

A MATHEMATICAL MODEL FOR CELL/MATRIX GROWTH ON 3D SURFACES USING THE LEVEL SET METHOD.

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INTRODUCTION

The kinetics of in vitro cell growth has been shown to depend on the local surface curvature of the substrate, an observation that lead to the description of curvature-controlled cell growth [1]. Additionally, Rumpler et al [1] proposed a 2D computational model capable of capturing in vitro cell growth with a curvature-driven velocity advecting the cell surface. Inspired by the results of Rumpler et al, [1], the work presented here aims to extend their model to 3 dimensions to capture 3D in vitro cell growth, in this case applied for cell-seeded open porous scaffolds cultured under static conditions.

METHODS

To account for the curvature dependent nature of the mathematical model, an initial Level-Set function is computed all over the domain, with the zero-level corresponding to the cell/scaffold-culture medium interface. The curvature is computed at each time step and subsequently the Level-Set function is advected with a certain velocity (Figure 1). This velocity is a constant plus the curvature, resulting in a layer by layer growth as well as an acceleration of cell growth where the curvature is high. In this prospective study, the value of the constant part of the velocity was chosen to be independent of the actual in vitro culture conditions. The model was implemented in FreeFem++ (<http://www.freefem.org/>), a dedicated language for Finite Element Analyses based on C++.

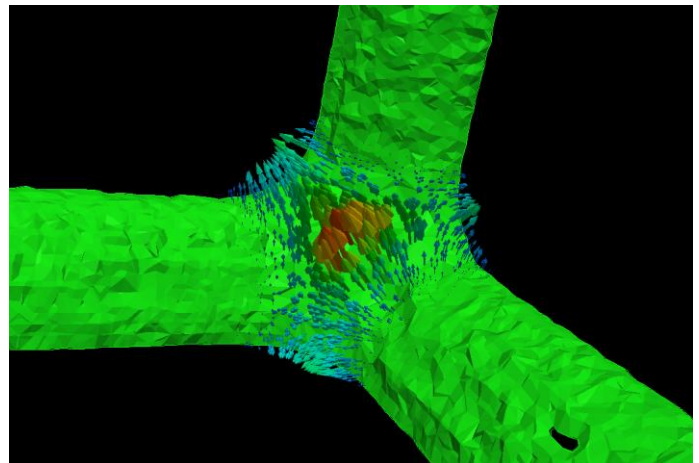


Figure 1 : Close-up on the Cell/Matrix interface and advecting velocity to illustrate the curvature-controlled cell growth principle

RESULTS

In a first step, this model was applied to simulate cell growth in a cell-seeded regular scaffold with a squared unit cell (Figure 2) cultured under static conditions. A preliminary qualitative assessment was carried out using in vitro experimental data [2]. The model was able to simulate 3D cell

growth in this scaffold. In a second step six other regular scaffold geometries (with unit cells ranging from hexagonal to triangular [3]) were implemented (Figure 3). The model was able to predict cell/matrix growth under static conditions in these six additionally tested geometries with a same time scale factor for all geometries and pore sizes.

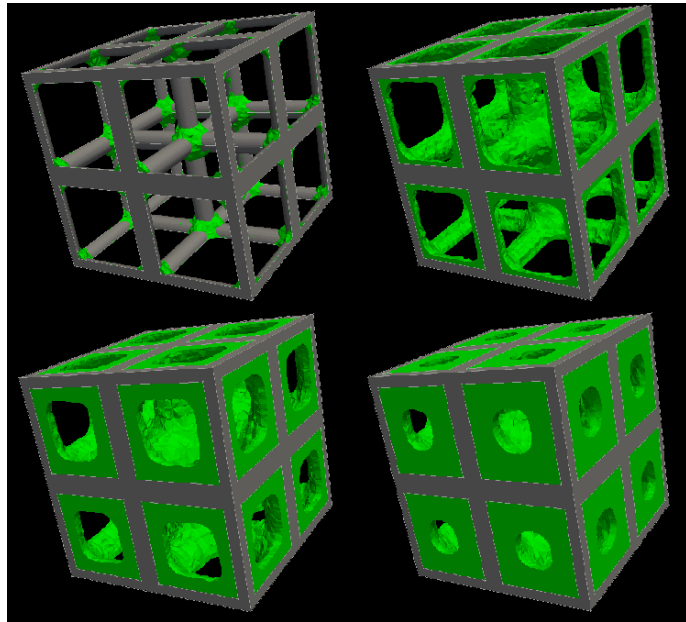


Figure 2: Cell growth over time in a cell-seeded scaffold with a squared unit cell cultured under static conditions

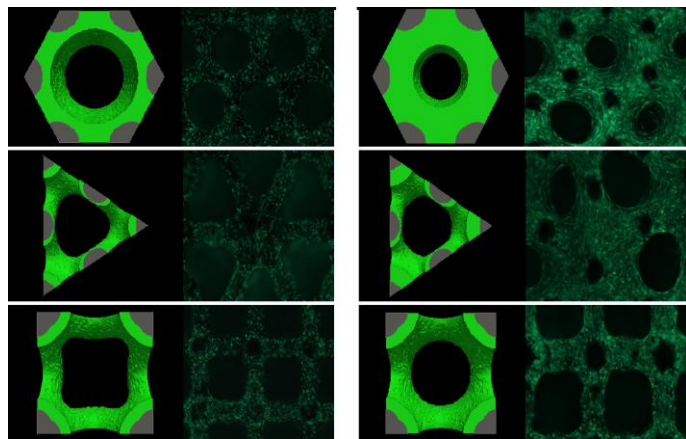


Figure 3: Cell growth on different scaffold geometries (hexagon, triangle and square) as observed from the top of the scaffold. Columns 1 and 3 show the calculation results and columns 2 and 4 show the experimental results (titanium scaffolds seeded with human periosteal derived stem cells) at 7 days (columns 1 and 2) and 14 days (columns 3 and 4).

The proposed model is an interesting computational tool to investigate the behavior of 3D cell growth in regular scaffolds with different unit cell geometries. In a next step, the velocity of cell growth will be made dependent on specific culture conditions (e.g. fluid flow for perfusion culture), and the computational tool can then be used as a tool to design optimal combinations of in silico scaffold geometry and culture conditions to, e.g., maximize in vitro cell growth.

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REFERENCES

- [1] Rumpel M. *et al* J. Roy Soc Interface, 2008; [2] Papantoniou I. *et al*, in preparation, 2012 ; [3] Van Bael S. *et al* Acta Biom, 2012.

DISCUSSION