122nd ASEE Annual Conference & Exposition
June 14 - 17, 2015
Seattle, WA
Seattle Making Value for Society
Paper ID #14060

Enhancing the STEM Curriculum Through a Multidisciplinary Approach that Integrates Biology and Engineering: Biomaterials Modules

Ethan Sclarsky, Rensselaer Polytechnic Institute

Chemical Engineering undergraduate student at Rensselaer Polytechnic Institute.

Tyler Marquis Cooper, Rowan University
Dr. Johannes Strobel, Texas A&M University

Dr. Johannes Strobel is Director, Educational Outreach Programs and Associate Professor, Engineering & Education at Texas A&M, College Station. He received his M.Ed. and Ph.D. in Information Science & Learning Technologies from the University of Missouri. His research/teaching focuses on engineering as an innovation in pK-12 education, policy of STEM education, how to support teachers and students' academic achievements through engineering, engineering 'habits of mind' and empathy and care in engineering. He has published more than 140 journal articles and proceedings papers in engineering education and educational technology and is the inaugural editor for the Journal of Pre-College Engineering Education Research.

Dr. Jennifer Kadlowec, Rowan University
Prof. Andrea Jennifer Vernengo, Rowan University

Jennifer Vernengo is an Assistant Professor of Chemical Engineering at Rowan University. Jennifer received her Ph.D. from Drexel University in 2007. She began work as a materials scientist at Synthes Biomaterials, then joined Drexel University College of Medicine as postdoc in 2009. Jennifer's research is in the area of injectable biomaterials for orthopedic tissue replacement and repair. She is particularly interested in developing innovative approaches to biomedical engineering education.

Enhancing the STEM Curriculum Through a Multidisciplinary Approach that Integrates Biology and Engineering – Development of Biomaterials Modules

ABSTRACT

Due to the increasing prevalence of cardiovascular and orthopedic disorders in today's modern society, there is a necessity to engineer biomaterials that improve the quality of life for people with painful and debilitating diseases. This will require educational institutions to provide specialized instruction in these areas. Yet, there have been relatively few published reports on biomaterials and tissue engineering-related lab activities, and existing activities lack a foundation in materials science. A primary deliverable of this project is to address this need and thus strengthen science, technology, engineering and math (STEM) education by developing interactive experiments that introduce tissue engineering through a biomaterials design perspective, emphasizing mechanics, cell behavior, and drug delivery. Cutting-edge methods in these fields have been adapted so they can be applied starting at the freshman level through upper level electives in chemical, mechanical, or biomedical engineering and cellular/molecular biology. The anticipated results of the project will be i) the implementation of curricular materials that fulfill a need in STEM education, ii) increased student interest in pursuing undergraduate and graduate study in STEM disciplines, iii) the development of a well-rounded workforce of engineers prepared to find multidisciplinary engineering solutions to the growing health care needs of the world.

1. INTRODUCTION

Biomaterials have received considerable attention over the past 30 years. A biomaterial has been defined as a material intended to interface with a biological system to evaluate, augment, or replace any tissue organ or function in the body [1, 2]. Therefore, the field of biomaterials encompasses the study of materials science, medicine, and biology. Biomaterials are a large portion of the healthcare market and represent a 9 billion dollar per year industry [3]. It is estimated that over 11 million people have implants utilizing engineered biomaterials [4].

This clinical need for biomaterials will require educational institutions to provide specialized instruction in these areas [5]. In fact, biomaterials is one of the twenty-three core topics within bioengineering identified by the Vanderbilt, Northwestern, Texas, and Harvard-MIT (VaNTH) Engineering Research Center (ERC) funded by NSF [6]. Despite the importance of the field, there are a very limited number of literature articles published on biomaterials education since the 1990s [5, 7-13]. Notably, VaNTH ERC established a taxonomy, or list of core competencies, within the area of biomaterials that educators should cover [14]. On this list of core competencies are i) the fundamentals of materials science, ii) methods of characterizing material properties, and iii) polymer synthesis and characterization. Obviously, materials design is an integral part of the field, yet the few existing educational modules related to biomaterials tend to focus biological performance and evaluation. This paper describes two experimental designs to engage students in the guided discovery of material science and its application to the i) characterization of polymers for meniscus replacement, ii) the design of magnetic nanobiomaterials for hyperthermia cancer treatment.

