Fall
2021

UC San Diego
Jacobs School of Engineering

BioEngineering Newsletter

Fall 2021 Issue! - Have you checked out the trolley? The new Sixth?

The People of BEN

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BEN

The BioEngineering Newsletter (BEN) is a student run publication that covers the people, research and events that occur within the U.C. San Diego Bioengineering Department. This Fall 2021 issue is dedicated to celebrate the inclusive nature of BioEngineering concepts and applications with sincerity and authenticity.

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Atkinson Hall or a magnified computer...?

The Big BENG

Introduction, Resources and Recruitment!

By Dalila Gonzalez-Mejia |Student Org Representative

Who is The Big BENG?

The Big BENG is an educational organization that strives to empower bioengineering undergraduate students with educational resources to succeed in their courses through educational videos on bioengineering topics. We want students to spend less time searching for resources and more time learning bioengineering concepts. Our mission is to provide bioengineering students with the opportunity to unlock their potential in this growing field. To keep up to date on what we're up to, fill \ out this form! https://forms.gle/SjtZTzqt2RZbnuKc9

Courses We Offer:

BENG 100: We offer 5 videos covering "how to survive" the course, and some basic but tricky concepts.

BENG 110: Our BENG 110 content is based on Dr. Andrew McCulloch's version of the course, and is split into two playlists-- one covering statics and dynamics (22 videos), and one concentrating solely on continuum mechanics (14 videos).

BENG 186B: Our bioinstrumentation design content covers a wide range of topics from input and output impedance to electrode kinetics. We have 28 videos that will teach you how to succeed in this class taught by Dr. Cauwenberghs!

BENG 130: Our content for thermodynamics is mostly application based-- we talk about how thermodynamics plays a role in everyday life, from your thermos to protein folding!

BENG 112B: We are currently developing a master resource list for this course. There are already many useful youtube channels and courses on fluid dynamics, but they are sometimes difficult to find. We expect to make this available starting Winter 2022!

BENG 103B: Our 5 video playlist on Bioengineering Mass Transfer takes a problem solving approach. We teach you how to consider assumptions, how to approach the complicated and nuanced problem sets, and a few of the core concepts of the course.

Call for feedback:

We think our videos are pretty cool. However, it's more important to us to make it **USEFUL to you**! And to do that, we need your feedback! Tell us what content sucks, what you love, what courses need more content, and what courses you think we should work on next! Fill out our short survey to win a starbucks gift card, we have a raffle every quarter:
https://forms.gle/Vdb7nh7c4XGDJMBx5

Call for new members:

We are looking for new teammates! We are in need of people that are excited to: 1) help with our social media presence and 2) help us create an amazing website. If you think you would be a perfect fit for this role, please don't hesitate to reach out to us at thebigbeng@ucsd.edu or d8gonzal@ucsd.edu We can't wait to hear from you!

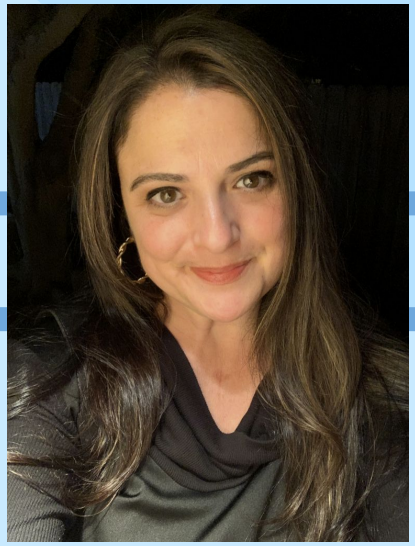
Interview with Physician

At Ellen Browning Scripps Memorial Pier

Dr. Rebecca Rakow-Penner

Adventures in Diagnostic Radiology

By Meenakshi Singhal | Deputy Editor-in-Chief



Dr. Rebecca Rakow-Penner, MD, PhD is an Assistant Professor of Radiology at UCSD Health. As a physician-scientist with an engineering background, she works at the forefront of translational medicine. Dr. Rakow-Penner is both a board certified diagnostic radiologist and the principal investigator of a lab dedicated to developing forward-thinking and noninvasive imaging technologies. Women's health is a key theme throughout Dr. Rakow-Penner's career; in this BEN interview, we learn more about her informed perspective on making meaningful strides in this underserved and necessary research area.

Q: **Can you share your career path as a diagnostic radiologist, and how you became involved in the subspecialty area of women's health imaging?**

I'm specifically interested in advancing women's health with engineering techniques. I started off as a bioengineering undergrad at Harvard and at some point realized I was the only woman in many of my engineering classes. I also started working in a lab as an undergrad where I was the only woman. Sometimes it takes a woman sitting at the table to think about diseases that are related to women's health. We have a large number of undergrads here at UCSD that are women in bioengineering, which I think is fabulous and a really nice change compared to my experience. I think that will redirect resources to ideas and challenges that face women's health—to be approached by women that think of the idea in the first place. Anyways, I decided to dedicate my career to women's health and imaging as an undergraduate.

A beautiful thing about engineering is that part of the training is to not just fix things, but to define a real need and then to address it. It's very empowering to define a problem and solve it, especially when its impactful. It's much easier to wake up every day and know you're going to love your job. I really enjoyed my electrical engineering classes like signal processing. I said "Okay, I want to play around with image processing". I wasn't definitely sure I wanted to do medical school in undergrad. That was a decision I made in the middle of graduate school. During undergrad I worked in a lab where we built MRI receiving coils, and we were specifically working on heart imaging at the time. I wanted to build a coil that allowed faster MRI imaging for breast cancer, so as an undergrad that was my senior design project. And that's how it all got started.

Interestingly enough, many of my career decisions were based on how much I enjoyed the people I was working with. I think happiness in a field is often contagious, and people who are passionate about their work are infectious. I have and had great teachers and mentors. I ended up going to Caltech for my master's degree. It was a

great program—I learned more in that one year of my life than any other year in my life—but at the time, they were not closely associated with a hospital. It took me a few months at Caltech to realize that's not the place for me, that my long-term career goals really involved translational research: I wanted to develop technologies that are going to be used for improving human wellness.

At that point I transferred to Stanford University; they were still developing the bioengineering program at the time when I went to grad school there. Therefore, I got my PhD in Biophysics because Bioengineering didn't exist there yet. In Biophysics there's a lot of crossover—I was able to take all of the electrical engineering and math classes I wanted for signal processing, and then also take any of the biology-related classes that I thought were necessary at that point. And then I did my PhD on developing MRI technology for breast cancer patients.

