Remembering Isabella Karle

Isabella Karle (1921 - 2017), retired from the Naval Research Laboratory (Washington, DC) after more than six decades there, passed away on October 3, 2017, at the age of 95, from a brain tumor. Early on Isabella was told by a teacher that chemistry was not a "proper field for girls" but she went on to become a member of the National Academy of Sciences. She received the 1988 Gregori Aminoff Prize from the Royal Swedish Academy of Sciences, the 1993 Bower Award and Prize for Achievement in Science and, in 1995, received the National Medal of Science. What follows are remembrances from several of her colleagues.

Jenny Glusker: Isabella Karle was a gifted scientist who was very active in determining crystal structures and advancing our understanding of chemical and biochemical reactions and their control. She also willingly made herself available to help anyone having difficulties with direct methods of phase determination.

Isabella's family was Polish-American and Isabella did not speak English until she went to grade school. However this did not cause her any problems and she rapidly excelled in classroom tasks, consistently at the top of her class. Her interest in studying chemistry and an excellent teacher of that subject led her to BS, MS and PhD degrees in physical chemistry by 1944 at the University of Michigan. This was done under the fine tutelage of Lawrence Brockway. In 1942 she married a fellow student, Jerome Karle, who was seated in the adjacent desk during studies. They were a devoted couple, married for 71 years.

Then came the time for Isabella to find a research position, not so easy for women in those days. However, she had very good credentials and was an excellent experimentalist, as shown when she worked for a short time at the University of Chicago on one part of the Manhattan project. The aim was to use chemical techniques on small lumps of impure plutonium oxide to obtain very pure plutonium chloride. This would be a step in the production of pure plutonium metal, the "new element discovered beyond the first 92." The chemistry of plutonium was not known at that time. Any equipment she needed had to be made by her in the laboratory, but fortunately she was a talented glassblower. Her description of this work on plutonium derivatives reminded me of the way Marie Curie worked in the laboratory to purify radioactive materials. It was as if Isabella had said to herself "I need to tackle this scientific problem, what techniques are available to help me do it?" and when she found out what they were she would solve the problem. In this case she worked with silica tubes that she had made, filled with crude plutonium oxide and chemical reactants, and inserted them in a hole in a large block of copper that was heated to high temperatures of 800 to 900 degrees Centigrade. After many experiments under difficult conditions, she ended up, triumphantly, with bright green crystals of plutonium chloride ($PuCl_3$) that she passed on to the physics branch of the Manhattan project.

Isabella approached direct methods in the same way, to the delight of her husband Jerry, who won the Nobel Prize for his work on them. She worked hard to find how to run direct methods correctly and then was able to help others. In fact, because of her contribution to the use of the method, Jerry felt she should share in the honors he received. Isabella, however, was just pleased to use and teach about direct methods. She pointed out that "I do the physical applications, he works on the theoretical. It makes a good team. Science requires both types."

Isabella was then able to use direct methods to study the structures of chemicals derived from, for instance, interesting creatures such as brightly colored frogs found in the tropical South American jungles. Her determinations of the chemical formulae of these compounds increased our understanding of their modes of action and how these modes might be controlled. She provided a knowledgeable intermediary between scientists trying to use the method and not having much luck and those who used mathematics to show how to do it but were frustrated that they did not know exactly how to use the method on crystallographic diffraction data. Now direct methods have been successfully incorporated in computer programs and three-dimensional results can come quickly.

Isabella also observed many of the courtesies that have made it so pleasant to be a scientists in this area. She came faithfully, with her husband, to all ACA meetings and added significantly to the smooth running of the meeting, calming an anxious Jerry when, in the olden days, members claimed they had difficulties using direct methods. She demonstrated the connection between the mathematical formulae and ways of handling phases for the measured structure factors. We often went to her for advice to get the method working for us. Not only was she a great scientist, she was a great teacher. She was also a good friend. She often phoned me to check that we were not working on the same structural problems. We never were but it was so nice that she asked. She also provided me with very helpful advice on raising children while doing a full-time job. She had plenty of experience with her three scientific daughters, Louise, Jean and Madeleine. My daughters greatly appreciated some of her suggestions.

Isabella also served as ACA president (1976) and left very useful information for future presidents such as how to make sure each committee does as asked. This took extra work on the part of the president before, not just during ACA meetings, but the results were constructive.

I am sad that Isabella is no longer with us and will miss her pleasant smile and interesting conversation, but I am proud to have known her and celebrate here her great contributions to molecular structure determination and her mentoring of early users of X-ray crystallographic methods.

