The Discovery of the Structure of Deoxyribonucleic Acid: The Contributors to the Watson and Crick Model (Including an Interview with Maurice Wilkins)

An Honors Thesis (ID 499)

by

Stephanie L. Johnson

Thesis Director

Dr. Thomas R. Mertens

Ball State University

Muncie, Indiana

April, 1989

Graduation: December, 1989

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In the April 25, 1953 issue of Nature, James D. Watson and Francis H. C. Crick made an announcement which proved to be the beginning of a revolution in molecular biology and genetics: they published their model of the structure of the genetic material, deoxyribonucleic acid (DNA). As with any scientific advancement, there was a great deal of experimentation done before the actual proposal of this model. In this particular case, Watson and Crick were not directly involved in the experiments they cited as references in their article "Molecular Structure of Nucleic Acids: A Structure for Deoxyribose Nucleic Acid," which was mentioned above. They were, instead, "model builders," providing ingenious insight into the puzzle of life (Watson, 1986, 48).

Who, then, were the experimenters who provided the valuable contributions necessary to help make the parts of the DNA puzzle fit together? Further, what information did they provide which helped Watson and Crick solve the puzzle? The answers to these questions can easily be found in the Nature article cited above, since Watson and Crick specifically mentioned their main contributors and briefly discussed their individual contributions. Furthermore, obtaining copies of the original articles cited as references by Watson and Crick facilitated an even fuller understanding of these contributions. And finally, one even more significant step, an interview with a contributor and Nobel prize co-winner, personalized the subject and fostered a very meaningful understanding of his specific contribution to the model of the structure of DNA.

THE CONTRIBUTORS

According to the reference list Watson and Crick set forth in their original article, the contributors to the development of their model were Linus Pauling and Robert B. Corey, Sven Furberg, Erwin Chargaff (S. Zamenhoff, G. Brawerman, and E. Chargaff), Gerard R. Wyatt, William T. Astbury, and Maurice H.F. Wilkins and John T. Randall. Of course, this list includes only cited references as they appeared in their article. It is obvious that these were not the only contributors to the model Watson and Crick constructed, considering the vast base upon which all of this knowledge most surely rested. However, Watson and Crick attempted in this context to give credit where credit was due.

Linus Pauling

Going through in logical order, as Watson and Crick did, the first contributor may be said to have been Linus Pauling. In conjunction with Robert B. Corey, Pauling published an article, "A Proposed Structure for the Nucleic Acids," which suggested a model for the structure of DNA. Ultimately, of course, this model was shown to be incorrect, but it was useful in some ways.

Linus Pauling discovered the alpha-helix structure of polypeptides. This discovery made a big impact on the field of structural crystallography because of the obvious prevalence of helices in biologically important molecules (Olby, 1974, 278). Pauling used his knowledge of helices to help him in his own quest to discover the structure of DNA.

Watson and Crick cite Pauling and Corey: "Their model consists of three intertwined chains, with the phosphates near the fibre axis, and the bases on the outside" (Watson & Crick, 1953, 737). This is the basic description which Pauling and Corey also gave: "We assume, accordingly, that the structure to be formulated is a helix. The giant molecule would thus be cylindrical, with approximately circular cross-section" (Pauling & Corey, 1952, 86). They went further to say that...

> the cylindrical molecule is formed of three chains, which are coiled about one another. *The structure that we propose is a three-chain structure, each chain being a helix with fundamental translation equal to 3.4 A, and the three chains being related to one another...by the operation of a threefold axis* (Pauling & Corey, 1952, 87). (Italics added).

In response to the Pauling model, Watson and Crick frankly stated that this structure was "unsatisfactory for two reasons." In the first place, they were not satisfied that Pauling was reading his X-ray patterns correctly, because they felt that the salt, not the free acid, was what gave the X-ray images. The phosphates in the center of the axis would not work because they would repel each other. Secondly, the van der Waals distances were too small in their opinions (Watson & Crick, 1953, 737).

Aside from his obviously valuable chemical and scientific contribution, Pauling also provided another type of help to Watson and Crick--incentive and urgency. Peter Pauling, the son of Linus Pauling, was sharing an office at Cambridge with Watson and Crick at the time they were working on their model. During that time, Linus would write enthusiastic letters to his son about the work he (Linus) was doing and the advances he was making in his work on the structure of nucleic acids. It was just such a letter which Peter received from his father that frightened Watson and Crick, making them fear that "Linus had a chance to steal the prize" (Watson, 1986, 125). This letter was the antecedent to the article Pauling and Corey wrote and published. Although the structure Pauling and Corey proposed was incorrect, Watson and Crick were motivated to step-up the pace of their work and they became fiercely more determined to discover the true structure.

