

GREAT EXPECTATIONS

The Path to Paraspeckles

From a childhood in India through running a lab in Perth, Archa Fox shares her story of balancing the personal and professional facets of her life.



Archa Fox with husband Charlie Bond, and children Anna and Billy, on the banks of the Swan River, 2011.

I am a scientist in my late 30s, with two small kids, a husband–collaborator and a lot on my mind! My childhood as part of a commune in India shaped my moral compass, and in some ways, led to me following my heart and becoming a scientist. What I have learnt along the way is that with great mentors, a bit of luck, as well as friends and partners for support, it might just be possible to combine family and career in this competitive and rewarding game of academic research.

A Hippy Upbringing in the Communes of India

I am going to start from the very beginning and talk about my childhood, as it was pretty out-of-this-world wacky. When I was three, my family moved from Perth to join a commune in India. We were all given new names: mine was ‘Ma Deva Archa’. I am the only one in my family who has kept their commune name – my name is part of my story, and I have learned to try to react with grace to quizzical comments when introduced at conferences!

The religious sect was led by ‘Bhagwan Shree Rajneesh’, later known as ‘Osho’ – we were the orange people, as we wore clothes the colour of the sunset. My life in India was a seemingly idyllic life of freedom. For the adults, it was daily meditations, group therapy sessions and discourses, and for the kids, it seemed to be endless days of just playing. I don’t remember much about this period of about four

years, but I can recall refusing to eat the vegetarian curries and instead living off a steady diet of Indian roti spread with vegemite (sent in the mail by worried grandparents), being completely freaked out at the dyed red hands and faces of the Holi festival, wandering around looking for my mum during the daily power blackouts, dancing like a whirling sufi in the huge mediation hall, living in a ‘kids house’ with no adults, and munching on raw



Archa in India aged 6.

sugarcane as a snack. When the Indian commune folded, we followed Bhagwan to America, in what was a huge experiment in social engineering: The Ranch in the state of Oregon. The orange people built a mini-city in the middle of nowhere, with an airport, hotel, shops and a lake. Kids were given the option of working or going to school: so, of course I chose working – but I am afraid to say I don’t remember being very good at anything I tried my hand at, so I spent a lot of time roaming around, looking for things to do. This was the time when Bhagwan was famous for owning a hundred Rolls Royces. We were told that the rationale was to laugh in the face of convention, but really – this was utterly bizarre behaviour. Inevitably, power corrupts, and the commune collapsed in 1985, and my family returned to Australia, settling in Sydney. From that time on, this chapter of my life was closed. We left behind the new-age lifestyle and beliefs, and essentially returned to a normal life.

The Roundabout Path to Science

Starting high school was daunting, but it turned out to be wonderful: because of my patchy education, I had a thirst for knowledge. I loved most subjects, particularly English, History, Biology and Chemistry.

I can vividly remember the moment when I first got a glimpse of the molecular nature of biology. In my Year 10 Science class, we were discussing how water is drawn into roots through osmosis, and our teacher added that salt is also taken up, even though roots are already more salty than the surrounding soil. I pushed my teacher to explain this and she said that they used energy to overcome the osmotic pressure – but what sort of energy? What kinds of machines needed this energy? She could not answer. I will always remember this, but I do pity that poor teacher having to put up with an arrogant student!

On reaching the final year of high school, I was faced with the inevitable question of what to do next. Although I had moved on from my strange hippy upbringing, I was still in some sense morally influenced by the doctrines of my early years: that life should be a spiritual journey of self-discovery, striving for a state of ‘enlightenment’, whatever that means. Busying yourself with a career was seen as distraction from the spiritual path. Even choosing a life trying to help others was frowned on: immersing yourself in the problems of others was another distraction from yourself. As a young adult, I was faced with something of a dilemma when it came to choosing what to do with my life. I was now a part of normal society, but I did not want to strive to make money or build a career. So I chose to follow what fascinated me,

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and I studied Science at the University of NSW, majoring in molecular genetics. What a good thing I went into science without needing monetary reward!

