Why science?

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Why science? It was really all the fault of one of my High School teachers! Maybe only a year after the structure of DNA had been proposed by Watson and Crick, one of our teachers explained to us that the 'structure of the genetic material had been discovered'. How amazing, we thought – the structure of the genetic material; it seemed impossible! In those days we didn't even know that wonderful acronym (DNA ≡ National Dyslexia Association).

During school holidays I was working on my grandfather's dairy farm in North Taranaki, and had the awesome responsibility of driving the horse and cart, by myself, taking the milk to the local dairy factory. It was maybe a quarter of an hour down Norfolk Road, an equal time along the main road toward Stratford, waiting in line with the other horse and carts (and an occasional old lorry) until it was our turn. Then it was myself with 6–7 large milk cans on the cart, each about 2 feet in diameter, and 5 feet high (sorry, it was before SI units on the farm). Then, tipping each large can slightly so that they would balance on their edges and could be rolled toward the large vat, tipped, the milk poured in, and the total weight of the milk recorded. The next step was a few yards around the corner, fill the large milk cans with whey (the remains of the milk after cheese was made) for the pigs; and then repeat the trip back to the farm. So, stop at the pig sties, tip the whey from the milk cans into the farm vat, and turn on the taps to each pig pen to fill the troughs. The pigs got their front feet into the trough, then their snouts, and off they went.

While the pigs gulped away, it was time to relax and daydream: Wow, it really was amazing, 'they' had discovered the structure of the genetic material. Maybe I should take the full science course next year?? Was that better than feeding pigs all my life? Maybe, one day, I could do something with that knowledge about the 'genetic material'. Hence my advice to students, 'feed the pigs, and daydream about DNA'. Enough of daydreaming, the pigs had finished gulping, take the horse and cart back to the shed, take the harness off the horse, rub the horse down, wash the large milk cans, and it was time for breakfast. Back to reality.

So anyway, I did take Science in the 6th form (hell, must be Year 12 now?), even though, the year before, General Science had definitely not been my best subject. And in the 6th form I did best at Maths and English, then Physics, then Chemistry, and finally Biology. I hated the essay-type questions in Biology, but enjoyed the possibility for ideas.

So, off to Canterbury University College; right to the end I was keeping my options open to do engineering, but science won out. Maths, Chemistry and Botany were great; but I really hated Zoology. It was brilliantly taught, but right out of the 19th century – Thomas Huxley would have loved the descriptive comparative anatomy. Yes, brilliantly, brilliantly taught. I can still remember (50 years later) differences between *Lumbricus terrestris* and *Maoridrilus uliginosus*. 'Observe, observe, observe', was the catch cry – but what about 'think, think, think', or 'test, test, test'? Why just 'describe, describe, describe'? But (if we had had such things then) I would certainly have given the staff very high marks for assessment of their teaching skills – though it alerted me to a point still not accepted even yet, that good teaching is not enough – modern content and thinking are also vitally important. New Zealand still seems to have University courses decades out of date in their content. Anyway, I vowed I would never, never, never again take another course in Zoology. I was cured of that subject (so I thought).

So Chemistry and Botany it was. I loved the physical chemistry, and Botany had all aspects of biology – biochemistry, physiology, ecology, genetics, life histories, as well as even a little comparative anatomy. Lecturers did have personalities, but fortunately we never took too seriously one beloved Welshman in Chemistry. Taffy would say in third-year Chemistry labs, 'How do you make a biochemist?' (and then proceed to answer his own question). 'You take a physical chemist and blow his brains out, so then you have an organic chemist. Now take the organic chemist and blow out what's left of his brains, then there's your biochemist'! Fortunately, I liked the biochemistry, even though it was decades and decades behind in accepting evolutionary ideas. I managed to sit in on Statistics, then a third-year Maths course. Apparently the course assumed one theorem that wasn't taught until second-year Applied Maths, so 'obviously' you couldn't take the Statistics course until the third year! And matrices were not introduced until third-year Pure Maths – which century were we in? Yes, most subjects were extremely well taught, but being up-to-date was not a requirement for all subjects!

