CHAPTER 4

SEX, SEXES AND SELFISH ELEMENTS

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It was a chance conversation that led to me doing a DPhil (as they call their PhDs in Oxford) under Bill's supervision. In the summer of 1986, just prior to my final undergraduate year studying Zoology at Cambridge, I happened to talk to Nick Davies, our lecturer in behavioural ecology. We chatted about what I found interesting. The idea that male birds show off their parasite status to females was a really fascinating idea, I remarked. He suggested that I should therefore do a DPhil with Bill Hamilton in Oxford. Nick kindly wrote a letter of introduction and, sometime later that year, I found myself in Bill's office in the Zoology department, being interviewed by him and Alan Grafen for a DPhil position that they would jointly supervise.

At that first meeting I didn't know what to expect. Bill came over as quiet and thoughtful, but also more than a little bumbling. His hair was rather unkempt, his face rugged, his hands large and hardened. He was 50 that year but, not knowing this, I guessed he must be nearer 70. I was proud just to say that I had met him.

At one point the conversation turned to the question of what I might like to research. Parasites, birds and the MHC came up, but we moved off that quite fast. What else did I find interesting, they asked? *Chlamydomonas* and uniparental inheritance of chloroplasts, I said. Like humans, zygotes of this single-celled green alga inherit all their cytoplasmic organelles (chloroplasts, mitochondria) from just one of the two parents. Unlike humans, however, the gametes of *Chlamydomonas* are all the same size. I had met this in genetics lectures and thought it bizarre. Why, when you have made a zygote with cells the same size, each contributing equally in terms of chloroplasts, is one of the parental cell's organelles destroyed? This seemed to me no different from any of the other paradoxes that I had been introduced to in behavioural ecology lectures. We had a discussion about the relevant facts, but none of us were especially well up on the details. Bill and Alan agreed that these were interesting questions. There was some talk of mating types and I confused matters by bringing up relative sexuality, the still poorly understood ability for some species to make up their minds what sex they might be after meeting a potential partner.

Anyone might think that it was then a straight line from this interview to the paper Bill and I published together,[1] relating the control of uniparental inheritance to the evolution of mating types. Nothing could be further from the truth. Soon after my arrival Bill and Alan sat me down to decide what I should do. The parasite and showy birds story was being heavily worked on and neither thought this a good area to go into. I suggested looking for phylogenetic inertia in behavioural traits. Alan squashed that one early on (to my eternal gratitude). Bill had an idea. He was interested in the wood formation of members of the *Compositae* and suggested that I see what literature there was on the subject. I asked why this was interesting and got back an answer, but not one that I understood nor, consequently, one that I can now relate. I guess it was something to do with parasites. Alan looked somewhat sceptical, but, as I had no better idea, I hit the libraries. I would report back in a month and they would see what progress had been made. There was, it turned out, quite a bit of literature on wood formation in the *Compositae*, although for the most part, it is rare within the group. I copied all the papers for Bill and duly handed them over. I remained none the wiser. Alan suggested this topic wasn't going anywhere. I could only agree, and Bill was happy for me to look in a different direction.

In the end, I fumbled my way onto a project. Much inspired by Hamilton and Axelrod's ideas,[2] I had been thinking what might happen when parasites mix. I thought sperm might be small to avoid such mixing of vertically transmitted parasites.[3] Quite by accident, uniparental inheritance of cytoplasmic factors was back on my horizons.

Bill was very encouraging and commented extensively on early drafts of this, my first, paper.[4] In one such draft, I had noted that pollen infected with viruses compete less well than uninfected ones. Bill picked up on this and added that this suggests '*a possible advantage to long styles*'.[5] In the margin he scribbled: '*It might be interesting to consider whether plants with exceptionally long* *styles are unusually plagued with vertically transmitted viruses. One thinks immediately of the long flowers of Nicotiana and tobacco mosaic virus—if that really is a special disease of Nicotiana*'.[6] Later he notes that one of the few cases that I found of efficient pollen transfer (Alfalfa Mosaic virus) is in a plant with very short flowers. Bill might have thought immediately of the long flowers of *Nicotiana* and the short ones of alfalfa, but I had no idea what they looked like. I was, nonetheless, happy to add the conjecture to the paper.

So where should my studies go next? Bill at the time had been working with Richard Stouthamer on the problem of asexuality induced by vertically transmitted microbes.[7] That maternally transmitted microbes should distort sex ratios was clear in Bill's early papers.[8] I asked Bill if anyone had ever written a review of the incidences of these as, if this literature had not been trawled, it seemed like an obvious next step for me: from why have uni-parental inheritance, to what happens if you have it. Bill said he knew of no such review and thought it an excellent idea. Alan agreed and so, while not knowing it at the time, I had started using Bill's own research method: sit in a library and read.

