

Re-Engineering Engineering Education

BIOMATERIALS

FORUM



OFFICIAL NEWSLETTER OF THE SOCIETY FOR BIOMATERIALS

Third Quarter 2010 • Volume 32, Issue 3



Biomaterials Forum, the official news magazine of the Society For Biomaterials, is published quarterly to serve the biomaterials community. Society members receive *Biomaterials Forum* as a benefit of membership. Non-members may subscribe to the magazine at the annual rate of \$48. For subscription information or membership inquiries, contact the Membership Department at the Society office (e-mail: info@biomaterials.org) or visit the Society's web site, www.biomaterials.org.

It is the policy of the Society For Biomaterials that all articles reflect only the views of the authors. Publication of articles or advertisements within *Biomaterials Forum* does not constitute endorsement by the Society or its agents of products, services or views expressed herein. No representation is made to the accuracy hereof, and the publication is printed subject to errors and omissions. Articles that do not have an author byline may originate from press releases. The Society For Biomaterials retains press releases on file for a period of one year from the date of publication.

Editorial contributions to *Biomaterials Forum* are always welcome. Contributions should be sent to the Executive Editor and are subject to the terms and conditions of the Editorial and Publication Release. Authors should refer to the Author Guidelines, which are available on the Society's web site, when writing submissions. The publisher accepts no responsibility for return or safety of artwork, photographs or manuscripts. Submission of editorial content does not guarantee acceptance or publication.

Address corrections should be sent to *Biomaterials Forum*, 15000 Commerce Parkway, Mt. Laurel, NJ 08054.

Requests for advertising information should be directed to Frank Scussa at fscussa@ahint.com or (856) 439-0500, ext. 4427. Information is also available on the Society's web site, www.biomaterials.org.

Unauthorized reproduction of this magazine in whole or in part is prohibited without the permission of the publisher. Requests for permission should be directed to the Managing Editor.

Scientific photos may be submitted for cover consideration in future issues. Submit color photo, no larger than 4" x 6", along with credit information and scientific description, to the Executive Editor.

Copyright© 2010 ISSN 1527-6031
Society For Biomaterials
All rights reserved

BIOMATERIALS FORUM

The official news magazine of the **SOCIETY FOR BIOMATERIALS** • Volume 32, Issue 3

Executive Editor	Karen Burg, Clemson University, Department of Bioengineering 401 Rhodes Engineering Research Center, Clemson, SC 29634 Phone: (864) 656-6462 • Fax: (864) 656-4466 E-mail: kburg@clemson.edu
Managing Editor	Erik Caplan, Society For Biomaterials 15000 Commerce Parkway, Mt. Laurel, NJ 08054 Phone: (856) 793-0901 • Fax: (856) 439-0525 E-mail: ecaplan@ahint.com
Government News Contributing Editor	Joy Dunkers, National Institute of Standards and Technology E-mail: joy.dunkers@nist.gov
Government News Contributing Co-Editor	Christine A. Kelley, National Institutes of Health E-mail: kelleyc@mail.nih.gov
Industrial News Contributing Editor	Steve T. Lin, Exactech Inc. E-mail: steve.lin@exac.com
Society Business & Membership News Contributing Editor	Michele Marcolongo, Drexel University Department of Materials Science and Engineering E-mail: marcolms@drexel.edu
Special Interest Group News Contributing Editor	Christopher Siedlecki, Penn State University Department of Bioengineering E-mail: csiedlecki@psu.edu
University and Research Institution News Contributing Editor	Guigen Zhang, Clemson University, Department of Bioengineering Email: guigen@clemson.edu
Book Review	Liisa Kuhn, University of Connecticut Health Center Center for Biomaterials and Regenerative Medicine E-mail: Lkuhn@uchc.edu
AIMBE News Contributing Editor	Alan S. Litsky, The Ohio State University Biomedical Engineering Department Email: litsky.1@osu.edu
Education News Contributing Editor	Jan P. Stegemann, University of Michigan Department of Biomedical Engineering Email: jpsteg@umich.edu
Graphic Designer	Jenelle Rittenhouse

Special Interest Group Reporters

Biomaterials Availability & Policy	Carl R. McMillin, carl@syntheticbodyparts.com
Biomaterials-Cell/Organ Therapies	Todd McDevitt, todd.mcdevitt@bme.gatech.edu
Biomaterials Education	Elizabeth A. Friis, lfriis@ku.edu
Cardiovascular Biomaterials	Peter G. Edelman, peter.edelman@bsci.com
Dental/Craniofacial Biomaterials	Hyun Joon Kong, hjkong06@illinois.edu
Drug Delivery	Thomas Dziubla, dziubla@enr.uky.edu
Implant Pathology	Janson Emmanuel, jemmanual@wlgore.com
Nanomaterials	Thomas Webster, Thomas_Webster@brown.edu
Ophthalmic Biomaterials	Ping-fai "Sidney" Sit, sidney@latech.edu
Orthopaedic Biomaterials	Lakshmi S. Nair, nair@uchc.edu
Protein & Cells at Interfaces	Carl Simon, Jr., carl.simon@nist.gov
Surface Characterization & Modifications	Jeffrey L. Schwartz, jlschwar1999@yahoo.com
Tissue Engineering	Jan P. Stegemann, jpsteg@umich.edu

Departments

The Torch

- 2 From the Editor
- 3 From the President
- 4 Staff Update

Chapter News

- 14 Members in the News

Education News

- 19 Inspiring the Next Generation of Biomaterials Scientists

Special Interest Group News

- 8 Human Microvascular Endothelial Cells Uptake Nanoparticles

University and Research Institution News

- 12 The Good and Peril of the Internet

Government News

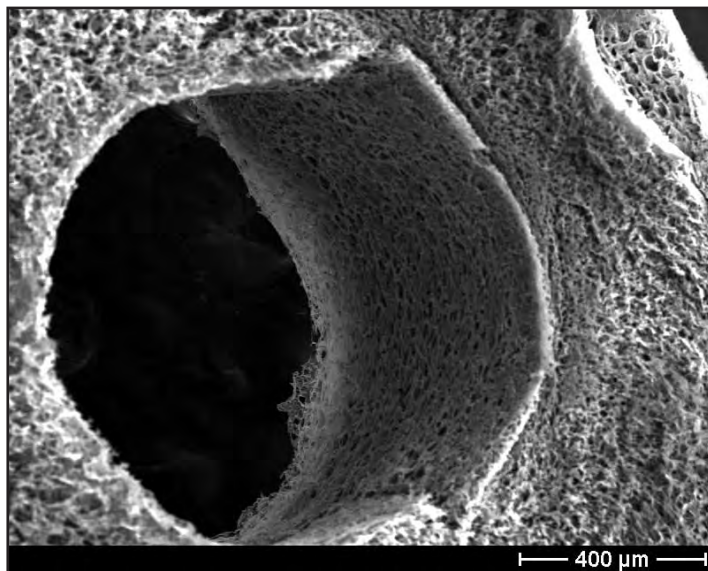
- 15 Imaging Cells in Polymer Scaffolds
- 10 AIMBE Update

Industry News

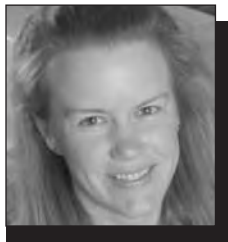
- 18 BioInk

Biomaterials Community

- 21 Community Calendar



On the cover: Scanning electron micrograph of a channel in an alginate scaffold used for bone tissue engineering. The scaffold includes macroscopic channels as well as microporosity throughout (scale bar = 400 microns). Photograph courtesy of Darilis Suarez-Gonzalez, M.S., and Dr. William L. Murphy, Associate Professor, University of Wisconsin.



My plans for this editorial changed with the death of Shalaby Shalaby in August. Dr. Shalaby was a recognized pioneer in the field of absorbable biomaterials. What may not be so widely known is that he was an advisor and mentor to many, including me. More than 20 years ago, he collected me from aimless wandering of the halls at Clemson University, a new,

lost and advisorless graduate student. I discovered over time that Dr. Shalaby consistently “flew under the radar.” Unlike many, he did not seek recognition or awards; rather, he sought out a network of collaborators, business partners, friends and, most importantly to me, students in need of guidance. Since he was so humble, he would never have described his “success,” let alone “keys to success.” Hence, I am going to describe three points that were core to his philosophy.

The first point is that everyone is important; a title and/or ability to pontificate in a large group does not equal importance. I think those in the biomaterials industry understand this concept far better than those of us in the biomaterials academic world. Perhaps it is the drivers or rewards systems that cause this difference in comprehension—a functional industrial team requires personalities and talents of all types, including introverts and extroverts. A nonfunctional team can have major, devastating financial ramifications for a company. In the world of academia, the major drivers are publications, grants and awards, and these drivers can easily lead to a “verbose equals important” type of mentality. The process of moving a biomaterial from concept to clinical reality is so overwhelmingly complex that it almost seems obvious that one would need input from a vast array of individuals. I think the best example that showcases living the “everyone is important” mantra involves Dr. Shalaby’s purposeful corralling of those unnoticed, borderline-grade, advisorless students and extracting the very best out of each one with the belief that in each one was a nugget or glimmer of potential. These individuals, who may not have otherwise reached their full potential, are now successful in industry, government and academia. Indeed, everyone is important.

The first point leads directly to the second, which is to be persistent, to never give up and to never take criticism personally. One of my American Council of Education mentors, University of Maryland, Baltimore County President Freeman Hrabowski, once told me he collected a lot of “no’s” in a day because he made a lot of “asks.” The point being that, similar to asking for money from a federal agency to study an exciting biomaterials concept, one will expect a large percentage of denials, but unless one keeps asking, the answer will be automatically “no.” I remember listening, as a new student, to other senior researchers criticizing Dr. Shalaby’s then novel concept of building absorbable systems that would release specific drugs or therapies on change with pH or temperature. The criticism was loud and continuous—this idea was not worth pursuing, as events like inflammation could inadvertently cause drug dumping. It seemed like science fiction to me, too, and I remember wondering if it wouldn’t be more sensible for Dr. Shalaby to switch course for a more mainstream research track.

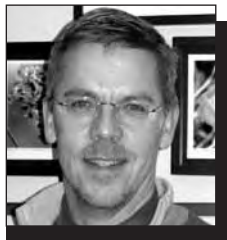
He doggedly continued in the face of verbal missiles, using the criticism as topics fueling his next series of patents. Today pH and temperature responsive absorbable materials research is commonplace and the questions do not focus on whether or not these types of systems are realistic, but rather on how to fine tune them, what groups with which to integrate them and so forth. Don’t take no for an answer if you believe in your cause.

