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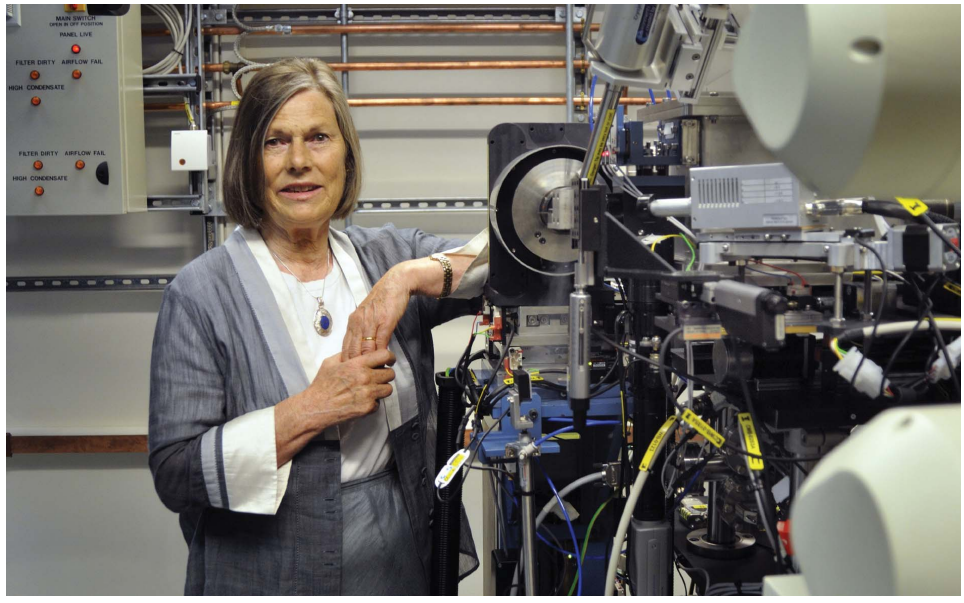
Professor Dame Louise Napier Johnson (26 September 1940–25 September 2012)



Professor Dame Louise Napier Johnson. Photograph by Anne-Katrin Purkiss, Wellcome Images.

One of my strongest recollections of Louise Johnson was in Molecular Biophysics in Oxford in 1971. An unusually animated Louise followed David Phillips, announcing as they approached that they needed my help. Would I like to co-author a review with Louise on protein crystallography? I happily accepted but, as I was just about to go on holiday, I nervously enquired when the review was due. A rather embarrassed David Phillips admitted that he had been asked sometime before but had not started writing although the manuscript was already overdue.

I was most unpopular with family and friends on our holiday as I travelled with piles of photocopies of recently published protein crystallography papers and laboratory notebooks. However, I returned to Oxford to find that Louise had written most of the diffraction theory, it was beautifully concise and illustrated with lysozyme crystallography; she clearly had an amazing grasp of the theory and experimentation of X-ray diffraction. I had written my sections using insulin structure analysis as my example. We put the text together easily and sent it to the Editor of *Biennial Reviews of Science, Technology and Medicine* as requested. We were very surprised to get a letter by return, accepting section 10, the conclusions, and suggesting we use the remaining sections as the basis of a textbook.

Publishers were amazed to find us with text. We had several offers to publish. We negotiated hard to obtain a large advance with which I believe Louise bought a horse. She rewrote many of her sections of the book during her pregnancy and following the birth of her son, Umar. The book was eventually published in 1976 and continued to be popular. I found it reassuring that the original copies in the laboratory were hard to find, being sought out by new graduate students. Louise eventually sacrificed her last copy to be broken up and copied for reissue by Elsevier in 2006.

I had first met Louise Johnson in 1965 when I was a graduate student at Oxford. Dorothy Hodgkin had encouraged us all to go to the Royal Institution in London where Bragg was Director and David Phillips had been working on the structure of lysozyme. In a wonderful lecture David unveiled the structure, the second solved by X-ray crystallography and the first of an enzyme. But even he was a little upstaged by Louise, who wowed us all with a marvelous talk on her PhD research. She demonstrated how substrate analogues (modified hexasaccharides) sat in a deep groove between the conserved catalytic residues. For the first time we could begin to understand how enzymes work!