My decision to go to medical school came out of my desire to understand the problems and ask the right questions. In graduate school, I worked on a project that was intended to improve breast cancer images and it didn't work out very well for breast imaging, and then I applied it to knee imaging. And the technique worked really well in the knee. I was frustrated that I developed a solution and then found a problem it solved. I wanted to define the problems. And that's what motivated me to go to medical school.

Thus, I went to medical school, and finished my MD and PhD together at Stanford. I then applied to residency—which brought me to UCSD. At UCSD, they have a special research radiology residency track, where you do an extra year of research as part of your training. I was able to start on many of the projects that are now part of the UCSD Women's Imaging Lab at UCSD as a resident.

I then did a special fellowship in women's imaging. I didn't want to do just breast imaging, and not just body imaging—I wanted to be able to do both of them. Clinically, body imaging involves everything from the diaphragm through the pelvis. And I didn't understand how the ovaries were anymore related to the liver than they were to the breast. So I felt that women's imaging was an appropriate specialty, where I can relate ovarian and breast disease clinically and in the lab. In addition to my clinical work in breast and female pelvis, I perform all the other clinical radiology work involved in the male and female abdomen and pelvis (and I secretly enjoy it all).

Back to women's imaging : there's really a disparity in radiology for women's health and in diagnosing diseases. I think prostate imaging is far ahead of where we are for female pelvis imaging—for ovaries, for endometrium—and I'm just very passionate about working on women's diseases and approaching it with gusto.

Q: **Given your focus on women's health, what do you see as the greatest challenges in effective treatment, and what role can imaging technology play in meeting these needs?**

There are so many questions to ask. In the female pelvis, there's cancer and then there's all the diseases that are not related to cancer, which still need to be figured out. The concept of pelvic pain has existed for a long time—historically, women were treated for hysteria with a hysterectomy – just surgically removing the uterus! Frankly, that's still the treatment for certain causes of female pelvic pain. A lot of gynecologists' diagnoses are still based on the physical exam because radiology has not done its best job in terms of making imaging useful for this subspecialty. One of the projects I'm working on now for cervical cancer is to be able to better evaluate response to radiation treatment with MRI, and that should help change the course of management compared to the standard of care right now.

Ovarian cancer screening is also a big challenge. There's currently no terrific way for screening a woman for ovarian cancer. Women who are *BRCA1* and *BRCA2* positive have a 10-40% chance of getting ovarian cancer; they just have their ovaries prophylactically removed around age 40, because the risk of ovarian cancer is so high. And there's a lot of value in keeping your ovaries until menopause, for your bones and your general health. If we can prolong a woman safely keeping her ovaries,, that would be great. We do that right now in breast cancer, with patients who have a higher risk of getting breast cancer. We do annual MRI screening for them, and then minimize prophylactic mastectomies.

Q: **What do you see as being the most innovative or crucial technologies/practices currently being developed within diagnostic radiology that could translate to some kind of clinical benefit in the coming years?**

AI is hot, but AI has been involved in radiology for a long, long time. It's just now, more hands are involved in solving radiology problems with AI. AI affects radiology by potentially improving efficiency, decreasing human error and even altering how we acquire and process images.

Additionally, I think radiology in combination with blood markers is really going to be the future. To be able to make a diagnosis based on a blood test and imaging technology together, and being able to predict outcome and diagnosis would be pretty cool. Radiology can be really helpful at catching diseases at the earliest time point (and possibly localizing the origin of disease detected by a circulating blood marker). One goal is to catch disease when patients are still curable. I think we do a pretty darn good job of that with breast cancer screening—but there's definitely room for improvement in breast cancer and other disease processes. Currently, for breast cancer MRI screening we have to give IV contrast, and although there's really no proven long-term effects in humans, it has been demonstrated that contrast used for MRI can deposit in the brain. This makes a lot of patients uncomfortable to know this, and then they don't want the exams. Trying to figure out ways of doing imaging without exogenous contrast is important, and that's something that people are working on currently. We [at UCSD] are also developing a non-contrast breast MRI protocol.

Q: **How have your experiences as a practicing physician informed your research interests? Have you noticed any significant clinical needs during your practice?**

Because of my clinical involvement in breast cancer imaging with *BRCA* patients, I can't help but notice how many of them have prophylactic oophorectomies where they just take out their ovaries around age 40. I think a true need is to be able to figure out a way to screen for cancer, without having to do aggressive surgeries.

And then I think pelvic pain and dysfunction are other ones. There are lots of causes of pelvic pain and dysfunction that can be imaged. For example, many women are ashamed to come to the doctor after pregnancy, with issues with going to the bathroom. There's some dignity involved with this and we need to help women keep their dignity and solve their medical problems. I think these are all things we can better evaluate with improvements in imaging, particularly with MRI. We could then help direct our surgical clinical partners with how to better treat these patients, rather than just telling them "I'm sorry you have pain" and expecting them to live with pain. We want to help give them opportunities to fix it. The better we become as physicians and scientists, the better we can understand the causes of pelvic pain and dysfunction. Hopefully, some of them can be addressed. An example is pelvic congestion syndrome.

There are now imaging and interventions now to treat this cause of pain, that have really surfaced within the last decade. With endometriosis, it's crazy. I think the standard is still to go in there and do a laparoscopic surgery to see if you have endometrial implants; we're working on MRI techniques to be able to look for endometrial implants with high sensitivity so that we can decrease the number of surgical operations required. Also, even if there is a surgical operation planned, we can better direct the gynecologist on where to go to evaluate the area of concern.

Q: **As a physician-scientist, you balance your time in the clinic with research endeavors. Could you explain a typical day in your life?**

Every day is a surprise. There are certain days of the week that are more weighted on the clinical side, and other days, like today, that are weighted more on the research side. On a typical clinical day, I try to minimize distractions so I can focus on my patients; patient care requires your full energy. I will often start at 7:30 in the morning—my first patient in breast imaging clinic is at 7:45 am. I'm either doing biopsies or diagnostic imaging until about noon. And then I'll try to squeeze in a research or teaching conference or lecture between noon and 1; and the afternoon is again filled until around 5pm with patient work. Then oftentimes if students in my lab need to meet with me, I head over to the lab and can have a meeting there for one or two hours. Then at home I put my two kids to bed, I sign clinical reports, I read literature until I can't keep my eyes open anymore, and then it's rinse and repeat the next day. You do have to love your job in order to survive and thrive like this.