2. PROJECT GOALS

The goals and objectives of this project are outlined below.

- To develop multidisciplinary curricula on biomaterials that enhances student knowledge of fundamental concepts in core STEM disciplines.
- To generate detailed experimental designs that can be disseminated and adapted by other faculty at 4-year universities on a national level.
- To increase student interest in pursuing undergraduate and graduate study in STEM disciplines.

3. MODULES

3.1 Structure-Property Relationships in Hydrogels

The meniscus is a crescent-shaped pad of cartilage that disperses stress during loading of the knee joint. Menisectomies are performed when the tissue is damaged beyond repair, most often the result of car accidents or sports injuries [15]. The patients who receive this procedure are usually young and active. In order to get them mobilized and rehabilitated as soon as possible, the best option may be to replace the meniscus with an artificial biomaterial. In order to prevent future degenerative changes in the joint, the optimal meniscus replacement would have similar compressive mechanical and viscoelastic behavior to the natural meniscus. In this challenge-based series of lessons, students will prepare and evaluate hydrogels as an artificial meniscus. Named 'Biomaterial of the Month' in 2007 by the Society for Biomaterials, a hydrogel is a three-dimensional water swollen network composed of crosslinked hydrophilic polymer chains [3]. PVA hydrogels chosen because it has been investigated for cartilage replacement [15-18] and it is safe, easy to prepare, and cost effective to purchase. Physically crosslinked hydrogels can be prepared from freeze-thaw (FT) cycles of aqueous solutions of PVA [19-21]. Research on the formation of PVA hydrogels from FT cycles [17, 22-25] has indicated that the mechanical properties can be varied as a function of the polymer molecular weight, concentration of the aqueous solution, and the number of FT cycles.

In junior-level Materials Science, students analyze the mechanical behavior of the hydrogels, both experimentally and computationally. The hydrogels are subjected to 2, 4, 6 or 8 FT cycles and stress relaxation testing is performed on an Instron mechanical testing system (Model 3362, Park Ridge, IL). PVA hydrogels are compressed with an anvil to 15% strain. Load and displacement data is captured by Instron BlueHill 1.2 software and converted to stress-strain values. Students use a Matlab GUI to investigate the suitability of three classic rheological models (Maxwell, Kelvin-Voigt and Standard Linear) in predicting stress relaxation behavior of the polymers. Students also determine how model parameters affect the output, similar in scope to what has been reported by Singh and Kahn [26].

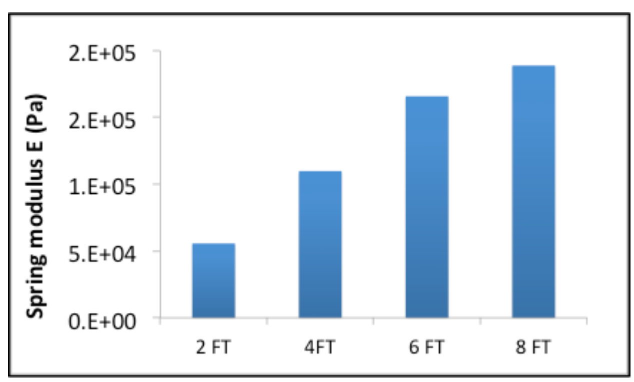

Figure 1. The spring modulus E for the Maxwell model as a function of number of FT cycles.

