MECHANOREGULATION SIMULATIONS USING FINITE ELEMENT MODELS OF WHOLE CELLS

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Introduction

Mechanobiological models can simulate observed patterns of tissue differentiation in many applications; e.g. facture healing and tissue engineering [Lacroix, 2002; Kelly, 2006]. Recent applications use lattice-models representing cells as points [Perez, 2007; Checa, 2010]. In this study, we hypothesised that a mechanoregulation simulation can be performed using an FE model of a whole cell rather than modelling the cell as a lattice point.

Methods

In this implementation, maximum strain on the cell membrane was hypothesised as mechanoregulatory stimulus for cell differentiation. A finite element model of a single cell consisting of continuum components, including a cell membrane, cytoplasm, nucleus, and a cyto-nucleoskeleton network modelled by multiple interconnected tensegrity structures was used (see Fig.1).

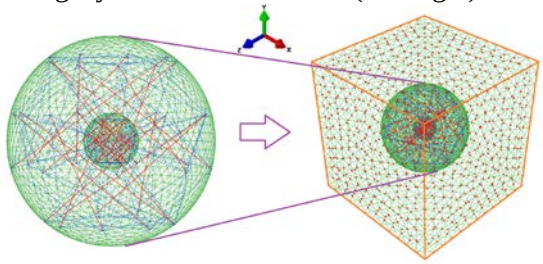

Fig. 1: The FE cell model is located at the centre of each block of tissue.

The threshold cell membrane strains for MSC differentiation to form cartilage and bone were found by computing the cell membrane strain under the threshold tissue octahedral shear strain γ of Prendergast et al (1997). If fluid flow is ignored, then the mechanoregulatory stimulus is $S = \gamma/a$ where a is a constant. Prendergast et al (1997) proposed that the mechanical environment in the tissue has a controlling influence on tissue differentiation as follows: high levels of stimuli ($S \geq 3$) promote fibrous tissue formation; low levels of stimuli ($S \leq 1$) favour bone formation; and cartilage is formed for intermediate levels of stimuli ($1 < S < 3$). An iterative simulation was performed on a piece of tissue that contains 8 cells (2×2×2) with its top surface strained along the x-axis. Simulations were started with mesenchymal stem cells in granulation tissue (iteration 1 in Fig. 2). Material properties of each block were updated according to the value of S calculated at the end of each loop.

Results

After the first iteration, all granulation tissue disappears with both fibrous tissue and cartilage forming (iteration 2 in Fig.2). Then, each of these tissue types continues to differentiate along an osteochondral pathway, eventually turning into bone at the fourth iteration (iteration 4 in Fig. 2).

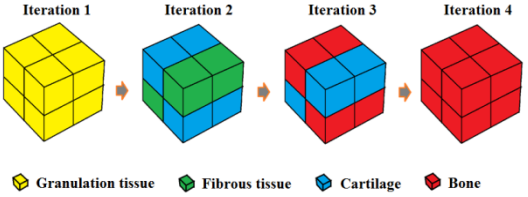

Fig. 2: Tissue differentiation using cell membrane strain as the mechanoregulatory stimulus.

Discussion

This work demonstrates that it is feasible to use whole-cell FE models to compute stimuli for mechanoregulation simulations. The approach using whole cell models offers the opportunity of using cell experiments to directly establish thresholds for mechanoregulation. It also widens the spectrum of applications of mechanoregulation models in the advances of mechanobiology and tissue engineering. However, a current problem is that massive computational resources are required to solve realistic problems.

References

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