The third point is that everything is an opportunity and one should seize opportunities. Obviously, one should establish bounds for this point so as not to pursue endless opportunities in all directions while partaking in none to a quality level. I can think of many times in my career when it would have been easier to keep my head down and not seize an opportunity, and it frightens me to think of the opportunities I would have missed. By way of only one example, when I first began life as a new faculty member, Dr. Shalaby asked me if I would co-teach an absorbable materials short course with him in Atlanta, Georgia. The course would be limited specifically to a very small group of industry participants. I agreed, but as the dates of the course approached and my schedule became overloaded, I questioned my own sanity in having agreed to participate in this seemingly time consuming, seemingly small impact, off-site event. I even mentioned my concerns to him, and he simply responded by assuring me this would be a great opportunity. We proceeded as planned, and I had a wonderful time getting to know the course enrollees, talking with them about absorbable materials research and potential and seeing Dr. Shalaby in networking action. I chalked up the event as simply a nice “break” from the higher priority tasks of an untenured professor, until a year or so later, when one of the participants mentioned to me that he worked as a consultant for a not-for-profit where I had applied for research funding. He said he had been so excited to see my proposal, and he had relayed to the powers-that-be how much he had enjoyed our Atlanta short course. Ironically, that initial grant blossomed into one of the most amazing networking and funding opportunities for which I could ever have wished over the past 10 years, that same not-for-profit has provided financial assistance, educational opportunities for my students and networking opportunities I could never have sought out on my own. I believe Dr. Shalaby’s comment framed my attitude and prompted me to travel to Atlanta with purpose to find opportunity. I now know to proactively keep looking, because everything is truly an opportunity.

As saddened as I am by Dr. Shalaby’s passing, I fully appreciate the sad, gut wrenching feeling is due to the large scale impact he has had and will continue to have on my professional career and who I am as a person. Indeed, a person’s impact and legacy extends far, far beyond technical prowess in a field.

Best wishes from Clemson,

Karen J.L. Burg
Hunter Endowed Chair & Professor of Bioengineering
Interim Vice Provost for Research & Innovation
Clemson University



Where's the Bio in Biomaterials? Where are the Materials in Biomaterials? A Vision for the Society For Biomaterials

This is the text of the speech I gave at the 2010 Annual Society For Biomaterials Meeting in Seattle, April 23, 2010, at the annual business meeting. It captures the vision I have for the Society.

As I take up the presidency of the Society For Biomaterials, I would like to say a few words.

The Society For Biomaterials has a unique and defining history. Each of us has our own sense of this history. To understand who we are today, we need to know how we got here.

The Society was formed at a time of great innovation and advancement in the field of medical devices and their use in the human body. The early days of biomaterials were filled with questions about how materials can be placed in the body to repair or replace tissues, organs and structures. Questions of biocompatibility arose—even debates about what biocompatibility was and what it wasn't. Some of these debates still rage. We explored medical devices and began to learn of all the wonderful and vexing ways the human body responds to these materials and devices.

In this early age of innovation—the late '60s to early '70s—the Society was deeply anchored in the materials science of biomaterials; what metals, polymers and ceramics could be used in medical devices, how they performed, how they succeeded and how they failed. These questions remain relevant even today.

Then, around 1980, future leaders of the field began to ask, "Where's the Bio in Biomaterials?" This question opened the door to more and more biologically-based questions. New ideas, not about simple passive interaction and biocompatibility, but rather about co-opting and controlling biology with materials, led, in the late 1980s and early 1990s to the advent of what we now call Tissue Engineering.

The concepts in Tissue Engineering opened up vast new areas of research and study as we, as a Society, began to explore questions that had, to this point, been mostly the realm of the cell biologist and the clinician.

However, by 1993, the pendulum had swung away from the early ideas of materials-science-centric Biomaterials to the other side of our Society, to the point where the future leaders of the field at that time began to ask, "Where's the Materials in Biomaterials?" Research presented at the Society was more and more focused on strictly biological questions and less and less on materials science-based questions.

These questions: Where's the Bio in Biomaterials? And Where's the Materials in Biomaterials?, I believe, are both the fulcrum

In all of this history, the central element of our Society has remained: working towards improved health and advanced medical treatments using biomaterials in medical devices.

of the debate that continues within our Society and are the essential defining questions that animate our Society and will lead us into the future.

In all of this history, the central element of our Society has remained: working towards improved health and advanced medical treatments using biomaterials in medical devices. This is, in my opinion, the core of this society: Materials Science and Biology (or Biology and Materials Science) in the pursuit of medical treatment.

The uniqueness of our Society is our members' backgrounds, expertise and collaborative efforts in materials science and biology.

The quantitative approaches engineering brings to medicine and the interdisciplinary teams of engineer, scientist and clinician, made it a natural step for the Society to move towards using engineering science principles to direct cell behavior with the ultimate goal of regeneration of organs and/or restoration of biological function; to make the next generation of medical devices and the next after that...

These are the core ideas that animate this Society today and set us apart from all other professional societies—this is our uniqueness proposition.

We all know there is a debate in this Society. These questions are discussed and debated with fierce support for one side or another, arguing that the Society needs to move in one or another direction. These debates are an important sign of health in our Society.

Where's the Bio in Biomaterials? Where's the Materials in Biomaterials?

Continued on Page 7

The Society For Biomaterials completed solicitation of abstracts for the 2011 Annual Meeting to be held April 13-16, 2011 at Disney's Contemporary Resort in Walt Disney World® Resort. A total of 1,000 abstracts were received. A preliminary program is available at the SFB website: www.biomaterials.org.

The theme for the 2011 Annual Meeting of the Society For Biomaterials, *Animating Materials*, plays off the Society's tagline "Giving Life to a World of Materials" with a decidedly Disney flair. The Annual Meeting will continue to focus on fostering development of new implant materials and devices for improvement of the human condition. The goal of the 2011 meeting will be to describe the latest innovations in materials science, molecular and cell biology and engineering; identify new opportunities and mechanisms for translation of these findings into new or improved medical treatments; and engage members from industry and academia in speeding the translation of research to clinical application. The program will include Symposia, General Sessions, Workshops, Panel Discussions and Tutorials covering all aspects of basic, applied and translational biomaterials science.

Committee Reporting: Each of the Society's committees is listed below, along with progress against the goals that each committee would like to accomplish during their yearlong term.

Awards, Ceremonies and Nominations Committee:

Art Coury (Chair); Jason Burdick, University of Pennsylvania; Monty Reichert, Duke University; John Fisher, University of Maryland; Todd McDevitt, Georgia Institute of Technology/Emory; Bob Latour, Clemson University Representative. The Awards, Ceremonies and Nominations Committee solicited nominations for the Society's 2011 awards as well as positions on the Society's Board of Directors. The Committee made recommendations to Council for the 2011 Awardees and the 2011 slate of officers at the October 15 Fall Council Meeting.

Bylaws Committee: *Joel Bumgardner, University of Memphis (Chair); Sachin Mamidwar, Orthogen Corp.; Lisa Friis, University of Kansas; Alan Litsky, Ohio State University; Lan Cao, Harvard University.* The Bylaws Committee is drafting language to formalize the creation of an Audit Committee and will review the bylaws for other possible revisions to bring before the Society's membership at the 2011 Annual Meeting.

Devices and Materials Committee: *Gabriele G. Niederauer, ENTrigue Surgical, Inc. (Chair); Warren Haggard, University of Memphis; Kristine Kieswetter, Kinetic Concepts, Inc.; Paul Spencer, Surmodics Pharmaceuticals, Inc.; Chris Loose, Semprus BioSciences; Ann Salamone, Rochal Industries; Bruce Anneaux, Zeus, Inc.; Jeremy Gilbert, Syracuse University.* In 2010-2011, the Devices and Materials Committee will continue its work in bringing together industry, government and academia to provide clinical relevance to biomaterials product development. It will also provide input to the Liaison Committee on naming representatives to standards organizations such as the American Society for Testing

"The Annual Meeting will continue to focus on fostering development of new implant materials and devices for improvement of the human condition. ."

and Materials and the International Organization for Standardization, and serve as a resource on relevant programs being developed for the Annual Meeting. Specific goals for the committee in the next months are to send out a survey to industry members to poll their unmet needs and investigate the possibility of developing a variety of educational webinars.

Education and Professional Development Committee:

Julie Hasenwinkel, Syracuse University (Chair); Sarit Bhaduri, University of Toledo; Lisa Friis, University of Kansas; Erin Lavik, Case Western Reserve University; Tom Slater, Medtronic Kyphon; Tim Topoleski, University of Maryland, Baltimore County; Heather Doty, University of Memphis (National Student Chapter President). The 2010-11 committee is currently administering the Biomaterials Days grant program and the C. William Hall Scholarship program, and evaluating endorsement requests from other organizations. The committee will also be working to develop a mentorship program and webinar series for Society members.

Finance Committee: *Laura J. Suggs, University of Texas at Austin (Chair); John Fisher, University of Maryland; Alan Litsky, The Ohio State University; Tony Mikos, Rice University; and Johnna Temenoff, Georgia Institute of Technology.* The Finance Committee continues to monitor the Society's long term reserve investments has developed of the 2011 budget. Budget priorities for 2011 include ensuring the success of our Annual Meeting, the productive relationship with our publishing partner, John Wiley & Sons, and recruiting and maintaining the Society's sponsors.

Liaison Committee: *Molly Shoichet, University of Toronto (Chair); Kristi S. Anseth, University of Colorado; Kevin Edward Healy, University of California, Berkeley; William Wagner, University of Pittsburgh; Ali Khademhosseini, Massachusetts Institute of Technology.* The Liaison Committee continues to seek opportunities for collaboration with other organizations at the Society's Annual Meeting and throughout the year, as well as seek qualified representatives to standards organizations. It expects to be active with the upcoming 2012 World Biomaterials Congress and possibly the 2020 World Biomaterials Congress as the International Union of Societies for Biomaterials Science and Engineering seeks preliminary ideas.

Long Range Planning Committee: Karen Burg, Clemson University, (Chair); Warren Haggard, University of Memphis; Helen Lu, Columbia University; Kris Kieswetter, Kinetic Concepts, Inc.; Erik Bland, Clemson University. The Long Rang Planning Committee is reviewing the plans prepared by previous committees and invites input from all members of SFB on the future direction of the Society and the field of biomaterials.