Sample data for the PVA hydrogels are shown in Figure 1. Here, experimental stress versus time data was fit to the Maxwell Model and the spring constant, *E*, is plotted as a function of FT cycles. Students will relate the trend in the data, increasing modulus *E* with increasing FT, to polymer structure. Increased degree of crosslinking between the chains generates a stronger three-dimensional network, making the modulus value of the polymer increase. At the end of the lab, based upon the experiment data and model parameters, students choose a formulation best suited for a high impact, high loading application such as meniscus replacement. The learning objectives of this module are to i) describe the underlying molecular mechanisms of stress relaxation in polymers, ii) quantify the impact of crosslinking of the stress-relaxation behavior of a polymer network and describe the underlying molecular mechanisms that cause this behavior, iii) use three viscoelastic models, Maxwell, Kelvin-Voigt, and standard linear, to predict the stress-relaxation behavior of crosslinked hydrogels, iv) practice using a mathematical package to fit experimental data and simulate the effect of varying model parameters, and v) describe key relationships between scientific principles, material properties and technological advancement in the field of biomaterials.

3.2 Module 2: Magnetic Biomaterials Nanoparticle Hyperthermia for Cancer Treatment

Hyperthermia is a relatively new approach to treating various types of cancers. It involves heating the cancerous tissues in order induce cell death. Conventionally, hyperthermia is achieved by ultrasound, microwaves, or infrared radiation, but these approaches are likely to heat the surrounding healthy tissues, causing damage [27, 28]. More recently, selective heating of tumors has been achieved by the application of magnetic nanoparticles to the tumor site, which will generate heat when exposed to alternating magnetic fields (AMF) [29, 30]. The heat output, typically quantified by the specific loss power (SLP), depends on the magnetic field frequency and strength, as well as the chemical and physical properties of the nanoparticles [31]. Optimization of the technology requires the application concepts across multiple disciplines, including chemistry, electrical engineering, physics, and materials science. Therefore, this technology presents an interesting opportunity to teach students foundational concepts in science and engineering.

Magnetite (Fe_3O_4) nanoparticles have been widely studied for hyperthermia applications, due to the strong magnetic properties and low toxicity [32]. In the following experiment, students synthesize their own nanoparticles according to the procedure outlined by Rashad et. al. [33] which is reported to produce nanoparticles in the range of 9-12 nm. Induction heating is achieved with the EasyHeat 0112 induction heating power supply (Ambrell Corporation, Schottsville, NY). The power supply operates at max power of 1.2 kW and the system operates in tandem with a workhead attached to a three-turn coil (0.12m long) that creates a resonant frequency of 280 kHz. Nanoparticles, suspended in water or water/glycerol mixtures, are placed in the center of the coil. The temperature of the suspension is measured with a FISO TMI Temperature Multichannel Instrument connected to an optical temperature sensor. The aim of this experiment is to investigate the effect of three variables (applied current level, suspension viscosity, and nanoparticle concentration) on the SLP magnetic nanoparticles. In hyperthermia studies, the SLP is calculated by Equation 1 [34].

$$SLP = c\frac{\Delta T}{\Delta t} \cdot \frac{1}{m_{magnetic}}$$ Equation 1

where c is the sample-specific heat capacity, $m_{magnetic}$ is the mass of nanoparticles per total mass of suspension, and $\frac{\Delta T}{\Delta t}$ is the initial slope of the time dependent temperature curve (usually taken during the first 60 seconds of heating). The heat capacity of the sample is calculated as the mass weighted mean value of the nanoparticles and water [35]. Sample data is shown in Figure 2. As current increases, the magnetic field strength increases, which will enhance the rotation of the magnetic moments within the particles, as well as the whole particle itself. This increases thermal dissipation, accounting for the increasing trend in SLP with current level. The learning objectives of the module are to i) explain the general properties of magnetic materials and magnetic nanoparticles, ii) describe the application of induction heating to hyperthermic cancer therapy, iii) describe the mechanisms of heating single and multiple domain magnetic materials, iv) to quantify the effect of applied current, suspension viscosity, and nanoparticle concentration on the SLP and explain the phenomenon within the context of induction heating of single-domain magnetic nanoparticles.

