Interview with Athel Cornish-Bowden

Athel Cornish-Bowden is Directeur de Recherche at the Centre National de la Recherche Scientifique, Marseilles, France. Dr. Cornish-Bowden obtained his MA, DPhil and DSc from Oxford University. He is the author of *Fundamentals of Enzyme Kinetics* and *The Pursuit of Perfection*

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Can you briefly describe your career to date? What are your main research interests? I obtained my doctorate at Oxford with Jeremy Knowles, ostensibly in organic chemistry but in practice in enzyme chemistry. I then spent three post-doctoral years with Daniel Koshland at Berkeley, where I developed an interest in the quaternary structure of proteins and its relevance to enzyme regulation. This led naturally to an interest in the principal mechanisms of enzyme regulation, cooperativity and allosteric inhibition. Subsequently I spent 16 years at Birmingham, where I worked on enzyme kinetics and regulation, especially in relation to mammalian hexokinases. Since moving to Marseilles 20 years ago I have become interested in the kinetics of multi-enzyme systems.

Systems biology has been described by some as the United Nations of the biological sciences, which hints at its trans-disciplinary nature. What is your working definition for this type of biology? In an ideal world systems biology would be an approach to biochemistry built on a recognition that to understand systems one must study them as systems and not as collections of components. In practice, systems biology seems to differ from traditional biochemistry and molecular biology chiefly in relation to the much larger body of facts that it tries to handle, but true systemic attitudes are not usually to the forefront. Whatever systems biology is, it is a development of biochemistry, not of, say, zoology, botany, taxonomy, etc., or even microbiology.

You have been quoted as saying that "systems biology in current practice is not easy to distinguish from old-style reductionist biochemistry applied on an ever-larger scale." Is systems biology a by-product of our inability to make sense of large data sets? I think there was a widespread belief in the 1990s that once the human and other genomes became known a broad understanding of the organization of living organisms would just emerge from the mountain of data. This didn't happen, of course, and people committed to a systemic view of systems never expected it to happen, so the failure of such an understanding just to "emerge" was certainly one of the driving forces for the explosive growth of systems biology. The term appeared in the scientific literature in 1998, but was used in fewer than 20 papers published before 2000, whereas it occurs in about two papers each day in 2007.

Could you give an example of the limitations of a genome sequencing approach? *Treponema pallidum*, the spirochete responsible for syphilis, now has a completely known genome, but not much more is known about its biochemistry than was known before its genome was sequenced. In the absence of any information about the kinetic and regulatory properties of its enzymes the best we can do is use sophisticated stoichiometric analysis, such as the methods being developed by Stefan Schuster, for example, to deduce from the genome some of its similarities with *Escherichia coli*. That is a step, certainly, but not really what we want to know, which is how it differs from *Escherichia coli*, which does not cause syphilis. Understanding syphilis will require much more than just genome information, and this will include a great deal of kinetic and regulatory information.

Who has had the greatest impact on your career to date? The people who taught me chemistry at Oxford, especially R. J. P. Williams and Jeremy Knowles, had a great impact on my way of thinking about it, as did Daniel Koshland a little later; he in particular encouraged me not to be frightened of building a career on a largely theoretical foundation. In the second half of my career the greatest influence has certainly been Henrik Kacser. He is unfortunately no longer with us, and the other three that I have mentioned have not been primarily interested in systems. Almost everything I have written in the past 20 years has been influenced by discussions with María Luz Cárdenas and Jan-Hendrik Hofmeyr. In the past few years I have been increasingly attracted by the ideas of Robert Rosen, which are also systemic, but at a much more fundamental level than Kacser's.

What advice would you give to a student looking to study biological systems? It would depend on whether the student wanted to make a successful career or wanted to make a real contribution to biological understanding; if the latter, then it would be essential to search for general principles, and to regard accumulating detailed information as a step towards that end and not as an end in itself. Existing methods are quite effective at making people computer-literate; the deficiencies are more on the side of biological literacy. There has always been a widespread feeling that biology is an "easy" subject compared, say, with physics, but this is only true if we just regard it as no more than a vast accumulation of facts. In reality biology needs not just knowledge of a long list of facts, but a broad understanding of how they are related. This is especially important now, at a time when we are witnessing an alarming growth of pseudobiology, a time when creationism, and the supposedly scientific version known as intelligent design, threatens biology teaching throughout the world, no longer just in the United States.

Readers interested in more details are encouraged to consult the following article: "Putting the systems back into systems biology," Perspectives in Biology and Medicine 49.4 (2006) 475-489.