From: B. Maddox, Rosalind Franklin: The Dark Lady of DNA (Harper: 2002)

TWELVE

Eureka and Goodbye

(6 January–16 March 1953)

'Rosy, of course, did not directly give us her data. For that matter, no one at King's realised they were in our hands.'

James Watson, *The Double Helix*

THE SECRET OF LIFE, four billion years old, was unpicked in a drama that moved day by day, almost hour by hour, in the first seven weeks of 1953.

News that Linus Pauling and Robert Corey had solved the structure of DNA started the clock running. On 6 January Rosalind, who somehow had got wind of the news, wrote Corey at Caltech and asked for details. They had been in correspondence since May when he had marvelled at her 'splendid X-ray photographs of nucleic acid fibres'.

Her notebooks show intense activity as January progressed. She herself had started to think of building a model of the A form based on her Patterson calculations. Might these represent a figure-eight shape – two coils crossed in the middle? Or paired rods? She knew of Chargaff's ratios and tried to squeeze the four bases of DNA into a structure with the phosphates on the outside. They would not fit. Still bemused by the discrepancies between the A form and the B form, she accepted that the B form was a two-chain helix but still had doubts about the other. As her later collaborator Aaron Klug was to comment, 'The stage reached by Franklin at the time is a stage recognisable 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.'

She had been at work for a week when Peter Pauling returned to Cambridge from his winter break in Germany and Austria. On 13 January he wrote his father to ask for a copy of the Pauling-Corey paper on DNA, adding that the Cavendish's MRC Unit would like one too. He prefaced the request with a joke:

> You know how children are threatened 'You had better be good or the bad ogre will come get you.' Well, for more than a year, Francis and others have been saying to the nucleic acid people at King's, 'You had better work hard or Pauling will get interested in nucleic acids.'

Pauling sent the paper, confident that he had scored another victory over Sir Lawrence Bragg, his old rival at the Cavendish. In fact, he sent two copies of 'A Proposed Structure for the Nucleic Acids' to England, one to Peter and the other to Bragg. Peter replied, 'We were all excited about the nucleic acid structure. Many thanks for the paper. Second sunny day since I have been in England.'

The paper appears to have arrived on 28 January, and there was indeed excitement at the Cavendish. When Peter brought the paper to the lab, Jim Watson had to restrain himself from grabbing it out of Peter's hand. He held back, impatiently listening to Peter's summary, until he yanked it out of Peter's outside pocket and read it for himself. Instantly he saw that Pauling's proposed structure – a triple-stranded helix with the phosphates at the centre – was much like the mistaken model that he and Francis Crick had built in November 1951. Worse – or better, from Watson's point of view – Pauling had made a fatal chemical error. The phosphates were not ionised – that is, Pauling had not built in the electrical charges phosphates acquire when in water. What he was proposing as a structure for nucleic acid was not an acid at all.

Pauling had made the silly mistake because he was in a hurry. But why? There has been much retrospective speculation on why one of the world's greatest chemists, the holder of the Presidential Medal for Science, the author of the classic textbook on the nature of the chemical bond, should have risked his reputation by rushing into print with a carelessly flawed proposal. One suggestion was that Pauling, having cracked the structure of protein, wanted credit for solving the other half of the cell's secrets. Another is that, for all his many honours, Pauling had never won the Nobel prize. Pauling later said that his wife once asked him why he hadn't cracked the problem and that, upon reflection, his answer was: 'I guess that I always thought that the DNA structure was mine to solve, and therefore I didn't pursue it aggressively enough.'

Watson's delight in the error was tempered by the news that the Pauling paper would soon be published in February in the *Proceedings of the National Academy of Sciences*. The mistake would immediately be spotted and Pauling would be on the trail again. Watson felt he and Crick had about six weeks' breathing space.

Also on 28 January Rosalind gave her leaving seminar at King's. Maurice Wilkins thought she was long-winded; he strained to hear the word 'helix' and did not. Neither did Herbert Wilson, who took notes. She did not refer to the B form of DNA, nor show the superb Photo 51, but concentrated instead on the recent experimental work of herself and Gosling that suggested that the A form of the molecule was not helical.