PhD-antics

I was really happy with my major at UNSW and rounded it off with an Honours degree with Tony Mackinlay, who announced his retirement at the end of my degree, leaving me searching for a PhD supervisor. I was incredibly lucky to be pointed in the direction of Merlin Crossley, then only just setting up his lab at the University of Sydney.

Merlin was, and still is, the most fantastic mentor and has been a huge part of helping me on my scientific journey. Anyone who has met Merlin knows that he is very charismatic and funny, and an amazing source of knowledge. I had the good fortune of being Merlin's first PhD student in Australia, and we worked well together and made some discoveries centered on some pretty important transcription factors in hematopoiesis, FOG-1 and GATA-1. The discoveries I made, and their subsequent publication, made it possible for me to contemplate a future career in science (which was lucky as I had not really set myself up for any alternatives!).

My time at the University of Sydney was great fun, but also extremely hard and harrowing, as every PhD must be. I was the president of the student Biochemistry society for a time. We had a blast organising trivia nights and BBQs at the front of the building. I had some great friends and mentors there, some of whom I now collaborate with. Of note here are Joel Mackay, Jacqui Matthews, and Matthew and Jackie Wilce. Merlin was adamant that his students make the annual pilgrimage to the Lorne Genome Conference. We rented out dodgy houses and had many exploits that I will not detail here, but fun (and great science) was had by all. This started my relationship with Lorne Genome that I still hold dear. For my sins, I have even been chosen to be the convenor for the conference in 2013.

It was also at this time that I met my husband, Charlie Bond, a protein crystallographer with Mitchell Guss. Fairly early on in our relationship, he told me that his next position was lined up in Dundee, Scotland. So, having to endure being the butt of Merlin's jokes about Hamish Macbeth (a popular Scottish policeman on TV at the time), I began to investigate possible labs in Dundee. This is part of the well-known 'two-body' problem that exists for academic couples, and was the first, but not the last, move that we would make together where we needed to take both our careers into consideration. So, I decided on the lab of Professor Angus Lamond, a renowned molecular and cellular biologist, working in the field of subnuclear organisation. Whilst I was writing my thesis, I also put together an application for a Wellcome Trust Fellowship. I was fortunate to be awarded this fellowship and arrived in Scotland ready to face my first winter at the end of 1999.

The bright lights of Dundee

Starting my postdoc, I felt like I had to begin everything again. Learning a new skill set seemed daunting, but I gradually took on the microscopy, proteomics and cell biology expertise that the Lamond lab is renowned for.

Living in Scotland was *mostly* wonderful: the Scottish countryside is exceptionally beautiful, the people are very friendly – but of course, the weather has a reputation that is justified! Joining a big lab was interesting, as most of the time, the lab had about ten international postdocs, with only one or two students. This postdoc-dense environment was very different to what I was used to, but was a great way of making life-long friends. Most of these postdocs are now scattered back around the world, starting labs of their own, and have become my extended scientific family.



Angus Lamond (centre, standing) and his lab, at a retreat in Glamis Castle, Scotland (Archa on Angus's left).

During my postdoc, I developed a somewhat esoteric project in which I discovered some new structures in the mammalian cell nucleus. Angus and I decided to call these things 'paraspeckles' as they were found close to the well-known splicing speckles. These little guys have become the focus of my research to the present date. I keep on trying to diversify, but they are pretty fascinating and keep me interested still. Originally, I discovered paraspeckles based on the localisation of a single protein, but recently, I was one of several groups that discovered paraspeckles are part of the murky world of RNA regulation, as they are built around a long noncoding RNA. Weirdly, John Mattick predicted a link like this, when he visited Dundee in 2002, and we chatted about my work. So there you go: either John got lucky, or perhaps RNA really is at the bottom of everything!

