Acta Crystallographica Section F
Structural Biology and Crystallization Communications
ISSN 1744-3091

Dame Louise Napier Johnson (1940–2012)

Keith S. Wilson[a]* and David I. Stuart[a]*

[a]York Structural Biology Laboratory, University of York, Heslington, York YO10 5DD, England, and [b]Division of Structural Biology, Henry Wellcome Building for Genomic Medicine, University of Oxford, Oxford OX3 7BN, England

One of the pioneering spirits of protein crystallography has passed away. Professor Louise Napier Johnson, DBE, FRS, died on 25 September 2012, the day before her 72nd birthday. Throughout her career Louise was a leading figure, applying an incisive physics intelligence to problems in biology. As a young graduate student at the Royal Institution, off Piccadilly in London, Louise published a landmark paper in *Nature* as Miss Louise N. Johnson [Johnson & Phillips (1965). *Nature (London)*, **20**, 761–763]. Many years later she assumed leadership roles at Oxford University and at the Diamond synchrotron in Oxfordshire, but never lost her delight in science and unassuming kindness towards those around her, to whom she was a remarkable example.

As early as 1934, J. D. Bernal and Dorothy Hodgkin had shown that it might be possible to decipher the structures of proteins using X-ray crystallography, and, working in Cambridge, initially overseen by Sir Lawrence Bragg, John Kendrew and Max Perutz eventually determined the first protein structure in the late 1950s. Enzymes remained uncharted, but in 1962 not only were Kendrew and Perutz awarded the Nobel Prize but, armed with a degree in physics from University College London, Louise started a PhD at the Royal Institution where Lawrence Bragg had moved from Cambridge. She joined a new group led by David Phillips, later Lord Phillips of Ellesmere [Perutz (1999). *J. Synchrotron Rad.* **6**, 945–946], which had set itself the task of explaining the mystery of enzymes using X-rays. They fortuitously chose lysozyme, an enzyme discovered by Alexander Fleming which breaks down the wall around bacterial cells, giving it anti-bacterial properties.

Louise took the story to a new level, entering the international stage at a meeting at the Royal Institution in 1965. The three-dimensional structure of the first enzyme was revealed in all its glory, with Louise presenting her analysis of its complexes with *N*-acetylglucosamine and tri-*N*-acetylglucosamine to show how they beautifully complemented the deep groove across the enzyme's surface and rationalized a wealth of biochemical data [Blake *et al.* (1967). *Proc. R. Soc. B*, **167**, 378–378]. This was the first use of the difference-map technique, apart from for heavy-atom location. Phillips then used model building to extend Louise's results, inferring a detailed mechanism for how the enzyme actually facilitated chemical change, founding structural enzymology. Despite early opposition, this is now accepted as the gold standard framework for understanding enzyme function. Furthermore, the methodology developed for lysozyme became a fundamental pillar of the pharmaceutical industry; indeed, many drugs currently on the market arose in some part through structural analysis of proteins.

After the Royal Institution, Louise spent a short postdoctoral spell at Yale, researching ribonuclease with Fred Richards, before returning to the UK in 1967 to join David Phillips' newly

established Laboratory of Molecular Biophysics in Oxford, first as a university demonstrator and as a lecturer in 1973.

KSW joined Louise's group as her second graduate student in 1971. Having solved the first structure of an enzyme in complex with an inhibitor, Louise had moved on to the even more challenging problem of glycogen phosphorylase, a subject which occupied her full attention for the next twenty or so years. The study of protein phosphorylation was in its infancy and this was the first such enzyme to be studied. It was typical of Louise to identify a topic which would lay down principles of relevance to so many biological systems. At that time a major problem in the project was the sheer size of the protein, with 841 amino acids in the chain and a molecular weight of 97 kDa. In addition, the protein formed dimers and in some forms tetramers. This may seem small beer nowadays with structures known for viruses and ribosomes, but in 1972 this was a daunting prospect especially for data collection.

The Phillips laboratory was famous for its development of single and multi-counter diffractometers and indeed the data for the first phosphorylase structure at a resolution of 6 Å were recorded on a Hilger and Watts four-circle diffractometer, requiring around three days per data set. Louise immediately recognized that this approach was not feasible for the extension of the analysis to higher resolution and was one of the first proponents of the use of a rotation camera with X-ray film for data acquisition, using first an in-house prototype and subsequently the Arndt–Wonacott oscillation camera. This enabled the resolution to be extended to 3 Å with data recorded on a rotating-anode source. Collection speeds remained slow, with a complete set requiring several days and several crystals, all done at room temperature. Louise was deeply involved in the construction of the model from the 3 Å MIR map, using a Richards' box, or rather two boxes due to the size of the protein.

