# TRANSCRIPT

## *Key Conversations with Phi Beta Kappa*

### Biophysicist Martin Gruebele on the Future of Scientific Discovery

He studies a broad range of fundamental problems in chemical and biological physics, and thinks deeply about the course of scientific inquiry, and finds fascinating ways to explain things to Fred in this episode, like what Zebrafish and chemical reactions in the Ozone layer can teach us about collaboration, and why more policymakers and scientists should be talking to one another.

Fred Lawrence: This podcast episode was generously funded by two anonymous donors. If you would like to support the podcast in similar ways, please contact Hadley Kelly at hkelly@pbk.org. Thanks for listening.

Hello and welcome to Key Conversations with Phi Beta Kappa. I'm Fred Lawrence, Secretary and CEO of the Phi Beta Kappa Society. On this podcast, we welcome leading thinkers, visionaries, and artists who shape our collective understanding of some of today's most pressing and consequential matters. Many of them are Phi Beta Kappa Visiting Scholars, who travel the country for us visiting campuses and presenting free lectures that we invite you to attend. For the Visiting Scholars schedule, please visit pbk.org.

Today it's a pleasure to welcome Dr. Martin Gruebele, who is the James R. Eizner Endowed Chair in Chemistry and Professor of Physics, Biophysics and Quantitative Biology at the University of Illinois. His research interests include protein and RNA folding, fast dynamics in live cells, vibrational energy flow in molecules, quantum computing and measurement, glass dynamics, and locomotion and sensing dynamics. He has been aptly described as a superstar in the sciences and in addition to his talents as a scientist and educator, he is a gifted endurance athlete in both cycling and ultra running. Welcome, Professor Gruebele.

Dr. Martin Gruebele:

Well, Fred, thank you very much for having me on the show.

Lawrence: Well, we're delighted to have you with us. We've got a lot of things to talk about in terms of your science work and science in the current moment in which we're living, but I want to take you back to the beginning. You were born in Stuttgart in Germany, right?

Gruebele: That's right. 1964. Nice, long time ago.

Lawrence: Is that where you grew up?

Gruebele: No. My family quickly moved from Stuttgart to Munich. I lived there for a few years. When Neil Armstrong landed on the moon, I remember that grainy, white, black and white broadcast in '69, we moved to Austria, where I went to a French full-day school. After that, my family moved to Spain, so I went to a Spanish school for a couple of years, and then finally my parents retired to the U.S. They later moved back to Germany, but all the kids ended up getting stuck in the U.S., and so that's how I ended up going to high school in San Francisco and going to UC Berkeley in the Bay Area for college.

Lawrence: When you came to the States for high school, were you thinking, "This is where I'm going to wind up," or did you not know that at that time?

Gruebele: You know, even to my whatever, you know 16-year-old mind, it wasn't obvious because we had already moved a few times. My dad was doing international construction financing, so where the big work was going on is usually where we ended up moving for several years. So, I was used to the idea of moving around and honestly, if you had asked me then would I be in the U.S. in the year 2020, I would have said, "Who knows? Probably not." But here I am.

Lawrence: Who knows tends to be a pretty good answer to most questions when you're 16. And so, then you went to Berkeley to start your undergraduate studies. Would you say Berkeley is where you became a scientist? Or is there a moment before that when you sort of had that epiphany moment, I think this is what I want to be, this is what I want to do?

Gruebele: People have this at very different times, and I've asked, actually a lot of scientists, because I'm always curious, you know, when this finally hit them. Mine actually hit me really when I was six years old. We had just moved to Vienna and my dad was mowing our lawn, which he did only twice a year, so it grew to a nice height. This was in one of those forested areas out of town where you could more or less do whatever you wanted. It wasn't like houses in the U.S., where the lawn is supposed to be nice in the neighborhood or anything like that.

Anyway, the mower ran out of gas and I asked my father, "So, what do you actually put into water to make gasoline?" Because in my six-year-old mind, orange juice is water with orange stuff in it, and tea is water with tea stuff, and milk is water with-

Lawrence: All liquids are water.

