“Genetical Implications of the Structure of Deoxyribonucleic Acid” (1953), by James Watson and Francis Crick

In May 1953, scientists James Watson and Francis Crick wrote the article “Genetical Implications of the Structure of Deoxyribonucleic Acid,” hereafter “Genetical Implications,” which was published in the journal Nature. In “Genetical Implications,” Watson and Crick suggest a possible explanation for deoxyribonucleic acid, or DNA, replication based on a structure of DNA they proposed prior to writing “Genetical Implications.” Watson and Crick proposed their theory about DNA replication at a time when scientists had recently reached the consensus that DNA contained genes, which scientists understood to carry information that determines an organism’s identity. Watson and Crick’s replication mechanism as presented in “Genetical Implications” contributed to the two scientists sharing a portion of the 1962 Nobel Prize in Physiology or Medicine. With their suggested DNA replication mechanism in “Genetical Implications,” Watson and Crick explained how genes are copied and passed along to new cells and organisms, thereby explaining how the information contained within genes is preserved through generations.

Watson and Crick began collaborating in 1951, two years before they wrote “Genetical Implications.” The two studied DNA at the University of Cambridge in Cambridge, England. Watson was a researcher from the United States, and Crick, twelve years older than Watson, was working towards his PhD at the University of Cambridge. Watson and Crick shared an office and frequently discussed their work over lunch.

In April 1953, before Watson and Crick wrote “Genetical Implications,” the two scientists described a novel three-dimensional structure of DNA in their paper titled “Molecular Structure of Nucleic Acids: A Structure of Deoxyribose Nucleic Acid.” That paper followed the recent scientific verification that DNA contained genes, which carry information that determines an organism’s distinct characteristics. Scientists had also identified the building blocks of DNA, but they did not agree on how those building blocks made up the three-dimensional structure of DNA. Using both information about DNA’s composition and results from experiments aimed at uncovering DNA’s structure, Watson and Crick developed a physical model of DNA. In “A Structure of Deoxyribose Nucleic Acid,” Watson and Crick described DNA as a double helix that contained two long, helical strands wound together. In their model, each DNA strand contained individual units called bases, and the bases along one DNA strand matched the bases along the other DNA strand. Watson and Crick argued that the sequence of DNA bases defined the genes contained within DNA. Many scientists immediately accepted Watson and Crick’s DNA model.

Watson and Crick expanded on their DNA model in “Genetical Implications,” which they published in May 1953. Having described a structure of DNA, Watson and Crick devoted much of “Genetical Implications” to discussing how that structure implied a potential replication mechanism for DNA. Watson and Crick had briefly mentioned DNA replication towards the end of their first paper, but they did not explicitly describe a mode of replication. Knowledge of how DNA replicates was important to scientists because it could explain how genes functioned. When a cell divides, that cell creates a copy of itself. During cell division, the DNA contained within a cell must be copied as well because the genes contained within DNA are needed for the cell copy to develop properly. Furthermore, when organisms produce offspring, the parent organisms need to replicate their own DNA to pass on genes to their offspring, which enables offspring to inherit genes from their parents. Until Watson and Crick wrote “Genetical Implications,” just shortly after they proposed their DNA model, no scientists had published a mechanism for how organisms copied genes.

In “Genetical Implications,” Watson and Crick devote two pages of text to discuss their proposed structure of DNA and how it might self-replicate. After a brief introduction, the authors use the first half of the paper to describe their previously proposed model of DNA replication, using multiple figures to accompany their descriptions. Throughout the second half of “Genetical Implications,” Watson and Crick detail their suggested DNA replication mechanism. Along with that description, Watson and Crick address questions they still have about their replication mechanism.

Watson and Crick start “Genetical Implications” by introducing DNA, its role in genetics, and the three-dimensional DNA structure that the scientists had previously proposed. They state that DNA is found in all cells that undergo cellular division. Watson and Crick also state that DNA carries a cell’s genes. Watson and Crick go on to say that no scientist before them had suggested a way for DNA, and thus the genes contained within it, to copy itself. Watson and Crick then refer to the structure of DNA they proposed in their last paper. The authors acknowledge that experimental data supports their model over previously proposed DNA models, though the authors still claim that available evidence is not sufficient to completely support their model. Despite that, Watson and Crick argue that their model of DNA has enough justification for them to discuss its role in genetics and inheritance.

In the next portion of “Genetical Implications,” Watson and Crick describe their DNA model. With the aid of illustrations, Watson and Crick state that their model of DNA consists of two helical strands twisted around each other in a double helix. Each strand, the authors explain, contains a chain of repeating units called nucleotides, where each nucleotide contains a sugar, a phosphate group, and a base. The sugar is a ring structure called a deoxyribose ring that exists in between the phosphate group and a base. A phosphate group is a negatively charged cluster of phosphorus and oxygen atoms attached to one end of the deoxyribose ring. The base is another ringed structure attached to the other end of the deoxyribose ring. Watson and Crick state that there are four possible bases: adenine, guanine, cytosine, and thymine. Adenine and guanine are called purines and are structures consisting of two fused rings. Cytosine and thymine are called pyrimidines and are single-ring structures.