Louise had studied physics at University College London, moving in 1962 to the Royal Institution to work on lysozyme for her PhD. She moved to Yale in 1966, working with Fred Richards, on the determination of the structure of ribonuclease-S at 3.5 Å resolution. This gave Louise experience of determining a second enzyme structure – probably the greatest number anyone had solved in 1967 – and gave Fred an enzyme where a helix was non-colvalently attached, providing a beautiful model for protein folding.

When Louise returned to the UK in 1967 to join David Phillips who had just moved to Oxford University as Professor of Molecular Biophysics, she began to work on the huge and extremely challenging project, the structure of the regulatory enzyme glycogen phosphorylase, the largest protein crystallized at that time. It was typical of Louise that she chose a really challenging project as well as one that would provide really new insights into enzyme regulation by phosphorylation and binding of metabolites. It was not surprising that it took many years before Louise and her team had X-ray data at high enough resolution to solve the structure. Indeed it was more than twenty years before she could explain, by bringing together her work with that of Bob Fletterick in the States, how post-translational modification by kinases and binding of small molecules at sites distant from the active site were mediated by conformational changes, a beautiful example of allostery.

Louise had married Abdus Salam, the brilliant Pakistani physicist and future Nobel laureate, in 1968. The two were obviously perfectly intellectually matched, with common interests in physics and philosophy. Abdus influenced her long-term interest in science in developing countries, which came to the fore much later after his death in 1996 when she was elected an Associate Member of the Third World Academy of Sciences in 2003. Louise influenced the development of science in Islamic countries, lecturing in Iran and Pakistan, and supporting the development of SESAME, the new synchrotron in Jordan.

However, she also got enormous pleasure from her children. Umar was born in 1974 and Sayyeda in 1982. It was fantastic to follow their progress through school, university and into professional life, to be able to have discussions with them, memorably at Louise's retirement symposium and dinner in Oxford, where I found them full of enthusiasm and with lots of stimulating ideas.

Louise progressed up the academic ladder in Oxford, from a University Demonstrator in Zoology and Janet Vaughan Lecturer in Biophysics at Somerville College in 1967, to a University Lecturer and Full Fellow of Somerville in 1973. She was the obvious successor to David Phillips when he retired in 1990, becoming Professor in Molecular Biophysics in the Department of Biochemistry and Professorial Fellow at Corpus Christi College in Oxford. In the same year her work on enzymes was recognised by election to the Royal Society.

In the following twenty years Louise continued her quest to learn more about enzyme structure, mechanism and regulation, as well as to advance the techniques of protein crystallography and structure analysis. On enzymes she pursued

her interest in understanding cell regulation through phosphorylation, including the role of protein kinases in the cell cycle. The structures she defined have not only informed molecular and cell biology, providing a general model as to how the protein kinases are regulated, but also have provided structural knowledge of targets for drug discovery in oncology, guiding the design of new inhibitors that have led to drug candidates in clinical trials.

Louise also extended her interest in physical techniques by accepting the role of Science Director for Life Sciences at the Diamond Light Source in the UK. She had always exploited synchrotron X-radiation in macromolecular crystallography, particularly for phosphorylase where an intense beam was really required. She championed the use of the powerful new source of X-rays in the UK in new areas, for example for X-ray imaging of whole cells. I remember how pleased she was to open Samar Hasnain's new Barkla X-ray Laboratory of Biophysics at Liverpool on 21 July 2011 (see photograph), just before she became very ill.

Louise Johnson with Tom Blundell and Samar Hasnain at the opening of the Barkla X-ray Laboratory of Biophysics at Liverpool University.

Louise was a very private person but a very generous colleague and an inspiring teacher. She influenced the lives of many, indeed a whole school of structural biologists who now lead much of macromolecular crystallography in the UK and elsewhere. This is a most significant contribution and one that will continue her philosophy of advancing science in a multidisciplinary and international context.

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