But the most 'useful' single course I took as an undergraduate, and I have to sincerely apologise for pointing out it was 'useful', was Stage I Philosophy for Science students. The Professor was Arnold Prior, who took the science students for a lecture a week on mathematical logic – ANDs, inclusive and exclusive ORs, if and only ifs, well-formed formulae, Lukasiewicz and Tarski logic, Polish notation – all brilliantly 'useful' later when starting with those new-fangled robots called computers. Then there was a lecture per week on classical logic (very useful), and another on the philosophy of knowledge. The latter was on Popperian logic of science; Karl Popper had spent several years at Canterbury, and had written '*The Open Society and its Enemies*' whilst there. However, we studied his '*The Logic of Scientific Discovery*' – brilliant.

So yes, the lesson I learned from that lecture course was never, never, never 'believe' your hypotheses, but 'use' them to generate tests, make new experiments. But still be 'realistic', and accept that you were approaching some closer version of reality. I now tell the students, 'Belief is the curse of the thinking class' (and then give apologies to Karl Marx and to Oscar Wilde for updating their statements). To continue with the Philosophy lectures, there was another lecture each week on the 'real philosophers', Berkeley, Kant, Hume. I don't think I learned anything whatsoever from them, but perhaps when I grow up I will try again. But it is really best not to grow up – adults know everything! Much better not to grow up; just keep learning.

But from this last lecture, we invented a game called 'philosophy' – could we misunderstand what you said? No matter how precise we were, anything we said could be misunderstood by some determined soul – who then was the winner at the game. It was hilariously amusing; no matter how careful you were, a determined individual could manage to misinterpret what we were saying. So we learned not to play that sort of 'philosophy'; the logic aspects were much more informative. I have recently been told that the game is a mirror image of the game 'politics'. In that game the intent is to mislead you, while apparently telling the truth. If you are not fooled, then you are the winner. Perhaps that is a harder game than 'philosophy', it just seems too easy to determinedly misunderstand someone.

What next? Maybe it was time to escape GodzOwn and do a PhD overseas. (Tom Scott had not even invented the term OE at that time.) The fastest way out was a 4-year Honours degree; quicker than a 5-year Masters. Okay, four papers in Botany, but one was straight description, as bad as Zoology. I was allowed to 'sit in' on a Physical Chemistry Honours paper, but not to 'sit it' – it 'didn't count' for Botany – no special topics allowed – do what we academics are interested in you dumb little student – we know what's good for you – you don't. But I loved the honours physical chemistry – Statistical Thermodynamics. Conceptually, it was so much more straightforward for a biologist than the classical thermodynamics that we had had drummed into us as undergraduates; why you couldn't build a steam ship to sail across the Atlantic taking heat from colder water and putting it in the warmer water. But I was not interested in designing and building ships, the statistical thermodynamics interpretation of entropy was a far simpler concept for a biologist. Okay, the formulae were probably more complex, but the concepts were more natural, and you had to get those first.

Fortunately Arthur Galston, a professor from Yale, was briefly visiting the DSIR at Lincoln, and strongly encouraged me to apply there – not following the tradition of the time of going to UK-land. So Yale's where I ended up for my OE. Lots of exciting things, molecular biophysics on the floor above, molecular genetics immediately below, dozens of visitors coming through and giving seminars. To we graduate students, Jacob and Monod were leading the excitement – by then Watson and Crick were considered old hat. They had just described the structure of DNA, Jacob and Monod were telling us how it worked, and how it was controlled and regulated in the cell. Being in a biology department I had to do a couple of zoology courses – in Developmental Biology. Despite my vow never to do Zoology again, the courses were really brilliant – real questions, real experiments, real progress (that continued to develop for decades, right up to the present). What did I say about some New Zealand university courses being proudly decades out of date? Yes, experimental zoology was great.

Because we demonstrated in first-year laboratory classes, we had to go to first-year lectures – so that we knew what the students had in lectures. Don't worry, said the older graduate students – the lectures are brilliant and informative. They were. It was a great honour to be allowed to lecture to the first-year students. The lecturers were told they had 50 minutes to tell the students what were the exciting things about their subject. So they did just that – and the students applauded at the end of each lecture. I have never seen that before or since – first-year students applauding their lecturers!!! Of course, the lecturers were not slaughtered by having to grade all the tests, assignments and exams – that's what we poor graduate students were paid for. (Years later, back at Massey, I found that we gave each first-year lecture twice (two hours) because the class was so big – but then we spent (on average) 10 hours marking tests and exams. Hold on, 2 hours teaching and 10 hours marking – isn't that the wrong way round – isn't 10 hours teaching to 2 hours marking a better ratio? Is that really why we employ academics for 'research-informed teaching'? Oh well!)

