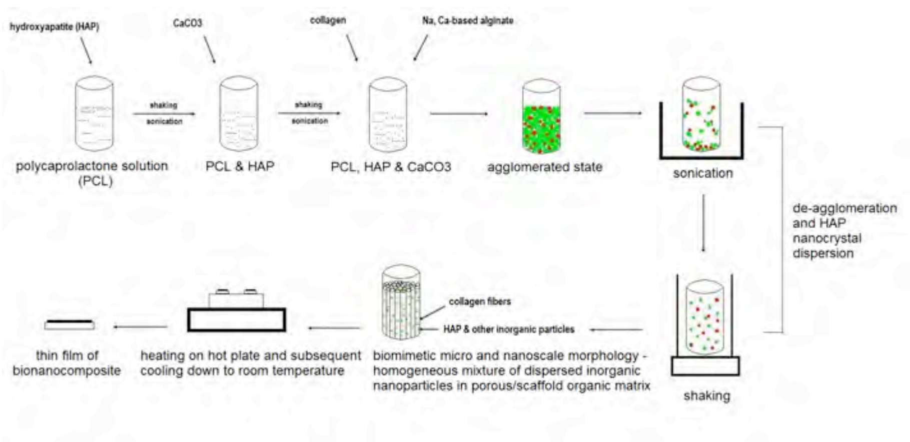
UNIVERSITY OF NOTRE DAME
NDnano
CENTER FOR NANO SCIENCE AND TECHNOLOGY

ND*nano* Undergraduate Research Fellowship (NURF) 2011 Project Summary

Student name: Matt Labriola
Faculty mentor name: Dr. Abhijit Biswas
Project title: Bone-inspired bionanocomposite scaffold for tissue regeneration and bone grafting technologies

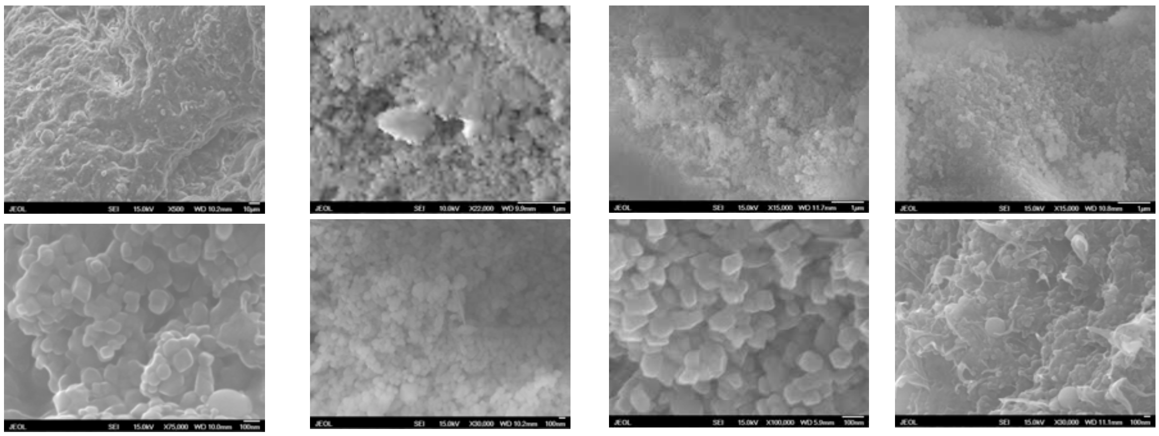
Bone is a specialized type of connective tissue that is built on the nano and microscale levels with unique self-regenerating and self-remodeling capabilities. It consists of a hard inorganic mineral phase embedded in a dense and elastic organic fibrous network, and its main constituents include hydroxyapatite (HAP), collagen protein fibers, phosphorous, and calcium. Given the complex morphology of bone tissue, there has been growing interest in the fields of nanotechnology and materials science to engineer an artificial multicomponent bionanocomposite scaffold that mimics natural bone tissue's content and structure. Such a scaffold could be used to treat bone defects by providing support and a framework on which cells can grow and proliferate if damage were to occur. There are many synthetic bone replacement materials, both single- and multi-phase, being utilized today that can execute their functions in vivo. Although notable advances have been made in tissue engineering for the purpose of replacing bone tissue, the current state-of-the-art bone grafting and bone replacement technologies have many limitations. Metals, ceramics, and polymers have been employed, but they lack the required biocompatibility and biodegradability that can be found in all natural bone materials. Therefore, expensive and invasive surgery is required for the implantation and removal of these scaffolds that could lead to pathogen transfer, physiological rejection, and patient discomfort. It is essential that a scaffold be designed that mimics bone tissue structural and mechanical properties using only biocompatible and biodegradable materials.

