Reinhard Laubenbacher Interview

Communicated by Alexander Diaz-Lopez

Reinhard Laubenbacher is a professor in the Department of Cell Biology and director of the Center for Quantitative Medicine at the University of Connecticut Health Center. He is also a professor of computational biology at the Jackson Laboratory for Genomic Medicine. Previously he held faculty positions at Virginia Tech, Wake Forest University, and New Mexico State University. The current interests of his research group include the development of mathematical algorithms and their application to problems in systems biology, in particular the modeling and simulation of molecular networks. An application area of particular interest is cancer systems biology, especially the role of iron metabolism in breast cancer.

Editor's Note: This month graduate student Melinda Lanius is the interviewer.

Lanius: *When and how did you know you wanted to be a mathematician?*

Laubenbacher: I wish I could say that I knew at an early age that I wanted to be a mathematician, but the fact is that I was actually not very interested in mathematics in high school and not very good at it. But I was interested in philosophy, which ultimately led me to mathematics. After a lot of soul searching, I ended up majoring in mathematics at the University of Munich, with a minor in philosophy. During my three years there, I developed an appreciation for mathematics as a form of abstract art, which I retain to this day. In part, I was inspired by a series of beautiful lectures on Hopf algebras by Bodo Pareigis, who also played an important role in my move to the United States, initially as an exchange student on a Fulbright scholarship. Still, it took a while for me to realize that I could possibly make a living doing mathematics research.

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Lanius: *Who encouraged or inspired you?*

Laubenbacher: The school system in Germany, where I grew up, provided at that time a single branching point to a higher education track after fourth grade. Few working-class kids like me took advantage of this option. It was my elementary school teacher, Frau Koenig, who convinced my parents to let me pursue this option, paid the application fee, and coached me for the entrance exams. Without her, I would surely never have pursued a higher education track.

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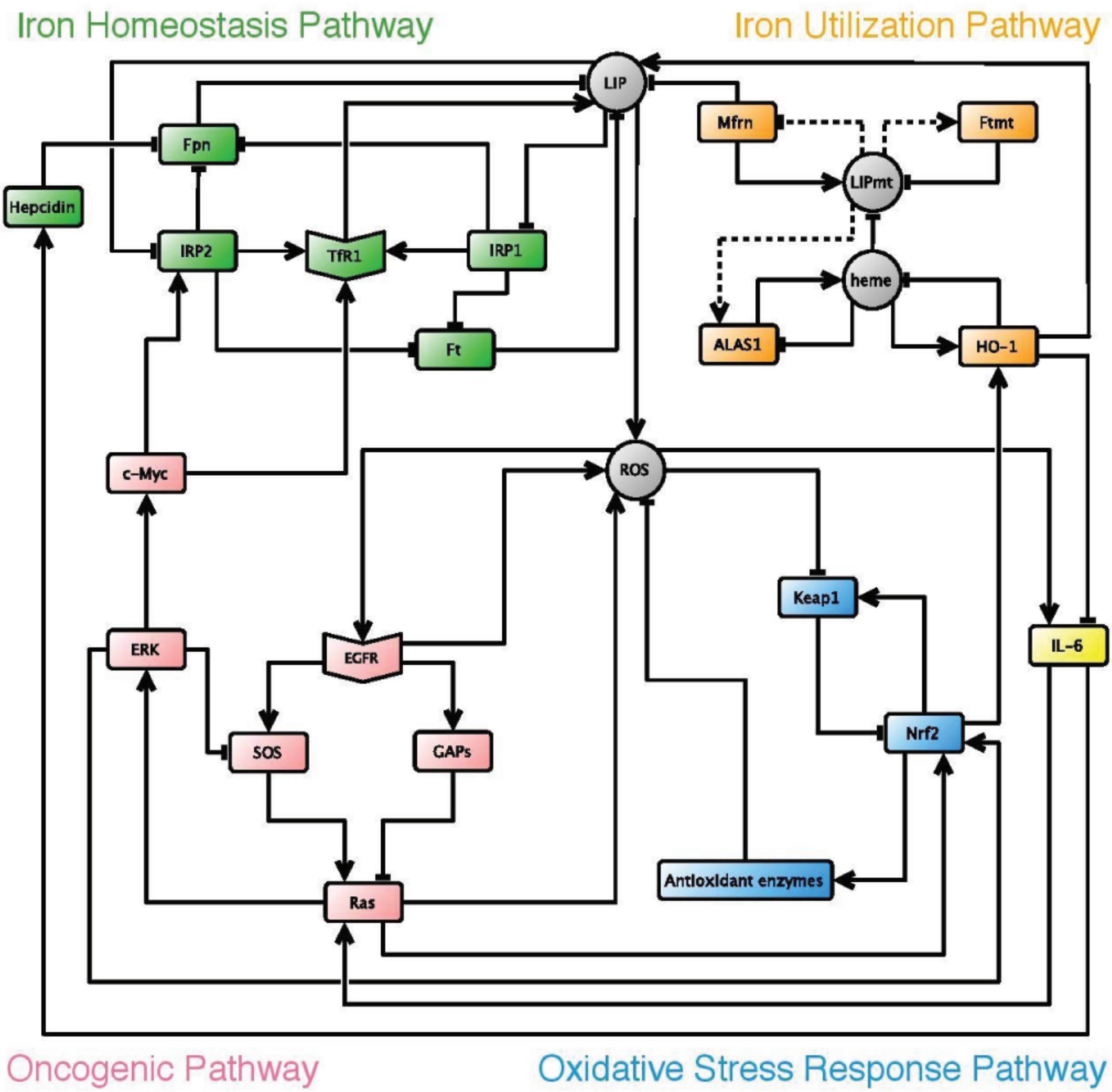