Back to Yale, I learned so many things. The Molecular Biophysics course was brilliant – well, in most parts. The real focus at Yale on 'educating' undergraduates was remarkable. It was accepted that most would not be, and would not want to be, professional biologists, but whatever they did we had to give them the widest possible knowledge and thinking skills. Professional skills were to be learned in Graduate School; undergraduate studies were for a broad education. An important lesson came from the founder of Limnology, G. Evelyn Hutchinson. We held him in awe, almost as a minor deity. Not only had he virtually invented a new corner of physical environmental studies, but he knew ancient languages, and wrote mathematical scribblings in the *American Scientist*. As Dean of the graduate students for biology, he told us simply, 'Our job is to turn you into better biologists than we are'. But that was impossible: we could never even equal him, let alone exceed him. But the thought stuck – that was our job as academics, and it is still our job! We must never forget it. Those damned graduate students must end up as better biologists than we are – its simply our job to make it happen – the quicker the better!

Whilst I was there, Roderick Thomas did a sabbatical from the DSIR in Palmerston North, and then transferred to Massey when it set up a Science Faculty. He wanted me to come back. So after a year in Canada it was return to New Zealand, where Massey had been highly innovative and had set up a Cell Biology course in the first year, and (apparently) I was to extend this to the second year. But by the time I arrived, the consensus had blown apart, and (40 years later) we still haven't got that basic and innovative second-year Cell and Molecular Biology course – academics can certainly dig their toes in and defend the past, defend the past!

I quickly found two themes amongst my colleagues: some aimed to educate students for the future (using the students favourite subject as a focus for their long-term education). Others wanted to train their students for the past – 'teach-em' what we ourselves had learned about this discipline 20 years ago. Okay, you've guessed it, I was for the 'good guys', wanting to educate students for the future – not training them for the past. Simple, isn't it? And I am not biased! I still call the education approach the 'University model', the training students for the past the 'Polytechnic model' – but that is rather unfair on Polytechs.

But there were lots of outside activities in Palmerston North, the piglet Muldoon as Prime Minister fired up quite a few academics to get involved in political activism. We founded a Massey ('Fitzherbert') branch of the Labour Party, organised and ran local election campaigns, and even rewrote the Constitution of the Party. Other activities included demonstrations and conferences against New Zealand involvement in the Vietnam war, we supplied the facilities for the first edition for *Amandla* (the Halt all Racist Tours – HART newspaper), marched up and down against all white All Black tours, helped organise a local branch of the Women's National Abortion Action Campaign (WONAAC), opposed nuclear armed ships in our ports. You name it, we were 'agin it'! A favourite parody was the children's book 'Hippy the Hippopotamus'. Hippy wore a flower behind his left ear, and carried 'a placard for a lost cause'. That was us! Other activities eventually became more respectable, being elected president of the Society for Molecular Biology and Evolution, NZ Association of Scientists, and the Society for

Systematic Biology (who are major users of the theoretical scribblings we play around with).

Teaching was fun, research was fun. Pauline and I started out following the work from Yale, studying the mechanism of action of plant hormones kinetically – this involved (with a little help from the physicists) designing and building equipment for measuring plant growth every minute, and timing the responses to a range of experimental treatments. It was good fun, and quite a few publications came out, including: pH and auxin-induced growth: a causal relationship? *Plant Science Letters 4*: 35–40 (1975); Early responses of excised stems to auxins, *Journal of Experimental Botany 23*: 23–36 (1972). The studies are summed up in a book chapter, Rapid responses to phytohormones, pages 537–597 in *Phytohormones and Related compounds*, Volume II (1978) (D.S. Letham, P.B. Goodwin, and T.J.V. Higgins, eds).

But in the meantime, fate intervened. In 1967 Fitch and Margoliash published their paper in *Science* using protein sequences to infer evolutionary trees. Wow, the power of the physical sciences applied to a stimulating evolutionary question from biology! It looked quite easy, and surely I could improve on those analyses. Wow, was I naïve! I think I was about the second biologist to start using the new IBM 1620 computer at Massey – no prewritten programs in those days; you had to start by writing your own. So thereafter it was a bit downhill for plant cell biology, but uphill for molecular evolution.

