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CELL SCIENTISTS TO WATCH

Cell Scientist to Watch – Elizabeth Hinde

Elizabeth Hinde received a Bachelor of Science majoring in physics and chemistry from the Australian National University in Canberra, followed by a Master of Arts in painting conservation and a PhD in fluorescence spectroscopy at the University of Melbourne. She then moved to the University of California at Irvine, USA, to work as a postdoctoral fellow with Enrico Gratton on quantitative imaging of protein diffusion within the nucleus. In 2013, Elizabeth returned to Australia and joined the research group of Katharina Gaus at the University of New South Wales (UNSW), Sydney, with a Vice-Chancellor Fellowship and subsequently established her own research group at UNSW with a Cancer Institute NSW Early Career Fellowship. In 2017, Elizabeth moved to the University of Melbourne as an NHMRC Career Development Fellow within the Department of Biochemistry and Molecular Biology, Bio21 Institute, and has recently moved to the School of Physics as the Jacob Haimson Beverley Mecklenburg Lecturer. Her research focuses on fluorescence microscopy methods to quantify live-cell nuclear organisation and the role chromatin dynamics play in maintaining genome function.

Elizabeth Hinde

What inspired you to become a scientist?

My dad was my physics teacher in high school and he had a huge influence on me. He made physics very interesting; for example, when studying projectile motion, we launched rockets off the building.

But you nevertheless 'escaped' from physics for a while, right?

Indeed. I wanted to go to art school, but my parents convinced me not to do that and to enrol in a Bachelor of Science majoring in physics. However, afterwards I did a Master of Arts in painting conservation. This involved restoring paintings and using tools like fluorescence and infrared spectroscopy to date a painting and figure out what materials the artist used to create it. This experience led to my PhD, which focused on the photo-physical properties of fluorescent pigments used throughout the history of art and how they can be used to authenticate an artwork or facilitate painting conservation. Then one day, I attended a workshop on fluorescence spectroscopy where Enrico Gratton (University of California, Irvine, USA) presented biological applications of fluorescence and I'd never seen that you could do fluorescence spectroscopy in real time or on a dynamic system. So, I applied to undertake a postdoc with Enrico, and it was in his lab that I started to realise that I wanted to be a scientist. So, in the end, my parents were right! I am now in the School of Physics and it's quite bizarre that I've ended up where I started.

Are you still in touch with the painting conservation field today?

Yes, together with Dr Petronella Nell, one of my PhD supervisors from the Centre for Cultural Materials Conservation, University of Melbourne, we are going to publish a paper looking at accelerated ageing of fluorescent pigments in paintings. I also think fluorescence lifetime imaging microscopy (FLIM), which is a method I currently use a lot now, would be a really good non-invasive way to analyse pigments in paintings.

What questions are your lab trying to answer just now?

My research is focused on the role nuclear architecture plays in maintaining genome function. In particular, there are three main lines of enquiry. The first is on the development of fluorescence fluctuation spectroscopy (FFS)-based microscopy methods to quantify the diffusive route of proteins take within the chromatin. The other two projects employ this technology to investigate the role chromatin dynamics play in facilitating DNA repair factor recruitment to a DNA double-strand break and transcription factor–DNA target search strategies. In the latter project, we are particularly interested in how transcription factors employ oligomerization or self-association to modulate the accessibility of the nuclear landscape, as well as their binding affinity and DNA sequence specificity.

Could you explain why you chose these techniques?

FFS is a great method to track the diffusive route of proteins within the nucleus of a living cell. In contrast to techniques based on single-particle tracking, which rely on a small number of molecules being labelled so that you can continuously follow their distinct paths as a function of time, FFS extracts this information from a population of molecules and, as such, has very good statistics. In the context of transcription, FFS is very valuable

Elizabeth Hinde's contact details: School of Physics, David Caro Building (192), Cnr Tin Alley and Swanston Street, The University of Melbourne, 3010, Victoria, Australia.
E-mail: elizabeth.hinde@unimelb.edu.au

Journal of Cell Science (2019) 132, jcs241489. doi:10.1242/jcs.241489

Elizabeth at her house in Melbourne enjoying time with her daughter Wren and her father Stuart.

since it can quantify the impact oligomer formation has on transcription factor dynamics. For example, we use FFS to look at transcription factor dimer or oligomer formation and how this affects their mobility and their capacity to bind DNA. For interrogation of chromatin architecture, we're currently using FLIM coupled with a histone-based Förster resonance energy transfer (FRET) assay. With this assay you have a real-time read out of nucleosome proximity (1–10 nm) within each pixel of a microscope image (~260 nm) as the chromatin compacts. It's an indirect way of looking at chromatin compaction, but the advantage is that you can do it within a living cell and our hope is to multiplex this readout with the FFS-based methods we use to track nuclear protein navigation.

"I had never realised how much administration is involved in managing a lab and other people."

What challenges did you face when starting your own lab that you didn't expect?

