

Biosensors and being fearless with Lin Tian

The 2021 Breakthrough Prize winner explains how reading widely shaped her worldview, and discusses the vomeronasal organ Tian discusses protein function and structure, and the historic city in China where she was born.

1 September 2024 | by BRADY HUGGETT

This transcript has been lightly edited for clarity; it may contain errors due to the transcription process.

[opening theme music]

Brady Huggett

Welcome to our podcast here at *The Transmitter*. This show is called “[Synaptic](#),” and it looks at the people, the research and the challenges of the neuroscience space. Thank you for joining us. This is Episode 17 of “Synaptic.” My name is Brady Huggett, and I host the show.

[transition music]

For today, I’d like us to go to Chicago, the third-largest city in America by population. I’d like to go back to the year 2000. That year, in Chicago, the city was home to 519,810 people aged 20 to 29 years. That is more than half a million young adults. The city had a bustling food scene even then. That year, the dining establishments in the Chicago area pulled in about \$10 billion in sales, which put it second among metropolitan areas in the U.S. behind Los Angeles.

While Chicago’s theater community has grown since then, even in 2000, it already boasted the Goodman Theater, the Chicago Theater, the Court Theater, and the Steppenwolf Theater Company. Of course, given its location along Lake Michigan, Chicago offers 26 miles of free beaches.

Right around this time, 2000, a recent college graduate in China named [Lin Tian](#) was looking to go abroad and attend graduate school. That’s our guest for today, Lin Tian. She had a serious boyfriend at the time—later they would get married—and they wanted to study in the U.S. together. They sent out about 20 applications and decided they would go to whatever school accepted them both.

That turned out to be Baylor University and Northwestern University. They chose Northwestern. It’s a big city, as Lin says in this podcast. And for young people like her and her boyfriend, the bustle that Chicago provided seemed attractive. Once at Northwestern, Lin came across the lab of [Andreas Matouschek](#), and she thought it was a good fit for her interests. “Biochemistry is the foundation for everything,” she said, and she already found protein structure and function fascinating. When she began to work with him, Matouschek pushed her to be collaborative, to approach other labs at Northwestern when she had questions that she could not answer herself. He challenged her to think about the ways that she could expand her skill set, as she said.

She would take that message forward into her career. We talked about that on this podcast. We also talked about how, for the first week of her postdoc, she felt so out of place that she considered quitting. We talked about how her father’s innate curiosity rubbed off on her as a girl. We talked about the future of exploring the brain, and how she wants her lab to do work that is high risk, high reward. All of that coming up in the next hour or so.

I interviewed Lin on August 14th, 2024, in her office in the Max Planck Florida Institute for Neuroscience in Jupiter, Florida. It was a hot Florida day, temperature in the low 90s, bright sun, and the beach not far away. I put the mics across her desk, and we began.

Let’s pick it up here, where Lin is telling me about her move to Jupiter, and what she likes about her new town. That should be enough to get us started. Here’s your episode of “Synaptic” with Lin Tian, starting right now.

[transition music]

Lin Tian

I have a Wikipedia page or something.

Brady Huggett

Yes. I also have never been to Jupiter before.

Lin Tian

Oh, welcome.

Brady Huggett

In my life. What do you think of it?

Lin Tian

Actually, I really like this place. Its people here, they come everywhere. I don't, haven't met people who actually grow up here.

Brady Huggett

Everyone's a transplant.

Lin Tian

Everyone's a transplant, I feel I live in a Northeastern neighborhood. All my neighbors, they moved at some point from Northeast.

Brady Huggett

Oh, really?

Lin Tian

Yes, a lot of New Yorkers, actually.

Brady Huggett

That's what my Uber driver was saying, that everybody here is from New York.

Lin Tian

Everyone from New York, they moved down.

Brady Huggett

They moved down to have beach houses, etc.

Lin Tian

Yes, exactly. Yes, my whole neighborhood, nobody actually grew up here, which is amazing.

Brady Huggett

That's, you're a transplant, they're a transplant. Everyone's a transplant here.

Lin Tian

Everyone's a transplant. People are very friendly here.

Brady Huggett

Oh, that's nice.

Lin Tian

They're nice and kind.

Brady Huggett

I'll take it.

Lin Tian

You'll take it. It's a nice beach town. I feel it's much better than what I expected. After living here for almost a year, I really like it. I live here, too. I'm five minutes from work. My kids go to school, and there are a lot of kids in the neighborhood. This is a whole campus, has Max Planck, Scripps, and FAU. It's a very dynamic campus.

Brady Huggett

I guess we'll get to this eventually, but when you first thought of coming to Jupiter, what did you think? Had you been to Florida before?

Lin Tian

No, it's never actually on my road map. I never have a thought about moving to Florida because I was just thinking I'm just going to retire at UC Davis. It's a very nice community. I just never thought about this. Actually, my family has never been on a road map.

Brady Huggett

It's funny because people retire here all the time.

Lin Tian

I know, exactly. Everyone should tell me, you moved a place maybe 20 years early.

Brady Huggett

That's right. You just started early.

Lin Tian

Start early.

Brady Huggett

Obviously you're not Floridian by birth. I'm not.

Lin Tian

No.

Brady Huggett

Where were you born?

Lin Tian

I was born in China.

Brady Huggett

What part?

Lin Tian

In the middle of China. It's a historic city called Xi'an.

Brady Huggett

Oh, Xi'an.

Lin Tian

I grew up there.

Brady Huggett

Historical in what way? Temples, pagodas?

Lin Tian

Yes, everything. I think it's the capital of 12th Dynasty in China.

Brady Huggett

Oh, I see.

Lin Tian

It's a very historic city. Everyone, like all the foreigners, they have to visit that place. Even for people growing up outside China, they go back to China, they visit the place, and they feel like, oh, they found their roots there. That's mean a really historic place.

