Rosalind Franklin and the Discovery of the Structure of DNA

by
A. KLUG
MRC Laboratory of Molecular Biology, Cambridge

In this article 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*.

ROSALIND FRANKLIN made crucial contributions to the solution of the structure of DNA. She discovered the B form, recognized that two states of the DNA molecule existed and defined conditions for the transition. From early on, she realized that any correct model must have the phosphate groups on the outside of the molecule. She laid the basis for the quantitative study of the diffraction patterns, and after the formulation of the Watson–Crick model she demonstrated that a double helix was consistent with the X-ray patterns of both the A and B forms.

Watson's account in *The Double Helix* does not pretend to tell more than one side of the story. The article by Dr L. D. Hamilton ("DNA: Models and Reality", *Nature*, May 18, 1968) does not do justice to Franklin's work*.

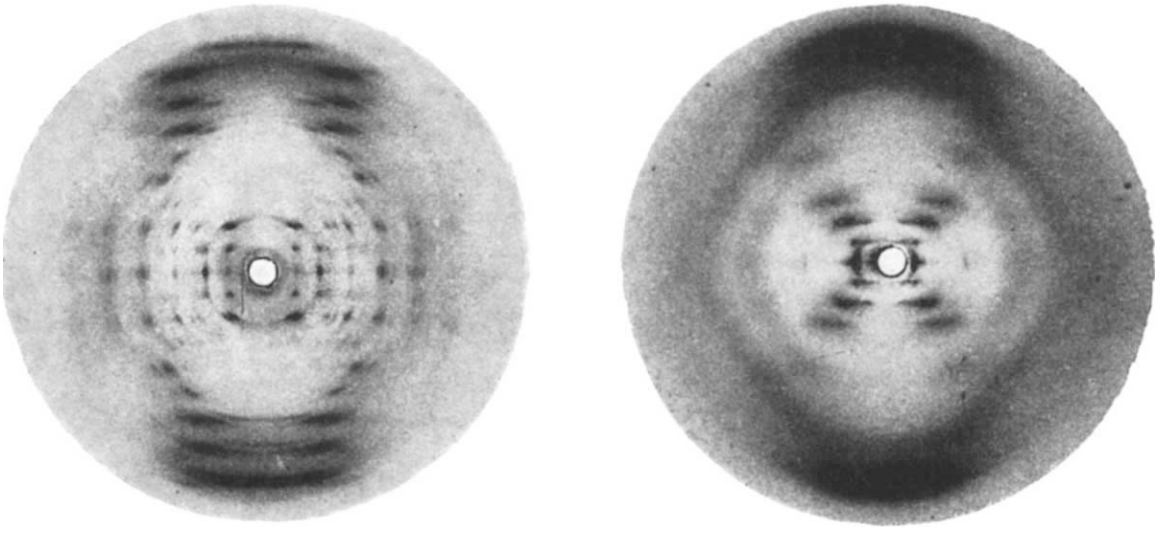
The importance of Franklin's work has been lost sight of, partly because of her untimely death. Because, as her last and perhaps closest scientific colleague, I am in a position to fill in the record, I have endeavoured here to give an account of what Franklin was doing in the period before the discovery of the Watson–Crick model, to place the helical question in context, and to summarize the contributions she made to the proof of the structure. I have not attempted to deal with the well recognized contributions made by the other protagonists in the story except in so far as they touch directly on her work.

* For example, although both the A and B types of X-ray patterns given by DNA fibres are discussed, it is not stated that it was Franklin who discovered the B structure and also took the particular photograph referred to by Watson in the passages quoted by Hamilton. Likewise her role in demonstrating the validity of the Watson–Crick model for both the B and A forms—once it had been proposed—is not brought out: ref. 4 is omitted. Hamilton refers, like Watson, to her "anti-helical" view, a term which does not fairly reflect her attitude from about the end of 1952 onwards. This might be more accurately described as one of questioning; the question being whether the structure of B—undoubtedly helical in her view—also applied to the crystalline structure A.

