STRUCTURAL BIOLOGY
ISSN 2059-7983

Rosalind Franklin 1920–1958[1]

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[1] A shorter version of this essay has already been published in the June 2020 issue of *Crystallography News*, the quarterly magazine of the British Crystallographic Association.

Keywords: Rosalind Franklin; DNA.

This year marks the 100th anniversary of the birth on 25th July 1920 of Rosalind Franklin, whose pivotal contribution to the discovery of the structure of DNA has been increasingly recognised since her untimely death from ovarian cancer at the age of 37 in 1958. There is now a general consensus that, if she had lived longer, she would have 'deserved' to be among the three awardees of the 1962 Nobel Prize in Physiology or Medicine. Each Nobel Prize can be bestowed on a maximum of three people and is never awarded posthumously. The Prize went to Francis Crick, James Watson, and Maurice Wilkins 'for their discoveries concerning the molecular structure of nucleic acids and its significance for information transfer in living material'. However, the debate still rages on as to whether, given the climate at the time, she would have been included instead of one of the three awardees.

A realisation of the vital importance of Rosalind Franklin's work has only gradually gained traction. Very belatedly, her name is becoming much better known and the public are being disabused of the veracity of the scurrilous comments about her in the famous book, *The Double Helix*, an account written by James Watson of the DNA structure discovery. It was not until 1999 that Watson finally said that '. . . the Franklin photograph was the key event . . . ' *i.e.* he at last admitted that Photo 51 was absolutely essential information for construction of the model.

So what was Photo 51 and why was it so important? I will try to give a brief and distilled account below. Much has already been written on the subject and the interested reader is referred to more detailed descriptions listed at the end of this piece.

Rosalind Franklin (RF) was born in London to Muriel and Ellis Franklin. Her brother, David, was one year older, and she had two younger brothers (Colin and Roland) and a younger sister, Jenifer. Rosalind showed early signs of wanting to challenge herself: her Aunt Mamie Bentwich, on holiday with the Franklin family on the Cornish coast in 1926, wrote to her husband that 'Rosalind is alarmingly clever – she spends all her time doing arithmetic for pleasure and invariably gets her sums right'. She attended boarding school at Bexhill-on-sea from age 9 to 11, and then in January 1932 went as a daygirl to St Paul's Girls' School, where according to the 'High Mistress', Miss Ethel Strudwick, 'every girl is being prepared for a career. The High Mistress considers that no woman has a right to exist who does not live a useful life . . . look beyond marriage as your goal'. Rosalind shone at both sport and in her studies, and her mother wrote: 'All her life, Rosalind knew exactly where she was going, and at 16 she took science as her subject'.

In the summer of 1938, Rosalind visited Paris and so began her lifelong love of France and all things French, including the people. She perfected her spoken French and developed a passion for hiking and mountains. On her return, from 1938 to 1941 she went to Newnham College, Cambridge University, to study Natural Sciences with a focus on Chemistry, at which she excelled. She thought nothing of riding her bike home to London at the end of term, a distance of 65 miles! In the 1st year exams ('Prelims') she came 2nd in the whole year group. She studied 'Crystal Physics' in the autumn of her second year, and became familiar with crystallographic space groups and various crystal forms. Her final year research project went well and was supervised by Fred Dainton, a photo- and polymer chemist. However, she did not actually 'graduate' until 1948 since degrees were not awarded to women by Cambridge until 1947, whereas in Oxford they did so from 1921 onwards.

Newnham gave Rosalind a 4th year research scholarship, and from 1941 to 1942 her supervisor was Ronald Norrish who was 'bad-tempered' and given to 'autocratic treatment of juniors'. She was housed in a claustrophobic small dark workspace and allocated

Figure 1
Rosalind Franklin (1920–1958).

an impossible project on the polymerisation of formic acid and acetaldehyde. She did not enjoy the experience and did not respect her supervisor, who said that 'confrontation when cornered was her tactic'. Generally it was known that she 'didn't suffer fools gladly'.

