

# DEPARTMENT OF BIOMEDICAL ENGINEERING

Biomedical engineers have created a pain-free drug delivery system that uses an array of microneedles made of silk protein.

# **PAIN-FREE NEEDLES** Silk microneedles take the pain out of drug delivery

Biomedical engineers at Tufts University School of Engineering have developed a new silk-based microneedle system able to deliver precise amounts of drugs over time and without need for refrigeration. The tiny needles can be fabricated under normal temperature and pressure and from water, so they can be loaded with sensitive biochemical compounds and maintain their activity prior to use. They are also biodegradable and biocompatible.

Professors David Kaplan and Fiorenzo Omenetto and their research team successfully demonstrated the ability of the silk microneedles to deliver a large-molecule, enzymatic model drug, horseradish peroxidase (HRP), at controlled rates while maintaining bioactivity. In addition, silk microneedles loaded with tetracycline were found to inhibit the growth of *Staphylococcus aureus*, demonstrating the potential of the microneedles to prevent local infections while also delivering therapeutics.

"By adjusting the post-processing conditions of the silk protein and varying the drying time of the silk protein, we were able to "This technology can be scaled up or down, shipped and stored without refrigeration and administered as easily as a patch or bandage. We believe the potential is enormous."

## IN THIS ISSUE

From the Chair2
Undergraduate Research3
Quick Hits 3
BMES4
Congratulations to our Graduates5
Alumni Relations 6
BME Retreat7

## FROM THE CHAIR



As human beings, we generally like to view things in packets or definable units. So, with 2012 we view our department from our first decade celebration. From the perspective of how far we have progressed over these 10 years, the view is both wonderful and incredibly exciting. We have a full cadre of engaged and committed faculty, an outstanding staff and an amazing group of students—from undergraduate to graduate to post-doctoral levels. We have progressed strongly by every possible metric, culminating

with our first accreditation review in the fall of 2011. Most importantly, after 10 years, we can now watch our earliest students progressing well in their careers, and our current cadre of students fully engaged in learning.

So for the next 10 years—what should we expect, anticipate, prepare for? There is no field in science and engineering to better prepare students for what is ahead—Biomedical Engineering not only sits at the forefront of the future, but helps to establish what this will be—the research ideas and discoveries of today in our labs and others, along with the inspiration, creativity and hard work of our students, will drive this future.

We remain committed to our students, to our program, and to our vision for the field of engineering and medicine where highly trained and creative students generate this foundation—in clinics, academics, and industry. As always, we welcome our former alums, colleagues and friends to stay in touch, stay involved and help guide this next 10 years.

We hope that many of you participated in the Alumni-Student Career Networking Night and BME reception—something we hope will become an annual event in February. If you missed it, catch up with your classmates and colleagues on our new BME alumni page: http://engineering.tufts.edu/bme/alumni/

If you're coming back to campus for Commencement, please be sure to join us for our alumni reception on May 18<sup>th</sup>.

David Kaplan Spring 2012

### **BME Reunion Banquet**

Please mark your calendars for the first annual BME alumni reunion banquet dinner on May 18, 2012. The dinner will be held in Scitech, "where it all began." Look for e-mails from BME\_Alumni@tufts.edu and check for upcoming details on our alumni page. Please e-mail us with inquiries.

## Take Note

## **ABET Accreditation**

In the summer of 2011, the BME department applied for accreditation of its undergraduate program by the Engineering Accreditation Commission of ABET, **http://www.abet.org** 

The ABET site visit occurred on November 6–8, 2011. ABET evaluators made a thorough examination of the academic program for the first major in BME: the processes in place for its evaluation, assessment, and continuous improvement; department facilities; and interviews with students, alumni, staff, and faculty.

Of the eight Tufts engineering programs being considered for accreditation by ABET, the undergraduate program in biomedical engineering is the only one applying for accreditation for the first time. A final decision about accreditation will be communicated by ABET in the summer of 2012.

