Rosalind Franklin and the double helix

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A draft manuscript shows how near Rosalind Franklin came to finding the correct structure of DNA.

SOME years ago I gave an account[1] of Rosalind Franklin's contribution to the discovery of the structure of DNA, based on published sources supplemented by references to her notebooks and reports. I pointed out how close Franklin had come in the progress of her work to various features of the structure contained in the correct solution. At the time, however, I did not know of the existence of a draft manuscript which confirms how close she had got to the answer. This only came to light later. I therefore take the opportunity of this 21st Anniversary issue to fill out the record and to highlight a dramatic element in the 'race' for DNA.

In my article I told how the analysis of the B form of DNA in terms of helical diffraction theory, which is given in Franklin's paper with Gosling in *Nature*[2] on April 25, 1953, can be found in her notebook for the period January to March 1953, that is before the Watson–Crick structure had become known to her. I went on to say, however, that she apparently did not feel convinced enough of the relevance of this analysis to publish it (because she had not solved the A form). This is erroneous. The typescript I have found is dated March 17, 1953 and is clearly a draft of the *Nature* paper. This suggests a different explanation from the one I gave, namely that she was proposing to publish what she knew on the B form, two other papers on the A form having already been submitted (before March 6) to *Acta Crystallographica*. This draft contains all the essentials of the *Nature* paper, and much of the wording is carried over intact. It required only slight modifications to take into account the Watson–Crick structure, news of which reached King's College on March 18, one day later.[4] In the final (undated) typescript, there is inserted by hand the sentence "Thus our general ideas are not inclnsistent with the model proposed by Watson and Crick in the preceding communication."

In the draft it is deduced that the phosphate groups lie on a helix of diameter 20 Å, that is, on the outside of the molecule, in accordance with the conclusion Franklin had reached earlier on the basis of physicochemical reasoning, including her own work on the water uptake by DNA fibres undergoing the A–B transition. Moreover, on the basis of the intensity distribution in the X-ray pattern, she concludes that there is not one chain in the helix, but probably two, coaxially arranged, and that these are separated by $\frac{3}{8}$ of the period, or 13 Å, along the fibre axis direction. The wording is so couched, however, as to show Franklin had not yet understood that the two chains must run in opposite directions, although she had already observed in her notebook that this must be the case in the crystalline A form (which has a two-fold axis of symmetry). I have already argued that it would not have taken long for her to see the true relationship between the two forms—at the time she was thinking of the A form as an unwound version of the helices in the B state (rather, I imagine, like the β-sheet structure is to the α helix in polypeptides).

This would have brought her to the final and crucial step necessary to the complete solution, base pairing. Franklin had thought from an early stage that the bases must lie on the inside of the molecule and be linked by hydrogen bonds, and she had already formed the notion that the two purines were interchangeable with each other and also the two pyrimidines[3]. An entry in her notebook shows that she was considering Chargaff's analytical data, though there is nothing to show that she knew the correct tautomeric forms of the bases. The step from base interchangeability to base pairing is a large one, but the idea would have been essential to fitting the variable parts of the structure, the bases, in to the regularly repeating part, the double helix of phosphate-sugar chains at which she had arrived by March 1953.

1 Klug, A., *Nature*, **219**, 808–810, 843–844; also 880 (1968).
2 Franklin, R. E., and Gosling, R. G., *Nature*, **171**, 740–741 (1953).
3 Franklin, R. E., and Gosling, R. G., *Acta Crystallogr.*, **6**, 673–677 (1953).
4 Olby, R. C., *The Path to the Double Helix* (Macmillan, London, in the press).