For J.T. Randall, an unwelcome sight at the end of that month was Jim Watson. The gawky young American from the Cavendish seemed always to be turning up at King's College London. One morning Randall went in to the coffee club that met daily in Angela Brown's room and there was Watson, grinning. 'Here's the Dean of St Paul's!' he wisecracked. Randall's pompous Christmas letter to *The Times* had been the subject of general mirth in the lab.

No one else talked to the inventor of the cavity magnetron like that. Randall was furious. Once Watson was gone, he boomed out, 'Never let that man in my sight again!' Out of sight, however, was not out of mind.

Rosalind did not like the sight of Watson either. On 30 January the door to her office opened and in he came. The only published account of what ensued is his: a pivotal scene in *The Double Helix:*

> Since the door was already ajar, I pushed it open to see her bending over a lighted box upon which lay an X-ray photograph she was measuring. Momentarily startled by my entry, she quickly regained her composure and, looking straight at my face, let her eyes tell me that uninvited guests should have the courtesy to knock.

Watson asked her whether she wanted a look at Pauling's manuscript, and getting little response, rushed on to point out where Pauling had gone astray. She countered with her own evidence that a helical structure was by no means proven. But Watson had heard from Wilkins that Rosalind was 'definitely anti-helical' – neither of them having seen her evidence. (The Birkbeck crystallographer, Harry Carlisle, wrote in his memoirs, 'I am convinced from Rosalind's excellent X-ray studies on both the A and the B forms of DNA that she was not in the least "anti-helical" at that time as suggested by Watson in *The Double Helix*.') He felt that Rosalind was more concerned with extracting positive arguments from her X-ray data.' For his part, Watson decided that she did not know what she was talking about:

> I was more aware of her data than she realised. Several months earlier Maurice had told me the nature of her so-called anti-helical results. Since Francis had assured me that they were a red herring, I decided to risk a full explosion. Without further hesitation I implied that she was incompetent in interpreting X-ray pictures. If only she would learn some theory, she would understand how her supposed anti-helical features arose from the minor distortions needed to pack regular helices into a crystallising lattice.

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

'Fearing that in her hot anger she might strike me': the patent absurdity of this remark has caused much scorn. Rosalind was of slim build and medium height, Watson a stringy six feet plus. But the male fear of the female has always been absurd – the stronger afraid of the weaker – but no less real for that. To dismiss it is to dismiss the Medusa, the Loathly Lady, the Wicked Witch of the West and all the other guises for whatever the male resents and recoils from in the female; that led even the mild-mannered graduate student John Cadogan to say of Rosalind, 'She nearly terrified the living daylights out of me.'

Watson's own bewilderment with women is well chronicled in *The Double Helix*. He could not approach them unselfconsciously: they were either prey – 'popsies' or 'au pairs' – or goddesses such as his aristocratic Scottish hostess Naomi Mitchison or his sister Elizabeth. Rosalind was neither; worse, she was an angry woman. And she had reason to be angry. Courtesy might have demanded that Corey send a copy of their DNA paper to her, not to the Cavendish.

Watson portrays Rosalind's 'hot anger' as entirely unmotivated. There is another possible explanation for her rage – indeed of the whole incident. Early in 1953, very upset, she complained to a friend at King's that she had come back to her room one day and found her notebooks being read. If Randall and Wilkins saw themselves as her bosses, she stormed to her confidant, they should have protected her work better. Instead, she knew Wilkins to be in open and frequent communication with the Cavendish pair. She voiced her fears also to an old colleague from BCURA.

