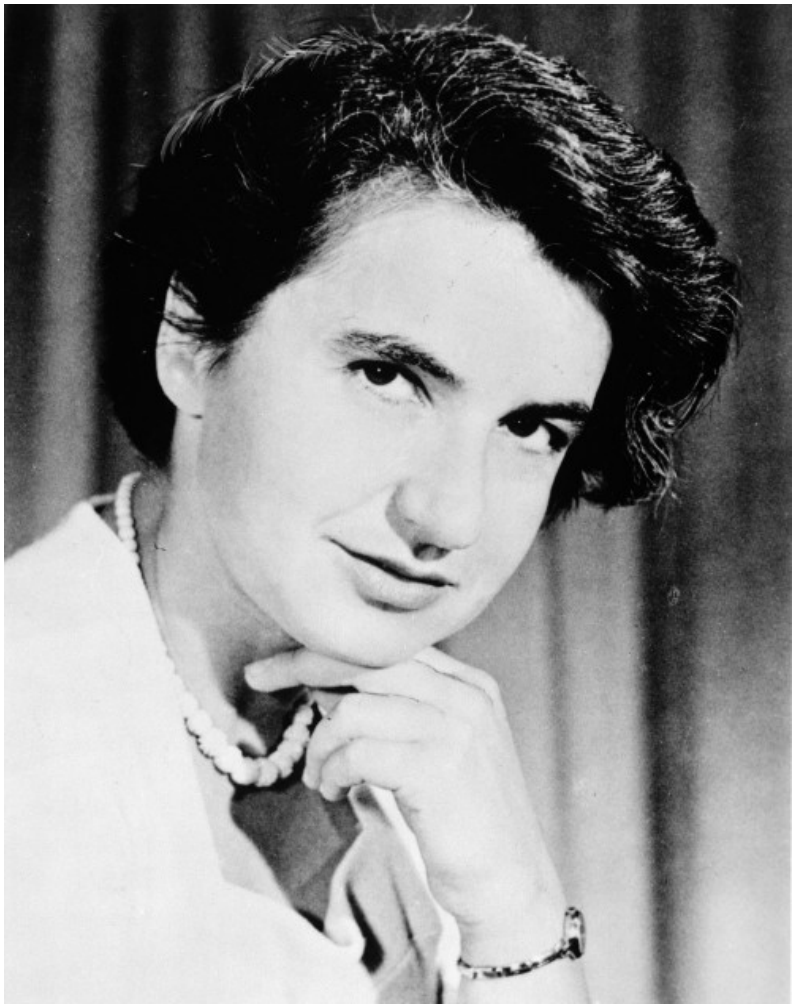
THE SILENT PARTNER OF DNA
By Julie Leitch



Rosalind Elsie Franklin
(1920 to 1958)

"Science and everyday life cannot and should not be separated.
Science for me, gives a partial explanation of life, in so far as it goes, it is based on Fact, experience and experiment"
Rosalind Franklin
(In a letter to her father)

