

“A Proposed Structure for the Nucleic Acids” (1953) by Linus Pauling and Robert Brainard Corey

In February 1953, Linus Pauling and Robert Brainard Corey, two scientists working at the California Institute of Technology in Pasadena, California, proposed a structure for deoxyribonucleic acid, or DNA, in their article “A Proposed Structure for the Nucleic Acids,” henceforth “Nucleic Acids.” In the article, Pauling and Corey suggest a model for nucleic acids, including DNA, that consisted of three nucleic acid strands wound together in a triple helix. “Nucleic Acids” was published in *Proceedings of the National Academy of Sciences* shortly after scientists came to the consensus that genes, the biological factors that control how organisms develop, contained DNA. Though scientists proved Pauling and Corey’s model incorrect, “Nucleic Acids” helped scientists understand DNA’s structure and function as genetic material.

In the early to mid-twentieth century, scientists investigated DNA’s structure using X-ray crystallography. X-ray crystallography is a technique where scientists shoot a beam of X-rays at a crystalline substance like DNA and analyze how the X-rays scatter, or diffract, off the crystal. Scientists collect the scattered X-rays on a film, creating a diffraction pattern or diffraction image of dark spots that can provide scientists with information about the structure of the crystalline substance. To write “Nucleic Acids,” Pauling and Corey relied on X-ray diffraction patterns collected in 1938 by William Thomas Astbury, an X-ray crystallographer. Astbury worked at the University of Leeds in Leeds, England, and collected some of the earliest X-ray diffraction patterns of DNA.

Shortly after they published research about the structure of proteins, Pauling and Corey wrote “Nucleic Acids” during late 1952. Pauling began studying chemical bonding, or how atoms connect to form larger molecules, in 1926. In 1934, he began to apply those concepts to protein structure. Pauling later won one of his two Nobel Prizes for that work. Corey, who had experience with X-ray crystallography, worked with Pauling specifically on protein structure. Pauling later admitted that he was one of many scientists who remained skeptical that DNA was genetic material and argued that proteins were responsible for genetic phenomena instead. Pauling stated that because he was not completely convinced that DNA could be genetic material, he thought about how DNA might interact with proteins to achieve a genetic function while he worked on the structure of DNA. “Nucleic Acids” was published in the journal *Proceedings of the National Academy of Sciences* in February 1953.

“Nucleic Acids” broadly applies to all nucleic acids, including DNA and a different nucleic acid called ribonucleic acid, or RNA. RNA, like DNA, can carry genetic information. The paper contains diagrams and tables of mathematical data, but no subsection headings. The first part of Pauling and Corey’s paper features a discussion about DNA’s importance and available experimental findings relating to DNA’s chemical composition and structure. In the second part of the paper, Pauling and Corey provide an in-depth description of their proposed structure of DNA and include calculations to support their claims. In the last part of their paper, the authors compare their model to a model Astbury suggested years earlier and describe how their structure of DNA could function as genetic material.

Pauling and Corey begin “Nucleic Acids” by discussing the biological significance of nucleic acids like DNA and RNA and reviewing structural data about nucleic acids. The authors mention that nucleic acids have roles in cell division, growth, viruses, and heredity, which is the passage of traits from parents to offspring. While they write that nucleic acids function in heredity, the authors do not explicitly use the word gene. Pauling and Corey explain that they relied on the known sizes of atoms in nucleic acids and on available X-ray diffraction patterns of DNA to develop their model.

Before introducing their model, Pauling and Corey acknowledge that their model is not completely proven because it is not based on a full mathematical analysis of the available X-ray diffraction evidence.

Continuing the first part of their paper, Pauling and Corey provide background information on the constituents, or building blocks, of nucleic acids. Pauling and Corey state that nucleic acids are large molecules made of units called nucleotides. The authors describe nucleotide composition in terms of three major components. They state that nucleotides contain phosphate groups, which are negatively charged clusters of one phosphorus atom bonded to four oxygen atoms and a hydrogen atom. Next, Pauling and Corey state that nucleotides also contain a sugar, a ring-shaped molecule containing carbon, hydrogen, and oxygen. RNA contains a sugar called ribose, and DNA contains a sugar called deoxyribose. Then, the authors describe and name the final components of nucleotides, the purine and pyrimidine bases, which stick out of the side of the nucleotide. Purine and pyrimidine bases are single or double ring molecules that contain nitrogen, carbon, hydrogen, and sometimes oxygen. Pauling and Corey go on to describe how the three components of nucleotides are connected. For example, they describe the atoms involved in connecting the phosphate group to the sugar. Pauling and Corey cite related studies previously published by other scientists, information about nucleotides, and explanations about how the parts of nucleotides are bonded together to justify their model.

Pauling and Corey conclude the first part of "Nucleic Acids" with a brief mention of DNA, specifically X-ray diffraction patterns of DNA. They cite scientists who obtained X-ray diffraction images of DNA, including Astbury at the University of Leeds. Pauling and Corey admit that they collected X-ray diffraction patterns of DNA, but because their images were not as successful as Astbury's, Pauling and Corey rely on Astbury's patterns to develop their structure.