The Published Record

Rosalind Franklin published, together with her student, R. G. Gosling, five papers on DNA[1–5]. Much of the material in these papers is not readily intelligible to the non-crystallographer, which may account for the lack of attention they have received. I have used chiefly these published sources, supplemented by reference to Gosling's thesis[6] and to Franklin's notebooks and reports which passed to me on her death in 1958.

The first two papers[1,2] were sent to press in March 1953 before Franklin knew of the Watson–Crick model. The first[1] describes the observations on the types of X-ray diagram given by highly orientated specimens of sodium DNA at different humidities. Two forms of DNA fibres, named A and B, are described and the conditions are given for producing them. In this paper are reproduced the beautiful X-ray photographs which were used in the subsequent analysis of both forms (Fig. 1). The accompanying paper in *Acta Crystallographica* describes quanti-



A B

Fig. 1. X-ray diffraction patterns of the A and B forms of the sodium salt of DNA, reproduced from ref. 1.

tative measurements on the X-ray pattern of the A form and gives the plan of the crystallographic campaign on which Franklin had set out.

The next paper[3] was one of the pair from King's College[3,7] which accompanied the announcement[8] of the Watson–Crick model in *Nature* on April 25, 1953. In this paper Franklin and Gosling show, by application of helical diffraction theory to their key photograph of the B form, that the B structure is compatible with a double-helical structure of the type proposed by Watson and Crick, although differences of detail are found from the proposed model. In a communication[4] published in *Nature* in July 1953, which has often been overlooked, Franklin and Gosling show conclusively by crystallographic analysis that the A form also contains two-chain helical molecules[1] with somewhat different helical parameters, but of essentially the same type as found in the B structure, and therefore also compatible with the Watson–Crick model (Fig. 2). The demonstration of the correctness of the structure is thus doubly convincing because the double-helical structure may be arranged to fit the X-ray data of both forms. The last paper sent to *Acta Crystallographica*[5] in 1954 contains an interpretation of the three-dimensional Patterson function of the A structure which enables the orientation of the helical molecules in the unit cell of the crystal to be deduced and presents a detailed picture of the arrangement of the phosphate groups.

Historical Outline

The following outline of events may help to put this summary of Franklin's work into historical perspective. Before 1951, Wilkins at King's College had succeeded in obtaining well orientated thin fibres from a specimen of DNA prepared by Signer at Berne. A research student, R. G. Gosling (now at the Medical School, Guy's Hospital, London), had found that a bundle of these fibres gave X-ray fibre photographs showing a high degree of crystallinity, and therefore a much more detailed pattern than those produced by Astbury and Bell in 1947. It became evident that a photographic system of higher resolving power might be expected to show more fine structure in the diagram. Furthermore, the bundle of fibres could not easily be maintained in parallel alignment and it was evidently desirable to be able to work with single fibres of small diameter. In January 1951, Franklin was appointed Turner–Newall Fellow at King's College with the support of Professor J. T. Randall, who suggested that she, with Gosling under her supervision, should undertake a systematic X-ray investigation of DNA

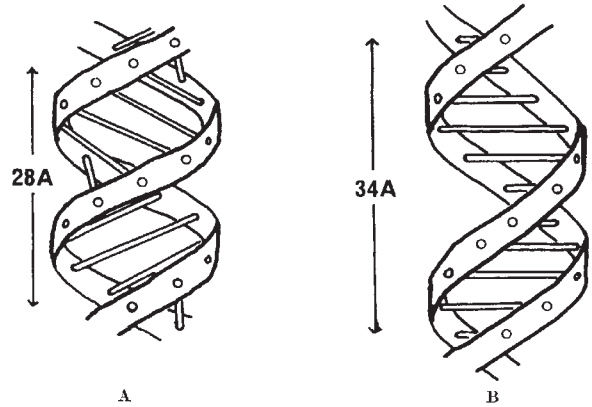


Fig. 2. Diagram (for reference) to show the principal differences between the A and B forms of DNA. The ribbons symbolize the phosphate–sugar chains, and the rods the pairs of hydrogen-bonded bases holding the chains together. In the A structure, in which the molecules are tightly packed in a crystal, each chain contains eleven nucleotides in the axial repeat distance of 28 Å. In the B structure, in which the molecules are essentially free, there are ten nucleotides in the axial repeat of 34 Å. The molecule is 30 per cent shorter in the A than in the B form. (Drawing adapted from ref. 9.)

