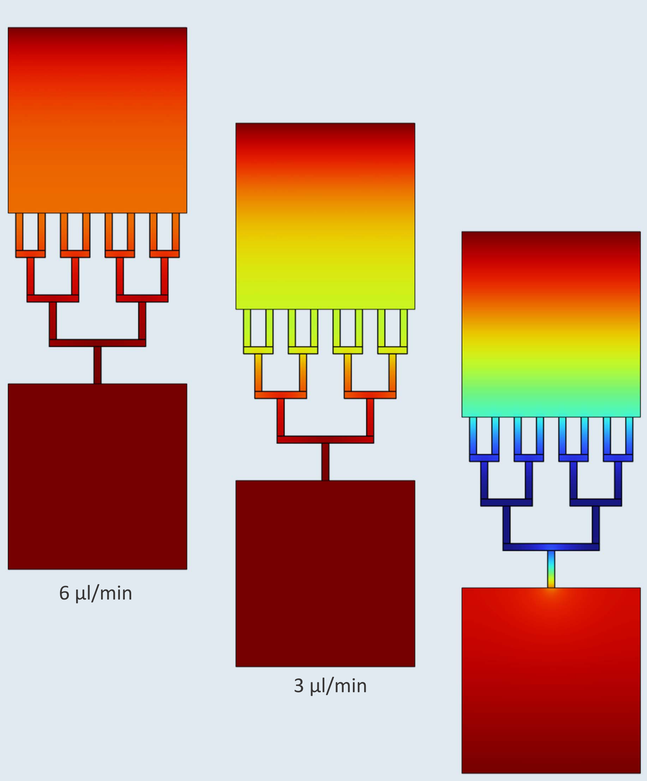

Optimization of the Oxygen Supply in Dynamic Cell Cultures

In this study, the oxygen supply of living cells inside scaffolds with different channel structures was simulated and fundamental rules for optimal supply were derived.

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Introduction

In artificial tissue regeneration living cells are often cultivated in scaffolds with a complex channel structure. A well-known problem is that cells colonize the outer areas of the scaffold but do not grow into the interior. As a possible cause an insufficient supply of oxygen to the cells in the interior regions of the scaffold is discussed[1]. In order to improve the oxygen supply, the cells' nutrient medium is usually pumped through the scaffold in a dynamic cell culture.

Therefore, in this study the oxygen supply in different channel structures at different flow rates was investigated using COMSOL Multiphysics®. It was assumed that the scaffold was completely populated with cells and the local balance of consumed and newly supplied oxygen was calculated for different flow rates. From the simulations basic principles were derived how channel structures should be arranged in scaffolds so that optimal cell colonization is possible.