To begin the second part of their paper, Pauling and Corey introduce their structural model of nucleic acids, starting with their argument for why nucleic acids form helical fibers. They make a theoretical argument in which they compare nucleic acids to proteins. The authors explain that proteins, composed of a variety of building blocks called amino acids, can fold into a spiral shape called an alpha helix. Pauling and Corey argue that, like proteins, a chain of nucleotides also folds as a helix because that structure would be the only way nucleotides could connect to produce the type of fibers scientists observed in nucleic acids. The authors then pose a more experimental argument for their helical structure. They cite electron microscopy evidence. Electron microscopy is a technique scientists use to view microscopic substances at high resolution, or detail. Pauling and Corey state that when scientists observed DNA under an electron microscope, they saw fibers that appeared to have a circular cross section, characteristic of a helical structure or a spiral staircase.

Pauling and Corey make a second argument for the helical structure of DNA in the second part of "Nucleic Acids." From the X-ray diffraction images and physical properties of DNA, like its weight and density, Pauling and Corey calculate that each repeating unit of DNA contains three nucleotides and that those nucleotides must come from three separate chains. A repeating unit of DNA can be visualized as one step of a spiral staircase. Pauling and Corey provide a diagram of a top-down view of three DNA strands wound together, showing the three different nucleotides.

Once they establish that there are three helical strands in their model of nucleic acids, Pauling and Corey continue the second part of "Nucleic Acids" by discussing what component of the nucleotide occupies the core of the triple helix. That part occupies the empty space in the middle of the triple helix, faces neighboring strands, and is responsible for connecting the strands together. Pauling and Corey state that the core of the triple helix could contain either the bases, the sugars, or the phosphate groups. They argue that the core should be packed with a part of the nucleotide that can pack closely enough so bonds can be formed without being too crowded. Because of the shapes of the bases and sugars, Pauling and Corey argue that the bases and sugars could not pack in the core of the helix in a way that allows the nucleotides to chain together into a helix shape. Therefore, authors claim that the phosphate groups, composed of phosphorus, oxygen, and hydrogen, must make up the core of the helix. Not only would the phosphate groups be bonded to the sugars of the same strand, but they would be attracted to the phosphate groups of neighboring strands through relatively weak interactions called hydrogen bonds. The hydrogen bonds between the hydrogen and oxygen atoms of the phosphate would hold the strands together. Pauling and Corey calculate bond

lengths based on the known sizes of each atom to support their claims. They include diagrams of a nucleotide helix, of a protein helix for comparison, and of a single nucleotide. The authors include multiple diagrams showing the phosphate groups at the core of the helix.

In the third part of their paper, Pauling and Corey compare their structural model to a model Astbury suggested in 1938. The two models are based on the same images. Pauling and Corey discuss how Astbury's model consisted of a single strand with nucleotide bases stacked one on top of the other. According to the authors, Astbury's model was not helical because Astbury claimed that a helical structure would not allow the nucleotides to pack close enough together. Pauling and Corey state that they kept the close packing of nucleotides in a helical structure by having three DNA strands wound together, instead of just one strand. The authors summarize how their model of DNA fits with most of the x-ray diffraction evidence.

Pauling and Corey end their paper with a discussion of how DNA may interact with other molecules. The authors argue that the nucleotide bases have atoms that can easily bond to neighboring molecules, like proteins, especially since the bases face outward. With three separate DNA strands and variable base sequences, Pauling and Corey argue that their DNA structure has the capacity for specificity, meaning that their DNA structure can produce the genetic variation scientists observe between different organisms and species.

Scientists rejected the structure of DNA that Pauling and Corey proposed in "Nucleic Acids." Horace Freeland Judson, a historian of science, articulated some reasons why scientists did not accept the model. According to Judson, Pauling and Corey claimed that their model worked for all nucleic acids, including RNA, even though much of the data was based on X-ray diffraction images of DNA only. Scientists later found that RNA has a different structure. Judson noted that another error in Pauling and Corey's model was that they had the atoms of the phosphate groups at the core of the triple helix packed too tightly together, and that they added extra hydrogen atoms to balance the negative charge of the phosphate groups. In an interview with Judson, Pauling stated that he and Corey did not devote a significant amount of effort to their structure of DNA and that they based their findings on Astbury's flawed diffraction images. Another historian, Robert Olby, discussed a calculation error Pauling and Corey made when determining how many strands of nucleic acid were needed in the helix. Olby claimed that the justification for having three nucleotides within each repeating unit of the nucleic acid was based on incorrect calculations.

In April 1953, James Watson and Francis Crick, two scientists at the University of Cambridge in Cambridge, England, proposed a different model of DNA in which two helical strands wound together. In his autobiography, Watson states that in late 1952, when he and Crick learned that Pauling was going to publish a model of DNA, they felt a great urgency to develop their own structure and publish it at the same time. Historian Frederick Lawrence Holmes stated that Watson and Crick's efforts were inspired by Pauling's model building, as Watson and Crick also built a physical model of DNA. In their paper on DNA, Watson and Crick respond directly to Pauling and Corey, challenging specific aspects of their triple helix model. First, the Watson-Crick model had the bases pointing inward rather than outward like in the Pauling-Corey model. Second, instead of placing the phosphate groups at the core of their molecule, Watson and Crick placed the phosphate groups along the backbone. Watson and Crick stated that the DNA bases formed hydrogen bonds that connected the two strands together. The Watson and Crick model also explained how specific pairings of certain types of bases and the many possible sequences of bases allowed DNA to function as genetic material. Watson and Crick based their model on X-ray diffraction images collected by Rosalind Franklin, who worked at King's College London in London, England. Franklin's images were significantly improved over Astbury's, allowing Watson and Crick to determine a more accurate structure. As of 2018, the Watson-Crick model of DNA is still the accepted model for the most common structural form of DNA.

Sources

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