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INTERVIEW

Transitions in development – an interview with Thibaut Brunet

Thibaut Brunet is a group leader at the Institut Pasteur in Paris, France, where he works on choanoflagellates (known as 'choanos' for short). These unicellular organisms are close relatives of animals that have the potential to form multicellular assemblies under certain conditions, and Thibaut's lab are leveraging them to gain insights into how animal morphogenesis evolved. We met with Thibaut over Zoom to discuss his career path so far, and learnt how an early interest in dinosaurs contributed to his life-long fascination with evolutionary biology.

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

I grew up in a very urban setting in a neighbourhood of mass housing, which was basically a series of brutalist, concrete buildings. The only biodiversity that I had around me as a kid was cats, dogs, pigeons and the two species of trees you find in most French cities. So, I learned about biodiversity largely from television documentaries and books. I was born shortly before the film Jurassic Park came out, so there was a big media focus around dinosaurs when I was a kid, and that came with a lot of excellent popular science about extinct life and palaeontology. I remember learning about dinosaurs and being struck both by the organisms themselves, but also by the fact that they were extinct; I felt a sense of cosmic injustice that these organisms had existed only to be taken away from us before we got a chance to meet them. When I grew up, that matured into the understanding that there was much more biology in the past than in the present. As a teenager, I stumbled upon the books of Stephen Jay Gould; they showed me not only that palaeontology and evolutionary biology have visual shock value, but that these were very conceptually engaging, deep and stimulating fields. Such books about evolution motivated me to become an evolutionary biologist, but, in a sense, this really grew indirectly out of my childhood interest in dinosaurs.

You completed your PhD at the European Molecular Biology Laboratory (EMBL), Germany. What were you working on at the time, and how did this relate to your early interest in evolution?

I was in the lab of Detlev Arendt, which focused on comparing cell types between diverse organisms. This came out of an interest in trying to understand how animals had diversified before and during the Cambrian explosion, from the last common ancestor of animals to the main lineages that exist today. The lab was using a model organism called *Platynereis dumerilii*, which is a marine annelid worm. Most of the lab was interested in the nervous system, but I was working on the evolution of muscle cells. So, I was studying an unusual cell type in an unusual organism. One of my projects was about the evolutionary origin of the notochord and the possibility that it might have evolved from muscle, and that was a great collaboration with another PhD student named Antonella Lauri. I've been very lucky to have amazing collaborators over the years, Antonella being one of the first ones. I also had a project about when the split between smooth and striated muscles occurred. I also had a lot of projects that just didn't work, so were never published. One of them was to try to use CRISPR technology on some genes in *Platynereis* and, for diverse reasons, that just never came into fruition. I think one of the important things I learned during my PhD was when to give up if something doesn't work. If you have several research directions going on at once, and some of them are progressing faster while some others are a bit stuck, at some point it becomes important to overcome the sunk cost fallacy, and to cut your losses and focus on what's working. For me, this wasn't trivial, as I had a tendency to want to finish everything. I think learning to give up was actually very important.

After your PhD, you moved to UC Berkeley for your postdoctoral studies, where you joined Nicole King's lab to work on choanoflagellates. What inspired you to switch to this organism?

It grew out of an intellectual random walk. During my PhD, my focus was muscle cells, and cell contractility more generally. When I started writing my thesis, I was struck by the fact that collective cell contractility seemed to be fundamental for animal complexity in two ways. One way is that contraction of muscle cells in adult animals allows movement, and the other is that the irreversible contractions of embryonic cells underpin morphogenesis. I also knew that cell contractility was very ancient. You find contractility in the unicellular relatives of animals, and even in more distant unicellular eukaryotes, such as amoebae. For example, *Dictyostelium* crawl by using actomyosin machinery that's not dissimilar to the one that animals use. I was very curious about how this ancient machinery for

Thibaut Brunet's contact details: Institute Pasteur, Université Paris-Cité, CNRS UMR3691, Evolutionary Cell Biology and Evolution of Morphogenesis Unit, 25-28 rue du docteur Roux, 75015 Paris, France.
E-mail: thibaut.brunet@pasteur.fr