It rapidly became clear that the in-house resources were insufficient to allow extension of the resolution beyond 3 Å; collection of a 2 Å-resolution 0.5°-rotation image required an exposure of about 15 h after which the crystal was 'dead'. Louise rose to the challenge by identifying the need for synchrotron radiation for subsequent data acquisition. Synchrotron radiation beamlines for protein crystallography were in their infancy, and Louise arranged for her group to work at the LURE synchrotron beamline run by Roger Fourme. This provided a fantastic gain in data quality. Exposure times for a 0.5° oscillation fell from 15 hours to about five minutes, reflecting both the enormous increase in intensity but most importantly the greatly reduced divergence of the synchrotron beam [Wilson *et al.* (1983). *J. Appl. Cryst* **16**, 28–41]. Over the next few years Louise attracted a set of scientists, including DIS, who struggled with early molecular graphics devices and developed the refinement programs to provide a refined structure. Eventually the phosphorylase project led to a full understanding of its mode of action and regulation, described in a monograph published in 1991 [Acharaya *et al.* (1991). *Glycogen Phosphorylase b: Description of the Protein Structure.* London: World Scientific]. To put the advances in data collection into context, while working as a postdoc in Louise's group, DIS brought a phosphorylase *b* crystal to Hamburg when the first imaging plate had become operational; complete 2 Å resolution data were recorded in six hours from a single crystal.

During the early 1970s Louise also managed to find time to co-author a book with Tom Blundell [Blundell & Johnson (1976). *Protein Crystallography.* London: Academic Press]. This rapidly became the bible of protein crystallography, necessary reading for all those working in the field. The book not only reflected Louise's outstanding breadth of knowledge but in addition her wish to communicate her knowledge and enthusiasm to others.

In 1990 Louise was appointed to the newly established David Phillips Chair of Protein Crystallography in the Oxford Laboratory of Molecular Biophysics, a post she held until her retirement from the university. In the same year she was elected a Fellow of the Royal Society, and in 2003 was appointed a Dame of the British Empire in recognition of her contribution to science. Louise went on to make major contributions to our understanding of the role of protein kinases in the cell cycle, providing continuity with her fundamental contribution to the rationalization of how phosphorylase worked, the first phosphorylated enzyme to be understood at a structural level. The protein kinases which she worked on are frequently mutated in cancer cells and Louise applied the methodology originally developed for lysozyme to search for new therapies, taking great delight in the success of Imatinib, an anti-cancer agent for chronic myeloid leukemia, and the first drug designed to target a protein kinase.

In 2003 Louise was appointed as Life Sciences Director at the Diamond Light Source, a recognition of her long-standing contributions to the application of synchrotron radiation for structural biology. She oversaw the vital construction phase of the first set of life science beamlines, ensuring that they were equipped with the appropriate optics and detectors, and in addition would provide automated facilities for data acquisition. The success of her guidance can be seen in the position of Diamond Light Source as a world leader for macromolecular crystallography, and in the fact that some half of the users of Diamond come to use this technique.

In addition to championing crystallography, she was always on the look out for new techniques. She had the idea for an embedded laboratory for membrane proteins, and, having secured external funding, she drove the idea into reality: the Membrane Protein Laboratory is now a successful user facility linking Diamond and Imperial College. She was particularly intrigued by the possibility of imaging living cells, for instance by ultrafast X-ray scattering on the free-electron laser (FLASH) in Hamburg. She took great delight in having the opportunity to take cells to Hamburg and actually participating in 'flying' them on the free-electron laser.

Louise followed on in the footsteps of those with a firm grounding in physics who applied their skills to the understanding of complex biological systems. She carried the baton of the major role played by women in crystallography, following a tradition started in Oxford by Dorothy Hodgkin. Her contributions were not limited to UK science. She was a wonderful exponent of the needs to advance science in developing countries, particularly through her role in the Third World Academy of Sciences. A fine example of her influence was her support for the SESAME synchrotron in Jordan.

For both of us the time spent in Louise's group was a fantastic experience. It was a privilege to have a supervisor who was so expert in the techniques of protein crystallography. Despite her intellectual rigour we remember Louise as a warm-hearted human being, with great understanding and always sympathetic to the needs of her postdocs and students, who remained a friend and mentor over the decades. Louise's husband, the physicist Abdus Salam, died in 1996, and she is survived by her two children Umar and Sayyeda.