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INTERVIEW

An interview with Paul François

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Paul François is an Associate Professor at McGill University, Canada. His group is interested in biological physics, using theoretical and computational modelling in collaboration with experimental biology. Paul recently joined the Development team as an Associate Editor, focussing on the field of computational and theoretical biology. We caught up with Paul over Skype from his home in Montreal, Canada, to find out more about his background and research – and what he is excited about in the field.


Photographer: Owen Egan

Let's start at the beginning – when did you first become interested in science?

I don't really know! When I was a kid, I don't think I was specifically interested in science. It's always easy to say 'oh, at that time I was interested in science', but if I'm truly honest, I was mostly interested in Greek mythology and all the ancient civilizations. My first contact with science was through my parents. My father is almost retired, but he used to be a maths teacher and now he is the head of a high school. I was a kid in the 1980s when there was this programme in France about coding at home, and my parents were very much into this. My mother teaches programming, so I got early contact with computers and I learned coding very early. I guess that was my real first contact with actual science. As a teenager, I got more interested in science in general. My father had a comic book called *Einstein for Beginners*, which I really liked a lot. I was trying to make sense of the equations in there – that was difficult for me to understand as a teenager. When I got to 16-18 I was really good at maths. At first, I wanted to do pure maths for my undergraduate studies but actually my degree ended up being maths and physics; it's only later on that I switched to physics.

Yes, you went on to study theoretical physics for your masters and your doctorate in Paris, France. Can you tell us about what you studied during that time?

I liked maths very much, but also realised that showing theorem was not really what I wanted to do; I wanted more-concrete stuff, so physics sounded like the right thing to do at the time. I was interested in physics formalism, which was a good midway between doing maths and more applied stuff. But very quickly traditional physics was not applied enough. Even when I studied in physics, I got interested in weird problems that are not very well defined, related to out-of-equilibrium statistical mechanics. My first paper was about particles diffusing on a network, like a truck diffusing within the flow of cars (Boutillier et al., 2002). I was interested in real problems like that; weird stuff – based on classical physics – but not very well understood.

For my PhD in the early 2000s, I got introduced to biophysics by my future PhD supervisor, Vincent Hakim, in Paris. At that time, there were three very nice seminal papers related to biophysics. There is the 'toggle switch' paper, which is a synthetic biology paper in Nature (Gardner et al., 2000), the 'repressilator' paper, which is how you build synthetic oscillators in cells (Elowitz and Leibler, 2000), and then there was a very famous paper on extrinsic/intrinsic noise inside cells (Swain et al., 2002). I thought those papers were really fascinating and they drove me towards biophysics. During my PhD, even though it's officially theoretical physics, I was already interested in biological problems. I did a lot of nonlinear dynamics – for example, studying dynamics of gene networks, oscillators, multistable systems. Also at that time I started my work on simulating evolution – that was actually a big chunk of my PhD thesis.

What contributed to your decision to go to Rockefeller University, USA, for your post-doc?

My post-doc was with Eric Siggia. He's fantastic, just fantastic! He was very well known in physics for his work on turbulence, but was one of the first theoretical physicists to switch to biophysics in the 1990s. He is a pure theorist by training, and at that time he sounded like the best to deal with applying theoretical ideas from physics to biology. So, I just wanted to work with him! Although working specifically with him was really one of my main motivations to go to Rockefeller University, there was a very strong Rockefeller/Princeton school in biophysics that was very influential and

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I really wanted to be part of it. It was a very cool environment because there were many connections with experimental biology. Surprisingly, I didn't work so much with experimental people when I was actually there, but I met a lot of people and I'm working with them now. I also met people through visiting labs. In any case, especially when you do collaborative interdisciplinary science, the timescale is very long. You build collaborations over years, maybe even decades. For instance, my collaborator in immunology, Grégoire Altan-Bonnet, was at Memorial Sloan Kettering, just next door to Rockefeller in New York. It really took years for me to identify something I could do with him, and now we're working very closely together. I got interested in segmentation (somitogenesis) and it was at that time that I met Olivier Pourquié. What was fantastic is that he invited me to come to the Stowers Institute in Kansas City to spend a few weeks, just hanging around and talking (and learning to do some simple experiments). I met fantastic people there, e.g. Bertrand Benazeraf and Alexander Aulehla, and we have been developing work together – still very cool and interesting collaborations.