* * *

She herself was engaged in a race against time. Due to move to Birkbeck in the middle of March, she was rushing to finish up as much as possible of the Patterson interpretation of the A form of DNA before she left King's. She was working hard on three papers (to be published jointly with Gosling) so as to hand them to Randall before she left; his permission was needed before anything was sent out to other readers, let alone for publication. Two papers were for *Acta Crystallographica*. In them she was formally announcing to the scientific world what she had discovered at King's: the existence of DNA in two forms, and the conditions for readily and rapidly changing from one to the other. She described the DNA molecule. Its phosphates were on the outside, thus exposed and ready to take up water: making hydration, and therefore stretching, easy. Thus shielded in a sheath of water, the DNA was 'relatively free from the influence of neighbouring molecules'. She appended to the first paper the startlingly clear X-ray photographs she and Gosling had taken of both forms. The second paper gave the measurements on the x-ray pattern of the A form on which she and Gosling had concentrated in the past six months: full of the kind of information that crystallographers would appreciate. The third, a shorter paper, was a more general summary of their findings on the B form.

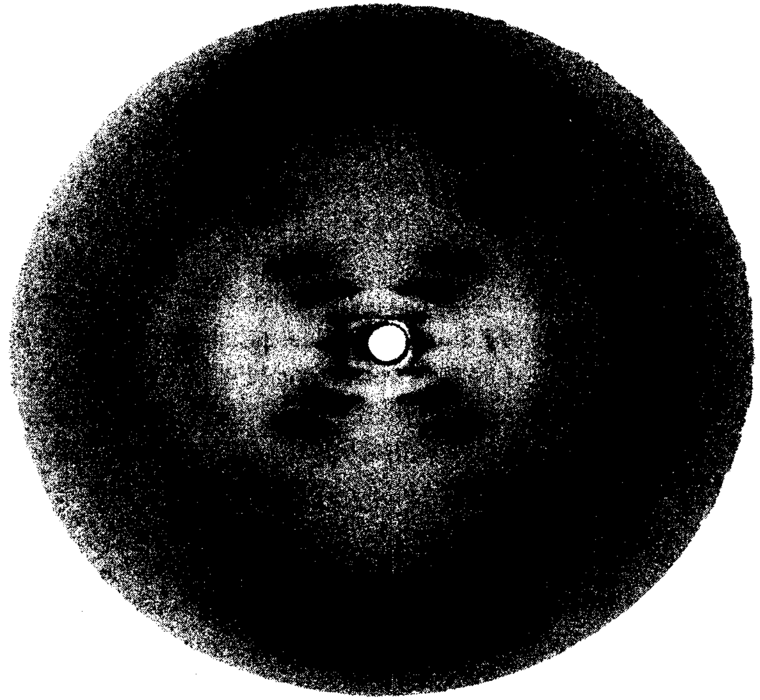
As Watson retreated from Rosalind's wrath, he was rescued from his fantasised assault by Maurice Wilkins, who had put his head round the door. Wilkins consoled him that some months earlier, 'she had made a similar lunge at him' and had blocked the door when he wanted to escape. As Wilkins poured out his 'see what I'm up against' tale of woe, he reiterated what Rosalind had said in her 1951 colloquium about the two forms of DNA and complained that he had been left to use only samples given him by Erwin Chargaff in New York, which would not produce the A to B transition. Rosalind's Signer fibres had produced much better patterns. 'She's got a very good B,' said Wilkins.

Wilkins had not known of Rosalind's excellent diffraction photograph numbered 51, taken eight months earlier, until Gosling brought it to him sometime that January. Gosling, preparing to complete his thesis without Rosalind's supervision, had every reason to show what was also his own current work to the assistant head of the department. 'Maurice had a perfect right to that information,' Gosling said, looking back. 'There was so much going on at King's before Rosalind came.' Both he and Wilkins knew the DNA research would continue after she left.

Unguardedly, Wilkins showed Watson Photo 51. There were many diffraction photographs of DNA around the lab; this one was simply the best. As the information in it was not new to Wilkins – Rosalind had related many of the details in her symposium in 1951 – he had no idea it would strike Watson with the force of revelation. Nor did he have any idea that Watson was about to make a new stab at building a model of DNA.