On a research day like today, I came in at 8 o'clock instead of 7:30 which is kind of nice. My first meeting today was at 9—researchers tend to not have meetings as early as clinicians which is a nice change of pace for me because I do not love the early morning. On research days, I'm still paged by the clinic about biopsy results or imaging questions from clinical colleagues, so I still have to make a call or two and give patients results and help a colleague. But in general, I'm busy with my students during the day. I had multiple meetings with students today and am doing my own writing—and checking email, which is never-ending. And then I'll wrap up probably around 5 or 6 o'clock today and take care of some reading and what not before bed. Usually I work about one weekend day; each weekend I'm either in lab or at home and putting in a full day of effort to keep up with everything. It's intense, but I think when you love your job it doesn't feel like a job. I know people always talk about work-life balance, and work-life balance is whatever you feel like you need to do to keep sane and everyone has a different threshold. This threshold may vary depending on different stages of work and life.

Q: **If you could give one piece of advice for an undergraduate student who is going on to pursue graduate school—whether med school or graduate school in bioengineering—what would your advice be?**

The best piece of advice I can give is to be passionate. You are more likely to love what you do and are more likely to make an impact. I'm going to make the assumption that everyone is smart who's in the field already. It's really hard to be an engineer in the first place, and to graduate from a program successfully and get into graduate school. So at baseline you're smart; the next level is to be passionate.

Interview with Professors

At San Diego's Balboa Park

Dr. Alysson R. Muotri

A journey to understand human brains

By Meenakshi Singhal | Deputy Editor-in-Chief

Dr. Alysson Muotri is a Professor of Pediatrics and Cellular and Molecular Medicine, as well as the Director of the UC San Diego Stem Cell Program. His visionary research is fundamental to our current understanding of brain organoids. Here we explore the unique ethical implications of working with this model system, and how Dr. Muotri envisions a future enriched by the potential of brain organoids

Q: **Can you provide an overview of your lab's journey with brain organoids/current research endeavors?**

My lab has a mix of experimental and philosophical questions and uses brain organoids as a tool to answer them. Some projects are related to disease modeling, aiming to better treat neurological conditions. Other projects are more on the fundamental side: we ask questions like, what makes us humans? Or, can humans develop and live on other planets? Thus, by using brain organoids to answer these, we can gain a deeper understanding of how the human brain has evolved and develops in utero. These early stages of neurodevelopment are crucial for proper brain function and adaptation.

Q: **What are the ethical challenges associated with generating brain organoid models with increasing neural complexity? How do you see researchers navigating these questions?**

As we build better models of the human brain, we get closer and closer to make them function like a brain. One of the functionalities of the human brain is to become aware and conscious. The brain is so attached to who we are, that we think that if something has a brain, it is conscious. Thus, the ethical dilemma we have is to determine when these organoids could become self-aware. While we are quite far from it, it is a nice exercise and forces us to discuss difficult topics, such as the definition of consciousness and how to measure it in the lab. We have partnered with the UCSD Center for Ethics in Biomedical Research, so we are constantly discussing these issues. You might ask how we can determine whether something is conscious or not—that is a difficult question. In the lab, we can stimulate organoids and see how their electrical networks react. We can also perform experiments applying anesthesia to generate a kind of coma state in the organoids, and see how the networks respond.

From there, we can look at an index of complexity, through which we can then classify the organoids.

Moreover, we promote public debates to gain input from the public as well. So far, what we know is that if we get to that stage (of having conscious brain organoids in a dish) we will pause the research and discuss what is the moral status of these brain organoids. Practically, we will need to define how to treat them in the lab, perhaps following the same rules we have to work with conscious animals, such as mice: how to grow them with no stress, how many do we need to perform a single experiment, how to discard them, and most importantly, how to consent people who donate their cells for us to generate these organoids.

Q: **Your lab has utilized brain organoids to study autism. Could you talk about what kind of information you hope to gain from this research and what inspired you to pursue this direction?**

There are two main goals for the lab: 1) To understand how autism arises and how the genetic alterations—since most of autism is genetic in nature—how those alterations in the genome affect the behavior of the person. This is still an open question. So we all know, and again maybe because we never had the right tools to do it, many people have turned to the mouse model to answer these questions. But what is an "autistic mouse"? We use some of the behavior in animals, but we don't really know how to correlate that with humans. Stem cell modeling, using brain organoids, can help fill the gap from the genetics to the network. Of course it's an organoid, or cells in a dish, which don't have the behavioral component; but we can go up to the circuitries or networks and it allows us to dissect that.

For example, from a single mutated gene, how that creates an individual who has either a remarkable ability—for example, to learn events and have a super special memory, or to have disabilities—for example not to talk: to have an intact brain that doesn't show any sign of alteration, but the person doesn't talk. So we try to understand that. For those who have disabilities, we want to see if we can help that person to do better in their social interactions. Something that bothers people is that often when you talk to autistic individuals, they want them to be able to interact more with other people. Regarding my motivation—initially I had a more academic view of autism—that's how I started, I wanted to know how the human brain becomes so much more social compared to other species. And studying autism and other disorders helps me to understand why the human brain has such a notable social component. Then I had a son who has autism, and my motivation becomes more translational. Now, I really want to move the basic science to clinical trials, and help people with disabilities. It might be a simplistic definition, but it's really what makes us human: the ability to navigate our large social connections, this is what our brains seem to be programmed to do. And if you cannot do that, you can see how one can struggle in life.

Q: **What do you see as being the next "big thing" in brain organoid research to take the next step forward? (vascularization, etc.)**

I think vascularization is one of the biggest limitations, and there are so many labs working on that. What I like is that there are different strategies: even sticking the organoids inside the animals and having the host vascular system penetrate the organoids and vascularize them—similar to how it does with cancer—that's one strategy. It's not the one that we like the most because we don't want to mix species,

and we want the organoids to grow bigger—which would not be acceptable to do in an animal model. So we are taking a bioengineering approach, which I think is more systematic, and we can control it better. We are creating sensors within those systems, like embedding electrodes, so that we can take those recordings and not only show that yes, the vascular system is working, but also prove that it's making the neurons fire more, or mature more—these would be ways to show the vascularization actually improves the model. But other people are trying to stimulate a genetic program through endothelial cells in the hope that these cells will self-organize to create a vascular system. Right now, I think there are many people who are on the verge of creating something, but nobody has actually shown that you do have a perfusable vascularized system, and that it enhances the organoids.

