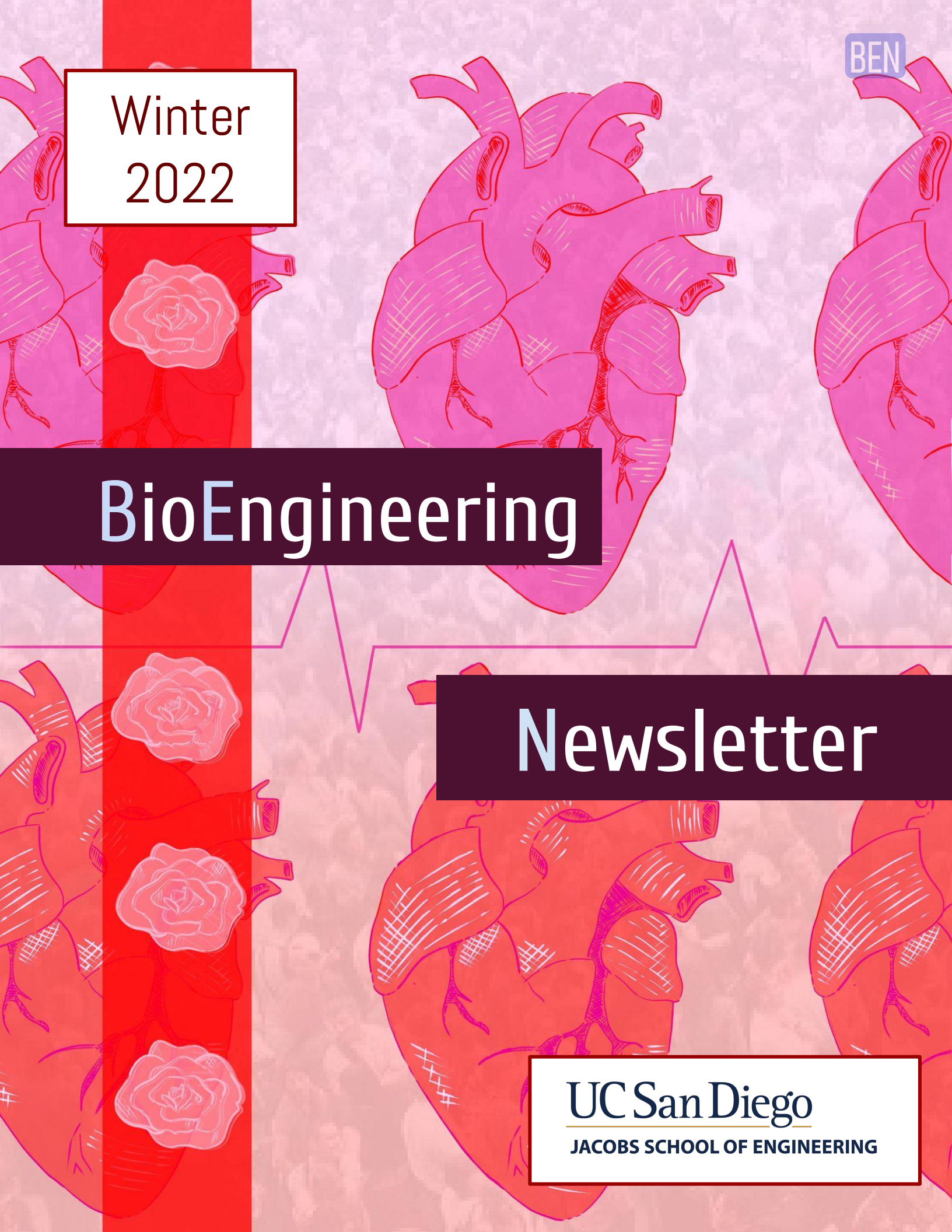

Winter
2022

BioEngineering

Newsletter

UC San Diego
JACOBS SCHOOL OF ENGINEERING

Winter 2022

- *It takes heart, immunology reigns supreme, and the elegance of systems biology*

The People of BEN

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The BioEngineering Newsletter (BEN) is a student run publication that covers the people, research and events within the UCSD Bioengineering community. We welcome in new year as we present the first edition of a new section, ***Physician Perspectives***. As always, the **Winter 2022** issue is dedicated to celebrating the resilience and ingenuity of our peers.

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Features

BENG Coffee Talks

A Biosystems™ Venture

By Theresa Slaiwa and Alice Tor | Coffee Talk Co-Chairs

The Bioengineering Coffee Talks are a weekly series of informal discussions between Dr. Bruce Wheeler, invited speakers, and undergraduate students. These talks began as an initiative to help Biosystems students better understand the meaning and value of their major, but have grown to encompass topics and speakers relevant to all tracks in the department.

All students are welcome to attend, and Coffee Talks are a great opportunity for students, especially those in the Biosystems track, to learn about their majors, meet and grow their peer support network, and explore the different pathways open to them after graduation!

Speakers, who are typically recent Biosystems graduates and/or current UCSD graduate students, provide students with unique post-undergrad perspectives in both academia and industry.

Here are a few Q&A highlights from a recent Coffee Talk, where we hosted **Lauren Midyett,** *a recent UCSD Biosystems graduate and current Bioengineering Master's student at Duke University:*

Q: **What motivated you to consider Master's degree as opposed to going into industry after graduation?**

A: Like most recent graduates, my decision was greatly impacted by the COVID-19 pandemic. The pandemic prevented me from getting as much industry experience in undergrad as I would have liked, and I still was unsure of what I wanted to go into after graduation. For those reasons, I decided that a Master's was the best next course of action for me.

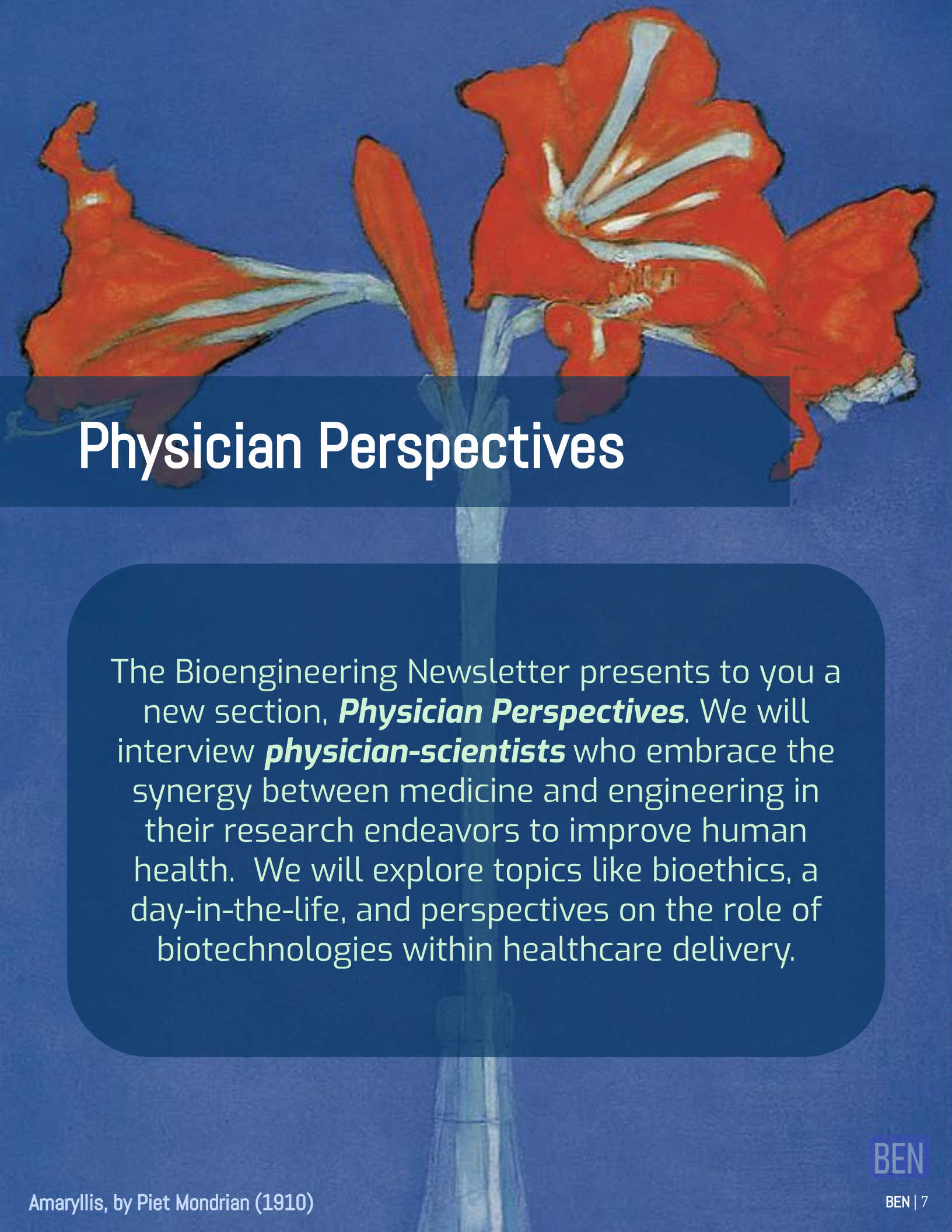
Q: **Which classes at UCSD helped direct your career path thus far?**

