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MULTI-OBJECTIVE OPTIMIZATION OF COST-EFFICIENT NEOTISSUE GROWTH INSIDE 3D SCAFFOLDS USING EVOLUTIONARY ALGORITHMS

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Summary: Introduction
Tissue engineering is a fast progressing domain where solutions are provided for organ failure or tissue damage. Computer models can facilitate the design of optimal production process conditions leading to robust and economically viable products. We developed a computational model describing the neotissue growth (cells + their ECM) inside 3D scaffolds in a perfusion bioreactor [1]. Here we apply multi-objective optimization (MOO) to maximize neotissue growth whilst minimizing the cost coming from medium refreshment and associated labor [2].
Methods
The model describes neotissue growth inside 3D scaffolds in a perfusion bioreactor with the speed of said neotissue growth depending on the flow-induced shear stress, curvature and the local concentrations of oxygen, glucose and lactate. Culture conditions can be varied by changing the frequency of medium refreshments and changing the amount of medium that is replaced at every refreshment step. In a single objective optimization study [1], it has been shown that frequent refreshment with a full medium replacement yields the highest neotissue volume. However, these frequent refreshments lead to a very high culture cost. In MOO, the goal is to reach a compromise between conflicting objectives (i.e. maximal neotissue volume and minimal cost). Here, we used four evolutionary algorithms: genetic algorithms, particle swarm optimization, multi-objective evolutionary algorithm based on decomposition, and differential evolution. In each algorithm, the MOO problem is solved using three different candidate solutions. Results are visualized by computing the Pareto-frontier, which is the border between suboptimal and infeasible solutions.
Results and Discussion
According to the obtained Pareto front, the most cost effective answer to the problem results in 84.5% filling of the scaffold in 21 days of culture at a cost of 46 euro. This point corresponds to refreshing the medium every 90 hours by 99%. There are other interesting points on the Pareto front resulting in higher neotissue filling, but at a dramatically increased total cost. The proposed optimal refreshment strategy now needs to be investigated in the laboratory to verify the model predictions.

Reference

[1] Mehrian M. et al., Biotech & Bioeng, revised version submitted (2017).
[2] Olofsson S. et al., ESCAPE Proceedings (2017).