In 1942 she registered for a Cambridge PhD but worked as an 'Assistant Research Officer' in Kingston for the British Coal Utilisation Research Association (BCURA) on the permeability and shrinkage of coals to gas (helium) and in water as a function of temperature. Activated charcoal was used in gas masks to very good effect in WW1, saving thousands of lives, and an understanding of the effect of gas on different coal types could be applied to make more effective masks and also had other industrial applications. During this period of WWII, RF acted as an air-raid warden. Her 1945 PhD thesis was entitled *The physical chemistry of solid organic colloids with special reference to coal and related materials* and in 1946 she published her first (of 37) peer-reviewed papers [*Thermal expansion of coals and carbonised coals*, Bangham & Franklin (1946)], putting forward the hypothesis of 'molecular sieves' to explain the variation in porosity of various types of coal.

For her first postdoctoral position she happily returned to her beloved France and worked from 1947 to 1951 in Paris, studying the crystallography of coal and graphite under Jacques Mering (who had been trained at the Royal Institution by W. H. Bragg) at the Laboratoire Central des Services Chimiques de l'Etat (a Government Laboratory). She was paid £5/week and in turn paid £3/week rent, she became 'unEnglished' and she felt that at work 'women engaged as equals'. She carried out powder diffraction on amorphous solids with monochromatic X-rays and identified the carbons that turned into graphite when heated to 3000°C ('graphitising carbon') and those that did not ('non-graphitising carbon', a rigid finely porous mass). She worked closely with Vittorio Luzzati from Argentina, becoming an expert in the crystallography of such samples. Five papers were published in 1948 on various aspects of her coal studies and her first letter to *Nature* came out in 1950, *On the influence of bonding electrons on the scattering of X-rays by carbon*.

At the beginning of 1951 she moved back to England, taking up a three-year Turner and Newall Fellowship at King's College, London to work under John Randall on proteins in solution and changes in their structure when they are heated or dehydrated, causing them to denature. She was concerned about her lack of knowledge in the new research field: 'I am, of course, most ignorant about all things biological, but I imagine most X-ray people start that way' (as an ex-nuclear physicist, I can sympathise with this view!). However, just before she arrived, Randall suddenly changed her project to the investigation of some DNA fibres that Maurice Wilkins, also working at King's with Randall, had obtained in May 1950 from Rudolf Signer in Berne. Randall wrote to her that '. . . This means that as far as the experimental X-ray effort is concerned there will be at the moment only yourself and Gosling . . . '. Unfortunately, Randall neglected to tell Wilkins about this new arrangement, even though Wilkins and Ray Gosling (a research student supervised by Wilkins) had already obtained good X-ray diffraction patterns from the DNA fibres. This set the scene for difficulties between Wilkins and RF which quickly escalated over the first six months of 1951 while RF was building new equipment to control the humidity of the DNA fibres using hydrogen gas bubbling through different salts.

The situation between RF and Wilkins reached such an impasse that, in October 1951, Randall directed RF and Gosling to work on the A (dehydrated) form of DNA using the fibres from Signer and the best X-ray camera, and Wilkins to work on the B (hydrated) form with some other fibres that did not crystallize well. Photo 51 was taken by RF and Gosling in May 1952 using a micro-camera, and was the clearest photo yet obtained, but it was of the B form (92% humidity) on which they were not supposed to be working, so it was put away. The X-ray generator was a prototype fine-focus device built at Birkbeck by Werner Ehrenberg and Walter Spear which had been given to Wilkins and Gosling, but was then used solely by RF and Gosling.

By January 1953, Gosling wanted to finish his thesis and he showed Photo 51 to Wilkins, who in turn, unknown to RF, showed it to James Watson (JW) when he visited King's from Cambridge. JW was working there with Francis Crick (FC) on building a model of DNA with newly obtained permission from W. L. Bragg, the head of the Cavendish Laboratory. Bragg had previously banned them from pursuing further DNA modelling following an embarrassing incorrect model (helical with the bases on the outside) that they had trumpeted the year before. From the 1938 X-ray diffraction work in Leeds of William Astbury and the crystallographer Florence Bell on DNA from calf thymus, it was known that the DNA