#### **Internship Program**

Assistant Professor Qiaobing Xu is developing a new program to help BME undergraduate students find internship opportunities. Internships enable students to gain practical experience and apply the theory learned in the classroom to solve real-world problems. This spring, Dr. Xu will organize a discussion panel from several local biomedical and biotech companies to introduce students to research and internship opportunities.

#### **Concord Academy InSPIREs**

This past summer, the department initiated a joint internship program with Concord Academy's InSPIRE program. The program, led by Amy Kumpel, E01, and fostered through the Academy's science department, provides students with internship research opportunities in the Boston area. Three outstanding high school students spent their summers working on various research projects in the laboratories of professors Xu, Fantini and Kaplan. In all cases, the students did an outstanding job contributing to research. As a result, the plans are to expand the program next summer with additional students.

## Pain-Free Needles Continued from page 1

precisely control the drug release rates in laboratory experiments," said Omenetto. "The new system addresses long-standing drug delivery challenges, and we believe that the technology could also be applied to other biological storage applications."

While some drugs can be swallowed, others can't survive the gastrointestinal tract. Hypodermic injections can be painful and don't allow a slow release of medication. Only a limited number of small-molecule drugs can be transmitted through transdermal patches. Microneedles—able to penetrate the upper layer of the skin without reaching nerves—are emerging as a painless new drug delivery mechanism. But their development has been limited by constraints ranging from harsh manufacturing requirements that destroy sensitive biochemicals, to the inability to precisely control drug release or deliver

sufficient drug volume, to problems with infections due to the small skin punctures.

The process developed by the Tufts bioengineers addresses all of these limitations.

The research was based on work supported in part by the U.S. Army Research Laboratory, the U.S. Army Research Office, the Defense Advanced Research Projects Agency-Defense Sciences Office, the Air Force Office of Scientific Research, and the National Institutes of Health.

Tsioris, K., Raja, W. K., Pritchard, E. M., Panilaitis, B., Kaplan, D. L. and Omenetto, F. G. (2011), Fabrication of Silk Microneedles for Controlled-Release Drug Delivery. Advanced Functional Materials. doi: 10.1002/adfm.201102012

## UNDERGRADUATE RESEARCH



On May 5, 2011, the department held its second annual Research Day symposium featuring the work of students from BSBME classes of 2011, 2012, and 2013.

The symposium began with senior project presentations and continued with a research poster session.

### Senior Projects

**Eddie Hong:** Silk Microneedle Array Formulation for Transdermal Delivery of Biotherapeutics

**David Hessler:** Induction of Limb Regeneration in a Non-Regenerative Frog Species

Mark A. Brenckle: Towards a Novel Silk-based Biosensing Platform with Broad Biomedical Utility: A Multifaceted Approach

Joshua Wilner: The Effects of Photostimulation on Stem Cell Proliferation and Differentiation

Valerie Luks: Optimizing Endothelialization within Microchannels of a Prevascularized Tissue Construct

Doohyun Park: Mouse Tail Regeneration with Biodome

Brian Canter: Synthesis and Materials Testing of Silk-elastinlike Proteins for use in Chembots

Atur Patel: Osteoarthritis Modeling Using a 3D in vitro Osteochondral Scaffold

Ryan Orendorff: Esoma

Trevor Stack: Characterization of Perfused Silk Microtube-Silk Sponge Composites

## **QUICK HITS**



Professor Fiorenzo Omenetto was named a Fellow of the Optical Society of America (OSA) for

contributions in ultrafast nonlinear optics, photonic crystal fibers and for pioneering the development of silk optical applications and silkbased photonic structures and devices. Professor Omenetto is the second OSA Fellow in biomedical engineering. Last year, Omenetto's research earned him a fellowship from the John Simon Guggenheim Memorial Foundation.