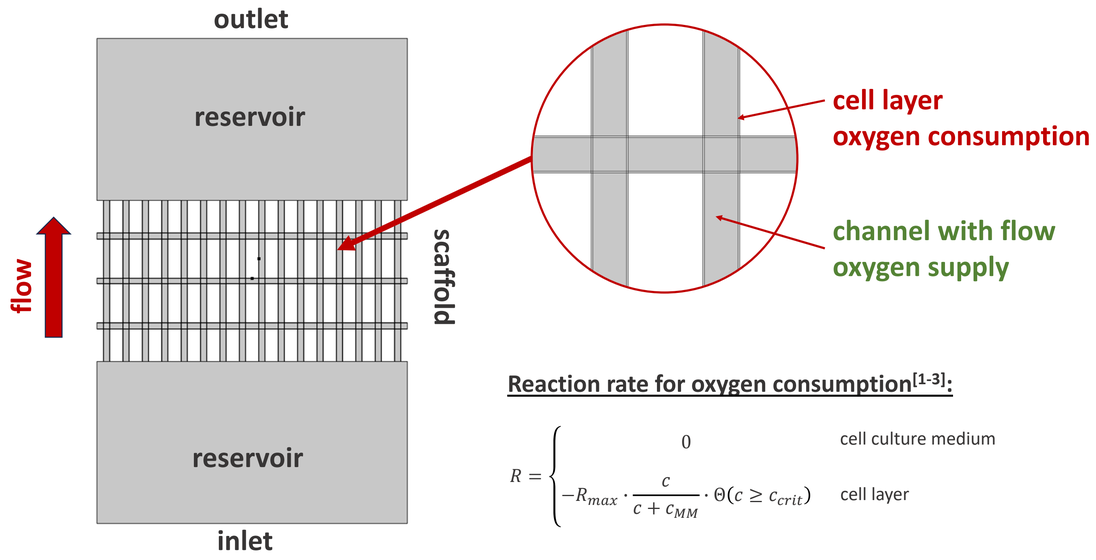

Figure 1. Structure of the simulation box. The system consists of two large reservoirs with the medium inlet at the bottom and the outlet at the top. In between there is the scaffold with the channel structure to be examined. The channel width of the scaffolds shown here is 200 µm.

Methodology

The simulations were carried out by combining the "*Laminar Flow*" and "*Transport of Diluted Species*" interface. It was assumed that the walls of the channel structure were completely populated with cells and the balance of supplied and consumed oxygen was calculated. The cells were represented as thin layers in the channel structure. Oxygen consumption was simulated in this layers by assigning a negative reaction rate with Michaelis-Menten kinetics[1-3]. All model parameters were based on osteoblastic cells and are listed in Ref. 1 in detail. The reservoirs above and below the scaffold had periodic boundary conditions on the right and left side. The inlet and outlet were assumed to be far away from the scaffold and set to constant concentration.

Results

The simulations show that without flow a critical undersupply of oxygen inside the scaffold occurs. Therefore, cells cannot colonize the inner areas of the scaffold in a static cell culture. At low flow rates, the undersupplied areas shift towards the outlet, because flow and diffusion counteract each other. Adequate oxygen supply is only achieved at high flow rates at which high shear rates occur. Sufficient oxygen supply at low shear rates is possible through cross channels or branches, since these channels only have low flow velocities and the oxygen supply occurs through diffusion from the nearby main channels. The simulations demonstrate that cross channels or branches are crucial for a physiological supply of the cells.

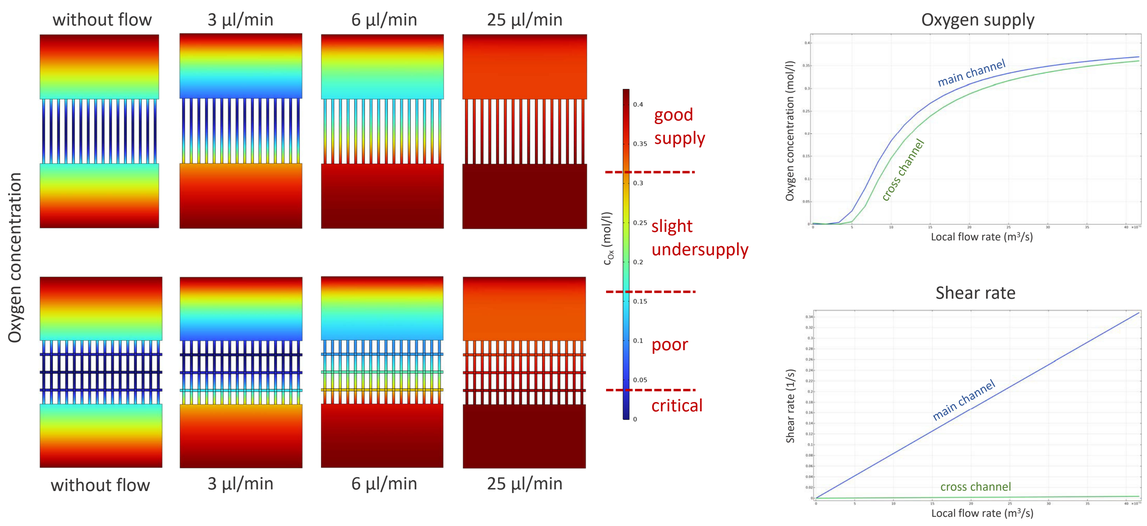

FIGURE 2. Local oxygen concentrations and shear rates in the scaffold for different flow rates. Without flow there is a critical undersupply of oxygen to the cells in the interior regions. For small flow rates the undersupplied area only shifts in the scaffold because flow and diffusion counteract each other. For high flow rates pathological shear rates arise.

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