Francis Crick: Hunter of Life’s Secrets

An intellectual biography by Robert Olby

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FRANCIS CRICK: HUNTER OF LIFE’S SECRETS is a fascinating and scholarly biography of the man whose ideas and discoveries provided the basis for the remarkable revolution in the biological sciences in the second half of the twentieth century, comparable—if not exceeding—in importance the revolution in the physical sciences in the century’s first half. It takes full advantage of the many contemporary records and archives which cover the intellectual history of these times, and also of the extensive contacts that author Robert Olby had with Crick and his family beginning in the 1960s and continuing up to Crick’s death in 2004 at age eighty-eight.

However, this has not prevented Olby from dealing very fairly with some well-known matters of controversy. The book extends to some 538 pages, including about 50 pages of source notes for the numbered text references, chapter by chapter, and a 24-page index. It is an extraordinarily interesting story from many points of view, with sufficient scientific detail to explain most of the issues involved, and it provides a very clear picture of Crick and his work, though perhaps without some of the color, force, and light-hearted humor that only a recording of a conversation with him could convey (also, the large photograph of Crick as a very young graduate student, which appears on the front dustcover of the book, will be quite unrecognizable to those familiar with his strong characteristic features in subsequent years).

Olby does a particularly good job in placing the DNA structure in the context of the uncertainty in some quarters at that time about the nature of the gene—whether it would have to contain proteins as well as DNA in order to give a structure which contained sufficient information to define other protein molecules, given that DNA itself was apparently a relatively simple polymer of only four different nucleotides and formed fibers whose X-ray diagram indicated a very regular structural repeat. The structure that Watson and Crick arrived at was indeed very regular. From model-building, they determined that adenine-thymine base pairs between two chains would fit into a perfectly regular sugar-phosphate backbone in precisely the same way as the guanine-cytosine base pairs did—provided the two chains ran in opposite directions. Thus, any sequence of bases along one chain was permissible, and would give a regularly repeating structure, provided that the complementary sequence was present on the other chain. If DNA was the sole repository of genetic information (as it was seeming more likely at that time), then the genetic message must be written in the sequence of the bases which must be translated into the sequence of amino acids in the proteins by a specific genetic code. During replication, the two chains would separate, each would pick up a complementary set of nucleotides, and an exact duplication of the original gene structure would have been achieved. In principle, it was an extraordinarily simple solution to what had seemed two of the most difficult problems in understanding life without invoking miracles.

Much has been written about the ethics of Crick and Watson (in Cambridge) using Franklin’s data without her permission or knowledge and without detailed acknowledgement of the work in King’s College London in their initial Nature paper, (though it was composed with Wilkins’ agreement). Wilkins believed, perhaps correctly, that Franklin would not agree to be a joint author with him and he refused Crick’s invitation to be a joint author on the Watson-Crick paper because he had not participated in the model building. That is why there were two papers from the King’s group (Wilkins, Stokes, and Wilson; and Franklin and Gosling) immediately following the short Watson-Crick paper describing the structure, in April 1953.

When a more detailed paper about the structure was written by Crick and Watson (submitted in August 1953

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and published in Proc. Roy. Soc. A in April 1954), in the section headed “Crystallographic Considerations,” it is stated that “the information in this section was very kindly reported to us prior to its publication by Wilkins and Franklin, and we wish to point out that without this data the formulation of our structure would have been most unlikely, if not impossible.” The section then goes on to spell out what that data was—that the paracrystalline B-form of DNA had a very strong meridional reflection at 3.4 Å and a fiber axis repeat of 34 Å, with a sideways repeat of 22–25 Å—vital facts for the modeling, given that on general grounds the structure was thought to be helical (the “details of their X-ray photographs” which were not known to Watson and Crick, would have been the spacing of the Bessell functions’ maxima on the various layer lines). Reading this, Franklin must have been aware that these measurements of hers had been given to Watson and Crick prior to their solution of the structure, yet there is no evidence—in fact quite the contrary—that she raised any complaints, as surely she would have done if she felt she had been treated unfairly. But clearly, she should have been told directly.