I had a more gradual transition to independence. After my first postdoc with Enrico, I joined the group of Katharina Gaus (UNSW, Sydney) as a senior postdoc with a Vice-Chancellor Fellowship. She provided a lot of infrastructure for me and once I was awarded a Cancer Institute NSW Early Career Fellowship and a National Health and Medical Research Council (NHRMC) project grant, she let me branch out into my own group within her centre, which is an EMBL Australia node in Single Molecule Science. Moving to Melbourne afterwards and being officially on my own in 2017, I found difficult in the beginning; I had to establish and raise funds for the microscope system – it wasn't a given that the infrastructure I needed would be there. I found that to be a significant challenge – learning to have to ask for money and to push things through. The second thing that I was shocked by was the level of administration. I feel like I had never realised how much administration is involved in managing a lab and other people. I've had to become much more organised.

Are you still doing experiments yourself?

I don't do any cell culture work anymore, but I definitely do at least one and a half days of imaging per week – usually to help set up experiments for students in the lab or to teach them a method. More so for collaborations – doing different experiments with another research group. However, the largest part of all is analysis, of which I still do a lot.

How did you go about recruiting new group members?

When I moved to Melbourne, I had funding for a postdoc and one of my colleagues, Jieqiong Lou, in Katharina's group went with me. She helped me start up everything and we have a very good relationship, so that made it an incredibly smooth transition. Overall, it has been difficult to recruit students because initially I was embedded in the Biochemistry and Molecular Biology department and people were frightened of the physics component in our research; now, I'm in the School of Physics and I feel the students think again that what we do is completely foreign [laughs]. Nevertheless, I was able to recruit students after giving talks or the odd guest lecture in an undergraduate course, and I have two great students with zero previous experience in microscopy, but they're perfect.

You mentioned recruiting students after giving talks. Do you feel that making your techniques accessible has been key to your success so far?

I dedicate a lot of time to preparing my lectures and figures in papers, and I always try to make fluorescence fluctuation spectroscopy as accessible as possible. Because my interest is in the nucleus and studying transcription or DNA repair factors, I have modified the methods and the way I present their output to target those specific biological problems. So most of the collaborations I have now are with people who are studying transcription or DNA repair, which is great because, initially, I made collaborations with people studying any biological question, but I haven't optimised these methods for other aspects of the cell. Now I really understand how to measure chromatin dynamics or diffusion in the nucleus, and so I think the methods are more understandable because of those applications.

What is the best science-related advice you ever received?

I still Skype with Enrico once a week. He's been a huge influence and his advice to me has been to 'never worry in advance' – I try to follow this advice, although anyone that knows me well would know that I am always worried about something. As a group leader, I try to be flexible. I am not one to plan an experiment or project too far ahead and I prefer to just try to test things and figure out what is happening as I go along. I therefore like students who are open minded and give it a go, even if they don't understand everything initially – by doing experiments they'll learn and understand. In terms of mentorship, I try to be accessible and I feel as a result, in the lab we're behaving like a team.

What is the most important advice you would give to someone about to start their own lab?

Senior colleagues give a lot of help and advice and if you don't know what to do or you need input on something, you should ask them. Having a mentor outside your department is great because then you can run questions by them before you go to the person who is actually in charge of the outcome. I think that's something that I've really valued.

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How do you get the most out of the meetings you attend, particularly in the early stages of your career?

Now that my research has headed toward the nuclear landscape and chromatin field, my group is attending more chromatin-focused meetings rather than only biophysics conferences. For example, I recently went to an EMBO workshop on 'Chromatin dynamics and nuclear organization in genome maintenance' held in France and now we've got a couple of really strong international collaborations from it. I remember being at that chromatin conference and I had a poster. I felt it was a big risk to go to this meeting, and it could have ended up amounting to nothing, but after listening to the talks I introduced myself to speakers whose talks I enjoyed and invited them to view my poster. To be honest, in the beginning I didn't want to approach them but I spent so much time travelling to get there that I had to force myself! In the end, it was really worth it because they were interested and it has led to fantastic collaborations. I highly recommend inviting speakers to view your poster!

With your background in painting conservation, do you spend a lot of time at museums? Could you tell us an interesting fact about yourself that people wouldn't know by looking at your CV?

No, I don't spend so much time at museums. I mean, my husband does since he is an artist, but I don't, actually [laughs]. I like jigsaw puzzles a lot, and rowing. I used to do a lot of rowing in Sydney harbour and I planned on picking it up again in Melbourne because the Yarra river is really good for rowing. However, since I had my daughter in 2017, I have not really found the time to start again. So, jigsaws and running for now, nothing too unusual. Actually, one of my last rows in Sydney was in an eight and a ferry came too close to our boat so as we hit the wake from the ferry the boat snapped in the middle, sank and we had to swim to the nearest house and call an Uber.

I hope everybody was fine, though?

Yes, but there are bull sharks in Sydney harbour so everybody was quite panicked! We saved the oars though.

Elizabeth Hinde was interviewed by Manuel Breuer, Features & Reviews Editor at Journal of Cell Science. This piece has been edited and condensed with approval from the interviewee.