The world lost one of its most gifted biochemists on 14 February 2015 following the death of Professor Richard Nelson Perham, FRS, FMedSci at the age of 77. An active, renowned member of the scientific academic community until the last, Richard Perham was distinguished for his work on the chemistry of proteins and the assembly of giant protein complexes, and was a leader in bringing the power of protein engineering approaches to problems of protein structure and function.

He pioneered the development of chemical tools to understand protein structure and function, revealing how enzymes are able to generate energy from glucose (via the remarkable, massive, 2-oxoacid dehydrogenase multienzyme complexes) and how viruses assemble their capsid coats. By protein re-design Richard was the first to switch the co-enzyme requirement of an enzyme (altering glutathione reductase from using NADPH to NADH for catalysis and lipoamide dehydrogenase from NAD⁺ to NADP⁺). He also made outstanding contributions to our knowledge of the structure and assembly of filamentous bacteriophages, and was amongst the first to use these ‘phages to display foreign peptides on their surface, opening the door to their use for the production of novel vaccines. In essence, Richard was a pioneer of the important, and hugely topical, areas of protein engineering and its use to understand the fundamental principles of protein structure and function. His lectures on these topics were stunning. He would delight audiences with his descriptions of multi-enzyme complexes and how they worked, using entertaining and real-world analogies (e.g. the ‘hot potato’ hypothesis for ‘handing over’ reaction intermediates) to communicate his ideas. What came through was a strong passion for his science, a tenacity and long-term commitment to his work, a charm and charisma that captivated his audience, and a deep respect for the contributions made by collaborators, students and ‘competitors’ alike.

Recognition for Richard’s achievements are equally outstanding, including election as a Member of the European Molecular Biology Organisation (1983) and the Academia Europaea (1992), and as a Fellow of the Royal Society (1984) and the Academy of Medical Sciences (2005). He was awarded the Max Planck Prize (1993), the Novartis Medal of the Biochemical Society (1998) and the Diplôme d’Honneur from the Federation of European Biochemical Societies (2011).

Richard was born on 27 April 1937 in Hounslow West, Middlesex. He went to Latymer Upper School in Hammersmith, London, having secured a Scholarship. For Richard, the time at Latymer was heaven: the School’s liberal outlook and broad curriculum, including the arts and sport (both of which remained passions of his for life), inspired and nurtured the budding scientist. Richard’s experience at Latymer founded his strong belief in the importance and value of education for all, irrespective of background and/or wealth. Richard remained a loyal devotee of Latymer School, first by election as Governor of the Latymer Foundation in 1991 and then as Chairman of Governors from 2005 until 2010. Having completed A-levels in pure and applied maths, physics and chemistry in 1955, Richard was encouraged by Latymer to sit the examination for entry to the University of Cambridge. The first of his family to go to University, Richard was offered a place at St John’s College. This had the bonus that St John’s is the home of the Lady Margaret Boat Club. Richard learned to row at Latymer, and ultimately rowed in the College’s First Boat. After deferring his entrance for 2 years to fulfil the requirements of national service, Richard joined St John’s, firstly as an undergraduate in Natural Sciences (1958), then post-graduate (1961), Fellow (1964), President (1983-87) and ultimately Master (2004–7). In all, a 57-year long devotion to the College.

In the 1950s the field of biochemistry was a hothouse of discovery and achievement: the structure of DNA had been solved in 1953; the first sequence of a protein (insulin) in 1955; and the first three-dimensional structure of a protein (myoglobin/haemoglobin) in 1956. A whole new world was opening up and Richard was inspired to join this exciting and burgeoning field.
A PhD with the double Nobel Laureate, Dr Fred Sanger, at the then newly-formed Laboratory of Molecular Biology, was his next step. Richard worked on the structure and mechanism of glyceraldehyde 3-phosphate dehydrogenase under the immediate supervision of Dr J Ieuan Harris. Together Richard and Ieuan identified a key cysteine residue required for protein activity, and went on to hold the world record in the mid-1960s for determining the longest amino acid sequence (over 330 residues) of a protein. This work led to Richard’s first major article in Nature, which was published in 1968.

In 1965, Richard had been appointed Demonstrator in the University’s Department of Biochemistry and, at the same time, was awarded a Helen Hay Whitney Fellowship to study at Yale University with Professor Frederic Richards in the Department of Molecular Biophysics. There he met (over a shared electron microscope) the young and gifted biologist, Dr Nancy Lane, later to become his wife. Nancy and Richard returned to Cambridge, married in Halifax Nova Scotia in December 1969 and had two children, Temple and Quentin. Today, the family is increased by their son-in-law, Barney Schauble, and grandchildren Isabella (just turned 11) and Tristan (aged 8).

Richard made many significant contributions to science in the 50 years he worked in the Department of Biochemistry in Cambridge. In the late 1960s he uncovered the importance of charge-charge interaction between protein subunits in the self-assembly of tobacco mosaic virus capsids, and later elucidated the novel mechanism of protein-DNA charge interaction that governs the assembly of filamentous bacteriophage virions. He introduced a number of important techniques in chemical modification of proteins, in particular based on reversible amidination and trifluoroacetylation of lysine residues. After some 30 years of effort, he and his colleagues produced the first complete description of the structure and assembly pathway of the pyruvate dehydrogenase complex (whose molecular mass is 10 MDa). He also uncovered a new mechanism of active site cooperativity, distinct from allostery, in enzyme activity, and elucidated unexpected mechanisms of active site coupling in his multienzyme complexes based on motif protein domains. His scientific achievements were juxtaposed with his strong commitment to serving the scientific community, not only as a senior academic at the University of Cambridge, but also in his membership of the Executive Council and Trustee of the Novartis (formerly CIBA) Foundation; Chair, Scientific Advisory Board of the Lister Institute of Preventive Medicine; Scientific Advisory Committee and Vice-President of the Fondation Louis-Jeantet de Médicine in Geneva. Richard also took over as Editor-in-Chief of European Journal of Biochemistry in 1998, revolutionizing the journal into what is now FEBS J, and remaining at the helm until 2013.

Richard made lifelong friends with all he met. He was a truly exceptional scientist with an impressive knowledge of art, literature, history, sport and all types of music. He was an inspired teacher and mentor, loyal to his students, and passionate about the University of Cambridge and St John’s College. He leaves a legacy of more than 350 scientific papers, just a few of which are noted below, an array of well-trained graduate biochemists, and family, friends and the scientific community proud of such a brilliant man.

Sheena E. Radford (The University of Leeds) and Nigel S. Scrutton (The University of Manchester)

References: