MASSACHUSETTS INSTITUTE OF TECHNOLOGY

April 2011

The BioTECH

Volume 7, Issue 2

BIOLOGICAL ENGINEERING-BIOMEDICAL ENGINEERING SOCIETY

At the Intersection

By *MASHAAL SOHAIL '11*
BIOTECH EDITOR

What's the connection between scale-free networks and cell cycle, cancer drugs and gold, between proteins and control theory and wintergreen and bacteria? Frans Johansson who asks similar questions about connections between termites and architecture, candy and computer, between sneakers and hummer and techno music and Martin Luther King would say that the answer lies in a term coined the Medici Effect. He defines this effect as 'the breakthroughs that happen when new connections are made at the intersections between ideas, concepts and cultures.'[1]

Increasingly, science departments are appreciating the strength of the Medici effect and developing programs that foster collaborations and transcend artificial boundaries that have traditionally separated disciplines. Lee Fleming at Harvard Business School studied the connection between a person's creativity and innovation and their social-network structure.[2] He looked at U.S. patent data since 1975 and created interaction maps for innovators across the U.S. He found that 'brokers', defined as 'influential persons connected to many others who don't know each other', tended to be the most innovative due to their central position with regard to the movement of information. On the other hand, it was connectors, 'influential individuals with a habit of introducing their collaborators to each

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New Faculty in Emerging Biotechnology

Jeff Gore

By Mashaal Sohail '11

Jeff Gore joined the Physics faculty in September 2009 and started a biophysics lab studying evolutionary dynamics and systems biology. He spent the last few years before that as a Pappalardo Postdoctoral Fellow working at the Alexander Oudenaarden Lab where he studied the evolution of cooperation using sucrose metabolism in yeast as a model system.

Professor Gore completed his PhD from UC Berkeley in Physics where he worked at an experimental single-molecule biophysics lab. As an undergraduate at MIT, he earned bachelor's degrees in Physics, Mathematics, Economics and Electrical Engineering.

Picture from his personal website

His group combines experimental and computational work using different microbial systems to study fundamental questions in evolutionary dynamics . These questions range across conditions favoring evolution of cooperative behaviors, ruggedness of fitness landscapes, reversibility of evolutionary adaptations, the cooperative nature of antibiotic resistance and co-evolutionary dynamics between species.

Tim Lu

By Matthew Luchette '11

Tim Lu, a newly appointed assistant professor in Course 6, hates biofilms. When bacteria self-adhere and aggregate, they create a slimy substance called a biofilm. These aggregates can form on living and non-living surfaces, from the surface of teeth to the inside of wounds, and can cause devastating infections. Biofilms are typically treated with various chemicals or antibiotics, but as Lu states, "sometimes that's not enough."

Lu's lab, which focuses on synthetic biology, has developed a way to defeat the bacteria from the inside out. His group has engineered a strain of bacteriophage that inserts a gene into the bacteria which makes them more susceptible to antibiotics and chemical treatment. "The phage don't kill the bacteria," says Lu, "only weakens them." Yet the genetic information inserted into the bacteria makes once benign treatments devastating to the biofilms.

Picture from MIT rLe website

Lu, a 30-year-old MD/PhD graduate from the Harvard-MIT HST program, attributes his early success to a mix of hard work and being "at the right place at the right time." "This is an exciting time to be in

Continued on page 17

Domitilla Del Vecchio

By Hattie Chung '11

Domitilla Del Vecchio is an assistant professor in Course 2. She received a B.S. and M.S. in Electrical Engineering at the University of Rome, and received her Ph.D in Control and Dynamical Systems from Caltech. Prior to joining the faculty at MIT, she was an assistant professor at the University of Michigan in the Department of Electrical Engineering.

Her research interests lie in the design and analysis of biomolecular control networks. Del Vecchio's recent work has focused on studying the non-modularity of synthetic circuits, called retroactivity. This effect occurs when the load from connecting two components changes the system behavior; this is equivalent to circuit behavior when two connected resistors result in a system change. Probing this behavior will increase the predictability of complex system dynamics. She is currently designing a circuit to measure retroactivity in cells, similar to a voltmeter for electrical circuits.

Picture from MIT website

Professor Del Vecchio is teaching 2.993: Biomolecular Feedback Systems this semester, a course that will equip students with analytical tools to assess systems. The second half will focus on employing these tools to design a feedback system.

Stem-Cell Skirmish

By Sabina Sood '13
BioTECH Editor

Synthetic-organs.yolasite.com

Over the past decade, much debate has been centered on research involving stem cells, undifferentiated cells that have the potential to develop into more than 200 types of adult cells. Many researchers agree that stem cells can replace or repair damaged cells in the body and significantly influence the treatment for many diseases, such as Alzheimer's, Parkinson's, and cancer.

Controversy arises, however, when discussing how stem cell research should be conducted. So far, scientists have been working with embryonic stem cells which come from four-to-five-day-old fertilized cells that have been discarded by fertility clinics. Critics of embryonic stem cell research argue that using fertilized cells for research is inhumane and should be banned.

Legislation has been passed to address this research issue, the most important being the Dickey-Wicker amendment. The amendment prevents tax dollars from being used to create human embryos in the lab (a common procedure in fertility clinics) or for funding research that involves destroying, discarding, or injuring embryos. The amendment was ratified in 1996 and has been renewed every year. This legislation became an obstacle for tax-funded embryonic stem cell research because the embryos are damaged when stem cells are taken from them. As a result, President George W. Bush made an exception to the law in August 2001, stating that tax dollars may be used for research involving a small number of stem cells that have already been extracted from embryos as long as the extraction was not done by federal researchers. In March 2009 after President Obama came into office, he eliminated the restrictions that had been previously established by Bush and announced that stem cell research is supported by the government.

Chief Judge Royce C. Lamberth from the Federal District Court vetoed Obama's executive order in August 2010, deeming it a violation of the Dickey-Wicker amendment. An appeals court is currently considering the case.

