the largest difference between them. Only the profile in the first cluster that contains one of the two observations is used to recalculate the distances between the remaining unclustered profiles to find the next nearest profile or cluster, and so forth. The opposite of this is to use the smallest rather than largest observed differences and is called single linkage, but as this tends to produce an effect called 'chaining', where the tree lacks fine detail, it is not usually used for microarray data. Complete linkage generally produces compact, well-defined clusters and works well where there are strong patterns in the data. It does not perform as well when the data are noisy, as microarray data often are. Average linkage is an intermediate between single and complete linkage and tends to perform well with microarray data.

The reliability of hierarchical clustering

It should now be evident that the choice of distance measure and linkage method can have a profound effect on the outcome of hierarchical clustering. This is illustrated by the differences between the four dendrograms in Fig. 6. The reliability of hierarchical clustering can be assessed objectively. A permuation test can be applied to determine whether the clustering differs from that which would occur by chance alone. I gave a detailed explanation of permutation tests in the first article of this series and thus it will not be repeated here [2]. The advantage of this method is that it returns an exact probability and is free from subjectivity.

In the next article of this series, principal component analysis will be explored.

Patricia de Winter

References

Gaborit N, Le Bouter S, Szuts V, Varro A, Escande D, Nattel S & Demolombe S (2007). Regional and tissue specific transcript signatures of ion channel genes in the non-diseased human heart. *J Physiol* **582**, 675–693.

de Winter P (2009). *Physiology News* **76**, 24–27.

Letter from America – To study motion, how closely must you live with it?

Having bookended extensive time 'on the road' with studies into human movement, I have mirrored my work in the lab with a life filled with motion. Travel has long been described as a function for a state of peace and knowledge, but just as Kurtz in Conrad's *Heart of Darkness* is driven mad by the environment and his distance from 'home', how would I fare with movement research, while on the road?

Over the past two years, I have had the pleasure of roaming through India, living in Australia, climbing volcanoes in Guatemala, sun baking in Mexico, snorkelling in Belize and finally living in New York. I began my journey studying and writing my Honours thesis on the neurophysiology of movement, and ended it working in motor control at Columbia University in New York. To my knowledge, I have escaped Kurtz's fate and my movements and travels have clarified my ideas and thoughts on my studies.

After my degree in my hometown of Sydney, Australia, I was lucky to take an optional year of research at the Prince of Wales Medical Research Institute, supervised by Richard Fitzpatrick. This meant my previously purely academic studies were supplemented with 'home mechanics' forays into welding, wood construction, circuit design, beginner's programming and How To Use Bicycle Parts To Create A Terrifying Apparatus 101. I became very good at diverting the attention of subjects from the steel-, cog- and bolt-ridden planks upon which I conducted my experiments. To study our perception of ground height as we walk, I measured healthy subjects' limits of height detection between their feet – their height threshold – by making them stand or walk over increasingly smaller changes in height. The year was an intense one but I enjoyed it and moved along a very steep learning curve about physiology research.

My best friend, Bonnie, and I (left) enjoying the ambient static electricity on top of a Guatemalan volcano. Two minutes later lightning struck!

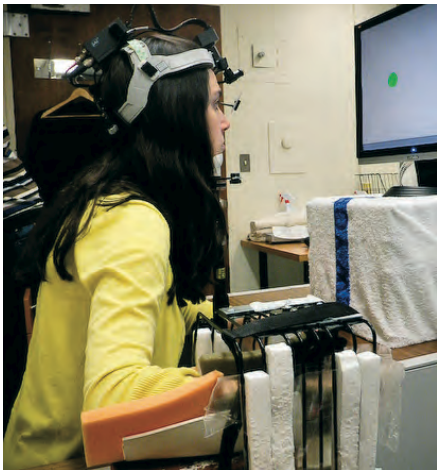
By the time I had finished writing up my thesis and presenting it in November of 2008, my feet were itching. During the year my interest in studying medicine had grown but the year-long application process looked, well, long. I had left for India by 1st December. Watching snake charmers and intricate Indian dances fed my interest in neuromotor research, while days suffering with bouts of 'Delhi belly' fuelled my desire to go to medical school. By the time I returned to Australia, I sent in my application and decided to spend the year living in New York City with my best friend to stretch myself both professionally and academically. Or at least that's what I told my parents. With friends, we diverted through Central America for 2 months.