I spent the next two years solidly sifting through any paper that might even mention a strange sex ratio, anything to do with cytoplasmic factors and anything that took my fancy just because it looked odd. When I found a particularly good report of this or that I would often go into Bill's room and announce that I had found a really intriguing paper and present him with a copy. This I discovered was a good way to start a conversation and to pick his brains. Rich Ladle, who joined to do a DPhil with Bill after me, solved the same problem by 'bribing' him with interesting beetles that he found while out sampling. His greatest success were some metallic green chrysomelids that had sex continuously. These prompted, from Bill, some energetic impromptu speculations on the efficacy of mate-guarding and sperm competition.

My offerings of interesting papers rarely raised Bill's interest as much as Rich's beetles. Nonetheless, if not berating me for pronouncing coccid like psocid and thereby getting him very confused, Bill would helpfully say that he had met something similar and go in hunt for the references. After much searching through his extensive card index, he would pull out a dozen or so cards and hand them to me, insisting that I return them when finished. On each was scribbled the details of a paper and usually some notes on its contents. Many of these feature as some of the more obscure references in his papers.

These cards were, he often told me, his 'extra-bodily grey matter'. He couldn't remember all the papers he had read, so this was his only record of many of them. The note cards were extremely valuable to me as a way into the literature. I don't recall ever finding great insights in Bill's notes on them, but that was not what I was looking for. I thought that Bill had contributed a lot to the review that subsequently appeared several years later.[9] He, didn't want to be co-author, saying that I had done just about all of the work. I did, however, make a point of providing a special acknowledgement of the extra-bodily grey matter.

While Bill certainly did rely on these note cards, I am sure he also had a special place in his real grey matter where he left a compendium of matters outstanding. One day while Alan and I were having coffee, Richard Dawkins and Bill joined us. The coffee room was just outside the library and that morning Dan Promislow came out and announced that he had a just read a paper about a coccid (definitely not a psocid) in which the males were minute appendages on the females' legs. Bill was ever so animated. Which species was it, he asked? Dan and Bill rushed into the library. Clearly a missing piece of some Hamiltonian jigsaw puzzle was about to be put in place. Richard and Alan asked me to remind them just what a coccid was.

It was a similar episode that led to the shorter of the two pieces I wrote with Bill.[10] I had, as usual, been reading that day's new journals when they arrived in the department's library. There was a very interesting paper on the discovery of a sexual representative of a group otherwise thought to be asexual.[11] I chatted it over with Rich Ladle who was doing his thesis with Bill on the evolution of sex. We decided that it would be worth writing up as a news piece for TREE. I handed Bill a copy of the paper and asked him what he thought of the idea of a short commentary. At the same time, I had been working on cytoplasmic sex-ratio distorters, not least of which were the parthenogenesis inducers that Bill had written about earlier.[12] While the literature was patchy, it seemed clear that certain lineages had more of one type of sex-ratio distorter than others. Inbred wasps, for example, seemed much more commonly to have asexuals than other species, and at least in some cases this was due to the vertically transmitted microbes (now known mostly to be Wolbachia). Bill and I had talked about this and it was clear that it tallied with his view that there might be lineages that, for whatever reason, produce asexuals at a higher rate than others. What we then see in such clades is mostly asexuals, doomed to failure probably, with a central core mother species spawning off her asexual descendents. The paper by

Pernin and colleagues[13] seemed to fit with such a pattern. Bill was happy to use this paper as a hook for the idea.

Bill's contribution came mostly in the latter third of the published paper. The references to *Rubus* and *Taraxum* possibly matching the pattern were Bill's insertion. It was Bill's idea to put in the reference to martians observing (or rather failing to observe) human sex. The close reader might also note a change of style in the last paragraph. This was all Bill's work. I remember when I first read it, it seemed almost poetical ('the softest, moistest of moss cushions where life is most benign'). Bill, as I now discover,[14] had an inordinate fondness for moss.

Bill's contribution to the other paper we published together was more substantive. It was an obvious jump for me to go from asking about uniparental inheritance and its relationship to the sexes in anisogamous organisms (i.e. why have small sperm), to asking about mating types in isogamous ones and the control of organelle inheritance. I came up with a simple verbal model in which biparental inheritance is bad, as it permits the spread of organelles that are aggressive to others. This would lead to the spread of a nuclear enforcer of uniparental inheritance, which in turn makes the conditions for the evolution of choice and hence of mating types. I was very much thinking at this time in behavioural ecological ways and only later reworked the model to have greater genetical relevance[15–17] (see also[18]). A very similar idea had been put forward, but dismissed, by Rolf Hoekstra.[19] I never understood why he dismissed it. I had reviewed as much of the mating type and organelle inheritance literature as I could find and things seemed to fit very nicely. That ciliates and fungi, which didn't allow cytoplasm to mix, often had very many sexes was just as expected. I talked the evidence through with Bill. He remarked that, in his mind, he would know that an idea was right when the exceptions started to fit into place. This, no doubt, informed our emphasis in the brief introduction.

