John Boccacino:

Hello and welcome back to the 'Cuse Conversations Podcast. I'm John Boccacino, senior internal communications specialist at Syracuse University.

Shikha Nangia:

My work at Syracuse has led to, for the first time, a molecular model of what the blood-brain barrier is. So we can see which drug molecule can go through the blood-brain barrier, which is like a very narrow tunnel, if you will, between two cells, which is very selective of what goes through. So water can go through, ions can go through, and alcohol goes through. Caffeine goes through. But any other molecules that are Alzheimer's treatment or for cancer treatment, they are large and cannot go through that tunnel.

So we would have to either push the walls of the tunnel to make it bigger for a bigger drug molecule to go through the brain, or we'll have to modify our drugs to be so small that they're at the same order of magnitude as a molecule of caffeine. The trick is, how do you modulate the blood-brain barrier, so it becomes a little bit large when the drug molecule goes, but it closes back and becomes small again after the drug has gone into the brain.

John Boccacino:

Our guest on this episode of the 'Cuse Conversations Podcast, she is Shikha Nangia, the Milton and Anne Stevenson endowed professor of biomedical and chemical engineering, and also the biomedical and chemical engineering department chair here in the College of Engineering and Computer Science.

Nangia's research group focuses on studying blood-brain barrier, which is a tightly locked layer of cells that protect and defend your brain from harmful substances, germs, and other things that could cause damage. But while this barrier serves to protect our brains, in the case of finding cures for Alzheimer's and Parkinson's, the blood-brain barrier has been a big obstacle.

We'll enter Nangia's research group, which uses theoretical and computational techniques to figure out how to best enable the transport of drug molecules across the blood-brain barrier. Now, this group is conducting fascinating and timely research, and on this episode, Nangia will explain the findings of her research, share how students help advance this work, discuss the interactive biomaterials REU site on campus, and also explore her role as a Syracuse University Art Museum faculty fellow.

Shikha, thanks for making the time to join me on the podcast today.

Shikha Nangia:

Thank you, John. I'm really excited to talk to you and tell us about the various things we do on campus with our students.

John Boccacino:

Give our audience a little background on yourself, and what really motivated this interest in studying biomedical and chemical engineering.

Shikha Nangia:

Growing up as a child, I've always thought that, as a person of the society, I need to give back to the community, and my education set me up for that. I felt that helping people with new inventions that can help their daily life was best served by engineering solutions to diseases that we cannot cure easily. So my interest in blood-brain barrier or how to treat Alzheimer's disease and brain-related diseases led me to this field.

And I'm very happy to where I'm here today as a faculty member who's not only teaching, but also able to do research with stellar students, and make that breakthrough that we need for this disease. So, in my role as a chair, I am also able to oversee other things that our department does in this area. So overall, it's a very fulfilling experience from my childhood through this education and being now in the biomedical and chemical engineering department.

John Boccacino:

Was there any sort of personal connection that you had, growing up with someone who was afflicted with Alzheimer's or Parkinson's that maybe fueled this research for you?

Shikha Nangia:

Yeah, there have always been people around me, whether it is extended family or grandparents of my friends. And I have always found that it is such a debilitating disease that you see a person, you lose a person while they're in front of you, because Alzheimer's is something that happens gradually. And, in every sort of situation, it's always difficult to see that a person has forgotten their loved ones, and that had a very huge impact.

And if you look at the statistics, which actually really, really inspired me, were that out of the 10 leading causes of death in America, Alzheimer's is a six, or brain-related diseases is sixth, and it is the only one for which there is no cure. So even if there are drugs on the market, they are only to slow it down, there's no cure, and that fueled the statistics, and knowing people around me felt that we needed to do something about it and motivated me.

John Boccacino:

Tell us about this blood-brain barrier and a little bit more about how it is a prevention to finding a cure for Alzheimer's and Parkinson's.

Shikha Nangia:

Yeah. So the interesting thing about the blood-brain barrier is that it is a defense mechanism of a living organism to protect its brain, its spinal cord, all the functions the body does, to protect it from anything that is in the bloodstream. So if you ingest food which was infected by bacteria, you would like that bacteria never to make it to your brain and change your bodily functions, your motor skills. And so, this blood-brain barrier is in place to keep bacteria out, keep viruses out, keep any toxins out as long as it can, based on its behavior.

Now, how it was discovered is also very interesting. If you go back to the late 1800s, an experimental was done on mice in which a blue dye was injected in the tail of a mouse, and the blue dye colored the body of the mouse blue, except the brain and the spinal cord.

