A Study on Nutrient Mass Transport Through Porous Channeled Flat Sheet Membrane and Prediction of Maximum Scaffold Thickness for Viable Cell Culture (in-vitro) By 3D Modeling for Tissue Engineering Application

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Abstract

Tissue engineering (TE) is a multidisciplinary field involving principles of engineering and life sciences to improve the health and quality of life by repairing, restoring, maintaining, or enhancing tissue and organ function using cells, scaffolds, and growth factors alone or in combination. There are several artificial tissues that are already being used which include fabricated skin, cartilage, blood vessels, bone, ligament etc. The main issues in TE are scaffold fabrication that closely mimics the tissue to be regenerated and nutrient transport in 3D constructs as the proliferating cells themselves act as a barrier. In nature, arterial branching of blood vessels in the tissue of the body plays a critical role to supply nutrients and remove waste. The development of vascularization within the tissue engineered constructs remains a challenge. A common approach for in-vitro tissue engineering is the assembly of a hybrid construct consisting of a porous biodegradable matrix or scaffold to which cells can physically adhere after seeding. This in-vitro tissue precursor is often combined with bioactive molecules to stimulate proliferation and/or differentiation during the in-vitro culture period. Finally, the hybrid construct is implanted into the defect site to induce and direct the growth of new tissue of interest as the scaffold material degrades. Conventional fabrication techniques are not often suitable to control scaffold structure to modulate cell alignment and nutrient transport. Within novel scaffold fabrication processes Phase Separation Micro Molding (PSμM) (see Figure 1) is one of the promising techniques wherein flat sheets with micro patterning (for cell alignment) and interconnected porous structure (for nutrient transport) by phase separation can be fabricated in one step [1]. 3D scaffold is obtained by stacking these flat sheets with required orientation of channels. 3D porous scaffolds so prepared promote new tissue formation by providing interconnected surface and void volume that promotes the attachment, migration, proliferation, and differentiation of cells throughout the region where new tissue is needed. Critical variables in scaffold design and function include the bulk material/s from which it is made, the 3D architecture, surface chemistry and the mechanical properties. Apart from above general scaffold characteristics all cells require access to substrate molecules (glucose, oxygen and growth factor) or otherwise

nutrient permeability. A balance between consumption and local delivery of these substrates is needed in-order to obtain cells survival. In-vitro cultured cells on a TE scaffold are particularly vulnerable for low feed rate due to lack of vascularization. In this work, nutrient diffusion properties of the porous membrane and cell alignment within the channel were analyzed. Based on these results a model has been developed to describe the mass transport and its distribution through single layer and 3D scaffold [2] with respect to different thicknesses and cell density. The model also predicts the time dependent changes in mass transfer considering the growth rate and reducing nutrient concentration in the bulk of the static bioreactor (see Figure 2). These predictions will allow the optimization of bio-reactor cell culture system, for multilayer PSμM construct well within the interior of the TE scaffold.

Reference

[1] One-step fabrication of porous micropatterned scaffolds to control cell behavior, Papenburg B.J., et al., Biomaterials, Volume 28, Issue 11, April 2007, Pages 1998-2009

[2] COMSOL User guide (www.comsol.com)

Figures used in the abstract

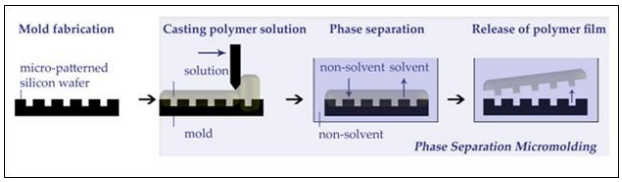

Figure 1: Illustration of Phase Separation Micro-molding (PSμM) flat sheet membrane casting.

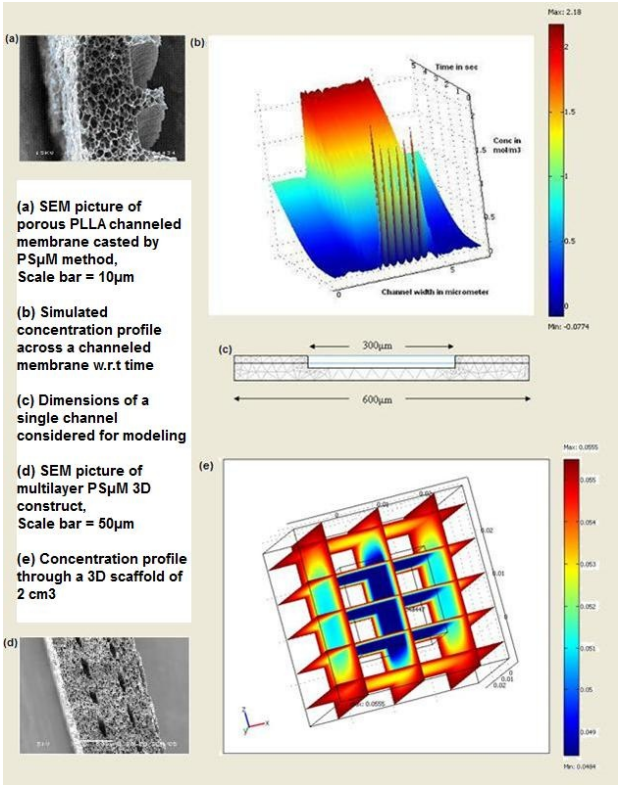

Figure 2: Simulated result of nutrient mass transport through PSμM flat sheet membrane and 3D scaffold.