Meetings Committee: Jeremy Gilbert, Syracuse University (Chair); Warren Haggard, University of Memphis; Chris Siedlecki, Pennsylvania State University; Phil Messersmith, Northwestern University; Ben Keselowsky, University of Florida. The Meetings Committee will be re-evaluating the Society's meeting website and will also be evaluating social event options and future meeting locations. In addition, the committee received approval from the Board of Directors to hold a symposium in New Orleans in the Fall of 2012 (October 3-6, 2012).

Membership Committee: Bob Hastings, DePuy Orthopaedics, Inc. (Chair); Horst Von Recum, Case Western Reserve University; Mariah Hahn, Texas A&M University; Julie Stenken, University of Arkansas; Stephanie Bryant, University of Colorado. The Membership Committee has been working on new ideas to increase the value of SFB membership, attract and retain more industry members, attract new members from the Biomaterials Days events and make online membership registration more user-friendly. Information is being gathered on how to most effectively use the advertising budget money available this year, with both print and online advertising options being investigated.

Program Committee: Nicholas Ziats, Case Western Reserve University (Chair); Warren Haggard, University of Memphis; Christopher Siedlecki, Pennsylvania State University, Phillip Messersmith, Northwestern University; Guillermo Ameer, Northwestern University; Anthony Brennan, University of Florida; Monty Reichert, Duke University; Suping Lyu, Medtronic, Inc.; Peter Edelman, Boston Scientific; Andres Garcia, Georgia Institute of Technology; Anne Meyer, University at Buffalo; Liisa Kuhn, University of Connecticut Health Center. The Committee has reviewed more than 90 ideas submitted from the Society's Special Interest Groups and from the general membership, invited full proposals, evaluated those proposals, and compiled the preliminary list of sessions for the 2011 Annual Meeting in Orlando, Fla. The quantity and quality of abstract submissions will determine how many of the proposed sessions are actually presented in Orlando.

President's Advisory Committee: Lynne Jones, Johns Hopkins University (Chair): The President's Advisory Committee was active in the development of several program proposals for the 2011 Annual Meeting, and has organized an SFB-supported symposium at the Orthopaedic Research Society Annual meeting to be held in January 2011. The committee members continue to support the student initiatives, including the C. William Hall Scholarship for undergraduate students, sponsored through the royalties of the *Biomaterials Science* textbook. Potential exists to expand the scholarship program to other student categories.

Publications Committee: Ashutosh Chilkoti, Duke University (Chair); David Grainger, University of Utah; Jack Ricci, New York University; Helen Lu, PhD, Columbia University; Karen Burg, Ex-Officio, Clemson University; Tom Webster, Ex-Officio, Brown University; Jeremy Gilbert, Ex-Officio, Syracuse University; Jim Anderson, Ex-Officio, Case Western Reserve University. The Publications Committee is working to finalize the new Wiley contract for the *Journal* in order to present it at the October 15 Board and Council meeting. Coming soon is the creation of "virtual" Journal issues. The groundwork for this exciting project is being laid now; more details to come later. Terms for both the website and *Forum* editors are ending, and the committee is planning for the beginning of the new terms. Finally, work still continues on the book series.

If you are interested in knowing more about a particular issue, policy or committee activity, or if you have any suggestions for improved membership services, please contact me directly at the SFB headquarters office:

Sincerely,



Dan Lemyre, CAE
Executive Director
Society For Biomaterials
15000 Commerce Parkway, Suite C
Mount Laurel, NJ 08054
Phone: 856-439-0826
Fax: 856-439-0525
E-mail: info@biomaterials.org
www.biomaterials.org

In Remembrance



Dr. Shalaby Shalaby with recent Clemson University bioengineering graduate Dr. Scott Maxson.

Poly-Med, Inc. sadly announces the passing of its founder, Dr. Shalaby W. Shalaby, August 18, 2010.

Dr. Shalaby was a long-time member of the Society For Biomaterials and adjunct Professor of the Clemson University Department of Bioengineering.

A native of Dairut, Egypt, Dr. Shalaby earned undergraduate and graduate degrees in chemistry, botany, pharmacy, textiles, organic chemistry and polymer science. He was a former professor of Clemson University's Department of Bioengineering. Additionally, he served as the manager of the polymer research and development team at Ethicon and was director of the Johnson and Johnson Polymer Technology Center. In 1993, he founded Poly-Med Inc. at the Clemson Research Park in Anderson, South Carolina, where he was president and director of research and development at the time of his death.

Considered a pioneer in the field of absorbable biomaterials, over the course of his career, Dr. Shalaby created innovative drug-delivery systems for the controlled release of antimicrobial agents and patented absorbable liquid tissue adhesive and wound closure devices, as well as a broad spectrum of other biomedical and pharmaceutical innovations. In honor of his many contributions, he received the Society For Biomaterials Technology Innovation and Development award.

His innovative and insightful contributions have been an integral part in creating Poly-Med's reputation as an industry leader in designing, developing, and manufacturing specialty medical devices and materials.

Continuing Poly-Med's mission, Board member Waleed Shalaby, MD, Ph.D. will be responsible for directing all Poly-Med Research & Development activities. Additionally, Board member David Shalaby will preside over corporate operations. All inquiries may be directed to Poly-Med's Secretary/Treasurer, Dr. Joanne E. Shalaby at Shalaby@poly-med.com.

From the President

Continued from page 3

We are defined by the dichotomy of these questions and we are anchored in our science by the desire to improve health by finding new ways to treat disease, trauma and disability. We are stronger as a Society if we do not stray too far from these core elements.

We are a Materials Society where materials science and engineering plays a central role.

We are a Biological Society—we seek to understand and use quantitative biological principles to treat human health conditions.

We are a Medical Device Society because we want to create devices and therapies that can treat patients.

We are a translational research society—more so than any other society out there. We were focused in this area well before The National Institute of Health or the Coulter Foundation recognized the U.S. national need to translate basic science advancements into real devices and therapies for real people with real diseases.

Thus, the medical device industry is another core element of our Society and it must continue to play a central role in the life of the Society.

We are a Society of academic researchers—clinical, basic life science and materials science and engineering—but we are also industrial medical-device researchers and developers, with all of the additional concerns that come with bringing medical devices to patients and government scientists and engineers studying and regulating medical devices.

Just like the dichotomous balance between Bio- and Materials, there is a dichotomous balance (or trichotomous perhaps?) that is a core strength of our Society that comes from industrial and government presences. We need strong industry participation to translate our ideas into therapies and new devices, to recruit the up-and-coming students, and provide a means to bring our new ideas to those who need them most—the patient. We need to work with government to assure the proper relationship between regulation and innovation.

We all once were students (many of us still are). The students with us today represent the future: The future of academic research, the future of industrial R&D and the future of the membership and leadership of this Society.

The Society For Biomaterials has always prided itself as being a student friendly place, where students can meet the leaders of the field, and the established among us can find the rising new talent. The opportunity to see industry and how it works, to see academia, to establish professional roots and connections – these are central values of our Society.

I have found that in life, strength comes from balance. Our Society was founded on such a balance. It is an exquisite balance between fundamental and applied, between academic and industry, between clinical and laboratory. Our strength into the future rests on us understanding this balance, acknowledging, respecting, and valuing “the other” and sharing not only in the benefits of membership, but also in the responsibility of leading the field and our Society. It also comes from embracing this balance – it is what has led us to this point.

I look forward to the daunting task of leading this Society for the next 12 months and I welcome your comments and efforts on behalf of the Society. Most of all, I value your friendship and your commitment to the Society—I will continue to work to make this vision the defining vision for our Society.

Thank you.

Jeremy L. Gilbert, Ph.D.
President

Human Microvascular Endothelial Cells Uptake Nanoparticles

Special Interest Group News

Christopher Siedlecki, *Special Interest Group News*

Contributing Editor

Carl Simon, Jr., *Proteins and Cells at Interfaces*

Special Interest Group Reporter

Qinghe Zhao¹, Patrick L. Apopa², Diane Schwegler-Berry², Yong Qian², Bingyun Li^{1,3}

¹Department of Orthopaedics, School of Medicine, West Virginia University, Morgantown, WV 26506, USA

²The Pathology and Physiology Research Branch, Health Effects Laboratory Division, National Institute for Occupational Safety and Health, Morgantown, WV 26505, USA

³WVNano Initiative, Morgantown, WV 26506, USA

Abstract: The uptake efficiency of nanoparticles by human cells may play an important role in molecular diagnostics and intracellular drug delivery. We studied the uptake of polystyrene nanoparticles by human microvascular endothelial cells (HMVECs). We quantified and imaged the cellular uptake of nanoparticles using fluorescence absorption and confocal laser scanning microscopy. We found that polystyrene nanoparticles could enter HMVECs within minutes and uptake of nanoparticles by HMVECs was dose and time dependent. The findings may help design future nanoparticle systems for intracellular drug delivery.

Introduction

Nanotechnology is a technique that manipulates materials in the range of 1-100 nanometers and utilizes the quantum effect of materials in the nano scale that is distinct from their bulk materials. Advances in nanotechnology provide opportunities in biotechnology and nanomedicine; for instance, nanoparticles were utilized to diagnose and image diseases and to treat tumors by targeted delivery of drugs to the tumor sites [1].

Nanoparticles can be taken up by living cells and tissues and are very promising as intracellular drug delivery systems. There are a few studies on the efficiency and mechanism of nanoparticle uptake into human cells [2-4]. In general, the cellular uptake of nanoparticles is believed to depend on nanoparticle size, surface chemistry, and type of cells and nanoparticles [2, 3]. Studies by des Rieux and coworkers assessed the influence of physical-chemical properties of nanoparticles on the translocation of nanoparticles across the intestinal epithelial cell monolayer, and found that nanoparticles with positive charges had a higher penetration rate than nanoparticles with negative charges [4]. However, Geiser and coworkers found that nanoparticle uptake by pulmonary macrophages and red blood cells was not affected by nanoparticle surface charges and surface chemistry [2]. Therefore nanoparticle uptake may be cell specific.

We studied the uptake of polystyrene (PS) nanoparticles by human microvascular endothelial cells (HMVECs), which may play a key role in cellular uptake of nanoparticles as intracellular drug delivery systems or nanoparticles from the environment. PS nanoparticles were used due to their narrow

size distribution and well characterized properties [5].

