“Molecular Structure of Nucleic Acids: A Structure for Deoxyribose Nucleic Acid” (1953), by James Watson and Francis Crick [1]

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In April 1953, James Watson [5] and Francis Crick [6] published "Molecular Structure of Nucleic Acids: A Structure of Deoxyribose Nucleic Acid" or "A Structure for Deoxyribose Nucleic Acid," in the journal *Nature*. In the article, Watson and Crick propose a novel structure for deoxyribonucleic acid or DNA. In 1944, Oswald T. Avery and his group at Rockefeller University [7] in New York City, New York published experimental evidence that DNA contained the biological factors called genes [8] that dictate how organisms grow and develop. Scientists did not know how DNAás function led to the passage of genetic information from cell to cell, or organism to organism. The model that Watson and Crick presented connected the concept of genes [8] to heredity, growth, and development. As of 2018, most scientists accept Watson and Crick´s model of DNA presented in the article. For their work on DNA, Watson and Crick shared the 1962 Nobel Prize in Physiology or Medicine[9] with Maurice Wilkins.

The collaboration that led Watson and Crick to write "A Structure of Deoxyribose Nucleic Acid" began in October 1951 soon after Watson arrived at the Cavendish Laboratory at the University of Cambridge in Cambridge, England. At the time, Watson was a twenty-three-year-old postdoctoral researcher from the United States and Crick, at the age of thirty-five, was a PhD student at the University of Cambridge. Watson and Crick started studying the structure of DNA together soon after Watson arrived at the Cavendish Laboratory. They frequently ate lunch together and discussed their work and the work of others in the laboratory. Eventually, senior members of the laboratory gave Watson and Crick an office space to share.

In 1944, Avery´s group at Rockefeller University [7] Hospital published an article that provided experimental evidence that DNA contained genes [8]. Decades before the publication of Watson and Crick´s article, scientists found evidence of the building blocks of DNA called nucleotides. Nucleotides are composed of three parts. The middle part of the nucleotide is a deoxyribose sugar attached to one side of the deoxyribose is a negatively charged phosphate group composed of phosphorus and oxygen and at the opposite side of the deoxyribose is one of four nitrogen bases, which varies between nucleotides. Scientists had published on the structure of the four bases in DNA: adenine, thymine, guanine, and cytosine. Adenine and guanine are made of two fused rings and called purines. Cytosine and thymine are single rings structures called pyrimidines.

When Watson and Crick wrote their article, they relied on the results of x-ray [10] crystallography experiments. To conduct x-ray [10] crystallography, scientists shoot a beam of x-rays, which are high-energy electromagnetic waves at a crystal. Once the beam hits the crystal, the x-rays scatter in a way that depends on the three-dimensional arrangements of the atoms in that crystal. The experiment results in an image, called a diffraction pattern, which scientists use to determine the three-dimensional structure of the crystal they observe. During the years leading up to the publication of the article, scientists used x-ray [10] crystallography to learn about the three-dimensional structure of DNA. While Watson and Crick never conducted x-ray [10] crystallography experiments themselves, they used data from experiments conducted by other scientists to develop their model of DNA.

Watson and Crick proposed a new model for the three-dimensional structure of DNA. The article consisted of less than two pages and had one illustration. To begin the paper, Watson and Crick respond to another DNA model proposed by Linus Pauling and Robert Corey, two scientists at the California Institute of Technology [11] in Pasadena, California. Pauling and Corey proposed an alternate model just a few months before Watson and Crick wrote their article.