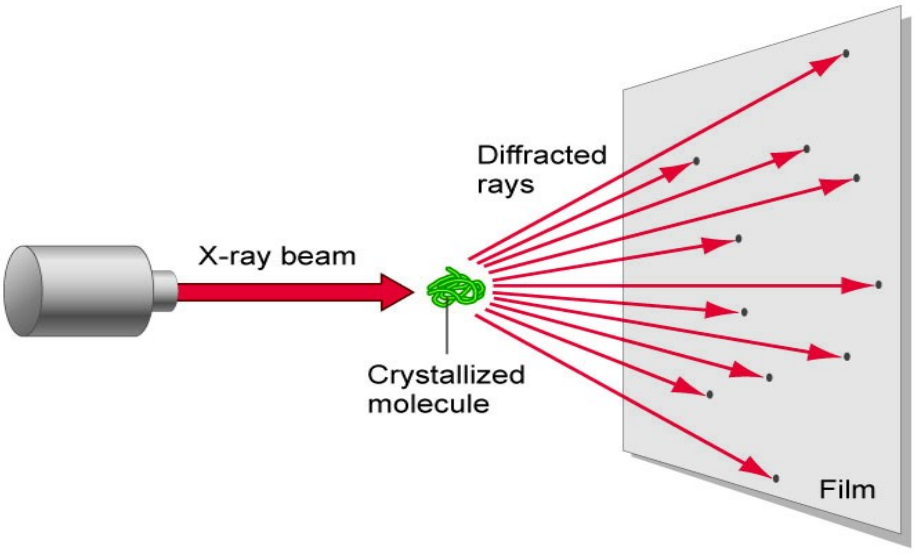
Planning the investigation

To be completed by November 27th

1. Find basic background information on Rosalind Franklin
2. Use the internet to find out about her discovery of the DNA molecule along with The relevant data, to include graphs, photographs and any of her notes from that Time.
3. Try to find out if I think she should have been included with Watson, Crick and Wilkins in the sharing of the Nobel Prize.
4. Aim to have summary and project completed by the 22nd of February.

Deoxyribonucleic acid is the exceptional machinery for the copying of all of life's hereditary material. Little was known about this molecular substance until the 1950's. In fact it was thought by many to be proteins that carried out life's copying blueprint. There were many scientists from all over the world working on DNA at that time, the most notable were Francis Crick, James Watson and Maurice Wilkins. They jointly received the Noble Prize for physiology and medicine in 1962 for their molecular model of the structure of DNA. However one name is missing that of Rosalind Franklin. Her x-ray diffraction photo of DNA (Fig.1) was quoted as "The most beautiful x-ray photo ever taken" by J.D Bernal, better known as photo 51. This photograph along with other data belonging to Franklin was shown to Watson and Crick. Had they not been shown Rosalind's work would they have been so quick with their molecular model?

Rosalind Franklin was born in 1920 into a wealthy British family. From an early age all Rosalind wanted to be was a scientist! She obtained her degree in chemistry in 1941. She was then further awarded her PhD, in 1945, for her work during the Second World War, during which time she wrote several scientific papers, on the study of coal for the British Coal Utilization Research Association. In 1947, she moved to Paris where she became experienced in X-ray crystallography. This is the way that three-dimensional structures are viewed, the operator has first to remove the named substance and convert it into crystal form. X-rays are then shone onto the crystal which in turn, throws the atoms, which are in the crystals, onto photographic negatives. The three dimensional shape can then be read from the X-ray photograph.



In 1951 she was head hunted because of her expertise, by Sir John Randall of the MRC Biophysics research unit, at King's College London, and appointed to lead a team into the investigation of certain biological material, namely DNA. This was the cause of much confusion as she was hired while Maurice Wilkins, one of her colleagues at Kings was away on holiday. Upon his return he was under the

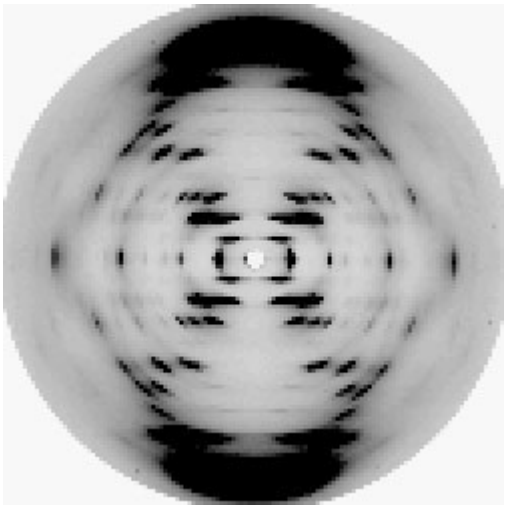
impression that Franklin would work under him, on the research into DNA. Given these circumstances she did not enjoy her time at King's and chose to work alone on the DNA project, leaving Wilkins to work on another form of DNA, which turned out to be unsatisfactory for diffraction studies.

Franklin, with the help of her graduate student Raymond Gosling, studied calf thymus DNA which had been extracted and purified by Rudolf Signer. Owing to her knowledge of physical chemistry she was able to produce thinner fibres of single strand DNA which produced more exact X-ray photographs. She was able to keep them at a very high humidity, by bubbling hydrogen through salt solutions. This produced easier to read X-ray patterns. She first discovered there were two forms of DNA, a dry crystalline form (A) and a wet form (B). The "B" form which is derived from the "A" form when the fibres take up quantities of water. The X-ray patterns of the "B" form showed a helix shape, although it was fuzzy. Since water in the molecules will be attracted to the phosphates, she rightly guessed that the backbone was on the outside with the bases on the inside.