Materials and Methods

Fluorescein isothiocyanate (FITC) labeled PS nanoparticles (20 nm) with carboxylate end groups and penicillin and streptomycin antibiotics were obtained from Invitrogen (Eugene, OR, USA). Endothelial basal medium-2 (EBM-2) was purchased from Lonza (Boston, MA, USA). Fetal bovine serum was obtained from Atlanta Biologicals (Lawrenceville, GA, USA). Epidermal growth factor (EGF) and hydrocortisone were from Sigma (St. Louis, MO, USA). All antibodies used in this study were purchased from Invitrogen (Eugene, OR, USA).

HMVECs were obtained from a previous study [6], and were cultured according to the reported protocol [6, 7]. Briefly, HMVECs were seeded in 24-well tissue culture plates and incubated in EBM-2 supplemented with 10% (v/v) fetal bovine serum, 100 U/ml penicillin, 10 µg/ml streptomycin, 1 µg/ml of EGF, and 50 µg/ml hydrocortisone. The cells were cultured at 37°C with 5% CO₂ to a confluent monolayer before adding PS nanoparticles. To determine the effect of concentration on nanoparticle uptake, PS nanoparticles of 2 µg, 10 µg, 20 µg or 40 µg were added to HMVECs in 1 ml medium and incubated for 30 min. The cell plates were then quickly put on ice for 10 min and the cells were washed three times with ice-cold 0.1 M phosphate buffered saline (PBS, pH7.4). Subsequently, the cells were fixed with 4% formaldehyde for 15 min at room temperature and washed three times with PBS. To determine the effect of incubation time on nanoparticle uptake, 2 µg PS nanoparticles were incubated with HMVECs for 10, 20, 30, 60, 180, 300, and 720 min. The fluorescence of the cells was recorded with a Cytoflour Series 4000 plate reader (PerSeptive Biosystems Inc., Framingham, MA, USA) at a wavelength of 505 nm for excitation and 515 nm for emission. Fluorescent images were acquired with a ZEISS LSM 510 confocal microscope (Thornwood, NY, USA) at an excitation wavelength of 488 nm, 543 nm, and 633 nm. All pictures were taken under the same instrumental parameters. For confocal microscope imaging, the cell membrane was labeled by incubating permeabilized cells with antibody to VE-Cadherin followed by FITC-labeled secondary antibody. The actin cytoskeleton was labeled using TRITC-phalloidin. The relative fluorescence of PS nanoparticles within cells was analyzed using software Image J 1.42q (NIH, USA).

Results and Discussion

The results showed that PS nanoparticles were taken up by the HMVECs within a short time (e.g. 10 min). Fig. 1a-c shows the three channel confocal images of control HMVECs. The cell membrane and actin cytoskeleton were clearly observed. No nanoparticles were seen in the control HMVECs (Fig. 1a-c).

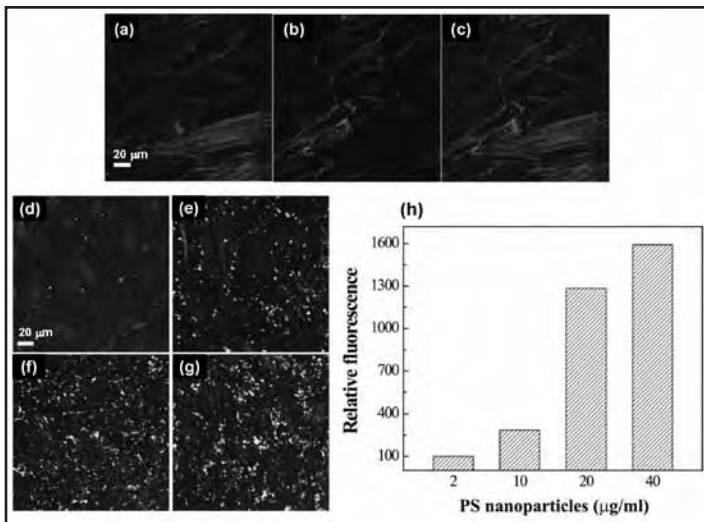


Figure 1: (a-c) Control-HMVECs. (a) Blue fluorescence: actin cytoskeleton. (b) Red fluorescence: cell membrane. (c) Combination of (a) and (b). The scale bar is 20 µm. (d-g) PS nanoparticles uptaken by HMVECs at dose of (d) 2 µg/ml, (e) 10 µg/ml, (f) 20 µg/ml, and (g) 40 µg/ml (blue = actin cytoskeleton, red = cell membrane, green = PS nanoparticles). (h) Relative fluorescence intensity of PS nanoparticles inside HMVECs vs. PS nanoparticle dose.

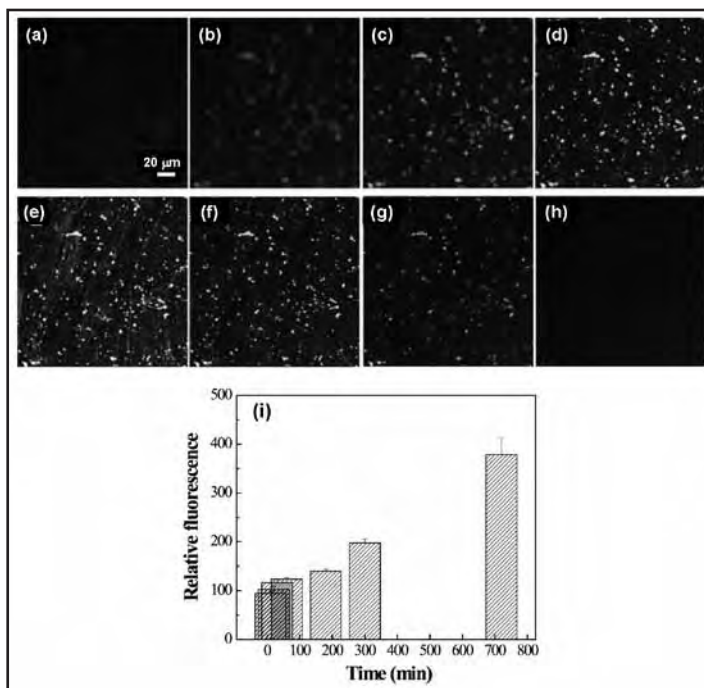


Figure 1: (a-h) Confocal images of HMVECs after uptake of 10 µg/ml PS nanoparticles for 30 min. Cross-sectional view from the apical aspect (a) to the basolateral aspect (h), with a vertical interval of 2 µm. Cell membrane is red, PS nanoparticles are yellow and green, and actin cytoskeleton is blue. (i) Time dependent uptake of PS nanoparticles (2 µg/ml) by HMVECs. Time points studied were 10, 20, 30, 60, 180, 300, and 720 min.

In comparison, PS nanoparticles (i.e. green fluorescence labeled particles) were found in HMVECs (Fig. 1d-g); this observation was confirmed in 3D confocal images (data not shown). The amount of nanoparticle uptake increased with an increasing amount or feeding dose of PS nanoparticles, as shown by the increase of fluorescence intensity inside the cells (Fig. 1d-h). Similar to other reports [5], the nanoparticles aggregated to some degree within HMVECs. Cross-section images (Fig. 2a-h) of HMVECs further

confirmed that PS nanoparticles were located within HMVECs. Moreover, it was found that the uptake of PS nanoparticles by HMVECs was time dependent (Fig. 2i). The uptake of PS nanoparticles occurred within a short time period, e.g. 10 min, and then gradually increased up to 720 min. Fluorescence of PS nanoparticles uptaken at 720 min was approximately four times that of nanoparticles uptaken at 10 min (Fig. 2i). The increase in nanoparticle uptake is probably because the efficiency of nanoparticle uptake depends mainly on cell trafficking rate and amount of delivery vehicles [5].

In conclusion, we found that PS nanoparticles can be taken up by HMVECs within minutes and the uptake process is feeding dose and incubation time dependent. Further studies to determine the trafficking mechanisms of nanoparticles into HMVECs and the distribution of nanoparticles in their organelles are under investigation and may provide new insights into early disease diagnosis and intracellular drug delivery.

Acknowledgements

The authors appreciate the use of confocal laser scanning microscope at the Microscopic Imaging Facilities at NIOSH, Morgantown, WV. The authors also thank Suzanne Smith at WVU for proof reading. No commercial associations, current and within the past five years, that might pose a potential, perceived or real conflict of interest, were reported by the authors of this paper. The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the National Institute for Occupational Safety and Health.

References

- Allen TM. Ligand-targeted therapeutics in anticancer therapy. *Nat Rev Cancer* 2002; 2:750-65.
- Geiser M, Rothen-Rutishauser B, Kapp N, Schürch S, Kreyling W, Schulz H, Semmler M, Hof VI, Heyder J, Gehr P. Ultrafine particles cross cellular membranes by nonphagocytic mechanisms in lungs and in cultured cells. *Environ Health Perspect* 2005; 113:1555-60.
- Caliot E, Libon C, Kerneis S, Pringault E. Translocation of ribosomal immunostimulant through an *in vitro*-reconstituted digestive barrier containing M-like cells. *Scand J Immunol* 2000; 52:588-94.
- des Rieux A, Ragnarsson EG, Gullberg E, Preat V, Schneider YJ, Artursson P. Transport of nanoparticles across an *in vitro* model of the human intestinal follicle associated epithelium. *Eur J Pharm Sci* 2005; 25:455-65.
- Yacobi NR, DeMaio L, Xie JS, Hamm-Alvarez SF, Borok Z, Kim KJ, Crandall ED. Polystyrene nanoparticle trafficking across alveolar epithelium. *Nanomedicine: NMB* 2008; 4:139-45.
- Apopa PL, Qian Y, Shao R, Guo NL, Berry DS, Pacurari M, Porter D, Shi XL, Vallyathan V, Castranova V, Flynn DC. Iron oxide nanoparticles induce human microvascular endothelial cell permeability through reactive oxygen species production and microtubule remodeling. *Particle Fibre Toxicology* 2009; 6:1-14.
- Shao R, Guo X. Human microvascular endothelial cells immortalized with human telomerase catalytic protein: a model for the study of *in vitro* angiogenesis. *Biochem Biophys Res Commun* 2004; 321:788-94.

