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Editorial

A life writ large: Chris Dobson 1949–2019

I first met Chris Dobson at a scientific conference close to 30 years ago. At that time I was a starting assistant professor, and Chris was a famous scientist who had made seminal contributions to our understanding of the protein-folding problem. Despite his involvement with conference organization, Chris spent the time to make me feel welcome, guiding me on a fantastic tour of Oxford University. His kindness, sharp wit, and caring personality were evident in abundance. This was the start of many rendezvous with Chris, in different venues associated with scientific conferences across Europe and North America, where I had the distinct pleasure of spending time with a truly exceptional human being.

Chris was a scientific giant who focused on big questions that often required foray into areas well outside his comfort zone. Trained as an inorganic chemist whose first paper focused on iron corrosion, he quickly cultivated an interest in biophysics and NMR spectroscopy. In a seminal study with the late Iain Campbell that was to foreshadow the importance of NMR spectroscopy in the investigation of biomolecular dynamics, Chris demonstrated experimentally that aromatic rings in protein interiors can flip, which is only possible if the hydrophobic cores of proteins are dynamic. Additional NMR evidence of this effect was provided by Wagner and Wuthrich and the group of Brian Sykes. Although this result seems rather obvious now, one has to understand that the dogma of the day, based on static high-resolution X-ray structures, was that proteins were static. Chris Dobson played a very significant role in changing this perception.

Studies of protein folding were a natural progression from Chris's early dynamics measurements and he and his team made outstanding contributions in this area. Working first with NMR and subsequently introducing new techniques, such as mass spectrometry, as was to become the hallmark of the Dobson approach to science, Chris focused on a number of protein systems, including his famous lysozyme, to identify pathways and mechanisms of folding. A curious result involving an NMR sample of an SH3 domain which formed deposits of fibers after sitting on the bench over a long weekend took Chris and his team in a new direction that was to form the basis of much of his subsequent work. This directional shift was renforced by the realization, at about the same time as the SH3 work, that human lysozyme forms fibrils in organs of individuals with key mutations. For the next two decades until his death, and based on a wide range of biophysics, bioinformatics, biochemical, cellular, and animal model experiments, Chris and coworkers made a series of incredibly exciting discoveries pointing to how the formation of aggregates might give rise to pathological conditions associated with neurodegenerative diseases. During this time a very dynamic group of investigators was assembled, including Michele Vendruscolo and Tuomas Knowles, the Cambridge Center for Misfolding Diseases was established, and Wren Therapeutics, a biotechnology start-up whose mission is to develop novel therapeutics for Alzheimer's disease was launched.

Despite Chris's prodigious achievements that involved the use of a plethora of different biophysical techniques, he remained partial to NMR spectroscopy. I remember fondly Chris's last visit to Toronto where I was lamenting the large amount of work that was required to translate my Varian pulse sequences to the Bruker language. Always an optimist and looking for ways to turn 'bad into good' Chris suggest that I write an article focusing on the subtle details that are so important for every good NMR experiment. This suggestion lead to a recent JMR paper chronicling the evolution of modern triple resonance pulse sequences, through the 'eyes' of the HNCA.

Chris's remarkable scientific accomplishments, his curiosity and appetite for science and his unique human qualities, including a genuine concern and interest for a great many of us, his students, will continue to live on. In this regard, I am absolutely delighted that Chris Waudby and John Christodoulou, two of Chris's former trainees, agreed to contribute a research paper in the present edition, focusing on the use of solution NMR to study protein folding on the ribosome, one of Chris's favorite scientific topics.

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