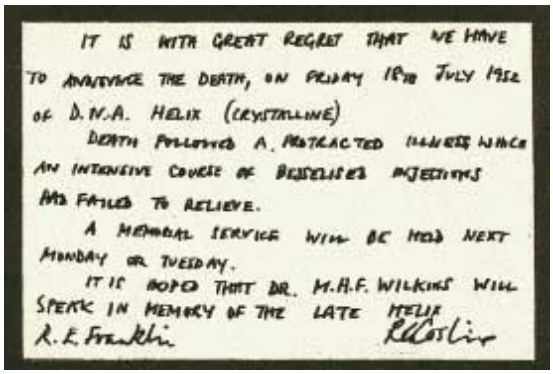
She wrote in her notes that she thought this would probably take the shape of a ladder with the bases as the rungs. She revised her thinking on the 24th of February 1953 when she wrote in her notebook that she now thought it to be a three dimensional helix. The A form however was not showing signs of a helix, but was showing the best X-ray spots in 'this dry' form of the molecule. She continued to work on the "A" form using the approach of experiments rather than guesswork because she did not like speculation.

Franklin gave a talk in November of 1951 to bring the unit up to date on her work so far. She presented the A and B form data. In the audience was James Watson of the Cavendish Laboratory, Cambridge who took on board what he could remember of her findings. Watson and his colleague Crick built their first model of DNA. Franklin was invited to view this model which was a triple helix, with the backbone on the outside, Franklin quite rightly pointed out that it would not hold up in this shape.

Franklin got the first clear picture of the "B" form of DNA in May of 1952. No one had been able to photograph the "B" form before. Looking down the molecule, and taken by long exposure the previous day this X-ray diffraction picture (Fig.3) proved a definite double helix formed by the X that ran through the middle!!



Franklin was able to analyse the smears' diffracted onto the negatives which showed that the DNA molecule makes twists at regular intervals. She however did not release this data, but continued to work on the "A" form getting bogged down with calculations which did not support a double helical shape. Her notes from this time however say that she guessed an antiparallel idea for this form. Finally after months of trying to link the two, on Friday the 18th of July 1952 she posted a prank death note certificate (Fig.4) for the crystalline "A" form of DNA.


IT IS WITH GREAT REGRET THAT WE HAVE TO ANNOUNCE THE DEATH, ON FRIDAY 18TH JULY 1952 OF D.N.A. HELIX (CRYSTALLINE)

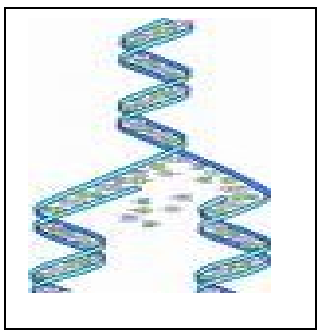
DEATH FOLLOWED A PROTRACTED ILLNESS WHICH AN INTENSIVE COURSE OF BIBLICAL INJECTIONS HAS FAILED TO RELIEVE.

A MEMORIAL SERVICE WILL BE HELD NEXT MONDAY OR TUESDAY.

IT IS HOPED THAT DR. M.H.F. WILKINS WILL SPEAK IN MEMORY OF THE LATE HELIX

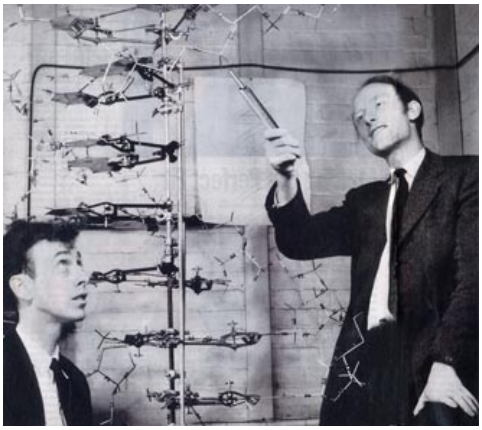
R.E. Franklin R.G. Gosling

She continued to waste most of the winter on the "A" form only returning to the "B" form in February of 1953. In March of 1953 it is seen from her notes that she had been able to apply the helical shape to the "A" form and had also found using Chargraffs' rules, that it had specific base pairs adding to her first antiparallel ideas. She now just had to apply this to her "B" form.