Sven Furberg

A second contributor was Sven Furberg. Like Pauling and Corey, he published a proposal for the structure of nucleic acids before Watson and Crick did. He actually proposed two different models, although he preferred his first, and, indeed, it was nearer to being correct than was his second. The article, "On the Structure of Nucleic Acids," was published in 1952 in the <u>Acta Chemica Scandinavica</u> volume 6, pages 634-640. His explanation of his model is as follows:

> In model 1, the pyrimidine and purine rings are piled in a central column directly on top of each other, 3.4 A apart, with the ribose rings and the phosphate groups in a spiral enclosing the column (Furberg, 1952, 638).

Loosely translated, this means his model was a single helix, with the sugar being perpendicular to the attached base. The bases were in the inside of the helix, and the phosphates on the outside. This observation is what caught the interest of Watson and Crick.

In their article, Watson and Crick say that their model is a "radically different structure for the salt of deoxyribose nucleic acid" (Watson & Crick, 1953, 737). They pointed out in their article that the structure they presented had two chains in a helix, each of which "loosely resembles Furberg's model No. 1, that is, the bases are on the inside of the helix and the phosphates on the outside" (Watson & Crick, 1953, 737). In other words, Watson and Crick here noted the similarities between the proposed structure of Furberg and their own proposed structure of DNA.

Erwin Chargaff

Another contributor, or team of contributors, was Erwin Chargaff and his co-authors, Stephan Zamenhof and George Brawerman. In 1952 they published the article, "On the Desoxypentose Nucleic Acids From Several Microorganisms," in Biochimica et Biophysica Acta volume 9, pages 402-405. In their laboratory at Columbia University in New York City, they were working with bacterial transformation, in an attempt to distinguish DNAs derived from different species.

The most significant contribution Chargaff made was the fact that he noticed that the purine/pyrimidine ratio in DNA always was approximately one-to-one. That is, A/T = 1 and G/C = 1. These are called the Chargaff ratios, and they helped Watson and Crick infer the structure of DNA.

> It has been found experimentally that the ratio of the amounts of adenine to thymine, and the ratio of guanine to cytosine, are always very close to unity for deoxyribose nucleic acid....In other words, if an adenine forms one member of a pair, on either chain, then on these assumptions, the other member must be thymine (Watson & Crick, 1953, 737).

Chargaff, in his experiments, disproved what had been known as the tetranucleotide theory. This theory stated that DNA was chemically made up of a repeating sequence of the bases, G A C T in animals, and G A C U in plants. It was Chargaff's work that finally conclusively disproved this.

Gerard Wyatt

Another contributor to the Watson and Crick model of DNA was Gerard Wyatt. In 1952, he published results of one of his experiments in the Journal of General Physiology volume 36, page 201. In his data came even more conclusive evidence that the Chargaff ratios were, indeed, a correct interpretation of the equality of content between purines and pyrimidines. Wyatt analyzed DNA from wheat germ, herring sperm, and viruses that attacked insects, and he found the one-to-one ratios of adenine to thymine and guanine to cytosine. He also found a "5-methyl-cytosine, which is a cytosine with an extra group of atoms attached at one point around the ring..." in some viruses (Wyatt, 1952, 201). This initially caused some alarm because it was a new base, but he showed experimentally that the ratio of this variant of cytosine also fit in the one-to-one ratio with guanine. This discovery finally demonstrated that the ratios were valid.

William Astbury

Still another contributor to the Watson and Crick model was William T. Astbury. He was a physicist and scientist that helped popularize the term "molecular biology" (Olby, 1974, 59). His contribution to Watson and Crick was his X-ray diffraction photographs of DNA. He was one of the pioneers of the use of X-ray crystallography in textile research and biology. In addition, he succeeded in obtaining one of the first clear X-ray photographs of DNA. This X-ray photograph was published in his 1947 article "X-ray Studies of Nucleic Acids," which appeared in Symposia of the Society for Experimental Biology, volume 1, pages 66-76. This X-ray photograph was of good quality, but not entirely sharp. However, it was helpful to Watson and Crick, and thus was cited in their article (Olby, 1974, 357).