Gruebele: Yeah. White stuff, right? I mean, water and liquid to me were the same thing essentially at that age. And he said, "Well, there is no water in gasoline." And I was completely taken aback and asked him, "So, who are the people who figured this out?" And he said scientists. And that's when I thought, "That's what I've got to do." So, a couple years later I had a chemistry kit in the basement and all of that sort of good stuff, and it went on from there, so by the time I got to Berkeley, I pretty much had decided that I wanted to study physics, and chemistry, and math.

Lawrence: You know, at Phi Beta Kappa, we always talk about the liberal arts and sciences. I'm always careful to say the and sciences part, and you seem to have explored almost all of the and sciences part of liberal arts and sciences. Chemistry, physics, biophysics, quantitative biology, little bit of astronomy on the side, mathematics. That pretty much runs the gamut of the pure sciences. In an era of specialization, this sounds fairly wide ranging. Did you set out to be so wide ranging in your interests? Or did your studies and investigations just kind of take you there?

Gruebele: Yeah, or maybe it's just attention deficit disorder, who knows? You know, I've always been interested in a lot of different things, and what I've found is that almost any problem if you study it for a while and you begin to understand what's not really known gets really interesting. And so, that's one of the reasons why I've been pretty eclectic, because I read the literature and I find things that I don't know about, like I'm trained as a chemist, but a few years back I was in Heidelberg visiting a center on zebrafish, and they had these incredible aquaria along the walls, with mutant zebrafish, tank after tank after tank, and I looked at this and I thought, "Wow. Actually, I've never thought of doing experiments that involve animals, but this is so exciting looking. I've gotta do something there."

And a couple of years later I read a paper on zebrafish locomotion where I didn't agree with what the authors were saying just from reading it, and so I thought, "You know, I got to figure it out by myself." And so, we went out and built a zebrafish facility and did locomotion research and we've got a student, actually I just came off the phone with a student maybe an hour ago, discussing some of our data analysis on zebrafish swimming. So, you know, that's how as a chemist you somehow end up doing work on zebrafish observations.

The bottom line is it's actually not as hard as it might seem to become expert in very different looking things, but you're still an expert only in that area. I might know a lot about zebrafish swimming right now, but that certainly doesn't make me a behavioral ecologist. You know, I have high kudos and respect for the training of those people. Like my friends say as a joke, I know very little bit about a lot of things. You could put it that way.

Lawrence: I think it's fair to say you know a fair amount about a number of things. In some ways, it's a sense that reality, nature, is not disciplinary. We are. We need disciplines in order to organize our thoughts and in order to approach certain problems, but the problem itself is not disciplinary. And I think sometimes we commit an error when we take an investigation or a problem and we pre-limit the inquiry by our own disciplinary preconceptions, as opposed to looking at the problem on its own terms, like this is not an issue about chemistry, or biology, it's about fish. And that will take you in lots of ways, even if chemistry is your port of entry.

Gruebele: Yeah. That's exactly right. Like the analysis techniques that we use on the fish, for instance, are actually from an area in chemistry called chemometrics. That's an analytical chemistry, you know, where you take a lot of complicated data and basically do the right kind of data science on it to filter out the information that you want. Looking back at my publications from recent years, I'd say probably about a third of them, maybe more, are actually with other groups, other people that may be in physics, or in biology, or in imaging. All over the country, all over the world. And that's because that's really the only way to solve problems.

Human knowledge has grown to the point where it really is impossible, whether that's in the arts or the humanities, or in science, for any single person to even master a small fraction of it. And so, we better get used to the idea of rolling up our sleeves and looking at these things together.

Lawrence: Well, I think there really was a time when one could say that one had read everything in the field. That expression I think is no longer coherent.

Gruebele: Yeah. The journal that I edited until a few years ago, the Journal of the American Chemical Society, it publishes I think something like 14,000 pages a year, and that's one journal out of hundreds of chemistry journals. So, yeah, no, that is just not going to happen.