Brady Huggett

Oh, so people from China come to your town because that's one of the original cities of the Chinese Dynasty.

Lin Tian

Yes. Even people who grew up outside China. For example, American-born Chinese, they go back to China, they visit. They still have to go back to my town because they think that they go there, they see the history, they can see their roots. They feel like, "Oh, that's where actually I'm from."

Brady Huggett

I came from. What was it like to grow up in this historical city? You're walking around as a child, can you feel the history or is it just you didn't think about it?

Lin Tian

The history is everywhere. It's like Rome. I know a few of you have been to Rome before.

Brady Huggett

I have, yes.

Lin Tian

It feels exactly like Rome. Everywhere you go, you turn around, it's a historic site. When you grow up there, you don't feel it. It's just normal. Then when I left, I feel like, "Oh, my gosh, I actually grew up in such a historic place." I guess I haven't really get chance to really study Chinese history because I grew up there.

Brady Huggett

When you go someplace new, you realize what the old place had.

Lin Tian

Yes, exactly.

Brady Huggett

How is it that your family was there?

Lin Tian

Oh, yes. I'm the only child in my family. My dad is engineer and my mom is HR manager. I just grew up in a very normal family. I'm actually the first scientist in my family.

Brady Huggett

What engineer was your father?

Lin Tian

My father is a civil engineer.

Brady Huggett

Oh, civil?

Lin Tian

Yes, civil.

Brady Huggett

OK. When you're growing up, you don't have a model for science.

Lin Tian

No, I don't have a model for science. I'm the first scientist in my whole family. Both on my mom's side and my father's side.

Brady Huggett

How did you find your interest?

Lin Tian

I guess it just the life takes a course, right? The life take you where you go, and also opportunities. Now I think about when I was young, my mom told me- I still have a picture, actually. My mom framed it after I became a scientist. I was really into figure out how things works. For example, I was once really fascinated about the fruit fly sample. Then just to look at the wing patterns on the microscope. I was like a kindergartner.

Brady Huggett

Wait a minute, you were looking at fruit flies in kindergarten?

Lin Tian

Yes.

Brady Huggett

Your school was doing that?

Lin Tian

My school was doing that.

Brady Huggett

That's amazing.

Lin Tian

Yes. Then after that, I've been doing a lot of small experiment. I'm fascinated about how the caterpillar transformed to a butterfly. I did some experiment in my own house and grow the caterpillar. To just watch the whole course of the- how the life transformed.

Brady Huggett

The cocoon.

Lin Tian

Yes, exactly. I guess I'm just very curious. That's my nature. I'm always curious to find how things works. Then after I grew up, I went to a very science and technology-focused university. It's called University of Science and Technology.

Brady Huggett

Science and Technology.

Lin Tian

China, it's just interesting that majority of the students there, after they graduate, they come to U.S. for graduate study. I guess from a long time ago I have—Also my dad, because his work, he always travel abroad, and he will bring me a lot of new things. Back when I grew up, China is not like today. It's still very closed environment.

Brady Huggett

When did you grow up? What decade?

Lin Tian

I'm 45 years old. [laughs]

Brady Huggett

It would have been the-

Lin Tian

I grew up with that. How many decades?

Brady Huggett

The '80s?

Lin Tian

The '80s. Yes, the '80s when I grew up.

Brady Huggett

Right. China was just beginning to open up in the '80s.

Lin Tian

Exactly. China just being opened up, and you feel like there's inspiration to go abroad, to explore. I also have this curiosity kind of nature. I just always want to see, oh, what's outside my world? My father, at the time, he also travels abroad a lot. He always bring me some souvenir from Paris. He traveled to Europe a lot so he brings me souvenir. I'm always thinking, "Oh, what's my outside world looks like?" I guess that time, now I think back, there are actually a seed planted in my heart. I really want to go to explore the world beyond.

Brady Huggett

Beyond. Two things, I guess. Number one, you could say maybe that a civil engineer also likes to figure things out.

Lin Tian

I guess so.

Brady Huggett

Maybe you might have got some of this from your father.

Lin Tian

I guess, yes.

Brady Huggett

If he's traveling around, is he also curious like that?

Lin Tian

He's a very curious person, and he always tell me about—His philosophy, always, I feel like really guided me for my whole life. He teaching me how to do multitasking when growing up. He always said, "Oh, you need to hang on for things. You don't give up. Never give up, and then just hanging on there and you will eventually overcome the challenges." He always teaching me how to do multitasking, like during the cooking.

He will tell me like, "Oh, let's cook dinner together, but this you should do first because it takes time." It's like a biological experiment. When you plan experiment, you need to think about, "What's my goal for this week, and what I need to prioritize? While doing this, maybe the time I saved, while I'm waiting, I can do something else." He taught me how to do that, making dinners, how to multitasking. I feel like because of my work, I have to really multitasking to integrate my life to science, to my work, juggling between family and my job. I feel like I just learned how to multitasking when I was young.

Brady Huggett

Saying don't give up-

Lin Tian

Don't give up.

Brady Huggett

-that's perfect for a life in science, right?

Lin Tian

For science. Exactly.

Brady Huggett

Was that because of his job that he was like that, or he was just like that?

Lin Tian

He's just like that. [chuckles] He taught me when I was young, and during my grow up how to multitask things, how to prioritize things, and also be open-minded. He always showed me, he'd bring me the souvenir and tell me, "OK, you should see the whole world." He always wanted me to think about beyond where I live, think about bigger pictures.

Brady Huggett

When he brings a souvenir, do you mean like he goes to Paris and see Eiffel Tower or is it something-

Lin Tian

Yes, Eiffel Tower.

Brady Huggett

Oh, OK.

Lin Tian

He bring me Eiffel Tower. I still have that Eiffel Tower on my desk, and he passed away a few years ago.

Brady Huggett

Oh, he did?

Lin Tian

Yes.

