How to Live with a Golden Helix

by Francis Crick

A DNA pioneer takes another look at his seminal discovery

The discovery of the structure of DNA has been described in print several times already, not only by Jim Watson in that rather breathless fragment of his autobiography he called *The Double Helix* (perhaps *Lucky Jim* would have been a better title), but also, in a more sober, detailed and scholarly way, by Bob Olby (*The Path to the Double Helix*). At least one TV documentary has been made about it. Leaving more ephemeral effusions, whether girlish or soured, on one side, we have an excellent account by Horace Judson. His book, *The Eighth Day of Creation* (Simon and Schuster, 1979), covers not only the discovery of the double helix, but also the search for the genetic code and the three-dimensional structure of proteins. Very well researched, scientifically accurate and written in a lively and readable style, it reveals more about the way molecular biology was done and about the people who did it than any other account I know.

What more can I add? Before the whole thing gets out of hand and becomes an academic cottage industry, I think a dose of cold water could do no harm. No doubt it is fascinating to read just how a scientific discovery is made; the misleading experimental data, the false starts, the long hours spent chewing the cud, the darkest hour before the dawn, and then the moment of illumination, followed by the final run down the home straight to the winning post.

And what a cast of characters! The Brash Young Man from the Middle West, the Englishman who talks too much (and therefore must be a genius since geniuses either talk all the time or say nothing at all), the older generation, replete with Nobel Prizes, and best of all, a Liberated Woman who appears to be unfairly treated. And in addition, what bliss, some of the characters actually quarrel, in fact almost come to blows. The reader is delighted to learn that after all, in spite of science being so impossibly difficult to understand, SCIENTISTS ARE HUMAN, even though the word "human" more accurately describes the behavior of mammals rather than anything peculiar to our own species, such as mathematics. Surely the script must have been written, not in heaven, but in Hollywood.

Unfortunately a closer study shows that real life is not always exactly like a soap opera. Not everybody was competing madly, with one eye on Stockholm. In actual fact there was a considerable amount of cooperation mixed in with the inevitable competition. The major opposition Rosalind Franklin had to cope with was not from her scientific colleagues, nor even from King's College, London (an Anglican foundation, it should be noted, and therefore inherently biased against women), but from her affluent, educated and sympathetic family who felt that scientific research was not the proper thing for a normal girl. Rosalind's difficulties and her failures were mainly of her own making. Underneath her brisk manner she was oversensitive and, ironically, too determined to be scientifically sound and to avoid shortcuts. She was rather too set on succeeding all by herself and rather too stubborn to accept advice easily from others when it ran counter to her own ideas. She was proffered help but she would not take it.

The soap opera has many other distortions and simplifications. I need not elaborate further. The plain fact that science is largely an intellectual pursuit, that it involves an enormous amount of hard, often grinding, work (both theoretical and experimental), that it is based upon an immense body of closely interlocking facts and theories, much of which must be thoroughly mastered before any progress at all can be made—all this tends to be submerged in the popular mind beneath those personal aspects which ordinary people relate to more easily. It is certainly an excellent idea to kill the stereotype of the cold, impersonal scientist in the white coat—such people do exist but they are as dull in science as they are in life—but we must not let the public think that because they understand some of our motives they thereby understand what science is about. The most surprising characteristic of modern Western society is that in spite of its being largely based on science and technology, the average citizen understands so little about the scientific enterprise. It is not only that elementary scientific facts are not known (the shape of H_20, for example) but there is an almost complete lack of any scientific overview, a lack of any description, even in outline, of what is well established, what we still have to discover, and how we hope to go about discovering it.

I think what needs to be emphasized about the discovery of the double helix is that the path to the discovery was, scientifically speaking, fairly commonplace. What was important was not the way it was discovered but the object discovered—the structure of DNA itself. One can see this by comparing it with almost any other scientific discovery. Misleading data, false ideas, problems of personal interrelationships occur in much if not all scientific work. Consider, for example, the discovery of the basic structure of collagen. It will be found to have all these elements. The characters are just as colorful and diverse. The facts were just as confused and the false solutions just as misleading. Competition and friendliness also played a part in the story. Yet nobody has written even one book about "The Race for the Triple Helix." This is surely because, in a very real sense, collagen is not as important a molecule as DNA.

Of course this probably depends upon what you consider important. Before Alex Rich and I worked (quite by accident, incidentally) on collagen we tended to be rather patronizing about it. "After all," we said, "there's no collagen in plants." After we got interested in the molecule we found ourselves saying, "Do you realize that one-third of all the protein in your body is collagen?" But however you look at it, DNA *is* more important than collagen, more central to biology, and more significant for further research. So, as I have said before: it is the molecule which has the glamour, not the scientists.