Maurice Wilkins

Finally, the last cited contributor to the Watson and Crick model of DNA was a man named Maurice H.F. Wilkins. Working at King's College in London in conjunction with John T. Randall and Rosalind Franklin, Wilkins and his colleagues obtained clear X-ray diffraction photographs of crystalline "desoxypentose nucleic acid" (Wilkins & Randall, 1953, 192).

In the article Wilkins and Randall published, "Crystallinity in Sperm Heads: Molecular Structure of Nucleoprotein in vivo," Biochimica et Biophysica Acta, volume 10, pages 192-193, Wilkins says, "One may reasonably hope to make an unambiguous structure determination of the nucleate fibres because of their high degree of crystalline perfection" (Wilkins & Randall, 1953, 192). This, indeed, is the advice which Watson and Crick took when they proposed their structure of DNA.

THE OPPORTUNITY

In an attempt to gain undergraduate credit in Biology 498, a course which offers credit in biologically-related independent research by students, my professor, Dr. Thomas R. Mertens, and I designed a project whereby I would visit the laboratories where the famous Nobelists, Watson, Crick, and Wilkins worked, and I would take photos and write a short human interest article about these important places. These laboratories were located in England, with Watson and Crick's being in Cambridge, and Wilkins's in London.

The name of the laboratory where Watson and Crick worked was the Cavendish Laboratory. The laboratory where Wilkins worked was called the Wheatstone Physics Laboratory, inside the King's College building. Unfortunately, I found that the laboratories were not at all similar to what they had been in the 1950s during the time the important discoveries were made by the future Nobelists. The laboratories were victims of the technological change happening around them. The Cavendish Laboratory was completely redone and consumed by the political science department at Cambridge, and the new Cavendish had been relocated. The Wheatstone Physics Laboratory in London was once a very high-ceilinged room, and had since been divided into two separate floors.

The equipment which I desired to see at King's College was in a storage area on an alley off of the Strand in London, the cosmopolitan location of the King's College building. I was taken to this place by a man named Dr. Fredrick Eagles, who proved to be most helpful.

When I saw the storage room and the old X-ray diffraction "dinosaurs" with which I did not have much familiarity, I became quite discouraged. This, of course, was evident to Dr. Eagles. I had recently made the fruitless two-hour trip to Cambridge, only to find that the Cavendish was now part of the political science department, and I had told him about this distressing news. He listened very sympathetically, and he very kindly showed me the equipment I had requested to see. He gave me a tour of the College and the "campus" (building), and showed me their view of the river Thames and the National Theatre. He also told me that the original Watson and Crick model was located in London at the British Museum, but it was inside glass, and with my unsophisticated camera, I might have difficulty obtaining an acceptable photograph.

Then I casually asked him about the status of Dr. Wilkins at King's College. He told me that Dr. Wilkins was in semi-retirement, but he came in on certain days of the week to teach a course about Medical Law and Ethics. I wondered if he might like to talk with me, if he could fit me into his schedule. Dr.

Eagles was thrilled at this suggestion, nearly assuring me that Dr. Wilkins would not mind talking with me. He called immediately and made an appointment for me to talk with Dr. Wilkins three weeks later, at my convenience! This was the stroke of luck I so desparately needed, and I thanked Dr. Eagles ever so graciously, and left King's College whistling and strolling along the Strand.

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APPENDICES

The first appendix is an original manuscript which my professor, Dr. Mertens, and I submitted to be published in the American Biology Teacher. The second appendix is a reprint of the article as it appears on pages 151-153 of the March 1989 issue of the above periodical.

An Interview with Nobel Laureate Maurice Wilkins

Stephanie Johnson

and

Thomas R. Mertens

Stephanie Johnson is an undergraduate biology major at Ball State University. While studying at Ball State's London Centre in Autumn, 1987, she had the opportunity to interview Dr. Wilkins. Her faculty advisor is Thomas R. Mertens, Distinguished Professor of Biology Education at Ball State University and former president (1985) of NABT.

Office Telephone (TRM): 317-285-8827

Home Telephone (TRM): 317-284-6942

In 1962, three men, Maurice Wilkins, Francis Crick, and James Watson, shared the Nobel Prize in Medicine and Physiology for what many have called "the greatest discovery in modern biology" (Sourkes & Stevenson 1966). This discovery, the elucidation of the structure of deoxyribonucleic acid (DNA), was first published in the April 25, 1953 issue of Nature. This work, which included that of the X-ray crystallographer Rosalind Franklin, has virtually paved the way for the entire field of modern genetics.

