**191a Mass Transfer Rates and Initial Conditions Modulate the Growth Rates and Structure of Bioartificial Tissues**

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Mass transfer limitations lower the availability of nutrient and growth factors in the interior of scaffolds used for tissue engineering applications. The extent of nutrient or growth factor depletion inside a scaffold will depend not only on the cell density, but also the cell phenotypes and the rates at which nutrients and growth factors are metabolized and processed. Finally, it has been observed that the operating conditions of a bioreactor and the initial spatial distribution of seed cells can have significant effects on the growth rates and structure of developing tissues.

In order to investigate the relative importance of these processes and identify the dominant system parameters, we have developed a comprehensive model that describes how populations of cells with multiple phenotypes migrate, interact and grow in porous scaffolds under conditions that lead to significant transport limitations. This comprehensive model consists of (a) partial differential equations quantifying the simultaneous diffusion, convection and consumption of nutrients and growth factors; and (b) a discrete model that tracks the migration, collisions and proliferation of heterogeneous cell populations on a 3D cubic lattice. The local concentrations of nutrients or growth factors are computed and used to modulate cell migration speeds, persistence, and division times. These parameters are different for each cell phenotype. The model also allows for cell death when the nutrient or growth factor concentrations drop below a certain level that can be different for each phenotype.

Simulations are carried out to determine how the cell phenotype, the initial seeding pattern and the operating conditions of the bioreactor affect the tissue growth process. Our results identify the key parameters that lead to severe transport limitations and prevent the full development of tissues. More interestingly, our simulations show that large differences in the migration speeds or metabolic requirements between cell subpopulations lead to the formation of stratified tissues, where cells are segregated according to their phenotype. Finally, our model identifies possible mechanisms through which the spatial distribution of seed cells and the initial conditions of the process can influence the growth rates and structure of developing tissues. The simulation results are discussed to provide guidelines for the optimal design of tissue growth experiments.