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CELL SCIENTISTS TO WATCH

Cell scientist to watch – Yanlan Mao

Yanlan Mao graduated in Natural Sciences from the University of Cambridge, UK, followed by a PhD in developmental biology and genetics at the MRC Laboratory of Molecular Biology (MRC-LMB), Cambridge, UK. During this time, she studied cell signalling and epithelial patterning in *Drosophila*, under the supervision of Matthew Freeman. For her postdoctoral research, Yanlan moved to the Cancer Research UK London Research Institute (now part of the Francis Crick Institute), to study the role of mechanical forces in the orientation of cell division and cell shape control in Nic Tapon's laboratory. She established her own research group in 2014 at the MRC Laboratory for Molecular Cell Biology (MRC-LMCB), University College London, where she addresses the importance of tissue mechanics during development, homeostasis and repair. She was awarded a L'Oreal UNESCO Women in Science Fellowship and the Lister Institute Research Prize in 2018. In 2019, she was awarded the Biophysical Society Early Career Award in Mechanobiology and also became part of the EMBO Young Investigator Programme. Yanlan is the recipient of the 2020 Women in Cell Biology Early Career Award Medal from the British Society for Cell Biology (BSCB).

Yanlan Mao

What inspired you to become a scientist?

I think probably two things. First, as a child, I was always really interested in patterns in nature, such as the ones you find in leaves, flower petals or shells. I was always fascinated by the diversity and how beautiful nature is, just by walking around and seeing the world. Second, someone that's really influenced my career has been my dad. He's a mathematician, and he's very passionate about his maths. As a result, I grew up always trying to think of the world in a very mathematical way. He introduced me to physics, chemistry and maths very early on, as those were subjects he studied, but not biology. Maybe that's why I was drawn to biology; it was more of an unknown world, with more to be discovered. I really wanted to combine biology with maths, at some point in my career. In a way that's what I'm doing now: mathematical modelling of physical forces in biology, and still tackling patterns, shapes and sizes of systems.

Patterns can help deconstruct more complex systems. Does your interest in patterns come from a curiosity to understand the basics?

Absolutely. Although I don't exactly work on patterning per se right now, it is still a part of some of my current work on tissue size and shape. The biophysics aspect is probably where the maths comes in; I want to break things down into simpler problems or first principles, and try to understand, in as simple a way as possible, how shapes and patterns form and how sizes develop. My PhD was in genetics; very hardcore, traditional biology, which was great to train me as a biologist, scientist and experimentalist. I think maths really helps to deconstruct things. We can't possibly understand all of biology. The important message that I always give to people is that trying to mathematically model something isn't about creating the perfect cell or the perfect fly; if you can get a perfect model then you already understand everything, so there's no point in making the model. You need to convert the problem into simple components and understand its basic core. Maybe it's just three interactions or four proteins. Is that sufficient to already give you 99% of the behaviour of a system? If so, then that already helps you understand a lot about the system. It's the logic of breaking things down and putting things back together, but through simplification.

So how did biophysics become the main aspect of your research interests and your current work?

I guess I got more into physical modelling because of my postdoc. A year before I started my postdoc, a beautiful paper was published from the lab of the late Suzanne Eaton and Frank Jülicher on generating a vertex model, a mechanical model of epithelial development. At the time, I felt this was the perfect kind of model for us to understand [*Drosophila*] wing shape. I actually learnt how to code by generating and adapting that model. Despite my background in maths and physics, I hadn't learnt any computer programming, which is a huge problem these days. That was what

Yanlan Mao's contact details: Medical Research Council Laboratory for Molecular Cell Biology, University College London, Gower Street, London WC1E 6BT, UK.
E-mail: y.mao@ucl.ac.uk

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Keeping the kids entertained during lockdown: learning how to cook and bake lots of new things together.

got me into biophysics, because the model was very much a physical model of tissues growing. To explore it, I had to learn biophysical experimental skills in order to test the predictions from the model and hypotheses, as well as generate new ideas with a biophysical spin. But I always linked back to my background in genetics and signalling. In a way, that's what I'm doing now in the lab – trying to combine the genetics and biology with mathematical and physical analyses to understand how changes in size, shape and form occur. Thinking back now, I'm not sure if it was an active and conscious decision. Maybe it was a lucky accident, this semi-conscious decision of moving into the field of tissue mechanics. First of all, I think I was very driven by the core question, which is tissue size and shape control – growth control. You need forces to move something. It's fundamental. Embryologists a century ago already knew that, even before molecular biology and genomics were available. Actually, they were doing what we're doing now, but just in a less technically advanced way. By the end of my postdoc, the 'renaissance' of cell and tissue mechanics really helped me define my focus. I was still in a fairly niche field and I could create my own little area of expertise. Since then, the field has increased more and more. People are starting to recognise and appreciate biophysics and mechanics again.