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individual cell movement had been repurposed to give rise to collective multicellular movements, and so I became interested in studying the transition to multicellularity via the closest unicellular relatives of animals, which are the choanoflagellates. I learned from the literature that choanoflagellates could become multicellular under certain conditions, and that Nicole King's lab in Berkeley was developing them into tractable model organisms for cell and developmental biology. Thanks to the work of David Booth, who was already a postdoc in Nicole's lab when I joined, they were also starting to establish functional genetics. So, I wrote to Nicole asking if she had the openings for postdocs, saying that I was interested in studying contractility. She replied that she wasn't sure if choanoflagellates had much contractility, but I could interview anyway, and try to find out; in the worst case, if they didn't, I would investigate something else, which was fine with me. I wasn't sure they would have contractility either, but I was sure I wanted to find out.

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You went on to start your own lab, where you continue working on choanoflagellates. Is this how you established your research niche, by taking that contractility project with you?

Yeah, that's exactly the way it went. It was easy because I came to Nicole's lab with my own project, and with the understanding that I would be able to take it away with me when I left. Nicole is an amazing mentor in that respect; she's very generous with postdocs who establish their own niche and take their project with them. There was also some serendipity since, during my postdoc, I accidentally co-discovered a new species of choanoflagellate named *Choanoeca flexa*. *C. flexa* has spectacular collective contractility, which was exactly the kind of thing I was interested in studying. When I started my postdoc, I wasn't sure it would exist, and in fact it doesn't exist in that form in the more established choanoflagellate models. So, that finding also contributed to creating my niche in a somewhat natural way.

Can you summarise the research themes of your group at the moment?

Generally, we're interested in understanding the cellular basis for the evolution of animal morphogenesis. One entry point into that is to try to understand cell shape and movement in choanoflagellates, which is a rather broad theme. We have specific research directions about understanding how the canonical choanoflagellate shape, with the ring of microvilli around the flagellum, is established. We also want to understand how that shape is remodelled, for example when choanos become amoeboid under confinement, or when they switch to a different type of motility. So, that is linked to questions of cell differentiation, and also cell mechanics and cell shape. We are also interested in how shape and movements at the cellular level are converted into movements at the multicellular scale during the collective contractility of *C. flexa*. Of course, the fact that very little is known about choanoflagellates means that when you do live imaging, you see a lot of things that no one has seen before. Many of the projects therefore end up growing out of accidental observations, so in a way that sometimes creates directions that don't really fit into a preordained, global plan for the lab. But, often, they still fit into this global interest in morphogenesis and shape.

You mentioned discovering a new choanoflagellate species, *C. flexa*. Does fieldwork form an important part of your research as well?

Fieldwork is more of a hobby that grew accidentally into a research direction. When I started my postdoc, I saw myself as a developmental biologist who was trying to learn cell biology, and becoming a field biologist on top of that would have seemed like a bit too much. But in Nicole's lab, most people had a hobby (which for some of them was also a part of their research) of collecting samples of aquatic environment wherever they went and looking for choanos. You can find choanos in pretty much any aquatic environment in the world; fresh water or sea water, cold water or hot water. You'll find different species, but choanos are everywhere. Once I joined Nicole's lab, I caught the bug almost immediately; there are very few joys in the world like scooping a few millilitres of a lake, or a river or ocean, and then looking through the microscope and discovering a world that was completely hidden. Sometimes it's wonderful, sometimes it's terrifying, and it's often a little bit of a mixture of both, but it's always fun. One year, we went to Curaçao for a workshop, and I collected the sample in which we ended up finding *C. flexa*. When we first saw it, we thought we were on drugs. The movements of these organisms were so different from what we were used to seeing choanos doing that it felt unreal. We were also lucky that this organism could be found repeatedly in the same location, so we could study it in its natural environment. This is not necessarily the case for other choanos; some of them have been in culture for a long time, and we haven't always been able to re-isolate them from where they were supposed to come from. When we have questions about the life history of *C. flexa*, we can go back to the field to test our hypothesis *in situ*. We actually have a recent preprint about how the *C. flexa* multicellular life cycle is regulated in its natural environment (Ros-Rocher et al., 2024 preprint). Whenever we do fieldwork scientifically, we try to team up with professional field biologists, such as microbial ecologists or protistologists, to avoid beginner mistakes. But, on the side of that we also keep it as a hobby, because looking at plankton samples is just so captivating.

