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IN MEMORIAM

David Harker—a life for crystallography

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Abstract
David Harker (1906–1991) was an American crystallographer. He was a pioneer in the determination of protein structures. He and his colleagues determined the structure of ribonuclease, which was the first protein structure determination in a US laboratory. They introduced important innovations in crystal structure analysis, some of which proved to be forerunners of the direct methods. For many years, his research was among the dominating factors internationally in crystallography.

Keywords David Harker · Herbert Hauptman · Harker section · Harker-Kasper inequalities · Protein Structure Project · Ribonuclease

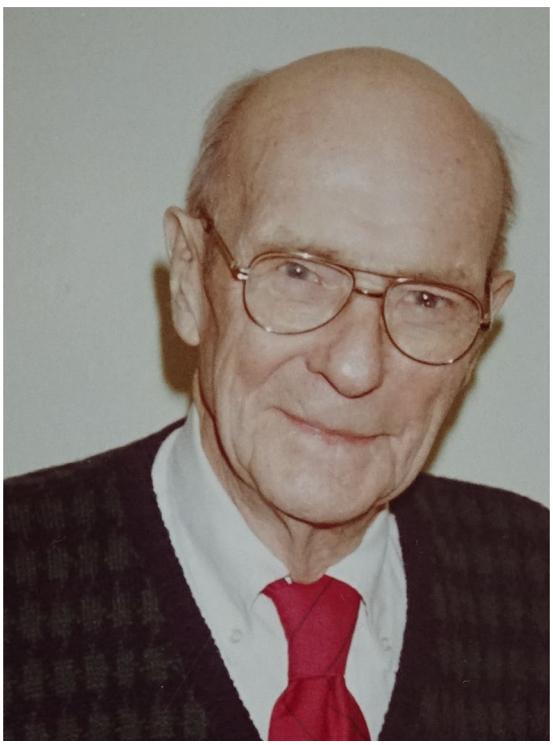

Fig. 1 David Harker in Buffalo, 1989 (photograph by I. Hargittai)

When David Harker (1906–1991, Fig. 1) died, the Nobel laureate Herbert A. Hauptman prepared an eloquent biographical memoir about Harker's life and research achievements [1]. Hauptman did not mention in this memoir, but had revealed to me in a personal conversation, that he felt uneasy about his own Nobel Prize: he thought that it should have been awarded to Harker. Nobel laureates seldom entertain such thoughts. According to Hauptman, "To crystallography he gave everything – his time, his energy, his total devotion. So complete was his dedication to his science and so fundamental and many-faceted were his contributions that he influenced forever the course of its development" [1].

The Harker family lived near San Francisco and Harker was 5 years old when he lost his physician father, but not before his father inculcated in him a lasting interest in "shape, symmetry, and structure" [1]. His strong-willed mother, also an MD, raised him and his brother paying meticulous attention to their education. Harker completed his chemistry undergraduate studies at the University of California, Berkeley. In 1930, he married Katherine de Savich of an upper-class Russian refugee family. She helped Harker in translating Russian science books into English and for a decade the two were involved in translating the papers of the Soviet crystallography journal, *Kristallografiya*, into English. After she died, Harker married Deborah Maxwell in 1974.

Following graduation, Harker worked for a research laboratory in Solvay, New York, but his readings moved him to continue in academia. He became Linus Pauling's graduate student at the California Institute of Technology. His thesis

Contribution to the Column "Foundation of structural science."

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work was the determination of a few crystal structures by X-ray diffraction. He was among the first who utilized the technique of Patterson function right after A. L. Patterson presented it in 1934. Not only did Harker apply this technique, he also extended it for cases that were not readily amenableto it—this was the introduction of the *Harker section*. Subsequently, his approach facilitated the determination of macromolecular structures containing a small number of heavy atoms. When Patterson learned about Harker's contribution, he wrote: "Mr Harker, I'm so glad you pointed this out to me. If I only could have thought a little more, I'd have seen this myself before you did. I could have kicked myself" [2].

Harker's interactions with Pauling did not end with his receiving his PhD in 1936. Those interactions were not always amicable either. Harker joined Johns Hopkins University where his teaching included freshman chemistry, crystal structure and crystal chemistry, and quantum mechanics. He was building up his X-ray crystallography laboratory. At Johns Hopkins, he came across the British crystallographer Dorothy Wrinch who was engaged in a fierce controversy with Pauling about protein structures. Pauling was not very good in tolerating dissent, was bluntly critical of Wrinch, and even tried to prevent her from publishing her papers. Harker resented Pauling's actions and was critical of his former mentor, earning Pauling's angry rebuttal [3]. When, in 1950, Harker embarked on his ambitious project of protein structure determination (vide infra), Pauling considered it a direct competition [4]. Nonetheless, Pauling recognized the importance of Harker's contributions to structural chemistry as illustrated here with two examples. There are 4 references to Harker in Pauling's opus magnum, *The nature of the chemical bond* [5], including one about the determination of decaborane by Harker and his co-authors in 1950. Pauling writes that it was "a great contribution to the structural chemistry of the boranes" [5]. Another recognition by Pauling appeared in the Patterson memorial volume where he wrote: "There was a period of about 20 years when the whole field of X-ray crystallography was dominated by Patterson's contribution and, of course, David Harker's contribution too" [6]. Harker attended the celebrations of Pauling's sixtieth birthday. He told the gathering that while being a graduate student he asked Pauling about the origin of his many good ideas. Pauling told him that he had many ideas, but kept only the good ones. This anecdote has been told many times without attribution.

