Bioengineering: Branching Out

BioE Quarterly

A LETTER FROM THE DEPARTMENT CHAIR

Dear Fellow Bioengineers and Friends,

Welcome to the Year of 2018 and the end of second Academic Quarter! As the new department chair starting this January, I would like to congratulate Professor Geert W. Schmid-Schoenbein on his tremendous achievements in our department during the past few years. Under his leadership, we built a very strong momentum going forward as one of the top bioengineering departments in the country, tied at #3 by US News and Reports.

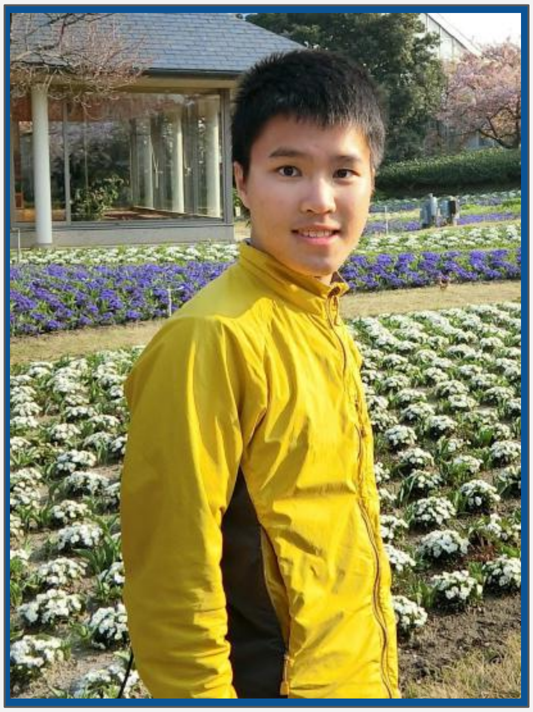
Bioengineering is at the interface of multiple more traditional disciplines. This newsletter captures a few highlights of the exciting activities and achievements unique to bioengineers. We showcase a very young bioengineer, a senior undergraduate student in this case, on her passion, learning experience and career dream. The Department is exceptionally strong in research, and here we cover a spectrum of research activities: a new BE professor studying tissue injury and repair taking advantage of his dual trainings on electrical engineering and medicine; a new BE affiliate faculty who has made significant achievements on tracking biomolecules within live cells in real time at a resolution beyond the standard light microscopy; and a partnership between a bioengineering professor and a cancer biologist investigating how tissue stiffness affect the metastasis of cancer cells. We also provide an example of how bioengineering is making an impact in a medical device company.

These stories only capture a miniscule fraction of all the great achievements by our students, staffs, scientist and professors in this department. The Spring is coming and we are looking forward to seeing these exciting activities going into full blossom in the coming months!

Cheers,

Kun Zhang
Professor and Chair

An Introduction



Dear Readers,

Every now and then, people are mesmerized by stories of novel drugs being synthesized, groundbreaking medical devices being invented, and pioneering research being published. Yet, the avant-gardes—bioengineers, scientists, students—behind the continuous revolution in medical technology are often overlooked. To most, bioengineering is a ray of white light. It certainly illuminates human society, but its very components—the assiduous engineers and the interactions across multiple academic disciplines that make innovations possible—are largely concealed from viewers. We at Bioengineering Quarterly strive to be a prism that refracts this singular white light into multiple colors, displaying not only the fruit of a research or the launch of a life-saving product, but also the motivations, aspirations, inspirations, hardships, and triumphs of current and future bioengineers.

This winter quarter issue *Bioengineering: Branching Out* celebrates the multidisciplinary and multifaceted nature of bioengineering. Though professors featured in this issue may not be biomedical engineers by training, their desire to save human lives eventually propels their research to converge in bioengineering. Utilizing their knowledge on electrical engineering (Dr. Kevin King), chemistry (Professor Jin Zhang), molecular biology (Dr. Jing Yang), and biophysical engineering (Dr. Adam Engler), these vanguards have published influential and astounding biomedical research. Meanwhile, the student body has also made incredible contributions to the bioengineering community. For instance, Lab Expo—a student-run event—featured a panel of economists, science policy specialists, and journalists who discussed the social and economic impacts of biomedical technology. That professionals from non-engineering backgrounds participate in this discourse suggests that bioengineering seldom happens in a vacuum; the interaction among various academic disciplines is essential for patients to benefit from biomedical breakthroughs. Our theme *Branching Out* thus have two important implications. First, it depicts the mode in which various fields of engineering and science unite to partake in the exhilarating field of bioengineering; second, it displays the intricate relationship between bioengineering and other academic disciplines in shaping public policy.

Each interviewee in this article has a unique and riveting story to tell. In essence, there is something fundamental and human about their stories. It is about passion, perseverance, and, above all else, the altruism that empowers them to indefatigably innovate in patients' healthcare. We at BioEQ invite you to listen to their stories and be inspired to create yours.

Sincerely yours,
Chak (Julian) Ho | Deputy Editor-in-Chief

The BioEQ Team

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The Bioengineering Quarterly (BioEQ) is a student run publication that covers the people, the research and the events that occur within the UC San Diego Bioengineering Department. For Spring 2018, we decided to examine how the Bioengineering field has grown, evolved, and branched out to become what it is today.

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STUDENT ORGANIZATIONS

Showcasing UCSD's Student Bioengineering Communities

Biomedical Engineering Society

The Biomedical Engineering Society's winter quarter was a busy one! We started off the quarter by hosting our first ever winter retreat in Temecula, a three day bonding experience for our members. Soon after, we held our first big event of the year, Lab Expo, which featured research ranging from the sciences to humanities as well as industry demos. Translational Medicine Day also took place, featuring some amazing speaker seminars, graduate school admissions panel, translational researchers panel, and industry demos. We have many more events planned for next quarter, including industry tours and Bioengineering Day, so stay tuned!

