At Work: Computational Biologist Joao Xavier

Joao Xavier

Computational biologist Joao Xavier studies computer models and quantitative experiments of biofilm and cancer growth. We spoke with him shortly after he joined Memorial Sloan Kettering in 2009.

I was pretty bad at math until I was about 13 years old. At that time, I had a very good teacher in high school who really pushed me and my classmates to learn more. She helped us to understand the bigger picture, and suddenly things started making sense to me.

After graduating from high school, I studied chemical engineering at the Technical University of Lisbon, in Portugal, where I was born and raised. I liked both physics and chemistry, and I found that chemical engineering provided a broad, multidisciplinary scientific education.

I was not necessarily attracted to working as an engineer, but I was very interested in having this solid groundwork. I had the opportunity to specialize in biotechnology as an undergrad, which was unusual. Thanks to the multidisciplinary education I received in the program, I was prepared to go on for a PhD in biomathematics at the New University of Lisbon after I graduated in 1998.

Biomathematics and Biocomplexity

One of the pioneers in biomathematics at the time was my mentor at the New University, Jonas Almeida. Jonas is now a professor of biomathematics at the M. D. Anderson Cancer Center, in Houston, and it is a bit of a coincidence that we are now both at the top two cancer centers in the United States. As his first PhD student at the New University, I was drawn to the study of biocomplexity, specifically how we can use the tools of mathematics to understand the dynamics of complex biological systems.

I did my first postdoctoral fellowship in 2002 in the Netherlands at an environmental engineering lab. In that position, I went back to being an engineer doing applied science. One of the problems I was given was to understand how microbial biofilms, which are communities of bacteria, develop.

I worked out a computational model of this process that had a good deal of applied science potential, but we also managed to stir up interest among colleagues in the basic sciences, who were trying to understand the genetic and molecular mechanisms of how these biofilms develop. As a result of that response, I decided to turn my attention back to basic research.

Back to top

Evolutionary Cooperation in Bacteria

In 2004, I met Philip Stewart, director of the Center for Biofilm Engineering at Montana State University, which is a mecca for biofilm research. Phil offered me a temporary position, and I ended up working at the center for six months in 2005. Then, in 2006, inspired by work there, I decided to do a second postdoctoral fellowship at the Center for Systems Biology at Harvard University.

There, I worked on fundamental problems applied to evolutionary biology with another young researcher, Kevin Foster, who studied social evolution as applied to insects. We started working on a general theory of how cells interact with each other to develop cooperative interactions. During this time, I learned how to speak about my work to people from different fields and tried to understand my research from the perspective of their fields.

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We were studying the concept of evolutionary cooperation. For a long time evolutionary biologists have wondered how organisms evolve cooperation if natural selection acts at the level of individuals. Why do some organisms expend resources helping others? We were studying this from the perspective of bacteria, and I applied my computational models to do evolutionary simulations. Instead of running experiments in the lab, we were running computational experiments using our model.

In 2007, we discovered that the very formation of the bacterial biofilm structure may be a consequence of competition among bacteria, rather than cooperation within the biofilm's bacterial communities. From a distant perspective individual bacteria appear to be working together, but when you look closely you see they struggle for their individual interests. Interestingly, this ends up benefiting the society as a whole. The work we did changed the way people looked at biofilms.

We then went on to develop experimental versions of these same computational models. I benefited from being at Harvard, where you have such an inspiring mix of scientists. The groups are kept very small, and individual group members are allowed to interact very closely. Personally, I had a postdoc colleague, Wook Kim, who helped me learn the basics of laboratory research.

Back to top

Cellular Interaction and Cancer

At the same time I was looking at bacterial biofilms, it became very clear to me that many biological problems derive from how cells interact with each other and how they react to environmental changes as a population. I started thinking about developmental biology in multicellular organisms, and what happens when that developmental process goes wrong, as it does in cancer.

Cancer has many parallels with biofilms in the sense that there is great dynamic complexity in terms of how cells interact with each other, as well as how groups of cells grow and develop spatial structures. Giving a lot of thought to how my specific skills could be applied to cancer biology played an important role in my decision to come to the Sloan Kettering Institute at Memorial Sloan Kettering Cancer Center.

The big draw for me to come was, obviously, the tremendous resources available for cancer research. In many ways, they are unparalleled. But what also really attracted me throughout the entire interviewing process was that I met so many people from so many different disciplines, all of whom have very productive interactions with each other.

I was already well aware of the work being done here in the Computational Biology Program, especially what Grégoire Altan-Bonnet was doing in systems biology and immunology, and what Franziska Michor was doing in her studies of evolution and cancer. If you Google “evolutionary dynamics and cancer,” the first thing you get is her work.

Back to top

Research Goals

In my lab, we combine computational models with quantitative experiments to answer a number of questions. How do multicellular behaviors emerge from interactions among individual cells? What makes multicellular systems robust to the many challenges that they face? Our goal is to identify the underlying physical, biological, and evolutionary principles that are common among, and confer robustness to, multicellular systems.

In the next three to five years, I hope to experimentally explore a model system I developed in bacteria based on swarming motility. (Swarming motility is the coordinated movement of a bacterial population across solid or semi-solid surfaces.) I believe this model will have many applications and will help us to understand how cells interact. At the same time I want to apply my computational models to cancer biology, collaborating with colleagues who are experimentalists at the Center.

One of my first collaborations here at the Sloan Kettering Institute is with Johanna Joyce in the Cancer Biology and Genetics Program. Johanna studies how cancer cells interact with cells in the tumor microenvironment, which is exactly the type of subject to which I think my skills can be fruitfully applied. She brings the perspective of understanding the molecular mechanisms behind the process, while I can help to elucidate what happens in the physics of intercellular signaling.

I’m also working with Eric Pamer, who is interested in how microbiomes, the microbes that are naturally part of our bodies, interact with the body’s immune system. Both Eric and I are members of the new Center for Microbes, Inflammation, and Cancer. The center, with Eric as its director, is a multidisciplinary research initiative designed to shed new light on the role that microbes and the body’s inflammatory and immunological responses play in the development of cancer. In my work with Eric, I hope to understand how the composition of diverse microbe consortia changes in response to the immune system.

It is exciting to be working with people here who are at the top of their fields, and it’s particularly gratifying to know that they are extremely accessible. You can go knock on their door, and they are there for you. This collaborative spirit will be a great help to me in achieving my research goals.

Back to top