In the Journal of Polymer Science Part B, Professor Mark Cronin-Golomb and colleagues demon-

strated the optical sensitivity made possible by azo modification of the silk that has high enough spatial resolution to enable holographic recording. The cover image shows reconstruction of a holographic image recorded in a thin film of azo modified silk fibroin. The curved lines around the image result from refraction through the wavy piece of silk that was used in the experiment. Azo-modified silk retains biocompatibility and may be suitable for use in implantable optical sensors and optically patterned substrates for tissue engineering.

## **BMES 2011**

The BME department was well represented at the Biomedical Engineering Society (BMES) 2011 Annual Meeting held in Hartford, Conn., on October 12–15, 2011. Professors Black, Cronin-Golomb, Fantini, Kaplan, Kuo, Omenetto and Xu attended and chaired several of the meeting's tracks and sessions. A large contingent of students, both undergraduate and graduate, and postdocs also attended.

## Posters:

**Mia Yang (Advisor: Omenetto):** Direct Printing of Frequency Tunable RFID Antennas on Shrinkable Substrates

**Michele Pierro (Advisor: Fantini):** Monitoring The Relative Phase of Oscillations Of Cerebral Oxy-Hemoglobin and Deoxy-Hemoglobin Concentrations During Sleep in Human Subjects

Amy Hopkins (Advisor: Kaplan): Recombinant Silk Fibronectin Fragment Fusion Peptides for Growth Factor Binding to Silk Fibroin Hydrogel for Engineering Extracellular Matrices

Vikas Yadav (Advisor: Kaplan): In Vivo Cartilage Tissue Engineering with Lysozyme Susceptible Bacterial Cellulose as a Scaffold

Waseem Raja (Advisor: Kaplan): Silk as an Alternative Biomaterial for Microneedles System

Alex Nectow (Advisor: Kaplan): An Automated Algorithm for the Quantitative Analysis of Nerve Cell Alignment on Anisotropic Silk Films

**Tessa DesRochers (Advisor: Kaplan):** A 3D Tissue Model of Human Kidney for the Study of Disease Progression

Kelly Sullivan (Advisor: Black): The Development of a Fibrin Gel Based Engineered Myocardium Model of Myocardial Infarction

Alex Mitropoulos (Advisor: Omenetto): Portable Nanoimprinting of Silk Fibroin Films

Jason Bressner (Advisor: Omenetto): Fabrication of Silk Films via Electrogelation

**Amy Thurber (Advisor: Kaplan):** Inhibition of TRPV1 in Osteogenic Differentiated hMSCs Increases Mineralization

**Violet Finley (Advisor: Kuo):** Synergistic Effects of Mechanical and Soluble Cues on Embryonic Tendon Cell Gene Expression

**Beibhinn O'Donoghue (Advisor: Omenetto):** Development of a Thermally Programmable Biomaterial Substrate for Cell Cultures

Yuji Zhang (Advisor: Omenetto): Manipulation of Silk Film Refractive Index through Doping and Annealing Treatments Joanna Xylas (Advisor: Georgakoudi): The Diagnostic Utility of Fourier-Based Metrics for Assessing Cellular Organization

**Katherine Tang (Advisor: Black):** The Effects of Infarcted Cardiac Extracellular Environment on MSC Growth and Differentiation

Zachary Schiller (Advisor: Kuo): Modulating Cytoskeletal Tension Regulates the Effects of Hypoxia on Adipogenesis of Mesenchymal Stem Cells

### Talks:

Lauren Black: Controlling Cardiac Differentiation of Stem Cells Via Changes in Stiffness and Composition of ECM

Kathy Ye (Advisor: Black): The Effect of Varying Frequency of Mechanical Stimulation on Engineered Myocardium Twitch Force

**Roberto Elia (Advisor: Kaplan):** A Novel Securable Hyaluronic Acid-Silk Hydrogel Composite for Controlled Drug Release

**Kyle Quinn (Advisor: Georgakoudi):** Quantification of Engineered Adipose Tissue Development Using Multi-Photon Microscopy