Deoxyribonucleic acid, better known as DNA, is an essential component of all living cells. It is composed of four different nucleotides, each of which is made up of a nitrogenous base, a 5-carbon sugar (deoxyribose), and a phosphate subunit. The nucleotide components are arranged in two complementary polynucleotide chains forming a ladder-like structure, twisted about itself to constitute what is called a "double helix." The importance of DNA is its function in cells; it carries the genetic code and establishes patterns of heredity. The discovery of its structure has answered many questions about genetics, as well as raising many others which have been and are currently being researched by scientists all over the world.

Maurice Wilkins

One of the men involved in the discovery of the structure of DNA was the British biophysicist, Maurice Wilkins. Born in Pongaroa, New Zealand in 1916, Wilkins was brought to England at age six to be educated at King Edward's School in Birmingham. He then earned his B.A. degree in 1938 from St. John's College, Cambridge (Reidman & Gustafson 1963). He did graduate research under Sir John Randall at the University of Birmingham on luminescence and phosphorescence as related to radar screens, thus earning his Ph.D. degree in 1940 (Moritz 1963).

During World War II, Wilkins came to the United States with other nuclear physicists to work on the Manhattan Project which developed the atomic bomb. Specifically, Wilkins worked on the separation of uranium isotopes at the University of California in Berkeley. After the war, he returned to England and focused his interests on the field of biology (Reidman & Gustafson 1963).

After his return to Britain, Wilkins became a lecturer on physics at St. Andrew's University in Scotland in 1945. In 1946, he joined the Medical Research Council at King's College of the University of London (Moritz 1963). He became an honorary lecturer in the sub-department of biophysics at King's College in 1958, and he was a professor of molecular biology at the same institution from 1963-1970 (Who's Who 1987).

In the early 1950s, Wilkins was working with a gel of DNA, into which he inserted a glass rod and extracted a fiber. He examined the fiber under a microscope with polarized light and recognized that the fibrous nature of DNA was a hint that its structure was crystalline. He then began to employ the X-ray diffraction technique in studying DNA. X-ray data led him to believe that the structure of DNA was in a helical pattern. He discussed this information with Crick and Watson, who incorporated it in building their model of the structure of DNA. This contribution by Wilkins led to his sharing with Watson and Crick in the 1962 Nobel Prize (Reidman & Gustafson 1963).

In 1960, the American Public Health Association recognized the accomplishments of Wilkins, Watson, and Crick by presenting them the Albert Lasker Award. In 1964, Wilkins was named an honorary member of the American Society of Biological Chemists and in 1969 became president of the British Society for Social Responsibility in Science. In 1970, Wilkins became an honorary member of the American Academy of Arts and Sciences, and in 1984, a member of Food and Disarmament International (<u>Who's Who</u> 1987).

The interview

In November, 1987, the first author had the opportunity to visit with Dr. Wilkins in his office at King's College, London (Fig. 1) and to ask him several questions concerning his receipt of the Nobel Prize and its effects on his professional life and career. Wilkins also commented upon the direction in which he feels modern genetics is headed, and upon his current research interests. His thoughts and insights will, no doubt, interest all who admire his contributions to modern biology.

<u>The Nobel Prize</u>. When asked, "What effect has sharing the Nobel Prize in 1962 had on your career and professional life?", Dr. Wilkins responded as follows: "More and higher quality people want to work with you." He also noted that there was an "increase in [my] salary and professional status." As might be expected, a Nobel prize winner receives an increased number of

invitations to speak and "more invitations to speak at meetings and conferences on wider topics than [one's] own field; for example, 'Science and the World' or 'Science and Religion'." Wilkins believes that the receipt of the Nobel Prize "opens doors" to speak at conferences on such widely divergent topics.

Wilkins recalled that during World War II he had worked on the Manhattan Project at Berkeley, California. In more recent years, however, he has turned his attention to significant global problems such as "World Hunger" and "Nuclear Weapons and Peace." Because of his status as a Nobel Laureate, he has opportunities to address conferences on such topics. Furthermore, Wilkins believes that it is "in Alfred Nobel's spirit to accept some responsibility in this area. Some Laureates feel [that] it's wrong to speak on other topics"--i.e., topics beyond one's field of scientific expertise. Furthermore, Dr. Wilkins asserted that he thinks this may be just "a weak excuse to get out of responsibility." He believes that Laureates have a responsibility to the public and should study the problems of science and society.