Q: **Do you think a potential avenue of brain organoid research will be tissue transplantation, or will organoids remain a model for studying developmental disorders and disease progression?**

I do see the regenerative part growing as well. I'll give a simple example: people are moving forward with the dopaminergic neurons for Parkinson's disease: so you create dopaminergic neurons, which produce dopamine, and you can transplant it into the 'Parkinsonian brain'. So you go directly to the striatum—since that's where they reside and are dying—and there are now two FDA protocols that have been approved to move forward with this idea. But, this was all before we learned how to grow striatum organoids. Now, the level of dopamine that we can get with these organoids is hundreds of orders of magnitudes more than the single neurons. So maybe, we should adapt these protocols—not to go with dopaminergic neurons, but with intact organoids and just transplant them there. And I can see that this approach might work for brain lesions as well,

or regions that you need a functional unit. And what I like about this approach is that because it's kind of an embryonic and "fetal", or a kind of naive state, it will adapt better to the region where you transplant. So it might form functional connections and adapt very well. We have precedent by transplanting these into the mouse brain, and they become functional there, so I think the next stage is to do that with humans. I think Parkinson's disease is a low-hanging fruit, and there are other conditions where this approach may also work.

Q: **I understand that the protocols to successfully grow brain organoids took quite some time to establish. Could you walk through the process of new efforts to combine different brain structures together using organoids?**

You basically have to learn how to create each piece with a new protocol, then put them together. Just to clarify, there are two ways of growing brain organoids. The first one is what we actually do: you add factors to drive the pluripotent stem cells to become specific brain regions. So you have a cortex, the striatum, the hypothalamus, and so on. We are still learning how to do that, and there are regions that are more difficult because we don't have really good embryology for that region.

Most of the protocols are empirically defined or extrapolated from mouse embryology. And we know what the factors that control mouse brain lesions are, and then adapted that to human cells. But this does not always work: most likely, it's just a good start, but it requires optimization. The second protocol takes a different approach. We call them unguided organoids: you guide the cells to become endothelial cells, then you let them differentiate, and you end up with a single unit that contains many brain regions in there. The beauty of this approach is that you can establish all these brain regions that are made from the same cell. But the problem is that each one of those are so variable that you lose this ability to do for example, disease modeling. In the future, I think this idea of a guided organoid, so building the different pieces and fusing them together to create this circuitry of interest, I think it might pay off. One example—that we're doing as a collaboration with Karl Wahlin from the Department of Ophthalmology—is attaching a retina to the thalamus, and then that to the brain organoid. By having this three way organoid that mimics the neurodevelopment of the visual system, we are hoping to learn how the visual system makes these connections, and how the cortex becomes a visual cortex. We can start learning how this system works and of course there are diseases where people have an intact retina at birth, but the connections to the other structures are defective. We might help these people recover sight by just learning how to stimulate this external process to find the right targets in the visual cortex.

Q: **If you could give one piece of advice for undergraduate students interested in pursuing research in the regenerative medicine/stem cell field, what would it be?**

Get inside a lab as soon as possible. If you like the lab, offer to volunteer and just get your foot inside the door. Then, you can grow from there. It's important to have tissue culture experience—stem cell biologists spend lots of time inside the tissue culture room—so by exposing yourself early on, you know if that's the lifestyle that you want or not. When you gain some experience, you can start moving or rotating in different labs, and find the one that you like the most. I remember when I was a first year undergrad, I wanted so much to learn how to do things in the lab and got involved early on.

Dr. John T. Watson

Breaking the Mold in Search of Innovations to Replicate the Function of Vital Organs

By Nabaan Mir | Interviewer

Dr. Watson is the first scientist from the National Institutes of Health (NIH) to be inducted into National Academy of Engineering (NAE), and he is also the current Director at Whitaker Center for Biomedical Engineering, co-Director at MAS Medical Device Engineering at UCSD. He is a founder of The William J. Von Liebig Center. Moreover, Dr. Watson has been our Community Advisor for 2 years!

Q: **What made you accept the invitation to be the community advisor for BEN? What are your thoughts on BEN as a concept and in its function?**

First, I was honored to be asked to be the Community Advisor for **BEN**. Second, in my role as Head of the BE Outreach Committee I suggested the value of a newsletter for student leadership experience . I think that a newsletter adds to the communication within the department and as something to look forward to each Quarter. But the Newsletter was also something that had to be developed organically from the students rather than having someone from the administration staff trying to make the newsletter or dictating what was being done. The students themselves had to decide, and I think BEN has done a fantastic job so far. The faculty and staff like it, and it has all come from the students' hard work. My role really to see that BEN as the resources it needs and we're not violating any university policies.

I'm also on an advisory board for another UC campus and their newsletter is not from the students but from the administration. In my view, at times it is quite political and I think that's a totally wrong approach. Campus should be non-political in terms of positions they take, and I think a newsletter has an important responsibility to not choose sides supporting a political candidate or belief, but rather be a channel to allow for communication. To that regard, I think **BEN** has done a great job.

Q: **Can you tell us about your childhood experiences and how they influenced your development?**

I grew up in the Indianapolis, Indiana, the Midwest. In the mid-20th century so a very different setting from California now. My mother passed away when I was ten and my father had some construction jobs he managed outside the city. During the week, my older sister and I were latchkey kids who had a lot of

freedom to do what we wanted within the boundaries set by our father. The opportunities that I had available to me were terrific.

Growing up we lived across the street from a large park, and I was in the park just about every day. I didn't study much and hung out with different friends getting into all kinds of fun. We built tunnels since we had construction ideas and built boats. We used to use to take old-time car hoods. They weren't flat like they are now, but very curvy and deep in the front. After patching all the holes, we would get some little old motors from the guys that ran the boat marina and overhaul the hoods into little makeshift boats. We went onto the river to move around and would sometimes by accident sink a boat. I also got interested in cars and I overhauled a Jeep engine in the backyard during the Winter. To my surprise it worked the first time we tried to start the Jeep Station Wagon.

So that was my experience in terms of learning early on. Technical capabilities were very self-taught along with the advice I got from my father and the people that I met in these situations. The curiosity I had and my adventures really taught me a lot.

I also worked shoveling snow, delivering papers, and mowing lawns. My first W-2 job was as a plumber's appreciate working during the summer at Purdue University. Little did I know I would eventually do research on the plumbing of the heart of a patient with heart failure.