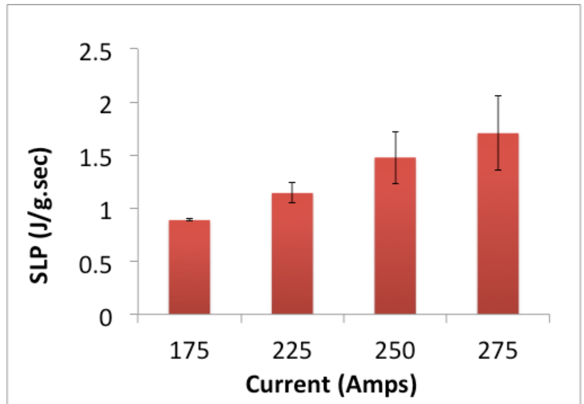

Figure 2. SLP of Fe3O4 nanoparticles as a function of current level.

4. EVALUATION PLAN

Summative and formative project evaluation will be carried out according to the recommended practices of the National Science Foundation [36]. The following instruments will be used as a *formative assessment* of whether the project is meeting its goals.

- Pre and post-tests: The questions (written and collected by PI) will be mapped to ABET and NCSES learning outcomes for pre-college and undergraduates.
- Rubrics: For each experiment, the undergraduate students will design an experimental plan, state what measurements will be made, and how they will analyze and interpret the data. On lab reports and oral presentations, students will be graded with respect to how well they document, execute, and communicate their results. These outputs will be graded with rubrics mapped to learning outcomes from ABET.
- Student pre and post-surveys and course evaluations: Pre and post-surveys before and after each experiment will probe achievement of project goals, such as improved attitudes towards STEM areas and the building of confidence in conducting research [37]. These instruments have been developed by an external evaluator and will be collected by PI.

A *summative* evaluation will be conducted with the following instruments:

- Career aspiration and design self-efficacy survey for undergraduate students: These surveys (modified, tested, and validated by Dr. Johannes Strobel) will be used to assess the long-term impact of the curricula on student interest in bioengineering, and the impact on their career choices, and self-confidence in their engineering expertise.

5. PRELIMINARY RESULTS

To evaluate the impact of the experiments on student learning, quizzes were administered to the students before and after each lab. The quizzes were of comprised multiple-choice questions (14 for magnetic biomaterials and 10 for the stress-relaxation lab), which were mapped to lab objectives and ABET objectives. As shown in Figure 3, there was a significant increase in the average class score between the pre and post-test for both labs.

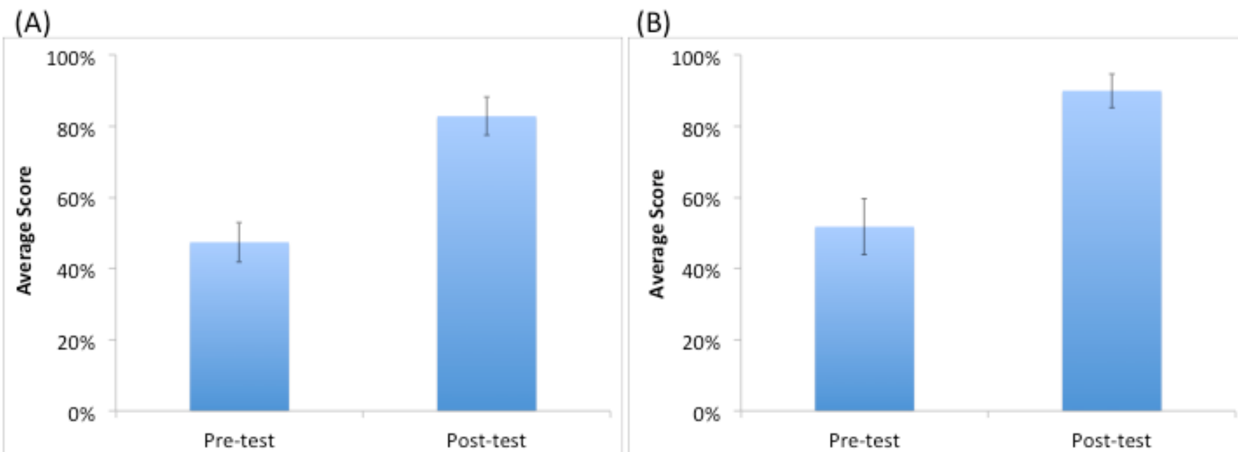

Figure 3. Average quiz scores for the (A) magnetic biomaterials lab (n=24 students) and (B) stress relaxation lab (n=28 students). Both post-tests scores were significantly higher ($p<0.05$) than the respective pre-test scores. The errors bars represent the 95% confidence interval.