And then a reverse experiment was done a few decades later in which a blue dye was injected, the same blue dye was injected in the brain of the mouse, and the brain stayed blue, the spinal cord turned blue, but not the rest of the body. And that led to this name of the blood-brain barrier, that there was something preventing that blue dye to go across that.

And now, after 150 years or so, we are still not able to get our drugs through just like the blue dye doesn't go through. So from that fundamental understanding of there is a barrier to now where we want to treat brain tumors, Alzheimer's, and others, all our drugs, chemotherapy, all that acts like the blue dye, and is not able to go into the brain. So any long-term solution, or a brain tumor to be treated, has to happen surgically.

You'll have to open the cranium to remove the tumor of the brain. You will not be able to sustainably give chemotherapy for cancers of the brain, or tumors of the brain. And also the same extension to, if

Alzheimer's is spreading over years and people are experiencing Alzheimer's-like symptoms, there is no drug that you could give for that extended period of time that will reverse it or cure it. And the blood-brain barrier, although a necessity is also the hindrance for treatment, and understanding that is critical.

John Boccacino:

What type of research are you doing with your group to advance the study of how we can one day come up with a cure, potentially, for Alzheimer's and Parkinson's?

Shikha Nangia:

Our work is based on computational modeling. We study the interface of the blood and the brain cells using computer models of the brain. And the rationale for doing this is to complement experimental work that has been going for decades around that.

And it's a very tough experiment to study, and none of the experiments are able to give you a very nanoscale. Nano means, if you're splitting hair, it's thinner than that. That resolution that you need to understand what the blood-brain barrier is. So experiments are not able to always provide enough information, but if you'd use this complimentary tool with the advances of computer science and computer modeling, we are able to study at a very, very molecular atom level detail, what this blood-brave barrier interface is.

And so, our work, my work at Syracuse for the last 10 to 12 years, has led to, for the first time, a molecular model of what the blood-brain barrier is. So we can see which drug molecule can go through the blood-brain barrier, which is a very narrow, angstrom-level tunnel, if you will, between two cells, which is very selective of what goes through. So water can go through, ions can go through. And, I am sure the audience will not be surprised if I tell them alcohol goes through, caffeine goes through.

And all these molecules that we get used to, addicted to, or feel in our brain, of our motor skills changing or enthusiasm when we have coffee and caffeine, and those are examples of molecules that cross the blood-brain barrier, but any other molecules that are Alzheimer's treatment or for cancer treatment, they are large and cannot go through that tunnel. So we would have to either push the walls of the tunnel to make it bigger for a bigger drug molecule to go through the brain, or we'll have to modify our drugs to be so small that they're at the same order of magnitude as a molecule of caffeine, so that it goes through.

So we are at that interface that we now understand what it is, it's time now to design better drugs, or to push the walls of the blood-brain barrier. Obviously, we cannot break the blood-brain barrier because it's essential for our survival. So, the trick is how do you modulate the blood-brain barrier, so it becomes a little bit large when the drug molecule goes, but it closes back and becomes small again after the drug has gone into the brain.

So, we are tweaking with that interface of how to better serve the community who's suffering from this debilitating disease.

John Boccacino:

What are the next steps? How do you take the research that we've developed here on campus and work with drug makers, work with the pharmaceutical companies to try to advance the research and make this where we might be able to come up with a cure one day?

Shikha Nangia:

The first test would be in the modification that we are trying to do at the interface, and we will do mouse model, just like 150 years ago with the blue dye. We'll have to take the same kind of approach where the modulators that we are using to make the blood-brain barrier wider will have to be tested in mice.

And so, I have collaborators that are in Brigham and Women's Hospital, Harvard Medical School, the University of Michigan and Rensselaer Polytechnic Institute, and other places where they are seeing the models that we have created, and testing them in mice. And once we see that we are able to achieve that, at the next level, we'll have to think about clinical trials, think about how do you get FDA approvals, talk to industry who's interested in this area. And so, this is a long road, but it starts with the first fundamental understanding that we obtain through our models.

John Boccacino:

And how does Syracuse University enable you and your group to pursue this research? What gives us a leg up when it comes to making progress and strides in this field?

Shikha Nangia:

I will give kudos to the research computing that we have available on campus. The research computing group on campus provides state-of-the-art computer facilities. We have extensive array and sets of computer systems that we are able to use. So my research lab uses extensively cluster called Zest, where all our simulations run over extended period of time, sometimes even weeks and months, which enables us to do that.