A: **BENG 152, 135**, and the more hands-on engineering classes definitely stand out to me. However, taking classes outside of engineering that just interest you is also instrumental in figuring out what you want to do. In my case, I took a lot of Global Health courses, which helped me better understand the market and purpose of engineering, and ultimately what role I wanted to have as an engineer.

Q: **What's your biggest piece of advice for current students?**

A: Join orgs! I was involved in Engineering World Health, which allowed me to develop both technical and social skills while keeping me connected with people and opportunities in Bioengineering. It's definitely important to take a step back from school and do some extracurriculars -- in the long run, they give you experiences and skills that carry farther than most classes.

You can sign up for upcoming Coffee Talks here!
https://tinyurl.com/beng-coffee



Physician Perspectives

The Bioengineering Newsletter presents to you a new section, ***Physician Perspectives***. We will interview ***physician-scientists*** who embrace the synergy between medicine and engineering in their research endeavors to improve human health. We will explore topics like bioethics, a day-in-the-life, and perspectives on the role of biotechnologies within healthcare delivery.

Amaryllis, by Piet Mondrian (1910)

Sandip Patel, MD

By Meenakshi Singhal | Editor-in-Chief

Immunomedicine: the next frontier in cancer therapeutics

Dr. Sandip Patel, MD, is an Associate Professor of Medicine at UCSD Health. As a board-certified oncologist in the Precision Immunotherapy Clinic, Dr. Patel treats cancer patients with the next generation of experimental therapeutics. In addition to leading a lab that studies the tumor immune microenvironment, Dr. Patel runs several Phase I clinical trials for novel immunotherapies. Personalized medicine and big data go hand-in-hand; in this first edition of ***Physician Perspectives***, we learn more about Dr. Patel's informed perspective on the data-driven future of cancer research.

Q: Could you give an overview of the main research questions that your lab seeks to answer?

Our lab focuses on the role of spatial orientation, in particular of immune cells in the stroma, and how it relates to cancer immunotherapy response resistance. Traditionally we've had diagnostics that tell us *what* something is—you have a mutation in EGFR (epidermal growth factor receptor), you have a PD-L (programmed death-ligand) of 80%—but *where* is that mutation of PD-L coming from? Does spatial configuration inform us of those patients who are particularly able to benefit from cancer immunotherapy, versus those who may be more resistant, versus those who need an alternative approach? And so what we're trying to do is add the *where* to the "what" question, in terms of how we understand a patient's cancer.

Q: Translational Medicine is the concept of turning lab discoveries into bedside therapeutics. One important step of this process is clinical trials. As the leader of multiple oncology clinical trials, can you share how the insights these trials advance the drug development process?

I think clinical trials are really the essence of what we try to do. Every therapeutic, every diagnostic we've had has been in the context of clinical trials. Probably the most famous example recently is the COVID-19 mRNA vaccine clinical trials, which have really helped us find probably our most important tool in handling the pandemic. So this was a basic science discovery of an mRNA vaccine, that was very rapidly translated in clinical trials; and these were the vaccines that are in use today and that are able to help us. Clinical trials really are crucial. And biomarker-driven clinical trials—looking at genomic markers that relate to specific populations so you can give a targeted therapy and maximize a

patient's benefit—are really key. Immunotherapies that try to stimulate a patient's own immune system to fight their cancer, and the diagnostics that help us understand what those specific targets are, are equally key in helping us understand how we can help patients.

We've had several examples here at UCSD: we're the first in the world to administer a pluripotent stem cell-derived NK cell (natural killer cell) product, we've been first for multiple targeted therapies. And the reason it's important is that it gives cancer patients opportunities to try something new that can help them. So fundamentally, I really view what we do in clinical trials as key in linking the *"bench to bedside"* and ensuring that the discoveries we have really get to as many patients as possible so that they can benefit from them.

Q: The role of genomics in medicine is only growing. Looking forward, what do you believe the role of the clinician is in managing and interpreting patients' genomic data?

I think increasingly, if you're a medical oncologist, *you need to understand genomics*. The central dogma of biology is DNA to RNA and protein; and especially in oncology—but also in multiple other diseases—we have to understand disease at a DNA level, RNA level, and at the protein level, for the most part to best help our patients. In some contexts it's more DNA and in other contexts it's more protein, and even other contexts it's more RNA. I think this is really a critical skillset for us to have in training programs, and continuing in medical education, because these therapeutic targets will develop throughout a physician's career.

But it's also thinking about tools and building tools that make it easy to interpret this data, and to help patients to understand their data. I think it's key for patients to be informed in their own healthcare—and as these tests get complex, I think it's equally key for us to think about ways to relay that information in ways that are meaningful to patients. So doing the appropriate tests is usually important, but doing them in a way in which the doctors—and more importantly patients and their caregivers— can understand, I think is increasingly becoming something that people realize is important for us to be able to advance healthcare on.

Q: How do you envision the future of immunotherapy looking like as a part of standard clinical practice?

I think different immunotherapies find themselves in particular roles. For example, immune checkpoint blockade drugs that target anti-PD-1, anti-PD-L1, anti-CTLA-4 (an immune cell protein receptor): these are FDA-approved, and have been transformative in melanoma, lung cancer, kidney cancer, and a variety of different cancer types. And then there's specific biomarker cohorts in which an immunotherapy may be particularly good; for example, in patients who have what are called microsatellite unstable tumors, that have a very specific DNA repair defect. Or, in patients whose tumors have a high mutational burden. So the other angle is cellular immunotherapies like CAR (chimeric antigen receptor) T cell therapies, which are used in liquid tumors like lymphomas and leukemias, and myeloma increasingly as well.

To me this really represents the floor, not the ceiling, of immunotherapy. Understanding which patient population may benefit from a particular therapeutic approach—whether immunotherapy, targeted therapy, or others—I think is increasingly key. And the tools that we develop in biomedical engineering and in diagnostics at a larger level, are really influential in ensuring that we can make sure that patients are on the right therapy approach. This is crucial given how toxic these therapies can potentially be, but also because of how serious the illness we're fighting is in terms of cancer. So we may not get a second chance to make a first impression of whether we're on the right path.

Q: Do your clinical and research practices guide or influence each other? How have your experiences as a practicing physician informed your research interests?

