Design and Fabrication of Durotaxic Tissue Engineering Scaffolds

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Statement of Purpose: Substrate stiffness is a crucial parameter that modulates the behavior of many cell types in motility, apoptopsis, phagocytocis and differentiation[1]. However, tissue engineering community's response to durotaxy has been minimal. While the current stiffness modulations are controlled at the ultrastructural biomaterial level, we present a novel minimal surface geometry based strategy to modulate the substrate stiffness at the architectural level. The proposed strategy promotes an opportunity to design customized biomorphic and durotaxic scaffolds and might have significant role in the "bench-to-bedside" transition of tissue analogs.

Methods: Schwarz Triply periodic minimal surfaces[2] (curved, bicontinuous, non-intersecting, zero-mean curvature surfaces) with 50% porosity was modeled implicitly with the trignometric function $cos(x) + cos(y) + cos(z) = C$. Modulated surfaces (Fig 1) were realized by varying the level-set value C. The resultant modulations were tessellated to form the respective scaffolds with pore-solid labyrinths. A cubic partition based scaffold with identical porosity was also constructed. Multiple copies of the $5mm^3$ scaffolds and unit cells of the modulated minimal surface and cubic partitions were fabricated with the PatternMaster rapid prototyping (RP) machine (Solidscape, Merrimack, NH). Mechanical characterization of the unit cells was performed with bulk compressive simulation on ABAQUS (HKS Inc, Plymouth, MI) and uniaxial compression on Dynamic Mechanical Analyzer (DMA: TA Inst., New castle, DE). The scaffolds were tested using DMA. The loading conditions and material properties were identical for all the configurations.

Results/Discussion: FEM simulation (Fig 2) reveals the modulation of the stress and strain concentrations and hence the stiffness of the modulated minimal surfaces. The modulation, however, is optimal in comparison to that of the conventionally used cubic lattice which shows high stress and strain concentrations at the sharp edges. DMA testing validated the simulation and demonstrated the modulation of substrate stiffness.

Conclusions: Substrate durotaxy is preferred across the hierarchy of the tissue analogue. While currently durotaxy can be realized only at the ultrastructural level, the proposed strategy promotes durotaxy at the architectural level. This novel synergistic combination of material science and mathematics might have profound implications in the ultimate deployment of tissue engineering scaffolds as viable bench-side tools to help in reducing the everwidening gap between the demand and supply of tissues and organs.

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References:

1.Georges PC, Janmey PA. *J Appl Physiol,* 98:1547-53,2005.
2. Schwarz HA. *Gesammelte math. Abhandlungen*, 1890.

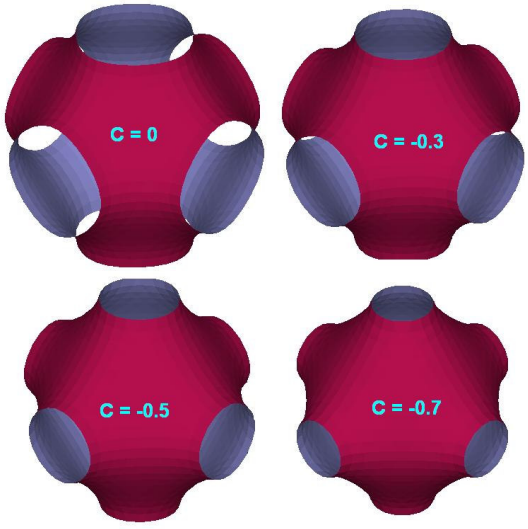

Figure 1. Representative modulation of Schwarz minimal surfaces. The Level set values are shown for the respective modulations.

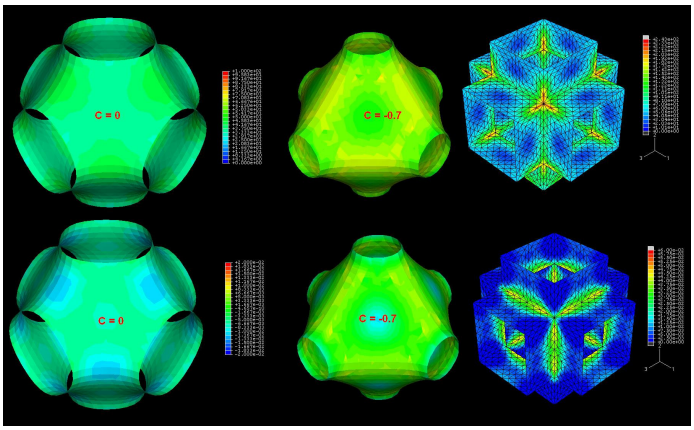

Figure 2. Von Mises Stress (top) and Principal Strain (bottom) modulation of Minimal Surfaces. Note that even at drastic modulation (C=-0.7) the stress and strain are optimally distributed in comparison with the conventional cubic lattice layout.