Lin Tian

Then two years ago, we went back to Paris as a whole family, he was not there, and I bought another souvenir, the Eiffel Tower.

Brady Huggett

Is it here?

Lin Tian

No, it's not here. It's at home.

Brady Huggett

Oh, at home.

Lin Tian

Yes. It's really basic Eiffel Tower, you will see everywhere. I don't know. This actually make me think about mentoring, right?

Brady Huggett

Yes.

Lin Tian

How do you enable others, how you inspire others, how you teach them those small things, like building the character set up for success, it's very important.

Brady Huggett

There's either a base level of talent, and you just nurture that by giving them advice on how to do things.

Lin Tian

Right.

Brady Huggett

I'm sorry your father died. I didn't know that.

Lin Tian

He passed away.

Brady Huggett

A couple of years ago.

Lin Tian

A couple of years ago.

Brady Huggett

Was he in the States?

Lin Tian

Yes, he was. He was in the States. Both of my parents immigrated-

Brady Huggett

Oh, they did.

Lin Tian

-about 10 years ago.

Brady Huggett

That would have been California.

Lin Tian

That would have been California, yes.

Brady Huggett

When you moved here, did they move here?

Lin Tian

My mom is still thinking about it.

Brady Huggett

I see.

Lin Tian

I'm really hoping-

Brady Huggett

She's in California.

Lin Tian

-she can move here.

Brady Huggett

Again, you're like, "This is a great place to retire. There's all these retirees."

Lin Tian

I know, yes. California has its own charm.

Brady Huggett

It definitely does. You're going to the University of Science and Technology, right? I do know where that is, I think. It's Anhui Province, right?

Lin Tian

Exactly.

Brady Huggett

That's more eastern in China.

Lin Tian

It's very eastern in China.

Brady Huggett

What was that like?

Lin Tian

It's about five hours drive from Shanghai.

Brady Huggett

Oh, I see. You knew at that point that you wanted to do science? Because you were talking about the caterpillar, that's more like biology.

Lin Tian

I'm neuroscience major.

Brady Huggett

You knew that going in.

Lin Tian

I guess, now I think back, I'm not sure. I was really not sure at the time, but I knew there's something I probably want to do. I would be good at it because I'm always a good kid at school. You're in STEM in China, they put a lot of emphasis on STEM. All the top students go to STEM. It's a natural way going to this great school to study science and technology, especially biology.

Brady Huggett

Did you have to take the Gaokao? You did, obviously.

Lin Tian

No, I was just recommended by the school. I didn't take it.

Brady Huggett

Oh, wow.

Lin Tian

I don't have to do that.

Brady Huggett

Oh, that's nice. I hear how stressful that is.

Lin Tian

It was very stressful. I still think it's stressful today, but I'm just lucky. I guess because my merit at the school, so they just recommended me for direct recruit to that university.

Brady Huggett

You must have done well in the sciences in your high school.

Lin Tian

Yes. I did some science competitions.

Brady Huggett

When you get in there, you're thinking maybe biology, maybe neuroscience?

Lin Tian

Yes, it's biology because I don't know in the '90s people always think in China, they think, "Oh-" I was always told the 21st century-

Brady Huggett

Biology.

Lin Tian

-is biology, is about technology. At that time, I have no idea what that means, how the technology would really change humanity. I have no idea. I took it because everyone telling me, and my dad telling me, you should study biology because that's the new era of science. Then going to the university, the first two years will actually study very broadly, not just biology. We have to really study mathematics, physics, chemistry and biology, so those four different areas.

I think it's really important because the first two years because of the foundation, it's equipped me with a skill set to migrate through different disciplines. You know how to study. When you have a question you're trying to answer, you think about, not just from one perspective, but from many different perspectives.

Brady Huggett

That's very useful. I can see how that pertains to your career today, for sure.

Lin Tian

I think because of early days, I studied everything—I don't remember anything. I feel like I gave back to all my teachers. I think the ways of learning really help you to think about our tackles on different questions today.

Brady Huggett

Because this was a science university, you did not need to take social sciences, literature, you didn't take things. It was all science.

Lin Tian

No, I didn't take any of that. It's a very heavy STEM.

Brady Huggett

You finished that degree, and then, as you said, your father often talked about, maybe going abroad. Had you planned to go abroad for your Ph.D.?

Lin Tian

Yes.

Brady Huggett

You did.

Lin Tian

Right, I did. I started when I was in second year in university. I started studying English. I have to take GRE, I have to take a TOEFL test. I really study hard, English, and to be able to pass those tests. Not just pass, you have to get a really high score. At the same time, we have to be really good at GPA because it's very selective and competitive as a foreigner-

Brady Huggett

For sure.

Lin Tian

-during the process. I started to prepare everything when I'm in second year in university.

Brady Huggett

You had not studied English yet.

Lin Tian

We studied English, but it's not for test-driven.

Brady Huggett

I see.

Lin Tian

It's not like for GRE and those are test-driven tests.

Brady Huggett

You'd taken English growing up-

Lin Tian

Yes, I'd taken English growing up.

Brady Huggett

-but this was specifically for these tests.

Lin Tian

-for test. yes.

Brady Huggett

Because you did come to the U.S. to study.

Lin Tian

I did come to the U.S. Back then, there's no internet. I think the internet just started to dot com, like www dot com. The Silicon Valley just started to take off. For us to apply, we have to go to the library and get the admission office's application form, get their address and phone number. We do have e-mails back then. Then you have to really write, type out all your application and put it in the mail, and then send it to U.S., and you have no clue what's going to happen. Now I think about it, it's actually amazing. You have this hope, right? You have this hope. You think the best thing is going to happen to you. It's amazing.

Brady Huggett

How many schools did you look at?

Lin Tian

I think I applied to probably 20 schools.

Brady Huggett

Oh, that many?

Lin Tian

Yes.