When Two Became Three: a Wee Scottish Lassie Born Under the Aurora Borealis

My time spent in Dundee was supported by two fellowships, and I see now that this gave me a great sense of independence within the Lamond lab. Angus was also very supportive scientifically and emotionally, including having an understanding of the young scientists in his lab who wanted to have children. So, after getting married, Charlie and I duly did the done thing and had a baby. This is an easy thing to write in one sentence, but belies the fact that actually the pregnancy was very stressful, with complications that meant it was hard to focus on working. The last three months were particularly difficult, eventually culminating in hospitalisation with suspected pre-eclampsia. It was a momentous relief when Anna Aurora Bond was eventually born on a cold night with Aurora Borealis flashing across the Scottish sky. She turned out to be a healthy, happy and

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Archa and baby Anna enjoying a burst of Scottish sunshine.

delightfully easy baby. This was a big part of my decision to go back to work when she was six months old, and she settled well into the nursery we had chosen. However, I have to be truthful and say that this was probably the one time in my career thus far where the chances of me leaving science for a long break were high. Because of the difficult pregnancy, I felt that her happiness was paramount, and

I was prepared to put her needs first. Support for young working mums is critical: Charlie was my lifeline, my backbone of support, and is an amazing father and partner. I was also fortunate to have other postdoc mums working in the Lamond lab, all in the same position, with children in childcare. We often discussed the working mother guilt dilemma: feeling that you never spend enough time either at work or with the children. But, our love of science, love of our families, and friendships helped us find a way to balance everything as best we could.

Flying Home to Start my Own Lab in Perth

After six long and cold winters in Dundee, Charlie, Anna and I finally boarded a plane bound for Perth and a new start back in Australia. Charlie was appointed to a tenure-track position at the University of Western Australia. We were fortunate that UWA, with the support of the research community in Perth, had decided to prioritise structural biology. It was too much to hope for two positions, but I had a Howard Florey NHMRC Fellowship to start a lab at the Western Australian Institute for Medical Research (WAIMR). Peter Klinken, WAIMR's Institute Director, was instrumental in bringing both of us here to Perth, and I am very grateful for his support and mentorship ever since.

The last five years here in Perth have been a huge learning curve, as I have had to figure out a whole range of people-management skills, learn grantsmanship, juggle rapidly growing collaborative networks, and try to get enough publications to feed the ever-starving, growling and ugly publication-triffid in the corner of my office. I have also seen my collaboration with Charlie go from strength to strength. Our labs recently solved the first structure of the RNA-binding proteins within paraspeckles, and this has led to new insights about the formation of these bodies. Collaborating with your partner is a strange and wonderful experience, and is incredibly rewarding, but also leads to some stressful moments when both of us are tired and grumpy from lack of sleep, and there are deadlines looming.

We have since had another child, a little scamp called Billy, who is now three and a half. Luckily, the pregnancy this time was uneventful. I have recently been fortunate to

be awarded a Cancer Council of WA Research Fellowship and a new NHMRC Project Grant. I am really happy with my lab at the moment, with two PhD students, a dedicated postdoc, several other students and support staff.

Running a lab and having young kids means you have to be very organised, and I generally only spend an eight-hour day at work. Whilst I do computer work after the kids are asleep, I have a continual feeling of trailing behind my peers, who are expected to, and continue to, work very long hours. This is something I have had to reconcile, but it is a constant juggling act.

My recent modest successes have made me feel perhaps there is a way of doing science that allows you to have fun with your family as well. The truth of the matter is that I find it joyful to be with my children, and I simply do not want to miss their childhood by spending too much of each day away from them. Charlie feels the same – I guess all parents do. Interestingly, I think that the values instilled in me within the commune as a child are also dictating my choices to some extent. They give me a sense of perspective on what is important in life, and also remind me that there are many alternatives, should I need to step off the traditional career path!

I am just like other scientists in wanting to discover great things and make a difference to people's lives. But I think my childish perspective of my spiritual upbringing might be wrong: I don't think family is a distraction from the spiritual path, and nor do I feel that wanting to leave a legacy of discovery, even help cure diseases, is egotistic. I feel instead that I am learning many important lessons about myself from being part of a loving family unit, and that being a scientist is also fulfilling a larger sense of purpose. Perhaps the intensity that comes with being a scientist is keeping busy that philosopher's part of my brain that would otherwise need to be tamed by meditation. Or perhaps I have it all wrong and I am just using my twin distractions of career and family to prevent me from walking the path to 'enlightenment', whatever that may be. I think you can see that it may be my life-long struggle to reconcile my upbringing with my life choices, but I am happy that on the whole I get it right most of the time.



Archa with Joel Mackay (left) and Merlin Crossley at the Lorne Genome Conference 2012.