MASSACHUSETTS INSTITUTE OF TECHNOLOGY

November 2005, Volume 4, Issue 3

The BioTECH

NEWSLETTER OF THE BIOMEDICAL ENGINEERING SOCIETY AND THE BIOLOGICAL ENGINEERING COMMUNITY

MIT BMES Wins Awards, Talks Shop at the National Conference in Baltimore

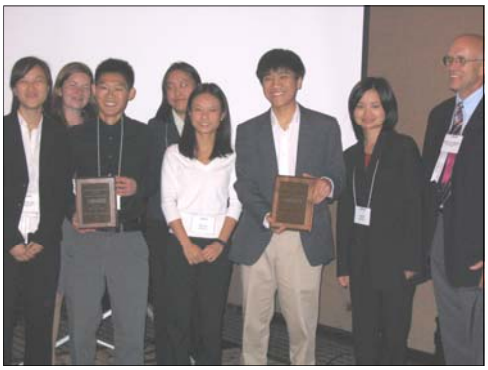
By *Brian Chase '06*,
MANAGING EDITOR

On Thursday, September 29, six members of the MIT BMES Executive Board traveled to Baltimore, site of the 2005 National BMES Fall Conference. The trip was graciously sponsored by the MIT Biological Engineering (BE) Department, and the students were proud to return with a plaque for winning the BMES Chapter-of-the-Year Award.

The journey started early Thursday morning, with the students leaving MIT at 5 a.m. for their flight to Baltimore. Ironically, their flight was delayed for three hours at Logan Airport, but everyone eventually arrived at the Baltimore Hyatt in time for the chapter development workshop and the award ceremony in the afternoon.

The award ceremony was conducted in conjunction with the BMES Annual Business Meeting, where the outgoing national BMES president summarized his accomplishments and the incoming president outlined his future goals. In between, the society handed out a number of awards, including the BMES Student Chapter Meritorious Achievement Award, which is given to the student chapter that has achieved the most for BMES at its institution. This honor was given to MIT and the University of California-San Diego for their 2004-2005 performance.

Also, awards for Commendable Achievement and Honorable Mention were given to the University of Wisconsin-Madison and both the Worcester Polytechnic Institute and the University of Rochester, respectively. This is the second year in a row that MIT has won the Meritorious Achievement Award.



MIT and UCSD received the Student Chapter Meritorious Achievement Award at the 2005 National BMES Fall Conference in Baltimore, MD.

In addition, MIT is the only school that has also earned the Outstanding Undergraduate Student Research Award and the Outstanding Graduate Student Research Award, adding to its plaque two additional certificates.

The award-winning student chapters shared their respective programs during the chapter development workshop held in a 3-

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Griffith Offers Graduate School App Primer

By *Emily Pfeiffer '07*,
VP OF INFORMATION TECHNOLOGY

On the evening of Tuesday, September 27, the BE lecture hall 56-154 was packed with students listening to Professor Linda Griffith's Graduate School Application Primer. Griffith explained the ins and outs of attending graduate school, from choosing a graduate program to preparing a competitive application and procuring funding, and offered a summary of the general graduate school academic path.

Griffith classified graduate school program decisions according to a series of levels, starting with choice of degree, and narrowing to choice of discipline, school, and lab group. In differentiating between a Master's and PhD as terminal degrees, Griffith explained that a Master's degree is most applicable to a career in industry, while a PhD is commonly required for BE and BME research. The PhD degree, typically requiring 4-6 years of study, sup-

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The BioTECH

MIT (Biological Engineering)-
Biomedical Engineering
Society Publication

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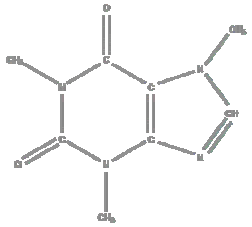
The *BioTECH* is a publication by the MIT (Biological Engineering)-Biomedical Engineering Society (BE-BMES) as a vehicle to inform, involve, and mobilize our membership regarding the complex and evolving bioengineering landscape at MIT and nationwide. Founded in Spring 2003, the *BioTECH* has grown from a campus publication to one with wider constituencies, a bridge for inter-chapter relations and a catalyst to spark discussions on the national scene — the BMES Bulletin, for example, printed our *Letter to the Editor* in a full page coverage (p.3) of its summer 2004 issue <http://www.bmes.org/pdf/vol28_2.pdf>.

BMES Caffeine Study Break was held on Tuesday, October 18, 5:30-6:30 pm in 56-614. Drinks offered include Starbucks® coffee, iced chai tea, exotic black/green teas, soda/pop, hot chocolate, Red Bull®, and more.



New England Science Symposium 2006

Sponsored by Harvard Medical School Office of Diversity and Community Partnership Minority Faculty Development Program and the Biomedical Science Careers Program, the New England Science Symposium is an annual event for post–docs, medical/dental, graduate and undergraduate students to present their research projects through oral or poster presentations. The Ruth and William Silen, M.D. Awards will be presented to the first ($300), second ($200), and third ($100) place winners of both the oral and poster presentations. There is no registration fee to attend the symposium but participants are responsible for their travel and lodging expenses.

Date: March 12, 2006
Location: The Conference Center at Harvard Medical
Cost: $0
Contact: 164 Longwood Avenue, 2nd Floor, Boston, MA 02115-5818
617.432.3834
http://www.bscp.org/events.asp

Pre-registration is required for presenters and for attendees. To obtain a registration form, please contact Lise D. Kaye at lise_kaye@hms.harvard.edu.