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What was it like for you to move from France to the USA?
It was a shock! I think I was a bit naïve. The scientific culture was very different, the environment was very different, the timescales were very different. I realised that there are good and bad things on both sides of the Atlantic and not necessarily in the way that I was expecting! For example, during my PhD, I was very stressed by time because, in France, you have funding for three years. After three years, you're done, and that's very high pressure to some extent. When I went to the USA, I did not feel this time pressure so much and I was very grateful. I think it's really thanks to Eric Siggia, he allowed me to explore for a little bit. In my scientific thinking and in my scientific training, it's really about taking time to think deeply about problems. You would never think that the USA will give us this opportunity. In my mind, I thought that the French were relaxed and people in the US were stressed and, to some extent, this was reversed. I think deep down I'm still a European. Now I am in Canada, which I see as the best of the two worlds: it's just like the perfect midway for me!

You've been in Canada at McGill University since 2010, where you've now established your own research group. What was that like as a process?
I think, like everybody else, it was both very exciting and very stressful. Early on, I was lucky because I could hire fantastic graduate students. It has been extremely important to me to be around good people: Jean-Benoit Lalanne, Daniel Tufcea, Mathias Beaupeux. Some of my favourite papers are coming from that period, because I had met people while I was a post-doc and, when I moved to McGill, all those collaborations really flourished. I could really find my own scientific path. I was lucky, again, because I had very good collaborators.

I should also point out that I'm a theorist, so it's also easier to start a group, to some extent, than for experimental researchers because you rely a bit more on yourself. You don't have as many external constraints. I have colleagues who have lab renovations taking forever, when I can work with my computer, my pen and paper. On a more personal note, my wife was already in Montreal and we had our daughter in Montreal, so family-wise it was much better for me, after having been in New York for years. Just settling in Montreal, for me, has been a big relief.

What are the main themes of your research now?
I have very broad interests now. I have a good-sized group of six or seven people; pretty much everybody has a project on a different subject/topic. I can see three main themes; they're different, but also a bit related.

My first theme is really something that I started during my PhD, the computational simulation of evolution, and more recently, I connect that to machine learning. Broadly speaking, it's studying how simulations can tell you something about biology, like simulating evolution, or trying to! You see the rules emerging by making many, many simulations, and then you try to see if they apply to biology.

Development is a big part of my work. More specifically, I'm really interested in segmentation, so I am doing a lot of work on somitogenesis, but these days I'm going back to insect segmentation; there's a lot of modelling there, but also data analysis. Again, I'm using computational methods and mathematical models to understand what's happening there.

My last big interest is immunology. I got really interested in the early immune adaptive response: how cells detect an infection, how they talk to one another. We've been doing a lot of cool modelling and also experimental validation of models with my experimental collaborator, Grégoire Altan-Bonnet, now at the National Institutes of Health.

The big difference with an experimental biology lab is that we are very broad in terms of topics, and of course mostly focused on theory, which allows us to find unexpected connections. The kind of mathematical models you write to model development can be connected to, say, differentiation of immune cells. There are even deeper theoretical connections, for instance we've discovered connections between the way immune cells take decisions and the way artificial neural networks also take decisions.

I'm a big believer in cross fertilisation: getting an idea from one field to another field. I think that new ideas come out when you do that. I guess my scientific path is a fractal illustration of this – I'm a physicist, I'm interested in biology and, even within biology, I try to cross pollinate different subfields of biology. I like that very much.

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Do you think it's important for early career researchers today to have an interdisciplinary focus?
Yes and no. I think disciplinary thinking and training is important and I think at some point you need to expand your horizons, but when do you do that? As a PhD student? I did it as a post-doc. I used to think that a solid core training was really useful, and then you can branch out – but now, I'm not so convinced. There are many programmes where people study physics and biology at the same time, and I find that the people coming out of such programmes are really good. I guess it depends also on people's personalities. Just don't wait too long before branching out, because at some point you lose the energy.

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For someone that's interested in branching out, do you have any advice about how to develop a more diverse skill set?
I think it depends very much on the people. For people like me, I would advise them to do disciplinary training in one field, and then branch out, get curious and start talking with other people. I think most of my training outside of physics really came through interactions with colleagues; discussion with people in different fields, through which you learn to find common ground. You need to find people who think like you in different fields. That is a difficult thing. Find those people and then work with them, it's when you learn: working by training – at least, that's the way I learn. Again, it depends also very much on people. It's very much down to teamwork; I would be nothing without my collaborators, my students. It's very important to interact.