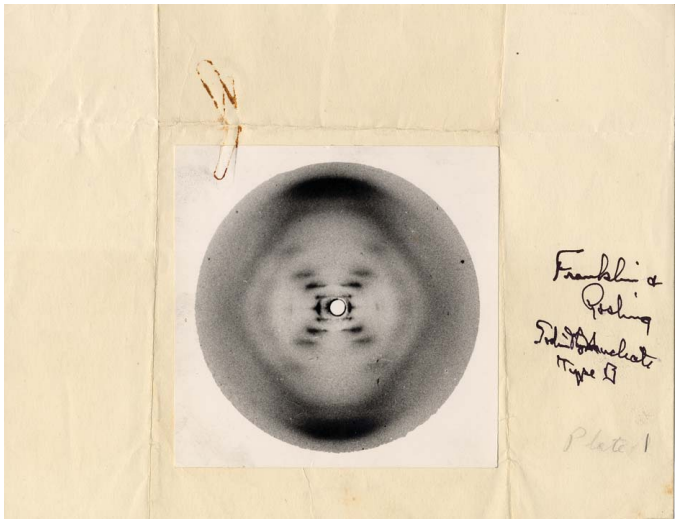

Figure 2
Photo 51. Courtesy Ava Helen and Linus Pauling Papers, Oregon State University Libraries.

structure repeated every 27 Å and that the bases were stacked 3.4 Å apart and lay flat, but they did not discover that it formed a helix. Wilkins had requested a physicist colleague at King's, Alex Stokes, to calculate the diffraction pattern arising from a helical structure, and as a result Stokes was the first to show that DNA was probably helical. However, it was not known how many chains constituted the helix. Wilkins also told JW the RF experimental helical parameter values: a 34.4 Å repeat with the bases stacked 3.4 Å apart. Meanwhile, RF found that someone had tampered with her laboratory notebooks, and her longing to leave King's intensified.

On the 9th February 1953, FC and JW were shown RF's December 1952 MRC Review Committee report by Max Perutz. This report was not marked confidential, but the results in it were unpublished. It gave the space group of the A form DNA as face-centred monoclinic (*C*2), and specified the unit-cell dimensions and angles. FC realised that this space group gave a vital clue as to the structure, because it meant that the DNA looked the same both ways up, so that it must consist of two antiparallel helical chains, not three chains as some had postulated. Erwin Chargaff had already found that in DNA the number of adenines (A) + guanines (G) was equal to the number of thymines (T) + cytosines (C), and also that the numbers of A and T were the same, as well as the numbers of G and C. Another critical piece of the puzzle was solved when Jerry Donohue, a postdoc who shared an office with the model builders and was watching them at work, suggested that the bases were the keto and not the enol forms that they had been trying to use.

By 7th March 1953, FC and JW had built a model that seemed to fit with all the known information. Each purine (A,G) was paired with a pyrimidine (T,C) across the inside of the double helix formed by two antiparallel carbon-phosphate backbones. Wilkins went to see it on 12th March and told everyone at King's about it on his return. RF was about to leave King's where she was miserable and felt she could no longer work in the same environment as Wilkins. She and Gosling had already sent off two papers on the structure of the A form and had almost finished one on the B form, of which she was very near to having the structure. How much RF ever knew about which of her results were shown to whom and when they were shown, remains a matter of current debate.

In mid-March 1953, funded by the Agricultural Research Council (ARC) as a senior scientist, RF moved to Birkbeck College where John D. Bernal ('Sage') provided a supportive and happy environment for her new research group working on virus structure. Her office was on the 5th floor of a bomb-damaged house: 'I swapped a palace for a slum'. The X-ray laboratory was in the basement and leaked, so that an umbrella was required during experiments! Here she worked on RNA and on Tobacco Mosaic Virus (TMV), the first virus to be discovered in 1892. Bernal thought the world of her and supported/protected her, calling her a 'brilliant experimentalist' and writing after her death: 'As a scientist, Miss Franklin was distinguished by extreme clarity and perfection in everything she undertook. Her photographs are among the most beautiful X-ray photographs of any substance ever taken'. Aaron Klug, a future Nobel Prize winner (Chemistry in 1962) who had come from South Africa to do his PhD at Cambridge and then won a Fellowship to work under Bernal, met Rosalind and transferred to study viruses in collaboration with her. By 1955 her group consisted of three postgraduate students: James Watt, John Finch and Ken Holmes, and also Don Caspar (who first coined the phrase 'structural biology') from the USA on a Fellowship. From interpreting fibre diffraction patterns, and using multiple isomorphous replacement methods, RF hypothesised that all TMVs were the same length and had a hollow core with the RNA deeply embedded in protein units and coiled inside (published in *Nature* in 1955). Together, her group determined the first virus structure, showing that indeed the 50 MDa TMV had a diameter of 150 Å with the RNA coiled round a hollow inside. The first model had been made using 288 bicycle handle bar grips! However, Norman Pirie, a plant virus physiologist at the Rothamstead Experimental Station in Hertfordshire, fundamentally disagreed with this result, and as a result stopped sending her virus material on which to work, so she and Klug then had to prepare their own viruses.