For Those Who Want to Present Their Work

Please submit abstracts electronically to Janine M. Mathó at Janine_matho@hms.harvard.edu, including

Name of author(s)
Mailing and e–mail addresses, phone numbers
Institution, academic level, and expected year of graduation
Research title and research sponsor(s)
Statement summarizing the work to be presented (summary not to exceed 400 words).

The deadline for submission of abstracts is **December 2, 2005**. Applicants are notified of their acceptance before the end of January 2006. Please also complete a registration form—see above.

Interview with Dr. Robert Langer

Renowned MIT Institute Professor shares thoughts about his career

Prof. Robert Langer

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Professor Robert Langer is an Institute Professor well known for his research in drug delivery and tissue engineering. He is the recipient of the Draper Prize, the equivalent of the Nobel Prize in engineering, among many other awards.

By *Joao Paulo Mattos '08,*
FEATURES EDITOR

BioTECH: How were your undergraduate years? What did you do to prepare for your future and your career? For example, what clubs did you join, what internships did you take?

Langer: Sure. I was an undergrad at Cornell, from '66 to '70. I don't think I did many extracurricular things as I look back on it now. We didn't have time to do much except classes. I remember one term I had five 8 o'clock classes including one on Saturday. I really wasn't involved in more than trying to get through them. My first 3 terms were hard for me. I probably shouldn't say this, but I wasn't great at going to certain classes and I sometimes had difficulty paying attention in large lectures.

Starting my second term sophomore year, I realized I was having this difficulty. So I started doing more and more problems on my own time, and I found that practicing them and working them out over and over was even more important than class lectures. And it worked. My GPA went up more than a point.

BioTECH: From what we've read, you don't give up easily. You had your first nine grants turned down, and you've pursued projects that people were convinced were unimportant or impossible, and yet you continued pursuing them. Have you ever encountered a project that had to be given up altogether? How do you know when to quit or keep going?

Langer: That's a good question. I guess to answer it we have to think of the projects I pursue and the projects that I ask people in my lab to pursue. I don't want to come up with a project and have some student get to a dead end. I like to think that I've been good at designing projects for students that they can get something out of.

"When I was younger, it was much harder to do as much good as we can today. Back then it was just a dream, and now I know we can do it."

Prof. Robert Langer

But if I'm going to work on something, and I feel that the science is good, I would never give up. It's just a question of time, resources, and people. I don't see why one should give up, if what you're doing is important and if the science is sound.

BioTECH: Research requires a lot of creativity and inspiration. Where do you get your inspiration from? How do you feel about what your lab has done?

Langer: Well, I look at the impact that the people in our lab have made. I see that what we've done has made a difference on two levels. First, there are the things that have come out of our lab: our patents, products, and scientific principles, many of which are influencing other researchers and hopefully helping many people all over.

Second, there's all the students who have come out of our lab. I get inspiration from seeing many of them going to top places like Harvard, Yale, Penn, Columbia, etc. To me, it's very inspiring that we're able to train the next generation of people who will train the next generation and so on. When I was younger, it was much harder to do as much good as we can today. Back then it was just a dream, and now I know we can do it.

BioTECH: In what countries are some of your innovations and treatments you helped develop available? Does a researcher that discovers a novel treatment have control over what happens to it, and to whom it becomes available?

Langer: Well, a lot of what we do is developing new principles; there are products, as well, but a lot of what comes out of our lab are principles. Drug delivery and release and such technologies are used in the US and Europe. In the third world, we've done work with the WHO and places like that. I believe that vaccine delivery will have an impact in the third world, but tissue engineering will not, at least not right now.

As for how much control a researcher has over his or her innovations, it might depend on what you're doing. What we do is pretty general and basic and in that sense I wouldn't say we have that much control. Anyone can adapt our principles for specific applications.

But everyone makes a choice; there's no reason why someone couldn't decide, well I'm going to work on malaria or diabetes, or something of that sort. In that case a researcher has control over

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Interview with Langer: insights on research, ethics, balance in life

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who his or her research can benefit. But what we've generally decided is to keep research more basic and general, not single disease focused.

BioTECH: What nations are currently the leaders in biotechnology and related fields? Why do you think this is so? How can one help these fields become more prominent worldwide?

Langer: Well, I might be prejudiced, but I think the US is the leader. To help other places, I really think one has to focus on the universities. The reason the US is doing so well is because of great universities like MIT.

In other countries, it would be important to help promote and develop research in their universities. There are places trying to do that, and we're involved with some of them with our programs in Cambridge and Singapore, for example. Interaction between foreign universities and places like MIT would certainly be a good strategy to make biotechnology and related fields more prominent worldwide.

BioTECH: What are some of the biggest challenges that the fields of bioengineering and biomedical research are facing these days?

Langer: I suppose one challenge is health care cost. On one hand costs are high, but on the other hand, the amount of research necessary for health care is incredibly high; there's animal trials, clinical trials, and so on. And I think you go through particular points in time where things are more difficult. Right now grants are harder, and the pay line has considerably dropped in the NIH in the last couple of years because of the Iraq war and things like that.

Of course there are also scientific challenges we face, and those are unlimited. To pick a few: gene therapy delivery, non-invasive delivery of complex drugs, targeting drugs to specific cell types; the list goes on.