By this time though, Watson and Crick had already received her MRC report on the "A" form and been

shown the “B” form photograph, by Maurice Wilkins, her so called colleague at Kings‘. Watson instantly found the solution to his and Crick s problems off deciphering the structure of the DNA molecule. Rosalind’s photograph allowed them to build properly, their model as a helix with the backbone on the outside.



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They now had all the information they needed to build their model which they did in March of 1953 (Fig. 5). They published their findings in “Nature” on the 25th April, along with their experimental data for the structure of the DNA molecule, included in that publication was no proper acknowledgement to Franklin’s contribution to their structure. Franklin also published in that issue saying how she thought a helical structure was highly probable.

She had come extremely close to finding the structure of DNA, but was unwilling to release data until absolutely sure. It was undoubtedly her downfall in the race to discover the structure of DNA. Franklin did not consider her to be in a race with Watson and Crick.

In spite of everything Franklin did not hold any grudges towards Watson and Crick and, in fact, used her own data on the “A” and “B” form to test their model. She calculated the measurements using the Patterson Function, and posted her findings in “Nature” along with the graphs shown below (Fig.6).

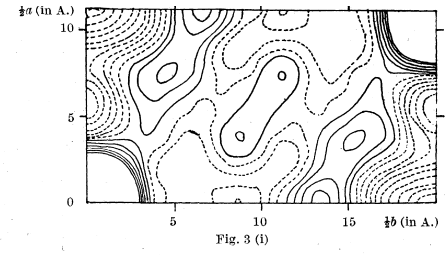

Fig. 3 (i)

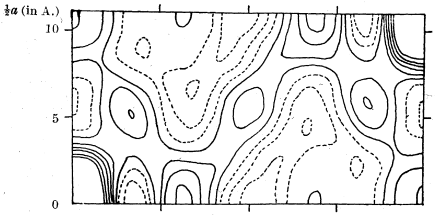

Fig. 3 (ii)

Three-dimensional Patterson function of crystalline sodium deoxyribonucleate. Sections in $a-b$ plane at (i) $c = 0$, (ii) $c = \frac{1}{2}$

Franklin went on to write five further papers on DNA, after she left Kings' College. She spent four happy years working on the tobacco mosaic virus and the polio virus at Birbeck College, until her tragic death to ovarian cancer at the early age of 37.

It is fair to say that no other scientist put so much work into the discovery of the double helix. The Nobel Prize is only given to living persons, and has never been given to more than three people, at any one time. Friends of the former scientist say she was never after the prize. Nor, was she worried about having been out run in a race she did not know existed. If she had been given proper recognition science classes would be saying her name along with the names of Watson, Crick and Wilkins.

While Franklin is increasingly remembered for her part in the discovery of the structure of the DNA molecule, her short scientific career went much further than that, she made essential contributions in science that went beyond how to take a good photograph. Francis Crick wrote in 1974 that "Franklin was only two steps away from the solution." Is it not more likely she was the solution? It seems all the evidence points to her being a co discoverer.

The DNA revolution has come a long way since its first discovery. We now have the ability to be able to trace a person just by their genetic fingerprint and more controversially, use of Genetic engineering to rid us of hereditary mutated genes in the cells, techniques that can also be used to produce "designer babies". In 1990 the Human Genome project was set up, their objective was to sequence the nucleotides of DNA in a haploid cell, all 3 billion base pairs. They completed this in 2003 which was an important step in the development of medicine, especially for people suffering from inherited Genetic disorders such as Huntingdon's Disease etc.

Did Franklin know her discovery would have had such an impact as to be able to revolutionise modern day Biology? We shall never know. A debate still continues to this day about the amount of credit due to Franklin.

Evaluation

I thoroughly enjoyed finding out all about Rosalind Franklin, the story of her life and how she was treated by her male peers was fascinating. I did, however, find it a struggle to obtain scientific papers and data on her work, what I could find I have included. In my opinion Rosalind should have been included in the sharing of the Noble Prize along with Watson, Crick and Wilkins, all the information I found pointed to her being a co-discoverer. Without her photograph, Watson and Crick would have been a lot longer in deciphering the structure, of the DNA molecule. Lets hope that the debates that continue, win in her favour.