

### John Desmond Bu'Lock



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Founding Editor of *Biotechnology Letters* and *Biotechnology Techniques*

Almost everyone who met John was immediately struck by his sheer intellectual brilliance. He dazzled us with his breadth of knowledge, and not just in biotechnology and chemistry which were his professional loves, but also in matters antiquarian, in medieval archaeology as well as being a devotee of Japanese gardens all of which received his immeasurable enthusiasm. Indeed just a few years ago, someone who had only known of John as a microbiologist asked him if he knew the 'other' J.D. Bu'Lock in Manchester who was an antiquarian. John, naturally, was highly amused but quickly pointed out that he was in fact both people. Although he contributed to many and varied activities, it will be his contributions to microbial chemistry, particularly for his epoch-making work on the biosynthesis of secondary metabolites, and to the development of biotechnology that he will be best remembered.

John was highly talented from the outset. He gained entry to read Chemistry at Cambridge University when he was still only 17. He graduated three years later and immediately continued in the same Department to complete his doctorate in 1951. He then took up the post of assistant lecturer in the Department of Chemistry at the University of Manchester in the same year, a Department that he loyally served until he officially retired in 1992 though, in fact, through his continuing editorial work with his journals, it was a Department that he never really left.

John's work in Cambridge for his Ph.D. had been concerned with the structure of several natural products including melanin, and this interest continued at

Manchester with investigations into the polyacetylenic compounds in fungi which were the very first biosynthetic studies to be carried out on microbial 'special' metabolites. This laid the foundation for his major work which was to follow on the biosynthesis and regulation of the polyketide secondary metabolites in fungi with the first demonstration of the role of malonyl-CoA and the first descriptions of secondary metabolism in terms of regulatory mechanisms in fungi. He described the growth of fungi as either being in the 'trophase', which was the balanced phase of growth, then going into the 'idiophase' which was where the idiosyncratic metabolic reactions occurred leading to the plethora of secondary metabolites. John often remarked later that these were two words he almost wished that he had never coined: but the words were apt descriptors and are still used by today's scientists to describe fungal metabolism.

Much of our current understanding of fungal metabolic processes, including the pathways to polyketide synthesis, originate from John's pioneering work in the 1960s. His output was prodigious and by 1973 he had been promoted, via full lecturer (1954), and senior lecturer (1968), to Reader in Microbial Chemistry. Manchester University though, until quite recently, was notorious for its parsimony in bestowing personal professorships to its own staff and in almost any other university John would have been welcomed to the professorial ranks many years ago. Indeed, several other universities did accord John professorial status in recognition for his contributions to microbial chemistry: Stevens University New Jersey, Kuwait University and Strathclyde University all asked John to be their visiting professors and with the latter University, this was a visiting professorship in perpetuity.

Although John's work and interests on fungal metabolites continued until his retirement, he could not resist challenges: in 1970 scientists at the CNR Institute in Pozzuoli, Italy, asked John to help them unravel the complexities of the lipids being recovered from bacteria isolated from volcanic fumaroles. These were the thermophilic, acidophilic archaeobacteria. John visited Italy many times to carry out this collaborative programme - set up long before European Union grants were available. From this work came the first structures of the isoprenoid ether lipids though other researchers elsewhere were also working hard to claim priority in this newly emerging area.

By the early 1970s John was sensing that biotechnology, which was then still referred to as fermentation technology, was going to be major determinant in industrial development. The antibiotic industry had indicated what was achievable; John's own work and his encyclopedic knowledge led him to the firm belief that biotechnology would be the next big development to happen, both nationally and internationally, for the production of a myriad of metabolites. John began this phase of his work by organizing a series of prophetic and highly influential meetings in Manchester from which came The Octagon Papers (1974-76). These took their name from the shape of the room in which the meetings took place and received considerable attention particularly by industrial scientists anxious to develop new products for rapidly expanding markets.

It also seemed obvious to John that many of the old processes such as ethanol production and the old acetone-butanol process could be made to work competitively if current biochemical knowledge and modern bio-engineering could be harmonized. John was then able to found his own laboratory devoted to biotechnology in 1975 with the aid of a start-up grant from the Wolfson Foundation. This was called the Weizmann Laboratory named after Chaim Weizmann, not just because of him being the first President of Israel, but because Weizmann carried out his pioneering work on acetone/butanol formation in 1915-6 in the old chemistry laboratories in Manchester University. The wheel had turned full circle.

