A Worm's Tale

written by

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There's something inherently amusing about worms. Perhaps it's just the sound of the words: 'I work on worms' which usually provoke at least the hint of a smile from the person who's just asked me what I do. It makes me think that, just perhaps, spending hours and days at a microscope discovering obscure facts about an obscure animal is not such a bad way to earn a living.

When normal people think of worms, if they ever do, it's long pink stretchy things being pulled out of lawns by birds, or crawling around in the compost bin. The worms that are my work mates are barely distant cousins of such earthworms. The only relatives of my worms that gardeners know are the nematodes you can sometimes buy for killing slugs. My worms are tiny, barely a millimetre long, just about visible to the naked eye as little white squiggles. Look at them down a microscope though and they're sleek, elegant animals, so thin and clear you can see right through them, beautiful as they glide effortlessly along. But then perhaps I'm biased and should get out more.

I'm not the only one– there's a growing community of worm workers around the world. These people have many backgrounds: some seek cures for cancer, others tackle aging, others want to understand the miracle of how the single cell we all start from, the fertilised egg, divides and divides to produce the intricacy of cells that make up any animal. What unites us is, at first sight, one of the least significant creatures on the planet, a lowly worm that doesn't even have an English name. Those who want a name have to use a scientific one: *Caenorhabditis elegans*, such a mouthful it's shortened to *C. elegans*, usually just 'The Worm'.

Worm workers are sociable– it was at the European Worm Meeting, that I first met Jonathan Hodgkin. That year the meeting was in England, at the beginning of July. Jonathan had realised that there would be some Americans there who would miss their Independence Day celebrations on 4th July, so he'd brought along some fireworks to stop them feeling homesick. I don't know how the Americans felt about it, but I, a young student, just joining the worm community, found myself helping Jonathan light up the sky of that Summer night.

Jonathan Hodgkin didn't just practice international relations, he studied them, in the worm world. He'd written an article, (ostensibly a scientific one) that told stories, stories of the origins of the worm. These weren't the stories I'd learnt, of an animal plucked from obscurity to become, by unprecedented feats of human endeavour, the best understood animal on the planet, the stories of scientists with great vision who, in 2002, finally won the Nobel prize they so richly deserved. No, these were stories of the worms themselves, of a richly diverse international community. They came from all over: German worms, plucked unceremoniously from a 'large compost heap on the edge of the Black Forest', Californian worms that had squirmed happily in a flower bed at a university, Australian worms, Hawaiian worms, not to mention the original Albanian worms described in 1899 in 'La mue et l'enkystement chez les nematodes' (a publication of such mystery even the title contained a word missing from my dictionary). The stories were not just of origins, they were of lives– French worms that were 'unhealthy', Americans who lived longer than anyone else and Brits who were the largest and most fertile of the lot. These worms didn't just have stories, they had personalities: some sociable, clumping together for meals, others loners, only congregating if they had to. There was even a voyeuristic peek into their sex lives where some males left their partners with, not only sperm, but a gift of gelatinous gloop, the purpose of which, to us mere humans, was entirely baffling.

To us wormophiles, these stories begged a question and planted a thought. The question was 'what is causing all this variety?' and the thought was 'maybe, just maybe, this could be the chance to finish, or start to finish, what the great father of modern biology, Charles Darwin had started, to really understand the process of evolution that made, not just the diversity of worms, but the diversity of all life, us included'. Whether Darwin went to the Galapagos and looked at exotic birds or a farmyard and looked at chickens, he was impressed by the diversity of life. He had deduced the existence of a process, 'Natural Selection', the survival of the fittest, responsible for the evolution of natural diversity. But Darwin had a problem, a problem he never solved: natural selection didn't work. At least, with the way he understood offspring got characteristics from their parents, it couldn't work– as he understood it, the characteristics of each parent were blended in their children, so the changes produced by natural selection would be blended away into nothing. Clearly there was something else going on, and that something was genes. Darwin didn't know about genes, but genes are what stop differences between creatures being blended away– genes don't blend– different genes may get mixed up a bit between parents and their children, but they stay distinct– either you’re blood group O or you’re not and that's that.