So the leg up that we get is the capability of extensive computational facility that we have. And the folks at Research Computing are very, very supportive. So anytime we have a glitch or need support, they are here to help us, so to keep the computers busy and keep the students making progress.

John Boccacino:

And then, how unique does that make us situated in the research landscape, to be able to produce results like this on a college campus?

Shikha Nangia:

I would say it is among the top few schools, or across the country, that have in-house capabilities of such a good research computing environment. And plus, it also is the focus. Not many schools or many research groups are using the computational modeling for this purpose right now. So I think the combination of the research interests I have, plus the availability of the computing environment, makes us unique overall. So I would say, just that being on a Syracuse campus is really, really enriching to this work.

John Boccacino:

The students themselves too, play a large role. How would you describe the impact that student researchers play in advancing your very timely research?

Shikha Nangia:

Students are critical, because all the work that I said we've been doing is all students, and these students are at the postdoc level, the graduate level, master's student, and undergrads. I mentor students at all levels, and over the years they have come from different backgrounds, whether it is biomedical engineering students or chemical engineering. I've had chemistry students, biology students, neurobiology students in the lab, and even physics and math students.

The idea is that computer science and modeling, that the way we work, sits at the interface of all these disciplines, and all it takes is a student who wants to contribute to this research area, and we in our lab have developed various onboarding mechanisms of students of different background to come and work with us. So within the next, a student joins in about two to three months, they're able to participate in doing these research projects that we have.

So, helping the student from where they are, to becoming researcher has been a very important part of what I do. And students overall, I would say I have mentored in these past 12, 13 years, almost a hundred students plus, at various levels total overall. I could have ideas, but if they are not students who are taking this forward, nothing can happen. So the success of the research program lies on the shoulders of these hundred plus students.

John Boccacino:

And what are some ways you're able to form a bond with the student researchers, and not only get them to understand the objective, but help them be in a position where they can thrive, grow, and contribute?

Shikha Nangia:

I strongly believe that for any student who performs well, they should be given the freedom to express themselves and give them a happy, healthy environment. And so, I give students a lot of flexibility in their schedules of when they want to come in.

What requires is, giving the student first a very simplified overview of what this research is before you pull them into the technicality of these things, because they will develop over time. But to simplify the things and say, this is what is happening. And if it's a undergraduate student, you pair them up with a senior PhD student or a master's student, and they can work in tandem and work with each other.

And overall, this is a team effort where the whole team is looking and working together to one common goal, and everybody's encouraged to express freely, and is respected. And that whole environment that we are a group of researchers who are happy in doing what we are doing, so it's a team, it's the environment, it's being a research family, I think, that enables this.

And it is otherwise hard to maintain a group of a large number of researchers with eight PhD students that I have and multiple undergrads. It's the family research, in it together, kind of an attitude that I feel helps students. And there's no bad question to ask. There is no worry about, I don't understand this. Can I... I'll be happy to explain and students help each other a lot. So there is that community or group feeling, family feeling in the group that really leads the way to doing good research.

John Boccacino:

Yeah, that collaborative family environment really does seem to be the key to being successful on all levels. And I'm wondering if you have any examples you'd like to share of some research success stories that your students have played a role in, specifically in advancing this type of biomedical and chemical engineering research when it comes to treating Alzheimer's and Parkinson's?

Shikha Nangia:

So I have several, but I'll focus on one. About four years ago, right after COVID, one of my PhD students graduated. She was deeply into understanding this blood-brain barrier interface. She worked as a postdoc in an industry and was looking at other ways, because when you are doing a postdoc, you want to broaden your horizon. So she started working and working in antibodies, which is another way to try and treat Alzheimer's and brain-related diseases. So she gained experience in that company.

And then, she was able to very quickly after the postdoc be a scientist at Genentech in the Bay Area. And right now she is doing research and development and has been able to bring computational tools that she learned here at Syracuse University to Genentech, and she's leading the computer aspect, modeling aspect at Genentech.

So, she is working at the interface of experimentalists, and she is the one who is able to progress Genentech's vision of what computational modeling of the next new drugs that they're going to put out.

The tools that she's using is what she learned at Syracuse through the research computing environment that she had, and she's able to make a difference in the real world, in a company that is looking at the blood-brain barrier very, very strategically.

John Boccacino:

Yeah, it's a great example of how the time here on campus set a student up for success in their career opportunities. And I kind of want to segue to another group that you're heavily involved with that also prepares students for successful careers in science and engineering. And it's the National Science Foundation-funded Interactive Biomaterials REU site here at Syracuse University. Give our audience a little background on the goals of the REU, and how it will position students who get involved for career success.

