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December 5, 2014
MHC 20301

Herbert Hauptman

The common saying, "knowledge is power," is often applied to the field of science, but it would be difficult to find a more applicable use than when describing the work of Herbert Hauptman. Using his research to identify the structures of molecules, scientists have engineered all of today's invaluable drugs. Although the common man may not know it, he or someone he knows has had their life saved by Hauptman. Whether this lack of appreciation is due to Hauptman's humble nature or the public's inattention to the scientific research that keeps them alive, this man has helped to drastically increase U.S. life expectancy by ten years.

Interestingly, this advancement in the field of medicine came from a mathematician. Contrary to this specification, Hauptman has had a self-described love of both mathematics and science ever since he began to read. This interest in science may have been the reason for his collaboration in chemistry that would eventually win him his Nobel Prize. The New York City native attended Townsend Harris Hall before graduating from The City College of New York in 1937 with a bachelor's degree in Mathematics and Columbia University two years later with a master's degree in the same field. Afterwards, the United States' involvement in World War Two forced Hauptman to take a break from his studies and become a Naval weather forecaster in the South Pacific.

In 1947, after returning from the war, Hauptman enrolled in a Ph.D. program at the University of Maryland and began a collaboration at Washington D.C.'s Naval Research Center. This partnership, with physical chemist Jerome Karle, became the focal point of Hauptman's career. The research he did on x-ray crystallography, a process by which molecules are identified, with Karle was the source of his eventual Nobel Prize and the dissertation that earned him his doctorate in 1955. He and Karle published their results in a book, *Phase Problem I: The Centrosymmetric Crystal*, but their findings were quickly dismissed because of the difficulty of the problem they had solved. The question of determining the exact structure of a molecule was considered unsolvable to most chemists at the time. It would take until the 1970s for their work to be accepted and 1985 for it to be recognized with the Nobel Prize in Chemistry. Hauptman would study this process of x-ray crystallography for the rest of his career.

In 1970, not wanting to shift his research towards laser-guided missiles, Hauptman left the research center. He continued his work in relation to endocrines at the Medical Foundation of Buffalo. He became the director of research for the foundation in 1972 and its president in 1988. By this time, Hauptman was an internationally renowned scientist: a member of the National Academy of Sciences, honorary degrees from universities worldwide, and recipient of a Nobel Prize. He became the first mathematician to win the award based solely on his work in mathematics. Due to these distinctions and Hauptman's contributions to the foundation, the Medical Foundation of Buffalo has since been renamed the Hauptman-Woodward Institute. Quoted as saying "There is no such thing as working too hard or too long," Hauptman exemplified his beliefs, working daily at the Hauptman-Woodward Institute even into his nineties. He died on October 23, 2011.

X-ray crystallography is the process of changing a compound to its crystalline form and analyzing the scattering patterns observed when x-rays are shone on this crystal. Scientists use this technique to determine the position of specific atoms in a compound and create an image of the molecule in three-dimensional space. This knowledge is key to the production of all drugs. It provides researchers with information about the substances they are studying and molecules they have created, both of which are vital to understand how a proposed treatment may interact with the body.

Hauptman and Karle made this process into what it is today. At the time of their research, the idea of calculating the position of an atom in a molecule was actually deemed impossible by most researchers. Prior to their research, x-ray crystallography could only be used to infer the structures of a compound. Chemists knew that there was a relationship between the scattering patterns of the x-rays and the composition of the molecule, but they could not determine the exact correlation. One major difficulty in x-ray crystallography is the phase problem. Inconveniently, the x-ray detector can record the intensity of different beams but not the phases of each electromagnetic wave. This limitation means that vital information, such as electron density distribution in the crystal, is lost. Hauptman used probability theory to devise a series of equations, called "direct methods", that could determine the phase and translate the diffraction patterns to pinpoint the positions of atoms in a small compound. In the 1980s Hauptman addressed this limitation, applying his research to larger molecules and successfully altering his equations to do so. Although they had revolutionized medicine and the pharmaceutical industry, Hauptman and Karle's theories were dismissed, unused until they were finally accepted twenty years later.

Hauptman's formulas even reduced the time required to determine a compound's structure. During the 1960s, it could take two years to find the structure of an antibiotic with only fifteen atoms. Using Hauptmann and Karle's research, it became possible to determine the structure of a compound with 100 atoms. Hauptman's later improvements to his own direct methods, made from his research at the Hauptman-Woodward Institute, further increased this limit to 1000 atoms. Currently, using direct methods in conjunction with modern computing capabilities, it is possible to quickly determine the position of atoms in a protein with over ten thousand atoms. A determination that once took years to complete is now done in hours with much larger molecules. Although computing power has a lot to do with this increase in efficiency, the impact of Hauptman's research is undeniable.

In an interview with the Associated Press, Eaton Lattman, chief executive of the Hauptman-Woodward Institute stated, "I don't think there's a single pharmaceutical that's been developed in the last 30 years that hasn't been studied using derivations of what Dr. Hauptman and his colleagues won the Nobel Prize for." Although Hauptman's influence on modern medicine is demonstrated by his prestige and awards, Lattman's quote is a much greater measure of his work. Hauptman's dedication to scientific advancement led him to further his research even after decades without recognition. The lasting impact of his work shows that society will forever be indebted to this commitment.

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