"It's a marathon, not a sprint."

Biophysics is an interdisciplinary field. What is your advice on establishing good collaborations?

Great collaborations take initiative to make that initial connection so that you form a link. The good ones I've had have always been where the two groups have different skills. For me, that's the whole point – slightly different skills and different backgrounds, and then you come together with a common vision or a common goal to answer the big question. Then it needs nurturing, just like in any collaboration. You have to be reliable and keep communication going, especially if it's long distance, because that momentum has to be kept. That's very hard. I've had collaborations where you have that initial conversation and then nothing really happens. Everyone has different priorities, different interests, but you can't be shy. If that collaboration is really important, you've just got to keep nudging them, keep emailing them, because you might not be their priority. As with many things, if you really want something, you just have to keep trying. We honestly don't mind getting multiple emails. Well, to some extent!

Is this a quality that you also encourage in your PhD students?

Yes, perseverance. At all levels, you've got to persevere. Don't be shy about annoying someone. It just shows you're passionate about something, and that you really care about it. I think most busy PIs wouldn't mind that. Another piece of advice is to work smartly. I just had a conversation with my students about how, in some labs, you have to work 18 hours a day, constantly pipetting. It's true that more work means more outcomes, but smart work is the important aspect. I stopped working weekends quite early on in my career. I worked very hard during the week, when necessary. I'd be the first to open the lab and I'd leave on the last tube train. I also knew that I couldn't maintain that rhythm consistently, because I would just burn out. It's a marathon, not a sprint. But that meant smart working and designing my experiments properly. I can see that students sometimes feel the pressure to constantly work, but you don't have to if you work smartly. With every experiment you do, you should ask yourself, 'what was the point of that, what was the purpose, what was the question, what was the hypothesis?', so you don't waste your time. At the beginning there is exploration and freedom, but hopefully you should quickly become more targeted. Being selective and smart about what you do is really important. And this also requires reading enough to know your field, to help you know what is a smart experiment. It's your job as a scientist to learn to manage that, so you can design experiments that have the highest chance of giving you something interesting. After all, you have a finite period of time and you can't do everything.

"You're only as good as your best postdoc or student."

What challenges did you face when you started your own lab?

The main one was probably hiring, and also learning to let go. Someone said to me once that you're only as good as your best postdoc or student. You rely on the staff you've recruited to do the core of the work, to generate the data and to push your ideas. But hiring is much easier said than done. How do you judge someone after a 30-minute interview, or even a day of interview? I've been saying this to postdocs about to start their own labs: if you know someone good, try to poach them if they're willing. Honestly, that's what I did! I offered a job to my first postdoc before I had my own

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job secured [laughs]. We still joke about that. I've always said people in my lab don't work for me, they work with me. That's really important. Once you hire well, trust the people in your lab to do their part of the teamwork. It's important to learn to delegate and to let go. When I went on my first maternity leave, which was about a year after starting my lab, I learned that I could let go for a bit. I wasn't completely hands off, but it meant that the students and postdocs didn't come running to me immediately with a question – they'd solve it themselves and, most of the time, they would be fine. I think that really forced me to learn that it's okay to step back. If you trust them then, more often than not, you realise they will learn faster, they will own their projects and take them to places that you probably wouldn't have initially thought about. Give them space and freedom to develop as unique scientists; you don't want a whole lab of 'mini-mes' [laughs]! That's when science gets exciting.

How are the challenges that you're facing now different?

A huge challenge I had recently was to find bridging or extension money to give students and postdocs enough time to finish their papers properly and get them published. When everyone's money is starting to disappear, but the projects haven't finished yet, what do I do? Do I make them redundant? Who will finish those projects? A person finishing someone else's paper always takes longer. Most of the time, studentships are three years. That's not really enough now to finish. And postdoc fellowships are two years! There's no way. Most of our papers weren't published until about five years in, when you include the revision process. Finding the money to extend people's time in the lab was a huge challenge, as there are not many 'flexi-grants' out there, even though it's the most efficient use of the money: the students and postdocs can finish and leave with publications to help them find good postdoc or PI positions. Very fortunately I got the Lister Prize, which saved my lab, because without it I would have had to close pretty much the whole lab down – all those 2019 papers might have still been sitting on the bench waiting to be published. But I was able to use that prize money flexibly to bridge a lot of the postdocs so they could stay and publish. I think it's important to help the community by creating more of these 'flexi-grants' or extensions, which would really make the initial investment into students and postdocs so much more worthwhile. More and more, the funding timescale doesn't match the time it takes to publish exciting stories, especially in biology and especially for those starting labs. The funding bodies haven't really taken this into account.

