Multiscale modeling of vascularized bone regeneration in hybrid constructs of soft collagen gels and rigid scaffold

Hua Tan1, Sungwoo Kim2, Weiling Zhao1, Yunzhi Yang2,3,4, Xiaobo Zhou1,\*

1Center for Bioinformatics & Systems Biology, Department of Radiology, Wake Forest School of Medicine, Winston-Salem, NC 27157, USA

2Department of Orthopedic Surgery, Stanford University, Stanford, CA 94305, USA

3Department of Materials Science and Engineering, Stanford University, Stanford, CA 94305, USA

4Department of Bioengineering, Stanford University, Stanford, CA 94305, USA

Presenter: Hua Tan

Grant No. 1 U01 AR069395-01A1

Engineering prevascularized scaffold-based and cytokine-regulated bone tissue holds great promise for regeneration or repair of bone defects but remains significant clinical challenge. While various scaffolds have been applied to promote bone regeneration in experiments or even in clinic, adequate vascularization for efficient bone repair is still a challenging issue in such kind of applications. We recently designed a novel hybrid construct of soft collagen gels and rigid macro-porous poly(ε-caprolactone)-β-tricalcium phosphate (PCL-β-TCP) scaffold and proved its efficacy in supporting endothelial cell growth and network formation. However, the structural and physical properties of the scaffold have not been comprehensively tested, and the best composition and stiffness of the gel for optimal neovascularization was not determined either. In fact, the number of combinations of parameters regarding the gel and scaffold properties is too huge to manipulate by wet-lab experiments alone. Therefore, we propose a multiscale computational model to simulate the bone regeneration process on hydrogel-filled scaffold. In this model, the endothelial and osteoblast cells will be loaded singly or in combination into the hybrid scaffold construct. The strut size, porosity of the scaffold, along with the composition, stiffness of the gel will be set as input parameters for the model. By simulating the cell growth process and checking the molecular and cellular output, e.g. dsDNA production and cell number, we can specify the best geometric and biochemical characteristics of the hybrid constructs. Calibrated with necessary experimental measurements, the model is applicable to more complex problems such as those involving cytokine delivery and mechanical stimulation.