When I came back from my first parole (aka sabbatical) I went to see a well-known statistician, Bruce Weir, and asked who could help with the problem of 'trees'. Its simple, he said, you just give a seminar to the mathematics department, and I am sure someone will be able to help you. Panic, panic, panic, 'I don't know mathematics', I said, 'I only did Stage One, and that was years and years ago.' 'No problem,' said Bruce, 'it's a very interesting question – how about Thursday next week?' I was trapped, and terrified, but there was no getting out of it now. But surely the mathematicians would know the answer.

From there on there was no way out – yes, some of the mathematicians were very interested. 'It should take a few weeks to solve your problem,' they said. That was over 35 years ago, and I am still enjoying the collaboration with Mike Hendy and colleagues. One just grew to love the mathematicians and their 'chicken scratchings', as Pete Lockhart affectionately describes their scribblings on bits of paper, backs of envelopes, blackboards, whiteboards, anything that doesn't move fast enough. Yes, there are lots and lots of stories about mathematicians, but I found that only the best ones are true! A favourite was the unfortunate mathematician visiting a foreign land, and whose behaviour was really suspicious – scribbling, scribbling, scribbling on bits of paper all the time. So he was charged and convicted of spying, and sentenced to life imprisonment. No problem really he decided; I hereby define the inside of my cell as the outside (and vice versa) and those poor guards on what is now the inside are condemned to always bring me food and paper. I am happy scribbling, scribbling away, proving theorems – what a cushy life!

One of our first successes was finding a way of making, and testing, quantitative predictions about evolution – thus answering a criticism of Karl Popper about the apparent lack of falsifiability of evolution. This was certainly putting my undergraduate education to good use. Initially, the problem looked so abstract that we wondered where we could find a journal obscure enough to publish such an esoteric problem. Then a controversy erupted in the pages of *Nature*, with claims that evolution was not falsifiable – was not real science. Wow, a natural home appeared! So luck does occur, but perhaps a prepared mind is necessary. The paper was: Testing the theory of evolution by comparing phylogenetic trees constructed from five different protein sequences, *Nature 297*: 197–200 (1982).

Perhaps our most successful paper, in terms of citations, is: Recovering evolutionary trees under a more realistic model of sequence evolution, *Molecular Biology and Evolution 11*: 605–612 (1994). This was the culmination of several years' work, finishing with Mike Steel fighting off sea sickness during a very bad ferry crossing across Cook Straight – but he got the final formula! But there were other ones with chicken scratchings that were useful – we love Hadamard matrices. Where would be without the mathematicos? In addition to the mathematical questions, there were many applications. A fun one was estimating the founding population size of Polynesian females arriving in New Zealand: Testing migration patterns and estimating founding population size in Polynesia by using human mtDNA sequences. *Proceedings of the National Academy of Sciences USA 95*: 9047–9052 (1998).

Nothing could be too sacred not to challenge. A very popular idea was that Darwinian evolution was not sufficient for macroevolution, and that some external physical forces were necessary to 'drive' macroevolution. The first question we tackled was the Cretaceous/ Tertiary extinctions, where it was assumed (without a single piece of evidence) that birds and mammals could not possibly out-compete dinosaurs and pterosaurs (that gave too big a role to competition, according to the North American Marxist scientists). But it was okay if dinosaurs and pterosaurs went extinct for some external physical reason, leaving 'vacant niches' for birds and dinosaurs to 'evolve in to'. Our challenge showed that modern birds were diversifying long before the extraterrestrial impact (which was certainly a real impact, but has never ever been shown to be necessary for the rise of mammals and birds). Our first test was: Mass survival of birds across the Cretaceous/Tertiary boundary, *Science 275*: 1109–1113 (1997). The work continues today.

So most of these projects still go on. We are very interested in the nature of the ancestral eukaryote, because it relates to the transition from the later stages of the origin of life, to modern biology – there is a lot of theory behind that. An early publication is: Relics from the RNA world, *Journal of Molecular Evolution 46*: 18–36 (1998). This subject is still very active, with a *Trends in Genetics* paper this year.

Finally, we now have amazing opportunities from the rise of genomics with an explosive increase in DNA sequencing ability. A whole range of new questions becomes available and the future is really, really exciting. When will it stop? Am I, too (like our mathematician friend), condemned to be ever-inquisitive and to continue to scribble away? Feeding the pigs would have been fine, but it is too late now to back out. DNA sequences give the power of the physical sciences to the interesting and challenging questions from biology. 'All organisms carry their history in their genes' is our slogan. But history is not enough, we want the processes that are going on even now. RNA viruses are evolving right under our nose. Ouch, we can't stop evolution. Can we be cured of science?