American Institute for Medical and Biological Engineering News

AIMBE News

Alan Litsky, AIMBE News

Contributing Editor

AIMBE, the American Institute for Medical and Biological Engineering, was founded in 1991 “to establish a clear and comprehensive identity for the field of medical and biological engineering” and “seeks to serve and coordinate a broad constituency of medical and biological scientists and practitioners, scientific and engineering societies, academic departments and industries.” The Society For Biomaterials is a member society of AIMBE as many of their interests overlap with ours and two SFB members serve on their Council of Societies. More about the organization can be found at their web site: www.aimbe.org.

The AIMBE staff publishes a bi-weekly Federal Update monitoring governmental activities and initiative relevant to their constituencies. Several events discussed in recent issues focus on the issue of increasing the number and percentage of women in science and engineering disciplines:

White House Nominates Materials Scientists for National Science Foundation (NSF) Director

The National Science Foundation announced plans for the leadership transition. In an announcement at the White House, President Obama announced Dr. Subra Suresh as the nominee for the post of Director of the NSF. Professor Suresh is currently Dean of the School of Engineering and the Vannevar Bush Professor of Engineering at the Massachusetts Institute of Technology (MIT). From 2000 to 2006, Dr. Suresh served as the head of the MIT Department of Materials Science and Engineering. He earned a bachelor's degree from the Indian Institute of Technology in Madras, an M.S. from Iowa State University and a Sc.D. from the Massachusetts Institute of Technology.

AAUW Report Details Possible Reasons Why Women Do Not Participate in Science, Technology, Engineering and Mathematics (STEM)

In an era where women are increasingly prominent in medicine, law and business, why are there so few female scientists and engineers? A new research report by AAUW presents compelling evidence that can help to explain this

puzzle. *Why So Few? Women in Science, Technology, Engineering and Mathematics* presents in-depth yet accessible profiles of eight key research findings that point to environmental and social barriers, including stereotypes, gender bias and the climate of science and engineering departments in colleges and universities that continue to block women's participation and progress in science, technology, engineering and math. The report also includes up-to-date statistics on girls' and women's achievement and participation in these areas and offers new ideas for what each of us can do to more fully open scientific and engineering fields to girls and women. An electronic copy of the full report can be downloaded at <http://www.aauw.org/research/whysofew.cfm/>.

Pay and Promotion Matter

A new working paper examines the exodus of women from the science and engineering fields, and upends some popularly accepted wisdom. The author, Jennifer Hunt, finds that the gap is primarily driven by the engineering field, and that “60 percent of the gap can be explained by the relatively greater exit rate from engineering of women dissatisfied with pay and promotion opportunities.” Family-related explanations, which are often blamed for the gap, play a much smaller role. Hunt finds a strong positive relationship between share of male workers and excess female exits, which suggests a need for policies aimed at improving female mentoring and networks and reducing discrimination across male-dominated fields. The full report can be found at <http://www.awis.affiniscap.com/associations/9417/files/Working%20Paper%20on%20Women%20leaving%20science.pdf>.

Save the Date for the 2011 Annual Event and Federal Symposium!

Save the date for AIMBE's 20th Annual Event, Medical and Biological Engineering in the Next 20 Years: The Promise and the Challenges, February 20-22, 2011 at the Mandarin Oriental in Washington, D.C. Immediately following will be AIMBE's 6th Annual Federal Symposium and Congressional Visits Day, February 23, 2011.

The perfect pair



Biofabrication and *Biomedical Materials* are in perfect harmony, together they deliver a complete package designed to keep you up-to-date in all areas of biofabrication and tissue engineering. New papers published online are free-to-read for the first 30 days.

Visit the journal homepages for more information iopscience.org/bf and iopscience.org/bmm

IOP Publishing

Society For Biomaterials 2011 ANNUAL MEETING & EXPOSITION

Animating Materials

SAVE THE DATE
APRIL 13 - 16, 2011

DISNEY'S CONTEMPORARY RESORT IN
ORLANDO, FLORIDA

<http://2011.biomaterials.org>



The Good and Peril of the Internet

In a pair of recent dual articles in the Wall Street Journal, Clay Shirky and Nicholas Carr made opposing arguments about the good and the peril of the Internet.

In Shirky's arguments, the open digital media are good for creating a new culture norm. "Digital media have made creating and disseminating text, sound, and images cheap, easy and global. The bulk of publicly available media is now created by people who understand little of the professional standards and practices for media."

"Similarly, open source software, created without managerial control of the workers or ownership of the product, has been critical to the spread of the Web. Searches for everything from supernovae to prime numbers now happen as giant, distributed efforts."

"Increased freedom to create means increased freedom to create throwaway material, as well as freedom to indulge in the experimentation that eventually makes the good new stuff possible. There is no easy way to get through a media revolution of this magnitude; the task before us now is to experiment with new ways of using a medium that is social, ubiquitous and cheap, a medium that changes the landscape by distributing freedom of the press and freedom of assembly as widely as freedom of speech."

However, Carr holds an alarming view toward the Internet. "The Internet grants us easy access to unprecedented amounts of information. But a growing body of scientific evidence suggests that the Net, with its constant distractions and interruptions, is also turning us into scattered and superficial thinkers."

"The richness of our thoughts, our memories and even our personalities hinges on our ability to focus the mind and sustain concentration. Only when we pay deep attention to a new piece of information are we able to associate it 'meaningfully and systematically with knowledge already well established in memory,' writes the Nobel Prize-winning neuroscientist Eric Kandel. Such associations are essential to mastering complex concepts."

"The Internet grants us easy access to unprecedented amounts of information. But a growing body of scientific evidence suggests that the Net, with its constant distractions and interruptions, is also turning us into scattered and superficial thinkers."

"When we're constantly distracted and interrupted, as we tend to be online, our brains are unable to forge the strong and expansive neural connections that give depth and distinctiveness to our thinking. We become mere signal-processing units, quickly shepherding disjointed bits of information into and then out of short-term memory."

"The cellular structure of the human brain, scientists have discovered, adapts readily to the tools we use, including those for finding, storing and sharing information. By changing our habits of mind, each new technology strengthens certain neural pathways and weakens others. The cellular alterations continue to shape the way we think even when we're not using the technology."

"What we seem to be sacrificing in all our surfing and searching is our capacity to engage in the quieter, attentive modes of thought that underpin contemplation, reflection and introspection. The Web never encourages us to slow down. It keeps us in a state of perpetual mental locomotion."

Since their arguments hinge on different anchor points, I will let you be the judge. But surely, it is worth thinking twice when you plan to exploit smart technologies aided by the Internet and multimedia either in your teaching or self learning.

Inspiring the Next Generation of Biomaterial Scientists

Department of Bioengineering, University of Washington, Seattle
By Eric H. Chudler and Buddy D. Ratner

The UWEB Research Experience for Undergraduate (REU) program (National Science Foundation grants EEC 9529161 and NSF 0647918) exemplifies a strong commitment to interdisciplinary undergraduate education and to increasing diversity in bioengineering and biomaterials science. This 10-week summer research program is a powerful tool to attract talented undergraduate students into the engineering field and to encourage them to pursue graduate study and eventual research careers.

The focus of the UWEB REU program is a carefully mentored research experience that teams undergraduate students with a graduate student or postdoctoral fellow and a faculty member. Mentors have diverse backgrounds and the teams focus on a project that exploits specific biological recognition mechanisms in order to develop a new generation of biomaterials for medical implants that will heal in the body in a facile, physiologically normal manner.

Planning for the REU begins in the autumn quarter prior to the start of the summer program. During this planning, application materials are placed online and students across the country are made aware of the program through online postings, program flyers, and promotion at scientific meetings. After the application deadline, a committee of faculty, staff and mentors is formed to evaluate the applicants. Each application is scored by at least three reviewers. Reviewers meet to discuss the applications and to select those students who will receive offers to join the REU program.

In addition to working in the laboratory, REU students participate in a series of interactive workshops (communications skills, journal club, laboratory safety, and bioethics).

All undergraduate researchers are required to write a journal style article (minimum of five pages) describing their research project. Many REU students publish their work in the UWEB publication, *Journal of Undergraduate Research in Bioengineering*; other

students co-author papers with their mentors and laboratory directors for other journals.

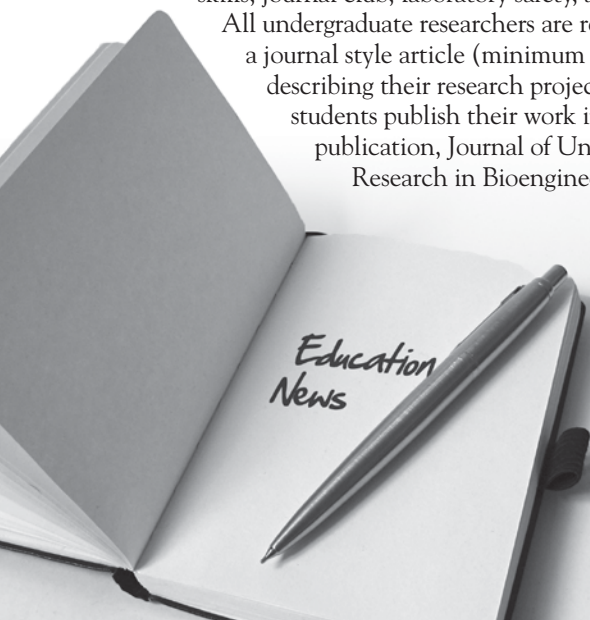
Each year, an REU bioethics lecture is presented that focuses on ethical concerns of importance to scientists and engineers (e.g., plagiarism, falsification of data, note keeping, statistics, animal welfare, human subjects) to stimulate discussion about the significance of ethics. One goal of this lecture is to make students aware of bioethical issues and to encourage responsible scientific conduct. Students also attend a laboratory safety class during the first week of the REU program. The safety class discusses issues such as chemical toxicity, handling, transport and storage, material safety data sheets, personal protection equipment, hazardous waste disposal and emergency procedures. As participants in the UWEB-sponsored program, REU students have the opportunity to attend a variety of University of Washington lectures and courses offered by scholars presenting their work in different departments across campus.

The 10-week research program culminates in two research symposiums. In the first symposium, UWEB REU students join approximately 100 other students who have participated in other University of Washington summer research programs (e.g., Amgen Scholars Program, Hooked on Photonics, National Nanotechnology Infrastructure Network, Environmental Health Research Experience Program, Intel Summer Research Experience for Undergraduates). Students construct large format posters that are displayed on easels set up in a conference center. During the poster session, students are assigned a time to present their results to the university research community in an informal setting. During the second symposium, students create a 10-minute PowerPoint presentation of their work. Each presentation is followed by a five-minute question/answer session with the audience. These forums provide valuable opportunities for the REU undergraduates to communicate their results to others and to provide the students with direct experience in poster preparation and oral presentation. This experience will be extremely valuable when they attend future scientific conferences.