Brady Huggett

That's what you mean. You have hope. There's 20 pieces of hope out there.

Lin Tian

Yes, 20. One of them will work out.

Brady Huggett

Yes. I know this, you end up going to Northwestern. You worked under Andreas Matouschek?

Lin Tian

Yes.

Brady Huggett

Were you specifically looking to work with him?

Lin Tian

Northwestern is the only university, actually, I take both me and my husband.

Brady Huggett

Oh, OK. We missed a step. You were both?

Lin Tian

I met him in college. We're both students at the same university. Also, he's a chemical engineering major. Northwestern, we applied many schools, and we decided we're going to pick the school we will both go together. Northwestern is one of the schools.

Brady Huggett

OK, all right.

Lin Tian

The other one is Baylor College.

Brady Huggett

Oh, those are the two?

Lin Tian

Yes, those are the two.

Brady Huggett

Baylor is good. Baylor's a great school.

Lin Tian

Baylor is good too, but then Northwestern is in Chicago. It's a big city. For young people, it's more attractive, right?

Brady Huggett

Yes, sure. Were you already married?

Lin Tian

No, we haven't married yet.

Brady Huggett

No, you were a couple.

Lin Tian

Yes, we're a couple.

Brady Huggett

OK, so the two of you came to Northwestern.

Lin Tian

We came together, yes.

Brady Huggett

All right, so that was the school. Then when you get there, did you find Andreas?

Lin Tian

We have to do rotations, so I did three rotations, and then I just found, Andreas Matouschek's lab is a good fit for me. Studying biochemistry, I feel like biochemistry is a foundation for everything that time, and studying protein structure and function. Again, think about, how you change some amino acid, and then you can change the function of the protein. We're trying to study how the protein aggregation, or the protein degradation can lead to activation of a new signaling pathway. I found that's really fascinating. Plus, he's a really great mentor.

Brady Huggett

Is he?

Lin Tian

Yes, he's a really great mentor. He always give a lot of positive reinforcement, and he always encourage you, and ask you to challenge, to think about beyond your skill set, right? Think about bigger pictures.

Brady Huggett

Meaning what? Let's say you're doing an experiment, he would come up and say, I don't know, "I can see you're working from this angle. Have you considered other angles?"

Lin Tian

Yes. Also, I think it's really important at time his lab is very biochemistry-focused, which means everything happening in a test tube, right? That's like classical biochemistry. Then the question, what is happening in cells? Things happening in a test tube, or in a purifier, protein, and *E. coli* doesn't mean the same thing will happen in a cell, or even in a neuron. When you cross the biological samples, things may not work the same.

He said, "Oh, this is happening in a test tube. Have you thought about take a step further to look at what's happening in a cell?" His lab is not equipped for that. Then I have to take initiative to go to other lab.

Brady Huggett

In Northwestern.

Lin Tian

In Northwestern, and to initiative some collaborations across lab. If you look at my publication as a graduate student, it's already started collaboration. I guess at that time, he already challenged me to think, "Oh, how can you collaborate to really expand your skill set?" We're asking questions beyond what the—You have to go to find the resources.

Brady Huggett

Yes, almost like, "Here's what you know, but there are other people who know other things. Let's ask them."

Lin Tian

Let's ask them.

Brady Huggett

Then you get this larger body of knowledge to tackle this problem.

Lin Tian

Yes. You have to, but as a graduate student, back then, you can think about it's actually quite daunting to go to another professor and work in another lab and really learn a brand-new skill set. For example, how to grow cells and how to measure protein with confocal microscope because his lab- you find it very comfortable in your own lab. If you have to learn new things in the other lab it's a challenge, right? The thing is, where I'm stuck in my project, and he will tell me, "Oh, maybe you

can think from different perspective,” then I will think about who actually can help me. I will bring this question to other professors and tell them, “This is my challenge. How should I tackle it?” That’s how the collaboration start.

Brady Huggett

You said it’s daunting.

Lin Tian

Yes.

Brady Huggett

Is it daunting because, well, you have to be a little vulnerable? You have to go say, I’m stuck. I don’t know how to do this. Can you help me? Maybe you don’t want to look that way. You’d rather, if I could just figure it out on my own, is that what you mean by it’s daunting?

Lin Tian

Yes. That’s what I tell my students these days as well. You can figure things yourself, but sometimes we can really use help. How did you build this collaborative environment? We all work as a group because everyone has your own strengths and weakness. We need to understand what are our strengths and what are our weakness. We can find help to overcome our weakness, but you can use your strengths. It’s the same thing as a student. When I was a student, I would go out and say, “Oh, I’m stuck. I need some help. Can I do some experiment in your lab?” It’s not easy to do. He encouraged me to do that and to initiate some collaborations. I guess, actually, I learned how to collaborate when I was a graduate student.

Brady Huggett

The more you did it, did it get easier to go up and say, “Hey, I have a problem. I want to learn more. Can I come into your lab?”

Lin Tian

Yes, definitely. That time, I also realized, lab has a wall. We don’t want the lab has a wall. We want the lab without borders. First, for trainees can freely migrate different lab. I think that’s really important. That’s actually prompt me to go to HHMI Janelia.

Brady Huggett

We should say your Ph.D., you’re looking at the proteasome for your Ph.D., right?

Lin Tian

Yes.

Brady Huggett

I think you had a [couple of papers](#) in there, like [Nature Structural & Molecular Biology papers](#).

Lin Tian

You know me well. You did your research.

Brady Huggett

You’re saying those had a bunch of authors on them because you collaborated across Northwestern, right? I think, I don’t know, maybe five or six years for your Ph.D.?

Lin Tian

Yes, five to six years.

Brady Huggett

Six years? I know that you did your postdoc at Janelia. I was curious because I think Janelia, it started in 2006. It had to be brand new.

Lin Tian

It’s brand new. That’s why it’s so exciting. I started my postdoc in April 2007. I’m one of those first cohort of postdoc at Janelia.