BioTECH: There are some students who are unsure about the ethics of biomedical research, especially research involving embryonic stem cells. What would you say to them?

Langer: Sure. I think we should break it down to two categories: one, bioengineering in general and two, human embryonic stem cells in particular. I think bioengineering in general doesn't have too many ethical issues—not that I've heard of, at least. Human embryonic stem cells, however, are a highly controversial issue.

> *"If I'm going to [pursue a project], and I feel that the science is good, I would never give up. It's just a question of time, resources, and people. I don't see why one should give up, if what you're doing is important and if the science is sound."*
>
> ***Prof. Robert Langer***

What I would say to them is two things: Number one is that I look at the good that can come out of stem cell research. To me, that good is enormous—potential good, I should say. They have the potential to save lives. But some people say that to do that you destroy lives. On the other hand, I would say that a lot of people are using cells that are already there, which means that life isn't being destroyed. There are also people getting embryos from fertility clinics, where they would be destroyed anyhow.

And that's my second comment: I haven't seen a similar uproar about fertility clinics. It seems to me that if there is an argument, it shouldn't start at stem cells per se; it should start in fertility clinics, where cells could be and were destroyed before it was ever possible (starting in 1998) to create human embryonic stem cells.

BioTECH: Biological Engineering is the first major at MIT in over thirty years. What made it possible for this major to be accepted?

Langer: Well, I think that on the one hand there is a change that has happened scientifically. Because of the revolution in molecular biology and cell biology in the last ten, twenty years, the biological aspects of engineering have become much more predominant and created more and more educational, scientific, and professional opportunities for students. I think that's one of the things that made it possible.

I think another thing that made it possible is the people. People like Linda Griffith and Doug Lauffenburger — there are others as well of course, all of whom were very committed to making this happen.

And of course the students themselves. Having a commitment from people who really want to do this played a huge role. So, there's the need and then there's the people making it happen. Both those things coming together are what I believe made this major possible.

BioTECH: Has your successful career and busy schedule ever interfered with family and friends? Are you able to keep a balanced lifestyle?

Langer: I think so. My wife is pretty good at telling me I need to be home at 7 PM every night to spend time with the kids and to help out. I try to do that, but the biggest problem is travel. It's hard because any one day I get four or five invitations to be on a national or international committee or university or to give a lecture outside of MIT. These are nice places, nice people, and worthy things, but I just can't do it most of the time.

I try to help in other ways if I can; for example, I can give lectures by video, or stay in touch with someone by e-mail, things of that sort. I want to spend time with my family so I couldn't possibly accept most of these invitations.

I travel a lot already, but I try not to be gone too many nights. Anywhere I go I rarely stay there for more than one night, without my family, that is. It's hard for me to remember in the last twelve years when I've been away from my family for more than 2 nights in a row. I try to make a particular point of never being gone very long, from either my family or the lab. I really value spending time with my wife and my kids and the people here.

MIT Research Highlight

Cultivation of Human Embryonic Stem Cells without the Embryoid Body Step Enhances Osteogenesis *in vitro*

By *Dr. Jeff Karp*, *POSTDOCTORAL FELLOW*, *Albert Kwon '08*, and *Hannah Seong '08*

Human embryonic stem cells (hESC) offer a potentially unlimited supply of cells that may be driven down specific lineages to give rise to all cell types in the body. Recently there has been great interest in exploring the osteogenic (bone growth) potential of hESCs, and to date two methods have been examined.

In one method, osteogenic cells are derived from 3-dimenstional cell aggregates called embryoid bodies (EB) (Fig. 1A). EBs mimic the structure of the developing embryo and recapitulate many of the stages involved during its differentiation including the emergence of multiple cell types. As an engineer it is very difficult to exhibit control over the multiple cell-cell and cell-matrix contacts that are inherent in this system.

An alternative method that has been tested but not well characterized avoids EBs through the immediate separation of hESC colonies into single cells which are then plated directly into a cell-adhesive culture dish (Fig. 1B). Using this method, one can presumably exhibit better control over the cell microenvironment and thus obtain more pure populations of progenitor cells.

We have recently found that by omitting the embryoid body step, a significant increase in the number of bone nodules (which correlates with the number of osteoprogenitor cells) can be more rapidly achieved. Specifically, 7 times more bones nodules formed when the embryoid body step was omitted (Fig. 2).

In addition, we found that these bone nodules formed after 2 weeks compared to after 4 weeks in cultures derived from EB. Furthermore, we found that regardless of the culture protocol, osteogenic cultures of hESC produced many of the hallmarks of *de novo* bone formation, including a mineralized collagenous matrix and an underlying cement line matrix (the cement line matrix is formed in the body during bone remodeling and serves to "glue" the old and new bone surfaces together).

Taken together, the results indicate that omission of the embryoid body step during the differentiation of hESC into osteogenic cells can be used to rapidly increase osteogenic cell numbers which may be useful in applications such as tissue engineering or cell therapy. In addition, these results might be useful in other cell systems where high numbers of particular cell types are required.

This research was done in the Langer Research Laboratory, with Albert Kwon '08 and Hannah Seong '08 involved as UROP students and Dr. Jeff Karp, Dr. Lino Ferreira, and Dr. Ali Khademhosseini serving as mentors.

Albert and Hannah share about their research experience on page 9.