Shikha Nangia:

An REU program is Research Experience for Undergrads. That's what REU stands for. And National Science Foundation has many, many universities that serve as an REU site. Every site that is funded through NSF has its expertise. What it entails is, giving students experience in a research lab over the summer. And depending on the size of the REU site, the number of students that participate in the summer research can vary.

At Syracuse, we have an REU site, which has been funded for now, almost 15 years. So many, many students have gone through this REU site. Every year, we bring 10 students from across the country to come to Syracuse campus for 10 weeks, and each of those 10 students are matched with a research lab of their interest. The faculty are the faculty on campus, plus we have a few collaborative faculty in SUNY ESF, and even upstate medical schools that participate in this, and they host one student each, so overall 10.

So the idea is to bring in the fold of the research enterprise more and more students who are studying all across the country, maybe are not able to do research at their home institution, but they apply to us around this time every year in February. So the applications are right now open. Students apply to us. We would select students who need this opportunity, who have research interests that match the faculty on campus. And the whole REU site, the 10-week program starts in around the first week of June.

And it culminates with the students learning what is happening on campus, the research that they're doing, and they're able to have professional development exercises that we do with them, how to write an abstract, how to go to a conference, how to present your research, things like that. And then, it culminates with a celebration, if you will, of students presenting their research as posters. And that's a big event on campus, and that happens in the first week of August.

So the cycle that I just described to you happens every year and has been happening for 15 years. So, I'm thinking if I were to just do a rough calculation, about 150 to 170 students have gone through Syracuse REU site in this past 15 years.

John Boccacino:

The fact that we've been continually rewarded by the NSF really shows what great work you and your colleagues across campus are doing to be trusted to get these student researchers to come in, and to thrive and grow in that environment.

Shikha Nangia:

Yeah, it's been a very ... I think from faculty point of view, we get to train new students, we get to bring a student into the fold. And these students, I have to tell you about the successes. These students have gone

on to stay in the STEM fields, either as PhD students elsewhere, because as part of the development here, the professional development, we tell them how to apply for grad schools and do PhDs.

So many of our students that we have tracked through the LinkedIn network that we have, are doing big strides in the field of biomedical engineering and in government jobs, in industry, as well as faculty in different universities. Some of the undergrads who were part of the REU program have even come back to us to do PhD on campus. So it has also become, they come, they love Syracuse University, and they want to come back to do their PhDs in the lab they did research in.

So it's helpful for the research community across the world, but also for Syracuse students as well, because we get to recruit from these students who enjoyed their research with us.

John Boccacino:

You mentioned that ECS has prioritized bringing in students from non-engineering backgrounds to come to Syracuse to study. Why has that been a point of emphasis, and how has that helped advance the department and advance the education that our students receive?

Shikha Nangia:

One good thing about what I describe to you in computational research is, it sits at the interface. And you can think of engineering as also at that thing. Engineering requires you having knowledge of, not only how to take this one thing and make it useful for the community, but you need the expertise, the major of, if you're thinking about a heart rate monitor, not only as a biomedical engineer, you need to build a monitor and know how the circuitry would work and how it measures, but you also want to know how does the heart work.

And a biology student who comes into the engineering fold, maybe through a master's program or a PhD, is able to take that biology knowledge and extend it towards the engineering of the heart rate monitor.

Similarly, if you have a new drug that you made for treatment of any disease, but what is that chemical? How do you purify it? What is its functional aspect? A chemistry student may be able to really bring in their chemistry knowledge to better design, or a process that can produce this chemical in a large quantity so that it can be marketed as a drug.

So there are many inputs to engineering from students who are maybe not undergraduate majors in engineering to bring in their expertise. So our college has been focused on telling students who are in these STEM areas, maybe not engineering, math, physics, biology, chemistry, neuroscience, biophysics, all these students who are at the periphery of engineering, but have in-depth major expertise, to come in and do engineering with us at the master's level to aggregate and amplify their knowledge and use their skills now to engineer stuff.

So we are trying to make these bridge programs for students to come in from different majors into engineering. Because when a student is in a high school, they are familiar with what is physics, what is chemistry, what is biology, what is math? Many schools across the country may not have an engineering elective, and it might be a missed opportunity for us to tell them that, if they come into engineering, they'll be able to take any new discovery and use it and amplify it and engineer it for the betterment of the society.

So we want the majors now who are in chemistry, biology, math, physics, biophysics, to say, all right, I can actually take my knowledge I already have. I call it a T-shaped skill. You have the depth in one major. And I say, cap it with a T-shaped, cross-disciplinary engineering degree, so that you have the depth and the width to take your knowledge and help the society. And that's what engineers do, they engineer solutions.