But Watson was now wiser than in late 1951 when he had botched his first model. A year of working on the tobacco mosaic virus had educated him, as had reading the Cochran–Crick–Vand paper on helices. He was now able to sweep up at a glance the meaning of Rosalind's photographic image: unbelievably clear evidence of a helix, with detectable parameters of tilting and spacing. It was with little exaggeration that he wrote in *The Double Helix*: 'The instant I saw the picture my mouth fell open and my pulse began to race.'

The two men had dinner that night in Soho. What Wilkins wanted to talk about was Chargaff's ratios and the possibility that they might hold the key to DNA's structure. Watson, however, pressed for numbers to go with the pattern he had just seen. He extracted a few. The repeat (the length of one turn of the helix) of the B form was 34.4 Ångströms – ten times the spacing between the bases stacked 3.4 Ångströms apart. On the train back to Cambridge, Watson drew the pattern from memory on the only paper available, the margin of his newspaper. It was stark enough to fit in the small space. In his mind there still lurked the possibility that the molecule might have three helical chains. As he cycled



Rosalind's Photograph 51 (shown original size) of the B form of DNA, which told Watson that the molecule was a helix.

home from the train, mulling over Rosalind's photograph with its dark cross, he decided on two. 'Francis would have to agree,' he later wrote. 'Even though he was a physicist, he knew that important biological objects come in pairs.' (According to Crick, the argument was more complicated than that.)

Events then moved fast. The following day, 31 January, Bragg unleashed Watson and Crick. He consented to Watson's request to order metal components from the workshop to begin model-building again. Having Linus's DNA paper in hand, Bragg was not about to repeat the worst mistake of his life. The thinking at the Cavendish seems to have been, 'We missed out on the fibrous protein. Now Pauling is going to get the DNA as well.'

When Rosalind started her modelling attempt of the A form, she found her paired-rod structures would not work. She then moved to a figure of eight in which a single chain formed a long column of repeating eights. But by Monday, 2 February, she ruled out the figures of eight as well.

On Wednesday, 4 February Watson started building. His sketch of Rosalind's Photo 51 confirmed to Crick that they had the right figures with which to put together a B-form model: 20 Å diameter, 3.4 Å vertical distance between the bases, repeat distance of 34 Å and helical slope of about 40 degrees. Although Crick was not entirely convinced that there should not be three chains, Watson was set on two. Once more the disputed phosphates formed the central core, ignoring Rosalind's argument in 1951 that these water-attracting groups had to be on the outside of the molecule. Crick has supplied the dialogue which shows teamwork in action: '"Why not," I said to Jim one evening, "build models with the phosphates on the outside?" "Because," he said, "that would be too easy" (meaning there were too many models he could build in this way). "Then why not try it?" I said.'

Watson obliged. Crick's other crucial action on 4 February was to invite Wilkins to come up to Cambridge for lunch on Sunday. Wilkins accepted, saying gullibly, 'I will tell you all I can remember and scribble down from Rosy.'

On Sunday, 8 February Wilkins arrived to lunch and found that the Cricks had two other guests, eager listeners: Watson and Peter Pauling. When the three men urged him to start model-building to get ahead of Linus, Wilkins vowed to do so as soon as Rosalind was clear of the premises. Watson and Crick wrung from him a grudging consent that they themselves could try again – without telling him that they had already started. Wilkins suddenly realised he was dealing with an awkward situation and left early for London. Had he said too much?

Perhaps he had, for sometime during the following week Watson and Crick got hold of the MRC report on the biophysics committee's December visit to King's. It was given them by their

Cavendish colleague Max Perutz, a member of the committee. Whether Perutz *volunteered* the MRC report, or merely handed it over in response to a direct request from Watson or Crick, has been the subject of some dispute over the years as its importance to their efforts has come to be realised. Defensively, Perutz wrote in *Science* in 1969, 'I was inexperienced and casual in administrative matters and, since the report was not confidential, I saw no reason for withholding it.'