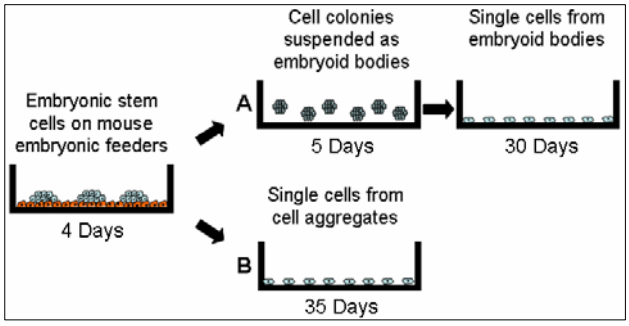

Figure 1: After hESC were cultured on mouse embryonic fibroblast feeder layers for 4 days, cell aggregates were removed with collagenase IV and either (A) suspended as EB for 5 days and then plated as a single cell suspension or (B) directly placed onto tissue culture petri dishes for 1 day followed by plating as a single cell suspension.

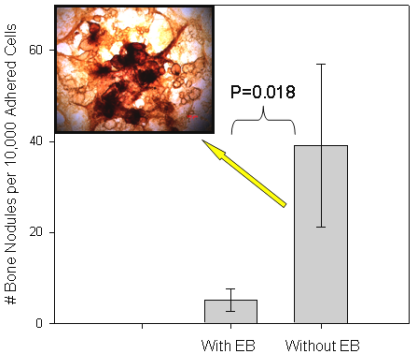

Figure 2. Cells grown from EB produced (5.1 ± 2.4) bone nodules (stained for von Kossa and alkaline phosphatase). In comparison, cells grown without EB (insert) produced 39.1 ± 17.8 bone nodules.

BMES-EMBS Distinguished Lecture Series

Wednesday, Nov. 16, 2005
MIT Room 66-110, 7 pm
(refreshment served at 6:30 pm)

Microsystems for Measuring and Manipulating Cells

Joel Voldman, Ph.D.
NBX Assistant Professor of EECS, MIT

Visit <http://web.mit.edu/bmes/www/lectureseries.html> for more details

The 2005 BMES National Fall Conference was held in Hyatt Regency Hotel in Baltimore.

Representing MIT at the National BMES Fall Conference were **Emily Pfeiffer**, **Judy Yeh**, **George Eng**, **Julie Tse**, **Prof. Douglas Lauffenburger**, **Ling Xu**, **Prof. Linda Griffith**, and **Brian Chase** (left to right).

MIT BMES at the National Conference

(Continued from page 1)

hour block just before the award ceremony. For MIT, co-presidents George Eng '06 and Julie Tse '06 gave the presentation, which focused on the growth and expansion of the MIT chapter to meet the demands of increasing interest in biological engineering and biomedical engineering, especially with the formation of the new BE major. They highlighted the expansion of the executive board from 11 to 21 offices, as a result of the creation of a multi-editor BioTECH staff and the appointment of past officers as student advisors.

The other award-winning schools offered some intriguing programs that had no equivalent at MIT. For example, Wisconsin-Madison generated a lot of interest in their Surgery Shadowing program, which works with the University of Wisconsin-Madison Medical School to offer undergraduates the opportunity to observe surgical cases in the operating room. Many other schools talked about programs that emphasized the social and societal outreach aspect of their BMES societies. The University of Rochester, for example, hosted a program in which they invited high school students to the university and helped them build simple endoscopes, to give them an idea of the process of engineering.

After all the presentations were delivered, the winning schools sat in a panel and fielded questions. This was followed by a two-hour roundtable (or in this case, circle of chairs) discussion of some ways to overcome common obstacles to running a BMES chapter, from fundraising to re-

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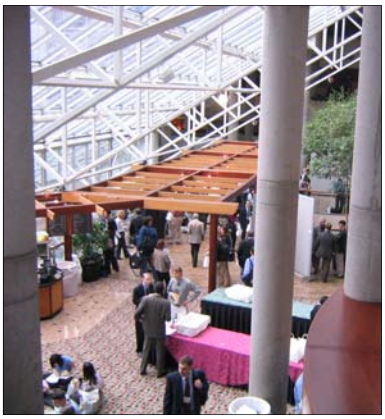
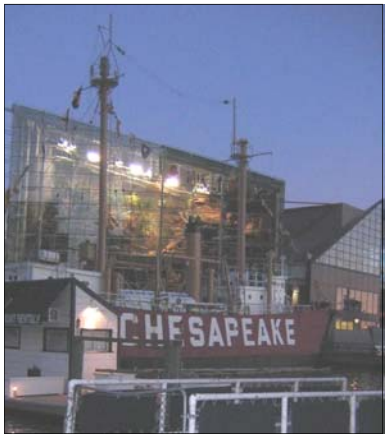


Conference attendants mingled during poster sessions held in the Hyatt lobby.

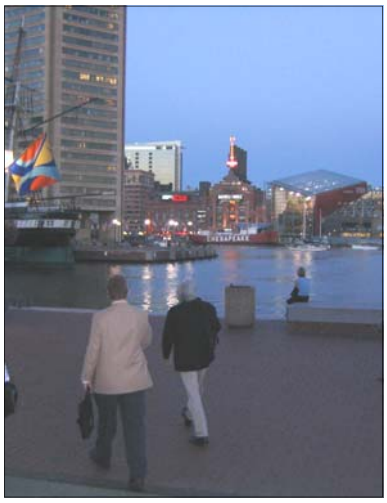
MIT BMES Co-Presidents **George Eng** and **Julie Tse** delivered a presentation during the Chapter Development Workshop.