This illustration comes from a collaboration between Laubenbacher's research group and a cancer biology group at UConn Health. It shows a dynamic model of a molecular regulatory network, represented as a graph. The model captures the process by which oncogenes can modify how a cell uses iron and how they can switch a normal cell into one exhibiting a cancer phenotype. The illustration is taken from the paper "Activated oncogenic pathway modifies iron network in breast epithelial cells: A dynamic modeling perspective," by J. Chifman, S. Arat, C. Lopez, S. Torti, and R. Laubenbacher; to appear in *PLoS Computational Biology*, 2017.

I have been very lucky throughout my career in meeting mathematicians and others who have influenced me in many ways, who have been generous with honest advice, and who have provided inspiration through their work. To mention one such person, I had the great fortune to get to know mathematician Bernd Sturmfels, whose work is a wonderful example of an organic symbiosis between what are commonly known as pure and applied mathematics. Throughout his very prolific career he has pursued research at the intersection of algebraic geometry and combinatorics and its applications to statistics, optimization, and the life sciences, among others. He was the reason I switched my research from algebraic *K*-theory to computer algebra soon after I met him.

Another colleague and friend who had a big influence on my work is mathematician David Pengelley, with

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whom I embarked on a wild journey through the history of mathematics and its role in teaching. David has carried on this work and has inspired many others to transform undergraduate mathematics teaching through the use of history and original mathematical sources. My historical work provided some of the motivation for my transition to applied mathematics.

Lanius: *How would you describe your work to a graduate student?*

Laubenbacher: Broadly speaking, my research program consists of three components: the development of mathematical tools and algorithms, their software implementation, and their application to specific health-related problems. Currently, my research group consists of several postdoctoral fellows; graduate and undergraduate students in math, computer science, and biology; a bioinformatician; and a software engineer. We work on a wide range of projects. As an example on the application end, my team works with several other research groups on ways to control the development of resistance to chemotherapy treatment in certain types of breast cancer. We use a mixture of bioinformatics, mathematical modeling, and control theory for this project, together with some new mathematical tools we are developing.

On the software development side, we are currently working to develop a crowd-sourced software package for the analysis of discrete polynomial dynamical systems that uses the novel tool of so-called Docker containers—lightweight software containers that can be used to easily package and connect implemented algorithms in a platform-independent manner.

Mathematically, we use a wide range of tools. One area of expertise we have developed is the construction and use of time-discrete, state-discrete dynamic models, which generalize Boolean networks. Such models can be viewed as maps from an affine space over a finite field to itself, described by a collection of polynomials with coefficients in that field. This makes them amenable to all the tools from computer algebra and algebraic geometry, as well as algebraic combinatorics. There are many very interesting mathematical problems related to such dynamical systems.

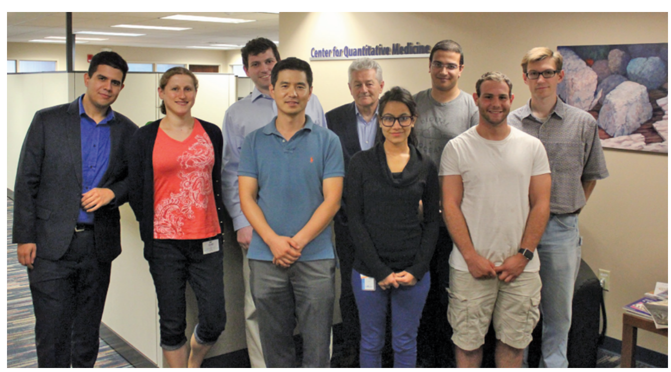
Lanius: *Do you have a favorite past project?*