Lou Massa: Isabella Karle was a remarkable scientist and a remarkable person who lived her own version of the American Dream: her parents were Polish immigrants to this country, and Polish was her first language until she went to school at the age of five or six. She was a great student all her life earning her BS, MA and PhD all before the age of 23. While studying at the University of Michigan, she met her future husband Jerome Karle in a physical chemistry lab. Their meeting was facilitated by the fact that they were seated next to each other alphabetically by surname; her maiden name was Lugoski.

Jerome and Isabella's mutual love of science cemented their relationship. They both earned their PhDs under Lawrence Brockway, a student of Linus Pauling. They worked in the field of electron diffraction, which would come to influence their work years later in the field of x-ray diffraction.

Almost immediately after completing their PhDs, they both went to the University of Chicago where they worked separately on the Manhattan Project. Among Isabella's many fascinating stories about that work is one about an occasion when she saved the lab from a potential catastrophe. The scientists carried portable radiation detectors, and one day Isabella noticed her detector going off beside the Coca-Cola vending machine, the type that dispensed soda directly into paper cups. As it turned out, the man who came to refill the machine needed to replace a hose in the machine and hastily grabbed one that had been exposed to massive amounts of radiation from a nearby laboratory. Because she spoke up, no one wound up drinking radioactive soda that day.

Isabella contributed to the field of Plutonium chemistry as a precocious recently minted PhD in her early twenties. She designed her own elaborate glassware to conduct her studies of plutonium chlorides for the Manhattan Project.

Isabella Karle's Curious Crystal Method, Story by Antonia Massa (@antoniabmassa), Photo credit: Rey Lopez a Washington, DC-based photographer, (narrative.ly/isabella-karles-curious-crystal-method .)

Perhaps her greatest contribution to science was to show that crystal structures could indeed be solved using the mathematical methods developed by Jerome Karle and Herbert Hauptman, work for which the two men eventually received the Nobel Prize. Isabella's meticulously designed x-ray experiments provided the all-important evidence needed to prove that their mathematical equations did work.

Those were the days long before you could buy computer-controlled x-ray diffractometers to measure intensities over the whole scattering sphere with electronic high accuracy. She was resourceful, borrowing an x-ray tube source and constructing an experimental arrangement to collect data. Her experimental design included use of the human eye to estimate the relative intensities registered upon photographic film. Imagine the confidence and the intellectual courage behind such an effort.

And the result was that she solved structures that no one else could. It took decades for science to widely accept that she could do this, but finally they did. That laid the groundwork for Jerome and Herbert's Nobel Prize for the mathematics. Though Isabella did not win the Nobel, she collected many other awards. She kept right on with her science, becoming one of the most important crystallographers of her generation. The prizes and accolades she racked up included the highest science award a US citizen can obtain, the National Medal of Science, which was presented to her in person by President Bill Clinton in 1995, in a ceremony held at the White House. She also received the Aminoff Prize, the highest honor in the field of crystallography. She was awarded multiple honorary doctorates, and published more than 300 scientific papers.

Isabella is revered as one of the greats of her generation. Only part of her greatness is as a scientist of historic importance. She managed to be a dedicated wife for more than 70 years and loving mother to three wonderful, accomplished daughters all while working at the highest levels of American science. Isabella will rightly be remembered by history for the greatness of her science. Those who knew her will also be remembering her humility and humanity. We loved Isabella, and she affected us deeply.

Connie Rajnak: I admired Isabella for a long time. She used to come to ACA meetings along with her husband Jerome and she welcomed me when I was a novice crystallographer and needed support. I was disappointed when Jerome shared a Nobel Prize with Herbert Hauptman that did not include Isabella. She should have shared that prize because she was the one who actually solved structures and made direct methods work. Jerome was strictly theoretical.

It was natural that when I had a sabbatical I selected Isabella to work with at NRL (the Naval Research Laboratory). She showed me how symbolic addition works and gave me a booklet that describes it. I liked the way she always published every structure she solved and did her best to find something interesting about it. When my 11 months at NRL were almost up she took me home with her and we talked with Jerome (Jerome and I share an interest in the piano but I couldn't persuade him to play anything). She then she rowed me around the lake just adjacent to their property and had a fine time talking about everything under the sun. I told her about my daughter's brush with breast cancer but she didn't mention that she was a breast cancer survivor herself.

After my sabbatical, I used to send her a birthday letter to which she always responded with a handwritten letter. After I married Stan I sent her an abbreviated version of our Christmas letter every year and she would respond similarly.