Absolutely. I think that most clinician-scientists, who are in the clinic and are also able to translate discoveries in their labs or to the community—in terms of sociological research—really play a key role. When I'm in clinic, I'm always thinking, ***what can I do in the lab to help the patient sitting in front of me***? And when I'm in the lab, I'm thinking, ***what have I learned in clinic that may help us drive forward a discovery to help a patient in the future?*** So it's a virtuous cycle ideally, and I learn different things from different angles. Even when I'm teaching courses it refreshes my memory and I think about things in different ways, so you can always be learning. And sometimes the best insights come from contexts that are very removed from the area in which you actually make the improvement, because having that mile-high view of the problem may give you additional insights.

Q: As a practicing oncologist at a large academic institution, could you share what a typical workday in your life is like?

I think every day is somewhat different in academic medicine. One thing that I really enjoy is the variety; so to give a perspective, I have two full days in clinic, and six full weeks on inpatient, and then once a month I have an outreach clinic. And so at that time I'm really focused on helping those patients, but there's issues that will arise for these patients outside of those hours as well. So helping patients in that context and for the rest of the week is really important and something that we want to be available for, for our patients.

On another day I may be giving a lecture in the morning, then going into the lab and working on a new experiment or meeting with the lab team and figuring out where we want to head together. Then I may be working on the clinical trials and trying to understand how we can best open clinical trials in a timely manner and make sure they're open for a broad community that really represents the strength of our diversity. Then we may have faculty recruitment meetings, meetings with undergrads, med students, residents, fellows; or national meetings, where we try to collaborate with other institutions and organizations on trying to improve the care of cancer patients. So every day is different. and that's one of the things that I really enjoy about being in an academic medical center.

Q: The 2018 Nobel Prize in Physiology or Medicine was awarded for the discovery of a kind of immunotherapy, checkpoint blockade inhibition. What do you foresee being the "next big thing" in immunotherapy?

Whether we start to think about diagnostics that help us understand the tumor microenvironment and the immune contribution in anti-cancer response, I think that's key and it's something that I'm focused on and collaborating on. I think focusing on new drugs to target different aspects of the immune system—this is very much an area of interest for active drug development, because we haven't moved the needle with immunotherapy for, by and large, the vast majority of patients—with for example, brain cancer, breast cancer, pancreatic cancer. So this is an opportunity to develop new drugs, and also think about **"living drugs"**, which are cellular therapies that are immuno-engineered to fight someone's cancer.

We've made great progress in cancer immunotherapy in a relatively short amount of time, but I think there's a lot left to be done, both in the diagnostic and therapeutic realms. And I view these as two sides of the same coin. The better our diagnostics are, the more refined our therapeutics get. And the more refined our therapeutics get, the more we need a robust diagnostic to understand which patients may benefit from that particular treatment.

I think it's a great time to be in biomedicine; our technology and our tools and ability to help patients has really transformed. I will probably in my whole career never do a chemotherapy clinical trial, because that era really is in the past—these are effective drugs, but newer drugs are either more targeted, or have an immune basis. So the future is really bright.

Q: If you could give one piece of advice for an undergraduate student who is going on to medical school or has interest in oncology, what would your advice be?

My one piece of advice would be to ***have an open mind***. I mean that in the sense that a lot of tools that you may think are not as related turn out to be hugely impactful in cancer, whether it be the ability to program in Python—for example, what I do in terms of image analysis—or statistical analysis in R, or thinking about cloud-based approaches to understanding datasets. These are all skills that are historically not taught in medical school, but what I think make all the difference in terms of cancer research.

And the other subpoint to make is that we've never really been in a time like the present, where it's relatively easy to get high level information; there's really been a democratization of cutting edge research. And that presents an opportunity to try to do something interesting and innovative that others may not have thought about to help patients and society. So the opportunities available at all levels have never been as ample as they are now. To my advice is to keep a broad mindset, because often our most innovative solutions to cancer come from approaches that are orthogonal or tangential at first glance, but turn out to be hugely influential in terms of moving things forward for patients.

Interviews with Professors

Flowers of the Four Seasons, Hiroshige (c. 1835)

Dr. Brian Aguado

By Nicholas Sada, Wei Ji Chen | Spotlight Writers

Precision Medicine: The Heart of the Matter

We welcome Dr. Brian Aguado to the Department of Bioengineering! Dr. Aguado is an Assistant Professor and Principal Investigator of the iBiomaterials Lab. His research focuses on integrating precision medicine with biomaterials for cardiovascular applications. In this interview, we learn more about Dr. Aguado's career path and his participation and leadership in crucial STEM diversity initiatives.

Q: Can you provide an overview of your academic journey?

My interest in Bioengineering started in high school. I didn't even know Bioengineering existed back then. My Anatomy teacher gave me an article in Scientific American called *Growing Replacement Body Parts* and I was instantly obsessed. It sounded like exactly what I wanted to do: apply math and engineering skills to biology and medicine.

I started at Stanford University with that motivation; after settling into a routine and figuring out what I wanted out of college, I started realizing grades weren't as important as experience so I focused on finding research positions. I looked for labs focused on tissue engineering and biomaterials and saw that Sarah Heilshorn—an assistant professor at the time—was starting a research group in biomaterials. I reached out and she offered me the opportunity to join her lab as an undergrad. I worked with a PhD student at the time and that introduced me to the research side of Bioengineering. Sarah treated me with a lot of independence: after getting acquainted with the lab for a year she gave me an independent project, which was focused on stem cell delivery and optimizing cell viability using hydrogels. I became obsessed with the research process, but when it came time to graduate, I knew I wanted to be a professor but I was unsure of the path I needed to take. I talked to Sarah and she encouraged me to apply to PhD programs - she's still supportive to this day.

I decided to go to Northwestern for my PhD. My first year, I was focused on classes. In my second year, I joined a junior professor's lab, but many issues eventually led me to change labs. I almost considered leaving graduate school, but came to the conclusion that I needed to try a different lab environment to be successful – I found the perfect fit in Lonnie Shea's lab. Lonnie continues to be one of my most valued mentors. When I joined his lab I started working engineering implantable materials for cancer detection.

I thought I would be working with stem cells or something similar, but Lonnie introduced me to the idea that you can be super creative with biomaterials and step out of your comfort zone. Applying biomaterials to cancer detection was such a cool concept because the idea was to implant a little implantable sponge—a polymer material—into a mouse model to detect and treat breast cancer. We found that we could redirect tumor cells to the material implant site before they would go to any other organs. My thesis was largely based on that technology. I generated different versions of that material: I added inflammatory factors to the material, I added extracellular matrix proteins to the material; I also investigated the primary tumor and saw how the primary tumor biology would change as a function of biomaterial implant. So there are all sorts of questions to be answered with the system.

I defended my thesis and graduated in 2015—it's still one of the best days of my life. Then in 2016, my Grandma (*mi Madrecita*) passed away suddenly from complications with heart valve disease. That was a really jarring moment in my personal life, but it motivated me to pursue research in heart valve disease. With that mindset, I joined Dr. Kristi Anseth's group in the University of Colorado, Boulder, and focused my postdoc research on aortic valve stenosis. I started thinking about how we can understand the mechanisms of and develop better treatments for this disease. At the moment, the only treatment is surgery; but not all stenosis patients are eligible for surgical procedures - my Grandma was one of them. So, we hope to develop non-surgical, drug-based strategies for treating valve diseases.

I did my postdoc research in collaboration with cardiologists to collect serum samples from aortic valve disease patients. We found that we could develop more personalized in-vitro models of valve disease by culturing valvular cells with serum from aortic valve stenosis patients. When we want to culture valve cells, we do so on a hydrogel matrix

Dr. Aguado and his grandmother at his PhD graduation

that closely recapitulates the stiffness of valve tissue so it's more physiologically relevant. In old models, we would use standard fetal bovine serum (FBS) to culture the cells. But in my approach, I took serum samples from human patients and cultured the cells. With human serum, myofibroblast activation varied as a function of the patient. We then found that we could correlate in-vitro results to patient echocardiography data, which gives us insight into a multitude of clinical scenarios. That got me interested in the idea that we could use biomaterials to generate personalized models of disease.