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Bioengineering Graduate Society

This was a busy quarter for us, and included our PhD recruitment weekends, as well as our Winter Town Hall with the department heads. Dr. Jeff Lievense and Dr. Julio Baez, both leaders in biotechnology, provided seminars regarding careers and the state of the field, and in March, we headed to PetCo Park for the San Diego Festival of Science and Engineering. In addition we held an assortment of social events including movie viewings, a paint night, afternoon tea, a hike up the Cowles Mountain Trail, and a night of dumpling making for Chinese New Year.

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Undergraduate Bioinformatics Club

In the past quarter, the Undergraduate Bioinformatics Club focused on developing projects and expanding their membership skillset. Highlights include technical workshops that taught members advanced Python techniques widely employed in bioinformatics research, completion of the Lego Sequencer Project and UBIC on Ice!

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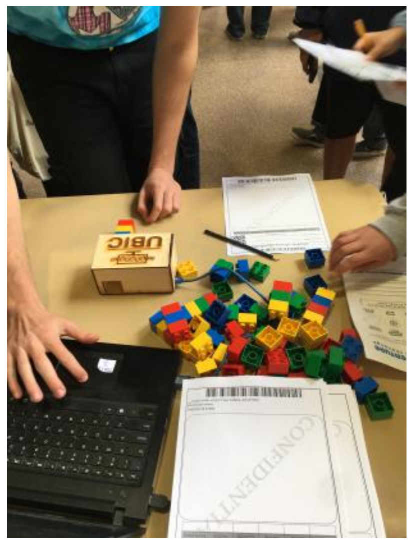

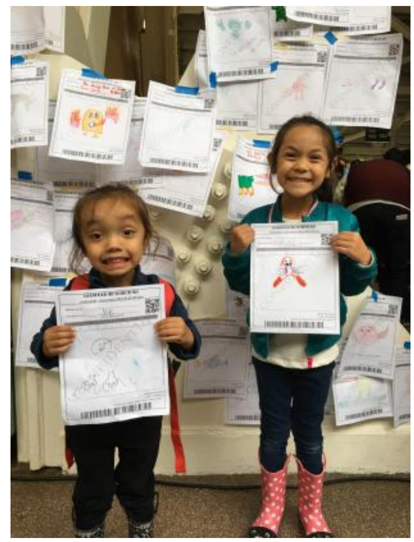

Tau Beta Pi

This winter quarter Tau Beta Pi put on a lot of fun events for our members and initiates. The quarter started off with a Decaf Resume Workshop with Triangle Fraternity where we invited engineers from industry to give their advice. We also put on a Honors career fair after Decaf for students to find internships and jobs. The following week we focused on community service by cleaning up the San Diego River Estuary. Every week we also host a volunteering event at Florence Elementary where we teach kids about STEM subjects. This quarter we went on a lot of social outing such as going ice skating, bowling, and hosting a retreat at Joshua Tree. Halfway through the quarter we had a ceremony to initiate the TBP candidates into members. For the latter half the quarter, we focused on new initiatives such as committees to increase our member participation. We also put on Pi Day which was a huge success with over 300 people attending! Pies were dropped and people's faces creamed.

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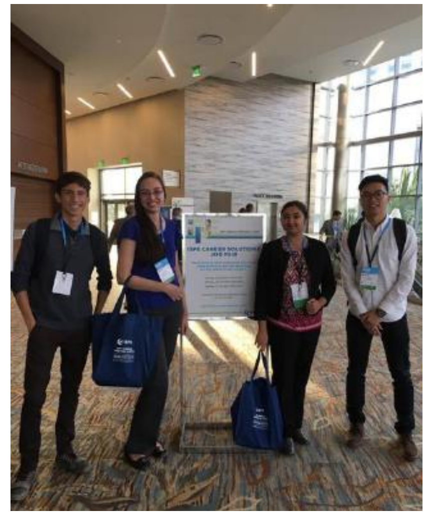
International Society for Pharmaceutical Engineering



ISPE kickstarted this quarter with Genentech Info. Session, one of our major annual events that provided each student an opportunity to have a one-on-one conversation with engineers in the company; furthermore, students gained valuable insights into the vibrant working culture and the patient-oriented maxim of Genentech. Our endeavor to connect students to biomedical industries continued with KGI Info. Session, during which representatives from the Kech Graduate Institute exposed students to summer internship and graduate programs. We concluded this quarter with ISPE mixer, an event that brought together students from multiple disciplines of engineering (i.e. bioengineering, chemical engineering) and offered them an occasion to discuss their academic and career paths, to share their experiences with internships, and to expand their interdisciplinary network.

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SynBio

SynBio has solidified the 2018 team for the international iGEM synthetic biology competition. The interdisciplinary team is comprised of undergraduates tasked with wet lab, dry lab, design, and logistics - congratulations to: Michael Herron, Zhijian Li, Claire Luo, Anser Abbas, Yiqun Jiang, Ishan Goyal, Tran Tram, and Varun Govil!

Former and current iGEM participants have been working to advise and mentor two prospective high school iGEM teams from Torrey Pines High School and Del Norte High School through conference calls.

Occasional socials and weekly journal club meetings were held to explore synthetic biology topics. One discussion was on a recently published paper authored by UCSD iGEM 2015 participant Walter Thavarajah and iGEM 2015 mentor Phillip Kyriakakis - "Biosynthesis of Orthogonal Molecules Using Ferredoxin and Ferredoxin-NADP+ Reductase Systems Enables Genetically Encoded PhyB Optogenetics".

