

Mathematical Biology: My Personal Journey

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When I first started doing mathematics (in 1981) the field of mathematical biology was very small. I had no idea it even existed. For me, it was all topology and graph theory and group theory and number theory, and all kinds of theories I've never used again. Then, one afternoon in the university library, I remember browsing along the shelves and picking up a little black book, published in some cheap and nasty font, called (I think) *Nonlinear Differential Equations in Biology*. By some guy called James Murray whom I'd never heard of. Well, when I read that book I knew that was it. That was the stuff I wanted to do. So I did. When I finished my undergraduate degree (at the University of Otago in New Zealand), I looked around for a place to do a PhD. My first choice, unsurprisingly, was Oxford, where James Murray was. But I have it on very good authority that Jim read my application, thought to himself "Sneyd? That's a funny name.", and threw it in the rubbish.

Oxford being unavailable, I started looking at places in the USA. I soon discovered that New York University offered courses on chemical kinetics, neuroscience, biological fluids, the visual system, and

a number of other cool things. That decided me, and a few months later, I trundled off to Manhattan. Small town New Zealand to New York City. It was a change, I can tell you.

At NYU I learned my very first real live Mathematical Biology. I did all the usual fluid mechanics - to this day I have only a vague understanding of fluids - but my real love, the stuff that motivated and inspired me, remained biology. I remember consulting with Charlie Peskin about the oral examination, the one you do after two years, before you start real research. Each student had to propose a list of topics to be presented to the examining committee, and I went to town on this. No sense of perspective, that's me. Charlie took one look at my proposed list, chuckled a bit, and said, in his usual kind and gentle way, "James, I'm not entirely sure it would be wise to cover ALL of these topics". At any rate, I ended up doing my PhD with Dan Tranchina on light adaptation in turtle cones. It's difficult to put into words the debt I owe to Dan and to Charlie. Their teaching, their mentorship, still forms the foundations of how I think today. I am standing on the shoulders of giants, but still don't see as far as they do. But I get to see very much further than ever I would if I was standing on my own.

The third major influence on my thinking was, as you might have guessed already, James Murray. After finishing my PhD, I went to Oxford for a year, to spend time with Jim and his group. We talked about patterns and morphogens, about honeybees, ants and termites, about alligator teeth, about infectious diseases, noninfectious diseases, forest fires, bugs, and cells. We argued about asymptotics and the value of nondimensionalization and whether we should prove things (not hard to guess which side I took). It was a wonderful group of people, and one of the most stimulating environments I have ever worked in. The friends I made there - most notably Jim Murray himself - remain today as a global network of inspiration to me.

Back in the USA, at UCLA, it wasn't long before I discovered the field that has formed the majority of my subsequent career - calcium dynamics. It was all rather serendipitous, I suppose. As a young assistant professor, with no set research direction, I was given some good advice by Ken Lange, who was chair of UCLA Biomathematics at the time. "James", he said, "go to every single talk in the physiology department. Every talk, every seminar, boring or inter-

esting, go to them all." Well, probably not his exact words, but that was the gist of it.

So off I went, as instructed. It wasn't long before this guy called David Clapham came by to talk about his recent discovery in *Xenopus* oocytes of spiral waves of calcium. At that time there were very few examples of spiral waves in the math biology literature, but here was a new one. Brand new. When I saw those calcium spiral waves, all lonely and unmodeled, I knew I had hit the jackpot.

That was the start of my interest in calcium dynamics. About the same time I also met Mike Sanderson, who has become one of my closest colleagues and friends. Mind you, it didn't begin well. Mike gave a talk in the Physiology Department, on the topic of intercellular calcium waves. Very cool, I thought. I could do that. So I went up to Mike's lab, knocked on the door, and said to him, "I really enjoyed your talk. You want to work with a mathematician?". Mike looked at me, paused, and said "No. Not really." Mike denies this ever happened, but you can trust me. It did.

Anyway, I wasn't going to be put off. I wanted to work on calcium waves, and I wasn't going to let a bit of grumpiness deter me. So I went back, and back, and back, until finally Mike realized that (as the Borg say) resistance was futile. After a few years at UCLA I went home again, back to New Zealand. I was a bit concerned. Would I find stuff to do? Would I find collaborators in New Zealand? Would I get bored? I decided to make sure I didn't, and began making plans to write a book. I'd read Jim Murray's wonderful book, *Mathematical Biology*, many times and used it extensively, but (let's be honest here) it didn't have a whole lot of physiology, and I'd always thought that a shame. Students kept asking me "Well, what is *Mathematical Physiology*", and I'd answer "Er... um... well...".

The book I was thinking of was too big a job for one person. I needed a co-conspirator. As it happens, I'd always been a great fan of Jim Keener's work on excitable systems and cardiac models, so I asked him to help me write it. Fortunately he had a momentary failure of rational thought, and agreed. The result was five years of effort for the first edition of *Mathematical Physiology*, followed by another five years of effort for the second edition. Still, at the time we didn't know it was going to take up ten years of our lives, so we rushed in where sensible people fear to tread.

Since then I've basically just kept doing the same thing. Calcium dynamics, mostly. I've moved around a bit, to and fro across the world; University of Canterbury, University of Michigan (where I met David Yule), Massey University, University of Auckland. I've always worked closely with experimentalists; Mike Sanderson and David Yule have been doing experiments for me for years. They like to think I do models for them, and I encourage them to think so. It makes them feel better, I think. I've been very lucky. I came out of my PhD (in 1989) just as mathematical biology was taking off. I rode that wave to my first job, and I've ridden it ever since. Now mathematical biology is an enormous field, widely valued across Faculties of Science, Engineering and Medicine, and one of the most dynamic and fast-growing areas of applied mathematics. It's rare nowadays to hear someone question the validity of mathematical modeling per se. (They might think your particular model is a pile of nonsense, but that is usually a rather different question.)

Although I was formally trained as a mathematician, I've never been one. Unapologetically. I don't care about mathematical rigor or proofs of theorems. I don't care what you can prove about your model, I care only about what your model can tell us about the physiology. I want to understand how cells work, how organs are put together, how they go wrong, and how you can fix them when they do. And mathematics is such a wonderful tool for doing just that.

List of Books:

- J. Keener and J. Sneyd, *Mathematical Physiology*, Second Edition, Springer-Verlag, 2008. Two volumes. 1049 pp.
- J. Sneyd (Editor), *Mathematical Modeling in Calcium Dynamics and Signal Transduction*, Lecture Notes in Mathematics, Springer-Verlag, 2005.
- J. Sneyd (Editor), *An Introduction to Mathematical Physiology, Cell Biology, and Immunology*, Proceedings of Symposia in Applied Mathematics, American Mathematical Society, 2002
- S. Camazine, J.-L. Deneubourg, N. Franks, J. Sneyd, G. Theraulaz, E. Bonabeau, *Self-Organization in Biological Systems*, Princeton University Press, 2001.

For more books, check out: <http://www.math.auckland.ac.nz/~sneyd/books.html>