

The Discovery of the Structure of D.N.A.

The Main Players.....

Excerpts from *What Mad Pursuit* by Francis Crick (Basic Books, 1988):

On Sir Lawrence Bragg...

It was at the Cavendish (laboratory at Cambridge University) that J.J. Thomson had “discovered” the electron by making measurements of both its mass and its charge.... Rutherford, fresh from New Zealand, had started his main research career there and later returned to succeed J.J. as Cavendish Professor. There, under his direction, Cockcroft and Walton had first “smashed” the atom. There original accelerator was still there. And in the early 1930’s, Chadwick discovered the neutron in a few short weeks.... The current Cavendish Professor was Sir Lawrence Bragg (known to his close friends as Willie), the formulator of Bragg’s law for X-ray diffraction. He was the youngest Nobel Prize winner ever, having been only twenty-five when he shared it with his father, Sir William Bragg.... Bragg was one of those scientists with a boyish enthusiasm for research, which he never lost. He also was a keen gardener. When he moved in 1954 from his large house and garden in West Road, Cambridge, to London, to head the Royal Institution in Albemarle Street, he lived in the official apartment at the top of the building. Missing his garden, he arranged that for one afternoon each week he would hire himself out as a gardener to an unknown lady living in The Boltons, a select inner-London suburb. He respectfully tipped his hat to her and told her his name was Willie. For several months all went well till one day a visitor, glancing out of the window, said to her hostess, “My dear, what is Sir Lawrence Bragg doing in your garden?”

On himself.....

Nowadays most people know what DNA is, or if they don’t they know it must be a dirty word, like “chemical” or “synthetic”. Fortunately, people who do recall that there are two characters called Watson and Crick are often not sure which is which. Many’s the time I’ve been told by an enthusiastic admirer how much they enjoyed my book - meaning of course, Jim’s. By now I’ve learned that its better not to try to explain. An even odder incident happened when Jim came back to work at Cambridge in 1955. I was going into the Cavendish one day and found myself walking with Neville Mott, the new Cavendish professor (Bragg had gone on to the Royal Institution in London). I’d like to introduce you to Watson,” I said, “since he’s working in your lab.” He looked at me in surprise. “Watson?” He said, “Watson? I thought your name was Watson-Crick.”

On Jim Watson.....

I first heard of Jim from Odile (his wife). One day when I came home she said to me, “Max (Perutz) was here with a young American he wanted you to meet and-you know what-he had no hair!” By this she meant that Jim had a crew cut, then a novelty in Cambridge..... Jim was distinctly more outspoken than I was, but our thought processes were fairly similar. What was different was our background knowledge. By that time I knew a fair amount about proteins and X-ray diffraction. Jim knew much less about these topics but a lot more about the experimental work on bacterial viruses..... Jim also knew more about bacterial genetics.

On Rosalind Franklin.....

People have discussed the handicap that Rosalind suffered in being both a scientist and a woman. Undoubtedly there were irritating restrictions-she was not allowed to have coffee in one of the faculty rooms reserved for men only-but these were mainly trivial, or so it seemed to me at the time. As far as I could see her colleagues treated men and woman scientists alike..... The only opposition I ever heard about was from Rosalind’s family. She came from a solid banking family who felt that a nice Jewish girl should get married and have babies, rather than devote her life to scientific research..... In any event, Rosalind’s experimental work was first class..... She was less at home, however, in the detailed interpretation of the X-ray photographs.

On Maurice Wilkins....

Maurice did not seem especially unusual to me. Even if I had known, say, that he had a taste for Tibetan music, I doubt if I would have considered that odd. Odile thought he was rather strange because when he first arrived for dinner at her apartment in Earl’s Court he went straight into the kitchen and lifted the lids of the saucepans to see what was cooking. She had become accustomed to dealing with naval officers, and they never did things like that. After she discovered that this was not the impertinent curiosity of a hungry man, but simply Maurice was interested in cooking, she looked at him in a new light.

The events....

Quotations excerpted from *The Eighth Day of Creation* by Horace Judson (Simon and Schuster, 1979)

In the summer of 1952, Franklin and Gosling (her research assistant at King's College) began the cumbersome mathematical technique, called a Patterson synthesis, by which they intended to find the structure of the a form of the DNA molecule. "The physical meaning of the so-called Patterson synthesis is one of the most difficult concepts in crystallography," Max Perutz and John Kendrew had said in a article they wrote....

By the beginning of July, Franklin had confirmed her opinion that the (D.N.A.) crystals were monoclinic, but she still failed to draw the conclusion that the molecule contained two chains running in opposite directions.

When Watson got back to the Cavendish from summer vacation, he found that he had two colleagues from Cal Tech, Linus Pauling's son Peter, and Jerry Donohue, a former student of Linus'.

Wilkins, when he got back to King's... began a microscopic study of plant cells, using the common spiderwort pollen in order to measure the total amount of nucleic acid in the cells, and the relative increase during growth and cell division. The method was a new one which he had devised himself.... That fall, he and Franklin were working completely separately.

The same fall, Linus Pauling (at Cal Tech) began to read intensively, though more selectively than he realized, through the literature about the physical chemistry of DNA, and to scrutinize X-ray diffraction pictures of the stuff...

By the end of November, Franklin and Gosling completed the first stage of the Patterson synthesis.... They could not discern the structural regularities...

At the end of November, Randall (head of the King's lab) asked each scientist in his team to write reports.... Franklin and Gosling's said several things about DNA expressly and precisely... The Biophysics Committee, including Max Perutz (one of the scientists at the Cavendish), visited on December 15, and copies of the reports were given to him. A fuse was lit.