Posing behind the Baltimore mascot were **Judy Yeh**, **Julie Tse**, **Ling Xu**, and **Emily Pfeiffer** (left to right).

Prof. Doug Lauffenburger waved his ticket on his way to the National Aquarium Reception. Also pictured were **George Eng**, **Judy Yeh**, **Prof. Linda Griffith**, and **Julie Tse**.



(Above and below) Baltimore Harbor offered great sightseeing opportunities.



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cruiting and involving new members. Altogether, 22 chapters were represented at the conference.

Besides the chapter development workshop and the award ceremony, the conference held many poster sessions and research talks where thousands of professors, investigators, and graduate students mingled and shared ideas, research summaries, and plans for future research.

Several MIT professors, including Prof. Douglas Lauffenburger and Prof. Matthew Lang, gave presentations on their areas of research. These sessions continued through all four days of the conference. Another room was set up for booths showcasing company products or school graduate programs. And in every other bit of space were posters for the myriad of graduate students showcasing their research. These posters were up all the time, and changed periodically. For an interested undergraduate, the conference kept one's eyes and ears on a permanent swivel, jumping from one thing to another.

The final perk of the conference was the reception after the meeting on Thursday at the National Aquarium down the street from the conference hotel. There, conference participants were able to observe thousands of different types of fish and other aquatic creatures, including caiman and turtles, while feasting on a buffet including crab cakes, a Baltimore specialty. It was an excellent ending to a very successful National Conference for the MIT BMES chapter.

The MIT BMES Executive Board would like to thank the BE Department for all of its generous support in making this trip possible for the students.

(Below) Chapter Development Workshop attendants posed for a picture. In the front row were representatives from UW-Madison, UCSD, U. of Rochester, and MIT (left to right).

Brian Chase (front) and **George Eng** (behind) had fun in posing with the Baltimore mascot, located in front of the Hampton Inn Hotel.

MIT Research Highlight

Biodegradable Microfluidic Systems for Tissue Engineering

By ***Chris Bettinger***, *PhD Student in Materials Sci & Engineering*

The field of tissue engineering and organ regeneration is an exciting and relatively new field of research born out of the high demand for transplants of vital organs. However, a critical limitation in the regeneration of vital organs is the lack of an intrinsic blood supply, which is required for highly vascularized organs such as the liver and kidney.

Vascular features such as capillaries can be as small as 10-15 microns and have intricate geometries and precise spatial locations. Regenerated organs lack this specifically placed vasculature. These intrinsic characteristics of vasculature invite the application of microfabrication technology, which has been typically used in the production of microelectronic devices, in developing complex scaffolds that require micron-scale resolution.

One thrust of research in the Langer Laboratory at MIT involves the integration of novel microfabrication techniques for vascular and liver tissue engineering applications in the context of a novel biodegradable elastomer.

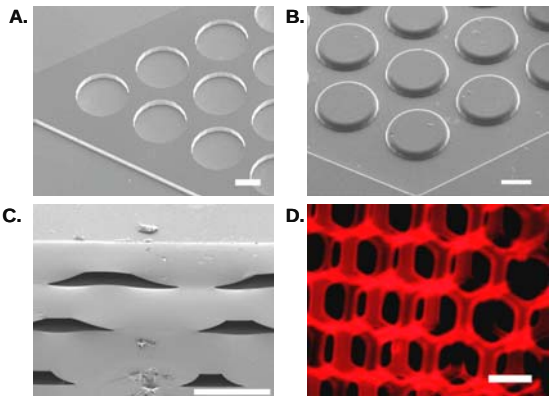
One important consideration in designing tissue engineering systems is the selection of a suitable biomaterial. Previous work utilizing microfabrication has used materials that are not suitable for scaffolds. Crystalline silicon and poly(di-methyl siloxane) (PDMS), while relatively biocompatible, are clearly not biodegradable, nor do they possess the proper mechanical properties that are ideal for a large implantable scaffold. In short, although these materials were not designed for tissue engineering systems, they are often employed due to their ease of fabrication.

The lack of a suitable material lead Yadong Wang of the Langer Laboratory to develop poly (glycerol-sebacate) (PGS), a novel biodegradable elastomer with superior mechanical properties and biocompatibility. With this novel biomaterial in hand, the focus was to adapt typical microfabrication methods to produce microstructures using PGS. Complex three-dimensional microfluidic scaffolds were produced using fabrication techniques tailored specifically for PGS.

A variety of cell types such as endothelial cells and hepatocytes were grown and sustained long-term using perfusion culture *in vitro*. These biodegradable microfluidic systems can be integrated with existing biomaterial systems and technologies for tissue-specific applications and increased functionality.

For example, drug delivery systems, cell patterning techniques, and co-culture systems for hepatocytes can be integrated within the microchannels to promote the organization of seeded primitive cells into complex tissues. Fully biodegradable systems suitable for implantation can be fabricated by integrating flexible, small caliber PGS tubes and affixing those using additional PGS as an adhesive. The end result is an adaptable tissue engineering device that can be integrated with the patient's existing vasculature.

Working in close collaboration with Jeff Borenstein of the Micro-Electro-Mechanical Systems (MEMS) group in the Draper Laboratory and Joseph Vacanti of the Organ Fabrication Laboratory at Massachusetts General Hospital, we are continually working towards developing the next generation of implantable scaffolds that are suitable for engineering complex vascularized tissues and organs. Our long-term goals include the design and fabrication of tissue engineering systems with liver function to be used as a diagnostic tool for drug discovery or as a fully functional liver-assist device.



