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Brian Charlesworth is a Senior Honorary Professorial Fellow at the University of Edinburgh. His work has involved the application of population genetics to a variety of issues in evolutionary biology. His current research is on population genetics theory, molecular evolution and genome evolution. He has published over 300 papers and three books.

What turned you on to biology in the first place? From an early age I was fascinated by living creatures, especially animals. My early childhood home was in Hove, where I enjoyed collecting snails from a bombsite and marine animals from rock pools, as well as going on walks in the nearby Sussex countryside.

Who were your key early influences? As a child I read a lot of natural history books and especially loved the ones about the Lake District by ‘Romany’, who I suppose is almost totally forgotten now. Gerald Durrell was also one of my favourites (he still is). I had excellent biology teachers at my high school and got into studying genetics and evolution in my teens — I guess I’ve never really grown up.

As a teenager and undergraduate I read the classic books on evolution by Dobzhansky, Fisher, Haldane, Maynard Smith, Rensch and Simpson, not that I really understood a lot of their contents. However, their writings stimulated me to take genetics for my final year at Cambridge and embark on a PhD in population genetics.

My postdoctoral advisor at Chicago, Richard Lewontin, was a huge influence on me: he was at the peak of his career with a group of very clever young people around him, several of whom became leading figures. His ability to ask critical questions and not tolerate bullshit, as well as do first-class science, was a real inspiration to me and my fellow postdocs. I was also fortunate to later work under Philip Sheppard and John Maynard Smith, both outstanding scientists in very different ways. I think that learning by example from really good people is very important for young scientists.

And what drew you to your specific field of research? Genetics attracted me because of its strong theoretical and quantitative content, combined with the rigorous testing of hypotheses against experiment and observation. An awful lot of biology, both ancient and modern, is tantamount to stamp collecting (to misquote Rutherford). I got into population genetics because of my interest in evolution and because I was attracted to the application of mathematical models to biological issues, although I am not especially good at maths. The application of molecular biology to evolution and population genetics was just starting when I was a PhD student, and the whole field has simply exploded over the past 50 years, so it was a lucky choice.

Do you have a scientific hero? You’d have to be an idiot not to name Charles Darwin as a hero if you are interested in evolution — his originality and profundity are amazing, and his intellectual legacy pervades evolutionary biology. After Darwin, the ‘Founding Fathers’ of population genetics, Fisher, Wright and Haldane, are my scientific heroes. Fisher was probably the greatest evolutionary thinker since Darwin, with an extraordinary combination of biological insight and mathematical virtuosity — but Haldane and Wright ran him pretty close.

Do you have a favourite paper or science book? Darwin’s On the Origin of Species is the best book on biology ever written: its English style is superb (greatly admired by Lytton Strachey, who was no slouch), the marshalling of facts to test the ideas is unsurpassed, it revolutionised our ideas about the position of humans in the natural world and it can be understood by any intelligent reader. My favourite paper is R.A. Fisher’s 1922 paper ‘On the dominance ratio’. This introduced all the basic theoretical content of population genetics, including selection at a single locus and the stochastic effects of finite population size. Everything we do in population genetics today flows from this paper.

What’s your favourite experiment? Mendel’s crossing experiments on peas. These were the first experiments on heredity where a clear hypothesis was tested against quantitative data obtained from a careful experimental design. All of genetics comes from Mendel’s ideas and results. I am particularly fond of Mendel because my father attended high school in Brno (he was a refugee from the Nazis).

What is your favourite conference? My favourite conference is the annual Population Genetics Group Meeting, which was founded over 50 years ago by the late Bryan Clarke. It is open to anyone who wants to attend, contributed talks and posters are assigned on a first-come, first-served basis regardless of academic status (old codgers like me get a look-in), there is no formal organisation (each year someone volunteers their university as a host) and the scientific quality is just as high as that at more prestigious meetings. It is also a lot of fun, with plenty of opportunities for people to get together, talk, eat and drink.

What has been your biggest mistake? As a postdoc in 1970 I analysed a model of selection in a density-dependent population. I found that sufficiently strong density dependence could result in limit cycles of population size. If I had pushed it a bit further, I might have discovered chaos, which made Robert May famous a few years later. One consolation is that John Maynard Smith made the same mistake.

What is your greatest research ambition? I think that I am being fairly honest in saying that I’ve never really had...
Quick guide

Balanced lethal systems

Ben Wielstra

What are balanced lethal systems? Balanced lethal systems pose an evolutionary mystery. Although natural selection should keep lethal alleles (dysfunctional versions of essential genes) in check, the frequency of lethal alleles in a balanced lethal system is highly inflated. Here is how it works: in a balanced lethal system, two homologous chromosomes each carry private, recessive lethal alleles, each of which is reciprocally compensated for by a functional gene copy on the other homologue. Therefore, an individual needs both chromosome forms — and in effect their linked lethal alleles — to survive. Yet, parents randomly transmit only one of the two forms via each gamete. As a consequence, progeny may receive two copies of the same chromosome form and miss the essential other one. In accordance with the rules of Mendelian inheritance, half of the offspring will be homozygous for either of the chromosomes and hence genetically pre-determined to die (Figure 1). Such a high mortality rate, recurring every single generation, appears to defy the basic tenets of evolutionary theory.

How could such a wasteful system evolve? Balanced lethal systems have been described in plants (the genera Isotoma, Oenothera, Rhoeo and Gaphytum) and insects (Drosophila tropicalis and Tribolium castaneum), but the best-known case is observed in vertebrates, in newts of the genus Triturus (Figure 2). This broad taxonomic spread suggests that a general evolutionary principle is at work. Yet, considering the incredible genetic load associated with balanced lethal systems, this seems counterintuitive. Natural selection is expected to: prevent a balanced lethal system from becoming established, because conspecifics that do not suffer from a balanced lethal system enjoy a considerable fitness advantage over, and should outcompete, carriers; and counter a balanced lethal system that is in place, because recombination should detach lethal alleles from a particular chromosome form, creating conspecifics liberated from the burden of the balanced lethal system. Explaining the evolution of balanced lethal systems requires a scenario in which short-term benefits ‘fool’ natural selection into opting for an arrangement that is actually detrimental in the long run, and in which two chromosome forms that amass private lethal alleles are involved. Sex chromosomes and supergenes could be implicated.

What could lead to fixation of the lethal alleles? Repressed recombination plays a fundamental part in balanced lethal systems. This explains why private lethal alleles cannot be purged from the two distinct chromosome forms. The acquisition of deleterious mutations is a well-known side effect of suppressed recombination, through a process known as Muller’s ratchet. Without recombination, purifying selection is less efficient in ridding an evolutionary lineage of deleterious mutations. Because genetic drift will eventually result in the