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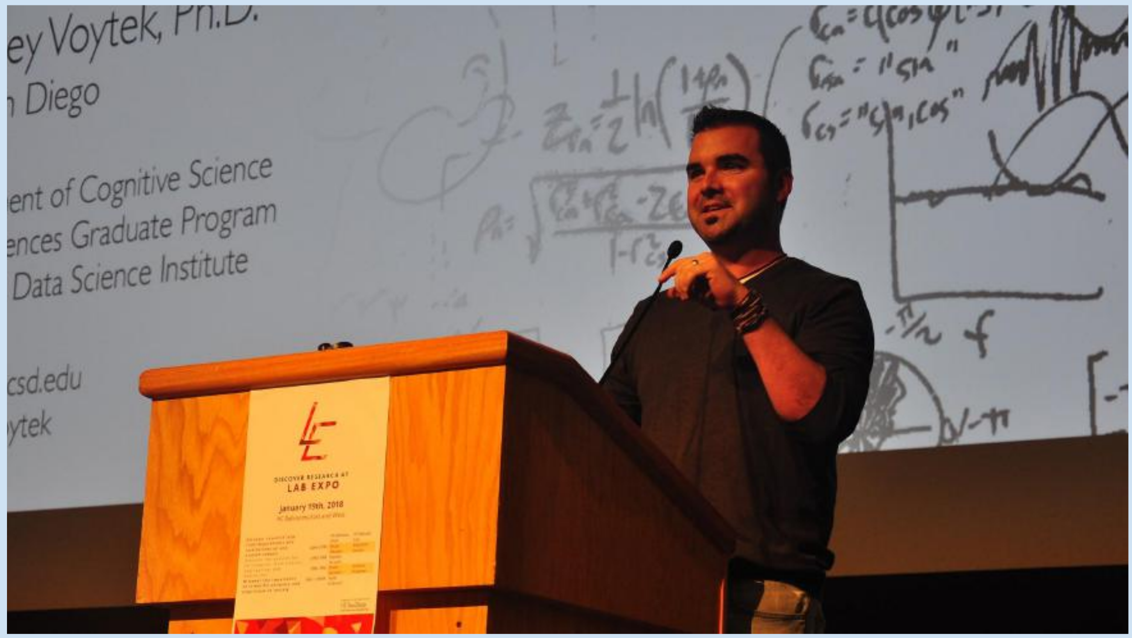
Lab Expo 2018

By Aditi Vaidya

If a passerby were to wander into UCSD's cavernous PC Grand Ballroom West on January 19, they would have found it peppered with both presenters and students, gathered around large, descriptive posters as dynamic conversation ensued. One such presenter, second year Aishee Das of the Cognitive Development Lab, expressed the positive atmosphere she experienced, stating that her initial nervousness was quelled by the attendees, who were "curious and forgiving if [she] ever stumbled."

The event was the annual Lab Expo, and by the end of the day, over 750 undergraduates and 50 researchers had converged in the PC Ballrooms. With the grand aim of galvanizing a passion for scientific literacy and discovery in the vast undergraduate population of UC San Diego, Lab Expo is a yearly event that takes place through the course of a day, complete with research poster presentations, speakers, and a panel of professionals. A dedicated committee—led by Troy Hussain and Arya Kaul of the Biomedical Engineering Society—helped bring this event to fruition.



Keynote speaker Professor Bradley Voytek spoke about, among other things, how he co-wrote a textbook about the zombie brain.

It is apt that this event takes place at a large university like UC San Diego, which allocates over $1 billion a year into funding for research. Because the university is so large however, research opportunities may get lost amidst the wave of information the average undergraduate is exposed to in a day. Lab Expo works to combat this issue and highlight the importance of the scientific process. As a testament to the many benefits of conducting research as an undergraduate, Aishee affirms, "When I became involved in my lab last quarter, I was not sure if I wanted to pursue research in the future or if I even enjoyed my field of study. However, with a quarter under my belt, I know that it is definitely something I am interested in and want to continue exploring."

A common thread that wove the event together was that of diversity in research. Troy states,

"To Lab Expo, ***diversity*** is a wide set of ***experiences*** ***&*** ***perspectives,***"

and this theme was evident throughout: the poster session featured research that ranged from the investigation of stress in Asian-Americans populations to the exhaustion of T-cells in the immune system. The panel brought together an economics professor, a journalist for the San Diego Tribune, and a science policy specialist to share their thoughts on scientific advocacy: a topic that brought out the multifaceted perspectives of each professional. Throughout the event, it became apparent that diversity in background as well as in experiences is essential for the cultivation of truly groundbreaking research. Due to an amalgamation of all of these factors, Lab Expo was a success. As Troy puts it, "A genuine sense of passion for discovery and researched [was] fostered."

Troy Hussain and Arya Kaul

Insight in the Industry: NuVasive, Inc.

By Vania Pena

NuVasive, the third largest medical device company in the spinal industry, develops minimally invasive surgical products and innovative procedures for spinal surgery. Operating under the philosophy of reproducibility and speed, NuVasive has been bringing innovation to the spinal industry for more than a decade. Solidifying their standing, the company boasts the creation of over 14 technologically facilitated procedures, 90+ specially designed products and implants, and over 2400 employees dedicated to providing life-changing solutions for those suffering from spinal afflictions.

NUVASIVE

Ryan Donahoe is the Vice President of the Global Implant Development sector at NuVasive. Working with a team of mechanical engineers, bioengineers, and biomedical engineers, he oversees the development of procedural implant and instrument systems for spinal surgery. Donahoe has agreed to be interviewed and provide insight on NuVasive and what they look for in their employees and interns.

NVM5®
NuVasive's Nerve Monitoring Machine, adding precision to each procedure

Lumbar Arthrodesis Plate Used in NuVasive's Anterior Lumbar Interbody Fusion (ALIF) procedure

"Nuvasive is focused on developing surgical technologies and platforms to help bring patients from a state of pain and disability back to doing what they love as fast as humanly possible," Donahoe explains. To make that possible, NuVasive strives to accompany their revolutionary products with minimally invasive surgical techniques. For example, their NVM5® system (formerly Neurovision) powerhouses the technology of computer-assisted surgery and helps to monitor and navigate the patient's neural anatomy, increasing the safety and reproducibility of the procedure. Another testament to this ideology is their industry changing XLIF (eXtreme Lateral Interbody Fusion) procedure. Using this method, surgeons access the spine through a small incision on the patient's side to preserve many of the existing spinal ligaments and musculature while also minimizing disruption to other anatomy. Over the last 15 years, the XLIF procedure has resulted in less time in the Operating Room, reduced blood loss, reduced risk of infection and other postoperative complications, and overall shorter hospital stays compared to traditional spinal surgery procedures, demonstrating significant value to patients and hospitals.