Laubenbacher: In my previous position at the Virginia Bioinformatics Institute at Virginia Tech, one of my roles for several years was director of Education and Outreach. The project that I am most proud of is Kids' Tech University, an outreach program for nine- to twelve-year-old kids and their guardians. Each year the program enrolls several hundred children at Virginia Tech, which hosts the program, and at other regional sites. The children come to campus on four Saturdays and engage with an internationally known researcher in one of the STEM fields, participate in hands-on activities, and explore what it is like to be a college student. Over a hundred Virginia Tech student volunteers work with the kids on all aspects of the program. The program is continuing, and this semester we have the first volunteer who participated when she was twelve and is now a computer science major. The hypothesis underlying the program is that in order to attract children to STEM careers, they need to get excited about the STEM disciplines, and nobody can convey that excitement better than a researcher. The program has proven to me that we completely underestimate the ability of children in that age range to understand complex scientific issues. Mathematicians who have served as faculty for the program include Erika Camacho, Keith Devlin, and Suzanne Weekes. Of all the work I have done, this program has been the most fun and rewarding for me.

Lanius: *What is a typical workday like?*

Laubenbacher: I have a few different hats I wear. At UConn Health, I am the director of the Center for Quantitative Medicine, a research center that has a very interdisciplinary faculty, ranging from mathematicians to clinicians. My tenure home in the School of Medicine is the Department of Cell Biology. I also have a joint appointment as a professor of computational biology at the Jackson Laboratory for Genomic Medicine, a not-for-profit research organization. I typically spend a couple of days a week there.

As I described earlier, my research group is involved in a number of different projects, with a host of interdisciplinary collaborators for each of them. This necessitates lots of meetings, in person or via phone or Skype. One hour we might talk about a detailed mathematical problem in enumerative combinatorics, and the next hour we might discuss the ambiguity of billing codes for medical procedures and their effect on the construction of patient profiles. I do a fair amount of grant proposal writing, since almost all research in medical schools is grant driven. I actually



Laubenbacher's research group includes postdoctoral fellows, graduate and undergraduate students, a bioinformatician, and a software engineer. They work on a wide range of projects, with an emphasis on the development of mathematical algorithms and their application to problems in systems biology. Front row, left to right: Byoungkoo Lee, Bandita Adhikari, Nick Monteleone. Back row, left to right: Albin Salazar, Anna Konstorum, Russ Posner, Laubenbacher, Abdelrahman Ibrahim, Cory Brunson.

enjoy this part of my job, because it provides a structure to work out new ideas and develop new collaborations.

I spend a fair amount of time reading and reviewing research papers. Together with Alan Hastings, I serve as editor-in-chief of the *Bulletin of Mathematical Biology*, the journal of the Society for Mathematical Biology. In this capacity, I see hundreds of manuscripts a year, which gives me a great view of all the exciting work that is being done in this field.

While I don't have any formal teaching duties, I have lots of opportunities to work with students and postdoctoral researchers on projects, which is tremendously enjoyable. A number of my former students and postdocs have gone on to become established researchers themselves, and I continue to collaborate with some of them. My PhD students typically come from the biomedical sciences PhD program or the MD/PhD program. I also work with students from the mathematics and the computer science and engineering departments, where I have adjunct appointments. For undergraduates, I direct a Research Experiences for Undergraduates program funded by the Division of Mathematical Sciences of the National Science Foundation, entitled "Modeling and Simulation in Systems Biology." That is a highlight of my summers.

Like most mathematicians and scientists, I travel a fair amount to conferences, other universities, and research institutes, and to meet with collaborators. Since my work intersects several different fields, I try to cover key conferences in mathematics, bioinformatics, the life sciences, and medicine.

Lanius: *What is the work culture like at UConn Health?*

Laubenbacher: When I moved to UConn in 2013, I had never been part of a school of medicine and was very curious about what the culture is like and what people do. So I spent much of my first year going around and talking to scientists, clinicians, and other healthcare workers. It was a fascinating experience, and everybody was so generous with their time and interested in ways that we could work together. Since research in a medical school typically requires grant funding, everybody is very focused on making their research maximally relevant, innovative, and impactful.