Brady Huggett

How did you get without seeing all the people who come through Janelia or the amount of research or the quality of research that was coming out—because it was brand new—how did you decide that’s where you wanted to go?

Lin Tian

Because I was just so inspired by their philosophy. We’ll work together as a team to tackle big questions or challenges. We’ll do that by inventing new technology. That’s what I always wanted. What I was already doing when I was a student, I want to go to a place there’s no walls. I can learn all the new skill set- to be able to gain a new skill set and to be able to tackle bigger picture questions. That’s what I just want to do. I want to be fearless. I don’t have to worry, “Oh, I’m going to go to ask that professor, can I work in your lab to learn this because I’m stuck? I really need to learn this to address this question.”

I feel like if you can go to a place, you only need to focus on asking questions. You don’t have to worry about whether you will be able to do it. There are a lot of support infrastructure to lower the barrier of accessing the resource. It’s just great because that’s really aligned with what I want to do, go after exciting ideas with all means and I don’t have to worry.

Brady Huggett

Let me see if I’m getting this right. At Northwestern, you have a problem. You’re working on a big question, and you’re stuck. You have to go around to professors and say, “Hey, I’d like to learn more about this. Can you help me with this? I have a question.” You actually learn to do that. You like that you got good at doing that. At Janelia, there’s like one question, and everybody already knows, they’re all working on it. You don’t have to go around and ask people. Everybody’s already focused on it. Is that what you’re saying?

Lin Tian

It’s not everyone already focused on it. What I mean is you can just focus on asking big-picture questions, but you don’t have to worry about, “Oh, I need this technology, but I don’t know it. How do I get access to it?” The Janelia already has this philosophy that we need to lower the barrier to access this technology. They have this supporting infrastructure system to help you. For example, if I want to do the two-photon imaging, I can just go to [Karel Svoboda](#)’s lab and I will be able to do it in his lab. I don’t have to get permission. I don’t have to feel like there’s a wall there. I only need to focus on, this is what I want to ask. This is a question, this is a challenge, and I do have a roadblock, but I can just—It’s so easy. I feel like that science should be done.

I know, but at the time, the Janelia just opened up. Nobody knew what’s going to happen.

Brady Huggett

Yes, exactly.

Lin Tian

They focus on brain research, right? Neuroscience, and also system neuroscience. I have no idea what system neuroscience even means. I’m a cell biologist.

Brady Huggett

That was a big change for you, too.

Lin Tian

It’s a big, big change. Yes, actually, after first week of postdoc, I was actually thinking quitting postdoc because I feel the questions they ask at a very different level, something I never thought about. I’m a cell biologist. I just don’t know how to—It’s just very overwhelming the first week, but then again, I think at that time, I really like the movie- I don’t know if you saw the movie called “Kung Fu Panda.”

Brady Huggett

Yes, I loved that movie.

Lin Tian

I love that movie because sometimes I’m that panda. You’re trying to do system neuroscience, but you’re a panda. You don’t look like a system neuroscientist. You don’t have the training to be the system neuroscientist, but eventually, the panda

becomes the king of Kung Fu. You can learn, be open-minded, and eventually, you'll be able to do it. I always think at that time, that movie really helped me because I just feel like, I'm a cell biologist. I came from Northwestern. I'm doing ubiquitin, protein and pathway signal, a very cell-bounded, molecular-driven question, and all of a sudden, I enter this place.

They're trying to ask a very big question about how the brain works. All this technology they use at time, for example, to photoimaging, I was like, "It's just so overwhelming." I never thought about I would be able to do those things.

Brady Huggett

The first week, longer than a week, or the first week? You're like, "I'm overwhelmed. I might've made a mistake."

Lin Tian

Yes, the first week. Actually, I have to say the first month.

Brady Huggett

First month.

Lin Tian

Feel that way. Then I tell myself, I can do it. I would just have to be open-minded and willing to learn new things.

Brady Huggett

I should ask, I don't know if you were married or not then, but did your husband come with you to Virginia?

Lin Tian

He actually, he works in D.C. by the time.

Brady Huggett

Oh, OK.

Lin Tian

That's why I also trying to find a postdoc with geographic limitation.

Brady Huggett

I see, OK. He, the both of you came to D.C., Virginia area.

Lin Tian

Yes.

Brady Huggett

You worked under Loren Looger there, I think.

Lin Tian

Loren Looger, yes.

Brady Huggett

I think he's also very collaborative.

Lin Tian

Oh, he's very collaborative, yes.

Brady Huggett

What was your time like working under him?

Lin Tian

He's also very supportive.

Brady Huggett

He was doing protein bioengineering at this point, right? This was a change for you too?

Lin Tian

It's not, actually, when I first applied, I was thinking, "Oh, that'd be great," because I was working on the proteins and the protein structure and function, but I'm working on one protein at a time. While looking at his work, I said, "Oh, I really want to learn computation modeling because I want to learn how can you work with a complex system based on simulation and prediction." You don't look at one protein at a time, you can look at network level. That's actually the beginning; I was really driven to that idea to be able to build a network model for postsynaptic proteins.

I was really hoping to learn protein modeling, how you can use a computation to design, to change a protein structure to the function. To understand how they work at network level, they collectively.

Brady Huggett

I think, I can't remember how long you were at Janelia, maybe four years?

Lin Tian

No, I was there for almost six years. Another six years.

Brady Huggett

I guess, postdocs have to end, right? Eventually, you're like, "Well, I need to go see if I can get a job as a proper professor."

Lin Tian

Yes. I just, at the beginning, actually, I was not really determined to become a professor. I was actually thinking about alternative careers because I don't know if you remember back in that time, I think there's a depression.

Brady Huggett

Oh, economic.