In order to achieve widespread influence and change, NuVasive requires the minds and skills of a wide range of individuals from different fields. Careers at NuVasive encompass a variety of areas, including CAD design, clinical research, testing and analysis, computer science, material science, and the fields of engineering: including mechanical engineering, electrical engineering, tissue engineering, and, of course, bioengineering.

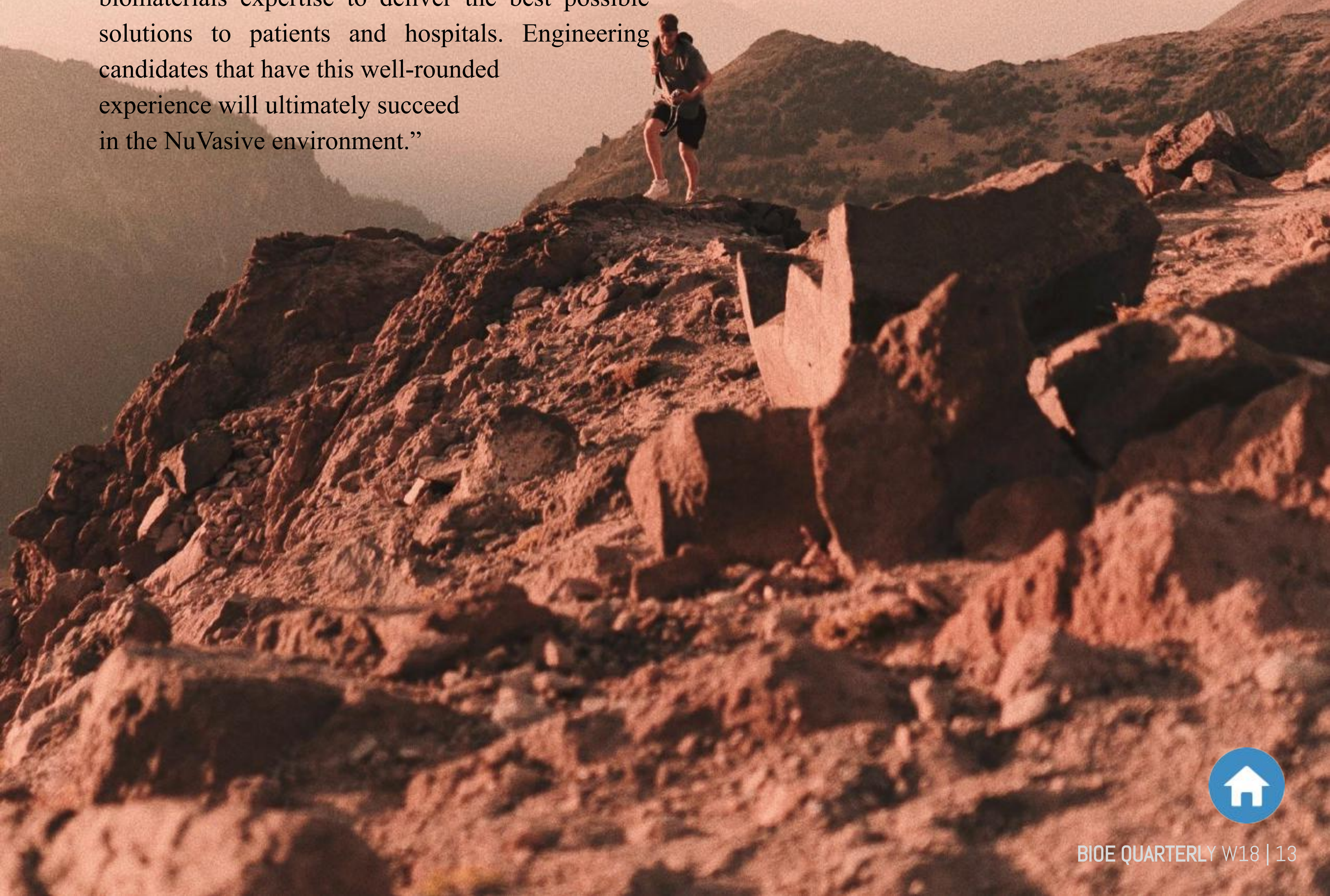
Ryan Donahoe: VP of the Global Implant Development Sector

Modulus XLIF, NuVasive's 3D Printed Titanium Spinal Implant

Reflecting on his own experiences with NuVasive engineers every day, Donahoe comments on the importance of practical skills when selecting applicants for internship or job positions.

“Within our global implant systems team, we employ heavy mechanical design work based on mechanical engineering principles and couple that with clinical knowledge of spinal pathologies, anatomy, and treatment methods in addition to biomaterials expertise to deliver the best possible solutions to patients and hospitals. Engineering candidates that have this well-rounded experience will ultimately succeed in the NuVasive environment.”

Donahoe recalls an encounter with a student he met at a career fair, commenting on the potential employee’s unique way of displaying what he knew: “This particular student knew how important CAD experience was to NuVasive, and instead of just having the standard CAD class on his resume he went home and took his HP printer apart, component by component, and 3D modeled all of them over a period of a month or two and reassembled it” This kind of work is a phenomenal display of application and it really raised the brows of the NuVasive employers because it spoke volumes about that individual’s design abilities, more-so than even his grades or coursework did. “It was impressive,” Donahoe says, “the fact that he took the time to do that indicated very strong initiative, drive, and passion for the opportunity”



There are a lot of candidates that seem to have the same qualifications going for them: taking similar or even the same classes in their respective universities, getting good grades and a high GPA, demonstrating good interpersonal skills, but often times the most valuable component to one's application can be to have (and to show) practical ability in the subjects taught at school. Having the valuable skills of a learned bioengineer, or mechanical engineer, or biologist, and more importantly, being able to demonstrate those abilities for employers to see, is what truly makes a strong candidate "Yeah, he got the job," Donahoe says referring to the student at the career fair, "he's still here [at NuVasive] and he's one of our top performers."