A few days later, Peter Pauling came into Watson and Crick's office and said he had just received a letter from his father who had mentioned that he had devised a structure for DNA.... In late January he mailed a copy of the manuscript to his son... Probably on Wednesday the 28th copies of the manuscript reached the Cavendish... "Peter's face betrayed something important as he entered the door, and my stomach sank in apprehension at learning that all was lost," Watson wrote. He remembered that he seized the manuscript before Crick could ask for it... To read a paper by a great scientist that's all wrong is an odd exercise....

When she (Rosalind) looked at (Pauling's paper) she could see that the structure could not be right because the X-ray diffraction photographs on which it was based were Astbury's - and she knew, of course, as Watson did not, that those pictures mixed the two forms of DNA. Watson... lectured her about the helical theory and repeated Crick's assertion that her antihelical evidence was a fluke. So she got mad. Watson later wrote (in *The Double Helix, 1968*):

Suddenly Rosy came from behind the lab bench that separated us and began moving toward me. Fearing that in her hot anger that she might strike me, I grabbed up the Pauling manuscript and hastily retreated toward the open door.

The scene would have been still more comical if Watson had reminded us that she was short and slim, he over six feet, if scrawny. Wilkins put his head into the door; Watson slid out; the two men walked down the hall in a new brotherhood. (They went into Maurice's office.) Watson wrote:

When I asked what the pattern was like, Maurice went into the adjacent room to pick up a print of the new form they called the "B" structure. The instant I saw the picture my mouth fell open and my pulse began to race. The pattern was unbelievably simpler than those obtained previously. Moreover, the black cross of reflections which dominated the picture could arise only from a helical structure. (*The Double Helix, 1968*)

The picture was Rosalind Franklin's.

Watson was hampered by the slowness of the shop at Cavendish in making his atom model parts..... He spent two days working with the backbones inside and the bases outside... Watson grumbled at the difficulty in fitting them together. Crick remembers suggesting that he put the backbones on the outside. Watson replied, "That would be too easy." Crick replied, "Then why don't you do it!"

Tuesday February 10, Franklin wrote in her notebook, "Structure B. Evidence for a 2-chain helix"

The paper with Pauling's three chain model appeared in print that month.

At some point Crick learned about the report from King's College the previous December 15. Crick asked Perutz for his copy. The report contained Franklin's precise measurements. (Much later Erwin Chargaff questioned whether Perutz had behaved ethically in giving the report to Crick. Perutz retorted that the committee had been set up-in the words of a letter from the Medical Research Council's (MRC) archives-expressly "to establish contact between the different groups of people working for the Council in this field.")

Franklin had written that the C-axis was parallel to the fibre axis. In the long row of candles that had to be lit, one by one, before the structure of DNA emerged out of darkness and was visible, Crick now set his spark to the one that stood closest to the center of the mystery. Watson had the shock of insight when he recognized the implications of Franklin's photograph.... Crick saw in Franklin's words and numbers something just as important.

When Watson showed Donohue the hydrogen bonds he had worked out to pair the bases, Donohue said, "But those are the wrong forms."..... They now had everything in mind they needed for the structure.

On Monday, February 23, Franklin headed the next page in her notebook, "Structure B: Photograph 51".... Five pages in, she stopped to sum it up. She had the diameter of the molecule right. She confirmed that the backbone was on the outside..... She concluded that the helix was made of two chains. She was tormented by the awareness that those two chains bore some strange relation that was eluding her. The fact remains that she never made the inductive leap.

On Saturday morning, February 28, Watson came in, cleared a place to work and got out his cardboard cutouts. He saw that the like-with-like pairs led nowhere. Suddenly he became aware that an adenine-thymine pair held together by two hydrogen bonds was identical in shape to a guanine-cytosine pair held together by at least two hydrogen bonds. All the bonds seemed to fall naturally, no fudging was required. Donohue said that the pairs agreed with what he knew. Crick immediately pointed out that the way the bases in these pairs would attach to the sugars meant that the two backbones would run in opposite directions, just as they had to do. Each chain could include the pairs flipped over. Chargaff's ratios were satisfied, too. The bases could appear in any order on one chain. Once that order was fixed, the base pairing determined the complementary order on the opposite chain. The last candle was lit.

Crick told everyone over drinks at the Eagle Pub at lunch, "We have discovered the secret of life."

Toward the middle of next week, the machine shop delivered the rest of the necessary model pieces. Watson and Crick began to build the model. They completed the full model on Saturday March 7. The same day, Maurice Wilkins wrote a letter to Crick: "...our dark lady leaves us next week..... at last the decks are clear and we can put all hands to the pumps!" Wilkins's letter reached Crick the following Monday. Crick didn't know whether to laugh or be sad.

Watson and Crick's first paper was published on April 25 in *Nature*. A coin toss determined the order of the author's names. Only a letter, but the first sentence must have gone off like a string of depth charges in a calm sea. "We wish to suggest a structure for the salt of deoxyribose nucleic acid (D.N.A.). This structure has novel features which are of considerable biological interest." At the end of the letter, what has been called one of the most coy statements in the literature of science, "It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material."

Crick later said, when an observer commented that the nature of the discovery process was strangely curious, replied "No, I don't think so. I think that's the nature of discoveries, many times: that the reason they're difficult to make is that you've got to make a series of steps, three or four steps, which if you don't make them, you won't get there, and if you go wrong in any one of them you won't get there."