**Philipp Seib (Advisor: Kaplan):** Doxorubicin Loaded Silk Films for Local Breast Cancer Therapy

Rachel Twardowski (Advisor: Black): Capacity of Cardiac Fibroblasts to Serve as Support Cells for Vacularization of Engineered Myocardium

**Joseph Marturano (Advisor: Kuo):** Collagen Crosslinking Contributes Significantly to the Mechanical Properties of Developing Tendon

Konstantinos Tsioris (Advisor: Omenetto): Silk Based Stabilization and Immobilization of FRET Protein Glucose Nano Sensors

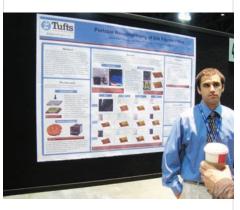
Jeff Brown (Advisor: Kuo): Embryonic Ligament and Tendon Cell Response to Mechanical Loading Varies with Developmental Stage



Zak Schiller, Violet Finley, Rachel Twardowski, Mark Paquette, Alex Mitropoulos, Katherine Tang, and Kathy Ye



Qiaobing Xu, Lauren Black, David Kaplan, Catherine Kuo, Fio Omenetto, Adam Collette, EG08, and Bruce Panilaitis



Alex Mitropoulos explains his research poster.

## Congratulations to Our 2010–2011 Graduates

## New Undergrad Admissions Policy

The engineering faculty has approved a change in policy for selection of students in the BME undergraduate major program. This change in the number of admitted students and admission policy is a result of strong feedback from students, alumni, faculty, and the BME department external advisory board.

Starting in AY 2012–2013, the number of admitted students will increase from the current 15 to 20. Fifteen students will still be selected on the basis of first-semester GPA, and an additional five admitted students will be selected on the basis of academic performance in the EN-64 (introductory engineering) course offered by the BME department. The first semester GPA will be computed by including a grade of "A" for each math, physics, and chemistry course for which the applicant has received AP credit. This will encourage students to use their AP credits and enroll in more advanced courses in their first terms at Tufts.



### Bachelor of Science in Biomedical Engineering

Mark Allen Brenckle Brian Spencer Canter David Patterson Hessler, Jr. Edward James Hong Valerie Louise Luks Ryan Daniel Orendorff Doo Hyun Park Atur Avni Patel Trevor J. Stack Joshua Irving Wilner

## Largest Entering Doctoral Class

In 2011, we received 150 applications for our graduate programs—our largest-ever pool. We extended offers to the most highly qualified and 29 of them decided to enroll, 15 as Ph.D. students. One of these, Kaori Graybeal, was a recipient of the School of Engineering's prestigious Provost's fellowships.

### **Doctoral Recipients**

#### **Debbie Ko Chen**

**Dissertation:** Diffuse Optical Signals in Response to Electrical Simulation of Peripheral Nerves **Advisor:** Sergio Fantini

#### **Cherry Anne Greiner**

Dissertation: Light Scattering Flow Cytometry for the Minimally Invasive Quantification of Circulating Leukemic Cells Advisor: Irene Georgakoudi

#### **Peter Hammer**

Dissertation: Simulating Heart Valve Mechanical Behavior for Planning Surgical Repair Advisor: Sergio Fantini

#### **Eleanor M. Pritchard**

Dissertation: Silk Biomaterials for Controlled Drug Delivery Advisor: David Kaplan

#### Michaela Ruth Reagan

**Dissertation:** Breast Cancer Osteotropism: Disease Models and the Roles of Mesenchymal Stem Cells **Advisor:** David Kaplan

#### Sarah Sundelacruz

**Dissertation:** Effects of Electrophysiological Manipulation on Differentiation and Wound Healing Capacity of Human Mesenchymal Stem Cells **Advisor:** David Kaplan

#### Yang Yu

**Dissertation:** Diffuse Optical Imaging and Spectroscopy of the Human Breast for Quantitative Oximetry with Depth Resolution **Advisor:** Sergio Fantini

