site (Brown et al., 2001). Other cellular processes, such as differentiation of stem cells, have been discovered to undergo massive structural changes upon changes in the cell state or function and involve nuclear changes needed for gene transcription and differentiation (Pajerowski et al., 2007). Also non-native processes, such as cancer progression, have been associated with changes in the rigidity of cells and with changes in the biomechanical environment of cells (Yu et al., 2011). This variability in cell mechanical properties adds a degree of complexity to biomechanical experimental and theoretical studies. Therefore, accurate in vitro phenotypic classification might be only possible in combination with numerical models.

The results from fluorescent images of the actin distribution on the two cell types tested with atomic force microscopy (AFM) (Barreto et al., 2013) showed different spatial arrangement of the actin networks as well as different rigidities for the two cell lines. Based on this observation, we will investigate, with a sensitivity analysis, if there is a relationship between material properties of the CSK and cell rigidity in defining the properties of a cell line that will help to understand the source of mechanical variability.

This will be investigated with a previously developed multistructural cell model (Barreto et al., 2013) using finite element (FE) analysis. The main assumption is that a multistructural model combines continuum and discrete approaches to represent the cell and the mechanical intracellular components of mechanical interest, including the cytoplasm, the actin cortex, the nucleus and the discrete fibres of actin bundles and microtubules. With this model, the first goal is to simulate AFM and MTC experiments, to evaluate the transmission of force inside the cells, and to determine which CSK component resists to specific external load, compression and shearing. The second goal of the study is the sensitivity analysis of the material properties of the cell model to investigate a wider mechanical variation associated with biological changes for different cell types.

This sensitivity analysis will be used to evaluate how alterations in material properties affect model predictions in terms of both rigidity and deformation, to build up the structure–function relationship of living cells. The ultimate goal is to understand which are the important parameters that need to be measured experimentally for: an accurate classification of the cellular mechanical behaviour for cell line; and to identify which biological parameters in cells influence tissue mechanics the most. The ability to model the mechanical responses of different cells may present many opportunities to medical research to identify changes from physiological conditions to disease (Ingber, 2003a; Slomka and Gefen, 2010).

2. Material and methods

2.1. *FE formulation for the adherent cell*

A FE model of an adherent cell with elastic material properties previously developed by Barreto et al. (2013) with Abaqus 6.11 (Simulia), is used in this study. Briefly, the cell model includes the cytoplasm and the nucleus covered by a layer at the cell edge representing the actin cortex and with deep actin bundles and microtubules representing the discrete fibres of the cytoskeleton (Fig. 1). Homogeneous, isotropic and elastic material properties were assumed for all the components and were taken from the literature (summarised in Table 1). Linear elastic properties were assumed for all the cell components, except for the actin bundles. The actin bundles are modelled as truss elements, that only resist tensile loads, with a radius of 12.5 nm (Deguchi et al., 2006). The nonlinear behaviour of the actin bundles was introduced in the model due to the simulation of a prestrained state of the bundles by redefining the stress–strain relationship of the actin bundles by taking into account the initial state of stress

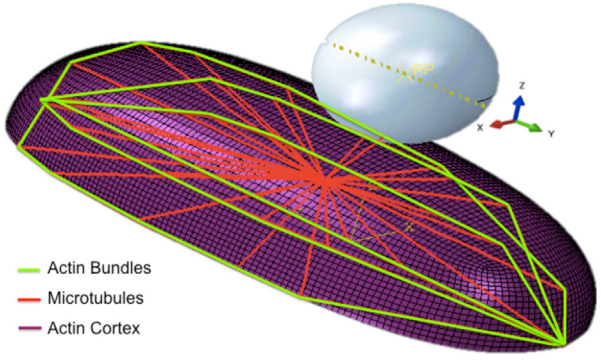

Fig. 1 – Discrete components of the FE cell model, actin bundles and microtubules integrated within the cytoplasm covered by shell elements representing the actin cortex.

Please cite this article as: Barreto, S., et al., Structural finite element analysis to explain cell mechanics variability. Journal of the Mechanical Behavior of Biomedical Materials (2014), http://dx.doi.org/10.1016/j.jmbbm.2013.11.022

Download English Version:

https://daneshyari.com/en/article/7208837

Download Persian Version:

https://daneshyari.com/article/7208837

Daneshyari.com