Looking for Gold

What then do Jim Watson and I deserve credit for, if anything? There are certain technical points which are sometimes overlooked. It took courage (or rashness, according to your point of view) and a degree of technical expertise to put firmly on one side the difficult problem of unwinding the double helix and to reject a side-by-side structure. Such a model was suggested by George Gamow, not long after ours was published, and it has been suggested again more recently by two other groups of authors. It is less well known that in 1953 we very briefly considered a four-stranded model—the structure eventually published by Stewart McGavin—and had the good sense to reject that also. But these are small points. If we deserve any credit at all it is for persistence and the willingness to discard ideas when they became untenable. One reviewer thought that we can't have been very clever because we went on so many false trails, but that is the way discoveries are usually made. Most attempts fail not because of lack of brains but because the investigator gets stuck in a cul-de-sac or gives up too soon. We have also been criticized because we had not perfectly mastered all the very diverse fields of knowledge needed to guess the double helix but at least we were *trying* to master them all, which is more than can be said for some of our critics.

However, I don't believe all this amounts to

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much. The major credit I think Jim and I deserve, considering how early we were in our research careers, is for selecting the right problem and sticking to it. It's true that by blundering about we stumbled on gold but the fact remains that we were looking for gold. Both of us had decided, quite independently of each other, that the central problem in molecular biology was the chemical structure of the gene. Hermann Muller had pointed this out as long ago as the early twenties and many others had done so since then. What both Jim and I sensed was that there might be a shortcut to the answer, that things might not be *quite* as complicated as they seemed. Curiously enough this was partly because I had acquired a very detailed grasp of the current knowledge of proteins. We could not at all see what the answer was, but we considered it so important that we were determined to think about it long and hard, from any relevant point of view. Practically nobody else was prepared to make such an intellectual investment, since it involved not only studying genetics, biochemistry, chemistry and physical chemistry (including x-ray diffraction—and who was prepared to learn that?) but also sorting out the essential alloy from the dross. Such discussions, since they tend to go on interminably, are very demanding and sometimes intellectually exhausting. Nobody could sustain them without an overwhelming interest in the problem.

And yet history of other theoretical discoveries often shows exactly the same pattern. In the broad perspective of the exact sciences we were not thinking very hard but we were thinking a lot harder than most people in that corner of biology, since in those days, with the exception of geneticists and possibly the people in the phage group, most of biology was not thought of as having a highly structured logic.

Of course it is obvious now that nucleic acid is the main if not the only genetic material, but in the late forties and early fifties this was far from clear. Everybody knew of the work on the transforming principle by Oswald Avery and his colleagues. Even the conservative Royal Society gave Avery a prestigious medal for the discovery as early as 1945. The citation shows clearly that they understood its genetic implications but not everybody else was convinced so easily. Alfred Mirsky in particular thought for some time that the effect was due to contaminating protein but I do not think that was the main stumbling block. The real difficulty was to decide whether transformation was of general significance or whether it was a freak. Initially it had been found only in pneumococcus—and it was not even known whether that organism had genes in the ordinary Mendelian sense. Moreover, it appeared to affect only one character, the nature of the coat. A little later the very careful work of Rollin Hotchkiss showed that other characters could be transformed. He also made the idea of a protein impurity highly unlikely. But transformation still remained an almost isolated case. Moreover, one could always argue that the experiments fitted equally well the idea that a gene contained *two* essential and specific components, nucleic acid *and* protein. The importance of the Hershey-Chase experiment on phage T4 was that it provided a second quite separate instance of the genetic specificity of DNA, even though, by comparison, the experiments were far dirtier than those of Avery and Hotchkiss. Hershey's results made a deep impression on Jim and myself, even though many people couldn't see what the fuss was all about. From then on we had few reservations that DNA was biologically important. Whether its structure would tell us anything interesting we could only guess—and hope for the best.