Last year, you won the Rutherford Memorial Medal in Physics for outstanding research. What does this award represent to you?
It's very humbling. I was happy, obviously! Not many biophysicists were awarded it in Canada. I thought it was a nice recognition for the field in general because, sometimes, people in physics think biophysics is not truly physics, because it's biology. Conversely, biologists think we're doing physics, we're not doing anything related to biology. As I've told you before, my work is really first and above all based on teamwork, so when I was awarded this medal, I thought about all the people who helped me over the years: my mentors when I was a student, my collaborators, students and post-docs in my group. I think I was very lucky to be a part of all these different teams. This medal might recognise me, but above everything it recognises our collective work.

I have to say Ernest Rutherford is a big name in Canada, and he used to be at McGill, so it made a lot of press and that was a bit intimidating. On this note, I was awarded this medal at the meeting of the Royal Society of Canada. It is a big meeting of many scientists from absolutely all scientific fields and all parts of Canada, and I really enjoyed interactions there. I talked with people studying philosophy of science, history of science, but also other fields I never thought about – that I didn't even know existed. It is very interesting to talk with people having completely different perspectives. The Royal Society of Canada is, in particular, trying to build a college of scientists with very different backgrounds that is going to discuss or reformulate standpoints, and maybe propose solutions to big issues. I think it's a great idea, especially these days where we need science. I think it's something to encourage for these kind of societies to bring different scientists together.

You recently joined the team at Development as an Associate Editor for computational and theoretical biology. Can you tell us a bit about what your role entails and why are you were interested in getting involved with the journal?
First, I love development as a field and Development as a journal. I was really honoured to be invited to join. At this stage of my career, I'm interested in giving back to the community – participating in the community – and definitely, reviewing and editing papers is an important part of the job. I've been interested in doing work on the publication side for a while, so when the opportunity came up, I just said 'yes!' – especially because I love Development. I also like the idea of having somehow this new direction for Development, building up on theory and computational work. I have published some theoretical work in Development and I think the journal has been quite open to it in the past, but having something a bit more formalised to encourage people to publish theoretical work in Development is important. As a physicist, being part of the team, I think it's important to hopefully bring physicists to publish in the journal and expand the field.

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What type of papers are you especially excited to receive?
I think the interesting things are at the boundary between fields. I think that we need different philosophies in this field, so theoretical papers on biology, but I'm really curious about specific theoretical work for very specific biological systems to make nice predictions and really bring new knowledge to biological problems. Papers combining theory and experiments are also of course always very interesting. I'm also interested in what things like machine learning or computational advances can bring to developmental biology. So, if you combine data science and developmental biology that would be of interest. I would be interested in seeing where we can go in this direction.

Along those lines, in which areas do you think there has been a lot of progress recently?
I think, especially from a physics standpoint, everything that is happening at the level of gastruloids and self-organisation is very interesting. I think there is a huge need for maths and physics to really understand what is happening there and it's important to move in this direction. Not only allowing self-organisation, but also hacking the system and really controlling it in a quantitative way.

I think 'big data' could also offer interesting perspectives if we are able to complement it with good theory, and building these things is something I'm really interested in in my own research. How do you use all this knowledge to make a compact, predictive model? At some point, you need to use all this data to corner a question and make a prediction on something specific.

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Finally, what would Development readers be surprised to find out about you?
I'm not sure there's anything really surprising about me! I'm really a big sci-fi reader; I have a big library of sci-fi books. When I was a teenager, my grandfather had a few sci-fi books and I just looked at them and loved them. I read all of Isaac Asimov's books at that time and some of my favourite authors are from this classical age of sci-fi. That said, I really like some more modern authors. I very much like the work of Nora K. Jemisin – she won three Hugo prizes in a row with her 'Broken Earth' trilogy. I also liked very much the recent *The Three Body Problem* by Chinese author Liu Cixin. What I like about sci-fi is that it is actually quite inspiring for our job, not so much because it anticipates what can happen in the future, but because it also makes unexpected connections between different fields of knowledge. Sci-fi does not shy from that: imagine how you can combine geology with biology or philosophy and computer science and physics – very good sci-fi books, they do that. I love that and I find it very inspiring. I think you can see the connection to my work!

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