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# INFLUENCE of the STRESS STATE on IN VITRO TISSUE GROWTH

## Mathematical Modelling and Simulation of Mechano-Physiological Processes

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In vitro tissue engineering has been investigated as a potential source of functional tissue constructs for cartilage repair, as well as a model system for controlled studies of cartilage development and function. Among the different kinds of devices for the cultivation of 3D cartilage cell colonies, we consider here scaffold-based bioreactors. It is well known that the metabolic activity of cartilage cells (CCs) is deeply influenced by the stress state to which they are exposed in the culture, this being able to favour cell proliferation or extracellular matrix (ECM) secretion. As a matter of fact, in the culture, CCs undergo a variety of mechanical loading conditions, depending on their location relatively to the scaffold or the surrounding biomass.

We investigate the idea [1] that when cells are in a local planar condition –as for example when they are initially seeded in a thin layer or are exposed to the shear stress exerted by a perfusion fluid- they tend to assume an ellipsoidal shape, orienting themselves along a polarization axis. Such an anisotropic conformation enhances the probability that the cell enters mitosis, the polarization axis representing the direction along which the cell will divide into two daughter cells. In contrast, when cells lay in the biomass bulk, they sense an isotropic condition, triggering ECM production, provided that enough nutrient has filtered through.

According to the above conceptual framework, in this talk a novel mathematical model of the mechanophysiology of engineered tissue growth at the microscale level is presented. The growing tissue construct is described as a mixture [2,3] of CC populations in proliferating, biosynthesizing or quiescent states and of ECM solid components immersed in an interstitial fluid [4]. Cell and ECM fractions dynamically evolve according to the cell metabolic response driven by time and space dependent biomechanical processes and nutrient availability. The resulting mathematical model is constituted by a coupled system of partial differential equations describing the diffusion process of the nutrient and the cellular metabolic response driven by biomechanical processes in a poroelastic multiphase medium [5]. Cellular response results into mass production that, in turn, determines the updated stress-state of the biomass, until the growth process is terminated.

Several simulation results accompanied by a stability analysis will be discussed, illustrating the role of the fundamental parameters and the possibility to tune them in order to enhance culture performance.

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