

# A lattice-based modelling approach to investigate the effect of loading on re-vascularization during tissue repair. Application to a bone/implant interface

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## Introduction

Understanding the formation of a capillary network is critical for any bone reparative strategy since sufficient supply of oxygen and nutrients is critical for bone cell survival and proliferation. In this study we have developed a discrete model to simulate angiogenesis and incorporated into an algorithm for the simulation of tissue repair.

## Methods

A mechanoregulation model for tissue differentiation based on fluid flow and shear strain [1] was combined with a stochastic model for cell migration and proliferation [2]. The mechanical environment was determined using finite element analysis and a lattice model was used for the simulation of cell activity (Fig. 1). Capillary formation was modelled by the random movement of endothelial cells at the capillary tips biased by the concentration of vascular endothelial growth factors. The effect of vascularity on the tissue differentiation process was included considering that at low mechanical environment cartilage instead of bone will form if there are no blood vessels within a distance from the differentiating tissue, since osteogenic precursor cells in regions of poor vascularity have been shown to follow a chondrogenic rather than an osteogenic differentiation pathway [3]. The model was applied to the regenerating tissue in a bone/implant interface under shear. Simulations were performed under force-control and displacement-control conditions.

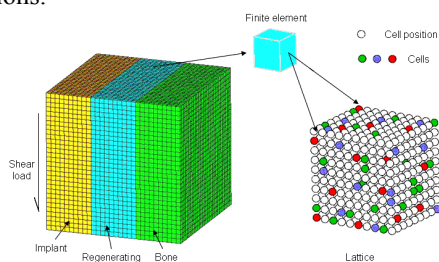


Fig. 1. Lattice contained inside each finite element for the simulation of cell activity.

## Results

The simulation predicted capillary networks with a realistic structure (Fig. 2). Under force-control conditions, with a shear force to obtain an initial relative displacement between the bone and the implant of 100  $\mu\text{m}$ , initially mesenchymal stem cells (MSCs) were predicted to differentiate into fibroblasts. As the repairing tissue started to stiffen, the mechanical stimulus decreased and chondrogenesis was favoured. When the mechanical stimulus was sufficiently low, MSCs surrounding the existing capillaries were predicted to differentiate into osteoblasts. Heterogeneous distributions of cells were predicted (Fig. 3). Under displacement-control conditions, with a fixed relative displacement between the bone and the

implant of 100  $\mu\text{m}$ , a very poor vascular network developed and a fibrous tissue layer formed at the bone/implant interface.

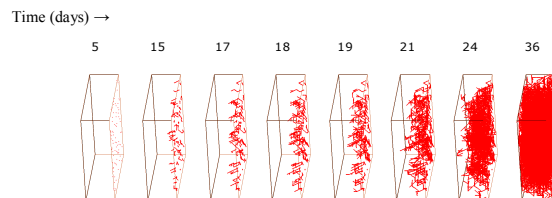


Fig. 2. Capillary network formation in the regenerating tissue between the bone and the implant under force-control conditions.

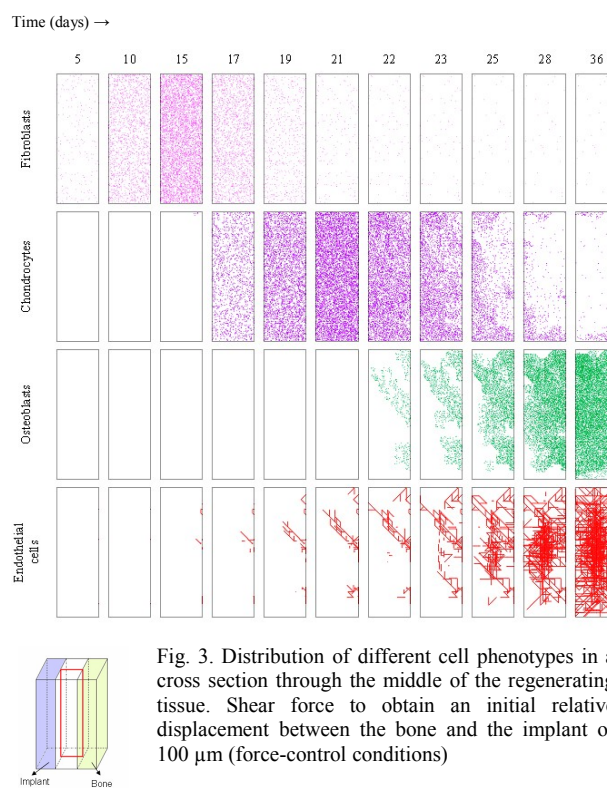


Fig. 3. Distribution of different cell phenotypes in a cross section through the middle of the regenerating tissue. Shear force to obtain an initial relative displacement between the bone and the implant of 100  $\mu\text{m}$  (force-control conditions)

## Discussion

Tissue differentiation patterns were predicted to be influenced by capillary network formation. The model will have to be continuously tested by attempting to simulate tissue differentiation in different circumstances, however it does suggest that it can predict the coupling between angiogenesis and tissue differentiation, and could be used as a tool in tissue repair and tissue engineering strategies.

## References

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2. Pérez, M. A. and Prendergast, P. J. J. Biomechanics, 40, 2244, 2007.
3. Kanichai, M., Ferguson, D., Prendergast P. J., Campbell, V. A., J. Cellular Physiology, 216, 708, 2008.