A Personal Perspective: My Four Encounters with John Kendrew

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Abstract

By celebrating the 100th anniversary of John Kendrew's birth in 1917, the Journal of Molecular Biology recognizes his seminal contributions to science in general and structural biology in particular. John was first to use X-ray diffraction to solve the 3-dimensional structure of a protein, sperm-whale myoglobin, worthy of a Nobel Prize in Chemistry in 1962. John was the Founder and first Editor-in-Chief of the Journal of Molecular Biology, Deputy Chairman of the Laboratory of Molecular Biology and Head of its Division of Structural Studies, a Founder of the European Molecular Biology Organization, first Director-General of the European Molecular Biology Laboratory, and 33rd President of St. John's College, Oxford. In this personal perspective I relate how I came to know John as his postdoctoral fellow at the Laboratory of Molecular Biology in 1967 and as his biographer 45 years later.

"It is the fate of every human being to be a unique individual, to find his own path, to live his own life, to die his own death."Oliver Sacks, 2015

Background

Fresh from graduate studies in biochemistry at Brandeis University, I traveled with my wife and three children from Boston to London in the summer of 1967. It was the first time any of us had been on an airplane, a BOAC VC10, let alone been abroad. I was to begin research as a Helen Hay Whitney Foundation Postdoctoral Fellow in the Division of Structural Studies at the Medical Research Council (MRC) Laboratory of Molecular Biology (LMB) on Hills Road in Cambridge. Trained in enzymology and protein chemistry at Brandeis, my Ph.D. supervisor, Nathan O. Kaplan, advised me to get some experience in protein crystallography if I planned to continue my career as a protein chemist. It was great advice. In the late 1960s, we felt that the very best place to gain this experience was at the LMB (Fig. 1), where X-ray crystallography and other experimental approaches to determine three-dimensional protein structure flourished.

My sponsor at the LMB was John C. Kendrew, Deputy Chairman of the LMB and Head of the Division of Structural Studies (Fig. 2). While in his early 40s and a member of the Cavendish Laboratory, John and collaborators solved the low-resolution (6 Å) and then the high-resolution (2 Å) three-dimensional structure of sperm whale myoglobin in 1957 and 1959, respectively [3,4]. The information about proteins provided in John's two Nature publications represented an achievement that had been thought impossible only a few years earlier. In fact, Max Perutz noted that he and John succeeded where others had failed because they did not know it was impossible to solve a protein structure.

John's tremendous achievements demonstrated at long last that proteins were not aggregates of small molecules but were true macromolecules and that their structures could be solved by X-ray crystallographic methods. For the first time, one could visualize structural features of proteins, such as the alpha-helices predicted by Linus Pauling, in some detail. John's research demonstrated the effectiveness of the heavy-atom isomorphous

Fig. 1. Photograph of the Governing Board of the MRC Laboratory of Molecular Biology on Hills Road in Cambridge in 1967 when the author was a postdoctoral fellow there. Front row, left to right: Hugh Huxley, Max Perutz, Fred Sanger, and Sydney Brenner. Back row, left to right: John Kendrew and Francis Crick. Five of the six Governing Board members were either at the time or subsequently became Nobel Laureates. Photograph reproduced with permission of the MRC Laboratory of Molecular Biology, Cambridge.

Fig. 2. Photograph of John Kendrew at work on the three-dimensional structure of sperm whale myoglobin. Photograph reproduced from the Kendrew Archives at the Weston Library, Oxford.

replacement method and the importance of electronic computing and model building in solving protein structures. It was certainly a watershed moment in the history of structural biology. It was not until 5 years later that a high-resolution structure of a second protein, the enzyme lysozyme, was published [1] and not until the late 1960s that several other high-resolution structures of proteins, including hemoglobin [6], became available. A low-resolution (5.5 Å) structure of horse hemoglobin [7] had been published in the same issue of Nature in 1960, in which John's high-resolution (2 Å) structure of myoblobin appeared.

In 1978, 18 years after the three-dimensional structure of myoglobin was published, the structures of more than 200 proteins had been solved, and by 2014, the Protein Data Bank included close to 40,000 protein structures solved at 2 Å or higher resolution. Today, protein structures are solved at a rate of several thousand each year, largely due to an enormous increase in the number of practicing crystallographers and to tremendous technological advances in the field. However, it should be remembered that John Kendrew was *nulli secundus,* "second to none", having determined a high-resolution structure for myoglobin in 1959.

For his research on the three-dimensional structure of myoglobin, in 1962, John shared the Nobel Prize in Chemistry [2] with his colleague and Chairman of the LMB, Max Perutz. This was the same year that John's two colleagues, Francis Crick and Jim Watson, shared the Nobel Prize in Physiology or Medicine with Maurice Wilkins for the determination of the structure of DNA. Watson had come to the Cavendish from Denmark to be a postdoctoral fellow with John and to work on protein structure, not on DNA. At the time, the Nobel Academy noted that "John Cowdery Kendrew's and Max Ferdinand Perutz's contributions are of the highest class and they are extraordinarily worthy of receiving a Nobel Prize." They went on to say that "…it has been considered that their (Perutz's and Kendrew's) contribution represents one of the most important results which has been obtained by use of the X-ray diffraction methods since these were introduced 50 years ago by von Laue and W.H. and W.L. Bragg."

For his scientific contributions, John was made a Fellow of the Royal Society in 1960 and Commander of the British Empire in 1963. He received the Royal Medal of the Royal Society in 1965 and became an Honorary Fellow of Trinity College in 1972 and Peterhouse College in 1975. John was awarded an honorary Doctor of Law degree by Peterhouse in 1997, shortly before his death.

Under John's sponsorship, I was to work with his close colleague, Herman C. Watson, who had joined