Polymer molding of microfluidic devices: Microfluidic layouts are designed using traditional engineering software such as AutoCAD (not shown) and etched into silicon to produce molds (A). Biodegradable polymers are replica molded to form sheets with microstructures (B), which can be stacked and bonded to form microfluidic devices. Three-dimensional devices were formed and sectioned (C) to verify the structure of the microfluidic channels. Devices were also perfused with fluorescent dye to demonstrate the ability of these devices to handle hydrodynamic pressures due to flow (D). Scale bars in all images are 200 microns.

This research was done in the Langer Research Laboratory by Chris Bettinger G in collaboration with Dr. B Orrick, Dr. Yadong Wang, Dr. Joseph Vacanti, and Dr. Jeff Borenstein.

Comments on the Value of an Interdisciplinary Undergraduate Research Experience

By ***Chris Bettinger***, *PhD Student in Materials Sci & Engineering*

Research, especially in the fields of biomedical and biological engineering, is becoming more interdisciplinary. Developing novel solutions to problems in the pharmaceutical and medical industries often requires unique approaches, which may draw upon expertise in multiple traditional disciplines.

The quintessential example of the impact of using an interdisciplinary approach to solving problems can be found in the experiences of Institute Professor Robert Langer. He developed novel cancer-fighting strategies that utilized chemical engineering and materials science principles.

Using this engineering-based approach, he was able to tackle and address the problem of angiogenesis in cancer tumors during the 1970s. Until that time, it was unheard of to think that an engineer would be contribute in the effort to eliminate cancer, medicine's most daunting task. However, bringing new perspectives to old problems oftentimes leads to new exciting discoveries.

With anecdotal evidence such as Prof. Langer's experience, as well as many other professors, the importance of excelling in multiple fields of science and engineering became clear to me early on during my undergraduate career. Therefore, I studied a wide range of subjects in the physical sciences and engineering, which was a simple first step toward developing an interdisciplinary perspective.

I found it is equally important, however, to engage in various UROP positions as well as industrial experience to attain adequate breadth of knowledge. In general, I found myself interested in a variety of technical fields and as a result, would never turn down the opportunity to learn. Oftentimes, it is easy to be complacent and dismiss a field of study or a branch of research simply because one is not interested or because it doesn't seem relevant at the time.

I am not arguing that one should study and work to become proficient in numerous fields because it is in fact very difficult to develop expertise in multiple disciplines. Rather, it is imperative to develop a fundamental awareness of the state of the art in various technical fields. In doing this, not only does one mature as a scientist by familiarizing oneself with a foreign topic, but one also increases the set of problem solving tools and techniques that they may draw upon in future research projects.

The traditional engineering and science education is the foundation for a future scientific career. In order to maximize the potential for solving current and future technical problems, this education must be supplemented with an interest in interdisciplinary studies. The added perspective gained by these pursuits, through coursework and hands-on-experiences alike, results in a well-rounded scientific education, which more than adequately prepares undergraduate students for post-graduate degree programs.

BioTECH would like to thank Merck for its generous sponsorship.

Research Experience

This column serves as an accompanying piece to the MIT Research Highlight on page 5.

By *Albert Kwon '08*, *Biology*, and ***Hannah Seong '08***, *Chemical Engineering*

This research experience was an incredible opportunity for us to gain research skills and to learn about the area of tissue engineering and stem cell research. This was our first UROP experience at MIT that we began during our freshman year under the mentorship of Dr. Jeff Karp, who detailed the motivation for this project and conveyed all the necessary background information.

Throughout this experience we learned aseptic cell culture techniques in addition to methods for performing various immunocytochemical and protein assays. As the project progressed, we observed how Dr. Karp and colleagues interacted to address various challenges that arose. We feel very privileged not only to have observed these interactions but also to have been given the opportunity to participate by contributing our opinions and ideas.

We have learned a tremendous amount from this UROP project, which in turn has already had a great influence on our short and long term academic and career plans. It is truly incredible to be part of this project and to have been involved from the very beginning. Our work was recently accepted for publication in the journal *Stem Cells* (published online on October 27). We feel that stem cells-based tissue engineering has great potential and look forward to help further advance this field to clinical practice.

Graduate School Application Primer with Prof. Griffith

(Continued from page 1)
plements the Master's roughly two years of technical training with instruction on research management, including problem identification and definition, approach development, and carrying the research through to publication.

Griffith defined the choice of discipline primarily as a choice of intellectual goals. She anecdotally related her own eleventh hour choice of graduate training in engineering over medical school to illustrate the personal nature of the decision to attend graduate school, and the choice between studying biological engineering or a "classical discipline" such as biology or mechanical engineering. Griffith also advised comparing faculty resources across departments at the graduate school selected before committing to a discipline.

Griffith acknowledged the role of location and other personal priorities in choosing a graduate school, but emphasized basing the decision on the curriculum and faculty of the school and departments in question. Griffith discussed the difference between the clinically based biomedical engineering and molecular life science based biological engineering as a distinguishing factor in classifying curricula.