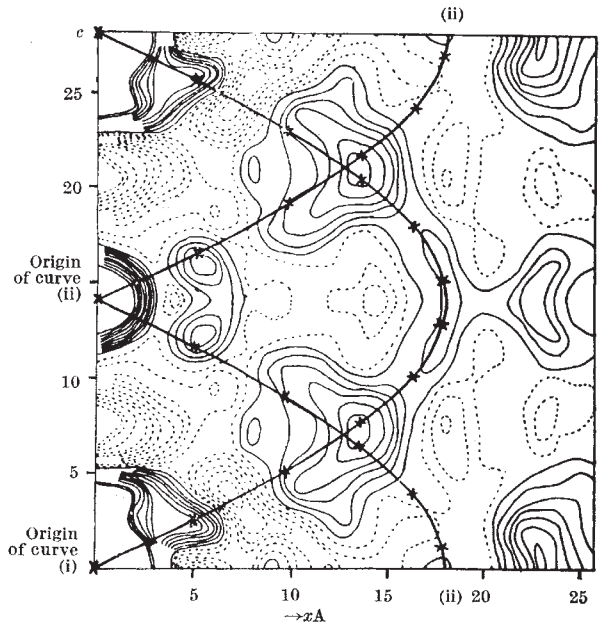


Fig. 3 (from ref. 4). Cylindrical Patterson function of crystalline sodium deoxyribonucleate, that is, the A form. The two curves (i) and (ii) show the theoretical Patterson function for two smooth coaxial helices of radius 9 Å separated by 14 Å (half their pitch) in the axial direction. The agreement is even better when account is taken of the fact that the real structure contains not smooth helices but eleven phosphate groups evenly spaced along such helices: the crosses mark the theoretical peak for *intra*-helical P—P vectors. (The remaining peaks on the maps are produced by *inter*-helical P—P vectors. See Fig. 2 of the same paper and also ref. 5.)

fibres. They assembled an Ehrenberg fine-focus tube together with a Phillips microcamera for taking high resolution photographs of single fibres of DNA. In order to search for further reflexions on or near the fibre axis direction, a microcamera was later designed specifically for the purpose of photographing specimens inclined to the X-ray beam at a series of angles.

The Discovery that DNA had Two Structural Phases

Simultaneously with the improvements in X-ray technique, a systematic search was also initiated to find the best conditions for producing fibres with high crystallinity, starting from the observation of Wilkins and Gosling that high humidity was required to produce good photographs. This work showed—for the first time—that at very high humidities a well defined structural change occurs leading to a new type of fibre diagram—structure B[1]. It was realized that all the earlier published X-ray patterns of DNA corresponded to a mixture of the crystalline form, structure A, obtained at about 75 per cent relative humidity and already found by Wilkins and Gosling, and this new structure B found by itself only at higher humidities. This different structure, structure B, showed a lower degree of crystalline order—that is, a paracrystalline structure—and, once formed, it persisted for a wide range of humidity and water content. The change from A to B was shown to be reversible. The existence was demonstrated of intermediate states consisting of mixtures of A and B, so explaining for the first time the difficulties of earlier workers who had been attempting to interpret such mixtures as a single phase.