John's prowess in biotechnology quickly became widely recognized and he was on constant call to speak at meetings, to participate in conferences, to sit on multitudinous committees, to be an adviser for the development of biotechnology around the world: in the UK, in Europe, in Japan and in India. John bestrode both British and world biotechnology. It was in this second highly productive phase that John launched his two journals: first *Biotechnology Letters* in 1978 and then *Biotechnology Techniques* in 1986. He even had time to co-edit with Bjorn Kristiansen "Basic Biotechnology" (published 1987) and with Bjorn and Charles Sinclair, "Kinetic Modelling of Fermentation Processes" (1986). All told, John published 160 original papers and reviews, edited some six books and wrote two classical books in the 1960s on microbial biosynthesis: *Biosynthesis of Natural Products* (published by McGraw-Hill in 1965) which was translated into Japanese, German and Spanish, and *Essays in Biosynthesis and Microbial Development* (Wiley, 1967) both of which are still worth reading for their highly perceptive comments as well as the amassed factual information.

The vision that John had for biotechnology though was never quite realized. He felt, and many of his colleagues felt likewise, that Manchester with its twin universities of the University of Manchester itself and the University of Manchester Institute of Science and Technology (UMIST), was uniquely placed to be the focal centre for the development of British biotechnology. However like many ambitious schemes, there were too many vested interests in maintaining the *status quo* to allow these visionary ideas to gain acceptance. Ironically, now in the mid-1990s, there seems a slight chance that this development could still happen but there is a long way to go. Nevertheless, John's own personal contributions can never be over-shadowed: he gave his subject everything and his subject became his lasting tribute.

John was hugely liked. For many of us, it was a privilege to know him and to listen to his views and opinions. On one occasion, he was visiting a small Department of Microbiology in a UK university and talked to each member of staff leaving each one bedazzled with his insight into their own personal research areas. This was one of many *tour de force* that John became famous for.

In 1991 John had to undergo major surgery. As he himself recognized, he was extremely lucky to come through it after having spent 8 weeks completely unconscious in the intensive care ward. Although he was dependent thereafter

on thrice weekly kidney dialysis, he continued to live life as fully as possible: holidays abroad were accomplished, meetings were still attended and invitations to conferences were still accepted. He still had much wit and wisdom to impart which he did with gusto and relish particularly if this allowed him to cock a snook at any received wisdom that he regarded as particularly unsound.

In these later years, John was able to return to his other interests: he played an active role in the Antiquarian Society of Lancashire and Cheshire having been a Fellow of the Society of Antiquaries for many years; he also helped in the founding of the Japanese Garden Society and was co-editor of their journal, a role which gave him enormous pleasure.

John leaves behind his devoted wife, Denise, his three married daughters: Auriel, Frances and Sarah, two grandchildren and a third who was born just a few weeks after his death. A loyal husband, a wonderful father and grandfather and, to us fellow scientists, a colleague and friend we were proud to know and whose memory we will always cherish. He gave us much to remember him.

*Colin Ratledge*

Since John's death, many tributes have come in from his friends and colleagues around the world. Some of these are given here.

*Professor Don Brown*, formerly of UMIST and now at Cranfield University, writes:

John started life as an organic chemist who refused an opportunity to carry out post-doctoral research in natural products, to then be asked, as his first job with Professor Birch at Manchester University, to grow up some micro-organisms! It did not take him long to be completely hooked and "microbial chemistry" became established at Manchester. His sense of history (and special second expertise - some people in the extra-mural area thought he was from the History Department!) resulted in his special new laboratory being named after his predecessor, Weizmann.

As a newly appointed lecturer in the Chemical Engineering Department at UMIST and determined to establish biochemical engineering there, it was with relief that I eventually discovered JD and his row of fermenters together with his microbiologists and chemists working in the so difficult field of secondary product metabolic pathways. Our early blunderings must have amused him and I certainly learned more from our "discussions" than he did from me. However, those early starts saw many collaborations in which he taught biochemistry and metabolic pathways to budding biochemical engineers while I taught basic chemical and biochemical engineering to bacteriologists and microbial chemists.

John was one of the original biotechnologists and for many of us, he invented the word. He realised early in its development that progress required a multi-disciplinary approach. We even enticed him into the field of biochemical

engineering where he showed that he could develop and analyse bioprocesses with great skill. His wide range of experience in biotechnology made him a bottomless pit of information and his observations and advice could always draw a circle of students and researchers at meetings and seminars. John had a strong belief in biotechnology and its importance for the future of all. He demonstrated this by serving on numerous biotechnology sub-committees of professional societies, extending his influence into Europe. His early up-bringing on a diet of *Tetrahedral Letters* directed his realisation that a similar publication was needed for the biotechnologist. I have a small pleasure, in supporting his plans for *Biotechnology Letters*, by occupying the first six papers of volume 1 number 1.