Ultimately, Griffith recommended gathering as much information as possible about each school, beginning with an internet search of school websites and the Whitaker Foundation (http://www.whitaker.org/academic/database/index.html) resources. She also recommended discussing fit of individual interests and specific schools with BE faculty contacts such as advisors and course instructors, or with current BE graduate students, who might offer perspectives on the other programs they considered.

Griffith outlined the following general schedule of application processes.

Summer through early fall of senior year: Research schools and gather application materials

October – December: Request recommendation letters and transcripts

Mid-December – mid-January: Meet application deadlines

Mid-January – late February: Receive decisions and schedule interviews

Early March – early April: Student visits

April 15th: Absolute deadline to accept or decline offers

Griffith reduced admissions qualifications to three categories: quality of recommendation letters, grades in engineering classes and GRE score. Recommending a compilation of 3-5 letters, she specified that a minimum of three letters come from faculty members. Griffith recommended approaching faculty at least a month in advance of deadlines, and (according to the preferences of the faculty member) emailing a reminder two weeks, one week, and daily in the last week before a letter is due. Griffith also advised applying for fellowship support during this time, possibly adding November or December deadlines.

Griffith summarized a common graduate school academic path as follows:

Year 1: Attend core classes, take a qualifying exam, explore and choose a thesis advisor and project

Year 2: In-depth study of literature. Learn about project feasibility, protocol, etc. Attend classes related to specific research

Years 3 and 4: Make progress on project, student begins to take ownership of project, as reflected by increased publication and presentations to meetings

Years 5 and 6: Conclude project and graduate

Griffith's Graduate School Application Primer presentation is outlined more comprehensively in a flyer available from the Biological Engineering office (56-651).

The BioTECH Staff would like to thank Prof. Griffith for reviewing this article.

BMES-Merck Poster Session Competition

MIT BMES and Merck are inviting all undergraduates to submit posters on their research!

AWARDS!!:
First Prize: $500
Second Prize: $300
Third Prize: $100
Everyone: A professional poster of your research printed courtesy of BMES and the Dept. of Biological Engineering

Poster Session:
When: Thursday, November 17, 5:30-8:30 pm
Where: Bush Room
Cost: $0! We will print the posters for you!

Submissions Due: Wednesday, November 9, 5pm
email to bmesposterssession@gmail.com

Guidelines:
* Research must be broadly related to biomedical engineering
* Posters must be original work, sized: 30" x 42" (required template available online at *web.mit.edu/bmes/www/*)
* Obtain supervisor approval to avoid breach of confidentiality
* Submit a separate Word document with a picture of yourself and a description of your personal involvement in the project

Timeline & Calendar of Events for Bioengineering Opportunities

November:

11/3 "Meet the Lab" (Schauer Group of MIT) *56-114 at 4:10PM*

11/4 "Deciphering the Binding Sites on Ras GTPases" (Dr. Carla Mattos of North Carolina State University) *4-270 at 3:00PM* [Computational and Systems Biology at MIT (CSBi) Seminar Series]

11/10 "The Met Receptor Tyrosine Kinase: Tubes, Tumorigenesis and More" (Dr. Morag Park of McGill U.) *56-114 at 4:10PM*

11/15 BME Minor, BMES Exec, and BME Faculty Luncheon

11/16 "Microsystems for Measuring and Manipulating Cells" (Joel Voldman, Ph.D., of MIT) *66-110 at 6:30PM* [EMBS-BMES Distinguished Lecture Series]

11/17 BMES-Merck Poster Session Competition for Undergraduates, Bush Room at 5:30-8:30 PM.

"Engineering Synthetic Multicellular Systems" (Prof. Ron Weiss of Princeton U.) *56-114 at 4:10PM*

11/18 Dr. Peter K. Sorger (MIT Professor of Biology) *4-270 at 3:00PM* [CSBi Seminar Series]

December:

12/1 "Hyaluronan-based Matrices in Inflammation" (Dr. Vince Hascall of Cleveland Clinic) *56-114 at 4:10PM*

12/2 Mark Trusheim (Massachusetts Biotechnology Council) *56-114 at 1:30PM* [BE Industrial Seminar Series]

"The Logic of Gene Expression: A Global View of RNA Processing" (Dr. Daniel Herschlag of Stanford Medical School, Dept. of Biochemistry), *4-270 at 3:00PM* [CSBi Seminar Series]

12/7 "Architecture, Algorithms and Circuits for Enhanced Chemical Sensing" (Sameer Sonkusale, Ph.D., of Tufts University) *66-110 at 6:30PM* [EMBS-BMES Distinguished Lecture Series]

12/9 Dr. Benjamin Blencowe (University of Toronto Dept. of Medical Genetics and Microbiology) *4-270 at 3:00PM* [CSBi Seminar Series]

Student Research Spotlight (cont'd.)

Student Research Spotlight

Why? Research is an ongoing dialogue — share your work and get feedback from faculty and peers with different backgrounds but similar interests!

Guidelines?
1. Undergraduate research in a BME-related field.
2. A concise and informative description of research in ~500 words.
3. Include a brief blurb on the context of research (lab affiliation, mentor, how you got involved, degree and length of involvement, etc).
4. Jargon-free, reader-friendly language accessible to the general MIT community.
5. Approval from mentor if research is UROP-based, or clearance from employer if research is industry-based.

Interested? Contact *TheBioTECH*@mit.edu for more info.