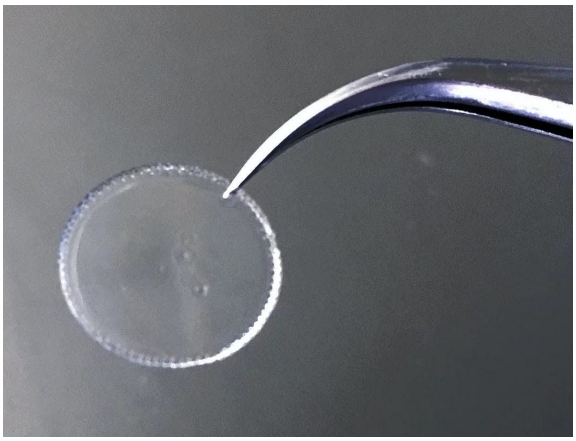
Given that motivation, my lab is focused on engineering precision biomaterials with the patient in mind. My group here at UCSD is interested in investigating sex differences in cardiovascular disease using biomaterial technologies as tools to dissect

underlying mechanisms. For example, heart valve disease manifests quite differently from patient to patient. Specifically, aortic valve stenosis is sexually dimorphic, both in clinical presentations and pathophysiology. For example, men tend to develop more calcifications in valve tissue, whereas women develop more fibrotic scarring in valve tissue. My lab is dedicated to uncovering the biological mechanisms that drive sex differences in valve disease and how we can customize treatments as a function of biological sex.

Q: The four main topics within your lab are: 1) using biomaterials to study sex-specific cell responses, 2) models of aortic valve disease, 3) sex-specific immunomodulations for cardiovascular tissue regeneration, and lastly 4) spatial transcriptomics to characterize sex differences. Can you give a brief summary of each of these areas?

Right now, the lab focuses on valve disease because that's where the dimorphisms I'm most interested in exploring are. I developed hydrogel formulations that helped reveal sex dimorphisms in cellular behavior—so if you were to culture male and female cells on the same hydrogel, they'd have different responses. *What is going on intracellularly that leads to different phenotypes?* **The first project is really focused on identifying the molecular and intracellular mechanisms that in-vitro drive dimorphisms.** I have evidence suggesting there are genes on the X chromosome that manipulate myofibroblast activation processes uniquely in female cells relative to male cells.

The second question is focused on further refining our patient-specific in-vitro models using serum samples from patients. The second project is extracellular; *what's going on outside the cell and how does extracellular environment exacerbate sex differences?* What is the complex milieu that you might find in a patient's sample? How does that impact cellular phenotype? The cells receive thousands of signals from this extracellular milieu, so how do these biochemical factors synergize with the intracellular mechanisms and lead to sex dimorphisms in cellular behavior? That's what the second project is focused on: identifying clinically relevant proteins that may be associated with valve disease in a patient/sex-specific manner.



Engineering patient-specific models of valve disease

The third project is an extension of my PhD research. I am super interested in sex differences in inflammation; women typically have increased inflammatory responses in response to injury relative to men. Thus, the goal of the project is to develop implants that modulate the immune system in a sex-specific manner during and after a myocardial infarct. There will likely be different

inflammatory populations that arrive at the heart as a function of sex; *so how can we manipulate those cell populations that arrive after a heart attack in a sex-specific manner, to better boost cardiac regeneration potential?*

The spatial transcriptomics project is the fourth. In RNA sequencing, you sequence a controlled and experimental sample. That tells you nothing about the location of the cells and where they were in the tissue because you're mashing up the entire tissue. In spatial transcriptomics, you take a slice of tissue section and mount it onto a glass slide that has spots of mRNA capture oligonucleotides. You first image the tissue and figure out its geographical features. Then you lyse it so the mRNA is captured at specific spots. Those spots are barcoded so you can align your spots and the transcriptomes of those spots with the original tissue sample. You now have the map and can identify where your cells are on that map. I want to use that technology to study sex differences in valve disease, because there are geographical features in male and female valves that are different. I'd love to learn how tissue geometry can influence cellular heterogeneities and how they can lead to sex dimorphisms.

Q: What motivated you to pursue becoming a professor and the PI of your research lab?

A lot of it was the support of my family and the motivation of my grandmother's death. I also really value the community aspect of academia. The people I've met and continue to meet throughout my career are all good people who want to do good for the world. Finding the support that you need is critical. There's so much underrepresentation in the sciences, for example, I'm a first generation Colombian-American.

Out of 27,000+ engineering faculty in the US, only 587 are Latinx, and 47 are US-born. There's this pipeline issue of Latinx students not making it to faculty positions, so why is that? It's a multivariate problem. To address it, my best friend Prof. Ana Maria Porras and I co-founded ***Latinx in BME***—a social media platform on Slack where we can communicate with Latinx biomedical engineers. We created this space because we had received so much help from our mentors but not everyone receives that kind of mentorship. Science can be an extremely isolating experience so that's why I focus a lot on trying to build a community of people.

Q: Why do you think diversity and inclusion are important for academia?

For starters, ***diversity saves lives***. One example is in pulse oximetry, for blood oxygen measurements. With pulse oximeters, you use a clip that goes on your finger. Those devices were engineered for White skin and the measurements are completely different for Black skin. If you put a group of engineers in a room to design a device and they're all White, they're going to design it for White people. We must have diverse perspectives when thinking about engineering the next generation of medical devices that are meant to help people of all backgrounds. Let's start with sex differences. Why is it that 8 out of 10 drugs taken off the market in the 90s had adverse effects on women? Because most of those drugs were tested on male animal models. Predominantly who are the scientists in these positions? Unsurprisingly, most are men.

You must diversify the people you're working with to be able to improve the products that you're ultimately trying to put out into the world.