So if you bring that expertise into this, I feel that we'll be able to really have a much bigger impact by not just training our engineers to keep growing up, but other majors to come in and work with us. And that has been a real focus of recruiting students into the engineering master's program.

John Boccacino:

I'm fascinated with another one of the roles, another one of the hats that you wear here on campus, as a Syracuse University Art Museum faculty fellow. Give our audience a little background on how that experience came to be and what are some of the ways your engineering experiences are being showcased as a faculty fellow.

Shikha Nangia:

The university faculty fellow opportunity came to me last year when my, Dean Goldsmith reached out to me and said, "You should apply for this program." Because he was aware that my personal time I spent doing electronic art, I use Adobe Illustrator to create graphics around my research, and I've been able to publish many of my graphic designs that I have done on journal covers, on scientific journal covers. So I think I have about 12 to 15 journal covers right now.

So he was aware of that, and he said, I think you should showcase your work and share it with the art museum. So that's how that opportunity came about. But once I became the fellow for the art museum, I wanted to connect the museum's artifacts to my class, which I teach. And I teach a very, very interesting class, which is about engineering materials, and materials of different types like wood and metal and ceramics, so I teach my students about that.

And, I was able to collaborate with Kate Holohan in the museum to bring out artifacts from the collection to show my class what, historically, humankind has been able to do. So for example, way back then, if we were building textiles of materials available, if there was no cotton growing, but there were feathers, so how was textile designed with feathers? Then cotton came along, how did people learn to weave it. To now, what is silk and silkworms. To now, what is all the athletic clothes that we have?

So I brought the museum artifact as history that my students should know. So we had a trip to the art museum, and they looked at the various cultures and timelines of the fabric, and then I gave them the opportunity to comment on the current clothing wear that we have. And I asked them to talk about athletic wear, because it's engineered to soak sweat and for you to feel fresh.

So how have we engineered from feathers to athletic clothes now? And then the challenge came is, I asked them, use AI to tell me what'll be the next best fabric that the humans would love to wear. What is not working for athletic wear now that you would like to change? So, the assignment for the class, the final project for the class became an arc from history to the future through, say, fabric. And then there was a similar arc for ceramics or metals used in the past to metals now, things like that. So what will be the future metal, or what will be the future coffee mug look like? What will be a kettle look like in the future? Those are engineering problems to solve.

And so, I gave the students a free landscapers, use AI and tell me what you think would the next thing be. So it ingrained in the students the history appreciation of, humans have been engineering things since forever, and that we will keep doing that in the future and they are important parts. So I tried to empower them that they are a critical part of the society that enables these inventions at the time which become commonplace later.

John Boccacino:

I also like your troubleshooting approach, because I'm curious how with your magazine covers, with the research journals, the fact that you're able to take and illustrate the research and have it then run on the

cover of a magazine to depict it, what's your process? How do you go about designing and capturing and representing your research and art form for these different publications?

Shikha Nangia:

It's an expression of science and creativity. I take liberties as an artist to simplify the details of what a blood-brain barrier is, but to communicate that, even a very tough, tedious problem that we have not solved in 150 years, can be appreciated in art. And that's the walk I like to walk, and use color and use humor in some cases and make it look eclectic.

And the process really is that, what is the message I'm trying to convey and how many different colors I could use. I love color, and that ultimately it's the colors that give that vibrance to it, and that's when I stop. You will not find me, just my personality, not making any black and white or gray images, just the way I think my brain works.

John Boccacino:

The fact that you can go from having a research group that studies blood-brain barrier and ways to treat Alzheimer's and Parkinson's to having art displayed that conveys your very complicated research materials and getting students involved in art as well. You've got a really well-rounded story to tell, and I can't thank you enough for making the time to join us here on the podcast to share your expertise.

She is Shikha Nangia, the Milton and Anne Stevenson, Endowed Professor of Biomedical and Chemical Engineering, and also the department chair of that group here in the College of Engineering and Computer Sciences. Shikha, keep up the great work and thank you for your expertise today.

Shikha Nangia:

Thank you, John. I appreciate you talking to me, and various aspects of things I do. I really appreciate what you do for Syracuse. So thank you for reaching out to me and making this possible. I appreciate you a lot.

John Boccacino:

Thanks for checking out the latest installment of the 'Cuse Conversations Podcast. My name is John Boccacino signing off for the 'Cuse Conversations Podcast.