In perhaps the only instance of a Canadian citizen flattering the USA, Sir Francis Head wrote, 'the heavens of America appear infinitely higher – the sky is bluer – the air is fresher – the cold is intenser – the moon looks larger – the stars are brighter – …' He goes on. This was when the USA was described as 'the new world', and needless to say, things have changed. My first contact with the States was in the suburbs of Anaheim, California, where not much can be described as 'fresh' except for the layer of paint on the Disneyland rides, and plenty of things are 'large', but the moon would be the last thing on my list.

On arriving in New York, I was eager to investigate the American style of

research and took an opportunity to meet and work with Pietro Mazzoni, co-director, with John Krakauer, of the Motor Performance Lab in the Department of Neurology at Columbia University, in uptown Manhattan. The experience of moving to a new city, finding a place to live, learning my way around and trying to avoid being run over was an overwhelming one. I expected to be similarly out of my depth when I met with Pietro and the lab at Columbia. I was, but in a different sense. The research being done at the Motor Performance Lab was incredible – it had the uncommon combination of being both clinically applicable and theoretically profound. As a 22-year-old from Australia, fresh out of my Bachelors degree, there were many 'little fish, big pond' moments. Despite this, learning about the lab made me feel much more comfortable than many of the other cultural lessons I had been discovering. Science research is arguably the most international of professions; pushing back the boundaries of knowledge requires sharing results and ideas. There was constancy to equipment, the techniques and the attitudes that made me feel a comfort that I'm sure many other researchers have found in a lab in a foreign city.
My work at Columbia University centred on a trade-off that exists in the motor system between speed and accuracy, called Fitts' Law. This describes a robust inverse logarithmic relationship between the speed of a movement and its necessary accuracy. Of particular interest was how submovements – the hypothesized simple components of gross movement – optimized the speed–accuracy trade-off.

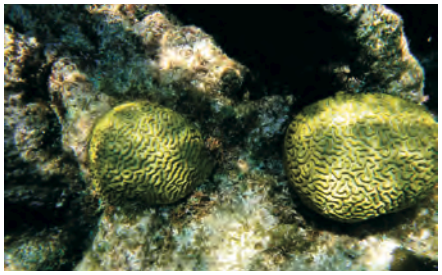
Meanwhile, life in New York started to feel more natural. I travelled back to Australia for my medical school interview and had the usual traveller's realisation that nothing much seems to have changed when you return. A highlight of the latter part of the year was attending the Society for Neuroscience Chicago conference. It was only the second conference I had ever attended



A fellow researcher, Sophie Ryan, demonstrating the motor study setup at Columbia University.

(the first was the 2009 Australian Neuroscience Society conference at which I presented a poster) so to say it was the largest is not a powerful statement. Nonetheless, nearly 31 000 neuroscientists descending on the Chicago convention centre is quite a sight!

As I write this in my final days at the Motor Performance Lab, I am excited to return home and start medical school, but am also filled with a sense of unfinished business. It seems that the more experiments you do, the more you discover you need to find out. I have spent the past two years moving through parallel experiences: treading across several countries with only a growing list of all the other places I must explore, and roaming around the realm of the neuromotor system asking more questions than I could ever have answered.



Brain coral in the Caribbean.

As Saint Augustine was reputed to have said, *solvitur ambulando* (it is solved by walking). I hope to keep travelling and return to physiology research soon, and with more ideas.

Joanna Offord

Measurement of gene expression using real-time quantitative PCR

29–30 March 2010, King's College London

The Physiological Society is sponsoring a 2-day 'hands-on' workshop to learn the principles of qPCR, focusing on the practical steps required to design, set-up, validate and analyse real-time qPCR assays.

Enquiries and registration: education@physoc.org

Course organised by David Sugden and Patricia de Winter

Meetings accommodation

Student accommodation has improved immeasurably in the 50-odd years since I started attending Society Meetings. I have memories of some very peculiar rooms, some so peculiar that it is best not to identify any of them. There was the high building in a gale-prone city that swayed so much it gave a nautical quality to ones sleep. In another residential block, the lifts served every other floor – specifically the floors that didn't have bathrooms. A particular challenge was mounted by the safety-minded university where overloading of electric circuits was prevented by a trip switch in the corridor outside each room. People arriving in the evening gloom could just about read the notice explaining how to reset the trip. Later arrivals went to bed in the dark and grumped all through breakfast.

Ann Silver