Learning curve

Teaching the scientists of tomorrow

A PhD student's passion for science

by Faye Thorndycroft
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Are you looking for freedom at work, job satisfaction and a chance to change the world? Hannah Baker, the Biochemical Society's Professional and Education Projects Manager, interviewed Faye Thorndycroft, a 24-year-old PhD student at the University of East Anglia in Norwich, about what biochemistry means to her and why she's sticking with research… the perfect job!

Would I give this job up? NO way!

Being involved in scientific research is all about answering questions. When you think you have solved one problem, the answer generally leads to another question! There are infinite Whys and this is what makes it so fascinating — it's a life-long puzzle.

Thinking back to being a kid it's now obvious to me where my enquiring mind comes from. I have always been interested in how things work and what they were made of, which, to my Mum's dismay, led to a lot of gadgets being dismantled.

I'm better at completing things these days! I took Biology, Chemistry and Physics A-levels, and studied Biological and Medicinal Chemistry for my BSc degree, followed by a Masters in Medicinal Chemistry. I'm now a PhD student at the University of East Anglia and work on researching the biochemistry of particular enzymes found in bacteria. The full title of my PhD is 'Mapping a proton channel in bacterial nitric oxide reductase from *Paracoccus denitrificans*'.

Perhaps this long run of 'education' seems a bit daunting to any readers still at school? It doesn't feel like that to me: studying science at university is not like being in a classroom, it's a combination of interesting lectures, seminars and practical work, incorporating cutting-edge science, interacting with top researchers and professors and what you make of the rest of the time is up to you — I'm into karate and snowboarding. I've come to realize that there aren't many experiences available like that! All the steps I then made after my first 3 years were gradual and each one slowly developed my scientific skills and my confidence. Taking this path through the broad knowledge gained in my degree and the lab experience during my MSc felt very natural to me.

Going on to be a post-graduate science student is a full-time job working in the lab— sometimes at the weekends too. Some people are horrified at that thought, but it's not bad because working in science isn't like being stuck in an office all day. You have so many different jobs to do all over the building, on the computer, using machines and meeting with people, it's a very flexible and extremely dynamic environment to be in. No two days are ever the same: even if you are carrying out the same experiment, you come up with new and better ways of doing things. I love the elated feeling you get when you have been working on a project for a while, run your last experiment and then get the result you were looking for. You can't quite beat that!

My laboratory group works on the nitric oxide reductase (NOR) enzyme, as we want to be able to understand the mechanisms of the reaction that it catalyses in bacteria (the reduction of nitric oxide to nitrous oxide):

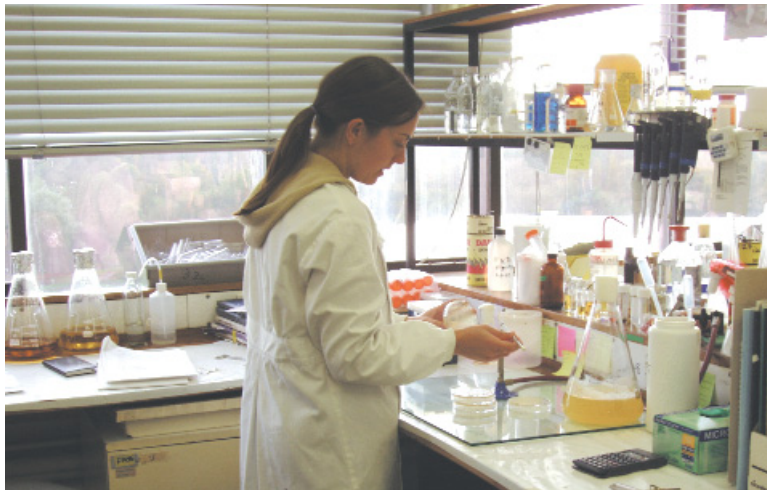
$$2NO + 2e^- + 2H^+ \rightarrow N_2O + H_2O$$

Two reasons for being interested in NOR are, first, some clinically relevant bacteria, e.g. *Neisseria meningitidis* or *Pseudomonas aeruginosa*, are able to defend themselves against the toxic NO released

by the host's macrophages by reducing it using NOR. Secondly, the product of NO reduction is N_2O, a greenhouse gas whose effect on global warming is 300 times greater than that of CO_2. Both of these reasons highlight the medical and environmental importance of research into NOR.

My research looks at how protons are able to get to the active site of the enzyme, which is buried inside a hydrophobic non-polar membrane. I have been focusing on some conserved amino acids that are likely to be responsible for passing protons down into the reaction centre. Using mutagenesis and a range of biochemical and biophysical techniques to study the mutants that I have made, I will eventually (hopefully) form an analysis of how this enzyme's structure and function contribute to the reduction reaction of NO to N_2O and therefore contribute to the bigger picture of discoveries into NOR.

Part of my PhD has been spent on exchange work, which has really helped broaden my experience of techniques, different institutions and, in this case, a new country. I worked for a month at The University of Stockholm, Sweden, with Dr Pia Ädelroth using flow-flash experiments. This experiment works by caging the enzyme in question with a molecule that has a photolabile bond. The enzyme must then be mixed with the substrate, whereupon a laser is fired at the cage, which in turn breaks off, and the substrate preferentially binds on to your enzyme. You can monitor various wavelengths optically and record any changes in the absorption of the enzyme. It is a technique that allows you to monitor very fast (microsecond range) reactions.



I love the topic area that I chose to do my PhD in. It is a real mix of genetics/biochemistry and biophysics, so I have had the opportunity to use lots of different techniques and I feel that my work will really make a difference in the understanding of how NOR works.

NOR is found in many different organisms and is studied by quite a few research groups around the world. Hopefully, once my work is published, others will be able to read what I have found and it will complement their research. The bigger picture of my work is to perhaps use NOR as a potential drug target as it is not found in mammals. So every step, no matter how small, leads us closer to understanding how this complex enzyme works.

I am currently preparing my first paper for publication and have formed enough results over the past 2 years to present posters at the 2004 and 2005 Nitrogen Cycle conferences in Norwich, UK, and Granada, Spain, and have just returned from the 62nd Harden Conference/EMBO workshop, 'NO: a radical in control', where I presented another poster and was also chosen give a short 20-minute talk. These conferences are a great way of sharing findings and meeting other people from all over the UK and the world working on similar areas of science. I have gained a lot of confidence as a scientist from being part of them.

I love the fact that I have freedom in my job, through determining my own schedule and speed of work, but mainly the fact that what I do every day is fulfilling and really does matter. Although I am at the beginning of my scientific career, I realized early on that if the experiments I'm doing show something positive, then they are just as important as the results of someone far more experienced. Researchers have a lot of responsibility at an early stage. That thought is a fantastic buzz and a big motivator. For me the important reason about being a scientist is the recognition of the tiny advances you make in trying to solve the massive puzzle.

To study for a PhD, I feel you need to be an enthusiastic individual with a passion for what you are working on. Being a scientist has given me lots of career options and I could get a good job in many different areas of work, but I have decided I want to stay in biochemical research and over the next year I will be looking at different research institutes and industrial companies. If I can find a lab working on issues that interest me I'll be sending off my CV… fast!