A FLUID-STRUCTURE INTERACTION MODEL INVESTIGATING THE MECHANISMS SURROUNDING BONE CELL MECHANOSENSATION IN RESPONSE TO FLUID FLOW

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Introduction

It is well established that fluid flow acts as an important biophysical signal in bone cell mechanotransduction. Several in vitro investigations have identified key mechanisms involved in the mechanotransduction process, where it has been proposed that the mechanical environment is monitored by mechanoreceptors on the cell body, such as integrins [Litzenberger, 2010] and primary cilia [Hoey, 2012]. However, precisely how these sensory mechanisms interact with an applied fluid flow stimulus and ultimately contribute to a biochemical response of bone cells remains poorly understood.

This paper outlines a computational model that characterises deformation in an osteoblast cell under laminar fluid flow regimes and investigates the role of focal adhesions and the primary cilium in mediating the response of the cell under a fluid flow stimulus.

Materials and Methods

A fluid-structure interaction (FSI) model is used to characterise the deformation experienced by an osteoblast cell subject to steady-state laminar flow, similar to that applied using a parallel plate flow chamber (Figure 1a). This is carried out using the ANSYS Multiphysics platform through a bi-directional coupling of the ANSYS CFX solver to the ANSYS Structural finite element (FE) solver, allowing the transfer of forces and displacements between fluid/solid domains.

We consider the behaviour of both discrete focal adhesions at the cell-substrate interface (Figure 1b) and the presence of a primary cilium (Figure 1c) under a range of fluid flow regimes. The osteoblast cell is assumed to behave as a Neo-Hookean hyperelastic material, where E = 4.47kPa and $\upsilon = 0.4$, while the perfusion media is assumed to have properties equivalent to water.

Results

It was found that, for an applied fluid shear stress of τ = 1Pa, significant strain amplification occurred at focal adhesion sites (see Figure 1b), while deformation on the cell membrane was relatively small. With the inclusion of the primary cilium on the cell model, similar strain magnitudes could be observed at the base of the primary cilium, however, these occurred upon application of a much lower fluid shear stress of τ = 0.02Pa (see Figure 1c). Furthermore, the strain magnitude at this location dependent on the length of the primary cilium.

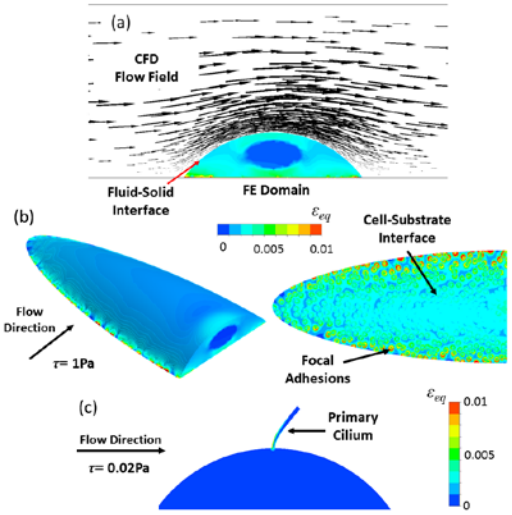

Figure 1: (a) FSI modelling strategy (b) focal adhesion sites and (c) primary cilium.

Discussion

This study highlights that focal adhesion sites and the primary cilium experience much greater levels of stimulation under a fluid flow stimulus than other regions of the cell. This finding has important implications as both these mechanoreceptors have been shown to mediate important cellular responses under *in vitro* fluid flow regimes [Litzenberger, 2010; Hoey, 2012]. We also found that the strain magnitude at the base of the primary cilium was directly affected by its length. It is already known that the primary cilium is capable of adapting its mechanical state by altering its length to become either more or less mechanosensitive [Hoey, 2012]. Importantly, it was shown that the primary cilium was stimulated at very low fluid shear stresses, suggesting it could play a pivotal role in bone cell mechanotransduction.

References

Litzenberger *et al.* Calc Tissue Int **86**:325-32 2010
Hoey *et al.* J Biomech **45**:17-26 2012