And that's all it needed, if you know about genes and about natural selection the system works– you can see how all the diversity of life on earth evolved. From the first stirrings in the primeval sludge to the diversity of a modern day coral reef, scuba divers and all, we understood how it happened. This understanding got a grand title 'The neo-Darwinian synthesis', scientists, and pretty much everyone who didn't try and dispute its existence on religious grounds, believed they understood evolution. End of story. Or maybe not. Despite many thousands of genes that scientists knew, in virtually no case was there a story stretching from a real, naturally evolved difference between two creatures, back to the gene that caused it telling how it did it. There was one gene that had a difference in it which made some fly maggots to wander around whilst others, without the difference, stayed put. And that was it, nowhere else could anyone point to a gene and naturally selected changes and say 'this is how it works'. There were many good excuses– there are thousands of genes in even very simple creatures and working out which is responsible for changes is hard. The creatures well known in evolution, like Darwin's finches, did not have well known genes and the ones with known genes were generally single, isolated creatures with no variation to study. But these were just excuses– we might understand the principle of how evolution worked, but we couldn't point to the practice. This is where another worm man comes in, one with foppish curly hair and a penchant for bright shirts. His name is Mario de Bono and he worked with Jonathan Hodgkin in Cambridge. He knew the stories Jonathan was telling about the diversity of worms and saw that here was where evolution met genetics– here there was real variation, the result of natural selection, as well as real knowledge about genes. Before the 'Human Genome Project' started, all 20,000 or so genes that make a worm had been identified. Every division from the first split of the fertilised egg into two, to the formation of the 959 cell adult worm, had been meticulously watched and documented. Here surely was the opportunity finally to trace the story of evolution, all the way from the differences brought in by natural selection to the genes.

The particular example of evolution that Mario chose to study was between sociable and loner worms. He started to look for what made Australian worms get together in groups, but British worms wander around on their own. The plot of the story is beginning to emerge: The difference that matters is in a gene, snappily called 'Neuropeptide Receptor 1 gene', *npr-1* to it's friends. Most genes are just long sets of instructions to make a particular chemical, a protein. *npr-1* is a gene that makes a protein 457 units long. It turned out that in sociable worms, just one of these units, number 215, was different to that in loner worms. It's a small change, but it seemed to be enough to make the difference between splendid isolation and a frenetic social whirl. But how? What does it do? (and how can I get it to improve my social life?) Well, apparently it's all in the nerves. Nerves that link between what the worms smell and what they do. If they smell food, that means, that a chemical from the food is being detected by a nerve in their nose (or the worm equivalent). What happens next depends on the nerve and how it communicates with other nerves that make the worm's body do things (like go and eat, or decide that mealtimes are too stressful and run away). With the help of his team, Mario worked out exactly which nerves these were (the worm has 302 to choose from), both the nerves involved in smelling the food and those involved in making the worms do things. The way these nerves communicate is again with chemicals, and this is where the decision is made– am I going to have a sociable meal, or am I going off on my own? It turns out that the chemical made by that gene, *npr-1* lives in those nerves Mario's team found were the important 'doing' nerves. The difference in the *npr-1* chemical changes how sensitive the nerve is to communications from the smelling nerves. The version in the British worms is very sensitive, so the nerves are much more likely to decide to turn off and decide that the worm is not going to the party. On the other hand the Australian version is much less influenced by what chemicals coming from the smelling nerves are telling it and so the doing nerves stay on and the worm keeps in with its friends. Many questions remain, but a story is appearing of how a big social difference came from a tiny genetic change, one small example of evolution.

Why does any of this matter? Beyond uncovering the mechanics of international worm society, about which human society hasn't previously shown much interest, does it matter at all? Or is it only good for keeping worm enthusiasts like me off the streets? Well, the way the nervous system of the worm communicates has lots in common with our human nervous system– the first reason to guess that the gene, *npr-1* had something to do with nerves was that it looked very similar to known nerve genes in mammals. So Mario's insight will be really important for designing new ways to treat human diseases involving behaviour and the nervous system, things like hyper-active children and depression. It might even be possible to reduce animal welfare problems in farming by helping animals become more sociable– reducing the stress of being cooped up in big groups. But, though I guess I believe in those sorts of benefits, much more exciting is the idea that finally, nearly 200 years after Darwin was born, we might start to uncover what lies behind the processes he discovered at work in evolution. Diversity in the international community of worms may not be as pretty as the diversity of a coral reef or a rain forest, but it's every bit as much a product of evolution. In seeing how the social lives of a few worms have come to be the way they are perhaps we're seeing a glimpse of God's thoughts after the fact– understanding what he, if he's out there, did to make the awesome diversity of life on this planet and indeed ourselves.