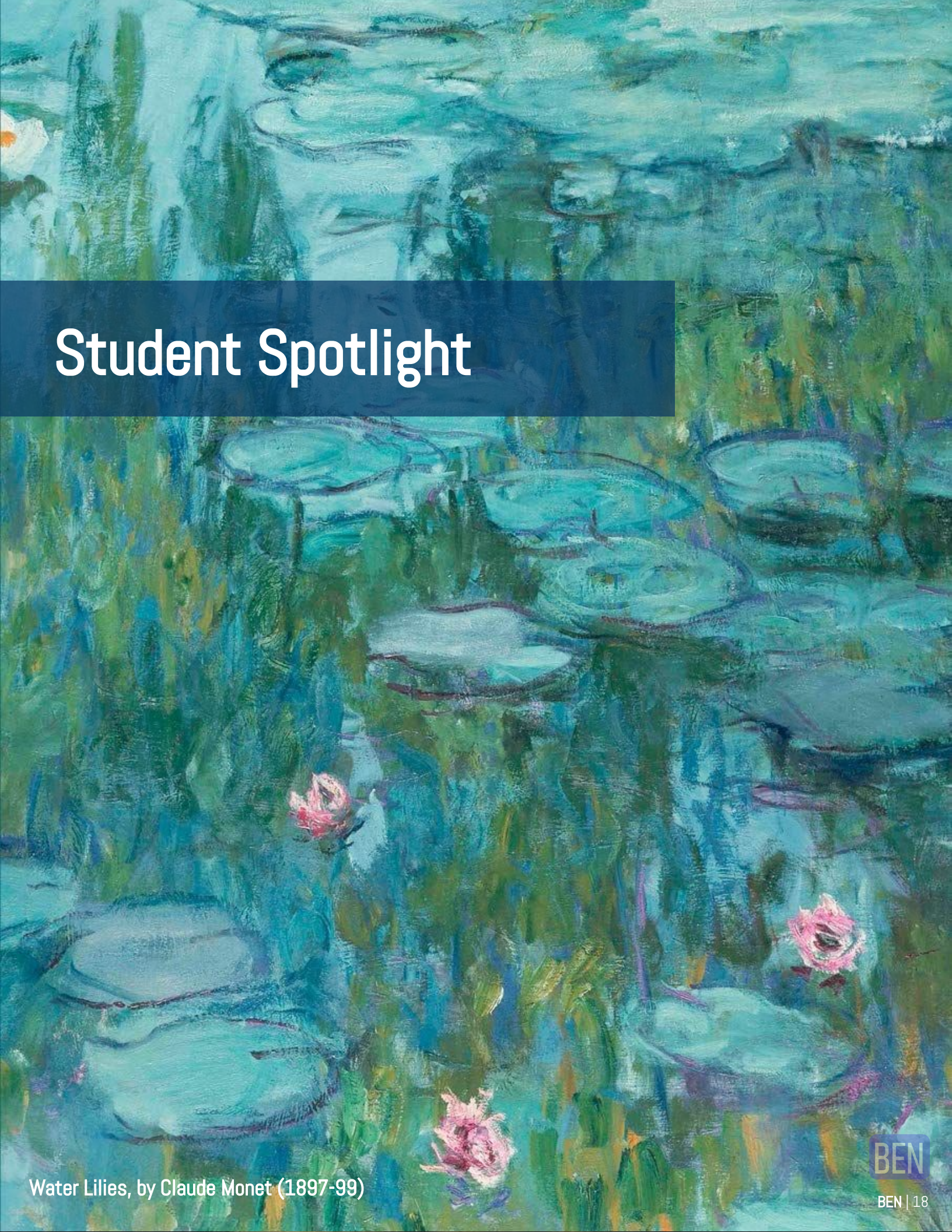
Q: You talked about how sex differences manifest in these different cellular and molecular mechanisms. Would you agree that the reason this is poorly characterized in women is because a lot of the mouse models used are male rodents and usually the ones doing the research are men and not women?

I would say the primary scientific reason it's not characterized well in women is because when scientists see a female rodent, they see fluctuations in hormones that impact the variables they're looking at. Science is focused on identifying mechanisms, on trying to reduce the number of variables that can impact a system. From a practicality standpoint, scientists do not focus on female models. They may think there are too many fluctuations of hormones in female animals that are difficult to control. Though that can be true, you'd be ignoring half the population. You can't just assume that a woman is a small man. There are fundamentally different ways in terms of how our bodies work at different length scales, from the sex hormone scale to inflammation. There's just so many dimorphisms that exist that it becomes unproductive to develop a medicine or therapy or device for men and just give it to women. It's becoming outdated to think that's an effective way to treat disease for everybody.

Q: Another aspect you focus on aside from research is science communication; how did your interest first start?

It came from the fact that I was unable to describe my studies to my family. In graduate school, when I was trying to explain what I was doing, my parents were just like, "Oh cool, he's doing cancer research," but not really understanding. That frustrated me—it made me feel like I couldn't describe my science to the lay public. It doesn't help that students never get any formalized education in science communication. So I applied for this program called "ComSciCon"—a communication science conference—and it taught me how important it is to be able to communicate your science to a wide range of audiences. By recognizing your audience, you can stimulate interest in science and help promote the scientific agenda. Along with ComSciCon, I also got interested in bilingual science communication. I'm bilingual in Spanish so that's what I use to communicate science to my parents. I'm certainly interested in ideas on how we can communicate sciences in different languages and to different demographics as well. For example, when I was in graduate school I worked to develop biomaterials laboratory modules for high school women that are historically excluded from the sciences, specifically Black and Latina communities. Part of the program was that we would invite parents to come to the laboratory. Lots of these parents didn't speak English, so we spoke Spanish with them and it was a really touching moment when one of the mothers said, "Thank you for doing this."

Student Spotlight



Water Lilies, by Claude Monet (1897-99)

Michael Fitzgerald

Bioengineering Graduate Student

By Meenakshi Singhal | Editor-in-Chief

Fitz is a 2nd year Bioengineering PhD student that studies neurodegeneration. He's currently using bioinformatics and systems biology tools to better understand common pathological mechanisms across neurodegenerative disorders, and he uses cerebral organoids to study the initiation and progression of Alzheimer's disease and potential drug interventions.

Q: Can you describe your research in the Subramaniam lab, and how your prior research experiences shaped your current interests?

I think my research in general is a bottom-up approach to how the brain works and how the brain aberrates—so how diseases arise in the brain. I started off my research by just looking at how neurons work. My first project was at the University of Oxford, and I was using CRISPR to study the development of neurons from stem cells. I asked the question, ***what are the processes that control neuronal development?*** My next research position was looking at *C. elegans*, which is a microscopic roundworm and actually regenerates its damaged neurons. So now we wanted to ask, ***how do neurons regenerate?*** If we can figure that out then we can hopefully have new approaches to cure conditions like paraplegia and central nervous system degeneration.

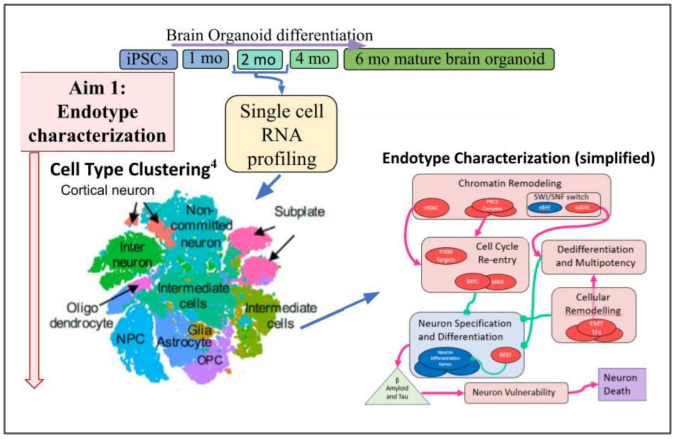
So we had this big laser table set up, big fancy microscopes, and we'd cut the neurons and see the way the neurons grew back.

But really to me, both of those projects led up to what I'm doing now in Shankar's lab, which is asking the questions: *What are the mechanisms that are occurring in the brain during Alzheimer's disease? What controls the onset and the progression of this disease?* And then I'm asking the question, ***how can we actually study that?*** There are two divergent ideas that we took. The first was "well hey, if we look at all the data that's out there in stem cell-derived neurons and in post-mortem brain tissue—and if we were to look at Alzheimer's disease, ALS, Parkinson's disease, Huntington's disease—***is there a common mechanism between neurodegenerative diseases?***

And if so, can we target them? So that's my project that I'm working on now. And what's really exciting is that we think the answer is yes. We believe there is a common mechanism that's driving these diseases and is upstream of disease onset and pathogenesis. So if we can target that specific mechanism, then you can potentially help treat every major neurodegenerative disease with one drug—which would be pretty cool.

However, there are a lot of limitations in how we currently study neurodegeneration; namely, in the post-mortem brain, you are only looking at the late end of the disease, and in stem cell-derived neurons, you don't really get the full cellular heterogeneity, the full neuronal morphology, or the full maturation—in terms of electrophysiology and other metrics. So to solve this problem, we started to look at brain organoids, which are essentially small spheres that roughly recapitulate the cellular heterogeneity and neuronal activity of a brain. And so using this model, we kind of went back to our roots and asked the question, *what are the mechanisms that control the development of the brain organoid?* Nobody really knows this; we've been working on developing protocols to just get us to the end stage, like our end point of a functional neuronal model. But we don't know the mechanisms that control that process. And understanding it more will help us develop better organoids, and in fact learn more about the brain.