The MRC report was all Watson and Crick could hope for – as valuable as an enemy's code book. The section on Rosalind's work explained the change from the first to the second type of DNA structure, and specified, with a neat little table, the measurements of the 'face-centred monoclinic unit cell' 'with certainty'.

One glance, to Crick's well-stocked brain, translated Rosalind's information into a recognition that the crystalline form of DNA belonged to the space group called 'monoclinic C2'. The DNA crystal, in other words, looked the same when turned upside down. Crick instantly knew, therefore, that one chain of the two helices must run up and the other down; they were anti-parallel, like up-and-down escalators. Watson took some persuading, but had to accept Crick's better judgement: 'monoclinic C2' was exactly the space group Crick had been working with for his thesis on horse haemoglobin.

During the same week, on 10 February, Rosalind wrote in her notebook: 'Structure B: evidence for a 2-chain (or 1-chain) helix?' She did some calculations on the photograph numbered 49, then laid the B form aside for two weeks. She had her two long *Acta Cryst* papers to finish and get to the typist. (These must have been completed shortly after, for they were received by the journal's English editor on 6 March, for publication in late summer.)

The paper by Pauling and Corey was published by the National Academy of Sciences on schedule in February. Their proposal for

DNA's structure may have been all wrong, but their explanation of DNA's importance was excellent:

> The nucleic acids, as constituents of living organisms, are comparable in importance to proteins. There is evidence that they are involved in the processes of cell division and growth, that they participate in the transmission of hereditary characters, and that they are important constituents of viruses. An understanding of the molecular structure of the nucleic acids should be of value in the effort to understand the fundamental phenomena of life.

To cover their British flank, Pauling and Corey also sent a letter to *Nature*, which appeared on 21 February, announcing their structure. From that, if Rosalind had not already gleaned the fact from Watson's traumatic visit three weeks earlier, she could see that Pauling had misplaced the phosphates. She wrote to Pauling and told him so. It took courage for a thirty-two-year-old 'Attached Worker' to correct a world authority but she was sure of her facts. She explained why her data indicated that the phosphate groups had to be on the outside rather than at the core of the molecule. She also mentioned, as if talking to a friendly associate, that she had three papers on DNA underway awaiting Randall's approval.

Pauling remained convinced that he was right. He was working without the fine-focus X-ray equipment or the pure DNA that Rosalind had, relying on Astbury's pre-war X-ray diffraction patterns, on which the A and B forms were superimposed. Nonetheless, he politely promised to try to meet Rosalind when he came to England (having succeeded at last in getting his passport back). However, he confessed in a letter to Peter that when in London he would much rather see Pauline Cowan, whom he had met at Oxford. He did not remember ever having met Miss Franklin but he had heard the previous summer that she was leaving King's; Corey had a very good opinion of Wilkins. Linus passed on to his son the information that Rosalind was working on three papers on DNA. As for his own structure, he could see

that it was a 'tight squeeze' but he and Corey were checking it over and expected things to come out all right.

Two chains, yes, but what held them together? If the phosphates were on the outside of the molecule, the four bases always found in DNA would have to be squeezed inside, somewhere between the chains. The problem was that each of the four – the two purines, adenine and guanine, and the two pyrimidines, cytosine and thymine (often abbreviated to A and T, G and C) – had a different shape.

Mid-February saw Watson wrestling with the problem. He tried various combinations, using cardboard cut outs because the metal pieces had not yet arrived from the machine shop. First, on 19 February, he tried pairing like with like: the resulting pairs were either too small or too large for the diameter specified in Rosalind's MRC table. Then he tried joining a purine to a pyrimidine – A to T, C to G. Still they didn't fit.

At another desk in Room 103 was Pauling's former student, Jerry Donohue. Like watching someone fumble with a jigsaw, Donohue suggested that Watson was using the wrong pieces. Bases might exist in two forms – that called 'keto' makes an oxygen atom available for bonding in a different position from that in the contrasting form, 'enol'. Why not use the 'keto' form? Donohue asked. Because, Watson answered, in effect, J.M. Davidson's *The Biochemistry of Nucleic Acids* and other textbooks showed the enol forms. The textbooks were wrong, said Donohue. As a chemist, he passed the news on to Watson that 'enol was *out* and keto was *in*'.