Using a low-cost, simple drop casting method for large-scale synthesis, we were able to design several nanocomposite scaffolds that mimic bone tissue's structural and mechanical properties using only biocompatible and biodegradable materials. A porous, three-dimensional, nanofibrous bioscaffold that is adequately mineralized with calcium, phosphorous, and oxygen is necessary for mimicking bone tissue. I synthesized four samples of differing composition to maximize the structural and mechanical properties of the scaffold. The interaction between calcium carbonate and HAP led to the formation of hexagonal calcium phosphate nanoparticles that were embedded in a dense and elastic collagen fibrous network. The presence of chitosan resulted in a scaffold with high interconnected porosity, which is essential for cell proliferation and growth. Without the pores, oxygen would not be delivered and cause cell death. The inclusion of both nano- and micro-scale features also improved the mechanical properties. High concentrations of HAP and calcium carbonate allow for better crystal packing and strong ionic interactions that maintain the hardness and elastic properties required for a scaffold that will undergo large amounts of stress. The scaffold using all natural bone materials exceeded the performance of metals and ceramics that are currently being used as bone substitutes. In addition, the mechanical properties of these scaffolds can be tuned to accommodate either high or low stress environments because of the variable hardness and modulus. By controlling mineral composition, we can tailor mechanical properties leading to new flexible designs for artificial bone substitutes that could be used in various parts of the body. The use of only biocompatible and biodegradable components overcomes the current technology gap. It is a solution to the problem of needing expensive and invasive surgery associated with the use of non-biocompatible materials. These results show the potential of biodegradable and biocompatible bone scaffolds as possible bone substitutes and could foster increased research on these new formulations.



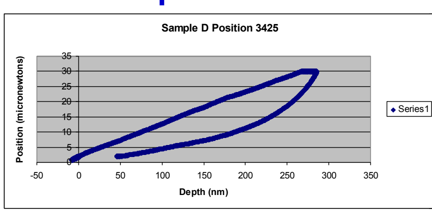
The simple, low-cost drop-casting strategy used in making the bionanocomposite scaffold samples.

Sample D **Sample E** **Sample F** **Sample H**



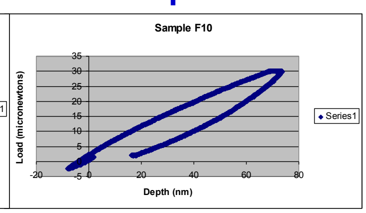
SEM images of my bionanocomposite scaffolds displaying the embedding of calcium phosphate nanoparticles in a collagen matrix. A porous structure was displayed with the presence of nanocrystals of calcium phosphate.

Sample D



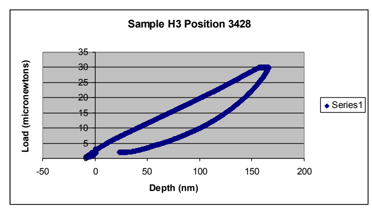
Hardness: > 350 MPa
Modulus (stiffness): ~4 GPa

Sample F



Hardness: ~ 4 GPa
Modulus: ~25 GPa

Sample H



Hardness: > 600 MPa
Modulus: ~ 4 GPa

Analysis of the hardness and modulus of three bioscaffolds with differing compositions. Bioscaffolds made of natural materials found in bone tissue exceed the performance of metals and ceramics used for bone substitutes.

Publications/Presentations

[1] Matthew Labriola, Michael Ashley, Ilker Bayer and Abhijit Biswas, Nanomedicine: Medical Applications of Nanotechnology, Vacuum Technology & Coating Magazine, Vol. 12, August, 2011.

[2] Matthew Labriola, 2011 SUMMER UNDERGRADUATE RESEARCH SYMPOSIUM, August 5, 2011, Jordon Science Hall, Notre Dame, Poster Presented.

[3] Michael Ashley, Matthew Labriola, Anindya Ghosh, Alexandru Biris, Ilker Bayer and Abhijit Biswas, Nanotech-Enabled Sustainable Energy: Green Nanoenergy, Vacuum Technology & Coating Magazine, Vol. 12, September, 2011.

[4] Matthew Labriola, Michael Ashley, Alexandru S Biris and Abhijit Biswas, Nanomedicine State-of-the-Art: Medical Applications of Nanotechnology, Review, to be published.

[5] Matthew Labriola, Enkeleda Dervishi, Michael Ashley, Ilker S Bayer, Tao Wang, George Csaba, Alexandru S Biris and Abhijit Biswas, Fabrication of bone-inspired porous bionanocomposite scaffold, manuscript under preparation

References/Acknowledgments

1. Labriola Matthew, Ashley Michael, Dervishi Enkeleda, Biris Alexandru, Bayer Ilker, Wang Tao, Csaba George, Lieberman Marya, Biswas Abhijit. Controlled Fabrication of Bone-Inspired Nanocomposite Scaffold with a Simple Sequential Drop-Cast Processing Strategy. Not yet published.
2. Biswas Abhijit, Ovaert Timothy, Slaboch Constance, Zhao He, Bayer Ilker, Biris Alexandru, Wang Tao. Mineral concentration dependent modulation of mechanical properties of bone-inspired bionanocomposite scaffold. Applied Physics Letters 2011.
3. Biswas Abhijit, Bayer Ilker, Zhao He, Wang Tao, Watanabe Fumiya, Biris Alexandru. Design and Synthesis of Biomimetic Multicompnent All-Bone-Minerals Bionanocomposites. Biomacromolecules 2010.
4. Murugan R, Ramakrishna S. Development of nanocomposites for bone grafting. Composites Science and Tehnology 2005.
5. Hollister Scott. Porous scaffold design for tissue engineering. Nature 2005

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