These structural changes discovered when the water content of the fibres was varied suggested to Franklin that the fundamental structural unit of DNA was a group of polynucleotide chains ("molecules" in her terminology at the time) so arranged that the phosphate groups are exposed and accessible to water. The group of chains would be linked together by hydrogen bonds between the bases which would be in the centre of the molecule turned inwards from the water. This, of course, is a correct

picture. It was arrived at by the following reasoning. In structure B the structural units of DNA would be relatively free from the influence of neighbouring molecules, each unit being shielded by a sheath of water. In support of this view, Franklin cited the electrometric titration studies of Gulland, Jordan and Taylor (1947), which were entirely consistent with the conclusion that the phosphate groups lie on the outside of the structural unit. Because the change from the crystalline structure A to the wet para-crystalline state B is readily and rapidly reversible, it seemed reasonable to suppose that the molecules or small molecular aggregates of the wet state could easily be derived from the grouping existing in the crystal structure. In structure A one might therefore also expect to find a small group of chains held together as a unit by hydrogen bonds between their base groups, and these units linked in crystalline array by intermolecular phosphate bonds, mediated by cations and water.

The careful, systematic experimental work, which made possible the characterization of the two states of DNA, also led to the production of the best specimens. When photographed on the high resolution apparatus, these specimens gave photographs of exceptional quality including the particular B pattern photograph—dramatically described in Watson's book as the key photograph (Fig. 1). The reason for this is that it shows in a direct manner that DNA in the B form is a helix with an axial repeat of 34 Å and an axial spacing between nucleotides of 3·4 Å. The model building by the Cambridge workers which gave the correct phosphate–sugar backbone was carried out to fit these parameters[10].

Analysis of the Diffraction Patterns

The paper, in which these results and interpretations are presented, was submitted for publication on March 6, 1953, before the announcement of the Watson–Crick model in April, but it was only published in September[1]. In this paper, the chief purpose of which is to report the observations on the different states of DNA and to present preliminary interpretations, Franklin states clearly that the B pattern photographs she had obtained were very strongly characteristic of a helical structure. (This refers to the "helical cross" as it is now sometimes called.) Her notebooks at this time show that, although Franklin knew the B pattern to correspond to that of a helical molecule made of a number of intertwined, coaxial chains each containing ten nucleotides per turn, she was not certain about the number of chains. Her measurements of density and water content on the A and B forms had indicated that there were either two or three chains per DNA molecule. She was applying helical diffraction theory to the B form and by March 1953 she was in favour of two chains per molecule. Measurements of the position of the innermost reflexions on the non-equatorial layer lines of the X-ray pattern pointed strongly to the presence of two chains, but the intensity distribution on the equator was, by its nature, more difficult to interpret. This analysis of the B pattern in terms of helical diffraction theory is given in her April paper with Gosling in *Nature*[3]. But in March she apparently did not feel convinced enough of the relevance of this analysis (because she had not solved the A form) to embody it in the paper referred to here. In any case, a premature proposal would have been contrary to her policy. At the same time she was studying the Patterson function of the A structure, which also indicated there were only two chains passing through the lattice points of the primitive unit cell, but her notebooks indicate that she did not understand the detailed relation between the two forms.

Indeed, despite her discovery of the simpler B pattern, Franklin's attention throughout 1952 was mostly directed towards the A pattern rather than the B, even though it did not lend itself to such immediate interpretation because it corresponded to a structure in which the molecules were not free but packed in a crystal lattice. The A structure offered the possibility of an objective crystallographic analysis because of the greater wealth and precision of the diffraction data available (Fig. 1). If correctly interpreted, the A pattern would yield more precise information about the DNA molecule, though, of course, any proposed model for DNA must be capable of forming either structure A or structure B. Franklin was proposing to analyse the Patterson function calculated from the X-ray data on the A pattern, perhaps even to obtain a direct solution of it by superposition methods. (The Patterson function, in essence, presents the information contained in the X-ray pattern in a generally more useful form for interpretation in terms of structural models: it embodies no assumptions, using nothing other than the observed intensities. In the case of nucleic acids, the principal features in the map of the Patterson function relate to the distribution of the phosphate groups, for these are the heaviest in the structure.) Most of the second paper in *Acta Crystallographica*[2] concerns the problem of treating the experimental data to deduce integrated intensities of reflexions from the fibre diagrams of the A structure—again a model piece of pioneering work which was to be the basis for later quantitative work in this field.