What advice did you receive that was really important for your transition to a PI?

Besides hiring the right people, another piece of advice I got was from someone who wasn't my direct advisor but a scientist I really admire. He said something that really stuck with me when I was a postdoc: 'Don't be scared of hiring people smarter than you.' He really meant people who have different knowledge and skills from you. He said not to be scared of that because you will learn from each other. That really has shaped how I recruit people. I hire people from all different fields. There's no way I could be as good as the person doing the modelling, but that's fine. If I were scared of hiring them, then that part of the lab would never happen. Let the experts be the experts in their own mini-fields. I'm completely comfortable with the fact that I can't possibly be the expert in everything. But hopefully, I've had the years of experience and guidance to know how to point my staff in the right direction. Together, we work as a team to really complement each other, and I'm constantly learning from my team (and vice versa, I hope). And that has been super exciting.

How did you and your lab cope with the lockdown due to the SARS-CoV-2 pandemic?

We had ten days to plan. We had to get all our flies ready and flip them onto fresh food so that they'd be okay for at least a month, because we honestly thought it would just be a few weeks; we never thought it would go on for four months. When the lockdown did happen, though, we were okay to stay at home for a while. Everything was then Zoom based. We continued our lab meetings once a week, and everyone had their own tasks to do at home. Most of them still had data to analyse. We're a quantitative lab, so we can analyse data to death! They have also been writing PhD theses, papers, proposals or reviews. It was a matter of every person thinking strategically about what they can do that will help them in the future and save them time when we do go back. We also have Zoom socials and Zoom coffee breaks, just to keep spirits up. I think the hardest thing was keeping everyone's motivation going, especially some of the students and postdocs who are living on their own; it's very isolating. So I would check in on them and make sure that they were ok, but also give them their space and not push them too much at the beginning. I said to them that physical and mental health are the most important things, and if you don't have those, you can't do science. More or less, people are still making good use of their time and being productive. Although we are really running out of things to do [laughs]! After all, we are experimentalists, and we need to generate experimental data. Luckily, our institute was one of the first selected as a pilot institute to open, so there has been a lot of amazing work to get that ready. Hopefully, we can start getting new data again soon.

You have been quarantined at home with your husband and two children. Recently, a US-based study came out that suggests that female PIs have been less productive, posting fewer preprints and applying for fewer grants, during this pandemic. What are your thoughts on this?

It's probably true. My husband's great and we try to share everything, but for example, I have a one-year-old and I'm the only one who can do some of the things needed. My husband and I basically work two-and-a-half days each, but I have maybe five hours per day, broken up by lunch time, nap time, dinner time and bath time, rather than full days, to do anything, whereas the days that my husband works, he really works the whole day. Despite our best effort to achieve equality in the household, there are still natural imbalances. I can just about keep the lab going, but I haven't been able to think enough to write a new grant, even though I should. Yes, we finished papers, but most of them have been papers that were already under revision. The brain needs continuity and time to start writing from zero, and I just haven't been able to do that with an hour or two here or there. My priority has been to make sure that everyone else in the lab is fine and happy. Basically, it's like another maternity leave for me. I've only been back in the lab since September, after my second child, and now I'm on 'leave' again! It's definitely a huge hit. It's hard to even quantify that. I just had to accept the fact that I was going to be less productive. It's a matter of adapting and taking on the right attitude. That's also something really important in science. You can always see things in a more positive way and then embrace it, and enjoy it. I have enjoyed spending more time with my children. That's been awesome and has kept me sane. Honestly though, the first day I was at home with my two kids full time, I thought, 'I can't do this!' Then, once you settle into a new routine, time goes very quickly.

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Could you tell us an interesting fact about yourself that people wouldn't know by looking at your CV?

I'm actually quite a good ballroom dancer. Only at conference parties do you see that appearing. I was on the Cambridge Dancesport team for two years; I was a beginner, but doing competitive dancing meant I improved fairly quickly. That was really fun. I started that during my PhD because I needed something new to do. A lot of evenings I would leave the lab at 6 p.m. for my dance training, and I'd be at competitions on the weekends. That really made me more productive in the lab. And ballroom dancing is fun.

So let's hope the conferences come back so we get to see your ballroom skills!

Yes, I miss the real conferences and the conference parties!

Yanlan Mao was interviewed by Inês Cristo, Features & Reviews Editor at Journal of Cell Science. This piece has been edited and condensed with approval from the interviewee.