Lin Tian

As economic was. A lot of professors struggling getting funded. Actually, I witnessed this during my graduate school. I just feel like maybe that's not the life I want. It's very stressful. I was actually thinking, "Oh, maybe I will do my postdoc, think about academia, but at the same time, I'm not really committed." I was thinking, I can maybe do some alternative careers, so we have alternative career committee form at Janelia. At that time, I'm a committee member. We arranged some alternative career workshop. It turned out only a couple postdocs showed up. I'm like, "Oh, OK. I guess my fellow postdocs, now they're interested in alternative career. They're all so dedicated in academia." I guess I don't have the confidence to know, I will be able to do it. That's why I'm thinking about a different path.

Brady Huggett

Like what? Maybe move to industry or work at the NIH?

Lin Tian

Industry or patent law, work at NIH, scientific writing, there are a bunch of those, alternative careers. They're also really good, important career. I guess, then I was thinking, oh, maybe my fellows still there. My fellow postdocs are now interested. I think that they're just so confident this will work out. At that time, when I first started my postdoc, I didn't have that confidence.

Brady Huggett

Then, but if you didn't have that confidence and you saw that no one else was really interested in an alternative career, why did you decide to start applying for?

Lin Tian

Because then I start to working on this develop a GCaMP, the genetically encoded calcium indicator. That's basically my project. I start to really learn different technology, from molecular biology all the way to systems neuroscience. Then, when I'd be able to do that, I feel like, "Oh, I'm capable. I'm capable to learn and to be able to overcome challenges, right?" Then I gain the confidence, I can give a try. At least I can try. If it doesn't work out, that's fine. I'll just try to find something else. If I

don't even try, how come I know? At the time, I was really naive when I'm in this postdoc. We don't even need to apply. Actually, we're not allowed to apply K99. It's an independent past grant. You then, people just think, "Oh, you come from this Disney World." In Janelia, you have no clue about academia, right? Because I never, I never done any grant writing. I don't even know what R01 is. The R01, the NIH system. It's quite naive, actually, when I first started my interview process.

Brady Huggett

I should say, though, when you were feeling like, I don't know if I can do this, and then you had the GCaMP [paper](#), right? This is quite a big paper for you, actually.

Lin Tian

Yes, it's quite a big paper. I think, that time, people haven't realized in 2009, I think a few haven't realized what's this technology going to lead us to. A few years later, you start to say, "Oh, that really can transform the system neuroscience."

Brady Huggett

Yes, I think that's still your most cited paper.

Lin Tian

Yes, it is my most cited paper, yes, for sure.

Brady Huggett

That puts you on the radar a little bit for other people. I like the fact that you're saying, "OK, well, maybe I can give this a try, right?" That sounds like your father saying, "Don't give up, don't give up, right?"

Lin Tian

Yes.

Brady Huggett

You get the job at UC Davis, assistant professor. That means crossing the country again.

Lin Tian

Actually, back, the same, I didn't know, where is the Davis? I have to Google Davis. Yes. that's before my first interview, I got invitation to visit school, OK, UC Davis sounds familiar, where it is, and I could go there, OK. It's northern, between San Francisco and Sacramento. I just decided to just to check it out. I just really like the community.

Brady Huggett

Yes, that's a great school.

Lin Tian

Then it's a great school. I like the sunshine in California because I visit in the springtime, like early springtime, when D.C. was still cold [laughs] and had a lot of snow. I feel like, "Oh, this is a great place." It's also small enough, because that time, I already have my son, my older one is 2 years old. I have to think about the place I need to—I can strive, but also I can have my family.

Brady Huggett

A family, yes.

Lin Tian

Yes, have a family life. Davis is a small town. It's a great place to raise your family. My colleagues are very friendly, very supportive. I just decided, "OK, I will just take it." [laughs]

Brady Huggett

Your husband was working in D.C., so that didn't matter.

Lin Tian

Yes, he works in D.C., and he decided to support me, so he quit his job.

Brady Huggett

Nice. OK.

Lin Tian

Then he eventually found a job in California. [chuckles]

Brady Huggett

He did?

Lin Tian

Yes, he did.

Brady Huggett

What's his career?

Lin Tian

He's a chemical engineer. He also has a Ph.D. in chemical engineer, but now he's a sales manager for South America. He in charge 29 countries in South America, and he speaks Spanish.

Brady Huggett

Oh, he does?

Lin Tian

Yes. [laughs]

Brady Huggett

He learned it?

Lin Tian

He learned it, yes. Because he have to learn it to be able to do his job.

Brady Huggett

What's the company?

Lin Tian

He travels a lot. Chevron.

Brady Huggett

Chevron?

Lin Tian

Yes.

Brady Huggett

Oh, the oil company?

Lin Tian

The oil company.

Brady Huggett

Oh, so you said 29 countries? [crosstalk] In South America?

Lin Tian

In South America.

Brady Huggett
That's amazing.

Lin Tian
Yes. He travels a lot. Yes, he decided to, again, to support me to move here. He took on this new role as a sales manager.

Brady Huggett
Yes. Right. Was he doing that in California?

Lin Tian
No.

Brady Huggett
Oh, no. That's what he's doing now. I said, "OK." You're in California. You're settling into this. I think you're there for 11 years, a long time.

Lin Tian
11 years, yes. A long time.

Brady Huggett
Yes. This is where I think, right? Because you'd had the success at Janelia, you begin to look at not only calcium, but other neurotransmitters and neuromodulators. How can we sense these in the brain, right? Can you tell me about some of that research?

Lin Tian
Yes. When we developed the GCaMP, right?

Brady Huggett
Yes.

Lin Tian
When we develop the GCaMP. I feel like having developing the GCaMP really help us to think about how can we verify those molecules in the brain. Developing GCaMP, this whole process, we develop the workflow, we learn a lot of knowledge, and build the foundations to be able to build a molecule that has a sensitivity and specificity to be able to probe the complex calcium dynamics in the brain. Calcium is not only molecule in the brain. The reason we look at the calcium dynamics, just because calcium is a proxy for-

Brady Huggett
Action potential.