Alternative Structures for the A Form

In the *Acta Crystallographica* papers of March 1953, which were intended to be the first of a series, Franklin offers no interpretation of the configuration of the molecules in the crystalline A form. The A diffraction pattern shows an absence of reflexions near the meridian, as would be expected for a helical structure, but it does not show the characteristic "helical cross" observed in the B pattern. This type of pattern could also be given by alternative structures in which rods or sheets are inclined to the fibre axis. In Franklin's view, a thorough and quantitative analysis, by use of the Patterson function, could decide between the possibilities, without resorting to any assumptions.

It is relevant to note that at an earlier stage in 1951–52, before the quantitative data had been collected, Franklin had been thinking of a helical structure for A, in agreement with the view of Wilkins and Stokes. This is clear from the report on her first year's work which she submitted in connexion with her Turner–Newall fellowship. The unit cell of the crystal in a plane perpendicular to the fibre-axis was near-hexagonal, that is, of a type which lends itself to the packing of cylindrical molecules, and the cylindrical molecule would itself be produced by the packing of a number of co-axial helical chains. The reason for Franklin's reversal in 1952 of this (correct) view involves technical matters which are dealt with at greater length in the appendix. Briefly, a diffraction pattern produced by inclined rods or sheets would also show departures from cylindrical symmetry (in the "form function"), and there was some clear evidence of such departures. Franklin, instead of dismissing these observations as resulting from a small perturbation in the molecular structure produced by the interactions in the crystal lattice (as Crick argued), seems to have been swayed by them into first questioning and then doubting whether the A structure was helical at all. She had early on observed a large decrease in length (30 per cent) of the fibres during the B to A transition, strongly suggesting some intramolecular re-arrangement. Could it be that the helices of the B state had been completely unwound to produce a quite different structure in the A state? But, whatever the case, any tentative opinion she held about the structure would, according to her plan of campaign, be settled by the analysis of the Patterson function: "No attempt will be made to introduce hypotheses concerning details of structure at the present stage."[2].

In summary, then, her resistance in the winter of 1952–53 to a helical structure, as described by Watson

(*Continued on page 843*)

(*Continued from page 810*)

and mentioned by Hamilton, applied only to the A form and not to the B form. In any case the whole question was to be resolved by a thorough crystallographic analysis. Franklin's notebooks show that a study of the Patterson function of the A form had indicated that there were phosphate groups lying 5·7 Å apart in certain directions. In January 1953 she began model-building to find what arrangement of the backbone chain could give such P—P distances. Furthermore, she had deduced that there were only two chains passing through a primitive unit cell in the structure, a conclusion not dependent on whether the chains were helical or not. Because the A to B transformation was readily reversible it seemed likely that the chains could also be arranged in groups of two in structure B, in agreement with her tentative interpretation of the independent data on that form.

It is interesting to note that—as she later told me—Franklin did not appreciate the significance of the fact that the space group of the A form was C2. This implies that the unit cell contains either four asymmetric molecules or else two molecules each with a two-fold axis of symmetry perpendicular to the fibre axis. The former possibility was ruled out by Franklin's density measurements, but she was not enough of a formally trained crystallographer—nor apparently was anyone else at King's—to infer that the DNA molecules must therefore possess perpendicular dyads. Of the protagonists, only Crick seems to have appreciated this fact—indeed the space group of the crystal of horse haemoglobin on which he had been working was C2, identical with that of the A form of DNA. (Franklin's background was that of a physical chemist and immediately before she came to King's she had been working on X-ray scattering from amorphous carbons—a field in which she made very important contributions (see obituary notice by Professor J. D. Bernal in *Nature*, **182**, 154; 1958).)