Lawrence: One of the things we talk about in terms of the liberal arts, including the sciences, is the pure sciences, pure science research as opposed to applied. You have spoken about and written about what you call the long-term prospects of science, and I was thinking about that in terms of one of the famous challenges to this, the otherwise admirable Senator William Proxmire and his famous Golden Fleece Award in which he was famous for picking out the names of some very odd sounding pure science experiments and giving them an award for having fleeced the public with tax dollars. And of course, if you wait long enough, some of those odd sounding pure experiments led to some pretty remarkable applied results.

But how do you explain that long-term prospect of science to a general audience, including policymakers like a Proxmire?

Gruebele: Yeah. I mean, so it's actually easiest through examples, because there are many of them. My favorite example of this is the discovery… Einstein's especially general relativity, who would have thought in the early twentieth century that, you know, about 100 years later, this is actually what was going to allow cell phones to give location information to within a few feet, right? And you actually need those corrections, you know. Simple classical mechanics alone doesn't actually do the trick. So, very often things that seem pretty obscure, like some chemical element like silicon that's, like you know, the main ingredient in sand doesn't seem to have an enormous use other than in construction, where certainly it gets used voluminously. It turns out later on, well, sand is actually the basis of our entire computer industry, right?

And so, it's those kinds of examples I think that show people that you have to look in the places that are not obvious to find things that eventually somebody can use to make really great new stuff.

Lawrence: So, let's dive into some of the science in which you've been involved, and we don't have time for all of it given the sheer breadth of what you've done, but I picked out a couple of projects, some of which you're gonna talk about in your year as a Visiting Scholar, and others just interesting work that you've done. Quantum dynamics of energy flow within molecules. How would you describe your work in that and what fields are you drawing on in that work?

Gruebele: So, energy flow in molecules is really the basis of reactivity and the products we get. And some of these are quite laborious to synthesize, and how energy moves around in a molecule when you put it in there via heat, via lasers, other kinds of methods, really determines in the end what you get. And about 70 years ago or so, mid-20th century, when people started seriously looking into this problem, they kind of had to throw up their arms and say, "Everything is statistical." So, we can use simple randomness to try and explain things.

But actually it turns out people were beginning to find discrepancies, for instance in chemical reactions like the ones that are actually necessary to govern the formation of the ozone layer or the structure of the ozone layer, or actually are involved in global warming, to talk about things that people have been worried about more recently. So, what our research did is it actually showed that a thing in mathematics called a fractal that people hadn't really worried about too much actually describes how energy spreads inside a molecule, so it's kind of this fractal that is self-similar and has little tendrils going out everywhere in the molecule.

And this decides where the energy goes, and this actually opens up a new hope in how we might be able to do chemistry. So, now if I take my crystal ball and I look, I try to guess what somebody might do with our research 50 years from now is what I call wave function chemistry. So, the idea instead of heating things, and the reason you do this is you need to get energy to go over a barrier and then you come back down on the other side, and then you get the thing that you want. What if we could actually just tunnel through that barrier and not even have it there at all? It would actually allow you to do chemistry with much less energy expenditure, like literally fractions of a percent of what we're using right now.

So, by being able to do chemistry playing tricks with quantum mechanics, things like synthesizing stuff ala Star Trek. They just say, "Computer, coffee please." And you know, a coffee shows up. I think actually those things are not completely crazy. These are actually things that 50 or 100 years from now that's how people will be doing chemistry.

Lawrence: I want to come back to fish swimming, which you have studied, and you suggest is actually a far more complex system than we might imagine. How did you come upon this, starting from watching the fish and being sort of fascinated with the dynamics of it? How do you understand it as a complex system? What do we learn from that?

Gruebele: Yeah, so the way and behavior people often in the past have done analysis is, you know, to actually make it qualitative, like you might take notes in a notebook on an animal and how it behaves. Or if you make it quantitative, pick out some parameters beforehand, like you might take the fish's bending angle or something like that as it bends its spine back and forth. And so, what we introduced into the analysis and other people did too around the same time, is the idea that you actually let the animal tell you what the variables are.