Capitalismmagazine.com

Your Lab, Chip-Sized

By Matt Luchette '11
BioTECH Editor

In 2006, researchers at the Massachusetts General Hospital (MGH) made an exciting discovery: they developed a device that could identify Circulating Tumor Cells in 99% of blood samples taken from cancer patients. This "lab-on-a-chip" (LOC) device, or device that integrates one or several laboratory procedures onto a centimeter-scale chip, consists of small channels with posts coated in EpCAM antibiodies. As blood flows around the posts, cancer cells in the blood attach to the antibodies and can then be stained and identified by microscopy. The MGH researchers believe that the device could be a non-invasive, inexpensive tool for diagnosing cancer and tracking the disease's progression in a patient. The current standard for diagnosing cancer is through a biopsy of a possible tumor, a potentially painful procedure that typically costs thousands of dollars. Yet as Daniel Haber, the chief of the MGH cancer center, told the Associated Press, "[The LOC device] is like a liquid biopsy." By integrating once complicated lab procedures on a single relatively inexpensive chip, this LOC device, and many others like it, may soon revolutionize diagnostic medicine.

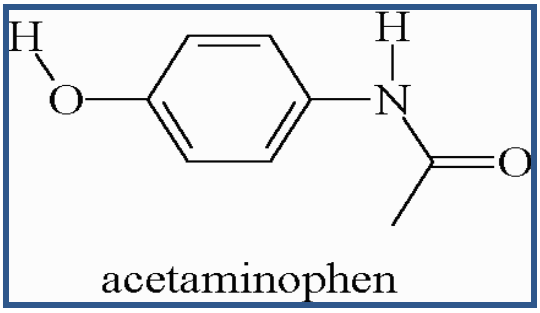
Similar LOC devices have also been developed and marketed for their low cost and ease of use. The Whitesides group at Harvard University, for example, has developed diagnostic devices on pieces of paper. The paper devices are coated in a color indicator which changes color based on the level of a clinically relevant marker, such as protein or glucose, in a patient's fluid. Traditional glass or silicon LOC devices can cost a few hundred dollars and the machinery used to make the devices work can cost thousands more. These paper devices don't require any supplementary machinery and cost only a few pennies, making them especially useful in the developing world, where lab supplies and money are both scarce.

Whiteside lab paper glucose assay for urine
Technologyreview.com

Furthermore the advantage of scaling down lab procedures onto a micro-device is not only financial; these devices often give more accurate diagnoses. A silicon LOC device developed at Bringham Young University uses its small length scale to detect single viruses. A patient's blood is flowed into the device through capillaries until it meets a wall. The bottom of the wall has a tiny slot just large enough for the viruses to enter. These trapped viruses can then be imaged with a camera and isolated for further study. As Aaron Hawkins, one of the supervisors for the chip's design, told Cnet News, "Most of the tests that you're given are fairly inaccurate unless you have a really high concentration of the virus." However these LOC devices can detect single cells or biomolecules, allowing for detection of biomarkers in relatively low concentrations.

The future success of diagnostic LOC devices depends on the effectiveness and reliability of these early products. The devices need to prove that in addition to being more convenient and cost-effective for the patient, they're also more accurate and easier to use than the existing technologies. Yet as these examples have already shown, the future looks promising.

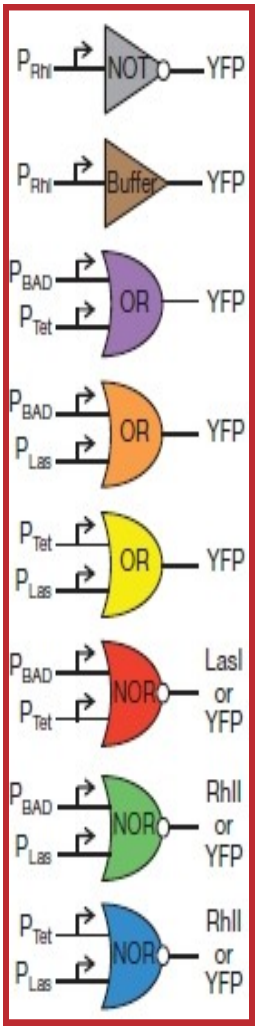
Courses: Hot or Not



Purdue.edu Chemistry Website

20.201: Mechanisms of Drug Action

This is an introduction to pharmacology. The class focuses on two aspects of pharmacology: pharmacokinetics (what the body does to a drug) based on a drug's absorption, distribution, metabolism, excretion, and toxicity, and pharmacodynamics (how the drug preforms its intended function). This class then moves into case studies on the development and study of various drug classes, including antibiotics and statins. One of the best features of the class is the guest lectures given by leading researchers in the industry. By the end of the course, I felt that I understood many of the considerations involved in developing a drug and how the effectiveness of a drug is measured.



Tamsir et al. Nature 463, 212-215 2011)

Principles of Synthetic Biology (20.949)

This course introduces many aspects of the diverse field of synthetic biology. Because it also attracts a diverse group of students from different backgrounds and experience levels, the professors began with a series of lectures on the basics of molecular biology and logic functions to get everyone on the same page. Topics such as noise in gene expression and manipulating basic logic gates are stressed. As the course progressed, the scientific and engineering tools introduced in lecture appeared on problem sets, which began to focus on modeling and analysis of biomolecular systems. After the one midterm exam, which mostly covered modeling tools, lectures shifted to a topic-by-topic overview of applications in synthetic biology, including the implementation complex logic functions, protein and nucleic acid engineering, and metabolic engineering. For a final project students chose any topic of interest from the course. Typical projects included some level of modeling and were presented in 10 minute talks during finals week along with a written report.