Throughout this I was also very close with my sister. She was a few years older and a much better student than I was, and really laid the groundwork in grade school and high school for me to follow before I went off to college. My sister ended up getting a doctorate, as did I, and I wonder if this would have happened had we not had these wonderful experiences.

During high school, Sputnik had gone into orbit and my High School Advisor said "we really need people in engineering to counter the Russians and Sputnik." Also, I entered a car design competition with a car design that you could "change" the color of the roof at any time the owner wished. Along with my mechanical interests, I ended up choosing mechanical engineering.

Q: **When you were in college at the University of Cincinnati you worked through a cooperative education, something that we don't have at UCSD. Looking back, how do you feel about the experience and how did it affect your path?**

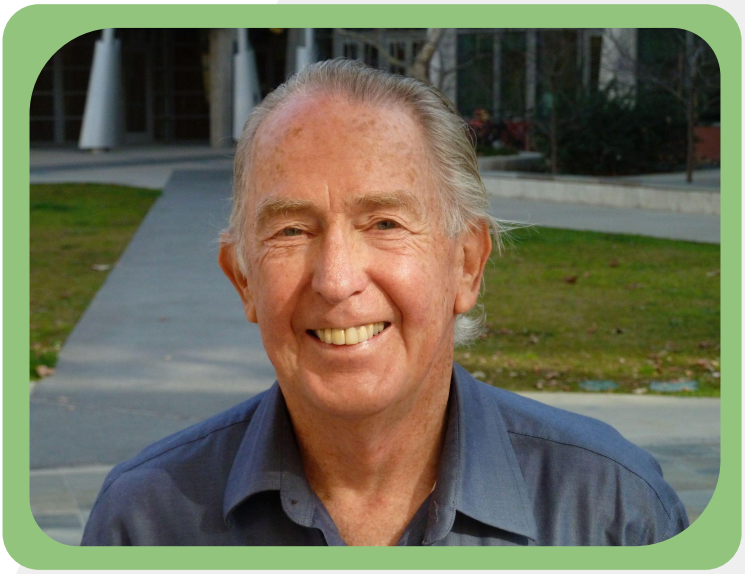
While I was at the University of Cincinnati, I was part of a co-op program that took five rather than four years. It helped pay for my college, but the experience and opportunities were most important. I got the chance to work in the business machine and power industries, so a wide breadth of experiences. When I graduated and was deciding on what job to take, I already had four job offers without an interview.

The power plant was most influential to me, where I worked for the Indianapolis Power & Light Company and balanced large rotating machinery. When dealing with large wind or fossil fuel turbines, there are usually three large bearings: The turbine part has two bearings while the generator part has one. When you turn the turbine off, the main shaft is no longer concentric and it sags between bearings. At the same time, during inspection and overhauling older turbines, blades are often removed for safety matters. So all these things need to be considered to balance the full system and compensate because of the high speed and momentum during function. I

got pretty good at determining the dynamics of rotating machinery (100 tons or more) and putting in the compensation weights for making the turbines operating concentrically and I even got a job offer to do that for the company that insured the turbine.

Having the opportunities in the co-op jobs and the experiences I had over those five years really taught me a lot; It had a lasting impact in the path I was able to follow, and eventually lead to my time at the NIH. I think the job experience is quite important for a developing student along with their coursework, and I wish we also had a similar co-op program here at UCSD.

When I graduated from college, the Vietnam War was going on and we still had the draft. I got called up to go to the draft board and went through physical and written tests. I scored very high on the written exams, so they were interested to make me an officer. As a result, I ended up with a critical skills deferment designing avionics control systems for military aircraft at Ling, Temco, Vought, in Dallas, TX. I worked some on the Crusader and Corsair II, aircraft that are displayed on the Midway



Aircraft Carrier, while I worked the most on the design and testing of the XC-142, a vertical-takeoff transport. So just out of college, I was put in charge of completing the validation testing of the thrust control system used in the propellers and pitch of the propellers on the engines to lift the transport and was involved in the first takeoff of a vertical takeoff transport; which is now in service as the Osprey at Naval Base San Diego. Again, my engineering background along with my co-op experiences both helped me tremendously.

While I was there fulfilling my draft commitment, I discovered Physiology and then designed a medical device for helping control high blood pressure. I contacted the University of Texas Southwestern Medical School and eventually met with the Head of the Department of Physiology and found out my device wouldn't work because I didn't know anything about blood coagulation. In fact, I'd never had a course in biology. But, because of that medical device experience subsequently they admitted me as a graduate student. The aircraft company gave me a scholarship to buy books, pay tuition, and sent me off to the medical school. I took essentially all the medical basic science and some of the clinical courses. My research advisor went on sabbatical in England, so I switched from exercise physiology to reproductive neuroendocrinology. My dissertation focus was in vitro and in vivo studies of the regulation of LH, FSH, and Prolactin in normal and orchidectomized male rats. I ended up going through my PhD training there and then became part of the faculty in physiology and surgery, with primary appointment in surgery where I had an active large animal research laboratory.

Q: **You served the Nation for 27 years at the National Heart, Lung, and Blood Institute (NHLBI). Please tell us about your various NHLBI program accomplishments and experiences at the NIH.**

My research focus is understanding and treating Heart Failure. Heart Failure is a condition equaling affecting men and women, all races, in all decades of life. At Southwestern I obtained NHLBI grants to study the combined effect of assisted circulation and adjuvant agents to increase endocardial blood flow for reversing the heart failure condition. We measured blood flow using radioactive microspheres while controlling cardiac output, heart rate, and blood pressure. The most important result was the inference that beta-blockers could reduce myocardial wall tension, likely improve endocardial blood flow, and improve cardiac function clinically. At a result of this research I was able to help treat dozens of heart failure patients at Parkland Hospital in Dallas.

My background in engineering, physiology, and heart failure research/practice together made me a candidate to work at the National Heart, Lung, and Blood Institute (NHLBI) where I was appointed the head of the artificial heart program and all programs dealing with the engineering in cardiovascular disease. Eventually I became head of clinical and molecular medicine that oversaw all the clinical trials of cardiovascular disease as well as the engineering in cardiovascular disease program.

The backstory for Bioengineering at NIH is quite interesting. Before accepting the NHLBI position I received conflicting views from professional friends about working in the extramural program at NIH. Half said that little could be accomplished because NIH was status quo and the other half said "go for it." Arriving at NIH I learned that in the Intramural program there were over 100+ bioengineers, technicians, and staff that comprised the NIH Biomedical Engineering and Instrumentation Program (BEIP). Murray Eden, a distinguished BE, was Head of the BEIP. But the BEIP was not allowed to do its own research but to be "job shopped" out to assist in other laboratory's research projects. I was shocked that Bioengineers could not conduct their own research programs just like I did at Southwestern.