## Master of Engineering

James R. Bochicchio (Bioengineering) Meghan Patricia Foley Jeremy Fryer-Biggs Brian Patrick Hurhula Jeffery Iudice Amelia H. Thomas Vu Anh Tran Robert D. Worsham

### **Master of Science**

#### Katherine B. Blanton

Thesis: Lentiviral Delivery of Osteoinductive Factors for Accelerated Bone Regeneration Advisor: David Kaplan

#### Xiao Da

Thesis: Dual-source Dual-detector Optical Probe for Improved Depth Discrimination in Functional Near-Infrared Spectroscopy Advisor: Sergio Fantini

#### Chia-Li Lu

Thesis: Enzymatic Degradation of Silk Fibroin Hydrogel Advisor: David Kaplan

#### **Douglas Howell McDonald**

Thesis: Intrinsic-Fluorescence Markers Reveal High-Risk HPV Infection and Cervical Precancer Advisor: Irene Georgakoudi

#### **Alexander Ryan Nectow**

Thesis: Development and Assessment of Drug-eluting and Anisotropic Silk Fibroin Scaffolds for Applications in Peripheral Nerve Regeneratio Advisor: David Kaplan

#### Xiao-Chi Zhang

Thesis: Biodome Project Biophysical Regulation of Murine Digit and Tail Regeneration Advisor: David Kaplan

#### Feng Zheng

Thesis: Phase Analysis of Low Frequency Hemodynamic Oscillations in Near Infrared Spectroscopy Advisor: Sergio Fantini



## **ALUMNI RELATIONS**

The Department of Biomedical Engineering is proud of the accomplishments of our alumni. From our first graduating class of undergraduate alumni to our doctoral recipients, we want to stay connected with all our biomedical engineering alums. We are pleased to announce the launch of our alumni web page: **http://engineering.tufts.edu/bme/alumni** 

We will post upcoming events, updates from fellow BME alums, and other highlights. Please check back regularly!

#### **BME Reception**

All undergraduate and graduate BME alumni were invited to the first BME alumni event on February 27, 2012. BME faculty and staff were in attendance at the Tufts Engineering Alumni Dinner and the *exclusive BME Alumni Reception*. Check our alumni page for photos from the event!



A soccer match, played between the faculty and grad students vs. the undergrads, was won (as usual) by the faculty and graduate students with the whopping score of 5–3.

## **ALUMNI SPOTLIGHT**

**'05, '09** Jonathan A. Kluge (B.S.M.E., 2005; Ph.D., 2009) started a post-doctoral research position in January 2010 at the University of Pennsylvania under advisement of Dr. Robert Mauck in the McKay Orthopaedic Research Laboratory. He moved back to Somerville in August 2011 and has been happily reintegrated in silk-based research endeavors since that time. Currently, he is back at Tufts part-time while also engaged with a Tufts-generated startup company called Spectrasilk, Inc. located in Woburn, Mass.

**109** Nate Zamarripa (M.S., 2009) recently returned to New England and is now working at Boston Scientific as an R&D Engineer in the Interventional Oncology group. He is currently working on a team whose focus is to develop new tools for interventional radiologists performing procedures such as transarterial chemoembolization (TACE), drug eluting bead embolization (DEB) and Yttrium 90 radioemembolization (Y90). **'10 charles Banos** (M.S., 2010) is currently working as an associate scientist in the Neurology Department at Biogen Idec in Cambridge, Mass. The group he is in focuses on drug discovery for different neurodegenerative diseases including Alzheimer's and Multiple Sclerosis.

**10** Michael Brown (B.S. 2010, M.S.E.M 2011) graduated from Tufts Gordon Institute (TGI) with his master's of science in engineering management. Brown's proposed business plan, Proximity Health Solutions, was the winner in TGI's 2010 Classic Business Plan category. **112 Violet Finley** (M.S., 2012) is now working at Draper Laboratory. Utilizing both her mechanical engineering (B.S.) and biomedical engineering (M.S.) backgrounds, she is focused on tissue engineering and medical device testing. "I've been really happy with the skills I gained through my time at Tufts. I feel prepared to do the work I'm supposed to do, and having gotten my master's in BME has opened doors to exciting work that I never would have been able to do with just my bachelor's in ME. Still living in Medford... feels strange to be right next to Tufts but not be a Tufts student anymore!"