As I mentioned earlier, essentially all of my projects are done within interdisciplinary collaborative teams, for which I might be the lead, co-lead, or provide a support role, depending on the nature of the project and the funding. Working in this way requires everybody to learn something about all the aspects of a project in order to have a common language, to understand the characteristics of the data to be used, to understand what a mathematical or statistical model can and cannot do. So I end up constantly learning new things about biology, medicine and its practice, population health, statistics, bioinformatics, new sequencing technologies, the intricacies of health insurance, and a whole host of other topics. And one learns about the culture in other fields, and how people think and approach problems. By necessity, most of this knowledge is fairly superficial but enough to interact in meaningful ways with professionals in other fields and understand their problems. At the same time, I spend a lot of time explaining mathematical techniques and concepts to my non-mathematical colleagues, and I enjoy the experience of having somebody "get it" in either a conceptual or technical way.

I am free to work on whatever projects I choose or design, as long as I am able to eventually obtain funding for them. Serendipity plays a big role in establishing collaborations and projects, so it is crucial to seek out as many opportunities as possible to talk about one's research and find out what other people do.

Having a network of colleagues and friends allows us to reach further than we might by ourselves.

Lanius: *How do you balance career and outside interests?*

Laubenbacher: As we all know, scientists in general, and mathematical scientists in particular, tend to be very passionate about their work, which makes it difficult to clearly delineate a boundary between work/career and other interests. And many of us are not very good at saying no to things, so we accumulate increasingly larger workloads over time; I am certainly guilty of that. But down time is a crucial component of any creative activity, because it helps one to clear the mind. In addition to spending some weekends in Boston or New York, my wife and I get much enjoyment from motorcycling through beautiful countryside. It is very relaxing, provides a great thrill, and allows us to spend quality time together.

Lanius: *What obstacles have you encountered and how did you handle them?*

Laubenbacher: In the course of my professional career, I have transitioned several times, from *K*-theory to history of mathematics, to mathematics education, computational algebra, mathematical biology, and biomedicine. Some of those transitions involved physical moves as well. While each has been difficult and challenging for different reasons, each one of them has been an incredible opportunity for growth. The unknown is always scary, and change also comes with self-doubt, worries about one's career, and plenty of anxiety about being a novice again after having been an expert in something. As it turns out, I needn't have worried, since each of the communities I have worked in has been very welcoming and supportive. It was invaluable for me to have friends and colleagues who were supportive during those times, who assured me that I was not just suffering from ADD, who provided a sounding board, and who gave me their honest opinions, whether I liked to hear them or not. The lesson here is that having a network of professional colleagues and friends that provide support allows us to reach much further than we might by ourselves.

Lanius: *What advice do you have for graduate students?*

Laubenbacher: We are living through a time of unprecedented opportunity for mathematical scientists. These opportunities extend far beyond the traditional careers many of us know about. The advent of data science on a big scale, for instance, has everybody looking for professionals with quantitative skills. The mathematical problems are often quite challenging and interesting, and the jobs come with good salaries and lots of flexibility. As my career shows, there are research opportunities in some very unlikely places. It is crucial for a student to know about them. I still meet too many undergraduate and graduate students who have no idea about what is out there and who start very late in their student careers to think about it. Graduate programs need to make an even bigger effort to provide this information to students. A key prerequisite for any professional today in an interdisciplinary environment is excellent communications skills, both verbal and written. Being able to engage people from diverse scientific, mathematical, and cultural backgrounds is a must, and, again, graduate programs need to prepare students for this.

Lanius: *If you could recommend one book to graduate students, what would it be?*

Laubenbacher: There are obviously many great mathematical and scientific choices for this. But I would recommend an old non-mathematical book with the unfortunate title *The Seven Habits of Highly Effective People*, which makes it sound like another self-help book that teaches time management and effective use of Post-it notes. Instead, it is a very thoughtful guide to making one's life as meaningful and impactful as possible.

Lanius: *Any final comments or advice?*

Laubenbacher: Seek and embrace change, continually challenge yourself, and always grow, professionally and personally. Of course, I am not talking about change for the sake of change, but about pushing one's boundaries and doing what feels right even though it might be very hard and maybe even likely to fail. One of my favorite inspirational readings along these lines is Theodore Roosevelt's 1910 speech "Citizenship in a Republic," better known as his "Man in the Arena" speech. It is important to remember that life is a journey, not a destination, in the words of Emerson, and we need to enjoy it as such, with all its highs and lows.

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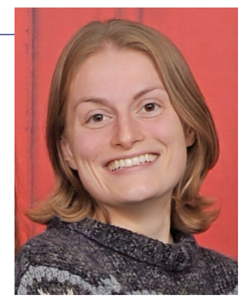
ABOUT THE INTERVIEWER

Melinda Lanius, a Wellesley College graduate, is currently earning her PhD in mathematics at the University of Illinois at Urbana–Champaign.



Melinda Lanius