Learning of the NIH prevailing view of BE, I had two goals: 1) to create a functional substitute vital organ for patients with advanced heart failure and 2) to level the NIH research opportunities for all bioengineers. Fortunately with the support of the community and my NIH colleagues I was able to achieve both. Let's focus on the first goal for this part of the interview.

Q: **With regards to the artificial heart program, what is the story behind its development so far?**

Transplantation of a donor organ is a successful procedure for premature failure of a vital organ such as the heart or kidney. The first kidney transplant was 1954 and heart was 1967. One of the first 10 heart transplant patients lived for over 20 years. It quickly became apparent that the availability of donor organs would never meet the clinical needs of patients with premature heart or kidney failure. Recognizing this need, Congress in the 1960s mandated that NIH should establish an artificial heart and artificial kidney programs. The NHLBI launched the combined Myocardial Infraction Research Unit – Artificial Heart Program In 1964. Dr. Peter Frommer, cardiologist/engineer, was head of the MIRU Program and Dr. Frank Hastings was appointed the first head of the artificial heart program.

The MIRUs became the prototype for today's cardiac and surgery intensive care units.

The heart is really amazing that it can actually produce about 2-3W of energy with a cardiac output of over 20L/min. You know we have about 40-50 million heartbeats in a year? With longer lifespans, if you live to be 100 that's about 4 billion heartbeats and you'd still be pumping away. It's quite an amazing organ that provides a vital function for the body. So the quest for the Artificial Heart Program was to create an alternative to cardiac transplantation as a treatment for premature heart failure.

I was the third Chief of the program(1976-2003). Dr. Hastings died suddenly of a stroke (1964-71) and the second chief was released shortly after arriving at the NHLBI (1974). While the program was mandated by Congress there were no set-aside fund for research and development. By 1977 we successfully competed within the NHLBI for RFP contract research programs to design blood pumps, implantable engines, and systems to transmit the needed power either percutaneously or transcutaneous across the intact skin. This was the first phase of a fifteen year plan to research a goal of **designing highly reliable systems that would function for two years or longer, provide a good quality of life and function; which society can afford.**

The prevailing wisdom from expert cardiologists, surgeons, engineers and scientists was only to duplicate nature with a pulsatile system capable of 10L/min output with normal blood pressure. There were really no other design, biological or medical inputs from the experts. Each phase of the fifteen year plan was approved by Advisory Boards and selected research awards were based on peer-review. Technical and non-technical (eg: ethics, death, culture) reviews were conducted essentially every other year. Each review ended with a "stop or continue" the program vote by the reviewers.

In Phase I we achieved our goals of multiple teams working on their designs while freely sharing their progress and problems with all the other teams. The second phase (1980) called for integration of blood pumps with electrical energy converters and energy transmission mechanisms. The third phase (1984) was to validate the "readiness" of these circulatory assist devices for human clinical trial. This phase included a two-year real-time reliability test of twelve devices on mock-human circulations and biological acceptability in shorter-term calf studies. The fourth phase was a randomized evaluation of mechanical assistance for the treatment of congestive heart failure (REMATCH Trial). The advanced heart failure patients who received the Heartmate I (HM1) had a meaningful improvement in survival and quality of life compared to the control patients receiving optimal medical therapy.

The HM1 demonstrated proof-of-concept but also the limitation of pulsatile systems with flexible pumping surface failure after 100 million cycles. The 15 year program required 16 years and was completed essentially within the estimated budget. Based on what was learned in this program and the research capacity that was developed we released the RFP Innovative Ventricular Assist Systems (1994) to start with a clean sheet to **design highly reliable systems that would function for five years or longer, provide a good quality of life and function; which society can afford.**

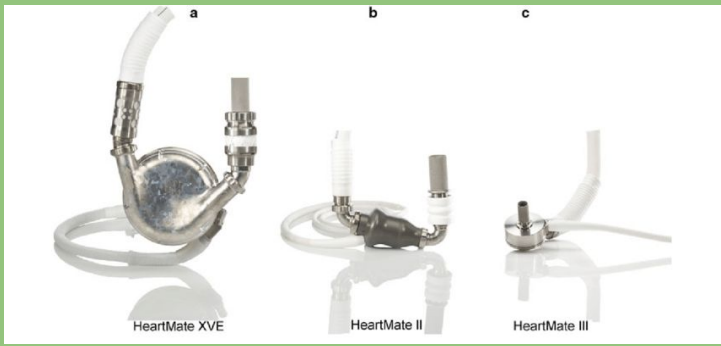
I've always felt that one of the strengths of engineering is that we aren't required to follow any predefined course to get from point A to Point B. We use different pathways to get to the goal, regardless of the perceived normal

way to engineer things. This is a very important concept that was used to duplicate the function of natural life-sustaining organ…the heart. We needed to make sure to perform the needed function, **to deliver nutrients and remove cellular wastes**, using an engineered approach rather than duplicating nature's design.

The heart is a complex four chambered system, but the function can be engineered in a single tube. When you duplicate the natural heart mechanical system that reciprocates – say fills and empties with blood as you pump – you have reverse bending motion and stress fatigue failure can occur quickly. With a rotating tube however, you can produce the same desired function with much lower fatigue and much longer lifetime.

The IVAS program team design concepts, included skeletal fatigue-resistance muscle, resulted in axial flow pumps showing the most potential. Interestingly, continuous flow pumps where the patient no longer has a pulse but a median blood pressure. This led to the creation of the Heartmate II (HM2), which is fully internalized except the primary power source. It met all the design objectives and the longest patients are approaching 20 years with the HM2.

When we started the artificial heart program and had advisory meetings with experts, they came up with only two clinical goals: 10L/min cardiac output and normal blood pressure. What we decided as teams of engineers, biologists, and clinicians was to move away from trying to duplicate the four chambered heart, but to still use the plumbing of the heart for distribution and find another way to produce the two watts of energy at the level of the blood needed to produce a 10L/min cardiac output. The first continuous pumps (HM2) operated 8000-10000 RPM, but newer



HeartMate Evolution of Engineering Design

centrifugal pumps (HM3) operate around 5000 RPM.

