

## Professor Dame Louise Napier Johnson 1940–2012

I 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 for the unveiling of the first X-ray structure of an enzyme, lysozyme, by David Phillips. The youngest member of his team was Louise.

The Royal Institution lecture theater had steeply stacked rows of seats and I looked down from the back at David Phillips way below. The fully extended polypeptide chain of lysozyme—129 amino acids—was suspended from the high ceiling and reached the bench where David had placed the model of the folded chain. This was only the second protein at high resolution determined using X-ray crystallography. I marveled at the achievement of Nature in folding this molecule into a globular structure that was so neatly packed. Phillips identified the active site as a well-defined groove in which evolution had conserved the catalytic residues through many divergently evolved species. But I remember most vividly the appearance of Louise Johnson, just finishing her Ph.D., who gave an articulate and stunning presentation of the enzyme bound to substrate analogs (Johnson and Phillips, 1965; Johnson, 1998). For the first time, we began to understand how an enzyme works; in this case, we had strong clues as to how it selectively cleaved the polysaccharide chain.

Louise Johnson was born in 1940 at Worcester. She studied physics at University College London between 1959 and 1962, moving to the Royal Institution to complete her Ph.D. in 1966. After completing her Ph.D., she moved to Yale in 1966 to work with Fred Richards, who was interested in protein crystallography but also had a deep interest in the principles of protein structure and folding. She contributed with Hal Wyckoff to the design of a flow cell system for X-ray analysis of crystalline proteins and to the determination of

the structure of ribonuclease-S at 3.5 Å resolution.

In 1967, Louise returned to the UK to join David Phillips who had been appointed the Professor of Molecular Biophysics at Oxford University. At the same time, the insulin team, led by Guy and Eleanor Dodson, moved to join David in Molecular Biophysics, based initially in the old Zoology building. As we struggled to define the structure of insulin, Louise began to work on a huge and extremely challenging project, the structure of the regulatory enzyme glycogen phosphorylase, the largest protein so far crystallized.

Fred Richards followed Louise across the Atlantic—I seem to remember he sailed his own boat—to join the growing Molecular Biophysics Laboratory and constructed the first “Richards Box” for superposing the model on the density, known in the lab as “Fred’s Folly.” It took some time before Louise and her team had data at high enough resolution to exploit the Richards Box. Only after more than 20 years could she (Johnson, 1992), together with Bob Fletterick, who was also working on the enzyme (Newgard et al., 1989), fully explain how phosphorylation and binding AMP at sites distant from the active site led to conformational changes that influenced the activity, one of the first examples of enzyme regulation by allostery (Johnson and Barford, 1990). And she was still publishing on phosphorylase 30 years later!

In 1968, Louise had married Abdus Salam, the brilliant Pakistani physicist and future Nobel laureate. The two were very happy together, perfectly matched intellectually. They had two children: Umar in 1974 and Sayyeda in 1982. Impressively, during this time Louise was appointed first in 1967 to a University Demonstratorship in Zoology at Oxford and to the Janet Vaughan Lectureship in Biophysics at Somerville College and then promoted in 1973 to a University Lecturership and an Additional Fellowship at Somerville College.

I came to know Louise well when we worked first on a review and then on the monograph “Protein Crystallography” (Blundell and Johnson, 1976). Louise proved to have an impressive knowledge and a deep understanding of our subject, which had not been described in a single volume before. She wrote clearly and accurately, always willing to debate topics. She continued to work on her sections of the book during her pregnancy and the birth of her son, Umar. The book was eventually published in 1976, and 36 years later it is selling on eBay at £425.78.

On the retirement of David Phillips, Louise was the natural successor, becoming Professor of Molecular Biophysics in the Department of Biochemistry and Professorial Fellow, Corpus Christi College, Oxford. In the same year, her work on enzymes was recognized by election to the Royal Society and in 2003 she was made a Dame (DBE) in the New Year’s Honors List.

During these years, Louise focused her research on understanding cell regulation through phosphorylation, including the role of protein kinases in the cell cycle. She defined some early crystal structures of phosphorylase kinase in complex with a peptide substrate, giving clues about kinase substrate specificity (Lowe et al., 1997). She worked on the structures of cyclin complexes with the cell cycle kinase CDK2, learning much about its activation and regulation (Honda



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et al., 2005). She unraveled the crystal structure of human CDK7, providing insights about its protein recognition properties (Lolli et al., 2004).

These studies provided the basis for a general model describing how the protein kinases are regulated. However, they also provided structural knowledge of targets for drug discovery in oncology. Her early work in 1997 on the relatively nonselective inhibitor staurosporine revealed some of the first details of how ATP competitive inhibitors interacted with CDK2 (Lawrie et al., 1997). She developed an active program in structure-based drug design with therapeutic applications for glycogen phosphorylase, the cell cycle kinases CDK2 and CDK7, and the transcriptional regulator CDK9. Indeed, her work, particularly that over the past decade on protein kinase inhibitors (Johnson, 2009), contributed to the development of many clinical compounds.

Louise remained fascinated by physical techniques and in 2003 accepted the role of Science Director for Life Sciences at the Diamond Light Source in the UK, which was commissioned in January 2007. She had exploited synchrotron X-radiation in macromolecular crystallography in her studies of phosphorylase. She spent 50% of her time with the University and 50% with Diamond developing beamlines for macromolecular crystallography, noncrystalline diffraction, circular dichroism, and infrared microspectroscopy (Duke and Johnson, 2010). Together with Professor So Iwata and Dr. Gwynndaf Evans and in collabora-

tion with Imperial College, she created the Membrane Protein Laboratory funded by the Wellcome Trust.

Louise had a passionate interest in international science, spending 4 years as Chair of the Scientific Advisory Board of EMBL and several years on the Advisory Board of the Swiss National Centre for Competence in Research. She played a role in the development of science in Islamic countries, lecturing in Iran, Bangladesh, and Pakistan, and supporting the creation of SESAME, the new synchrotron in Jordan. Her election as an Associate Member of the Third World Academy of Sciences reflected her activity and allowed her to network with a broad range of eminent scientists with similar interests in science in developing countries.

Louise remained always generous with her time, a huge influence on the emergence of structural biology in the UK and elsewhere, and gave wonderful support to the many new labs established by her students and research colleagues throughout the world.

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