My main project in the lab right now is to take this organoid model that we have, and use it to study Alzheimer's disease. And to give you



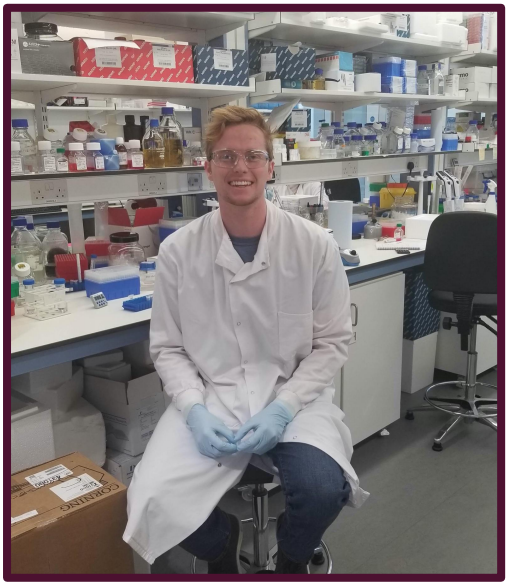
Brain organoid characterization workflow

a little bit of insight, nobody has ever shown spontaneous, widespread neuron death in any neuronal model that reasonably recapitulates Alzheimer's disease. All of the models in current use that show late-stage phenotypes are the result of unnatural overexpression of Alzheimer's disease genes, or exogenous toxic protein additions. But nobody's ever been able to take a patient's cell, without doing some kind of "protein assaults" or extensive genetic engineering, to show late-stage Alzheimer's disease pathology. And so what we hope to do is grow late-stage Alzheimer's disease organoids in an attempt to understand the disease onset and progression in an experimentally tractable and reasonably accurate model of the brain.

At the end of the day, **there's two big unsolved biomedical challenges: cancer and neurodegeneration.** The reason we've been able to develop some good therapeutics for cancer is because we have good models for it. There isn't a good model for Alzheimer's disease, in my opinion, as we currently speak.

So developing the right model, asking the right questions, and most importantly, using these powerful technologies like bioinformatics, cerebral organoids, CRISPR-Cas9. That's why I really love my research; it's a culmination of all of those put into one project.

Q: Mentorship is important in any field of study. Who inspires you to pursue bioengineering?



It's gotta be Shankar, it really does. I have the most crazy story about how I met Shankar—I met him as a high school student. My ex-girlfriend's best friend is friends with Shankar's son, and so that's how I met Shankar. I ended up getting his email, and shot him an email, and I was like, "Hey, I'm interested in bioengineering." I'd applied to UCSD and so I knew he was faculty there, and really wanted to meet him. I never got a response, emailed him again, never got a response, emailed him again, never got a response. Then like four months later, I get an email from him saying, "Hey, sorry I missed your email, I'd love to meet up." And I was like "Yes, anytime!".

And I met up with him and basically had this dialogue, where I thought I knew a bunch about bio because I'd taken AP Bio and had looked up stuff on his lab website. And we basically had a conversation where he told me the history of bioengineering and early agriculture and Leonardo Da Vinci. Then we started talking about more modern bioengineering concepts like genetic engineering. And it was cool because he'd say something at a pretty basic level, and then I'd say something to let him know that I understood what he was talking about. Then he'd bring it up a notch, and I'd say something, then he'd bring it up another notch where I didn't know it anymore. So it was cool.

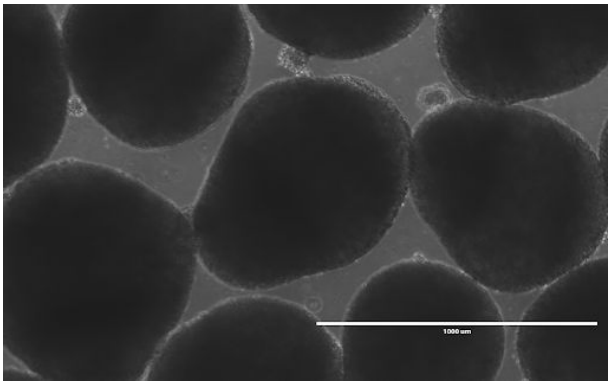
Shankar challenged me, but more importantly, he made me feel heard. Like he made me feel like the contributions that I could make to the field could impact lives. And just the fact that I was an 18 year-old who had an excitement about biology, and then he helped me turn that into a research career—in giving me guidance on how to apply for a lab position, or how to apply for a co-op, getting into grad school, things like that—to now, of course I want him as my PI. From a young age, he showed that I had value, and that if I applied myself I could make a difference in this field. And so that's where it starts. That was the turning point for me where I was like, "Yeah I can do this,

I could get really good at it". At a really young age, I was really interested in biology, so my Dad bought me a microscope. And that was pretty cool, because I got to look at a bunch of stuff. So that piqued my curiosity, but **Shankar turned curiosity into a career.** And I'll always be grateful to him for that. And not only that, but he also cares about the other things in my life. Like he's not just interested in me as a scientist, but as a person. So like developing my skills as a scientist, but also as a team member, as a leader, as a family member. So yeah, Shankar is the platinum standard when it comes to mentorship.

Q: What is the most crucial lesson you have learned during graduate school?

It might sound overplayed, but really just being able to fail. Like the ability to work so hard at something, and then realize you messed it up. Like to work so hard to write a grant—spending 250 hours on it—just for it to get denied. Like what do you do with that? After you spend so much time and effort saying "here is my work product", and then having someone else say "it's not good enough". What do you do with that? And I think this is a common theme, but it's true. Being able to work so hard towards something, and fail, and then being able to say, "Okay, despite this, I'm going to keep going. I'm gonna look at the path I took, and ask the questions: *Well what happened? What was beyond my control? How can I do better next time?*"

And in terms of that actually manifesting in research, this is the real lesson that I learned from that: the lesson was to become a **more efficient planner.** I think research is a very nonlinear process. You go from point A to point B, but along the way you're taking all these detours, all these other routes. And part of that is necessary. Part of research is taking detours and rabbit holes to learn about a process and to be able to apply it. But being able to have clarity of thought and being able to take a step back from your research project and say, *"Okay, what do I have? What do I need to have? And what are the steps I need to take to get there?"* And I think this is something that a lot of young scientists struggle with because research is such a multifaceted job—there's so many different components to consider.



Brain organoids in culture, photo courtesy of Fitz

And unlike any other job I've had in my life, nobody knows my project as well as I do. I mean Shankar is great for getting help; Andrew, a senior scientist in the lab, I wouldn't be able to do my research project without him. But at the end of the day, when it comes to deciding directions for the project, the onus is on me to make sure that the path I take—the choices I choose to make—are going to get me to where I need to go in an efficient manner. Because if I just think, "Oh I can do this," and then go do that, and it's like, "Well, okay, I did this but it didn't really get me to where I want to be." So being able to take a step back, have clarity of thought about what I'm doing and where I need to go, I think that's a really hard skill to learn as a scientist. But that is the most useful skill. And it's only coming after I kept trying; you don't learn it until you mess up. You can work for a month-and-a-half on something and then realize that it's useless, and if you'd had a little better foresight then, you would have realized that sooner. So being able to learn that process is hugely valuable.

Q: Work life balance is something that we all strive to achieve. How have you developed your sense of balance and what do you enjoy doing outside of the lab?

One thing I definitely didn't realize as an undergrad when I got my first full-time research position—it was a co-op where I stopped going to school for six months and worked in Shankar's lab—there was no time card, no one was keeping track of my little steps. No one knows when I leave lunch or when I get there. And it's even more true in the age of work-from-home. I think the important thing to realize is that the only person who gets hurt if you aren't making good progress is you. And so there's a really big accountability there. Especially if you're working on the same project for months and months, there's times when I wake up and it's like, I love my project, I love science and it's frankly bonkers that I get paid to do this, but it can be hard to motivate myself to get in R and do some coding.