The success of the UWEB REU program is made possible by the many dedicated mentors and lab directors who have devoted countless hours to share their knowledge and research projects with young scientists.

Education Quote of the Quarter:

“ Education is not the answer to the question. Education is the means to the answer to all questions.” — William Allin



Congratulations to:

Dr. Mauli Agrawal, Dean of Engineering at The University of Texas at San Antonio, who is the recipient of the fifth annual Julio Palmaz Award for Innovation in Healthcare and the Biosciences. This award, given by non-profit San Antonio corporation BioMed SA, honors individuals who have made significant contributions to advances in the healthcare and bioscience fields. Dr. Agrawal is a Fellow of the International Union of Societies for Biomaterials and the American Institute for Medical and Biological Engineering. His research, including developing and improving orthopedic implants, regenerative medicine devices, diabetic foot products and drug delivery stents, has led to the formation of three biomedical startup companies in San Antonio.

Dr. Ali Khademhosseini, Assistant Professor of Medicine and Health Sciences and Technology, at Harvard Medical School, Massachusetts Institute of Technology, and Brigham & Women's Hospital, who is the recipient of four prestigious awards honoring his development of micro- and nanoengineering approaches for controlling cell microenvironment and use of these techniques to regulate stem cell fate decisions. Ali is the recipient of the 2010 American Institute for Chemical Engineers Allan F. Colburn Award for excellence in publications by a young member of the Institute. This award is sponsored by E. I. DuPont de Nemours and Company and will be presented at the AIChE Annual Meeting. Dr. Khademhosseini is also the recipient of the TERMIS-NA Young Investigator Award, an award given to an individual who has demonstrated outstanding achievements within the tissue engineering and regenerative medicine field and is within 10 years of receipt of their terminal degree. Additionally, Dr. Khademhosseini was selected as the winner of the American Chemical Society Colloid and Surface Science Division Unilever Award for 2010. The award recognizes and encourages fundamental work in colloid or surfactant science carried out in North America by researchers in the early stages of their careers. And last, but not least, congratulations to Dr. Khademhosseini for receiving the 2010 Office of Naval Research Young Investigator Award, an award given to honor past research achievements and potential for continued outstanding research efforts of those individuals showing exceptional promise for conducting cutting-edge research.

Dr. Naren Vyavahare, Professor of Bioengineering at Clemson University, who received the Clemson University Alumni Award for Outstanding Achievement in Research for his contributions to cardiovascular research. Each year a recipient is selected by representatives from each of Clemson University's colleges who are members of the Sigma Xi and/or Phi Kappa Phi honor societies.

2010 Biomedical Engineering Society Fellows

Linda Griffith (Professor of Biological Engineering and Mechanical Engineering; Director, Center for Gynepathology Research, Massachusetts Institute of Technology)

Cato Laurencin (Vice President for Health Affairs, University of Connecticut; Dean and Van Dusen Endowed Chair of Academic Medicine, School of Medicine, University of Connecticut Health Center)

David Puleo (Professor and Director, Center for Biomedical Engineering, University of Kentucky)

(William) Monty Reichert (Professor of Biomedical Engineering and Chemistry; Director, Center for Biomolecular and Tissue Engineering, Duke University)

Christine Schmidt (B.F. Goodrich Endowed Professor of Materials Engineering, University of Texas at Austin)

Editor's note: Would you like to share some good news about an honor you or a colleague have received? We would love to hear from you; please email news items to kburg@clemson.edu.

Imaging Cells in Polymer Scaffolds by X-Ray Microcomputed Tomography

Shauna M. Dorsey, Sheng Lin-Gibson, Carl G. Simon, Jr.*
Polymers Division, National Institute of Standards & Technology,
Gaithersburg, MD 20899, USA

*Corresponding author. Polymers Division, National Institute of Standards & Technology, 100 Bureau Drive, Gaithersburg, MD 20899, USA

Introduction

We have investigated the ability of X-ray microcomputed tomography (μ CT) to make quantitative, three-dimensional (3D) measurements of cell adhesion and proliferation in polymeric tissue engineering scaffolds [1]. The most common method for examining cells in scaffolds is microscopy [2]. Sectioning followed by histology can image the scaffold interior but is destructive, tedious and only semi-quantitative [2]. Fluorescence microscopy can be quantitative when high-throughput approaches are applied [3] and confocal fluorescence microscopy can yield 3D images [4]. However, neither can “see through” opaque materials to image the interior of a scaffold. Other common methods for measuring cell presence include the colorimetric and fluorometric soluble assays for enzymes (dehydrogenase) [5], protein (bicinchoninic acid assay) [6] or DNA (Picogreen) [7]. These soluble assays are quantitative but do not yield information on spatial distribution. In contrast, μ CT generates 3D images, can penetrate deep into the scaffold interior, is non-destructive and is inherently quantitative [8-10]. For these reasons, we have investigated the sensitivity of using μ CT to image and measure cell adhesion and proliferation in polymeric tissue engineering scaffolds.

Cells were seeded onto polymer scaffolds at different concentrations (0, 5000, 10000, 25000, 100000 and 400000 cells per scaffold) and measured at different times (1 d, 7 d and 14 d). Poly(ϵ -caprolactone) (PCL) was chosen as the material for scaffold fabrication because it is biocompatible and has been used in FDA-approved devices. A salt-leaching approach was chosen because it is a common and effective method for scaffold fabrication. The MC3T3-E1 osteoblast cell line was used because it is a well-characterized murine osteoblast model which has been widely applied for regenerative orthopaedic models. Cell adhesion and proliferation on the scaffolds was assessed by three techniques: fluorescence microscopy, a soluble assay for DNA (Picogreen) and μ CT. Results from the three approaches were compared so that the usefulness of μ CT for detecting cells in tissue engineering scaffolds could be evaluated.

Results and Discussion

Experiments were performed with cylindrical scaffolds fabricated in 96-well plates from PCL by salt-leaching using sieved NaCl (0.250 mm to 0.425 mm dia.) (Fig. 1a,b) [11]. The scaffolds had pores of size range 0.2 mm to 0.4 mm and gravimetric analysis indicated that scaffolds were 97 % porous. Imaging of MC3T3-E1 osteoblasts by fluorescence microscopy showed that cell numbers increased with increasing cell seeding density and increasing culture time indicating that osteoblasts adhered and proliferated on the scaffolds (Fig. 1c). Similar results were obtained for the soluble DNA assay (Picogreen) where increased DNA levels were extracted from the scaffolds with increasing cell seeding density and culture time (not shown).

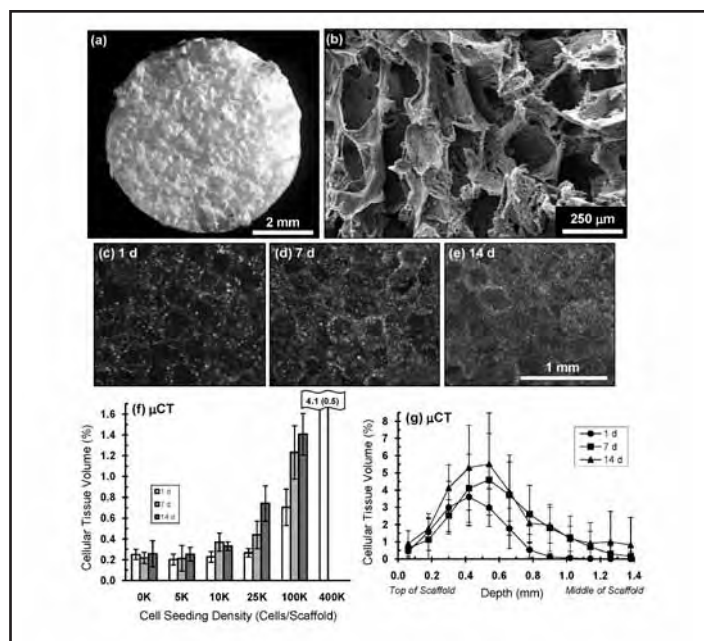


Figure 1: (a) Stereomicroscope image of PCL scaffold fabricated in a polypropylene 96-well plate. (b) Scanning electron micrograph of the scaffold interior. (c-e) MC3T3-E1 osteoblasts were seeded on PCL scaffolds in 96-well plates (25000 cells/scaffold), cultured (1 d, 7 d or 14 d) and imaged by fluorescence microscopy (fixed cells, nuclei stained with Sytox green). Scale bar in (e) applies to (c-e). Green dots in images are nuclei of cells adherent to scaffolds. (f) Cells were seeded on PCL scaffolds at different densities (0K, 5K, 10K, 25K, 100K, 400K cells/scaffold), cultured (1 d, 7 d or 14 d) and imaged by μ CT. Cellular tissue volume on the scaffolds was determined from μ CT images using a threshold of 34. ANOVA with Tukey's multiple comparison test indicated that 25K-14d, 100K-1d, 100K-7d, 100K-14d and 400K-1d scaffolds were significantly different from background (0K, scaffolds with no cells) ($P < 0.05$). [Only the 1 d is shown for 400K because cells were not viable at this high density in 96-well plates in 0.2 mL of cell medium.] (g) Cell penetration depth into the scaffolds was evaluated by μ CT image analysis. μ CT scans of scaffolds were divided in the Z-direction into 12 regions of 120 μ m for cellular tissue volume analysis (threshold 34). Plots from scaffolds seeded with 100K cells and cultured 1 d, 7 d or 14 d are shown. Error bars in panels (f-g) are standard deviation ($n = 6$).