So, you take very extensive videos of the behavior of the animal as it does its thing, swimming around in the case of the fish, and then you actually take those videos, create a physical model of the animal, so we have actually physical models of the animal that run on a computer, that have all of the elasticity that the fish has, the constraints, it can only bend so far but not this far, all of those sorts of things. And then combine that with a neural network that actually sends signals to this model and actually makes the model move.

And as people often say, if you can imitate something really well, then you're probably beginning to understand it. And so, we've actually gotten to the point where we can basically train this model on the fish that we observe and when you look at the movie of our computer fish, you wouldn't be able to tell that it's not the real animal.

Lawrence: So, let me connect you up with the ancient and the modern and talk a little bit about your fascinating work on glass. As you have described it, there actually are things about glass that we don't really understand that well, even though we use it and it's a major piece of our lives, so what have your studies been and what have we learned about glass all the way down on an atomic and subatomic level?

Gruebele: Yeah, so glass is a beautiful material, but actually one of the hardest to understand materials that humans have ever created. The reason glass is so hard is it never reaches thermodynamic equilibrium. So, many systems, even cells are actually not too far away from thermodynamic equilibrium, and a lot of the things that happen in them happen relatively quickly, so one can simulate them on a computer. But glasses move on such astronomically slow time scales that it's actually very hard to understand how their arrangements come to be and how they would rearrange.

And so, the experiments that we did were basically to say the following: You know, since things move so little and so slowly inside a piece of glass that it's hard to look at the dynamics of motion, why don't we actually just crack a piece of glass open and look at the glass surface? And so, we basically built a microscope that can look at the individual units of glass that are moving around, and there were discussions among the theorists, and there still are, whether these units tend to look more like little balls that hop around on the surface or in the glass, or whether they look more like little strings that snake around, you know, on the surface.

And what our movies of dynamics on the glass surface showed is that they actually were like little balls, and so when you look at one of these movies, you really see clusters of atoms that clump together to make one of these… We call them cooperative units in the glass. And then these clusters will hop from one place to another as a whole unit, instead of individual atoms, you know, hopping around, and this is really how glass surfaces flow. So, they flow actually by these little nanoscopic balls moving and hopping around on the surface. It's quite a sight, actually, when you see one of those movies.

And so, by observing that and seeing that basically with our own eyes, so to speak, for the first time, that was really a revelation, how glasses actually move about.

Lawrence: So, I want to look at science in a broader way with you given the moment that we're living in. The role of science and research during what can only be described as the largest public health crisis globally in a century has brought to the fore all sorts of questions. So, I'm wondering as you think about your work not just in the lab, but now on a more global scale, what kind of a time is this in the history of the world for science and the pursuit of science?

Gruebele: I think it's actually a very exciting time, because when humanity faces big problems and we face many of them, it's not just the current pandemic crisis, but, you know, global warming, industrialization of many of the nations that have not been industrialized in the past, there's a lot of complexities that are facing us. I think science has a lot to contribute to these questions. One of the things that science, scientists need to do more of, and that we perhaps have not been as forthcoming with, is communicating. It's very easy to get into the details of your lab work and, you know, be happy when the little balls jump around on the surface like I was just talking about, right? And so forth. But it's actually really critical I think for scientists to become more engaged, which is one of the reasons for instance I love this opportunity here.

Science sometimes creates problems, right? A lot of the things that we enjoy, refrigeration for instance, came with problems of let's say refrigerants that harm the ozone layer, right? But science often then also can focus on the solution to these problems once they become clear. They're often not clear to the scientists and the engineers, either, at all, any more than the general public, and so one of the messages that I like to have for people out there is that, you know, it's a double-edged sword, right? The things that you create can always be used in different ways, for the good or for evil, and they can work well, or they can have side effects, and it's almost impossible not to have one without the other.