Testing the Watson–Crick Model

While Franklin was busy with this analysis the Watson–Crick structure was proposed. Franklin thought the model entirely reasonable because it contained some of the features she was already familiar with and explained her puzzles away. Her first act was to test the B pattern[3] in terms of the model, for this pattern, rather than the A, lent itself readily to the direct application of helical diffraction theory. The X-ray data were shown to be compatible with a helix of two intertwined polynucleotide chains, each containing ten nucleotides per turn in a distance of 34 Å. The two helical chains are not equally spaced along the fibre axis, but one chain is displaced from the other by about three-eighths of the fibre axis period. The phosphate groups lie on the outside of the structure at a radius of 10 Å.

Next came the turn of the A structure, for which very precise data were available embodied in the map of Patterson function. In the second communication[4] in *Nature* published in July 1953, Franklin and Gosling showed conclusively that the A form also contained two-chain helical molecules of the same type as found in the B structure. This was done by a most elegant application of the cylindrically averaged Patterson function which Franklin and Gosling had already calculated. The run of the two helical chains and the intra-helical phosphorus-phosphorus vector can be seen directly in the map (Fig. 2). Each chain of the double helix has eleven nucleotides per turn (compared with ten in the B form) repeating in a distance of 28 Å, and the two chains are equally spaced along the fibre axis. (The number of eleven nucleotides per chain was suggested by the fact that the only near meridional reflexion in the X-ray diagram of structure A was a rather weak one on the eleventh layer line. This observation was made on the special X-ray camera specifically designed for photographing tilted specimens.)

This structure is sufficiently close to that of the B structure to explain the reversibility of the A→B transition (Fig. 2). In the A form the bases are no longer perpendicular to the fibre axis as they are in the B form, but are tilted about 25° from the perpendicular position in a way that allows the fibre to contract 30 per cent and reduces the longitudinal translation of each nucleotide to 2·5 Å. These conclusions were later confirmed by Wilkins and his co-workers in their first paper on the A form published in October 1953 (ref. 11), which took up the study of structure A where Franklin and Gosling had left it.

Franklin left King's College for Birkbeck College in March 1953 to take up the study of the structure of tobacco mosaic virus in the laboratory of Professor Bernal. But, before she finally gave up her work on DNA, a final paper was published with Gosling[5] reporting the interpretation of the three-dimensional Patterson function. The use of three-dimensional data made it possible to determine the orientation of the helical molecule in the unit cell and also the positions of the phosphate groups along the helical chains. The paper is not as complete as it might have been—she told me at the time that she was not very satisfied with it—for she had not been able to devote herself to the details of the analysis and to its writing. She was already deeply involved with her new work on TMV, and in any case the essential features of the DNA configuration had been established.

Appendix—The Helix Question

Watson and Hamilton have both written about Franklin's "anti-helical" view without explaining the context of this opinion. Franklin had decided that there were sufficient discrete reflexions in the diffraction pattern of the A form to settle the question of the existence of helices in this form by an objective crystallographic analysis, without any assumptions having to be made. Indeed, if there is a phase in Franklin's work that can be called "anti-helical", there is equally an earlier pro-helical phase. This can be found in the official report on her first year's work which she submitted in February 1952 in connexion with her Turner–Newall fellowship, and also in her notes for her talk at King's College in November 1951—the lecture which Watson describes attending in his book. In the report she states that general features of the crystalline (A) pattern—and also those of the wet form (later known as B)—suggest a helical structure and that the 27 Å layer line spacing of the A structure probably corresponds to one turn of a helix. Furthermore, she points out that the unit cell of the A structure is nearly hexagonal in projection, therefore suggesting that the structure is built up of near-cylindrical units, that is, molecules such as would be produced by the packing of a number of co-axial helical chains. The report concludes as follows: "The results suggest a helical structure (which must be very closely packed) containing probably 2, 3 or 4 co-axial nucleic acid chains per helical unit and having the phosphate groups near the outside."

