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INTERVIEW

David Colquhoun

Interviewed by David Bradley - *August 31, 2001 · Issue 109*

Biography: David Colquhoun , A.J. Clark Professor of Pharmacology and Honorary Director, Wellcome Laboratory for Molecular Pharmacology, University College at London (UCL), was born July 19, 1936, in Birkenhead, United Kingdom. He is a graduate of Leeds University and pursued his Ph.D. in Edinburgh. From 1964 to 1969, he worked on immunological problems at UCL and wrote a book on statistics, followed by a stint at Yale University where he studied nerve conduction. He returned to UCL as a member of the pharmacology department in 1979.
Colquhoun is currently working on ion channels and synaptic currents and, in particular, single ion channels and the theory that is needed to interpret their behavior in terms of physical and structural mechanisms.

What was the key event that pushed you into research? Working in a pharmacy. It made me realize I did not want to spend my life selling condoms and fraudulent homeopathic pills.

How did you get your current job? It was given to me by Heinz Schild, who held the chair here in 1964. I got someone to point him out to me at a meeting and asked him if I could work at UCL (no postdoc time was needed in 1964). Although I didn't publish much for the next five years, he kept me on because, I suspect, I could teach the bioassay statistics that he loved, having written a seminal paper on it while interned during the war. I did, however, write a textbook (*Lectures on Biostatistics*) during this time, and that provided much of the background that I needed later to understand single ion channels. These days I would certainly have been fired for lack of productivity, since time spent thinking does not

count for much now.

Who was your most influential teacher? I don't think I was much influenced by any of my undergraduate teachers, apart from developing an interest in statistics as a result of going to elementary lectures by B.L. Welch. He kept his back to the audience throughout his lectures as he slowly covered the blackboard with equations. I found it riveting (and later very useful). He would no doubt have been given a dreadful score by the Teaching Quality Assessment people, but since they seem to be more interested in paper-chasing bureaucracy than in the quality of what is taught, perhaps we should count that as an additional recommendation.
The real influences came later - first from Bernard Ginsborg in Edinburgh, who taught me the fascination of electrophysiology and the value of physics in understanding it. Later, Donald Jenkinson, at UCL, for his good science and total integrity. Throughout my life I have been especially grateful to Alan Hawkes, who has almost succeeded in giving me some sort of insight into stochastic processes, without which it is impossible to understand single molecules, and who showed me the power of matrix algebra and the beauty of choosing an elegant notation.

Which research paper has had the most effect on your work? Undoubtedly, Neher and Sakmann's first paper, which showed that it was possible to observe the opening and shutting of single ion channels - to see single molecules in action on a timescale of tens of microseconds. I also love the work of Jeffries Wyman. I bought Edsall and Wyman's *Biophysical Chemistry* as a Ph.D. student, but only later realized that they already knew in the 1950s about allosteric mechanisms and what later came to be called the binding-gating problem. I have also always been very fond of A.V. Hill (1909) in which he not only derived the Langmuir adsorption equation ten years before Langmuir, but did so in the context of acetylcholine receptors.

What was your best experiment? The experiments done with Bert Sakmann, which lead to a short paper in *Nature* in 1981, and a real paper in the *Journal of Physiology* in 1985. I liked them because Hawkes and I (with help from Bernard Katz) had predicted how ion channels would be expected to behave and, for once, it turned out that they did and that useful information about mechanisms could be found from measurements. In particular, they made it possible to distinguish between changes in the binding site and changes in the ability of the channel to open after the agonist bound - the old pharmacological distinction between affinity and efficacy or the new distinction between binding and gating.

What qualities do you need to be a successful researcher? To love what you do sufficiently to work 80 hours a week for the pay rate of a bus conductor. Actually, I am tempted to say that you what you need is ruthless self-promotion, an ability to exaggerate the importance of your results, and a willingness to sell yourself to commercial interests. But that is not a very good answer, because I would not count that as "success."

What advice would you give a younger scientist? Love what you are doing or try another job. Don't let yourself be pushed around by bureaucrats. Be aware that you can't do research, teaching, form-filling, and run a company; you have to choose. Be aware that in good departments, at least, that is if you want a

job, a few good and original papers are better than dozens of trivial ones. Be aware also that if you put your name on papers when you have had little to do with the work, any good interviewer will find that out very easily. Learn whatever amount of mathematics and physics are needed to understand the methods you use. Don't imagine that you can do this in most fields without knowing some calculus and in anything that involves much kinetics or statistics without knowing matrices.

Why do you think the public fears science? The usual answer is that it is because they don't understand it, but I suspect the problem is a bit deeper. The public - well, human beings, really - would like certainty and control in their lives, and some of the answers that science gives are uncomfortable, especially when the answer is "I don't know" or "I can't cure you." It is not surprising that people are tempted to replace uncertainties by wishful thinking (such as homeopathy and astrology). The public is not stupid. They understand perfectly well that genetically modified pollen does not stay restricted to one field and that the man in the white coat who is wheeled out to assure us that nuclear waste can be stored safely for 100,000 years cannot possibly know whether that is true.
One problem is that the simple questions that people really want to know the answers to (like what should I eat, or why can't you cure my cold) are mostly very hard to answer, largely because of the impossibility of using proper randomization. This is not helped by the tendency of scientists to exaggerate the importance of their results. On a morning radio news program recently the interviewer said to a scientist something like this: "I notice that this is the fifth cancer breakthrough that has been announced this month. Tell me, are you about to apply for renewal of your grant or talking up the shares in your start-up company?" The public is quite smart enough to understand this only too common behavior. If they don't trust us it is, to a substantial extent, our own fault.

The constant pressure to become involved in commercial enterprises is presumably one of the main problems? The universities should be the one place where people can seek truth without pressure from accountants and shareholders. If that is lost, then scientists will be trusted to much the same extent as [used-car salesman] salesman, and they will deserve it.

What scientific plans do you have for the next five years? I have got only three years left (officially). What I'd like to do is understand the NMDA (N-methyl-D-aspartate) type glutamate receptors and the glycine receptors at the same level as the muscle nicotinic receptor, though I fear that three years may not be enough. Then I want to finish a textbook on receptors and get my analysis programs converted to Microsoft Windows.

David Bradley, a freelance science writer, lives on the edge of Silicon Fen north of Cambridge, United Kingdom. Elemental Discoveries is his Webzine of science news, views, and interviews.