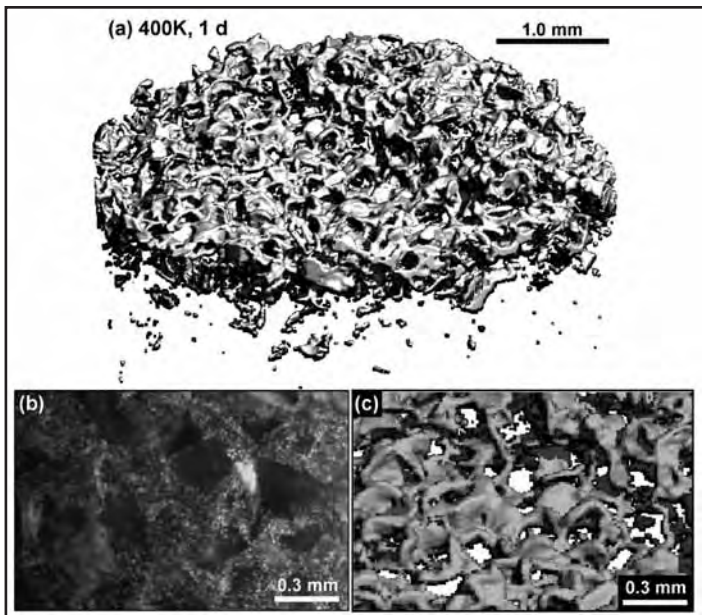


Figure 1: (a) μ CT image of a scaffold cultured 1 d with 400K cells (threshold 34; calculated cell volume is 4.0 %). Note that the opaque voxels are not scaffold but are from confluent cell layers on the scaffold. Side by side comparison of a (b) fluorescence micrograph and a (c) μ CT image from scaffolds cultured 1 d with 400K cells. Note that panels (b) and (c) are at the same magnification allowing direct comparison of fluorescence and μ CT.

For μ CT, cells on scaffolds were stained with osmium tetroxide to enhance their X-ray contrast. Osmium is a heavy metal that stains cell membranes, scatters X-rays and makes cells visible by μ CT. Stained and dried scaffolds were imaged by μ CT [Scanco μ CT 40, 55 kVp, 145 μ A, 8 μ m voxel size (slice thickness), 0.3s integration, 325 slices, sigma 1.2, support 2] and thresholded at voxel intensity 34. Threshold 34 was chosen because 95 % of the voxel intensity signal greater than 34 came from the cells as determined from voxel intensity histograms (background accounts for the other 5 %; background is scaffold or void).

Cell adhesion and proliferation during culture on scaffolds was determined by calculating the “percent tissue volume” in the μ CT scans which was defined as the percent of the voxels in a given scaffold volume that contained enough osmium stained cellular material (tissue) to give that voxel an intensity value greater than 34. Results showed a trend of increased cellular volume with increasing cell seeding density and increasing culture time (Fig. 1f). Cell penetration depth into the scaffolds was also evaluated quantitatively by μ CT image analysis (Fig. 1g). For the 100K scaffolds, the cells penetrated to 0.8 mm after 1 d and to 1.2 mm by 7d. From 7 d to 14 d, the cells did not penetrate further. Cell migration deeper into the scaffolds was probably prohibited by insufficient exchange of nutrients/waste since the 96-well plate scaffolds can only access medium at their top surface.

Cell adhesion and proliferation on the scaffolds was assessed by three techniques: fluorescence microscopy, a soluble assay for DNA (Picogreen) and μ CT.

A μ CT image of a 400K-1d scaffold is shown in Fig. 2a. Note that the 3D contours of the salt-leached pores in the scaffold are visible due to the confluent coating of osmium-stained osteoblasts adhered to them. The even X-ray contrast across the top of the scaffold indicates uniform cell distribution. The μ CT (8 μ m resolution) cannot resolve individual cells and can only resolve cell clusters (tissue, regions of confluent cells). A side by side comparison of a fluorescence micrograph and a μ CT image at the same magnification (Fig. 2b,c) demonstrates the higher resolution afforded by fluorescence microscopy. Cell nuclei are visible in the fluorescence micrograph (Fig. 2b) while cells in the μ CT image run together appearing as a pixelated, continuum (Fig. 2c). On the other hand, the μ CT image more clearly portrays the 3D nature of cells on a scaffold and enables imaging through the opaque scaffold.

Statistical analysis of Picogreen DNA assay data showed that > 5K cells had to be seeded on scaffolds to enable detection above background (not shown). For the μ CT volume calculations, statistical analysis showed that > 25K cells had to be seeded on a scaffold to enable detection of signal above background (Fig. 3a). These results demonstrate that the Picogreen DNA assay was \approx 5X more sensitive than μ CT. In addition, these results indicate that μ CT is best suited for situations where a high density of cells is present on a scaffold, such as in more mature constructs where cells have reached confluence and where tissue generation has begun.

The penetration depth data for the 100K-1d scaffold in Fig. 3b showed that after 1 d of culture the cells were present in the top 800 μ m of the scaffolds. If it is assumed that there are 100000 cells present in these scaffolds, then a volume calculation indicates that the cell density in the scaffolds during the μ CT imaging was 4 million cells/mL {cell number / ($\pi r^2 \times h$) = 100000 cells / [3.14 x (0.325 cm)² x 0.08 cm]}. The μ CT volume analysis (Fig. 1f) demonstrated that the 100K-1d scaffolds were easily distinguished from background, which indicates that a cell density of 4 million cells/mL is well within the detection limits of μ CT. A similar calculation for the 25K-

Id specimens indicates that cell density was 1 million cells/mL for these scaffolds, which was not significantly different from background by μ CT (Fig. 1f). Taken together, these results indicate that cell density between 1 to 4 million cells/mL is required for quantitative μ CT volume analysis.

Conclusions

The ability of μ CT to quantify cell adhesion and proliferation in polymer scaffolds has been evaluated. Fluorescence microscopy had better imaging resolution than μ CT and the Picogreen DNA assay was more sensitive for cell quantification than μ CT. However, μ CT combined imaging and quantification into a single modality, is inherently quantitative, can image through opaque scaffolding materials and yields 3D images which can be used to assess spatial distribution of cells in scaffolds. The μ CT required cell density to be > 1 million cells/mL indicating this approach will work best for constructs containing high cell density.

The three approaches for assessing cells in scaffolds addressed herein, fluorescence microscopy, Picogreen DNA assay and μ CT, are complimentary to one another. When evaluating cell adhesion and proliferation in polymer scaffolds, use of fluorescence microscopy is essential for establishing that cells are present and that they are evenly distributed about the scaffold, especially at early time points when μ CT cannot detect cells at low density. In addition, fluorescence microscopy is higher resolution enabling individual cells to be visualized. The soluble DNA assay is valuable because it is quantitative and provides a second measure of cell number. The μ CT provides both a 3D image and 3D quantitative analysis of cell spatial distribution within scaffolds. In sum, μ CT compliments fluorescence microscopy and soluble assays for cell components (DNA, protein, enzymes) to provide a comprehensive evaluation of cell adhesion and proliferation in polymeric tissue scaffolds.

Acknowledgements

We acknowledge valuable contributions from J. Sun, N. Lin, D. Zeiger, Y. Yang (NIST) and M. Alexander (University of Nottingham). S.M.D. acknowledge and support from the NIST-NSF summer undergraduate research fellowship (SURF). This work was supported by NIST and by NIH/NIBIB R21 EB006497-01.

References

- 1 Dorsey SM, Lin-Gibson S, Simon Jr CG. X-ray microcomputed tomography for the measurement of cell adhesion and proliferation in polymer scaffolds. *Biomater* 2009;30:2967-74.
- 2 Vacanti JP, Morse MA, Saltzman WM, Domb AJ, Perez-Atayde A, Langer R. Selective cell transplantation using bioabsorbable artificial polymers as matrices. *J Ped Surg* 1988;23:3-9.
- 3 Simon Jr CG, Eidelman N, Kennedy SB, Sehgal A, Khatri CA, Washburn NR. Combinatorial screening of cell proliferation on poly(L-lactic acid)/poly(D,L-lactic acid) blends. *Biomater* 2005;26:6906-6915.
- 4 Yang Y, Becker ML, Bolikal D, Kohn J, Zeiger DN, Simon Jr CG. Combinatorial polymer scaffold libraries for screening cell-biomaterial interactions in 3D. *Adv Mater* 2008;20:2037-2043.
- 5 Ishiyama M, Shiga M, Sasamoto K, Mizoguchi M, He P-g. A new sulfonated tetrazolium salt that produces a highly water-soluble formazan dye. *Chem Pharm Bull* 1993;41:1118-1122.
- 6 Smith PK, Krohn RI, Hermanson GT, Mallia AK, Gartner FH, Provenzano MD, Fujimoto EK, Goeke NM, Olson BJ, Klenk DC. Measurement of protein using bicinchoninic acid. *Anal Biochem* 1985;150:76-85.
- 7 Singer VL, Jones LJ, Yue ST, Haugland RP. Characterization of PicoGreen reagent and development of a fluorescence-based solution assay for double-stranded DNA quantitation. *Anal Biochem* 1997;249:228-238.
- 8 Barry JJA, Howard D, Shakesheff KM, Howdle SM, Alexander MR. Using a core-sheath distribution of surface chemistry through 3D tissue engineering scaffolds to control cell ingress. *Adv Mater* 2006;18:1406-1410.
- 9 Ho ST, Hutmacher DW. A comparison of micro CT with other techniques used in the characterization of scaffolds. *Biomater* 2006;27:1362-1376.
- 10 [10] Yang Y, Dorsey SM, Becker ML, Lin-Gibson S, Schumacher GE, Flaim GM, Kohn J, Simon Jr CG. X-ray imaging optimization of 3D tissue engineering scaffolds via combinatorial fabrication methods. *Biomater* 2008;29:1901-1911.
- 11 Simon Jr CG, Stephens JS, Dorsey SM, Becker ML. Fabrication of combinatorial polymer scaffold libraries. *Rev Sci Instrum* 2007;78:072207.

AtriCure Inc. (West Chester, OH) received regulatory clearance to begin U.S. sales of its AtriClip device, which protects against blood clots during certain heart procedures. Last year, AtriCure received FDA approval to sell Cryo1, a disposable medical device that uses extreme cold to ablate the heart.

Biomet Inc. (Warsaw, IN) plans to invest \$26 million in an expansion that will create about 280 new jobs. Biomet's project has four components—manufacturing, distribution, technology and research and development. The plan is to renovate existing property and add new equipment. The jobs will be added over a two-year period.

BioOhio (Columbus, OH) announced a new partnership with the Beijing Pharma and Biotech Center, aimed at bolstering the biomedical industry in the U.S. and China. The pact was recently signed in Beijing during a business development trip organized by the state Department of Development. Under the pact, the Beijing organization will help Ohio medical device companies look at market opportunities in China and help navigate paperwork hurdles. Both BioOhio and the Beijing center also will facilitate information-sharing between Ohio hospitals and Beijing-based researchers that specialize in cardiovascular innovations.