Watson and Crick then explain how the two DNA strands connect together in their model. According to Watson and Crick, the DNA strands join via the bases. The bases face inside the double helix and the phosphate groups face outside. The authors explain that each base from one DNA strand connects to exactly one base from the other DNA strand through a type attraction called a hydrogen bond. Watson and Crick highlight that the base pairing they describe is specific such that a base can only bond to one other kind of base. One base, the authors say, must be a purine and the other base must be a pyrimidine. Supported by experimental findings, Watson and Crick claimed that the pairs occurring specifically in DNA are adenine with thymine and guanine with cytosine. The authors then provide an illustration that shows how hydrogen bonding occurs between the bases.

After describing their DNA structure in “Genetical Implications,” Watson and Crick discuss how bases arrange themselves on DNA strands. According to the authors, the four DNA bases, adenine, thymine, cytosine, and guanine, can order in any arrangement along a single DNA strand. However, Watson and Crick argue that when two DNA strands are paired, the sequence of DNA bases in one strand determines the sequence of bases in the other strand because the bases along one DNA strand can only hydrogen bond to specific bases along the other strand. Based on that, Watson and Crick conclude that if one were given the sequence of bases along one DNA strand, they would also know the sequence of bases along the other DNA strand. Watson and Crick call the two DNA strands complements, and claim that the complementary nature of DNA leads to a way that DNA can self-replicate, which in their paper they refer to as self-duplication.

Next, Watson and Crick describe their proposed DNA replication mechanism. They state that their model of two-stranded DNA has two templates for replication. Each complementary strand functions as a template for the formation of a copy of the other strand. Watson and Crick state that to begin DNA replication, the hydrogen bonds between the bases connecting the two strands break. Then, the strands unwind and separate, though Watson and Crick do not explain how the strands are able to separate. The authors then state that each of the separated DNA strands serves as a template for new complementary strands. Since each DNA strand serves as a template for a new strand, by the end of a single DNA replication cycle, two DNA double helices are created from one original double helix. Within each DNA double helix, one strand is new copy, and the other strand is one of the original strands from the DNA double helix prior to replicating. Furthermore, Watson and Crick emphasize that the base sequences in both DNA double helices are identical to each other and to the original DNA double helix.

In the final portion of “Genetical Implications,” Watson and Crick pose questions about their model and speculate potential answers to those questions. While Watson and Crick develop a replication mechanism in principle, they state that they do not know how the cell carries out the chemical reactions required to separate the two strands and replicate DNA. The authors suggest that enzymes, proteins that facilitate chemical reactions in cells, may have some involvement. Watson and Crick admit that they do not know how the DNA strands unwind and separate without getting tangled, but they emphasize the need for DNA strands to untwist. In the last paragraph of their article, Watson and Crick re-summarize their DNA replication mechanism.

As with Watson and Crick’s first paper on DNA, “Genetical Implications” was well-received among scientists. In June 1953, Watson presented his and Crick’s theories about DNA structure and replication at a symposium in Cold Spring Harbor, New York. At that symposium, attended by seventy-two scientists, no scientists objected to Watson and Crick’s proposal. However, some questioned an issue Watson and Crick had brought up in “Genetical Implications” regarding how DNA strands could unwind and separate without breaking the DNA double helix.

Although Watson and Crick’s DNA replication mechanism detailed in “Genetical Implications” was well-received at the 1953 symposium, the following year the paper received some criticism. Max Delbrück, a researcher at the California Institute of Technology, or Caltech, in Pasadena, California, raised the issue of DNA strands unwinding both privately to Watson in letter correspondence and publicly in a paper Delbrück published in 1954. According to historian of science Frederic Lawrence Holmes, as well as Delbrück’s biographers, Delbrück was an influential figure for many scientists at the time, particularly Watson. Even before Watson and Crick wrote “Genetical Implications,” Delbrück had written to Watson expressing his concerns about how DNA could unwind and separate during replication. Delbrück stated that he did not think DNA as proposed by Watson and Crick could unwind at all. In 1954, Delbrück wrote an article that contested the Watson-Crick replication mechanism. He suggested a different way for DNA to replicate. Delbrück’s article sparked a debate over how DNA replicated that did not end until 1957 when Matthew Meselson and Franklin Stahl, two scientists at Caltech, experimentally supported Watson-Crick replication.

Watson and Crick shared a portion of the 1962 Nobel Prize in Physiology or Medicine for their theories about DNA structure and replication presented in both “A Structure for Deoxyribose Nucleic Acid” and “Genetical Implications.” As of 2018, scientists continue to support the DNA replication mechanism Watson and Crick suggested in 1953. Since the publication of “Genetical Implications,” scientists have answered the questions Watson and Crick proposed in that article. For example, scientists later found that multiple enzymes carry out the processes of unwinding DNA for replication and physically pairing the bases of replicating DNA strands with the bases of template strands. As of 2018, Watson-Crick DNA replication model and descriptions of the enzymes that aid the replication process are taught to high school and college students studying introductory biology.

Sources

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