It must, however, be remembered that the patterns she was dealing with were fibres or rotation photographs in which the inherent three-dimensional data are to be had only in two-dimensional form, leading to certain possible ambiguities of indexing of the patterns. As she proceeded with the collection of quantitative data, she noticed in 1952 that there might be a very definite asymmetry in the form function of the molecules in the crystal and therefore in this structure itself. If this were the case the structure could not be helical unless the helix were considerably distorted. Franklin also appears to have been greatly influenced in this back-tracking from a helical structure by the discovery[2] of double orientation of the crystallites in a fibre of the A form. It seemed unlikely to her that this phenomenon could have occurred at all if the individual molecules had a high degree of symmetry about the fibre axis. Furthermore, she had earlier observed that during the change "crystalline to wet" (that is, A→B, in the later terminology) a considerable

increase in length of the fibres occurs, and in the annual report referred to here she is careful to state that "the helix in the wet state is therefore presumably not identical with *that* [my italics, A. K.] of the crystalline state". With this *caveat* in her mind, it was quite natural in the context of the new observations to think that the A structure might not be helical at all and to explore structures that were not helical.

Her premises can be summarized as follows: although there were clearly helices present in the B structure, these might be so distorted, or even undone, by the intermolecular bonds in the crystalline A structure that she had to consider non-helical structures. But a plausible A structure would have to satisfy certain criteria which her own investigations on the A and B transition had established, namely, that, whatever happened to the chains, the transformation must be reversible, and the phosphates must lie on the outsides, that is, towards the water, in all arrangements.

Her notebooks for the winter of 1952–53 show her considering a variety of structures including sheets, rods made of two chains running in opposite directions with interdigitated bases and also a pseudohelical structure with non-equivalent phosphate groups which looked like a figure of eight in projection. In January 1953 she began model-building to limit the structures to stereochemically possible ones; she attempted to fit these structures to the three-dimensional Patterson function of the A form which had been calculated in 1952. This had told her that there were phosphate groups lying 5·7 Å apart in certain directions. What a Patterson function (by its nature) could not tell her directly was whether these vectors referred to phosphates on the same or different chains. Not surprisingly, however, none of these structures fitted the Patterson. Furthermore, some of them could be ruled out by reference to the B form which was also constantly in her mind. In her notebooks we see her shuttling backwards and forwards between the data for the two forms, applying helical diffraction theory to the B form and trying to fit the Patterson function of the A form. We also find her trying to fit in the bases, using Chargaff's analytical data, and returning again and again to the densities and water contents of both forms from which information she checked the number of chains. At the same time she was trying to solve the Patterson directly by superposition methods[5].

By February she knew that there were two chains per unit cell in the A structure and she was considering a structure with eleven nucleotides per chain. But, although she knew that there were ten nucleotides per helical chain of the B structure, and that there were very likely two such chains in the B helix, she did not see the relation between the two structures, perhaps because she could not extricate herself readily from her deep commitment to solving the Patterson function without *a priori* assumptions, a course which required consideration of non-helical structures. The answer, which she did not arrive at before the Watson–Crick model was proposed, is, of course, surprisingly simple. Both structures are helical and related in a simple manner as I have described.