At Johns Hopkins University, Harker learned about an interesting puzzle investigated by a fellow professor, Jose D. H. Donnay. It was about a possible correlation between the internal structure and the external face development of crystals. They joined forces and discovered what has become known as the Donnay–Harker law. In Hauptman's formulation, it states that "the order of decreasing prominence of the faces of a crystal is the same as the order of decreasing inter-planar lattice spacing due to the space group symmetries" [7].

In 1941, Harker moved to the research laboratory of the General Electric Company and his project was the investigation of metals by crystallography, especially, X-ray diffraction. This did not exclude dealing with other projects and one of them was the determination of the structure of decaborane. This was in cooperation with John S. Kasper with whom an even more widely-known joint achievement was the establishment of the famous Harker-Kasper inequalities among the crystal structure factors. This was the forerunner of the direct methods in X-ray crystallography.

The story of Harker's next move has been retold many times and has become a legend. Sometime in the fall of 1949, he was having a casual conversation with the Nobel laureate Irving Langmuir, the leading scientist of General Electric. Langmuir asked him what he would do with a million dollars. Harker responded that he would be happy to devote ten years of his life to determine a protein structure. Langmuir raised the money and Harker created his laboratory at the Brooklyn Polytechnical Institute, as it was then, or Brooklyn Poly. It became known as the Protein Structure Project, which aimed at the structure determination of ribonuclease. Brooklyn Poly at the time became a world hub for the science of macromolecules thanks to the presence of Herman F. Mark [8], Paul Peter Ewald, and David Harker. Francis Crick joined it for a short while at Harker's invitation. This happened right after James D. Watson and Crick published their seminal paper about their suggestion of the double-helix structure of DNA. Harker and his wife did everything they could to make the stay of Crick and his family agreeable, including a comfortable apartment at a price they could afford [9]. It was not the Harkers' fault that the Cricks did not enjoy their apartment on Fort Hamilton Parkway in Brooklyn and that Crick's one-year sojourn in 1953 with the Protein Structure Project was not too successful, especially in comparison with his previous year at Cambridge, England. Harker's project introduced methodological innovations, among them the multiple isomorphous replacement. Unknown to Harker, J. M. Bijvoet in Utrecht had already used such a technique, but did not sufficiently publicize it. This approach proved spectacularly successful a few years later for the structure determination of myoglobin by John Kendrew and hemoglobin by Max Perutz at Cambridge [10].

Harker's project stayed at Brooklyn Poly for a decade and in 1959 he moved it to Roswell Park Memorial Institute in Buffalo, New York (today, Roswell Park Comprehensive Cancer Institute), named after its founder, Roswell Park. Harker's research continued to thrive and it involved other renowned crystallographers on the staff or just visiting. The

structure of ribonuclease was finally determined in 1967. It took a long time, but it was still a pioneering deed, the first protein structure determined in an American laboratory.

Harker retired in 1976 at the age of 70 and continued as a scientist emeritus at the Medical Foundation of Buffalo, today, the Hauptman-Woodward Medical Research Institute. He focused his research on the mathematical aspects of crystallography, color space groups, and infinite polyhedra. His friendship with Herbert A. Hauptman, the principal scientist of the Institute enhanced the attraction of this venue for him. Hauptman was a mathematician and at the time Harker joined his institute, Hauptman was engaged in preparing stained glass polyhedra and determining the number of equal-size spheres possible to arrange in them—a mathematical curiosity of structural significance [11]. Thus, they shared interest in the object of their curiosity. In 1985, Hauptman shared the chemistry Nobel Prize, the one referred to above, with Jerome Karle, for their work in developing direct methods for the determination of crystal structures.

Harker's recognition started first on a more local level right after the publication of the ribonuclease structure and moved soon to national and international level. Only a few items are mentioned here. He served as president of the Society for X-ray and Electron Diffraction in 1946. He was a charter member of the International Union of Crystallography. In 1977, he was elected to the National Academy of Sciences and the American Academy of Arts and Sciences. According to Hauptman's memoir, Harker was nominated for the Nobel Prize in 1979. In 1980, he received the Fankuchen Award of the American Crystallographic Association and in 1984, the Gregori Aminoff Prize of the Royal Swedish Academy of Sciences, the highest recognition for achievements in crystallography. I had known Harker's name from the literature long before our meeting in person in Buffalo in 1989, and I have the warmest memories of that meeting.

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