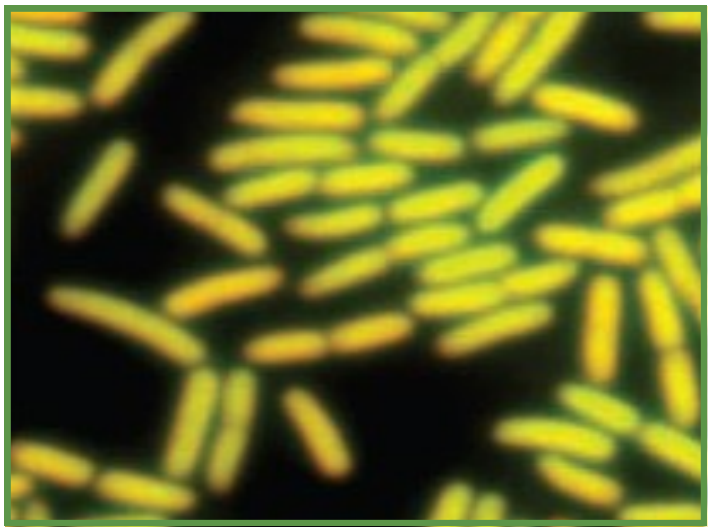
MIT OCW Website

6.041: Probabilistic Systems Analysis

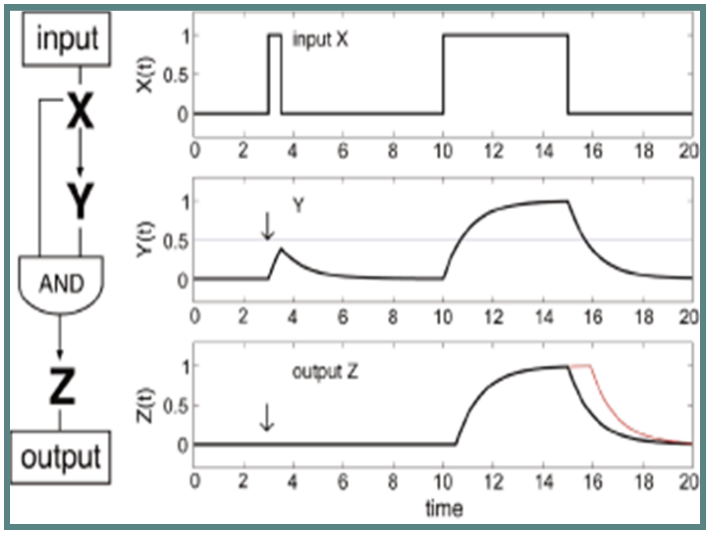
This is a very useful class, regardless of what your interests are. Although most of the examples are centered on computing and information processing, the concepts are very applicable to biology. Learning about the Poisson process and Markov chains is particularly helpful; these probabilistic models can be used to describe aspects of cellular behavior, such as transcriptional bursts and molecular binding events. Basic concepts like conditional probability or memoryless processes are taught as well. The format of the class is the same as any large lecture-style class – there are weekly psets, recitations, and three exams. Anyone interested in systems or computational biology should take this class.

8.591 /7.81 /7.32 Systems Biology

Although Systems Biology is only required for physics graduate students specialized in biophysics, it also attracts undergraduate students from various majors. In fact, half of the class is composed of undergraduates. Approximately two thirds of the course focuses on differential equations that capture the unique features of biological networks and circuits, while the other one third, newly added by Professor Jeff Gore, explores fascinating questions in evolutionary dynamics including population genetics and evolutionary game theory. There are two midterms, one final, and weekly problem sets that are carefully designed to build up computational skills in biophysics research. Besides covering textbook contents, Professor Gore also uses recently published research papers and conducts interesting in-class games during lectures. There is a high level of student participation in this class. Students actively answer and pose questions, leading to meaningful class discussions. In essence, if you wonder about physicists' viewpoint on biology, this is a wonderful class that you cannot miss!



Elowitz et al. Science 297, 1183-1186 (2002)



Shen-Orr et al. Nature Genetics 31, 64 – 68 (2002).

7.342: Systems and Synthetic Biology

Dr. Hyun Youk, post-doc in the laboratory of Alexander van Oudenaarden
This is one of the advanced undergraduate biology seminars. It provides a nice overview of the big questions in systems biology, which is the study of how biological components integrate to form complex system behavior. A particularly interesting topic was noise and stochasticity in cellular processes. We explored this topic through papers from a variety of perspectives, such as synthetic circuits that test extrinsic and intrinsic noise, and development studies in frog embryos. We read two papers a week and discussed them in a weekly seminar – one paper per hour. The most rewarding part was approaching the papers in a critical manner. Hyun encouraged us to think how the experiments could have been planned better, determine whether a paper was well-written, and develop what future steps should be taken. Unfortunately, Hyun will not be here next year to teach this enjoyable class again. But a similar seminar was offered in Fall 2008 – 7.342 Systems Biology: Stochastic Processes and Biological Robustness, which was taught by Jeff Gore and Arjun Raj (who then were post-docs in the van Oudenaarden lab). Be on the lookout for this class in the coming years – it will be worth it!

***Perspectives compiled from various students.**

Applications of Synthetic Biology

By *Matthew Luchette '11*
BioTECH Editor

In early 2000, when the U.S. Department of Energy stated that 30% of the nation's fuels should be made from renewable sources by the year 2030, Stephen Church was listening. In 2005, Church, a geneticist at Harvard Medical School, and his colleague Chris Somerville, a professor of plant biology at Stanford, formed a company called LS9 to design renewable biology sources to manufacture fuels. The company's technology relies on a new field called synthetic biology, which focuses on designing new intracellular pathways that do not exist naturally to perform a specific function. Church's company reengineers genetics circuits within bacteria, adding to and changing some of the cell's own intrinsic metabolic pathways, to manufacture the biofuels. While several other research groups have looked to ethanol as another possible fuel source, Church and Somerville believe that these bacterial-derived hydrocarbon fuels would require less energy to produce and could be further engineered to reduce production of pollution-causing sulfur byproducts.

While LS9 could change the fuels that run our cars, one of the more famous, or infamous, illustrations of synthetic biology today began at the J Craig Ventner Institute in Maryland and California. In 2010 Dr. Ventner and his colleagues synthesized an entire bacterial genome ex vivo and then transplanted the synthetic genome into a new bacterial cells whose genome was removed. These new cells were viable, meaning they are the first living cells without parents.

Researchers at the Venter Institute rave that, similar to Church and Somerville, the sophisticated technologies used to make their synthetic genomes could allow synthetic biology researchers to more easily reengineer genetic circuits in the future. The idea of improving the tools to engineer biology to standardize the design process is the basis of the BioBricks Foundation, a not-for-profit organization of Harvard, MIT, and UCSF scientists. The Foundation hopes to create a vast Registry of Standard Biological Parts. These parts would be tools for the synthetic biological engineer, like knuts and bolts for a mechanical engineer, that would be important for building a specific cellular network. If the Foundation is successful, the Registry could help streamline the design process for researchers like Church and Somerville.

MIT iGEM Team 2010 — from *The Tech*

Yet despite how young the field is, synthetic biology is not just reserved for sophisticated scientists and venture capitalists: high school and college students world wide can create novel synthetic biology projects at the annual International Genetically Engineered Machine (iGEM) competition, which takes place at MIT. According to the iGEM organizers, the goal of the competition is to promote the open engineering of tools to manipulate biology and to design biology to perform novel functions. Each year the competition draws participants from as far as Taipei and Slovenia. In the past, winning projects have included bacteria that could detect mercury in solution or can detect nitrates in soil. While the ethical implications of engineering biology are still an important consideration, the wide applications of these projects suggest that synthetic biology could grow to become a leading field of research in the years to come.

