

## From Physics and Chemistry to Plant Biology

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In 1967, at age 13, the English education system required that I decide between studying history and chemistry. Since history seemed a mass of unconnected facts, and science came easily to me, I chose chemistry, my grasp of the last millennium stops at William Pitt the Younger, and I fell in love with the Periodic Table. To this day, Mendeleev's insights continue to astound me; to have contemplated the known elements at the end of the 19th century, to have ordered them systematically and identified gaps, and to have correctly predicted the atomic weights and chemical properties of the missing elements in those gaps was a breathtaking achievement. I still regard the Periodic Table as an aesthetic masterpiece. I also enjoyed physics (especially optics and spectroscopy) and was competent in math. Out of school, I raced sailing boats whenever I could.

But my mother's love of nature, and my anxiety about ecological crises (yes, even then an issue), led me to feel at the time that I should do something more "useful" than physics and chemistry; the world needed to be saved and I should try to save it. At Cambridge University, studying Natural Sciences, I switched to biology. Alas, my first encounter was with another mass of apparently unconnected facts, as we waltzed through the invertebrate phyla with Prof. Parry. After 2 years it dawned on me that attractive as ecology might be to contemplate while watching David Attenborough programs, actually doing experiments seemed to mostly involve throwing quadrants and doing statistics, the prospect of which bored me to tears. After a failed attempt to resume physics—my mathematical faculties were burned beyond recognition by various extracurricular activities—I studied Botany in my final year alongside classmate Richard Michelmor, enjoying the genetics, biophysics, and biochemistry options taught by Harold Whitehouse, Enid MacRobbie, and Tom ap Rees, respectively. Plants always appealed to me as a physicist and chemist—I still find the capacity of plants to use light energy from the sun to fix carbon to be an astounding example of the creative power of evolution.

My genetics classes particularly caught my imagination when they dealt with mysterious, poorly understood phenomena, of which at the time there were even more than today. In 1976, I was able to pick up one such topic for my PhD, jointly with Gabriel Dover of Cambridge Genetics Department, and Dick Flavell at the (then publicly owned) Plant Breeding

Institute, and investigate repeated DNA sequences in heterochromatin of cereal chromosomes. My mentor in experimentation was an inspirational postdoc, John Bedbrook. This was in the earliest days of recombinant plant DNA, at a time when some said plant DNA couldn't be cloned. A special P2 facility with negative pressure was built for these experiments. During that period, I was lucky to be exposed to the talents of many other high-quality researchers in the Flavell lab—Jean Beggs, Wayne Gerlach, Roger Kemble, Richard Thompson, to name but a few, and of course Dick himself. But I discovered the project had an innate limitation; it was one thing to visualize repeated DNA sequences by *in situ* hybridization, but another to demonstrate function. For that, real genetics was required.

Luckily for me, John Bedbrook had managed to persuade Fred Ausubel that I would be an amusing character to have in his lab, if not a productive one. I was exposed to the incomparably greater rigor of bacterial molecular genetics, in Fred's lab at Harvard Biological Laboratories ("the Biolabs"), during 1981 to 1982. It was an extraordinarily exciting time, and I spent 2 years in the company of some stellar talents. In addition to Gary Ruvkun, Venkatesan Sundaresan, David Ow, Sharon Long, and Frans de Bruijn, there was the star-studded cast of the Gilbert, Ptashne, Kleckner, Wang, Maniatis, and other labs to meet, talk, and drink with. Scientifically, I developed an interest in gene regulation and in genetic criteria for function, and I made some modest contributions to symbiotic nitrogen fixation. I was unprofessional in more ways than one, and looking back at my 2 years in Fred's lab, I realized I had started 12 different projects, and partially completed two. But I sure learned a lot. I thank Fred for tolerating my various ups and downs.

John Bedbrook went on to found the modestly named Advanced Genetic Sciences in Oakland California, and in 1983, I headed West to join him. At the time, it seemed that the most interesting biological questions, such as "How are genes regulated? What does it take for them to express at high levels?" and the questions that needed answers in a genetic engineering company, were the same questions. I could be paid well and still do curiosity-driven research. It didn't last forever, but it did last a surprisingly long time (too long, if you were a shareholder). After 3 years working on maximizing gene expression, I switched to work with Hugo Dooner on the behavior of the maize (*Zea mays*) transposable element *Ac* in tobacco (*Nicotiana tabacum*) and Arabidopsis. Hugo

taught me how to think about Mendelian genetics. In a collaboration with Pal Maliga, I ended up engineering a Tn5 bacterial streptomycin resistance gene so that it worked in plants, and this enabled a very nice cell autonomous assay for *Ac* excision in cotyledons. This assay also finally enabled me to give the kind of talk on the job circuit that persuaded people to hire me for project leader positions. In 1988, at the age of 34, I started my current position at the Sainsbury Laboratory, a newly created institution dedicated to the study of plant-microbe interactions.

I suppose I was recruited because I plausibly made the case that by using my expertise with transposons, I would be able to isolate disease resistance genes. Remarkably, and luckily, it worked, and we developed a selection for transposon insertions in the *Cf-9* gene. Other genes were isolated by map-based approaches. It turned out that the *Cf-2* gene exists in two copies; if we'd tried to use a selection to tag it, we would never have succeeded. I am eternally grateful to Pierre de Wit for isolating *Avr9* before *Avr2*! Of such strokes of luck are careers made. I also gratefully acknowledge the key role that talented individuals in my lab played in the characterization of the full set of *Cf*-genes. Without former postdocs Dave Jones, Matt Dickinson, Colwyn Thomas, Martin Parniske, Mark Dixon, and Kim Hammond-Kosack, who all left to found their own groups, the *Cf*-projects would never have been such a success.

So now the cog of time has clicked through another tooth. Having spent my career working on DNA, I find myself more and more thinking about the properties of proteins, something for which I find myself singularly ill prepared. Fortunately, due to the generosity of the Gatsby Foundation funding of the Sainsbury Lab, I was able to recruit talented researchers such as another former postdoc, Tina Romeis

(who now has her own group), and many talented current colleagues, to enable this transition. We are now heading into the new world of figuring out the mechanisms by which the protein machines encoded by the genes we cloned deliver the phenotypes that got us interested in the first place. That's our main job now—in both *Arabidopsis* and various solanaceae—but we still do a little functional genomics in *Arabidopsis* using transposons. We also have a nice little project mining biodiversity in wild *Solanum* species for resistance against late blight. The resistance genes we identify will one day be useful in controlling this devastating disease.

It's been a long, strange trip. I never worried too much about the future, but I often worry about the present. I always had a blithe certainty that something would turn up, and I always made choices on the basis of what would be the most exciting thing to do next. At my most productive, I was a slave to my science. That's a little harder these days, with a young family, and a partner who's at least as talented and dedicated as I am. I've also made some great friends among the many terrific investigators in plant biology and plant-microbe interactions.

I've always believed that plant science was not only interesting but could be useful. I've been bemused at the public reaction to the plant genetic modification (GM) issue—it seems self-evident that this technology is better than that which it replaces. Many left-wing activists with whom I campaigned as a student against the usual suspects are now on the other side of the fence from me. So I spend some of my time trying to bridge the communications gap. But it's a massive task, at least in Europe. I'm not phased by this—though I get pretty annoyed sometimes—I just proceed on the assumption that truth will out. Even a scientist needs faith.

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