The only reason he did maths, Bill once told me, was to get his papers past the journal editors. I was never quite sure if he was joking. Nonetheless, for publication something more than a verbal model was needed, so I put together a mathematical model. I had come upon a technical problem that I couldn't see the way out of. Somewhere in my recursions I had generated a quartic equation. I just couldn't see how to provide a neat analytical solution. I had a chat with Bill. He asked me to leave my notes on the maths and let him think it over for the weekend. On Monday he returned with hand written set of equations (in pencil) and a printout from Mathematica, with prototypes for figures a and b. My own model was fine and tractable, but my nomenclature was utterly dreadful, he remarked. Coming from the author of the paper with the most impossible nomenclature,[20] this was pretty severe criticism.

Bill suggested we try *Nature*. Someone had told me that *Nature* papers were by necessity short but you could cram loads into figure legends without them noticing, hence the size of the figure legend. A few weeks after submission we got referees' reports back and a letter saying that, while the manuscript was interesting, one of the referees thought the piece was too speculative. The other two reviewers had been positive. I told Bill and showed him the letter. Bill commented how *Nature* had it in for him, that his PNAS sex review[21] should have been published there, but it had a bad review from a former colleague. Bill was a bit down at the time. He shrugged his shoulders and advised that we submit elsewhere.

The paper sailed through the system at *Proc R Soc B*, and *Science* picked up on the story, doing a two-page spread on it.[22] This was very much a case of the left hand not knowing what the right was doing, as after *Nature*, we sent the paper off to *Science* only to have it returned a few days later unrefereed, with the usual by-line that it was 'not of adequate interest to the readers'. Bill shrugged his shoulders at that one as well.

After the spread in *Science* the story became news for a short while (sex and selfishness are a good mix for science journalists). Bill was very gracious and refused to take any of the credit. On the back of it, I had the honour of presenting, along with Paul Sherman, the Crafoord lectures, at the time when Bill received the Crafoord prize in Stockholm, in 1993. A few days before the ceremony, the Zoology department in Uppsala invited Bill and me to visit and to present a talk. Bill gave a strikingly novel lecture on sphagnum bogs and Gaia. He concluded that while sphagnum bogs may be a level of selection, Gaia couldn't work. I had not the slightest inkling that he was thinking about such things.

Prior to this, I hadn't much socialized with Bill; that wasn't his style. He was always a little difficult in conversation and pregnant awkward silences were not uncommon, both socially and in lectures. On one occasion, presenting a talk in the department of Zoology in Oxford, when attempting to remember the name of a coccid (yes, them again), he took his hands to his face and stood in silence for what must have been many minutes, punctuated only by the strange humming noise of Bill musing. I doubt that anyone in the room would have heard about the species in question, which, on this occasion, Bill couldn't remember anyway.

In Uppsala, Bill and I both stayed in the same hotel and one day after dinner we took the lift up together. In the lift I thought I would try and lighten the mood, so asked him a playful question. It was what is sometimes called the good fairy question. What if a good fairy could answer any question you really wanted answering. Any question, no matter how big—a 'life the universe and everything' sort of question. He asked me to go first. A phylogeny of everything I thought would be fascinating, not least because we will not get it without neo-divine intervention. Bill's turn. Pregnant silence. Was I going to get an answer before the lift let us out? I pushed him for a reply. Not quite a question, he replied. What he really wanted was to be taken back in time. To the time of the dinosaurs. His gift from the good fairy, was to really know how big the dinosaurs were. Bill wanted to understand to the bottom of his boots, what Tyrannosaurus rex was really like.

Not long after, I left Oxford and my interactions with Bill became relatively rare as our interests diverged and Bill was spending more and more time in the tropics. Our paths crossed again when, in 1998, I edited a review by Stuart West and colleagues[23] that advocated the development of mixed models to understand the evolution of sex. Bill's parasite model, they argued, may be part of the explanation, but you also needed to factor in the sorts of forces that Alexey Kondrashov had discussed, relating to mutational decay. It was my responsibility to find authors to comment on the review, comments that would be published alongside the review.

As prime developer of the parasite hypothesis, Bill was an obvious candidate to write such a critique. At around this time Bill and I were both speaking at a meeting organised by G.C. Williams at Stonybrook, New York, so I broached the issue then. I followed up with a letter and then a phone call. He apologized but said he was not keen on writing the piece. Not only was he very busy preparing for a trip to the tropics, but he didn't see the point of exploring mixed models until someone could show him that he was wrong. Alexey Kondrashov also thought the enterprise premature until someone could show him that he was wrong. In the end Kondrashov did contribute a critique[24] but Bill, to my great regret, stayed silent.

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