On the last Monday of the month, 23 February, Rosalind probably after finishing her *Acta* papers, took out Photograph 51 and began her careful measurements of the B form. By the following day, she had accepted that the A and the B forms were both two-chain helices. 'Nearly home,' wrote Aaron Klug in his analysis of her notebooks years later.

It occurred to her that a way of explaining the Chargaff ratios – why DNA invariably contained the same number of A as T molecules and the same number of Cs as Gs – was that adenine and guanine were interchangeable, and so were cytosine and thymine. This interchangeability gave her a vision that 'an infinite variety of nucleotide sequences would be possible to explain the biological specificity of DNA'.

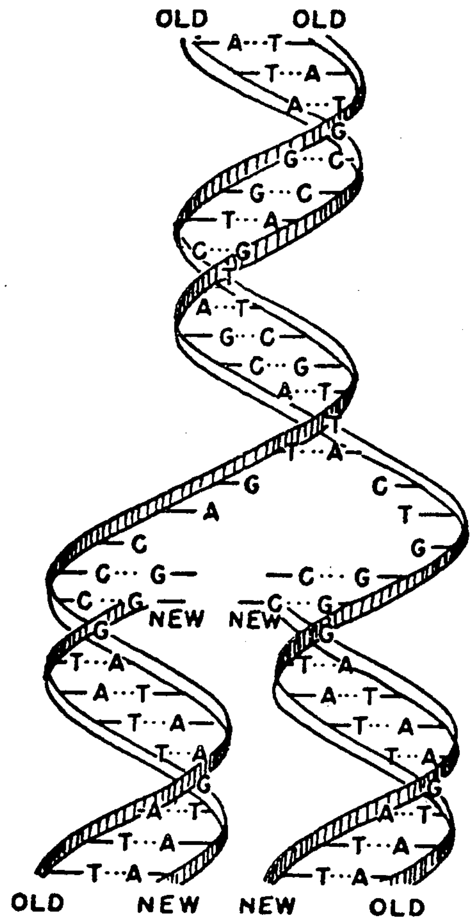
'Base interchangeability is, of course, a long way from the final truth of base pairing,' Klug acknowledged. She was two steps from the solution. Crick later ventured that she would have taken those steps within three months.

She did not. She failed to understand the significance of the monoclinic C2 space group or to figure out the bases joined in pairs to carry the genetic code. 'It is easy to feel sympathy with Franklin,' the science historian Horace Freeland Judson has written. 'The fact remains that she never made the inductive leap.'

But Rosalind had been trained, as a child, as a Paulina, as an undergraduate, as a scientist, never to overstate the case, never to go beyond hard evidence. An outrageous leap of the imagination would have been as out of character as running up an overdraft or wearing a red strapless dress.

The fact is that in two unhappy years, working in isolation except for Gosling, in a field new to her, she had come within two steps of answering the most exciting question in post-war science. What is more, she, unknowingly, had provided all the essential data for those who took the two brilliant leaps of intuition – to anti-parallel chains and base pairs – that cracked the problem.

Donohue's off-the-cuff advice about the 'keto' form tipped the balance for the Cavendish. Watson, fitting together his pieces of cardboard at the end of the month, suddenly noticed that adenine joined by hydrogen bonds to thymine formed the same shape as cytosine bonded to guanine. The paired pairs were congruent; Chargaff's ratios were explained. What is more, the same pairs were always found together. Adenine always grabbed thymine;



How the double helix copies itself. The two sugar-phosphate backbones are like the rails of a spiral staircase, with the paired bases, adenine and thymine (A and T) and guanine and cytosine (G and C), forming the steps. When the rails come apart, each of the bases seeks its invariable complement, and thus two staircases are formed, the new identical to the old.)

cytosine, guanine. Whenever any one of them appeared along the long DNA chain, the other was invariably across from it on the opposing chain. One side was therefore the inverted mirror image of the other. Split apart, each of the chains served as templates on which a new, complementary chain could be formed. Base pairs, therefore, held the secret of DNA – how characteristics pass from generation to generation, from cell to cell, from parent to child. The DNA molecule is a set of chemical instructions which reverses the tendency of matter to become disordered and allows new molecules to be the same as the old. The day was 28 February 1953. It was at lunchtime when (according to Watson's myth-making narrative) 'Francis winged into The Eagle and told everybody we had found the secret of life.'