### **Keep in Touch**

- E-mail BME\_Alumni@tufts.edu with your news, stories, and updated contact information. If you're not receiving e-mails from us, please let us know!
- 2. Join our graduate and undergraduate LinkedIn groups.
- 3. Visit Tufts Online Community: **www.alumniconnections.com/tufts** (go to "Classnotes," then click on "Submit/Edit a Class Note")

## **BME RETREAT**

The 2011 BME retreat took place at Point Sebago Resort in Casco, Maine, September 16–17, 2011. More than 80 students, postdoctoral associates and faculty attended. Fun activities at the conference site and nearby lake were held during the day. A banquet dinner was held to kick-off the evening science symposium of posters and talks given by students, associates, and professors.

For a full description of the retreat, please visit our Events page: http://engineering.tufts. edu/bme/newsEvents/

### Silk Art Contest Winners

#### VIDEO

		Leah Bellas, Lindsay Wray, Amanda Baryshyan, Joanna Xylas–Seriluxe Gary Leisk, Tim Lo–cocoon formation via human enactment	
ART			
1st	Place:	Xiaoshu Dai-silk jewelry	
2nd	Place:	Tim Lo–silk leaves and flowers	

3rd Place: Dan Hines-Tufts logo in silk

#### FOOD

- 1st Place (tie): Amy Hopkins, Lee Tien, Tom Valentin, Min Tang-Schomer–silk peach gelatin brain
  1st Place (tie): Eleanor Pritchard–silk chocolate dessert
- 3rd Place: Isaac Anderson—silk chocolate mud (ugh!)



Dan's "Tufts logo in silk" took third place in the "Art" category.



PhD candidate Cassie Baughman (Sackler School), Postdocs Rossella Calabrese and Tessa DesRochers



Tim's "silk leaves and flowers on tree" won second place in "Art" category.



Graduate students Pami Anderson and Antonio Varone



A silk, peach-flavored gelatin brain tied for first place in the "Food" category.



Xioashu's silk earrings won first place in the "Art" category.

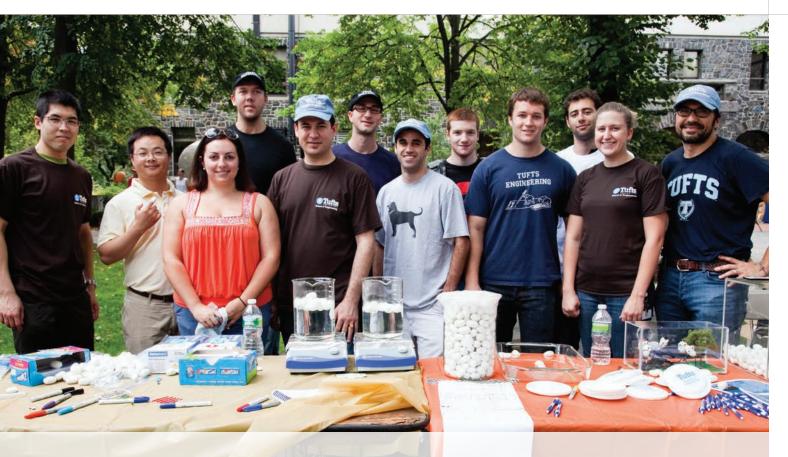


Biomedical Engineering Professors: (backrow): Qiaobing Xu, Mark Cronin-Golomb, David Kaplan, Lauren Black, Fio Omenetto, Sergio Fantini (front row): Catherine K. Kuo and Irene Georgakoudi



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Members of the Department of Biomedical Engineering share the process of silk transformation at Tufts Community Day, September 25, 2011.