Lin Tian
Action potentials. It's not even action potentials, but calcium is great because it's slow, right? You have more photons, so you have a better signal-to-noise ratio. It's not the only thing. Actually, indeed, the calcium dynamics, it's actually the synaptic plasticity, postsynaptic neuronal activity is modulated by all those input signals. There are neurochemical signals. I really just want to find out how the neurotransmitter system works across scales from molecule to behavior. The critical step is to be able to measure them quantitatively.

Brady Huggett
In real time.

Lin Tian
In real time. Actually, I started to build in glutamate sensor while I was in Loren's lab. Then I just, from there, I'm thinking, OK, I want to look at your modulators, for example, dopamine. I still remember [Alla Karpova](#), she's still a group leader at Janelia, and she came to us, asked, "Can we make a dopamine sensor?" [chuckles] That time, I'm like, "OK, dopamine? I never thought

about.” Then I start to look at those literatures. Dopamine is just such amazing molecule in everything. The hypothesis is, can we build a molecule that actually can transform the dopamine concentration to something like a light signal?

Brady Huggett

Do you use GFP for that?

Lin Tian

I use GFP for that.

Brady Huggett

I had a question about this. As you said, someone came to you and said, “Well, can we sense for dopamine?” Then, I think, you began to have thoughts, “Why can’t we sense for everything?”

Lin Tian

We can sense everything.

Brady Huggett

If we can actually figure all those things out, then you’d really start to figure out how these things work in tandem, right?

Lin Tian

Exactly.

Brady Huggett

If you’re going to do that concurrently, you need more than GFP because you have to have different colors show up. Is that right?

Lin Tian

Yes. That’s what actually we’re working on right now, to be able to expand the color spectrum, not just you have green-red, but now we want to do the far-red near-infrared, and we want to have the color spectrum. Actually, that’s what I show there.

Brady Huggett

Oh, on the left.

Lin Tian

Right, on the left. To be able to use a color spectrum to be able to differentiate or probe all those molecules simultaneously.

Brady Huggett

Not only do you have to build a sensor, but you have to build whatever that fluorescent protein is going to be?

Lin Tian

Yes.

Brady Huggett

Wow.

Lin Tian

Yes. Or leverage what’s already there and to transform that protein to a sensor, the sensing mechanism. A lot we do is we use, for example, today we use AI, AlphaFold, RoseTTAFold, those simulations to guide the protein engineering. Then we have to use engineering to be able to couple this signal event, for example, the binding, the ligand binding domain to bind the ligand. There needs some conformational change during protein binding. How we transform that conformational change to the chromophore changes, for example, proton state to deep proton state, fast enough to capture, mini-second dynamics.

Brady Huggett

I want to talk about how you got from UCD to here. It took 11 years.

Lin Tian

11 years.

Brady Huggett

You become the vice chair of the Department of Biochemistry and, I can't remember.

Lin Tian

Molecular Medicine.

Brady Huggett

That's right. Yes. Then, I don't know, were you looking for a new challenge, or what happened? Or did Max Planck come to you?

Lin Tian

Yes. MPI came to me in the middle of pandemic. Actually, I gave a Zoom talk I think the pandemic, 2000- It was 2020, right? Yes. 2020. In the summer of 2020, I gave a Zoom talk, it was like a seminar. I gave a talk here, and I was asked if I'm interested about this place. I said, "Most likely now," it's probably impossible for us to move because I love my community. It's not just work. Your kids are being raised there. My mum being raised there. Especially, Davis is a very, very close community. We always support each other. My kids grew up with my colleagues' kids. They play baseball together, right? We'll talk about science on the baseball field. [laughs]

Brady Huggett

It's a nice life.

Lin Tian

Yes. It just feel like why I want to move. I also realized the limitation. I feel like after 11 years at a public university focused on teaching and also, of course, research, I start to lose being—I want to be fearless again. I'm on the search committee for multiple faculty search. Whenever I see the new assistant professor come in, I would tell them, "I really miss that time when you start a new lab, you can be fearless. You can dream big."

Brady Huggett

When you say fearless, what do you mean? Because I don't think at times your work is fearful, but you're saying fearless like you can conceive of anything because you're just starting out, you can conceive of anything.

Lin Tian

You can conceive anything, right? You can dream big. You have a real light. This NIH-funded research, you have to submit a grant here and there. Of course, I still do that because I like to collaborate. I always writing grants, not a big deal, but I think you just can't—You do feel that there's a limit, right? You have to spend eight weeks in teaching. Actually, I love teaching, but still, that's take time from you to think about the bigger pictures.

Brady Huggett

From your research.

Lin Tian

Then you do realize you have to live on the resource you have. University is big. Your research may not be aligned with the bigger picture of this such a big university. Also, how can you be able to work like, for example, as an institute, you can work together because there's always internal funding. You don't have to worry about long-term project, high risk, because our research is always high risk, high reward. It's always long-term. It takes longer time to get things to work out and to be able to really- Because for me, I don't want to just develop a technology. I want to really think about, "Oh, this is a question we need to ask. In order to answer this question, we need this new technology."

Think about to build something from a molecule, from simulation in a computational method. It's a simulation to transform that all the way to a molecule that works in a living brain. Then you have to really understand, what's the question? I can tackle what's the killer app, we call killer application. We can move the field forward. It doesn't happen overnight. If you think

about sensor development, every single sensor, a major improvement takes about at least five years. It's a very long-term investment. Although actually I'm very lucky. I never need to be worried about funding.

I'm always well-supported by NIH. You always think about this long-term thing. I always have to use the funding to do something new. Then I will have preliminary data. I can write another grant. I never be able to do things I don't have to think about. I can just go after. I really miss the time I was at Janelia; I feel like that time I can be fearless or when I was an assistant professor. For example, when I start my lab, while I'm building things, but also apply GCaMP to Down syndrome, IPSC model, I have no clue how the IPSC cell works, but I'm fearless.