Watson and Crick begin their article by discussing the alternate model proposed by Pauling and Corey. While not described in detail by Watson and Crick, the Pauling-Corey model of DNA was a triple helix, where each of the three helical strands contained nucleotides strung together. In the Pauling-Corey model, the negatively charged phosphate groups faced inside the triple helix, and the bases faced outside the triple helix. In their article, Watson and Crick criticize the Pauling-Corey model. First, they argue that the DNA bases cannot face outward with the phosphate groups facing inward. Watson and Crick claim that the DNA strands bond together through the bases, so if the bases faced outward, there would be nothing connecting the DNA strands. The authors also argued that if the negatively charged phosphate backbones of the DNA strands faced inward they would repel each other. In addition, the arrangement of atoms in the Pauling-Corey structure would repel each other. That concludes Watson and Crick´s criticism of the Pauling-Corey model in their paper.

Watson and Crick continue with a description of their proposed DNA structure and a diagram to go along with their proposal. They define their structure as a double helix, with two helical chains coiled around a theoretical axis. According to Watson and Crick, the DNA strands run antiparallel to each other. That means that the strands run in opposite directions. Nucleotides are not perfectly symmetric molecules. They have a top and a bottom. So, when the DNA strands run antiparallel as Watson and Crick describe, one strand has the nucleotides facing right side up and the other strand has the nucleotides facing upside down.

Watson and Crick further the description of their structure by comparing it to a model of a chain of nucleic acids proposed by Sven Furberg, a crystallographer at Birbeck College, in London, United Kingdom, in 1952. Watson and Crick say that like Furberg´s model, their model of DNA has the bases facing inside the double helix and the phosphate backbones facing outside the double helix. Also similar to Furberg´s structure, Watson and Crick explain that the bases are perpendicular to the deoxyribose rings and phosphate groups of the nucleotides. In other words, the bases are like rungs of a ladder and the deoxyribose sugar and phosphate groups are like the rails of the ladder. After describing some remaining details about their structure, Watson and Crick finish their general description of their DNA model.

Watson and Crick then discuss the novel features pertaining to their DNA model. The first feature the authors discuss is how the two strands of DNA are connected. The authors state that a single base from one DNA strand attaches to a single base from the opposite DNA strand via hydrogen bonds. In DNA, hydrogen bonds occur between hydrogen atoms and oxygen or nitrogen atoms. While hydrogen bonds are weaker than the phosphate bonds connecting nucleotides together in each DNA strand, they are strong enough to hold the two helical strands together. Watson and Crick explain that for adequate hydrogen bonding to occur, within each pair of connected bases, one base must be a purine, a double ring, and one base must be a pyrimidine, a single ring.

Next, Watson and Crick describe is the specific identity of each base in a base pair. The authors assume that each of the four bases can only pair with one other type of base. Adenine, a purine, can only pair with thymine, a pyrimidine. Guanine, a purine, can only pair with cytosine, a pyrimidine. Based on that logic, Watson and Crick explain that the sequence of bases along one DNA strand automatically determines the sequence of the other strand. Each base along a DNA strand pairs with its only viable [12] counterpart on the opposite strand. To support their claim about specific base paring, Watson and Crick cite experimental evidence. Erwin Chargaff at Columbia University [13] in New York City, New York obtained that evidence. The authors explain that Chargaff determined that in DNA the ratio of adenine to thymine and guanine to cytosine is always roughly one-to-one. That means that the amount of adenine in DNA roughly equals the amount of thymine, and the amount of guanine roughly equals the amount of cytosine, which is the likely case if base pairing in DNA is specific.

After the discussion of base pairing, Watson and Crick conclude withx-ray [10] crystallography evidence that they used to generate their model of DNA. Watson and Crick acknowledge that the x-ray [10] crystallographic evidence of DNA published before they wrote their article could not confirm their model alone and there needs more experimental evidence to prove their model. Watson and Crick then postulate that the base pairing mechanism they proposed implied a possible DNA replication mechanism, though they do not describe that mechanism. The authors then end their article with acknowledgements.