The paper shows that for their structure to fit together properly, the two chains must run in opposite directions, which presumably their model building would have revealed anyway, but they do not mention the space-group evidence for this, which Franklin had overlooked, but which Crick realized immediately upon reading a circulated account of the DNA work written by Franklin and shown to him by Perutz. This also should have been acknowledged.

Another point that has been made much of by some writers is that, even after her early death in 1958, her contribution was not mentioned in the three separate Nobel Lectures given by Wilkins, Watson, and Crick as part of the Stockholm arrangements in 1962. This is only partially true. Wilkins was the only one who, presumably by mutual arrangement, spoke specifically of the genesis of the discovery of the DNA structure and subsequent work on it because he had started the work and continued to work on it later. He does say in his talk that Franklin “made a very valuable contribution to the X-ray analysis” and in his conclusion, he thanked Franklin “who, with great ability and experience of X-ray diffraction, so much helped the initial investigation.” It is notable, however, that he does not include any of her published papers on DNA in his list of 24 references (perhaps hardly surprising, after she had refused to let him collaborate with her on the X-ray work which he had started). This was the consequence of Randall’s unfortunately worded letter of appointment to her when she joined the King’s group. Crick and Watson talked exclusively about their work following up the implications of the DNA structure: Crick on the general nature and details of the genetic code and Watson on the role of RNA in protein synthesis. These were subjects on which they had been extremely busy since 1953, and where Franklin’s work was not directly relevant. However, at the very least, some special mention by them of her role in the discovery and of her tragic death in the intervening years would have been a kind gesture and a small price to pay. And since the unpublished experimental data from the King’s group had obviously been essential for the discovery of the structure, there should have been at least four names on the initial publication.

One of the best sections of the book relates Crick’s role in establishing the detailed nature of the mechanism of transfer of information, written in the sequence of the bases in DNA, to specify the amino-acid sequence—and, hence, the structure and function—of the proteins which carry out their cellular roles. His realization that it was unlikely to depend on direct reading of the shape of DNA base sequence by incoming amino-acids themselves so as to form a polypeptide chain of appropriate sequence, and his postulate, before the discovery of transfer RNA, of a whole set of 20 adaptor molecules to perform the recognition, were certainly logic carried to the point of genius (“the Adaptor Hypothesis”). Equally striking was his virtually simultaneous recognition, with Brenner, at a memorable meeting with Jacob in 1960 (when it had become clear from Jacob, Monod, and Pardee’s experiments that ribosomal RNA was not the information carrier), that it was in fact the Volkin-Astrakan RNA already found in phage infection which itself was the messenger RNA.

Crick was responsible for laying down the basic hypotheses and “dogma” defining the mode of expression of genes—that the genetic message is contained in the DNA base sequence, that DNA makes RNA, and that the messenger RNA makes a protein with a defined sequence, which folds up and performs its cellular function, and that any subsequent changes in the protein cannot feed back and change the original DNA sequence. In remarkable experiments with Brenner and other colleagues in the MRC “hut,” but carried out largely by Crick himself, he showed that the code must be written in triplets of bases, which earlier work had shown could not be overlapping. He did this, basically, by showing that three single base deletion mutants, lying close together near the start of a message, and each individually destroying the same function by shifting the reading frame by one step, would, when expressed together, give rise to the expression of a functional polypeptide chain, generated by the correct reading of the subsequent triplets in the corrected reading frame. The identification of all the actual triplets used—and its constancy throughout nature—was the work of many other scientists as well, many of them actively inspired and encouraged by Crick—but in Monod’s memorable words, “No one man discovered or created molecular biology. But one man dominates intellectually the whole field because he knows the most and understands the most. Francis Crick.”

So how and when did Crick become the towering figure and intellect that he was? His earlier development was not particularly remarkable. He came from a comfortable middle-class background of shoe manufacturers in...
Northampton, in the English Midlands. He was fascinated very early by scientific subjects and informed (as many others were!) by reading Arthur Mee’s excellent *Children’s Encyclopedia*, a multivolume, multi-author work. He won a scholarship at age 14 to Mill Hill School, one of the well-regarded “public” (i.e., private) boarding schools in North London, did well in the School Certificate Exam at the age of 15, moved in 1931 to the Science 6th form to take the Higher School Certificate (HSC) Exam (the gateway to Universities) the next year. He obtained distinctions in physics and mathematics for science and a pass in chemistry. He then stayed on for a further period to take the HSC again, getting sufficiently good results to win the Form Prizes in physics and mathematics. He was unsuccessful, however, in the Oxford and Cambridge University Entrance Scholarship exams and apparently not just because of inadequate Latin. His headmaster (later?) described him as being highly competent, but said that he had no expectations of Crick’s future brilliance. And so he did not go to Oxford or Cambridge, but to University College London, a perfectly good choice, but at that time with a rather dull physics department.