Ultimately, Donahoe's advice to any potential applicant would be an early start on gaining experience. "My encouragement to any of the students would be start your freshman year. If you really want to get into the industry, start as early as you can getting into internships, and gaining experience in organizations." He continues, "You need to understand how organizations work and how to drive results in heavily cross-functional projects." He explains how the team dynamics and responsibilities vary considerably between industry and academia. In the former, there is an emphasis on understanding your function in the group, understanding who does what, and the importance of your job to others' success and how to collaborate most effectively. "You don't really learn those things in a textbook so the real world experience is so important" Donahoe adds. Essentially one can expect their necessary experience to be part education and part real world experience, but not one alone. "The schooling and the education is so critically important but it has to be paired with hands-on, real world experience, there's just no replacement for it," Donahoe emphasizes, "if you come in with only the education you're missing half of it."

INTERVIEWS

Dr. Kevin King

Summer Joyce Batasin & Kevin Yu | Interview Writer

Bio: Dr. Kevin King is a new professor in the UCSD Departments of Medicine and Bioengineering. He completed his B.S. in electrical engineering from the University of Illinois where he focused on solid state physics, microelectronics, and microfabrication. He earned an S.M. and Ph.D. degrees in electrical and bioengineering at MIT where he discovered a pathway that spreads immune responses through solid organs such as the liver. His graduate program offered a unique opportunity to take medical school courses and learn to interview and examine patients. This inspired him to complete his MD at Harvard Medical School, internal medicine residency at Stanford, and cardiology fellowship at Brigham and Women's Hospital and Massachusetts General Hospital. Now, having joined UCSD, his time is spent caring for cardiology patients in the hospital; directing a interdisciplinary research lab studying tissue injury, repair, and regeneration in the heart and beyond; and promoting the education of future physicians, scientists, and engineers.

Q: *What made you interested in studying EE at first?*
A: I really enjoyed physics and math in high school and college. I was impressed by how seemingly-simple principles explained such a wide range of phenomena in the world. As an undergrad, electrical engineering classes were captivating - circuits classes were fun puzzles to solve, signals and systems opened my eyes to the amazing duality of frequency and time, and microelectronics introduced me to the scale, precision, and performance enabled by solid state devices and integrated circuits. Today, at UCSD, my lab asks biological and clinical questions, but we do this using engineering principles and technologies.

Q: *What attracted you to work in bioengineering later on? What kind of connections did you make between the two fields?*
A: My pivot from electrical to bioengineering occurred during an undergraduate "co-op" at Advanced Micro Devices in Austin Texas. I was there gaining real world industry experience and had free time after work, so I decided to volunteer at a local hospital ER one evening each week. This was really exciting for me because I had no family members in medicine, so everything about the hospital was new and exciting to me. I was impressed by the kindness and respect that the medical staff showed patients; if you were sick or vulnerable, the medical staff took care of you, no questions asked. This was very compelling to me and really changed my focus when I returned to University of Illinois. I started taking biology courses as electives and joined a research lab to apply engineering of microfluidic devices to study cells for medical applications. I spent the remainder of my undergraduate years dividing my coursework between advanced electrical engineering courses and life science courses such as molecular and cell biology, physiology, immunology, organic chemistry, and biochemistry. Looking back, my undergraduate education armed me with an outstanding toolkit to work at the interface of engineering and biology.

Q: *Can you go into more detail on what attracted you to medicine and cardiology?*
A: As mentioned previously, I was attracted to medicine because it is so fundamentally human. The interaction between a patient and physician is unlike other interactions in life. When a person presents to the hospital and is struggling with an illness or a disease, the person is usually very vulnerable, and every patient handles that differently. It's humbling to be able to help people think through what’s happening to them and what can be done about it. For example, when a patient presents with a heart attack, we talk about why it happens; we go through the pros and cons of different options for restoring blood flow to the heart (e.g. medicines, stents, or surgery); we talk about how to manage complications that can arise after the heart attack (e.g. congestive heart failure, arrhythmias); and we talk about what can be done to avoid having another heart attack in the future (quitting smoking, treating diabetes, and lowering cholesterol and blood pressure). While at first glance this may seem like a one-size-fits-all conversation, it turns out that treatment decisions are highly individualized and made in close collaboration with patients and their families.

Of all the specialties in medicine, cardiology appealed to me in particular because it is deeply rooted in physiology. In cardiology, we're fortunate to have highly quantitative diagnostics like multi-modality imaging, and sensors for measuring pressures, flows, forces, and electrical signals.

This allows us to continually improve our understanding and intuition for the cardiovascular system as we see more patients. Cardiology also has great therapeutics, such as statins, stents, valves, pacemakers, and pumps, so there is a lot we can do to make patients feel better and live longer.

Q: *What attracted you to return to bioengineering after medical training?*
A: Having trained in electrical engineering through PhD, I don't think I ever stopped being an engineer. Engineering strongly influences how I understand and think about cardiovascular physiology and disease. It also impacts how I approach the study of basic biological disease mechanisms in the lab. I was attracted to accept a joint position between UCSD bioengineering and medicine after clinical training because it will allow me to work closely with a wide range of students and colleagues. I think bioengineering students have a great toolkit for discovering how disease works and inventing creative ways to diagnose and treat disease earlier, at less expense, and with greater efficacy.