<u>Current Research Interests</u>. Although he began his professional career as a physicist, Dr. Wilkins is best known for his contributions to biology, a field which he entered through the "back door" of biophysics. His long and successful career demonstrates how other scientific disciplines have had a significant impact on the development of biology.

In discussing his research, Wilkins provided some background about his more recent interests:

> I did neurobiology, mainly nerve cell membranes, for some years, but this was not very exciting and I was not very interested in that. I was interested in neurobiology, but I couldn't find a suitable line of work which was really interesting, so I gave it up after a while.

More recently, Dr. Wilkins has directed his energies to broader issues at the "Science and Society" interface--food and famine, nuclear disarmament, and the social responsibility of scientists. His national and international leadership in organizations concerned with these problems has already been cited.

Directions of Modern Genetics. Although Dr. Wilkins is not a geneticist, because his work on DNA has had such an impact on the discipline of genetics, one could expect him to have views on the directions in which modern genetics is headed. Pursuing this issue with him led to some of Wilkins's strongest statements:

> I think there is one thing I can say, and that is that I am not very happy about the effect of molecular biology on people's minds. Crick has always been a very hard line materialist, and Watson has got like this, too. They think everything about life and human beings can be explained in terms of atoms and molecules. Now, I'm putting it very roughly.
>
> I think they've got a bit narrow minded, the molecular biologists. Molecular biology is, obviously, extremely important. It has enormous potentiality in many areas of science and medicine. But I think it would be a great mistake to think that it is going to comprhend everything. Nevertheless, molecular biology is a very powerful tool in science.
>
> I think it is, in some ways, doing molecular biology a disservice to somewhat misrepresent it. But I think they're quite right that the way it is

> developing, there seems to be an immense potentiality...this field. Quite where it's going to go, I don't know.

In his arguments against the mindset of many molecular biologists, Wilkins clearly reflects his interests in, and concerns for, humanity and education. He related his experiences at the Lindau meeting where Nobel Laureates held discussions before several hundred medical students, mainly German nationals. In discussions with four or five experts working in the area of recombinant DNA, the students "wanted to know all about the human implications of this work and what kind of ethical problems it might raise." Wilkins seemed to think that the students were very hard on the Laureates: The students seemed to think that the Nobelists "weren't concerned [enough] about the possible cultural, social, and philosophical effects of developments [in recombinant DNA work]."

Turning specifically to human genetics, Wilkins noted that "at the moment, you see, as far as genetic diseases are concerned, one cannot do an awful lot." He noted that there are ways to alter somatic cells to produce a certain result, but he said that the Nobel Laureates at the Lindau meeting seemed to agree that to alter the genes themselves would be wrong. "This would be, as people say, playing God. And who would decide what genes you would alter and what the forms of the new genes ought to be?" Clearly he believes human genetic manipulation raises serious ethical problems.

Wilkins went on to say, "My own feeling would be that this type of ethical problem will get more acute in the future." He believes that the sure way to deal with those ethical problems is through education. His belief in education has led him to teach a discussion course about the social impact of the biosciences at King's College, London. Dr. Wilkins noted that as scientific knowledge increases and give us increased power to control life, moral and ethical problems are likely to arise. He believes "we should have lots of discussion between scientists, lawyers, medical people, and the public" concerning what these people think we ought to do in dealing with science and society issues.

Impressions

Dr. Wilkins said that he agreed to a personal interview because he likes to encourage young people who are interested in science to pursue these interests. Certainly the opportunity to have a private interview with a Nobel Laureate whose work has had a major impact on biology, was an inspiration. Most encouraging, however, was Dr. Wilkins's personal "down-to-earth" approach in the interview, and his very evident concern for human values and for the well being of all humanity.

Maurice Wilkins, scientist, Nobel Laureate, and humanitarian, should stimulate the interest of many young people to pursue careers in science. As an advocate of science education and scientific literacy, he ought to have impact on the lives of all citizens for whom an understanding of science is essential for informed living in these last years of the Twentieth Century.

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Caption

Figure 1. Dr. Maurice H.F. Wilkins, photographed in his office November 19, 1987. (Photograph by Stephanie Johnson.)