There are hundreds of patients now with many years of use, but it's all by producing the function rather than duplicating the anatomy and biology of the human heart. It's amazing that these patients can function without the system incorporating sympathetic or parasympathetic input through innervation. They play volleyball, golf, climb mountains, just about any moderate level of exercise. There are many bioengineering opportunities to reduce the adverse events and the weight of peripheral equipment.

In the artificial heart program, we are currently entering the fourth iteration of devices with two main goals. One is pediatric devices for children. For example, those with hypoplastic left ventricle, a congenital malformation with underdevelopment of the left ventricle, you need a designed device that can be put into the malformed heart, which also varies for each patient. The goal is to have one last a few years while the child grows to become candidate for cardiac transplant.

The other goal is myocardial recovery. In cardiac transplants, sometimes you leave the

patient's heart in place so they have two hearts, and there is a chance that the natural heart recovers and you can take out the donor. About 5-10% of patients recover cardiac function, and so there is wide interest in the field of recovery of function for assisted circulation patients.

Q: **Are you currently continuing your work on the artificial heart program, and what are your current research interests?**

My goal for continuing work in this area are threefold. First to provide immediately a solution for patients with premature heart failure that are otherwise healthy. Their other organs are working well, but for some reason they develop heart failure in a relatively short period of time. The second objective is to have the actual recovery of the natural heart, if we could do that, then the artificial heart can be explanted. The third goal is to have a better understanding of heart failure so that it is treated more effectively. Heart failure is not a disease, but a condition caused by high blood pressure, valvular disease, cardiomyopathy, and other mechanisms contribute to the heart failure condition.

Another area, where I am acting in a limited way, is providing advice on developing artificial kidney innovation. The artificial kidney field has been without innovation goal for almost 50 years. I've been helping to advice the head of that program with the American Society of Nephrology, and I'm helping to try to bring new approaches to performing kidney dialysis.

Best of all, is working with our Bioengineering students to plan and implement activities beyond the classroom like BEN and this Newsletter.

Q: **Throughout your experiences, what are some of the most important lessons you've learned, and important skills to succeed in undergraduate, graduate, and professional settings? Did you ever have a challenge that was too big to overcome?**

Volunteer with confidence! My life has been blessed with opportunities both personally and professionally. My opportunities have appeared just-in-time. I recommend, working with stakeholders, to describe the problem on one-page and determining the top three priorities to succeed. Then develop an implementation strategy.

Growing up, my father always told me that there was nothing I couldn't do, and I always felt confident that I could successfully take on

medical and engineering challenges. That is advice that I would repeat to myself and students. Many things are different today than back then, but this sort of attitude is very powerful. Throughout my life I've never found a challenge that was too difficult to overcome through effort, but I have a realization now that when they talk about senior living and frailty that there is such a thing as frailty, and that probably has given me a challenge that I didn't expect through what I would call a third-party channel.

Let me share an "opportunity" story of a friend of mine. He was in school in Boston, and as a student had a car. They had a lecture series like we have a seminar series and he thought, "what can I do?". He volunteered to pick up the seminar speaker from the airport and bring him to the university. So he would pick up the person at the airport and first take them to his little office down in the basement of a building. He would get to really know them by having read about them and ask them questions as they had some coffee and signed their name

on a large wall with everyone's name, including Nobel Laureates. He went through graduate school picking up seminar speakers and had a really unique experience just because he took an opportunity, and I thought that was really cool. Something that I always tell people and students to do is to volunteer and find opportunities. A lot of things that happened in my life were just due to me taking a chance. Opportunities can be few and far between, and when they come, they often don't last for long so you should always "go for it."

Part II of our interview with Dr. Watson will be published on our next issue!

Warmest congratulations on your graduation, Nabaan!!

Hello, my name is Nabaan Mir. A recent Bioengineering: Biotechnology graduate, I hope to pursue a career in medicine and care for those living amongst our diverse communities. Being a member of the close-knit team of BEN has been a wonderful experience discovering the many stories and adventures within our Department of Bioengineering.

Nabaan has worked diligently on this interview article even after his graduation. We give the best wishes for his next adventure!

Student Spotlight

At San Diego's Balboa Park

Dalila Gonzalez-Mejia

Undergraduate Student

By Yichen Xiang | Editor-in-Chief

I'm a third year Bioengineering transfer student in Marshall College. I transferred from community college in the SF bay area, where I got my A.S.T in Biology and did research at Stanford for a year and a half. My research passion lies within women's health and health disparities. My dream career is to work as a research physician, splitting my time between seeing patients in the clinic as an OB/GYN and working on cutting edge women's health research. I am currently a member of and lab manager for the Smarr Lab on campus. My projects focus on gender disparities in academic achievement and using wearable device data to develop physiological signatures of pregnancy outcomes.

Q: Why are you passionate about women's health, besides the obvious fact that you are a female? Since when have you decided to pursue your research interest?

My passion for women's health started when I was in high school. Long story short, my mom was diagnosed with breast cancer and around the same time I went through a whole ordeal to find out I was born with two uteruses. It was a low-key traumatic part of my life, but through it I discovered my passion for women's health and medicine. I almost failed high school because I was going through all of this and didn't have the right support, but I made it through (barely) and used my community college experience to turn a new leaf and explore my passion for science, medicine, and engineering.

Q: What did you do as a research intern at Stanford University School of Medicine through Canada College, before you transferred to UCSD? Were you able to apply the skills you developed there to your current research projects?

While at community college in the bay area, I had 2 internships at Stanford. The first was with a postdoc at the VA, where I used wet lab techniques to explore immune cell differentiation and extravasation within endothelial cells. I learned so much in such a short time, including cell culture techniques, immunohistochemistry, mouse husbandry, organ preservation, slicing, and imaging, PCR, RT-PCR, ELISA assays, and probably a lot more that has totally slipped my mind. It was an amazing opportunity, but it was unpaid and eventually I had to move forward and seek a paid opportunity.

That led me to my second internship, which was a Stanford collaboration with my community college. A group of Cañada College students were selected to work with the Bogyo lab and look at the effects of non nutritive sweeteners on common gut bacteria.

This position helped me learn about teamwork, bacteria growth, and it gave me my first taste of the realm of biological data analysis.
My current research projects are purely dry lab, and I focus largely on big data and data science techniques to look at physiological time series data. While I haven't' used any wet lab skills from the first internship, I am still constantly using my critical thinking skills, and knowledge of lab culture to succeed in my research and lab manager position. Like I mentioned before, the second internship introduced me to biological data analysis, which I use on a daily basis. I work mainly with python libraries like pandas, matplotlib, and scipy, but occasionally work with R and MATLAB as well.