Q: *What is your lab currently working on at UCSD? How is bioengineering playing a role in this research?*
A: In the lab, we study "tissue biology." We study how solid tissues are organized; how they respond to stress and injury; and how they heal, repair, and regenerate. This involves drawing on knowledge from small length scales such as molecular and cellular biology but also thinking about how cells physically, electrically, and biochemically interact within large tissues. The toolkit for the tissue biologist is only just emerging. Single cell multi-omic technologies, intravital microscopy, and optogenetics are allowing us to measure and control molecular and cellular function inside complex solid organs, and I predict this field will make surprising and important contributions to our understanding of a wide range of tissues (e.g. heart, brain, liver, kidney) and diseases (e.g. ischemia, immune-mediated disease, metabolic disease, and cancer).

Bioengineering plays an important role in many of our projects. For example, we are building sensors and circuits that perform adherence-independent monitoring of heart failure patients without requiring them to remember to wear a device or perform a measurement themselves. Then we perform analysis of this sensor data to predict hospitalizations. We are using bioinformatics to analyze next generation sequencing data from large numbers of single cells. We are also using quantitative intravital imaging and time series analysis to study how cells communicate in solid organs. Finally, we are building microfabricated devices to mimic the mechanical, electrical, and chemical microenvironments inside solid organs during health and disease. These projects all rely on engineering, so bioengineering training has definitely served me well.

Q: *What advice do you have for students wishing to get involved in the field of biomedical engineering*?
A: As for advice to prospective bioengineering students, I would say do it! Biomedical engineering is a spectacular field. Important questions range from the fundamental to the applied and span everything in between. As a bioengineer, you have license to disregard the invisible lines that separate classical engineering disciplines. Bioengineers, perhaps more than other area of engineering, have to be very ambitious because they need to be truly excellent in many technical areas of engineering while also developing deep domain expertise in biology and medicine. This is a powerful combination, but it requires being an aggressive life-long learner, and not being afraid to explore outside of your comfort zone.

Dr. Adam Engler and Dr. Jing Yang

Matthew Chen | Interview Writers

The Study of Oncogenesis: A Multidisciplinary Endeavor

Throughout our academic careers, the specificity of our studies increases. Before college, the curriculum is broad and its exploration of subjects is superficial. It is not until university that students begin to specialize, branching out into distinct fields of study. Specialization is highly advantageous, but collaboration is essential for answering a broader question that requires a multifaceted understanding.

To study matrix stiffness and its impact on tumor metastasis, Dr. Adam Engler and Dr. Jing Yang designed a system that fused their training from different academic backgrounds. In order to investigate this subject, it was important to produce a material capable of simulating tissue's differing stiffness and elasticity. Dr. Engler's background in biophysical engineering allowed him to "bring the engineering technologies to the extracellular matrix so that he could change its mechanical properties." However, without a thorough understanding of molecular biology, the matrix itself is not a holistic approach.

This is where Dr. Yang's background in molecular biology makes this matrix system an effective simulation of tumor environments. As Dr. Engler explains, "Dr. Yang can bring in her expertise on the signaling side of tumor biology and say this is really what the tumor looks like so let's change the environment to look this way instead."

As they explain in their Nature Cell Biology paper *Matrix stiffness drives epithelial-mesenchymal transition and tumor metastasis through a TWIST1-G3BP2 mechanotransduction pathway,* TWIST1, the basic helix-loop-helix (bHLH) transcription factor, is essential for the activation of EMT(epithelial mesenchymal transition), a process critical for tumor metastasis. At lower matrix stiffness, cells develop an intact basement membrane. However, under higher pressures, this membrane destabilizes, and the cell begins to show a partial EMT phenotype.

In their project, Dr. Engler and Dr. Yang explored the role of G3BP2 (a cytoplasmic anchoring protein for TWIST1) in metastasis. They found that high matrix rigidity caused the release of TWIST1 from G3BP2 and the resulting EMT phenotype. Understanding the mechanics of TWIST1 release from G3BP2 and consequent induction of EMT came from Dr. Yang's expertise, and alongside Dr. Engler's understanding of generating matrix rigidity, isolation of stiffness' impact on induction of EMT was finally possible.

Looking towards the future, Dr. Engler and Dr. Yang hope to improve on the matrix model. In human tissues, stiffness is not static. As Dr. Engler emphasizes, "the tumor environment changes over time" and to introduce a new dynamic to their current model would help them to better "mimic the biology that occurs in-vivo but do that in a dish". Like before, such a complicated system would require the expertise of various backgrounds. Even Dr. Engler, with expertise in various disciplines, advises

"*there is very little training that will allow you to conduct research totally by yourself. Figure out what you are good at and what you are not good at. You just need to surround yourself with people that understand the areas you are weak at. That is what collaboration is."*

Featuring the Bioengineering Department's Undergraduate Student of the Quarter

STUDENT SPOTLIGHT

Julie Yip :

Bioengineering for Global Health

By Neve Foresti

Fourth Year Bioengineering student Julie Yip is well-known for her dedication to several organizations (EWH and BMES), mentorship, and supportive smile. Her varied curiosities from science writing to food business have led her to write for the UCSD Guardian and sell jam at local farmers markets. She's an excellent example of all that a bioengineer should be because she draws from her diverse interests and unique background to improve the health of the community.