ConvaTec (Skillman, NJ) announced that the U.S. Food and Drug Administration (FDA) has granted 510(K) clearance to market Vitala, an innovative, non-intrusive ostomy continence control device for people with an end colostomy. The Vitala Continence Control Device allows individuals to manage their colostomy without a pouch, belt or irrigation. A Phase II clinical trial has shown that the device is safe for use up to eight hours, and is recommended for use 6-12 weeks after surgery. It functions by sealing against the stoma to prevent the release of

stool while permitting gasses to vent through an integrated, deodorizing filter. When in use, stool is stored inside the body, negating the need to wear an ostomy pouch.

Elekta (Stockholm, Sweden), developer of treatment planning systems for radiation therapy and radiosurgery, has released a tool for the treatment of lung tumors that allows doctors to visually confirm a tumor's position during the breathing cycle by allowing the lesion to be treated with a continuous radiation beam. Lung tumors have provided a challenging radiation target because a patient's breathing causes the target to move.

Samsung (Seoul, South Korea) announced plans to invest 23 trillion Won (approximately \$19 billion) over the next decade in technologies including solar cells and medical devices, aiming to boost sales and increase work force. Samsung also announced plans to invest 2.1 trillion Won (~\$1.8 billion) in biopharmaceuticals and 1.2 trillion Won (~\$1 billion) in electronic healthcare equipment such as blood testing devices.

Other News:

The National Venture Capital Association is in discussions with senior U.S. Food and Drug Administration (FDA) Center for Devices and Radiological Health (CDRH) officials about establishing a separate, more efficient pre-market review pathway for especially novel devices, supported by a supplemental user fee. Under the proposal, the FDA would establish a formal definition of a "novel" device, and would determine whether a candidate device meets that definition within 30 days of submission. If so, CDRH would assemble a concentrated team of high-level review resources, including outside consultants, to review the submission. The review would be funded in part by an extra user fee, paid by the sponsor on top of the standard application fee.



One of the oldest institutions of higher education in this country, the University of Delaware today combines tradition and innovation, offering students a rich heritage along with the latest in instructional and research technology. The University of Delaware is a Land-Grant, Sea-Grant and Space-Grant institution with its main campus in Newark, DE, located halfway between Washington, DC and New York City. Please visit our website at www.udel.edu.

Faculty Positions in Biomedical Engineering

The College of Engineering at the University of Delaware invites nominations and applications for mid- and senior-level tenure-track faculty positions to lead a growing program in biomedical engineering (www.engr.udel.edu/biomed); exceptional junior-level applications will also be considered. Candidates with backgrounds in biomedical engineering or bioengineering, with research interests in proteomics and systems biology, biomechanics, rehabilitation engineering, bioimaging, bioelectronics, biomaterials and tissue engineering, and brain-machine interface and device design, are particularly encouraged to apply.

Appointments may be in a primary engineering discipline or as an interdisciplinary appointment across departments, and candidates will be expected to teach undergraduate classes in a new biomedical engineering major in the College. Successful candidates must conduct innovative and internationally recognized research, high quality teaching, and mentoring. Additional information about the biomedical engineering efforts on the UD campus can be found on the application website.

Applicants should submit a curriculum vitae, a statement of research and teaching interests and achievements, and the names, addresses, phone numbers, and e-mail addresses of four references at <http://www.engr.udel.edu/facultysearch>. Review of applications will begin as early as October 15, 2010, although nominations and applications will be accepted until the position is filled.

The UNIVERSITY OF DELAWARE is an Equal Opportunity Employer which encourages applications from Minority Group Members and Women.

Annual Meeting Announcements:

The newly elected officers for the National Student Section for 2010-2011 are:

- President: Heather Doty (University of Memphis)
- President-Elect: Scott Cooper (University of Florida)
- Secretary/Treasurer - Kristen Moffat (Columbia University)
- Secretary/Treasurer-Elect: Vahid Serpooshan (McGill University)
- Bylaws Chair: Daniel Alge (Purdue University)

Student Chapter Awards were awarded to:

- The University of Memphis
- Columbia University
- The University of Florida

The Student Chapter Travel Awards were given to:

- Case Western
- Purdue University
- The University of Memphis

Student Chapter Connections

Calling all student chapter officers and/or students interested in forming student chapters. We are planning a conference call this Fall to share ideas about how you have promoted biomaterials at your university. We hope to get input on successful fundraising, social, and educational events you have conducted, as well as give your club ideas for future semesters. Please have a representative from your chapter contact the SFB National Student Chapter president Heather Doty at hdoty@memphis.edu and let her know you would like to participate. We look forward to connecting with you all!

Remember to find the Society For Biomaterials on LinkedIn and Facebook!!!

University of Memphis Chapter Section:

Are we ready? Yes, we are! Thanks to the University of Memphis Biomaterials Chapter, Medtronic, Smith & Nephew, and Wright Medical. As one of the chapter events this past Spring, a mock interview was held for all biomedical engineering (BME) students, graduate and undergraduate, at the University of Memphis. Prior to the event students were encouraged to sign up for one of the 36 mock interview openings and submit their resumes to mock jobs that were created based on typical entry level BME positions at Medtronic, Smith & Nephew or Wright Medical. Students had the choice of one-on-one interviews, phone interviews and small group interviews. The faculty members were impressed when their students showed up in suits, ties and with portfolios in hand. The students prepared as though they were going to



SFB Student Section National Officers 2010-2011.
Pictured from left to right: Heather Doty, University of Memphis (President); Daniel Alge, Purdue University (By-Laws Chair); Scott Cooper, University of Florida (President-Elect); Kristen Moffat, Columbia University (Secretary/Treasurer).

an actual interview, and they surely dressed to impress. A total of nine representatives (interviewers) from the three largest biomedical engineering companies in Memphis reviewed resumes in individual rooms and waited for the students to arrive. Students filled the halls waiting for their 15-minute interviews. They were drilled with challenging interview questions asked by the interviewers. The top three difficult/unexpected questions for the students were:

1. "What would peers/advisor describe as one of your strengths and one of your weaknesses?"
2. "Do you think you are misconceived (misunderstood)?"
3. "What would make you not want a job?"

The phone interviews were, of course, conducted over the phone, with the student and interviewer in different rooms. All the students who participated in the phone interviews expressed satisfaction with the experience because as a company representative said "If you don't get through the phone interview, you won't get to the one-on-one." Some students found the phone interviews considerably more difficult than one-on-one interviews because of the lack of personal interaction. Tips we learned for mastering phone interviews were:

- Know your basic interview questions cold (e.g. List three of your strengths, three of your weaknesses, why should you be hired for the position, etc.).
- Use specific examples of experience you have that will be translatable to the job requirements when answering their questions.
- Ask questions to show that you are interested in the company

After each interview there was time allotted for the interviewers to critique the interviewee and comment on their resume. During this time one student discovered she was asked what her hobbies were to see if she chose more solitary or group activities. Everyone agreed that they received good feedback and can now feel more confident submitting their resume and going to an interview. As one soon-to-graduate Ph.D. student said, "I'm very glad I had the opportunity to participate in this because it was the first time I've ever had an interview."

From the students' feedback, the mock interview event was a success in building familiarity and confidence for the students to enter the real world of job hunting. The University of Memphis Society For Biomaterials chapter plans to host more professional development activities in the Fall. We encourage other student chapters to host mock interviews to help prepare their members for the next step after graduation.

We would like to recognize and specifically thank all the interviewers and people who helped organize this event from Medtronic, Smith & Nephew and Wright Medical, without them it would have not been possible.



Tips for setting up a mock interview at your university

- ✓ Contact local companies/universities and determine if they are interested in helping and how many interviewers they can send.
- ✓ Ask companies for mock job descriptions of typical introductory job or intern positions and if you can send them interviewee resumes for critique.
- ✓ Set a time and date for the mock interview that will work for most students and all interviewers.
- ✓ Reserve rooms on your campus (close by if possible) for each interviewer, or two rooms for phone interviews (one for interviewer/and one for interviewee).
- ✓ Create a schedule for the interviews and allow at least 15 minutes for the interview and 5 minutes for critique session.
- ✓ Notify students to sign up for time slots, review mock job postings and send their tailored resumes to a student chapter representative. (Approximately three weeks before the event).
- ✓ Send the interviewer the resumes for all the students they will interview. (Approximately two weeks before the event).
- ✓ Remind students to dress professionally, bring extra copies of their resumes and arrive early for their interview.
- ✓ Arrange for parking passes (off campus guests) and water for all interviewers for the day of the event.
- ✓ Make sure all reserved rooms are unlocked and set up for the interviews. Label the doors with notices that an interview will be taking place and show all the interviewers to their rooms.
- ✓ Start the sessions on time.
- ✓ At the end, collect contact information for each of the interviewers and show them out.
- ✓ Get feedback from students who participated to determine what worked well and what could be done better next time.
- ✓ Send thank you cards or emails to the interviewers.

Community Calendar

RESBIO Cells on Polymeric Biomaterials Short Course

Piscataway, N.J.
October 26 and 29, 2010
www.njbiomaterials.org

TERMIA-NA Annual Conference

Orlando, Florida
December 5-8, 2010
www.termis.org

2010 Annual Meeting of the Orthopaedic Research Society

Long Beach, California
January 13-16, 2011
www.ors.org

15th Annual Hilton Head Workshop: *Regenerative Medicine: Innovations for Clinical Applications*

Hilton Head, South Carolina
March 16-19, 2011
www.hiltonhead.gatech.edu





Developing next generation technologies is a complicated task....

Collaborate with Zeus.
We'll Bring Your Ideas to Life!

Electrospun Materials

- Nano-fibrous textiles and coverings
- High potential in medical markets
- Multiple polymers available

Aeos™ ePTFE

- Biomechanical conformity
- Enables anti-proliferative therapy
- Sheet membrane, monofilament, tubing, and more

Absorv™ Bioabsorbables

- Modulated degradation rates
- Varying strengths and hardness
- Multiple extrusion forms

Are you sure you want to go at it alone?

We continue to lead the medical device industry with new polymer solutions to complex problems. Collaboration is the foundation to innovation and new product development. Our partnerships have resulted in some amazing products that have revolutionized the market. We push the limits of material science beyond measure to help you quickly confront and overcome your challenges.

Who do you want on your innovation team?



ZEUS

VISIONARIES OF POLYMER SCIENCE