THE ROLE OF THE MICROENVIRONMENT FOR MICROBEAD CELL EXPANSION: MECHANICAL CHARACTERIZATION EMPLOYING AN INDIVIDUAL-CELL BASED MODEL

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Introduction

In cell-culture systems, the biomechanical properties of the microenvironment are of great concern as they can strongly influence cell behavior and even differentiation [1]. On the other hand, tissue engineering applications require 3d cell culture systems which offer a well-controlled cell environment and can accommodate a large number of cells [2].

In microcarrier systems, high densities of cells can be seeded and expanded on microbeads [3]. The biophysical properties of the microbead determine the physical microenvironment of the cells [4].

Using individual-cell based models (IBMs) , we study the relationship between microbead design characteristics and the mechanical microenvironment to which cells are exposed.

Methods

A lattice-free IBM is used which considers cells as deformable spherical particles. At each time point, the displacement of the cells is calculated from the equation of motion, which is derived for cells that move in a low-Reynolds number environment [5].

In the IBM, cells are considered deformable elastic spheres with a contact area dependent contact force described by the Johnson-Kendall-Roberts (JKR) potential.

The IBM describes the cell cycle of growing cells from a purely morphological perspective by splitting the cell cycle into two distinct phases: cell volume growth and cytokinesis.

In the simulations, cells are randomly seeded on the microbead at a fixed seeding density, and exponential cell growth is simulated until confluency is reached.

Results

The combination of elastically stored energy in the JKR potential and energy dissipation through drag forces determines the overall cell mechanical stress which changes due to microenvironmental conditions.

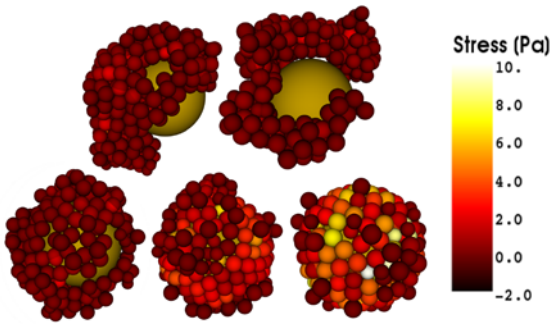

Figure 1: Cell Expansion on microbead for different cell-bead adhesion strengths: K_a = 2.5e-6, 5e-6, 10e-6, 20e-6 and 40e-6 J/m^2.

Simulations were performed for different levels of cell-bead adhesion energy (Figure 1). Higher values of cell-bead adhesion strength lead to higher mean compressive stress values and a higher rate of stress increase around the point of confluency.

Discussion

In this study an IBM was developed that describes cell expansion on spherical microbeads. Simulations reveal that the cell-bead adhesion energy, which is influenced by the adhesive coating applied to the carrier, is a strong determinant for the magnitude of mechanical stresses on the cells.

In general, the simulations give a proof of principle that a large biological heterogeneity is not required to result in a strongly heterogeneous mechanical microenvironment. Purely spatial and mechanical properties of the carrier system can result in localized differences in mechanical stress on the cells.

References

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