I find this story a little strange. Winning a scholarship was not a requirement for entry into Oxford or Cambridge, only a source of funding. The normal alternative at that time was a State Scholarship, which would cover the fees and other expenses, and was awarded on the basis of excellent results in the High School Certificate Exam, the requirement being, as I recall, a distinction in three subjects. If Crick obtained two distinctions in his first attempt, and had been strongly motivated to go to Cambridge to do physics—where he would have been in Rutherford’s department—and had he been encouraged by his teachers, he would surely have striven very hard for a third distinction in subsequent years. This was the same path that my sister and I followed (also in the mid-1930s in her case) without any family financial support. It was the standard way of getting there from such a background. I suspect that Crick’s teachers did not provide strong motivation in their approach to or their knowledge of their subjects. They did not interest him sufficiently in the extraordinary developments in atomic and nuclear physics, quantum theory and relativity, which were well under-way by the early 30s, when scientists in Cambridge were splitting the atom, discovering the neutron, predicting the positron, and exploring superconductivity.

This lack of inspiring teaching also seems to have been responsible for Crick not obtaining a first class degree at London University, although he did obtain a good grounding in classical physics. He was able to start on a research studentship to enable him to learn some more about biology at Cambridge. He was at first given a position at the Cavendish, a physics laboratory under Sir Lawrence Bragg. I had begun a similar studentship there about a year earlier, with John Kendrew as my supervisor. I found that Crick’s remarkable ability to understand, to formulate, and to clarify all different kinds of scientific problems was by now fully developed. A year or two later, Jim Watson and I were so impressed by Crick’s powers that when Bragg—who had invented X-ray diffraction and won a Nobel Prize at 24—was once again considering exile for Crick (because of his loud and tactless criticism of some of Bragg’s contributions to the current protein structure work and his continuous talking and penetrating laugh) that we appealed to the diplomatic Kendrew to beg him to intervene to save this priceless asset to the Unit—which Kendrew did, successfully, of course.

Watson was already convinced of the importance of knowing the structure of DNA, as was Crick, who realized that model-building might be a fruitful approach, as it had been in the case of Pauling’s α-helix; their collaboration then began. The success of the DNA work in 1953 and its ramifications into protein synthesis, and the paralleled success of Perutz and Kendrew in solving the structure of hemoglobin and myoglobin at Harrie Massey, a very successful physicist and mathematician. It is clear that Crick’s powers of analysis of a problem, his original and fruitful ideas, and his strong personality and self-confidence first began to show clearly during his successful wartime service, when thoughts and actions had early and significant consequences. His intellectual development was undoubtedly helped by his long friendship with Georg Kreisel, an eminent mathematical logician who, though younger than Crick, insisted on clarity and precision in the formulation of ideas and in their expression.

At the end of the war, he continued to work for the Admiralty in the Intelligence Department for a year or so, where he had sufficient free time for extensive reading in theoretical physics and in chemistry and biology. He gradually made up his mind that the areas of research that most interested him were the borderline between the living and the nonliving, and the working of the brain. In each of these he wanted to extend the range of clear scientific explanation, and to rescue these subjects from religious dogma and superstition, for he was “a strong agnostic bordering on atheist.” He would be very disappointed by the situation in many places today, despite his success!