The Next Frontier

Potential Harms of Synthetic Biology

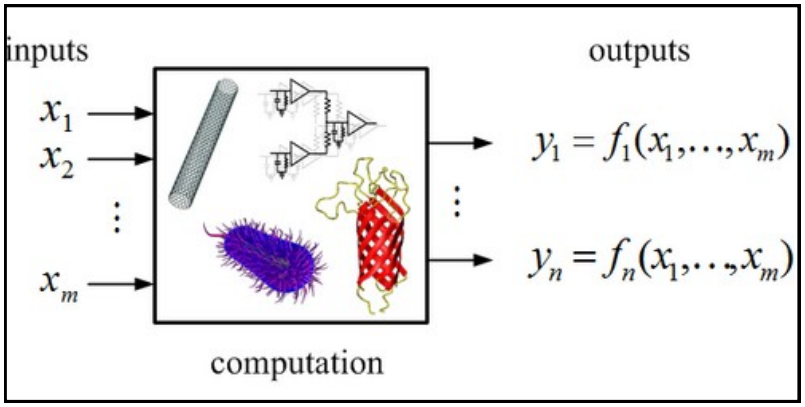
By *Hattie Chung '11*
BioTECH Editor

Following the announcement of the "first artificial cell" from J. Craig Venter's group in July 2010, President Obama issued a Bioethics Commission to explore the implications of synthetic biology. The panel, consisting of 13 scientists, public policy experts, and ethicists, met over a course of 13 months. Although the panel considered "an array of approaches to regulation—from allowing unfettered freedom with minimal oversight and another to prohibiting experiments until they can be ruled completely safe beyond a reasonable doubt," they "chose a middle course" approach (Report).

Perhaps an attempt to be science-friendly in contrast to the former president, Obama mainly appointed social liberals to the Bioethics committee (2). As a scientist and an engineer myself, I can't argue that I want more regulations, but I was slightly disappointed at the hands-off approach. Some of the problems posed by synthetic biology will warrant regulatory frameworks unlike any other, and it would be beneficial to both the scientific and policy communities to start a dialogue and co-evolve.

The synthetic biology community is relatively small — there are 19 principal investigators who are funded by the NSF-supported Synthetic Biology Engineering Research Center (SynBERC), 17 of which have their own laboratories. With such a small community mostly housed in respectable academic institutions, the breakout of a biosecurity threat seems unlikely. Supporting the opinion of the Bioethics Commission report, I do not think that "Do-It-Yourself" biologists will pose a huge security threat. As Andy Ellington writes in his blog, "There is no 'Radio Shack' for DNA parts, and even if there were the infrastructure required to manipulate those parts is non-trivial." Unless we build the Best Buys and the Radio Shacks for biological parts and research equipment, synthetic biology in the U.S. will be largely limited to academic institutions. However, the field has expanded rapidly on the international stage. The international Genetically Engineered Machines (iGEM) from only five U.S. teams in 2004 to over 138 teams from five continents in 2010. One of the objectives of iGEM is to share detailed information on each project and submit newly created biological components to the Registry of Standard Biological Parts. It is available to the public. That said, the real cause for immediate concern is more obvious - academic institutions in foreign countries that are managed under completely different regulations than that of the United States.

Although the Obama Commission did not instate any regulations or an organization to oversee synthetic biology activities, it would be prudent to start developing an international regulatory framework now. Biosecurity poses challenges that previous policies are not capable of handling: it has the ability to self-replicate. While the threats are not immediate, waiting for this capability to be developed and then



From the Riedel Lab, University of Minnesota

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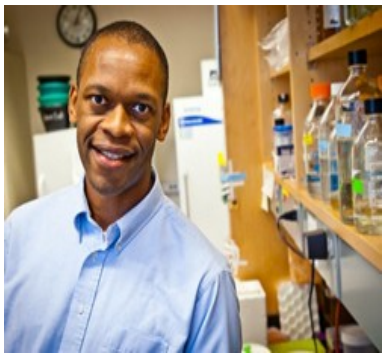
Briefings: Semester in Review

Career Panel, How to Choose a Major, Student Research Prizes, and more!

Every semester, our exec works diligently to share exciting events and opportunities with our community. Here is a brief overview of highlights from the past semester!

Industrial Relations

Life Technologies, a company founded by the merger of Invitrogen and Applied Biosystems presented an information session in September. Representatives from Life Technologies included MIT alumni and former interns and promoted recent graduate and intern opportunities in Biological Engineering/Biology, Chemical Engineering/Chemistry, and Computer Science/Electrical Engineering. In November, Genentech, a sponsor of *The Biotech,* hosted a career panel featuring current Genentech employees and MIT alumni, as well as a private luncheon with interested candidates. For more opportunities in industry, please check out MIT's Spring Career Fair and the Tau Beta Pi Career Fair!



Source: R&D Mag

Faculty Luncheons

Last semester, we had faculty luncheons with Professor Jacquin Niles, who teaches 20.109 in October. We had a great conversation about his education as a medical researcher as well as his work on malarial research with an RNA approach. In November, students were able to converse with Professor Scott Manalis, who teaches 20.330 and 20.309. With Professor Manalis, students were able to give feedback on course 20 classes they have taken and talk more generally about the major itself.

Source: Quake Group Page

Special Event: Lecture by Flagship Ventures CEO

This was a special joint event hosted by the BE Undergraduate Board and BE-BMES. The CEO of Flagship Ventures, Dr. Noubar Afeyan, gave a lecture to the members of both BE-BMES as well as the Biological Engineering Undergraduate Board on November 1st. He talked about his experiences in academia as Senior Lecturer at MIT's Sloan School of Management and his success in industry and start-ups as a co-founder of over 20 successful life science and technology companies. Dr. Afeyan entertained the audience with stories of his experiences starting out in the business world after receiving his Ph.D. in Biochemical Engineering from MIT in 1987. He ended his lecture with advice on how to be a successful venture capitalist and entrepreneur.