John was a great traveller and it is probably accurate to say that his work in the microbial chemistry of metabolic pathways had a greater following at an international level than it did nationally. In spite of the problems with his health, he continued to attend scientific conferences and enthral the audience with his latest findings. Although to many he was an irascible old devil, to those who knew him closely and had cause to work with him, we know that it was an outward characteristic of his desire for dedication and discipline in our work that few of us could match.

*Professor Arnie Demain*, Massachusetts Institute of Technology, USA writes:

When I was a young microbiologist at Merck and Co. Inc. in New Jersey and inquisitive about the control of fermentation processes, I read everything that I could get my hands on that was written by John Bu'Lock. I had no idea that he was basically a chemist, since he had such real insight into the biology of industrial microorganisms. Many of my apparently unconnected thoughts about secondary metabolism fell into place as I read John's clear interpretations of the biochemical life of fungi and actinomycetes. I was fortunate enough to meet him in the 1960's while he was taking a sabbatical leave at Stevens Institute in Hoboken, New Jersey. Once I spoke to him, my ideas about the metabolic control of secondary metabolism crystallized and allowed me to organize my thoughts into a conceptual basis that could be tested by experiment. John was the first person to make biochemical sense out of the myriad of descriptive and seemingly unconnected observations of fermentation microbiologists made in laboratories, pilot plants and factories throughout the world. Throughout his career, his work and publications were always thought-provoking and exciting. Not only was John a great scientist, but he also became a great friend. It was always amusing and exciting to be with John due to his sharp wit and ever-active brain. He and Denise Bu'Lock became wonderful friends of my wife, Jody, and me. John's mind continued to sparkle even after he became physically ill. I'll not forget the 1993 Ciba Foundation Conference in London<sup>1</sup> where John's ideas stimulated us all to new peaks of excitement and appreciation of secondary metabolism. I, and the world community of scholars and practitioners of secondary metabolism, will miss him dearly but will never forget his words<sup>2</sup> about the field he loved so much: "Now ever since Perkin, failing to make quinine, founded the dyestuffs industry, the organic chemists have found the study of 'natural products' an inexhaustible source of exercise, which can be performed out of pure curiosity even when paid for in the hope of a more commercial reward. As a result, the

organic chemist's view of nature is unbalanced, even lunatic, but still in some ways more exciting than that of the biochemist. While the enzymologist's garden is a dream of uniformity, a green meadow where the cycles of Calvin and Krebs tick round in disciplined order, the organic chemist walks in an untidy jungle of uncouthly named extractives, rainbow displays of pigments, where in every bush there lurks the mangled shape of some alkaloid, the exotic perfume of some new terpene, or some shocking and explosive polyacetylene."

<sup>1</sup> D J Chadwick and J Whelan (eds.) *Secondary Metabolites: Their Function and Evolution*. Ciba Foundation Symposium 171. John Wiley, Chichester (1992).

<sup>2</sup> J D Bu'Lock, *Adv. Appl. Microbiol.* 3, 293-342.

*Dr Zdenko Vanek* of Academy of Sciences of the Czech Republic, writes:

All the scientific staff of the Institute of Microbiology of the Czech Academy of Science have received the news of the death of John Bu'Lock with deep grief. We became acquainted for the first time in 1959 when I worked as a scholar of WHO in the Department of Organic Chemistry at the University of Manchester. Since then John has visited Prague many times at the occasions of various scientific conferences and symposia and all his presentations were always awaited with great expectation, because his performance was a creative act which always brought new and often provocative ideas about mechanisms regulating the biosynthesis of natural products. His personality combined outstanding chemical education with a deep knowledge of biochemistry and biology. He was the discoverer of approximately 12 polyacetylenes (*Progress in Organic Chemistry* 6, 86-134, 1964) and of a number of compounds including basic ideas of their biosynthesis. Thanks to a friendly and unselfish character of John Bu'Lock it was quite natural that a number of scientific workers from Czech Republic took advantage to work under his leadership at the University of Manchester and we will always be most grateful for that.

*Professor Jack Ziffer*, of Technion - Israel Institute of Technology, writes:

My thoughts about John have always been of a brilliant scientist who achieved the near impossible of establishing the two Journals, against all odds. I recall one incident that was typical of his kindness to me. Shirley (my wife) and I were attending an international meeting at the University of Manchester, and John accordingly invited the associate editors who were there, to a dinner at a Chinese restaurant. John knew that, at the time, I had a project on microbial rennet and thoughtfully he arranged to have me sit next to the late Professor Kei Arima from Japan. During the meal, I heard John, who was sitting on the other side of Kei, whisper to him whenever another dish was served "Tell him that it's kosher", which had me even more apprehensive, because Kei kept telling me every dish was only chicken.

John was truly a very special person. I have always felt strongly about him ever since my first contact at the time of the Octagon Papers. I was honored to have him as a friend and will miss him.