6. ACKNOWLEDGEMENT
This material is based upon work supported by the National Science Foundation under Grant No. 1245595.

7. REFERENCES

1. Williams D. The Williams Dictionary of Biomaterials. Liverpool: Liverpool University Press; 1999.
2. Polymer Characterization Techniques.247-56.
3. Ratner B, Hoffman AS, Schoen FJ, Lemons JE. Biomaterials Science: A Multidisciplinary Endeavor. Biomaterials Science: A Introduction to Materials in Medicine. San Diego: Elsevier Academic Press; 2004. p. 1-9.
4. Moss A. Use of Selected Medical Device Implants in the United States. Hyattsville, MD: National Center of Health Statistics, 1988.
5. Black J, Shalaby SW, LaBerge M. Biomaterials Education: An Academic Viewpoint. Journal of Applied Biomaterials. 1992;3:231-6.
6. Vanderbilt N, Texas, and Harvard-MIT Engineering Research Center. http://www.vanth.org/curriculum/curr_bio_domains.asp.
7. Saterbak A, editor Laboratory Courses Focused on Tissue Engineering Applications Proceedings of the 2002 American Society for Engineering Education Annual Conference & Exposition; 2002.

8. Pittsburg Tissue Engineering Initiative I. An Education Outreach Manual in Tissue Engineering. In: Pittsburg Uo, editor. 2010.
9. Birol G, Liu S, Smith D, Hirsch P Educational Modules in Tissue Engineering Based on the “How People Learn” Framework. Bioscience Education E-journal. 2006;7.
10. Bhatia S. A disease-centered approach to biomaterials education and medical device design. 33rd Annual International Conference of the IEEE EMBS; Boston, Massachusetts2011. p. 3617-9.
11. Reichert W, Harris TR, Lemmons J, Mikos AG, Puleo DA, Schoen FJ, Temenoff JS. 2011 Panel on developing a biomaterials curriculum. Journal of Biomedical Materials Research Part A. 2011;100A:802-16.
12. Feldman D, Gombotz WR. Biomaterials Education: An academic and industrial viewpoint. Journal of Applied Biomaterials. 1991;2:133-9.
13. Burny F, Donkerwolcke M, Muster D. Biomaterials education: A challenge for medicine and industry in the late 1990s. Material Science and Engineering Part A. 1995;199:53-9.
14. Vanderbilt N, Texas, and Harvard-MIT Engineering Research Center. http://www.vanth.org/curriculum/Curr_taxon.asp.
15. Kobayashi M, Chang YS, Oka M Masanori Kobayashia. A two year in vivo study of polyvinyl alcohol-hydrogel (PVA-H) artificial meniscus Biomaterials. 2005;26(16):3243-8.
16. Spiller K, Laurencin SJ, Lowman AM. Characterization of the Behavior of Porous Hydrogels in Model Osmotically-Conditioned Articular Cartilage Systems. Journal of Biomedical Materials Research Part B: Applied Biomaterials. 2009;90B:752-9.
17. Stammen J, Williams S, Ku DN, Gulderg RE. Mechanical properties of a novel PVA hydrogel in shear and unconfned compression. Biomaterials. 2001;22:799-806.
18. Spiller. Semi-degradable, Multi-functional Hydrogelsfor the Repair of Articular Cartilage Defects. Philadelphia, PA: Drexel University; 2010.
19. Peppas N, Merrill EW. Crosslinked poly (vinyl alcohol) hydrogels as swollen elastic networks. Journal of Applied Polymer Science. 1977;21:1763-77.
20. Thomas J, Lowman A, Marcolongo M. Novel associated hydrogels for nucleus pulposus replacement. J Biomed Mater Res Part A. 2003;67:1329-37.
21. Hassan C, Stewart JE, Peppas NA. Diffusional characteristics of freeze/thawed poly(vinyl alcohol) hydrogels: Applications to protein controlled release from multilaminate devices. European Journal of Pharmaceutics and Biopharmaceutics 2000;49:161-5.
22. Stauffer S, Peppas NA. Poly(vinyl alcohol) hydrogels prepared by freezing-thawing cyclic processing. Polymer. 1992;33(18):3932-6.
23. Urushizaki F, Yamagushi H, Nakamura K, Numajiri S, Sugibayashi, K, Morimoto Y. Swelling and mechanical properties of poly(vinyl alcohol) hydrogels. International Journal of Pharmaceutics 1990;58:135-42.
24. Hickey A, Peppas NA. Mesh size and diffusive characteristics of semicrystalline poly (vinyl alcohol) membranes prepared by freezing/thawing techniques. Journal of Membrane Science 1995;107:229-37.
25. Peppas N, Scott JE. Controlled release from poly (vinyl alcohol) gels prepared by freezing-thawing processes. Journal of Controlled Release 1992;18:95-100.
26. Singh KV, Khan, F, editor Interactive Module for Biomaterial Modeling and Characterization. 121st ASEE Annual Conference & Exposition; 2014; Indianapolis, IN.