Briefings: Semester in Review

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GBM with Mark Bathe

BE-BMES' first general body meeting of the semester took place on Wednesday October 13th from 7-8pm in Room 4-159. The meeting featured Mark Bathe, an assistant professor in the biological engineering department, who gave his perspective on where biological engineering is headed and briefly described his research on DNA based nanoscale design. The second half of the meeting was a very informal conversation on biological engineering at MIT. The executive officers also briefly described how students could make the most our of their academic experiences at MIT through BE-BMEs UROP information sessions, research competitions, poster presentations, and biotech tours.

Source: Lab Website

Lecture Series

Source: New York Times

September saw a lecture with George Church, who is currently affiliated with the Harvard Medical School and the Wyss Institute for Biologically Inspired Engineering.

Source: MIT News Website

He has helped with the Genome Project and is a leading voice in many biotech companies in the field of synthetic biology. He gave an overview of the activity in personal genomics in the Boston area and talked about his perspectives on the leading challenges and hot issues in bioinformatics, computational biology and synthetic biology. The next talk in the lecture series was given by Professor Manolis Kellis. As an associate professor of Computer Science at MIT and a member of CSAIL and the Broad Institute, he has been working at the cutting edge of computational biology and genomics. In november, Jose Gomez-Marquez and Soon Wan Gim led a seminar and discussion on "Technology for global health: Challenges and opportunities". This event explored the possibilities for using technology to address the huge unmet health needs and inequalities around the world. .

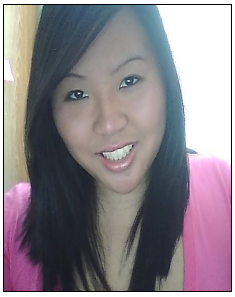
Marquez is director for MIT's Innovations in International Health (IIH) program, where he has spearheaded a number of ventures, including the X out TB program while Gim is the past IEEE GOLD chair and also chaired the 2009 IEEE Humanitarian Workshop held at BU.

BE-BMES
Excellence in Biomedical Engineering Research Awards 2010

The 6th Annual Merck/BE-BMES Undergraduate Research Poster Session took place in the MIT Bush Room (10-105) on Friday, November 12, 2010. Sponsored by Merck, this poster session gives an opportunity for undergraduates to display their research works in a broad range of Biology, Bioengineering and Chemical Engineering topics. There were a total of 11 entrants for this year's poster session. 1st place went to Michelle Dang '11 for her "EGF-ligand cleavage is regulated on the substrate level in a cell-specific manner" research work. Yingxia Wang '12 got second place, while Sabina Sood '13 and Jennifer Li '14 were tied for third place. We had an extremely high caliber of entrants this year and the judges were very impressed. Jose Otero (Manny), representative from Merck who also helped judge the poster session, concluded, "Absolutely our pleasure to be a part of this great event and organization!....Let's maintain strong connections."

Michelle Dang
EGF-ligand cleavage is regulated on the substrate level in a cell-specific manner

The dysregulation of EGF family ligand cleavage has severe consequences for the developing as well as the adult organism. Therefore their production is highly regulated. The limiting step is the ectodomain cleavage of membrane-bound precursors by one of several ADAM metalloproteases and understanding the regulation of cleavage is an important goal of current research. We have previously reported that in mouse lung epithelial (MLE) cells, the pro-EGF ligands TGF-alpha, NRG and HB-EGF are differentially cleaved depending on the cleavage stimulus (Herrlich et al., FASEB J. (22) 2008). In our current study in mouse embryonic fibroblasts (MEFs) that lack different ADAMs. we show that induced cleavage of EGF ligands can involve the same substrate-specific metalloprotease but does require different stimulus-dependent signaling pathways. Cleavage was stimulated by phorbol ester (TPA; a mimic of diacylglycerol and PKC activator), hypertonic stress, lysophosphatidic acid (LPA)-induced GPCR activation, or by ionomycin-induced intracellular calcium release (IM). Although ADAMs showed substrate preference (ADAM17: TGFalpha, HB-EGF; ADAM9: NRG), substrate cleavage differed substantially with the stimulus and cleavage of the same substrate depended on the presence of different, sometimes multiple, PKC isoforms. For instance, classical PKC was required for TPA-induced, but not hypertonic stress-induced cleavage of all EGF family ligands. Inhibition of PKCzeta enhanced NRG release upon TPA stimulation, but blocked NRG release in response to hypertonic stress. Our results suggest a model in which substantial regulation of ectodomain cleavage occurs not only on the metalloprotease level but also on the level of the substrate or of a third protein.



Yingxia Wang
Encapsulation of Single Cells in a Droplet-Based Microfluidic Device

Microfluidic devices have great potential in cell analysis due to their small scale, high-throughput operation, and adaptability to a variety of analytical methods. A droplet-based microfluidic device, when combined with electrochemical measurements, would allow for more robust single-cell measurements than conventional electrochemical methods, thus better revealing cellular functions and dynamics. For this idea to be

beneficial, cells must be individually encapsulated and stored in droplets of media in a continuous carrier phase, and high-throughput encapsulation of single cells is necessary. Therefore, this encapsulation process is tested and evaluated in this project. Soft-lithography techniques are used for PDMS-based chip fabrication. Tris buffer and perfluorinated polymer solution are utilized as the media and carrier phase, respectively. Lastly, polystyrene beads are used
to simulate cells. The devices have a high percentage of one-cell droplets, showing their potential to be useful for single cell measurements. Ultimately, microelectrodes will be
integrated into this device to produce an ideal tool for electrochemical measurements of immune cell exocytosis.

Sabina Sood

Measuring Histone Variant H2A.Z Dynamics at Budding Yeast Promoters to Determine Mechanisms Involved in Nucleosome Eviction and Reassembly

The chromatin structure in eukaryotes is inhibitory to most genomic processes. Multiple cellular mechanisms exist to ensure chromatin dynamics. One such mechanism is the site-specific incorporation of histone variants in chromatin. The histone variant, H2A.Z, replaces the canonical H2A in nucleosomes found at gene promoters. This phenomenon is conserved from yeasts to humans. It is also known that the promoter-specific H2A.Z nucleosomes have a high turnover rate. However, the mechanism by which these nucleosomes turnover is unclear.

The goal of our project is to find out the mechanism involved in nucleosome eviction and reassembly. To achieve this goal, we developed a sensitive assay, called SNAP labeling, to measure the kinetics of histone replacement.