His strong support from Massey and the personal impression that he made gained him the help of A. V. Hill who in turn enlisted the support of Sir Edward Mellanby, then the head of the MRC, who obtained a research studentship to enable him to learn some more biology at Cambridge. He was at first given a position at the Strangeways, an independent laboratory specializing in work on tissue culture. Here he spent some time studying the properties of cytoplasm using the movement of magnetic particles. He read extensively, before taking up a Ph.D. Studentship in 1949 at the age of 33 in the MRC Unit headed by Max Perutz and located in the Cavendish, a physics laboratory under Sir Lawrence Bragg. I had begun a similar studentship there about a year earlier, with John Kendrew as my supervisor. I found that Crick’s remarkable ability to understand, to formulate, and to clarify all different kinds of scientific problems was by now fully developed. A year or two later, Jim Watson and I were so impressed by Crick’s powers that when Bragg—who had invented X-ray diffraction and won a Nobel Prize at 24—was once again considering exile for Crick (because of his loud and tactless criticism of some of Bragg’s contributions to the current protein structure work and his continuous talking and penetrating laugh) that we appealed to the diplomatic Kendrew to beg him to intervene to save this priceless asset to the Unit—which Kendrew did, successfully, of course.

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atomic resolution (and thereby showing that this could be done for all crystalline proteins which could be labeled with heavy atoms) led to the great expansion of the MRC Group into the splendid large new laboratory of Molecular Biology on the Hills Road Hospital site in Cambridge, in early 1962. There they were joined by Sanger, working on protein and nucleic acid sequencing, Klug and his colleagues working on virus structure, and myself working on muscle structure and the molecular mechanism of contraction. Perutz was appointed Chairman. It was—and still is—a marvelous place to work, with a very happy atmosphere and a great esprit de corps; and for many years Crick was the star turn. Everyone went to the top floor cafeteria for morning coffee, for lunch, and for afternoon tea, where a huge amount of scientific information was exchanged and discussed, with Francis and Sydney playing prominent roles. The Lab’s record of discovery and innovation suggests that this was not time wasted.

The Lab glowed with success when Nobel Prizes were awarded in the same year (1962) to Crick, Watson (now back in the U.S.), and Wilkins (still at King’s London), and to Kendrew and Perutz—and to a remarkable number of others in subsequent years. To keep Francis (and everyone else) in touch with all that was going on in the different divisions of the Lab, “Crick Week” was organized in the autumn of each year. Representatives of all the different groups would explain what was happening in their own areas of research, in the Lab, and elsewhere, with Crick and Brenner in the front row, insisting, usually with good humor, on high standards of clarity, logic, and experimental purpose and design. I think that this extraordinary period could have been covered more extensively in the book.

It was a terrible loss to the Lab when Crick, then around age 60 but still apparently going at full flood, moved to the Salk Institute in La Jolla, California, in 1976–1977. The biography describes the various reasons for this very well. They were in considerable part financial, engendered by MRC rules. Retirement age had previously been set at 60, and only near that time was it raised to 65, still uncomfortably close for Crick. Scientific salaries in the U.K. were quite low at that time; and, because of his late start in MRC employment, Crick’s pension would have been very small, even for a modest life in Cambridge, let alone the extensive travel and Mediterranean holidays that had become part of Francis and Odile Crick’s life. Moreover, the government had recently changed the tax and royalties laws, so that foreign sources of income, such as lectures in America, would have become taxable at U.K. rates. Nevertheless, the Cricks and the stimulating social and intellectual environment which they had both generated and enjoyed, had become so much a part of the Cambridge scene that many of their friends were still surprised that they would consider moving to California.

I suspect that the beautiful year-round weather which they had already experienced from time to time in La Jolla, as compared to the long, dark, chilly and damp Cambridge winters was a factor, too, in addition to the prospect of a generous salary for the indefinite future. But I also think that Francis may have felt trapped by the expectation that he would remain the great guru of molecular biology if he stayed in the MRC Lab in Cambridge. He really wanted to move on to entirely new fields, and devote himself fully to the second of his original interests, namely the working of the brain, which he was able to do without impediment at the Salk, right up to his death in 2004.

These years and his vigorous pursuit of brain function are adequately described, but one is left with the impression that the field may not have been quite ripe for a man of Crick’s particular talents. There may have been too much very specialized experimental work still to be done and too many new experimental techniques to be developed, in order to approach the enormous intricacies involved. However, there is no doubt that he enjoyed to the full making whatever contributions he could, and inspiring others to work in this rapidly developing field.

But it was in laying the foundations of the enormous edifice of molecular biology that Crick’s genius found exactly the right expression. This book provides a detailed and authoritative account of the life in science of this very remarkable man and should have a wide readership, not only among scientists.