27. Verma J, Lal, S., Van Noorden, CJF. Nanoparticles for hyperthermic therapy: synthesis strategies and applications in glioblastoma. International Journal of Nanomedicine. 2014;9:2867-77.
28. Jordan A. Hyperthermia in Cancer Treatment: A Primer. In: Baronzio G, Hager ED, editor. New York, NY: Springer; 2006. p. 60-3.
29. Ito A, Shinkai, M., Honda, H., Kobayashi, T. Medical application of functionalized magnetic nanoparticles. Journal of Bioscience and Bioengineering. 2005;100(1):1-11.
30. Deatsch AE, Evans, B.A. Heating efficiency in magnetic nanoparticle hyperthermia. Journal of Magnetism and Magnetic Materials. 2014;354:163-72.
31. Gilchrist RK, Medal, R., Shorey, W.D., Hanselman, R.C., Parrot, J.C., Taylor, C.B. Selective Inductive Heating of Lymph Nodes. Annals of Surgery. 1957;146(4):596-606.
32. Shundo C, Zhang, H., Nakanishi, T., Osaka, T. . Cytotoxicity evaluation of magnetite (Fe3O4) nanoparticles in mouse embryonic cells. Colloids and Surfaces B: Biointerfaces. 2012;97:221-5.
33. Rashad MM, El-Sayed, H.M., Rasly, M., Nasr, M.I. Induction heating studies of magnetite nanospheres synthesized at room temperature for magnetic hyperthermia. Journal of Magnetism and Magnetic Materials. 2012;324:4109-023.
34. Lima E, Jr., Torres, T. E., Rossi, L. M., Rechenberg, H. R., Berquo, T. S., Ibarra, A. Size dependence of the magnetic relaxation and specific power absorption in iron oxide nanoparticles. . Journal of Nanoparticle Research. 2013;15(5):1-11.
35. Shete PB, Patil, R.M., Thorat, N.D., Prasad, A., Ningthoujam, R.S., Ghosh, S.J., Pawar, S.H. . Magnetic chitosan nanocomposite for hyperthermia therapy application: Preparation, characterization and in vitro experiments. Applied Surface Science. 2014;288:149-57.
36. Frechtling J, Mark MM, Rog DJ, Thomas V, Frierson H, Hood S, Hughes G, Johnson E The 2010 User Friendly Handbook for Project Evaluation. The National Science Foundation, Division of Research and Learning in Formal and Informal Settings, 2010.
37. Carberry A, Ohland M, Lee HS. Measuring engineering design self-efficacy. Journal of Engineering Education. 2010;99(1):71-9.