Looking back I can see that it is also important not to be too clever. Consider the following argument: DNA fibers show a very good x-ray diffraction pattern, implying that the microcrystalline structure which produced the many spots is very regular. But for a genetic material to have any interest it must necessarily be somewhat irregular. Therefore nothing of interest is likely to come from studying diffraction patterns of DNA. A similar argument could be used about its base composition. Only an imperceptive person could possibly spend time measuring the exact amounts of the four bases in DNA since how could that possibly reveal anything of genetic interest? Fortunately neither of these arguments influenced us at the time. We can see now that they are wrong because of the overwhelming importance of base-pairing and because one base-pair looks very like another in shape and, at that resolution, to the x-rays. The important thing is not to be deflected too much by negative arguments of this general type, even though they may indeed turn out to be correct and one's labors to have been in vain. The much stronger rule is that if something is of great scientific importance one can hardly learn too much about it, even by what, at first sight, may seem rather pedestrian methods. Of course, not everybody may be equipped to appreciate the significance of some rather simple observation (why the stars come out at night, for example) as the history of the double helix shows rather clearly.

The Secret of Life

But what was it like to live with the double helix? I think we realized almost immediately that we had stumbled onto something important. According to Jim, I went into the Eagle, the pub across the road where we lunched every day, and told everyone that we'd discovered the secret of life. Of that I have no recollection, but I do recall going home and telling my wife Odile that we seemed to have made a big discovery. Years later she told me that she hadn't believed a word of it. "You were always coming home and saying things like that," she said, "so naturally I thought nothing of it." W.L. Bragg, Cavendish professor, was in bed with 'flu at the time, but as soon as he saw the model and grasped the basic idea he was immediately enthusiastic. All past differences were forgiven and he became one of our strongest supporters. We had a constant stream of visitors, a contingent from Oxford which included Sydney Brenner among them, so that Jim soon began to tire of my repetitious enthusiasm. In fact at times he had cold feet, thinking that perhaps it was all a pipe dream, but the experimental data from King's College, when we finally saw them, were a great encouragement. By the summer, most of our doubts had vanished and we were able to take a long cool look at the structure, sorting out its accidental features (which were somewhat inaccurate) from its really fundamental properties, which time has shown to be correct.

For a number of years after that, things were fairly quiet. I named our house in Portugal Place "The Golden Helix" and eventually erected a simple brass helix on the front of it, though it was a single helix rather than a double one. It was supposed to symbolize not DNA but the basic idea of a helix. I called it golden in the same way that Apuleius called his story "The Golden Ass," meaning beautiful. People have often asked me whether I intend to gild it. So far we've got no further than painting it yellow.

Gradually DNA became better known. Paul Doty told me that shortly after lapel buttons came in he was in New York and to his astonishment saw one with "DNA" written on it. Thinking it must refer to something else he asked the vendor what it meant. "Get with it, bud," the man replied in a strong New York accent, "dat's the gene."

Nowadays most people know what DNA is, or if they don't, they know it must be a dirty word, like "chemical" or "synthetic." Fortunately people who do recall that there are two characters called Watson and Crick are often not sure which is which. Many's the time I've been told by an enthusiastic admirer how much they enjoyed my book—meaning, of course, Jim's. By now I've learned that it's better not to try to explain. An even odder incident happened when Jim came back to work at Cambridge in 1955. I was going into the Cavendish one day and found myself walking with Neville Mott, the new Cavendish professor (Bragg had gone on to the Royal Institution in London). "I'd like to introduce you to Watson," I said, "since he's working in your lab." He looked at me in surprise. "Watson?" he said, "Watson? I thought your name was Watson-Crick."

The First

The double helix is indeed a remarkable molecule. Modern man is perhaps 50,000 years old, civilization has existed for scarcely 10,000 years, and the United States for only just over 200 years; but DNA and RNA have been around for at least a billion years, if not longer. All that time the double helix has been there, and active, and yet we are the first creatures on Earth to become aware of its existence.

There was in the early fifties a small, somewhat exclusive biophysics club at Cambridge, called the Hardy Club, named after a Cambridge zoologist of a previous generation who had turned physical chemist. The list of those early members now has an illustrious ring, replete with Nobel laureates and Fellows of the Royal Society, but in those days we were all fairly young and most of us not particularly well-known. We boasted only one F.R.S.—Alan Hodgkin—and one member of the House of Lords—Victor Rothschild. Jim was asked to give an evening talk to this select gathering. The speaker was customarily given dinner first at Peterhouse. The food there was always good but the speaker was also plied with sherry before dinner, wine with it, and, if he was so rash as to accept it, drinks after dinner as well. I have seen more than one speaker struggling to find his way into his topic through a haze of alcohol. Jim was no exception. In spite of it all he managed to give a fairly adequate description of the main points of the structure and the evidence supporting it, but when he came to sum up he was quite overcome and at a loss for words. He gazed at the model, slightly bleary-eyed. All he could manage to say was, "It's so beautiful, you see, so beautiful!" But then, of course, it was. □