When developing their model of DNA, Watson and Crick relied on unpublishedx-ray [10] crystallography experimental data. Scientists at King´s College London in London, UK, collected that data. Rosalind Franklin, a chemist, and her graduate student, Raymond Gosling, collected the data. Watson and Crick acknowledged those individuals in their paper. From 1951 to 1953, Franklin and Gosling gathered x-ray [10] diffraction pattern images of DNA, which they obtained from the x-rays of DNA crystals. When Watson and Crick wrote "A Structure for Deoxyribose Nucleic Acid," Franklin and Gosling had not published their most clear DNA diffraction images, despite those images having improvements over the published data at the time. In early 1953, without Franklin´s knowledge, Maurice Wilkins a co-worker at King´s College showed Watson one of Franklin´s clear diffraction patterns of DNA. Later, Watson and Crick received a report Franklin wrote on her experimental findings. That report contained data Franklin presented at a colloquium at King´s College in 1951. When developing their own model of DNA, Watson and Crick drew conclusions from data contained within both Franklin´s diffraction image and her report.

In 1962, Watson and Crick shared theNobel Prize in Physiology or Medicine[9] with Wilkins for their findings relating to the structure of DNA and its role in genetics, many of which appeared in "A Structure for Deoxyribose Nucleic Acid." Franklin died in 1958 before the award of the 1962 Nobel Prize and did not receive the Nobel Prize, the award of the Nobel Prize is never posthumously. Some people speculate that if she were alive she would receive it for her contribution to solving the DNA structure. Others did not think she made crucial contributions to the solution of the DNA structure. The roll Franklin played in the discovery of the structure only realized after the publication of Watson´s book *The Double Helix: A Personal Account of the Discovery of the Structure of DNA* in 1968. Aaron Klug, Franklin´s last graduate student and colleague at Birkbeck College, in London, inherited her notebooks and papers when she died and published, "Rosalind Franklin and the Discovery of the Structure of DNA" a review of her notebooks and papers after publication of Watson´s book. Franklin and Gosling published five papers on DNA structure the first two sent to press before Franklin knew of the Watson-Crick Model. These papers were very technical papers dealing with x-ray [10] crystallography, which may why they did not receive more attention.

Watson and Crick´s structure of DNA has remains largely accepted among scientists through the twenty-first century. The three-dimensional structure of DNA Watson and Crick proposed called the B-form DNA, terminology Franklin coined when she first collected diffraction patterns of that form of DNA. The B-form DNA is the most stable conformation of DNA under physiological conditions, though DNA can adopt other three-dimensional confirmations depending on its base sequence and its surrounding environment. For the next seven years following the 1953 publication of "A Structure of Deoxyribonucleic Acid," Wilkins and his research team obtained higher resolution x-ray [10] diffraction images of B form DNA from a variety of species. From the higher quality images, Wilkins made small adjustments to the dimensions of Watson and Crick´s DNA structure.

"“A Structure of Deoxyribose Nucleic Acid" had immediate impacts on both the study of DNA as genetic material and the field of molecular biology. Watson and Crick´s article shifted scientists away from the question of how DNA was structured and toward the question of how DNA functioned. Later in 1953, Watson and Crick wrote a second paper, "Genetical Implications of the Structure of Deoxyribonucleic Acid," that addressed how DNA might self-replicate to pass on the genetic information encoded within it.

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In April 1953, James Watson and Francis Crick published “Molecular Structure of Nucleic Acids: A Structure of Deoxyribose Nucleic Acid” or “A Structure for Deoxyribose Nucleic Acid,” in the journal Nature. In the article, Watson and Crick propose a novel structure for deoxyribonucleic acid or DNA. In 1944, Oswald T. Avery and his group at Rockefeller University in New York City, New York published experimental evidence that DNA contained genes, the biological factors called genes that dictate how organisms grow and develop. Scientists did not know how DNA’s function led to the passage of genetic information from cell to cell, or organism to organism. The model that Watson and Crick presented connected the concept of genes to heredity, growth, and development. As of 2018, most scientists accept Watson and Crick’s model of DNA presented in the article. For their work on DNA, Watson and Crick shared the 1962 Nobel Prize in Physiology or Medicine with Maurice Wilkins.

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