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I guess the choanoflagellate community is relatively small. What are the benefits and challenges of this?

The advantage is that we all know each other; most people who do cell, molecular or developmental biology of choanos have largely come from Nicole's lab. There's a very healthy culture of transparency and mutual help. I think that comes down in large part to the culture that Nicole set up from the beginning, and maintaining that positive culture is facilitated by having a small community where it's still possible for everybody to know each other. The community is growing, so we will negotiate this transition to hopefully have a more established model organism-style community. That's something to hope for, because if choanos are as interesting as we think they are then the community will grow. At the moment, though, there's a lot of open space for exploration; there would be really no reason to compete with each other because there's just so much to do and there's still relatively few of us.

Of course, there are also disadvantages. One obvious one is that we have a relatively small number of people working on establishing

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new techniques compared to other model organisms. I think that issue is compounded by the fact that establishing techniques is not always sufficiently recognised by the scientific community in general, even though establishing, for example, genetic techniques in a new model organism is really the cornerstone on which you can then build everything else.

What were your most important considerations when looking for group leader positions?

Some personal considerations came into play. I had moved around a lot during my PhD and my postdoc, and I was looking for a place to settle more permanently. So, proximity to pre-existing friends and family was important, and it was really my hope to return to Paris. I was also looking for a job that was either a tenure track or tenured, where I could see myself long-term. In terms of choosing institutes, I was looking for a place with intellectually curious colleagues who would be open to working on unusual model organisms and would be interested in discussing science. I was also careful to tick a number of boxes that I thought were important to be able to do good research, such as access to good core facilities. I was also looking for good institutional support, such as a grants office to help with grant applications and mentorship by more senior PIs. Pasteur ticked all these boxes, and I'm very happy here.

Do you now have collaborators within the institute?

Yes. That was not necessarily decided when I interviewed; what really attracted me to Pasteur was initially the informal discussions with my colleagues, and some collaborations have emerged from those. We collaborate with Arnaud Echard, an expert on cell division, about the incomplete cell divisions in choanoflagellates, and with Jean-Yves Tinevez who created the wonderful image analysis hub in the Institut Pasteur. We are also working very well with the excellent proteomic and microscopy facilities in Pasteur. And we also have a lot of collaborations outside of Pasteur with people in Europe. A lot of people in Europe were interested in doing some work on choanoflagellates when I arrived. We were the only choano lab in France, one of the only three choano labs in Europe now (there's one in Norway and there is another one in Ireland that just started). So, people who were interested in doing some choano work didn't have a huge choice of potential European collaborators! We have collaborators in Cambridge, UK, at the CRG in Barcelona, at Utrecht University, and at EMBL among others, and we have collaborators in other Parisian institutes, such as Collège de France. It's a bit of a challenge when you start your new lab to have all these external scientists who you're also working with, but you get to see very diverse science and you benefit from the perspective of people who are coming at things from a completely different angle than you.

What has been the most challenging aspect of transitioning to a group leader role?

For me, switching from postdoc to PI was going from a job that was maybe two- or three-dimensional to a job that was suddenly 26-dimensional. The number and diversity of tasks just exploded, and that includes tasks that you didn't even imagine could exist! So, I would say if I had to single out one challenge, it would be that time has now become limiting. When I was a postdoc, I felt that I had ample time for my main research projects as well as for exploring side directions, writing reviews or simply thinking. Now, every activity exists in a temporal trade-off with another. I try to safeguard time for thinking because I feel that creativity really lives in the more unstructured exploratory space between tasks that have a clear purpose. It is important to protect this unstructured exploring, while striving to still do all the rest of the tasks well.