Q: How does your research experience at UCSD differ from that at Stanford? Was it smooth to find what you want to do and become part of the research team? (How can your experience in joining a research group be improved?)

When I first got to UCSD, I felt overwhelmed at how many different research opportunities there were. I also couldn't quite find one that I was excited to explore. I searched website and papers for an entire year, until one day I was in BENG 1 hearing a guest lecture on time series analyses. I was enthralled by the professor's work so I emailed him right after class, and he accepted me as his student! In reality, it was a longer process of meeting with him and discussing his papers and what I wanted to get out of my research, but it all worked out in the end and I couldn't be happier that I waited for the right opportunity. My current research is a 180 from what I was doing at Stanford, since it's purely data driven, but I love it. I am so excited to see where the physiological data science space will take me next.

Q: Did you experience any obstacle transferring to UCSD? Is there any information/resources that could better aid you in the process, but weren't known to you?

Acclimating to UCSD as a transfer student was really hard. I didn't get involved in many student orgs because I was worried I wouldn't have time for my academics. In the end, I ended up alienating myself and feeling very lonely and out of place. Thankfully, I was able to get more involved in Engineering World Health (EWH) and take the Transfer Year Experience course and that really helped connect me with resources on campus. After getting to know more of the campus and visiting places like the Raza Resource Centro and The Zone (they had free back and neck massages pre-pandemic no lie), I began to feel like I belonged here. I encourage anyone new to UCSD to get out of their comfort zone and try out different clubs and spaces on campus to see what communities feel special to them!

Q: Apart from research, you also actively contribute to multiple student organizations (Engineering World Health and the Big BENG). How did you balance work and life?

First of all, finding the balance is hard. Every quarter, I have to find a new balance depending on what my schedule looks like, what my family needs from me, and what research I'm working on. Sometimes I mess up. Just this quarter, I totally underestimated the amount of time an assignment was going to take and did really poorly on it. My go-to time management strategies are using google calendar *religiously,* scheduling time aside for mental health breaks and date days, and warding off procrastination by switching up where I study. I try to stay away from coffee, but every now and then it's just what I need to get that lab report done. It also just takes knowing yourself and what your bad habits are and trying to work around them. For example, I know that if I'm overwhelmed with how much stuff I have to do, I tend to shut down and binge Netflix. To avoid this, I break my assignments down into super small steps and reward myself after each one. 1) Open google docs. **eats a skittle** 2) Write the heading. **eats a snickers** 3) Look up one research article and spend 15 mins digesting it. **drinks a hot chocolate* etc.

You are a Triton Research and Experiential Learning Scholar (TRELS) and received grants for Fall 20 and Win21 quarters. What is TRELS and what projects were your grants for?

I was lucky enough to be a TRELS scholar for 3 quarters during the 2010-21 school year! They funded my research within the Smarr Lab, focussing on differences in student achievement between majors and gender. Previous research shows that women, on average, have higher GPAs than men when you look at all majors. However, when you look deeper into the data, the same trend does not hold for STEM majors. I'm currently exploring the role of circadian rhythms in this GPA gap, as well as the effect of having low percentages of women in STEM classes.

Q: Anything else you wanna share, be it tips in school/social lives, stories in women's health, or fun facts about you.

Fun fact: I'm married! I always get shocked looks when I tell people this, but I was honestly just really lucky to find an amazing partner early in life. He's a software engineer, a great cook, and super shy but also the silliest person you've ever met.

Academic Tip: Find a mentor that's in the career you want to be in-- ask them if they're happy, what they would have done differently, and what resources they recommend to help you get there. You can find a mentor through a student org, LinkedIn (yes, you can cold message/email!), professional organizations, or grad students on campus!

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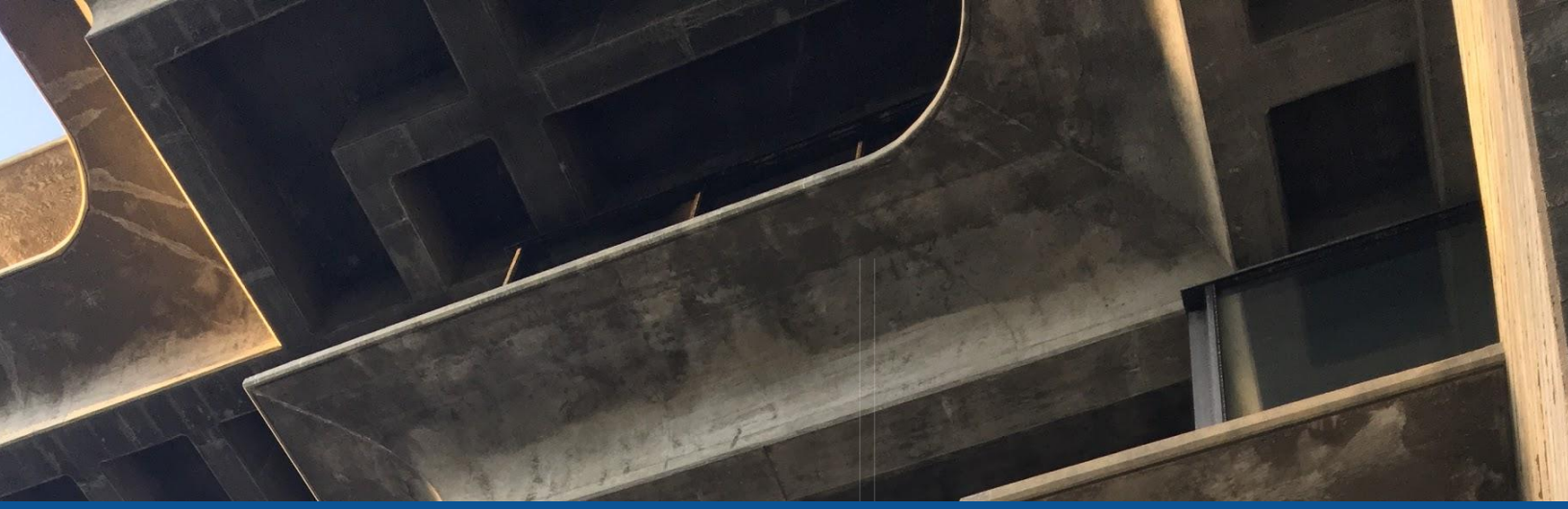

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University of California, San Diego Department of Bioengineering

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