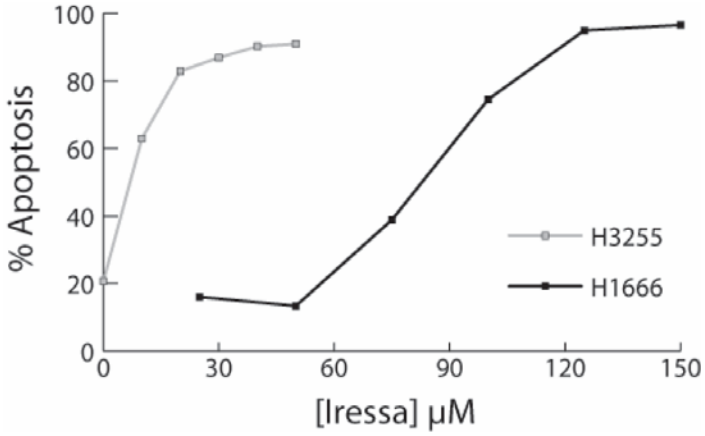


Figure 2. Cell death upon treatment with Iressa. Percept apoptosis as signified by staining positive for cleaved caspase-3 and/or cleaved PARP after a 3-day treatment with Iressa. H1666 and H3255 treated at

(Continued from page 12)
which the EGFR mutation contributes to proliferation and apoptosis.

These data are part of an even larger study of the mutant EGFR genes, in which the receptor trafficking, degradation, and signaling are also being quantified. When combined, these data will be mathematically modeled in the hopes of gaining additional insight into the development of more effective therapeutic strategies for the next generation of inhibitors.

Student Research Spotlight

Quantitative Effects of ErbB-Targeted Therapeutics on Apoptosis and Proliferation in Human Cancer Cell Lines

Danielle Carpenter, a sophomore from Houston, TX, has been doing research in Professor Douglas Lauffenburger's lab under the mentorship of postdoctoral Fellow Matthew Lazzara since the spring of 2005. She is currently majoring in Chemical-Biological Engineering (10B) but is also considering the new Biological Engineering (BE) major.

By *Danielle Carpenter '08*

Epidermal growth factor receptors (EGFRs) are a family of receptor tyrosine kinases involved in many cellular processes such as cell growth, cell death, migration, and differentiation. Given their intimate involvement in a wide variety of cellular processes, it may come as no surprise that dysregulation of EGF receptors can lead to a variety of cancers. Consequently, ErbB receptors are prime targets for cancer therapy, and pharmaceutical companies have put great effort toward the development of inhibitors (small molecules and antibodies) designed to interrupt the various steps in EGFR activation.

An example of such a drug is Iressa (a small molecule inhibitor which binds to the EGFR and inhibits the kinase activity of the receptor), which is approved for the treatment of non-small cell lung carcinoma (NSCLC), but has yielded disappointing results. Despite the fact that 40-80% of NSCLC tumors involve overexpression of EGFR, only 10% of NSCLC patients demonstrate tumor regression in response to the drug. It was quickly discovered that the 10% of patients who responded to Iressa harbored genetic mutations in their EGFR gene, which seems to aid in the development of cancer.

However, how these EGFR mutations affect normal receptor function, and the reason for their extreme sensitivity to Iressa remains largely unknown. The specific focus of my work is to investigate how the mutant EGFR genes alter cellular proliferation and death (apoptosis), with and without EGFR inhibitors such as Iressa.

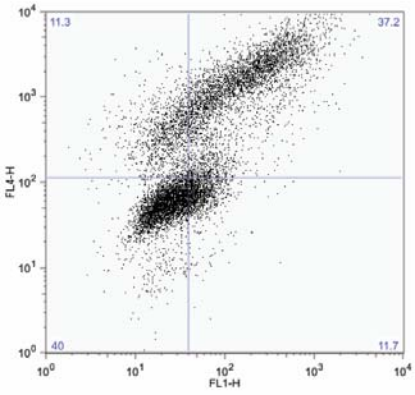


Figure 1. Levels of protein markers indicating cell death. FACS plot of cleaved PARP (FL1-H) vs. cleaved caspase-3 (FL4-H) of H3255 cells after a 3-day treatment with 10 μM Iressa. Each point represents a cell. Cells in the lower left quadrant stained negative for both cleaved PARP and cleaved caspase-3, and those in the upper right stained positive for both protein markers.

My project employs several basic protocols for quantifying cell proliferation and apoptosis. The assays involve incubating various cell lines (with and without EGFR mutations) with varying concentrations of inhibitor, and then determining the levels of proliferation or apoptosis.

To quantify levels of proliferation, I use a spectrophotometry-based assay to measure color change of a dye that correlates with the number of live cells in a tissue culture dish. To quantify cell death, I fix the cells subsequent to inhibitor treatment and use fluorescent antibodies to detect levels of cleaved caspase-3 and cleaved PARP (two protein markers that are indicative of cell death), and then quantify fluorescence using a flow cytometer. An example of the raw data obtained from such an experiment is shown in figure 1.

In figure 2, we are comparing cell death of two different cell lines, one of which has a mutant EGFR gene and the other of which is wild-type. Following a three-day treatment with 50 μL of Iressa, we see 91% of H3255 cells are positive for cleaved caspase 3 and PARP, as compared to only 13% of H1666 cells, suggesting that H3255 cells are 7-fold more sensitive to Iressa than H1666 cells.

By performing these experiments on a multitude of cell lines, containing either the mutant or wild-type EGFR gene, we will gain a quantitative understanding of the extent to

(Continued on page 11)