Description for a problem studied at the UK Mathematics-in-Medicine Study Group Loughborough 2008
< https://mmsg.mathmos.net/uk/2008/orthopaedic-tissue/ >

Modelling of the Growth of Engineered Orthopaedic Tissue in Zero Force and Variable Load Environments

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Mathematical and computational modelling are important tools for improving in vitro cultivation systems in order to obtain biologically and mechanically competent engineered tissue equivalents for potential clinical use (Sengers et al. 2007). Our aim is to analyze the role of the different processes during in vitro tissue growth such as nutrient transport and consumption, cell proliferation and moving, extra-cellular matrix (ECM) secretion, scaffold degradation, interaction forces between cells, ECM, scaffold, mechanical stimulation and to create mathematical model capable to predict tissue properties.

To build our model we select experimental data from Vunjak-Novakovic and Obradovic experiments (Obradovic et al. 2000) for creation of engineered cartilage by culture of articular bovine chondrocytes on biodegradable polymer scaffolds in bioreactors. In these works suitable experimental data for time evolution of cells and main component of ECM - Glycosaminoglycan (GAG) are available.

Nutrient consumption, ECM synthesis and deposition, expansion of the construct depends of cell concentration, which changes with time. Thus the main problem to be solved is to create model which could predict properly time evolution of space cells distributions and expansion of construct volume. This have to be done by using equations for balances of the forces acting between cells, ECM, scaffolds and obtaining from them displacement and velocities of cells. Following problems are found here:

- Having in mind that the number of cells is constant and cells are firmly attached to GAG and scaffold to find if the local cell density changes only due to stretch of corresponding part of the construct or there are additional mechanisms.

- To find out when synthesis of ECM at given place could increase concentration of ECM at this place or construct may start to expand and in this way to have increase of the size, not of the local concentration.

- To discuss proper application of novel Volokh growth model (Volokh 2004, Volokh and Lev 2005) according to which force which causes construct expansion is proportional to difference between GAG concentrations before and after tissue expansion.

- Our future work involves activation of GAG production processes by the application of cyclic loads to tissue constructs; again the problem of coupling of stresses, strains and construct growth are central to realistic modeling of the temporal development of the tissue

We are particularly interested in formulations that use Lagrangian frame of reference and Blatz–Ko constitutive equations as in Ambrosi and Mollica 2002.

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