From our research, we found that the HTZ1-SNAP chimera is fully functional and can be labeled with Biotin or a fluorophore both *in vitro* and *in vivo*. Future experiments will focus on measuring the kinetics of H2A.Z turnover by using the SNAP labeling method.

Jennifer Li

Sensitivity of Human Glioblastoma Cells to Temozolomide is Mediated by Glutathione S-transferase

Glioblastoma multiforme is the most frequent and incurable brain tumor in adults. Although temozolomide (TMZ) has become a standard chemotherapy agent against glioblastoma, patient survival is only slightly increased. Glioblastoma cells develop resistance to TMZ, limiting its effectiveness. It has been shown that GSTP1 expression in glioblastoma is associated with its drug resistance. This study aimed to determine the role of GSTP1 in TMZ sensitivity/ resistance of glioblastoma. We used Cell Titer-Blue cell survival assay and Caspase-3/7 activation assay to assess cell viability and apoptosis of a human glioblastoma cell line U87 after TMZ treatment. To investigate whether GSTP1 was indeed involved in sensitivity of U87 cells to TMZ, U87 cells with siRNA-mediated knockdown of GSTP1 expression were generated and the expression of GSTP1 was examined by Western blot. The TMZ sensitivity of these U87 cells with knockdown expression of GSTP1 was measured. We found that U87 cells were sensitive to TMZ. The U87 cells with knockdown expression of GSTP1 showed increased sensitivity to TMZ and the cell death of U87 cells was caused by apoptosis. Our results demonstrated that sensitivity/ resistance of human glioblastoma cells to TMZ was mediated by GSTP1. It is suggested that inhibition of GSTP1 expression together with administration of TMZ may provide a way for improving clinical outcomes of TMZ in the treatment of human glioblastoma.

BE in the World: News, Business, Policy Perspectives

Wooly Mammoth cloning project on the fast track, say scientists

Taken from Alaska Dispatch, Published Jan 23, 2011

According to The Daily Yomiuri (Japan), a team of geneticists in Japan has made a breakthrough on their long effort to clone a wooly mammoth, resurrecting the Pleistocene beast from 10,000 years of extinction. The team had been having trouble finding a viable sample of mammoth DNA to use for the cloning process. But the researchers have devised a method to extract intact nuclei from preserved mammoth eggs, which they will then insert into modern elephant eggs, hopefully resulting in a viable embryo. The leader of the project says the potential mammoth's birthday is at least five or six years away, and that if the clone survives, it may provide clues to the animals' extinction.

Article continued on Alaska Dispatch

23andMe presents top 10 most interesting genetic findings of 2010

Taken from Eurekalert Published Jan 12, 2011

Leading personal genomics company reviews last year's genetic milestones on the journey to understanding the role of genetics in personal health, human development and ancestry

REFLECTING ON 2010:

1. Genetics influences whether your body shape is "apple" or "pear" — and which shape you are has implications for disease.
2. Genetic variations newly associated with risk for childhood asthma
3. New Variants Influence Risk for Rheumatoid Arthritis
4. Understanding Alzheimer's disease
5. One size doesn't fit all — personalizing treatment
6. No clue yet to how long Geri-Boomers can expect to live
7. Baby's First Tooth May Be A Health Predictor
8. Before you call that relative a "Neanderthal," some more of what we've learned about our distant past
9. A Fresh Look at Latino Genetic Ancestry
10. Web-based research works!

Article continued on Eurekalert

Sanofi's Bid Puts Pressure on Genzyme

Taken from New York Times, Published August 29, 2010 by Andrew Ross Sorkin and Duff Wilson

Sanofi-Aventis, the French drug maker, publicly disclosed its $18.5 billion bid for Genzyme on Sunday, intensifying pressure on the American biotechnology company to engage in discussions about a sale.

Sanofi approached Genzyme in June, and the two companies were engaged in friendly merger talks. But, according to Sanofi's chief executive, Christopher Viehbacher, the discussions were stifled by Genzyme's management.

"We are disappointed that you rejected our proposal on Aug. 11 without discussing its substance with us," he wrote in a letter to Genzyme's chief executive, Henri A. Termeer.

"Our financial advisers finally met briefly on Aug. 24, but the meeting simply served as further confirmation that as throughout you remain unwilling to have constructive discussions."

Article continued on New York Times

Mice Study Shows Breakthrough in Treating Fetal Defects

Taken from Yahoo News, Published Jan 18, 2011

WASHINGTON (AFP) – US researchers have discovered why fetal stem cell transplants, once considered a promising field for treating congenital defects before birth, were failing: it was all mother's fault.

But mom's cells could also be the solution, according to a study on mice released Tuesday in the Journal of Clinical Investigation. The mistake

BE in the World: News, Business, Policy Perspectives

may have been that doctors were trying to match transplantable bone marrow stem cells to the fetus. The mother's immune system would recognize the new cells as dangerous and reject them.
Article continued on Yahoo News!

Scientists Make Chicken That Don't Spread Bird Flu

Taken from Yahoo News, Published Jan 13, 2011

LONDON (Reuters) – British scientists have developed genetically modified (GM) chickens that cannot transmit bird flu infections -- a step that in future could reduce the risk of avian flu spreading and causing deadly epidemics in humans.

Scientists from Cambridge and Edinburgh universities said that while the transgenic chickens still got sick and died when they were exposed to H5N1 bird flu, they didn't transmit the virus to other chickens they came into contact with.
Article continued on Yahoo News!

FDA Approves Second Advanced Cell Stem Cell Trial

Taken from Yahoo News, Published Jan 3, 2011

WASHINGTON (Reuters) – Advanced Cell Technology said on Monday it had won U.S. Food and Drug Administration approval to try out human embryonic stem cells for treating macular degeneration, a common cause of vision loss.

It is the second FDA approved trial for ACT's stem cell product and the third for the controversial and powerful stem cells.

ACT said it would start recruiting patients with dry age-related macular degeneration using retinal pigment epithelial, or RPE cells, which ACT makes from human embryonic stem cells.
Article continued on Yahoo News!

A Life of Its Own: Where Will Synthetic Biology Lead Us?