There is, of course, no telling what would have happened had the Watson and Crick structure not intervened, but I would venture to suggest that she would finally have seen—and perhaps not much later—the relation between the A and B forms. Whatever might have happened, one can see that the "anti-helical" view was not a fad or "mere perversity". The stage reached by Franklin at the time is a stage recognizable to many scientific workers, when there are apparently contradictory, or discordant, observations jostling for one's attention and one does not know which are the clues to select for solving the puzzle. As Watson's book has made clear, there was no inexorable logic on the part of any of the protagonists leading directly to the solution. For example, a question that might have been put at the time was which of the forms of DNA, A or B, was the one more closely related to DNA in its natural state. There must be some intramolecular rearrangement in the A and B transition. Was one of the two structures more fundamental than the other? With the benefit of hindsight the answer is obvious, namely, the one closer to DNA in solution, that is, the wet or B form which shows no further changes in structure as the hydration is increased right until the stage when the DNA passes into solution. It should be added that, near the end of 1952, Wilkins and Randall reported[12] a similarity between the X-ray photographs of sperm heads and those of fibres of pure DNA, but the periodicities were not sharply defined and no assignment to one of the two known—but as yet unpublished—forms was reported. The sperm head patterns were not classed as B until later[7]. It seems fair to conclude that there was no compelling experimental evidence on the biological side to persuade Franklin to switch her principal analytical effort from the A to the B form.

But if, for a time, Franklin was moving in the wrong direction in one aspect, then there are clear indications that equally she was moving correctly in another. In the first paper[1] Franklin also gave attention to the problem of the packing of the bases. She discussed the existence of small stable aggregates of molecules linked by hydrogen bonds between their base groups and with their phosphate groups exposed to the aqueous medium. She discusses the obvious difficulty of packing a sequence of bases which follow no particular crystallographic order and the state of her thinking can be seen in the following extract from her March 1953 paper:

"On the other hand it also seems improbable that purine and pyrimidine groups, which differ from one another considerably in shape and size, could be interchangeable in a structure as highly ordered as solution A. A possible solution, therefore, is that in structure A cytosine and thymine are interchangeable and adenine and guanine are interchangeable, while a purine and a pyrimidine are not. This is suggested by the remarkably similar crystal structures found by Broomhead (1951) for adenine and guanine hydrochlorides. In this way an infinite variety of nucleotide sequences would be possible, to explain the biological specificity of DNA."

Base interchangeability is, of course, a long way from the final truth of base pairing, but in the context of the crystallographic analysis in which Franklin was engaged—an analysis which could provide a solution to the regularly repeating parts of the structure—the idea would have been essential to fitting in the variable parts. In his book Watson wrote that Franklin's "instant acceptance" of the Watson–Crick model amazed him at first. But he went on to say that on further reflexion it was not so surprising to him. It is not in the least surprising when one studies her papers and notebooks and realizes how close she herself had come in the progress of her work—albeit in disconnected fashion at different times—to various features of the structure contained in the correct solution.

Papers by R. E. Franklin and R. G. Gosling

[1] The structure of sodium thymonucleate fibres. I. The influence of water content. *Acta Cryst.*, **6**, 673 (1953).
[2] The structure of sodium thymonucleate fibres. II. The cylindrically symmetrical Patterson function. *Acta Cryst.*, **6**, 678 (1953).
[3] Molecular configuration in sodium thymonucleate. *Nature*, **171**, 742 (1953).
[4] Evidence for 2-chain helix in crystalline structure of sodium desoxyribonucleate. *Nature*, **172**, 156 (1953).
[5] The structure of sodium thymonucleate fibres. III. The three-dimensional Patterson function. *Acta Cryst.*, **8**, 151 (1955).

Other references

[6] Gosling, R. G., thesis, Univ. London (1954).
[7] Wilkins, M. H. F., Stokes, A. R., and Wilson, H. R., *Nature*, **171**, 739 (1953).
[8] Watson, J. D., and Crick, F. H. C., *Nature*, **171**, 737 (1953).
[9] Sutherland, G. B. B. M., and Tsuboi, M., *Proc. Roy. Soc.*, A, **239**, 446 (1957).
[10] Crick, F. H. C., and Watson, J. D., *Proc. Roy. Soc.*, A, **223**, 80 (1954).
[11] Wilkins, M. H. F., Seeds, W. E., Stokes, A. R., and Wilson, H. R., *Nature*, **172**, 759 (1953).
[12] Wilkins, M. H. F., and Randall, J. T., *Biochim. Biophys. Acta*, **10**, 192 (1953).