So for me, I think part of it was realizing when I work best. When you grow up people are like, "Oh, if you're not waking up at 6am then you're not trying hard enough". But it's like, my hours when I work best are from 11am to like 1am. I don't work 14 hours a day, but that time period is when I get my best work done. So for me it was learning to wake up in the morning and workout. I really like rock climbing, so I like to go. To me it was a good way to accomplish a little thing. If you can accomplish a lot of little things, every day, then I think you're going to be in a good place to make good progress towards the big milestones you have in your life. So if I can wake up in the morning, go rock climbing at the gym, and finish climbing a route that I'm working on, then it makes the other things that you need to get done on that day seem a little bit more doable.

And for me a really big aspect of keeping my head on straight is my faith.

To me, science is my purpose in life—it's why God put me here. It's of those things that's just so easy to forget, and so I'm making sure to devote a little bit of my time every day to my faith. And on a weekly basis, setting aside time to take a step back and touching base with my Creator is the way I can make it through the tough times. You know, like when Shankar and I were writing a grant and I pulled two all-nighters back-to-back on three hours of sleep. So when life gets crazy, when you have your life built on a solid foundation, you will survive. ***But building your life on a solid foundation is a daily process.*** So accomplish the small things, continue to accomplish the small things, and for me, to realign myself with the person who put me here; that's how I maintain my work-life balance.

Q: Is there any advice you have for students interested in pursuing academia and/or grad school?

Do your best to find a research position. And it's hard. It's really hard a lot of the time. There are also fiscal barriers associated with that. Not everybody has the privilege to be able to volunteer in a lab 10 hours a week because they may have to work a job and get paid. So if grad school is something you want to do, then **1) Do your best to find a research position, and 2) Do your best to find a mentor who is faculty in your department.** Go to them and say, "Hey, I'm really excited about this topic area. I would love to pursue it in an academic research setting, or in grad school. Here's what I'm thinking about doing, do you have any advice for me?" I think if there's a hundred students who like the idea of going to grad school, 20 of them will actually go to somebody and say, "Hey, I want to do this." If you wait for the opportunities to come to you, then odds are you're too late. For me, I remember in high school I emailed like 25 faculty members at different universities trying to get an unpaid research position before I ended up getting a response from Shankar. So go out, try to find a research position, try to find a faculty mentor if possible.

The only other thing that I would say is that it's not worth doing if you aren't really excited about it. *Academia is not a luxurious route.* Grad school is a great way to be in poverty for an additional six years after you graduate. So if you really like the idea of research—of new, groundbreaking technologies—and if you find yourself falling asleep at night thinking about these research topics, then do it. **Go for it; it's one of the coolest jobs you'll ever have.** I get paid to look up stuff that I'm interested in. I don't get paid a lot, but it's a pretty cool position to be in. And the last thing I'd say is that not everyone's route is going to look the same. There are people in my cohort who went directly from undergrad to grad school, like me. But I was privileged enough to be able to take an unpaid intern position in undergrad. I was also able to get two co-ops—I stopped going to school for two separate periods for six months—and that gave me the research experience I needed

to be able to a PhD program right out of college. **But not everybody's path looks like that.** Other people work in industry for two, three years. Some people work in industry for upwards of a decade before going into grad school. And I think that's probably a little more difficult route because when you get used to industry, there's a lot of luxuries associated with it, like a salary. So right now in grad school, everything is dependent on me—me being able to decide what I need to do next, and me staying on top of my work. Meanwhile, industry has a lot more structure—and obviously depending on the position—is like, "Here's what I need from you" kind of a thing, so much more defined.

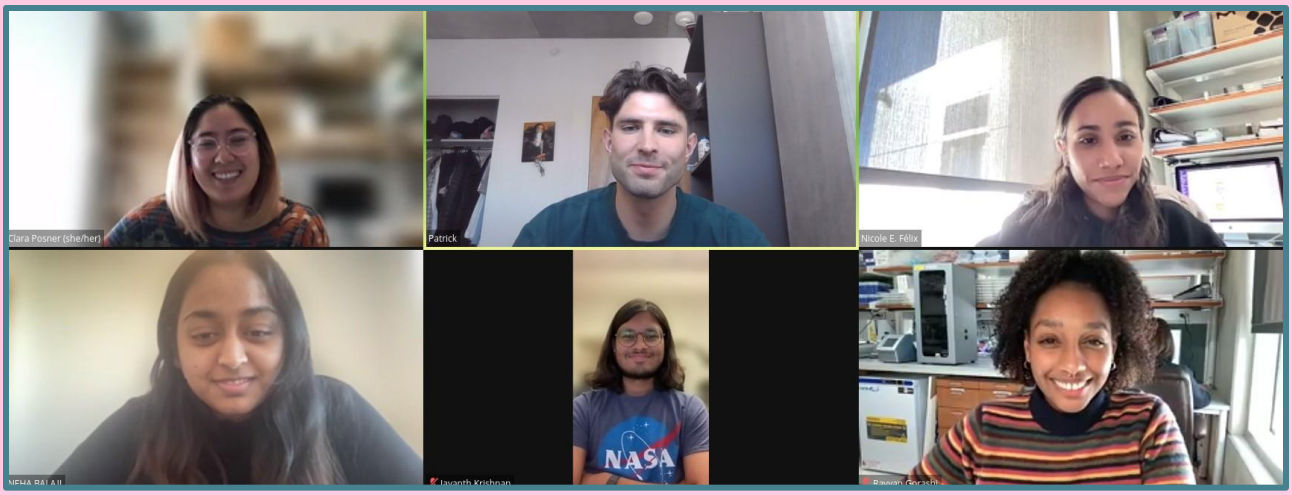
So the three things would be: **1) find a research position, 2) approach a faculty member and ask them for their advice, and 3) understand that not everyone's path is going to look the same.** Nobody knows your background, where you're coming from, the specific things you're struggling with at this moment. But that doesn't mean you can't go into a PhD program. It might just not happen in exactly the manner you might want it to. So I think those are the key things to keep in mind.

Hibiscus by Hiroshige (c. 1845)

Student Org Events

BEGS Mentorship Initiatives

By Tiffany Zhou, Clara Posner, Patrick Kasl | BEGS Representatives



BEGS Mentorship Committee, 2021-22

Graduate students face numerous challenges: stress over academics and research, conflicts with co-workers or PIs, work/life balance, imposter syndrome, time management, and more. The onset of the COVID-19 pandemic and the subsequent shift to remote learning created additional difficulties, especially for students who started their first year of grad school remotely and struggled to get to know their colleagues and build strong connections.

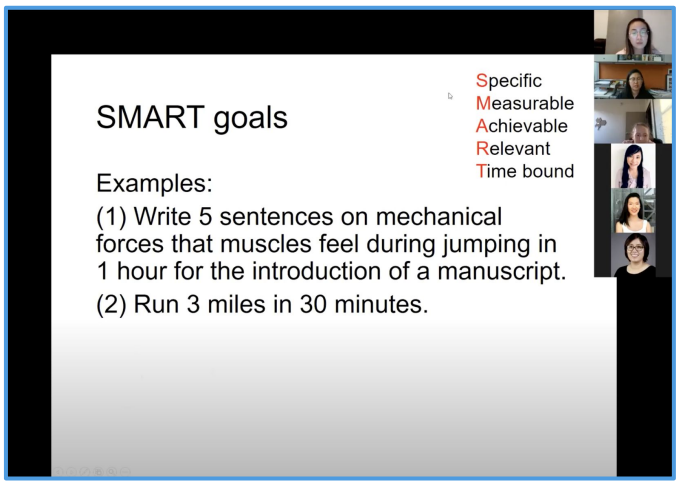
To better help students navigate these challenges, the **Bioengineering Graduate Society (BEGS)** significantly ramped up its mentorship initiatives over the past year. We believe that mentorship is highly important for student success, as it allows people to share knowledge and insights and offer support and guidance; no one should have to go through grad school alone. We officially formed the **BEGS Mentorship Committee** in the 2019-2020 academic year. Led by Bioengineering PhD student **Clara Posner** as Mentorship Chair, the committee has been hard at work ever since.