Taken from The New Yorker, Published Sep 28, 2009 by Michael Specter

The first time Jay Keasling remembers hearing the word "artemisinin," about a decade ago, he had no idea what it meant. "Not a clue," Keasling, a professor of biochemical engineering at the University of California at Berkeley, recalled. Although artemisinin has become the world's most important malaria medicine, Keasling wasn't an expert on infectious diseases. But he happened to be in the process of creating a new discipline, synthetic biology, which—by combining elements of engineering, chemistry, computer science, and molecular biology—seeks to assemble the biological tools necessary to redesign the living world.
Article continued on The New Yorker

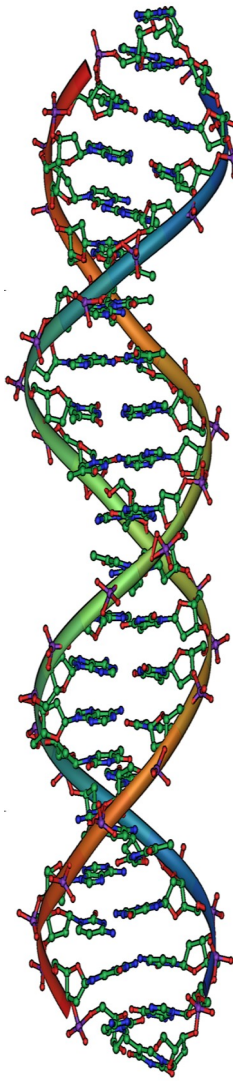
Neanderthal Relative Bred With Humans

Taken from Discovery News, Published Dec 22 2010 b

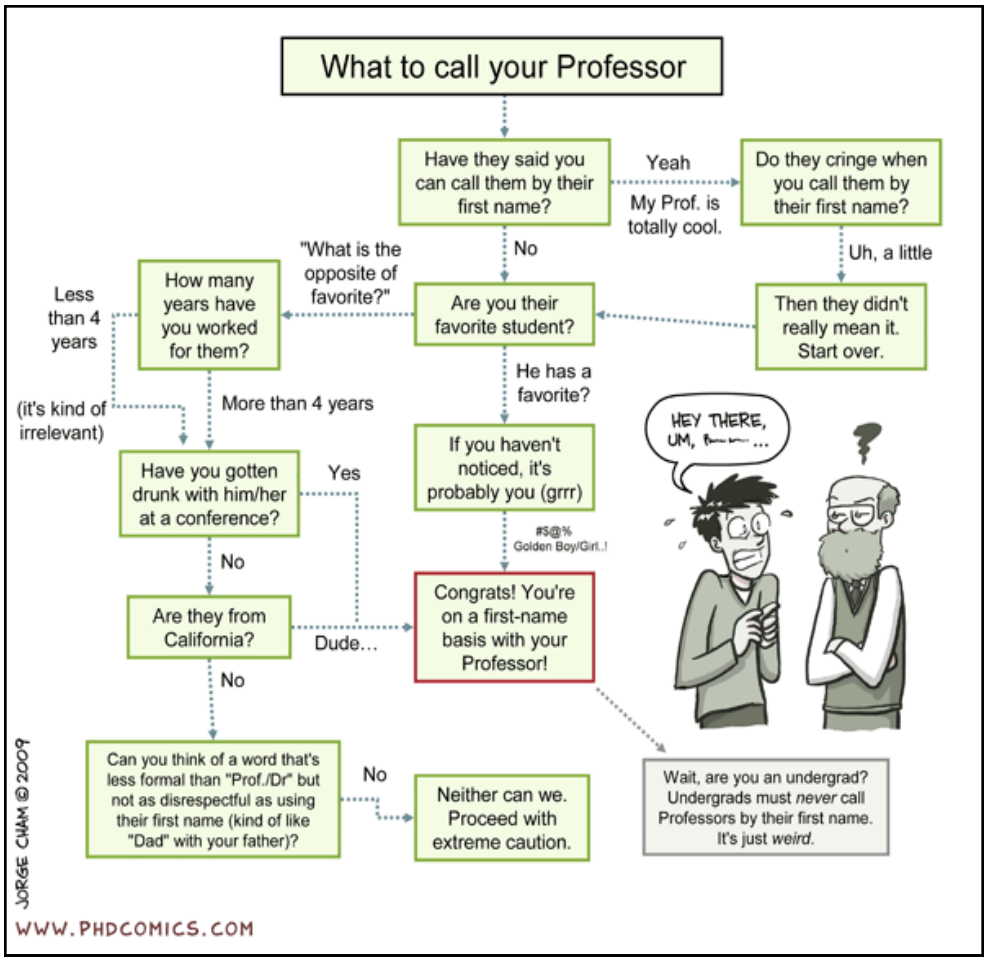
Neanderthals need to make room for a new kid sister in the early human family.

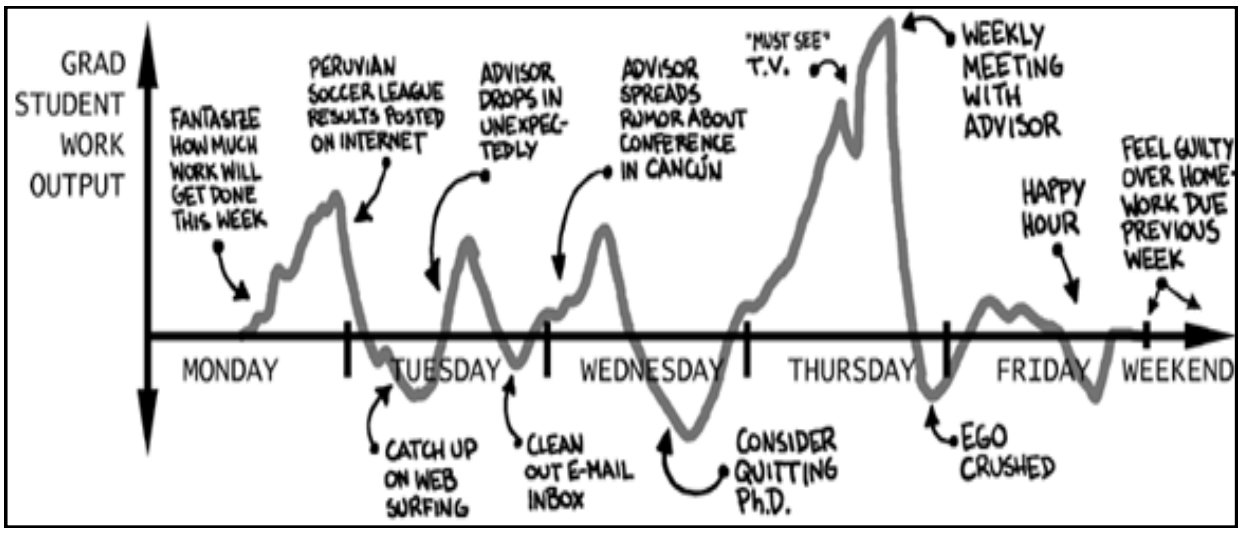
By sequencing the full genome of a girl's fossil finger bone found in a Siberian cave, researchers conclude that there must have been a closely related sister group of Neanderthals living in central Asia about 40,000 years ago. The data also show that, like Neanderthals, the mysterious group interbred with modern humans, in this case leaving behind a genetic fingerprint in modern-day Melanesians of Papua New Guinea and Bougainville Island, nearly 10,000 kilometers (6,213 miles) from where the fossil was found.