Jean Karle Dean: My mother's endless enthusiasm for crystal structure solving and relating 3-dimensional structure to function is why I became interested in crystallography. When I was a child, before computer graphics, I would sometimes help her plot calculated electron density on large sheets of rolled white paper held open on the dining room table by brass candlesticks. By age 18, I was operating an early version of an automatic diffractometer in her lab. Decades later when my workplace purchased me my own diffractometer, I was amused when the installer recommended that I start with a crystal of known structure to teach myself how to use the instrument and to solve the structure. I politely did not say anything and proceeded directly to crystals of interest of unknown 3-dimensional structure.

My mother was always interested in how structure related to function and the importance of intra- and intermolecular hydrogen bonding as well as other attractions between molecules. Earlier in her career, she would get very annoyed when short-sighted editors did not want to publish packing diagrams.

My mother had a natural instinct for solving crystal structures that allowed her to determine the crystalline structure of some of the largest molecules solved by direct methods, generally polypeptides. She also greatly enjoyed her collaborations.

In Stockholm, I was seated next to Nobelist Glenn Seaborg at a sit-down meal at the American Embassy. He told me that he could not understand why my mother was not sharing the 1985 Nobel Prize in Chemistry with my father, Jerome Karle, and Herbert Hauptman. I took that as an immense compliment to my mother's scientific contributions.

Sue Byram: Mrs. Karle was one of the pioneers in the solution of single crystal structures. I knew her over many years, particularly through visiting the Laboratory for the Structure of Matter at the Naval Research Laboratory in Washington DC from the 1970's to the present. She was a hands-on practical user of my company's single crystal diffractometers and we were immensely proud of providing hardware and software which we hope assisted in her important work. She was always eager to use the latest tools which would assist her in solving many difficult structures.

I just re-read the really nice words from the retirement ceremony of Isabella and Jerome Karle in 2009, where it was stated:

"Isabella Karle is one of the pioneers in the area of small molecule structural biology who developed the method on which so many important concepts in peptide structure and function were corroborated. Without her pioneering contributions to this field, much of the wonderful work that followed would not have been possible. Mrs19Karle's early research concerned the structure analysis of molecules in the vapor state by electron diffraction. In the fifties, her research was directed toward crystal structure analysis. She developed practical procedures based on the theoretical work developed by her husband in the Laboratory for the Structure of Matter at the NRL for the determination of phases directly from the measured intensities of x-ray reflections. These practical procedures have become adopted world-wide and have been essential to the explosive output of crystal structure determinations that are indispensable to the solution of problems in a number of scientific disciplines: chemistry, biochemistry, biophysics, mineralogy, material science, pharmaceuticals, drug design and medicinal chemistry, for example."

The whole Karle family is part of the wider crystallographic community and we treasure that. I recall many stories about the family, children included, attending many ACA and IUCr meetings. I started attending ACA meetings in the early 70's and have enjoyed seeing the Karle's at many of them. Indeed, Mrs. Karle was ACA president in 1976, exemplifying her love and devotion to our science. Most recently, I spoke with their daughter, Louise Karle Hanson and her husband Jon Hanson at the August 2017 IUCr meeting in Hyderabad, India. Mrs. Karle was both a distinguished scientist and a lovely human being.

Robert Henry "Pete" Bragg (1919 - 2017)

Robert Henry "Pete" Bragg, professor *emeritus* in the Department of Materials Science and Engineering in the College of Engineering at UC Berkeley, passed away on October 3, 2017, at the age of 98. He joined Berkeley in 1969, one of only six African-American faculty members on the campus. He chaired the department from 1978 – 1981.

Before earning his PhD, Bragg became an expert at x-ray crystallography and x-ray diffraction while working at the Portland Cement Association Research Laboratory. He went on to earn his PhD at Illinois Institute of Technology, working under his mentor Leonid V. Azaroff. Following receipt of his PhD, he worked for nine years on carbon-based materials at Lockheed Martin Missiles & Space Company.

The current Chair of the Materials Science and Engineering Department, Mark Asta, said "Professor Bragg pioneered the use of X-ray based techniques to characterize the structure of complex materials, particularly those containing light elements that had traditionally been relatively 'transparent' to these methods." Besides being a professor at Berkeley, Bragg was a principal investigator in the Materials and Molecular Division of Lawrence Berkeley National Laboratory. He served as an adviser to the U.S. Department of Energy, the Naval Research Laboratory, the National Science Foundation and the National Institute of Standards and Technology.