Donohue later was one of many who felt that his part in the great discovery was underplayed. 'Let's face it,' he wrote in 1976, 'if the fates hadn't ordained that I share an office with Watson and Crick in the Cavendish in 1952–53, they'd *still* be puttering around trying to pair "like-with-like" enol forms of the bases.'

The patronising attitude of the Cavendish team towards Rosalind continued. As Peter wrote his father in March about the rivalry between the Cavendish and King's:

> Wilkins is supposed to be doing this work; Miss Franklin is evidently a fool. Relations are now slightly strained due to the Watson-Crick entering the field. They have some ideas & shall write you immediately. It is really up to them and not to me to tell you about it . . . They are getting pretty involved with their own efforts, and losing objectivity.

Never had Maurice Wilkins's gift for metaphor served him better. Exhilarated by the imminent departure of his nemesis, on 7 March, a Saturday, he wrote to Crick:

> I think you will be interested to know that our dark lady leaves us next week . . . I am now reasonably clear of other commitments and have started up a general offensive on Nature's secret strongholds . . . At last the decks are clear and we can put all hands to the pumps!
>
> It won't be long now.
> Regards to all
> Yours ever
> M

It was too late. Nature's secret strongholds had fallen to the pitchmen from the Cavendish. The final model of the double helix of DNA (or at least one turn of it; one entire DNA molecule, reproduced on that scale, would have been 50,000 miles high) had been finished on Saturday, 7 March. Crick was looking at it as he read Wilkins's letter.

Rosalind could write a strong letter too. On 10 March, with no idea of what had happened at the Cavendish, she poured her heart out to Adrienne Weill in Paris, saying that her prime concern was to get out of King's as fast as possible.

> I start at Birkbeck next week. It got delayed repeatedly – first because I missed a month with flu and things in the autumn, then because I thought another month would give me a lot more results – but it didn't, and I'm abandoning an unfinished job now in order to get out of King's without further delay. I don't know yet what I shall do at Birkbeck. In theory I do what I like, which probably means I shall waste a lot of time playing around with odds and ends before I settle to anything. As far as the lab is concerned, I shall be moving from a palace to the slums, but I'm sure I shall find Birkbeck pleasanter all the same.

On 12 March Wilkins made the journey to Cambridge to see for himself what he had learned on the telephone from Kendrew, Watson and Crick apparently being too embarrassed to tell him directly that they had cracked DNA. There stood the model, its elegance proclaiming its accuracy. Wilkins (unfortunately for Rosalind, King's being over-modest yet again) spurned any idea of joint authorship: 'I felt the model *as such* was their work. Crick agreed with alacrity.' Separate publication was decided upon. Wilkins then returned to London and, in his words, 'I told *everybody*.'

For Rosalind, the news that the Cavendish had cracked DNA was an irrelevant parting gift. She had confidence in her own two papers, on their way to publication, that would give solid data on DNA's structure, not a mere hypothesis. In any event, she and Gosling had their shorter paper on the B form nearly ready and she would turn her hand to polishing it up the following week.

Rosalind came to say goodbye to Freda Ticehurst and to thank the photographer for all she had done for her. She said (in Freda's recollection), 'I'm not wanted here – we [meaning Wilkins] could never work together. It's impossible for me to stay.' Her valediction delivered, she packed up, and turned her back on King's College London. One thought that certainly never crossed her mind was that half a century later the institution she despised would name a building after her, coupling it with the name of the adversary who had branded her forever as the 'dark lady'.