A pioneer in X-ray crystallography, electron microscopy and biophysics

Ralph Walter Graystone Wyckoff, one of the most remarkable American men of science, died at the age of 97 in 1995. A study of his life gives us some glimpses into the early history and developments of X-ray crystallography, electron microscopy and biophysics in USA.

Wyckoff’s forebears came from Holland and settled in 1634 in the city of New Amsterdam which is now called New York. His father was a buildings contractor and Ralph was the first scientist in his family. Even when in school, he published papers in the Journal of the American Chemical Society and also took some patents. As a graduate student in Cornell University he made a serious but unsuccessful attempt to discover the missing element eka caesium from pellucite, a caesium containing mineral. This element, a short-lived radioactive one, was later discovered by Mlle Peres, one of Madame Curie’s collaborators. While searching for a new problem for his doctoral thesis, Wyckoff came to know that in Cornell there were two visiting Japanese scientists – Nishikawa and Asahara. Shoju Nishikawa was a student of the famous Tarahiko Tarada (1878–1935) who discovered ‘Bragg’s’ law independently of Bragg. As early as 1913 Nishikawa discovered X-ray fiber diffraction patterns of textile materials and of asbestos and did the structure of spinel. He was the first to realize the importance of the theory of space groups as a general and logical means for X-ray analysis.

Wyckoff, under the direction of Nishikawa, solved the structure of caesium dichloroiodide and sodium nitrate which were amongst the earliest structures to be solved in USA using single crystal diffraction. He used Laue photography – but soon shifted over to photographing Bragg reflections. After his doctorate and immediately after the end of the war, Wyckoff went to the Geophysical Laboratory, Washington where he set up an X-ray group to determine inorganic and mineral structures. In 1922 he published the famous tome – The Analytical Expression of the Results of Space Groups as Applicable to the Calculation of the Structure Factors. This book went into several editions and was responsible to a large extent in the spurt of the activity in X-ray crystal structure analysis. About the same time, many others including Kathleen Lonsdale in England and Hermann Mauguin in France derived similar expressions. These, together with those of Wyckoff were all incorporated in the International Tables published by the International Union of Crystallography.

When the physical chemist Noyes went from MIT to the California Institute of Technology (Caltech), he was intent on starting X-ray crystallography as he felt that determining the positions of atoms in a crystal would be very important to chemistry. Ellis, who was to be in charge of X-ray crystallography development in Caltech came to Wyckoff’s laboratory to familiarize himself with the subject. Wyckoff himself also went to Caltech to help set up the X-ray laboratory under Dickinson – with whom Linus Pauling was to work and create a major revolution in the field of X-ray crystallography, inorganic and mineral structures.

In 1927 Wyckoff went to the Rockefeller Institute for Medical Research in New York and started a new laboratory to investigate organic structures. Robert Corey trained in Wyckoff’s laboratory on organic crystals, solved the structure of urea there and then moved over to Caltech and became known for his work on amino acids, etc.

Wyckoff’s interest in crystals of biological interest was fostered by his close associations with P. Lecomte du Nouy, one of the pioneers of biophysics and with Alexis Carrel whose development of tissue culture made it one of the fundamental techniques of modern biology.

Wyckoff (and his collaborators) attempted to crystallize proteins to obtain their X-ray diffraction patterns. He felt that the ultra centrifuge could be used for purifying proteins. As a first step to preparing good crystals, he went on to design and construct comparatively large ultra centrifuges with air turbines. In his design he substituted the steels normally used in such instruments by light and strong aluminium–magnesium structural alloys developed by Dow Chemicals. He used these centrifuges for purification of plant and animal proteins and viruses and obtained extremely beautiful protein crystals including that of haemoglobin. Unfortunately he did not succeed in getting X-ray diffraction patterns (probably because he did not keep the crystals in their mother liquor during photography as Bernal and Hodgkin did later).

He then went on to newer applied fields. Equine encephalomyelitis virus was the first of the viruses to be purified by this method. Wyckoff and J.W. Beard made an effective formalin-killed vaccine from these purified preparations. In view of the serious encephalomyelitis epidemic among horses in the United States, Wyckoff was invited to work in the Lederle Laboratories, where he developed, tested and produced several million doses of this vaccine. Following their massive use, the epidemic ceased and there was no major recurrence of the disease in USA. Wyckoff’s laboratory then turned to the production of vaccine for typhus fever which was then raging. Large quantities of vaccine were made for the use of the US army. In response to the need for human blood plasma for treatment of war wounds in the Second World War, Wyckoff and his group next developed the process and built large-scale freeze drying plants for plasma with which they produced 2000 plasma packages per day.