And, on the flipside, what do you most enjoy about running a research group?

One obvious aspect on the scientific side is you get to explore many more directions. But the most enjoyable aspect is really the mentoring, I think. There is something fascinating about mentoring a brilliant student or postdoc, proposing a research project to them and then seeing them really wrap their own mind around it, and inject their own intellect and creativity into the project. They always bring in their own personal perspective. Each project will end up simultaneously reflecting the nature of the system studied, my personality, and the personality of the trainee who's taking it up. I find the three-way dialogue between nature, me and the trainee extremely interesting to experience. I think it's part of the reason I've always enjoyed collaborations in the past, and it's something that I really enjoy about being a PI as well.

You mentioned earlier that Nicole was a good mentor to you. Have your previous mentors influenced your own mentorship style?

Yes, absolutely – I learned a lot from both Detlev and Nicole, but also from all the other mentors I've had. I think I picked up more of a disparate bag of small tricks than a coherent philosophy. I just remember things that my mentors did that helped me progress or encouraged me, and I try to pay it forward with my own trainees. I was also struck by a quote from Claude Desplan in an interview I actually read in Development a few years back, in which he was asked about his approach to mentorship. He said, 'I don't think I really have a strategy […] my way of mentoring is just to talk to my people, to encourage them, to respect them and to like them.' I think that in a simple way this encapsulates something very important, which is the need to make people feel respected, valued, supported and encouraged. The exact way you get there will depend on the person, but it's something I constantly keep in mind.

What has been your approach for hiring new team members?

That's a key aspect in the beginning, because the first few hires are crucial and they obviously happen when you're the least experienced. So, my approach has been twofold: to maximise information, and to not do it alone but instead ask for advice. Maximising information can mean that students who would like to join for PhDs will work in the lab for a few months as interns so that I know them, they know me, we know if we work well with each other and they know if they like the project. For postdocs and for some students, it's not possible to do that, so I really try to get to know them as people. They'll give a long scientific presentation and spend at least one day in the lab to meet all the lab members and get a sense of each other's personality. Gathering references from earlier mentors and trying to get as honest and detailed feedback as possible is also important, of course.

Regarding the second aspect of my approach, which is to not decide alone, I take feedback from all members of the lab regarding potential new recruits, so it's really a collective decision. When I started hiring, of course, the lab was empty, so I got a lot of help during early interviews from my institutional mentor, François Schweisguth. He's been extremely helpful in sitting with me through interviews and giving very wise, honest, experienced feedback.

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What advice would you give to people starting their own labs?

It's a difficult question because I've only started my own lab once, and it was relatively recently, so I don't have infinite wisdom on that. But if I could go back in time to give some advice to myself, it would simply be to be patient, because things take time to start. A lot of things have to be in place before you can really start doing research, and as long as even one of these things is missing you cannot really start. So, there is a very nonlinear aspect to it: for long time you do nothing, and then all of a sudden you can start producing and you make progress quickly.

Did you ever consider a non-academic career path?

A little bit. Before my PhD, I got an accreditation as a biology teacher. That played an important part in my later career because it meant I always had a plan B in case research didn't work out. I wasn't sure how successful I would be as a researcher, especially since I was attracted to fairly unconventional topics. I didn't know in advance whether the experiments would work, or how interested the community would be. For me, it was good to have this backup plan always at the back of my head, because that really allowed me to explore the research directions I was interested in very freely. So, I would recommend always having a plan B if you want to take a career in research.

Finally, what do you enjoy doing outside the lab?

I used to be in a choir. I am not a religious person, but I get almost a mystical feeling out of singing in a group. There's something very unusual about the experience in which you almost feel like your ego is dissolving into the group. It's very strange. Nothing else has that effect on me. I haven't done it in a while, unfortunately (now I mostly sing in the shower), but I would like to go back to it.

Thibaut Brunet was interviewed by Laura Hankins, Reviews Editor at Development. This piece has been edited and condensed with approval from the interviewee.

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