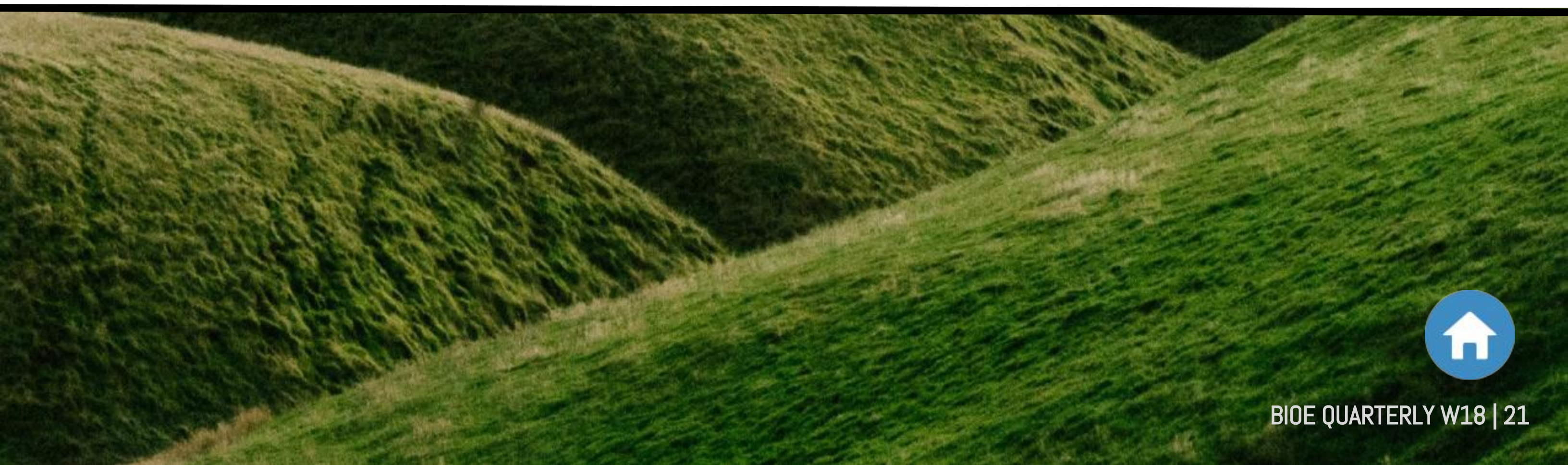
Julie's reasons for becoming an engineer are authentic as they can be, influenced by her childhood, personality, and upbringing. "I grew up in the kitchen with my mom, always helping her with chopping and baking. I've always really liked working with my hands and seeing things come together. It sounds really simple, but it's not something I realized until I got into engineering. I love the process of going from that idea to the final tangible thing and getting to enjoy it."

She uses “excitable” to describe herself when it comes to learning, but this can often make choosing a career difficult. While she does not know exactly what she wants to do immediately after graduation, she is interested in being a design engineer for devices that will aid and support women (maternal, reproductive, neonatal health), especially those with less resources. She says, “In the end, if I can help women and babies, it doesn’t really matter what I do.” Her volunteering with the annual “Vagina Monologues and Their Stories at UCSD” and biomedical device startup Hapty Hearts (previously called Amniotic Wrap) demonstrate her passion for women’s health.

Julie, as well as two other Bioengineering students Niranjanaa Jeeva and Ella Stimson, founded Hapty Hearts after the UCSD Engineering World Health’s “Health Hack” competition. For students interested in creating an engineering startup, she advises to start with competitions, such as the USD Social Innovation Challenge. “It was scary at first, but they connected us afterwards with other programs. It gets easier once you start, but you have to take the opportunities. We approach it as ‘We will learn something from this.’” In fact, Julie mentions that she thinks the most important lesson she has learned from this experience is the importance of understanding the market and its users. If you want to make a product for a specific population, you need to talk to people who will actually use it. *Will they even want to use the product? What priorities do they have in what they are looking for?* For this very reason, Julie is considering joining a women’s health Non-governmental Organization after graduation. While her initial position may not be an engineering position, she recognizes that this may be a necessary step for her goals of using bioengineering to aid women. “My goal right now is to understand the market and its specific users, which I can’t do just by taking a class. Because my future goals employ many different facets, I need to be more specialized, which is why I’m also considering grad school.”

Julie describes her current team for Hapty Hearts as one of the best teams she has ever been involved with because each of the three founders has something unique to offer. Although business has always been their weakest pillar, the skill that has most contributed to their success is the ability to communicate their passion for women’s health. If you can inspire someone else to care about an issue as much as you do, they might be willing to invest in you.

In the end, “everyone has something to offer, even outside of STEAM. Sometimes, people feel like they need to fit this cookie-cutter expectation,” but by striving to be free from those cookie-cutter expectations, Julie is forming her own path. Her unbounded dedication to health and STEAM demonstrate the untapped potential of bioengineering and its students.



Professor Jin Zhang

By Michael Hu

Professor Jin Zhang attended Tsinghua University in Beijing for her bachelor's degree, before moving to the US to earn her PhD in Chemistry from the University of Chicago. She then moved to UC San Diego for the first time to complete her post-doctoral research, before joining the faculty of Pharmacology & Molecular Sciences, Neuroscience and Chemical & Biomolecular Engineering at Johns Hopkins University, where she became a Professor in 2013. In 2015, Professor Zhang returned to UC San Diego to join the Department of Pharmacology, with affiliations in Departments of Bioengineering and Chemistry & Biochemistry.

Despite not formally being a bioengineer by training, Professor Jin Zhang exemplifies in her research many of the fundamental principles of engineering applied to living systems. Here, we examine more closely her work in the development of super-resolution imaging to visualize nanometer-scale interactions within individual cells, which draws from principles of chemistry and molecular biology, and applies them alongside principles of user-centered design to develop novel imaging technologies.

It is now well accepted that at the cellular level, nearly all processes are governed by molecular interactions, the totality of which is called the "interactome". In particular, the majority of cell functions comes specifically from protein-protein interactions[3], so understanding such interactions has now become essential in revealing the nature of the cell. Historically, a massive amount of work has gone into proteomics, particularly in elucidating the relationship between proteins and the genome via the translational process . However, spatiotemporal information, which is the key to the understanding of how cellular information is encoded, is often lacking in these studies. Thus microscopy methods are required for visualizing protein-protein interactions within living cells.

Presently, standard light and fluorescent microscopy is limited to 200 - 250 nm resolutions due to diffraction of light, making visualization of individual proteins nearly impossible[5]. Techniques that can offer higher special resolution are available, such as electron microscopy and x-ray crystallography[3]. While these methods allow for sub-nanometer resolutions, the necessary sample preparation requires killing the cell in question. As such, they can be used to see snapshots of interactions, but do not allow for live visualization.