The new genetic information, reported Dec. 23 in *Nature*, underscores the fluidity of human evolution and hints that even more groups are waiting to be uncovered, says paleoanthropologist Milford Wolpoff of the University of Michigan in Ann Arbor. "We're just scraping the outside of what's probably a much more complex picture."
Article continued on Discovery News



Bench Humor





Graphics from PhD Comics

At the Intersection

(Continued from page 1)

other', who were more successful in publicizing their ideas.

The face of research is changing and the most cutting edge discoveries and inventions in science and engineering are becoming harder to categorize neatly into any particular field. Electrical engineers are building genetic circuits to engineer bacteria for industrial and medical purposes. Physicists and mathematicians are modeling biological networks and designing experiments and simulations to study evolutionary dynamics and decision-making patterns in cells and organisms. Material scientists and engineers are developing drug-delivery carriers and engineering immune cells to fight disease more effectively. Economists are working with ecologists to detect impending regime shifts in time to avert them. Computer scientists and anthropologists are using bioinformatics and comparative genomic approaches to study genetic variation patterns and to reconstruct historical demographic and population differentiation events.

Some powerful examples of this 'new way of doing science'[3] are Systems Biology at Harvard, Integrated Program in Quantitative Biology at UCSF, Biophysics at UC Berkeley, Computational & Systems Biology at MIT, and Quantitative & Computational Biology at Princeton. Moreover, new center buildings for inter-disciplinary research are continuing to proliferate with some key instances being the MIT Media Lab, Center for Genomics and Systems Biology at NYU, Craig Venter Institute in San Diego, The Broad Institute, and the upcoming EBICS (Emergent Behaviors of Integrated Cellular Systems) centers at MIT, Georgia Tech and University of Illinois at Urbana-Champaign.

This issue of the Biotech showcases some of the more recent developments in these multi-disciplinary pursuits, the ethical and political issues that ought to be considered and some of the younger pioneers advancing these new scientific fusions. According to Michael Specter of The New Yorker, 'the industrial age is drawing to a close, eventually to be replaced by an era of biological engineering.'[4] Before the science can effectively tackle the current medical and intellectual challenges on a massive scale however, much more progress is needed with regard to open sharing of scientific methods, tools and data sets and the development of stronger scientific partnerships globally. As one American-Canadian science fiction writer puts it, 'the future is here, it's just not widely distributed yet.'[5]

1. Johansson, Frans. "Intersections 07: Innovation at the intersection of disciplines and culture". Design Cou cil. Feb 12, 2011. <www.designcouncil.org.uk>
2. Gudrais, Elizabeth. "Innovation at the Intersection". Harvard Magazine. Feb 12, 2011. < http://harvardmagazine.com>
3. "Our Approach". Broad Institute. Feb 12, 2011. http://www.broadinstitute.org/
4. Specter, Michael. "A Life of its Own". The New Yorker. Feb 12, 2011. www.newyorker.com
5. Gibson, William. "The Science in Science Fiction". Talk of the Nation. NPR. 30 Nov 1999.

Faculty: Tim Lu

(Continued from page 3)

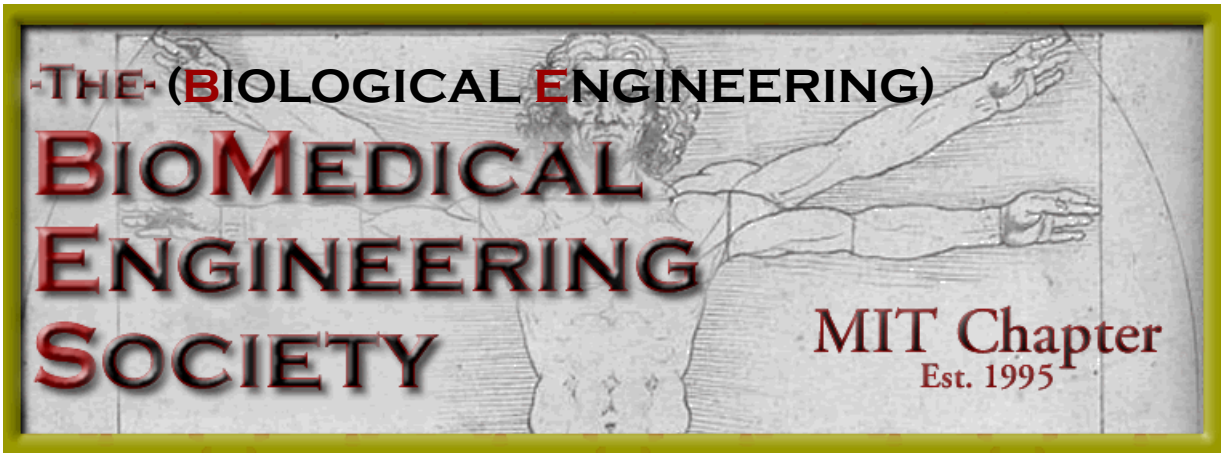
synthetic biology," Lu states.

"We have an amazing ability to write genetic circuits, but we don't know what to write." Yet in spite of the uncertainty, as one of synthetic biology's leading engineers, Lu's research stands to forge the future of the field.

Potential Harms of Synthetic biology

(Continued from page 9)

starting to build a policy framework to regulate self-regulating bioweapons will be ineffective. Building a new policy framework is no easy task, and it will be helpful to install safety mechanisms along the way as synthetic biology progresses.



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- ✓ Interact with fellow students with similar aspirations
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