I feel like, OK, I will be able to- Because I'm naive, I guess, when I was assistant professor. There's a whole empty lab, what I want to do. I have to recruit to get people in the lab. I have to learn how to do the IPSC technology. Then I have to find the collaborators and then eventually find some foundation grant to support me for those bold ideas. All my bold idea actually supported first by the foundation grant before the NIH grant.

At early stage, there's a lot of opportunity to apply early stage, this foundation funding, because you're early-stage investigator, they support you. Once you get to associate professor or by the time I'm already promoted to professor, the MET career, there are not many foundation willing to support MET career professor anymore. I do have a Keck Foundation, which allowed me to do some infrared protein engineering work, but that's it.

Brady Huggett

It's the funding. It's having to find funding that limits the work a little bit because once you get a grant, you have to stick to what that grant should be after.

Lin Tian

You have to stick to it, yes.

Brady Huggett

You felt like here at Max Planck, you would have more freedom.

Lin Tian

I have more freedom.

Brady Huggett

We should say, too, that you did just get a very large grant from the NIH, right?

Lin Tian

Yes.

Brady Huggett

In October last year, the NIH gave, I think, \$11 million for you to work with USC, UCD, Allen Institute, and Stanford, right?

Lin Tian

Yes.

Brady Huggett

Basically, it is to come up with new technologies to track neurotransmitters, neuromodulators, neuropeptides in the brain, right? The idea is, if you can do this, it'll open up new areas of research. That's the whole point, right?

Lin Tian

That's the whole point. This grant is about optimization to optimize technology, right? We already have the first generation. It's a GCaMP evolution. The first GCaMP actually developed in 1997, but it cannot be used in the brain, right? That's why I was supposed to optimize the GCaMP, make it meaningful in the brain. Then eventually it got further optimized until today, this past 15 years, optimization. Finally we have probably the best sensor we can use to have the sensitivity to robustly probe the single-action potential.

I can develop technology, but any technology can have the first generation, but in order to get optimization, it takes time. This grant is really about optimization. I think what I'm saying is if you want to try something new that's more risky, usually it's hard to get the funding for those new things. Max Planck gave me this opportunity so I can focus on optimization. I still have my financial grant going. I love the collaboration. At the same time, I don't have to feel like, "Oh, I'm only optimizing. I can't develop new things anymore."

Brady Huggett

Because you've got other funding to do the cutting-edge new things.

Lin Tian

The new things, the risky thing, like very risky research. I feel like It's really hard to do very risky things at the university setting. Also the long term, right? Like your grant can come and go. You always have to, especially when your lab gets bigger, I always have to worry about, what if I don't have funding, my senior scientists or soft-money positions, they're going to suffer. What I'm going to do, because my nightmare always like, "Oh, if I lose a grant, what about my people?"

Brady Huggett

Somebody suffers.

Lin Tian

Yes, somebody suffer. I have to ask them to do risky things because we want to be able to generate new technology. We have to take a risk. That's why I think it's a good time for me to move because I want to be fearless again.

Brady Huggett

Yes, I love it. Last thing. I have heard you describe the brain more than once. I think this was in a talk you were giving as, I think you said, a dark enclosed box, right? Or a dark enclosed space.

Lin Tian

Yes, dark enclosed space.

Brady Huggett

That's obviously true, right? I was thinking how we know more about the cosmos than we do about this thing that everybody has sitting above their shoulders. We know more about maybe the bottom of the ocean than we do this thing that sits right here. Of course, neuroscience has made huge strides in the past 40, 50 years. Sometimes it does seem daunting to me, right? If you start thinking about things like cognition, memory, consciousness, why do we dream? All these things that we're still trying to figure out. I'm wondering if you also sometimes find it daunting how much there still is to learn.

Lin Tian

Yes, of course. I feel like we just start to scratch the surface. We just start to understanding the brain. We still have a long way to go, but that's exciting because it's massive on no space. I found that's really exciting to go after those exciting ideas. That's making me stay up at night. [laughs] If you think about biology, molecular biology, cell biology, everything apply to neurons, but it's a network. The brain is so vulnerable, so fragile, but they have such a high speed, how those things works. It's a network. It's just amazing. On no space, it make me stay up at night. [laughs]

Brady Huggett

Thank you. This is perfect.

Lin Tian

All right. Thank you. Yes.

[transition music]

Brady Huggett

Fearless. I love that about how she wants her research to be fearless. Also, Jupiter. I wasn't there very long, but I enjoyed my 24 hours. I saw the beach. It was gorgeous. Suddenly, the attraction that people have to that whole area made sense to me. Thank you, Lin, for spending time with me and for a great talk. When we were done, she took me on a tour through her lab, so thank

you for that, too. This episode will be archived on thetransmitter.org, where we also have a transcript. In the transcript, we have inserted links to the main papers that we discussed, so check that out if you'd like more information.

This show can be found wherever you get your podcasts—YouTube, Spotify, Apple, or in whatever podcast app you use. Some of the information for our intro came from the Encyclopedia of Chicago, from the Illinois Census for 2000, and the website for the Chicago Park District. If you'd like to comment on this show or whatever we do with *The Transmitter*, you can find us on the social media platforms X, Blue Sky, Mastodon and LinkedIn. Our theme song was written and performed by Chris Collingwood. Thank you for listening to “Synaptic.” Until next time.

[ending theme music]

Brady Huggett

Do you know who that is?

Lin Tian

Lin Tianmiao.

Brady Huggett

Yes.

Lin Tian

I don't know.

Brady Huggett

She's Chinese; she does textile art and now she's doing installation art.

Lin Tian

Oh, interesting. No, I guess I don't Google myself. [laughs]

Brady Huggett

No.

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