The structure allowed the TMV infection process to be understood, and a famous model of the virus was displayed at the 1958 World Trade Fair (Expo1958) in Brussels. To aid the highly calculation-intense interpretation of the X-ray diffraction patterns, a 'computer' was employed: she was called Mrs Cratchby! Results on pea streak, potato, turnip, tomato and cucumber viruses were reported in seven papers in 1956 and six in 1957. The group then expanded their focus from plant viruses and started work on the Polio virus.

During her time at Birkbeck, RF went on a couple of two month-long tours of America (1954 and 1956) and she thoroughly enjoyed the recognition and respect she was given there. It was on the second of these that she experienced pains in her abdomen which were the first sign of the illness that would cut her life so short.

Rosalind has received much belated posthumous recognition that sadly she did not live to witness, with at least 39 buildings or projects named after her, including the 2019 European Space Agency's ExoMars rover. Newnham College, Cambridge have named a student residential building, there is a blue plaque on the house in London where she lived from 1951 to 1958, in 2000 King's College named their new Dental Education Centre the Franklin-Wilkins Building (a painfully ironic coupling of names), and in 2018 the Rosalind Franklin Institute was launched at the Harwell Campus in Oxfordshire as an autonomous medical research centre under the joint venture of 10 universities, and funded by UK Research and Innovation. Beyond the UK, among others there is the Rosalind Franklin University of Medicine and Science in Chicago.

There has been much controversy regarding Franklin's contribution to the unravelling of the structure of DNA. A balanced account was given in *Nature* by Aaron Klug in 1968: *Dr Klug discusses Dr Franklin's contribution to the discovery of the structure of DNA in the light of accounts given by Professor Watson in his book The Double Helix and by Dr Hamilton in a recent article in Nature*.

In 2017, under the Planning Act of 1990, Historic England listed her tomb as of 'special architectural or historic interest', with the official description (which sums up the her scientific impact very well): 'the tomb commemorates the life and achievements of Rosalind Franklin, a scientist of exceptional distinction, whose pioneering work helped lay the foundations of molecular biology; Franklin's X-ray observation of DNA contributed to the discovery of its helical structure'.

Notably, last year the University of Portsmouth announced that on 2nd September it was changing the name of its James Watson Halls to Rosalind Franklin Halls. Perhaps this act shows in microcosm the growing appreciation of the impact of Franklin's life and work, somewhat redressing the balance in the previous mis-allocation of credit.

Further reading: *Rosalind Franklin, The Dark Lady of DNA* by Brenda Maddox (2002); *My Sister Rosalind Franklin* by Jenifer Glynn (2012).

Acknowledgements

I am very grateful to Jenifer Glynn (RF's sister) and Daniel Franklin (RF's nephew) for checking this account, and also for helpful correspondence with Tony North and constructive comments from Randy Read.

References

Bangham, D. H. & Franklin, R. E. (1946). *Trans. Farad. Soc.* **48**, 289.
Franklin, R. E. (1950). *Nature*, **165**, 71–72.
Franklin, R. E. (1955). *Nature*, **175**, 379–381.
Glynn, J. (2012). *My Sister Rosalind Franklin*. Oxford University Press.
Klug, A. (1968). *Nature*, **219**, 808–810.
Maddox, B. (2002). *Rosalind Franklin, The Dark Lady of DNA*. HarperCollins Publishers.