After this very successful detour into applied and useful biophysics, Wyckoff returned to the life of fundamental research in the University of Michigan.
Because of his manual dexterity, he was able to repair an old and unusable electron microscope and in this process he suggested so many improvements that he was appointed consultant to RCA, USA and Philips, Holland. During his electron microscopy researches, Wyckoff had difficulty in estimating the size and height of virus particles. At that time he met Robley Williams, a Caltech astronomer who was coating some mirrors in the Dept of Physics and Astronomy in Michigan. Williams said that it was standard practice to get the height of lunar mountains by knowing the angle at which the sunlight falls on them and measuring the length of the shadows they cast. The solution was to make the viruses cast shadows by evaporating gold from one side and leaving a shadow on the far side. The technique of metal shadowing, so familiar to electron microscopists now, was one of the major contributions of Wyckoff and his group to electron microscopy.

For the first time the shadowed virus particle revealed its true three-dimensional shape and photographs of particles of several viruses were taken. A particularly satisfactory development that followed was the direct demonstration of the ordered arrangement of molecules within 'virus crystals'. So impressed was J. D. Bernal with these photographs and developments that he invited Wyckoff to an international meeting he was convening in London. The participants were amazed at the simplicity and effectiveness of the technique. It was this meeting that shadowing became a universal tool in the hands of electron microscopists.

It was also after this International meeting that the early confabulations took place between W. L. Bragg, P. P. Ewald, J. M. Bijvoet, R. W. G. Wyckoff and many others about the starting of the International Union of Crystallography and the International Union of Electron Microscopy. The former was established in 1948 with W. L. Bragg as its first President, J. M. Bijvoet its second (1951) and R. W. G. Wyckoff its third (1954). The International Union of Electron Microscopy was formed much later. When Wyckoff was at the Rockefeller Centre, he had started looking at collagen and later did much work on the electronmicroscopy of collagen in the National Institute of Health and other institutions in Washington where he went from Michigan. His old friend Nishikawa sent one of his students H. Noda to work with him. Noda went back to Japan and became one of the authorities on collagen and its fine structure.

After retirement, Wyckoff joined the University of Arizona and set up a laboratory for the study of the fine structure of biological solids. Here he extended his interest in collagen to other proteins. He was amongst the first to find collagen in fossilized bones of the animals of Pleistocene era. His laboratory went on to study older fossils and dino-saur bones. He also used paper and liquid chromatography for the analysis of the amino acids extracted from these bones. Using electron microscopy he studied the structures of proteins in fossilized bones and proved beyond any doubt that collagen can persist over the geologically significant periods of time. His laboratory also analysed the ancient proteins, especially collagen, to see how they differ from the present day ones and whether these differences are due to chemical and/or biological evolution.

One of Wyckoff’s life-long projects was the unified description of the results of crystal structure analysis. This resulted in the publication of his first group of volumes on the crystal structures (4 sections and 5 supplements, 1948–1960) and his later Crystal Structures (5 volumes, 1963–1967). He had put in an enormous effort into this but as it has been said 'his effort was much less and that he saved for thousands of crystallographers later'.

Wyckoff was recipient of many honours. He was elected to the National Academy of Sciences, The American Academy of Arts and Sciences and foreign member of the Royal Society, London and Royal Academy of Netherlands and a corresponding member to the Academie des Sciences, Paris. He was very proud of his election as Honorary Fellow of the Indian Academy of Sciences (1955). Almost every country in the world honoured him for his work on X-ray crystallography and electron microscopy. The American nation was grateful to him for his production of life-saving vaccines for which he was awarded many prizes.

I met R. W. G. Wyckoff in Washington in the spring of 1955. I first congratulated him on his election as President of IUCr. He said he cherished his election as Honorary Fellow of the Indian Academy of Sciences more. The reason he gave was that his attachment and ambitions in crystallography were not as much as his admiration for Indian philosophy, especially that of Ramakrishna Paramahamsa and Swami Vivekananda.

Wyckoff knew C. V. Raman well ('highly original guy and a bit too energetic'). They had met first in 1924 when Raman had gone to Caltech as a visiting professor and again later in 1948 in Boston. Raman had bought for his personal library all of Wyckoff’s books immediately after they were published, e.g. Structure Factors in 1922 and Crystal Structures in 1924. Wyckoff happened to be the examiner of my DSc thesis. He was not at all happy that I had not accepted the fellowship he had offered me to work with him in electron microscopy. ('You missed a lot as you were not there to participate in the exciting things that were happening'). I remarked about his work on the dispersion corrections in anomalous scattering and on the later epoch-making discovery of Nishikawa and Matsukawa of the failure of the Friedel’s Law under anomalous scattering conditions, on both of which some of my X-ray work was based. He talked most affectionately about Nishikawa and his association and life-long relationship with him. After the second world war Wyckoff resumed close contacts with him which were unbroken till Nishikawa’s death in 1952. 'I am eternally grateful to him for introducing me to Japanese culture, Japanese art and to the eastern philosophies.'

Wyckoff did much for the growth of X-ray crystallography internationally and in USA. To quote from one of the articles in The 50 years of X-ray Diffraction edited by P. P. Ewald — The meeting of Ralph Wyckoff with the shy and gentle Nishikawa in 1917 may be said to have an implicit significance to the growth of X-ray crystallography in USA.'

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