The Mentorship Committee's first major initiative was to create the **BEGS Graduate Student Mentorship Program**, a formal mentor-mentee program to pair first year graduate students with senior graduate students in the Bioengineering department. The aim of this program is to ease the transition into grad school for first year students and to provide them with someone to reach out to if they have questions or need advice. Pairings are determined by degree program, research interests, academic background, personal interests/hobbies, and underrepresented minority status. To encourage active mentorship, we set up an incentive system where mentor-mentee pairs can earn points by attending BEGS events together, and at the end of each quarter the pair with the most points wins a prize. We also had a quarterly mentor-mentee spotlight highlighting a nominated mentor-mentee pair, and an annual mentor award recognizing a graduate student's excellence in mentoring others.

The BEGS Graduate Student Mentorship Program is currently in its second year and has grown to 49 mentor-mentee pairs, compared to 30 pairs last year. We also expanded the program this year to allow undergraduate 3rd and 4th year Bioengineering students to be connected with a graduate student mentor; there are currently 20 of these graduate-undergraduate mentorship pairs.

BEGS x BMES Mentorship Olympics

Ideas generated in the weekly committee meetings by our amazing and engaged committee members have led to multiple other initiatives. Among these include increased collaboration between BEGS, **Women in Bioengineering (WBE)**, and **Biomedical Engineering Society (BMES)** at UCSD, including the introduction of application reviews and mock interviews with undergraduate students applying to grad school. We have also merged efforts with BMES to support and expand the network for casual professor talks, where faculty talk about their life story or interests/hobbies outside of research. In addition, our recent Mentorship Olympics was a fun social event in collaboration with BMES. Teams competed in a potato sack race, cornhole toss, soccer target shooting, and a mini obstacle course!



Setting SMART Goals with Dr. Kwon

Continuing the trend of new initiatives has been the establishment of the **Professional Development and Diversity Committees**, both of which are now chaired by Mentorship Committee members **Rayyan Gorashi** and **Nicole E. Félix Vélez**, respectively! Lastly, we'd like to highlight a particularly successful mentorship event: the **Graduate Student Success Workshop** hosted by **Professor Ester Kwon**. In this workshop, students learned how to set SMART goals for the week and were assigned *"productivity partners."* A week after the event, productivity partners were given Starbucks gift cards to meet in person and follow up on their SMART goal progress.

BMES Lab Expo 2022

By Kendra Worthington | BMES Representative

If you were to ask a bioengineer for one word they would use to describe their field, you would hear answers such as versatile, innovative, and fast-growing. However, among all the responses, one that shines through the most is interdisciplinary. Bioengineering sits at a unique cornerstone of many sciences, and it is this interdisciplinary nature that sparks the hosting of the annual Lab Expo research symposium.

Lab Expo 2022, the ninth anniversary of the event, was hosted on Friday, January 14th. The event, as described by the organizing committee, is *"a research symposium organized by undergraduate students with the purpose of increasing scientific literacy, developing interdisciplinary collaboration, and promoting scientific advocacy."* This may sound like a tall order from a one day event, but through the multiple activities of the day, each of these purposes were accomplished at this year's event.

One of the most phenomenal aspects of Lab Expo is how it is a launchpad for future scientists. Through this event, students are inspired to seek new research opportunities, with some even joining a research lab directly on the day of the event. More so, the purpose Of scientific literacy is to allow the event attendees to increase their ability to understand science. Through listening to 3 minute TED talk research presentations at the **Lab Expo Graduate Showdown,** learning from the impressive career of the experienced keynote speaker, **Dr. John Newsom, CEO of Tioga Research**, or having one-on-one conversations with presenters at the two poster sessions or networking session, students have a multitude of opportunities to increase their understanding of science.

Another key aspect of Lab Expo's mission is scientific advocacy, a concept which event **co-chair Rohil Ahuja** describes as the proper communication of science. He highlights the crucial need of researchers to explain their research in a way that allows a listener of any educational background to understand the impact of their work. By offering the opportunity for researchers to present their findings in a low stress environment, the event allows the presenters to gain experience in communicating and advocating for their research.

The last of the three main aims of Lab Expo is interdisciplinary collaboration. Coming from a background of bioengineering, the planning committee saw how important

the many different fields of research were to their studies. This year, the event featured a wide variety of fields, from bioengineering to computer science and anthropology to cognitive science. By including a wide breadth of research, Lab Expo brings together many parts of the research community on UCSD's campus and gives them a space to talk and seek out collaborations that they might not have otherwise discovered.

The success of this event merits a look into the planning behind it, which involved the year-long efforts of c**o-chairs Rohil Ahuja and Wesam Kanim** alongside their planning committee. Their planning is characterized by a sense of adaptability, as a rise in local COVID cases forced their event online a mere 3 weeks before its occurrence. Despite this hindrance, the switch from in-person to online was no setback for this team, as they persevered in their work to put on a phenomenal online event.

Lab Expo is one of the largest events that the Biomedical Engineering Society hosts, however our organization hosts many other informative events. This quarter, we began a **Bioprocessing Seminar series**, featuring professionals from various parts of the bioprocessing industry who taught students about their work. In addition, the annual **Translational Medicine Day** event held in early March guided students through the process of taking a product from the research to the clinical level. These events and more are all a part of an effort for BMES to serve our community and be a resource for anyone interested in bioengineering.

Check out the Lab Expo '22 website at https://sites.google.com/ucsd.edu/labexpo2022/home

ISPE Company Info Sessions

Bridging Undergrad with Industry

By Ryan Truong | ISPE Rep

A fear that is common between many undergraduates is the ability to land an internship during the summer or a job after graduating. Another aspect that goes hand in hand with this is a lack of information available to fully understand these companies' culture, principles, and job descriptions. This is why at **ISPE (International Society for Pharmaceutical Engineering) UCSD**, we strive to alleviate the pressure and unknowns by allowing students to network and learn about different biotech companies, such as the one shown here, **Genentech (2019)**! ISPE hosts many company info sessions throughout the school year and representatives from these respective companies come to our event to share their insights.

Because of the pandemic, we have transitioned these events to be online, but are ready to go back in person once we can! During these info sessions, the representatives give a small presentation, sharing their company's culture, the various jobs that they have, the process of applying, and etc. In addition, sometimes past interns and current engineers/scientists of the company come out as well to share their daily work life. Students then have a chance to connect with these representatives, ask questions they may have, and get a chance to follow up after the presentation to network with the representative. These events have also served as a great way for students to become more familiar with companies of interest, since there are so many of them!

Ultimately UCSD's ISPE Chapter strives to serve as the bridge to connect students to their future aspirations after college. Through events like resume workshops and company info sessions, ISPE UCSD hopes to help students get their foot through the door and drive them down the career path they want to take.

Visit us @ http://ispeucsd.weebly.com

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STAFF NOTE

All of us at the BEN would like to thank:

The Bioengineering Department for their overwhelming support of this project, Dr. Patel, Dr. Aguado, Dr. Watson, and Michael Fitzgerald for their ideas and suggestions. The Biomedical Engineering Society (BMES), The International Society of Pharmaceutical Engineers (ISPE), Women in Bioengineering (WBE), Bioengineering Graduate Society (BEGS), Engineering World Health (EWH), BE Student Outreach Committee, MS/MEng Coordinator & Undergraduate Advisor Sandra Marqas and Carol Kling for their help in publicizing and supporting the BEN, and The Jacobs School of Engineering. We give our special thanks to Dr. Watson for working meticulously with us and supporting us as our Community Advisor.