A Digital Micro-Mirror Device (DMD)-based Stereolithography System for the Microfabrication of Complex, Spatially-Patterned Tissue Engineering Scaffolds

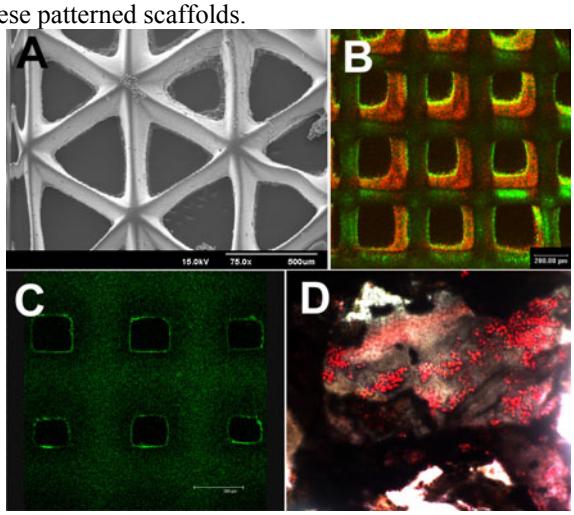
Gazell Mapili[1], Yi Lu[2], Gerry Suhali[2], Shaochen Chen[2], Krishnendu Roy[1]
[1]Department of Biomedical Engineering, University of Texas at Austin
[2]Department of Mechanical Engineering, University of Texas at Austin

Statement of Purpose: Recent advances in developing scaffolds for tissue engineering applications have yet to report methods in creating three-dimensional (3D) constructs that incorporate complex spatial-patterning of extracellular matrix components (ECM) and growth factors. Most 3D scaffolding systems are only capable of differentiating a single progenitor cell population into one specific cell lineage due to either (a) bulk incorporation of bio-factors within the scaffolding matrix or (b) exogenous delivery of hormones, chemicals, or growth factors in culture medium.

A key step towards achieving patterned 3D structures is the development of novel scaffold-manufacturing techniques by which distributed environments can be incorporated in a simple yet precise, reproducible fashion[1]. Here we report a novel, digital micro-mirror device (DMD)-based scaffold fabrication technique that allows precise, pre-designed patterning of multiple molecules and allows generation of complex architectures in a high-throughput, layer-by-layer fashion. This stereolithography system fabricates scaffold structures with pre-designed complex architectures using functionalized, poly(ethylene glycol)diacrylates (PEGDA) and particle entrapped soluble bio-factors. Our system combines a layer-by-layer stereolithography approach with controlled release-concepts to fabricate PEGDA scaffolds for applications in hybrid tissue engineering.

Methods: Pre-designed micro-fabricated scaffolds were created using a layer-by-layer, stereolithography process that combines a DMD chip to a conventional projector and an ultra-violet (UV) light source. Patterns of each scaffold layer were drawn in a series of PowerPoint slides, which were then executed on the DMD chip to generate a dynamic mask. The illuminated areas of the liquid macromer solution were solidified simultaneously under one exposure, while the dark regions remained in the liquid phase. The liquid macromer solution was formulated using PEGDA in PBS and a cyto-compatible, UV photoinitiator, Irgacure 2959. Degradable poly (lactide-co-glycolide) (PLG) particles were added to the macromer solution for entrapment during polymer crosslinking. Surfaces of hydrogels were also modified to be cyto-adhesive by covalently conjugating fibronectin to patterned scaffolds. Methacrylic acid (MAA) was added to the macromer solution prior to photo-polymerization, and the carboxyl groups were converted to amine-reactive esters via NHS/EDC chemistry followed by conjugation of fibronectin. Murine mesenchymal stem cells (mMSCs) were then seeded onto fibronectin-modified scaffolds, and osteogenic medium was added for a 4-week period.

Results / Discussion: The DMD-based stereolithography system successfully fabricated 3D scaffold structures in a layer-by-layer fashion with pore geometries ranging from hexagons, triangles, squares, and honeycombs. Fluorescently-labeled microparticles were effectively entrapped in a pre-designed method, both within a layer and in a layer-by-layer fashion, during the polymer-crosslinking process. Immunostaining and mMSCs attachment show successful fibronectin conjugation to MAA:PEGDA scaffolds when compared to negative control scaffolds. Additionally mMSCs seeded onto these micro-fabricated scaffolds efficiently differentiated into osteoblasts and produced scaffold mineralization, thereby demonstrating the ability of such structures to support cell proliferation and differentiation. We are currently investigating chondrogenesis and adipogenesis using these patterned scaffolds.



A shows a triangular-specific geometry for scaffold porosity. **B** shows entrapped, fluorescent particles in a multi-layered scaffold. **C** shows fibronectin conjugation via immuno-histochemistry. **D** shows scaffold mineralization (black) due to mMSCs differentiation into osteoblasts (nuclei stained red).

Conclusions: We have demonstrated DMD-based stereo-lithography to be a powerful system in creating pre-designed, spatially-patterned scaffolds for applications in hybrid tissue engineering. These micro-fabricated, spatially patterned scaffolds could ultimately consist of intricate architectures that combine both spatial and controlled-release kinetics of biochemical factors, thus creating an ideal environment for studying multiple tissue formation from a single stem cell population.

References:

1. Mapili G, Lu Y, Chen S, Roy K., Laser-layered microfabrication of spatially patterned functionalized tissue-engineering scaffolds. *J Biomed Mater Res B Appl Biomater*. 2005 Nov;75(2):414-24.

Acknowledgements: We would like to acknowledge the Whitaker Foundation and the National Science Foundation for their financial support.