Hoping to resolve this issue, in 2016, Professor Zhang developed a methodology called reconstituted fluorescent-based stochastic optical fluctuation imaging (refSOFI). Fundamentally, SOFI is accomplished through the use of blinking fluorescent emitters. Unlike standard fluorescent microscopy, which records the raw intensity of the emission from a fluorescing target to generate an image, SOFI records multiple images over a specific timespan. Subsequently, a super-resolution image can be computed by examining the stochastic fluctuations in fluorescence over time[1]. Professor Zhang made use of this methodology and combined it with a set of engineered proteins that only emit fluctuating fluorescent signals when engaging in specific protein-protein interactions (Fig. 1). In doing so, it became possible to visualize protein-protein interactions and obtain high resolution images in real-time[2].

In spite of this success, Professor Zhang acknowledged that an issue with the system was that the reactions involved were irreversible, meaning that it was impossible to apply this to monitor the dissociation of protein complexes [2]. Seeking to resolve this, she made use of a novel fluorescence phenomenon to generate a system of engineered proteins that could induce fluorescence fluctuation in response to proximity. This technique was dubbed fluorescence fluctuation increase by contact (FLINC)[4].

FLINC operates using two proteins, TagRFP-T and Dronpa. Simply put, TagRFP-T exhibits increased fluorescence fluctuations when in closer proximity to Dronpa. By separately fusing TagRFP-T and Dronpa to individual proteins of a pair involved in a protein-protein interaction, fluorescence fluctuations are produced whenever the pair interacts[4]. Thus, it becomes possible to selectively generate SOFI-compatible fluorescence signals during a protein-protein interaction of interest (Fig. 2a). For instance, by binding TagRFP-T and Dronpa respectively to the proteins FRB and FKBP, which bind in response to the addition of the immunosuppressing drug rapamycin, it becomes possible to visualize FRB and FKBP interactions at extremely high resolutions (Figs. 2b and 2c)[4]. Furthermore, this technique can be used to monitor dynamic biochemical reactions, e.g. protein phosphorylation and dephosphorylation, at superresolution.

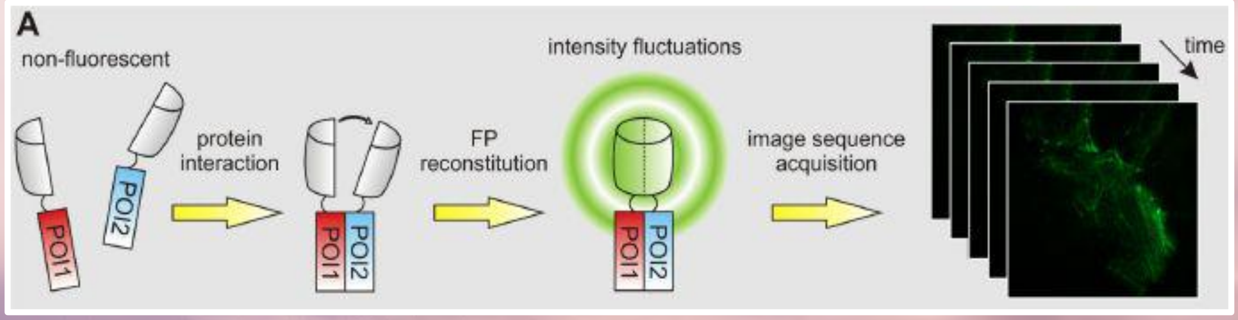


Figure 1: An example of refSOFI interactions facilitated by inducible fluorescent signals on engineered proteins.

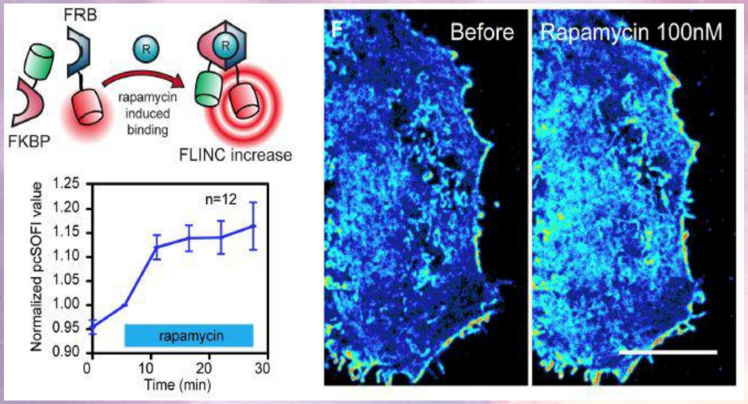


Figure 2: a) Design of the FKBP and FRB FLINC system, induced in response to rapamycin, b) fluorescence intensity in response to rapamycin exposure and protein-protein interactions, and c) cell surface visualization before and during induced protein-protein interactions.

In achieving this result, Professor Zhang was able to effectively combine her chemistry and life sciences background with computational signal-processing techniques to generate a novel imaging system that provides previously impossible-to-attain resolutions for the visualization of protein-protein interactions and biochemical activities. In doing so, she demonstrates perfectly that it is not at all necessary to be a bona fide bioengineer to apply bioengineering principles.

Citations

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A LETTER FROM THE EDITOR IN CHIEF

Dear Readers,

We are delighted that you could join us for another issue of the Bioengineering Quarterly. As the new year starts, our team continues to explore and investigate new aspects of the bioengineering community. In particular, we are excited to introduce a new industry section, where biotechnology companies can present their impactful products or services. As we will continue working to incorporate new, exciting sections into our publication, please do not hesitate to reach out to us with any questions, comments, or concerns about any aspects of BioEQ.

Thank you for your continued support for BioEQ, and we hope you enjoy the Winter Quarter 2018 issue of BioEQ - Bioengineering: Branching Out.

Cheers,

Linda Lei
BioEQ Editor in Chief

STAFF NOTE

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