When we think about new stuff and how we can apply it, also immediately start thinking about, "Well, what are some of the possible consequences that this has that might not be like our prime target?" And scientists in the past have not done necessarily that much thinking in that direction. It's been you develop the thing or engineers engineer it into something that actually works out there, and then you kind of just wait and see what happens, right? And then you find that there are aftereffects that you didn't think about, and sometimes they happen very quickly, and sometimes these things might take 20 years to develop, and those are the scary ones, right? Because if something takes a month to develop and then you pull the product or you figure out a science solution to it, harm has been done, but it's been, you know, it's limited. But when something takes

20 years to become a problem, it probably also will take 20 years to solve the problem, and so you need to have that foresight.

And so, that's why I think it's really, really important for scientists to spend time thinking about what could be the side effects of the stuff that I'm thinking about, of the stuff that engineers can make with it? And do that early on in the process. And so, I think scientists definitely have that responsibility and more so now than ever that things are moving faster, that we need to think about all the possible consequences our work can have, and not just the intended one.

Lawrence: Right. My late father worked on the Manhattan Project as a young engineer. This was the discussion with many of them. I think he would probably have said more around the water cooler than actually in the meeting rooms, but what were they creating? What were they inventing?

Gruebele: Exactly.

Lawrence: And of course, during the war, they were thinking of it specifically in terms of a weapon to end war, but none of them was naïve to think that and then it would disappear. Of course, it wasn't going to disappear. So, in some ways there were some scientists who thought about that, and there were some who thought less, and your suggestion that there's an obligation more generally now for scientists to play a role in it, maybe even the answer is you're in it one way or the other. You may choose to say that that's not my project, but if you do, that itself is a kind of normative position that you've taken.

Gruebele: Exactly. And that's exactly right, and it's just what you're saying there. It's not that everybody must do this, right? But we must have enough people, including people who are in the trenches and the sciences, who think about this. Scientists who talk to policymakers. Policymakers who listen to scientists.

Lawrence: So, I would not be forgiven by listeners if I didn't ask you a little bit about this extraordinary ultra racing career of yours, so tell us a little bit about your ultra racing career. You've done marathons, including Boston, solo Race Across America, Ironman competitions, including the last year, 2019, Ironman Hawaii World Championship. So, where does this interest come from and how does this connect with the rest of the scientist, who explores things to their very essence?

Gruebele: Basically, I was one of those kids in elementary, middle, and high school who did not want to do sports. But you know, you get a little more middle aged and start gaining a little bit here or there, and actually about… I don't know, it's maybe 16 years ago now, I decided dieting is not an option for me. I need something else. And so, I picked up a bicycle and I had a friend in town who was into something called ultra racing, so this is just doing things super long distance. So, there is something really fascinating to me about just the idea of endurance, and then enhancing it through contraptions like bicycling, we have this machine, the bike, that we've made so we can move faster.

And so, this just enormously fascinates me. It brings together the human intellect, the technology that we create, the teamwork, because this Race Across America you just mentioned, it's like the Tour de France, right? There's like three team cars that hand you food out of the car window while you're cycling, and you never stop. You ride 21 hours a day and hardly sleep at all if you want to make it to the finish a winner. So, it's a team effort, it's a technological effort, it's an intellectual effort, and it is this endurance effort that's really unique to humans.

Lawrence: Right. Well, I'm looking forward to a wonderful year for you as a Visiting Scholar. I hope you'll come back and join me and report back on what you've found in your various visits. They'll be virtual as much this year as in person, but we're delighted to have you as part of the Phi Beta Kappa Visiting Scholar family this year. Thank you for being with us today.

Gruebele: Well, Fred, thanks for having me on.

Lawrence: This podcast is produced by Lantigua Williams & Co. Cedric Wilson is lead producer. Virginia Lora is our managing producer and Hadley Kelly is the Phi Beta Kappa producer on the show. Our theme song is Back to Back by Yan Perchuk. To learn more about the work of the Phi Beta Kappa Society and our Visiting Scholar program, please visit pbk.org. Thanks for listening. I'm Fred Lawrence. Until next time.

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