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EDITORIAL

The Double Helix: Sixty Years On

Sixty years ago, on 25 April 1953, the journal *Nature* published three papers under a common heading, '*Molecular Structure of Nucleic Acids*'. The first of these is the iconic paper by Watson and Crick, simply titled '*A Structure for Deoxyribose Nucleic Acid*', which has a lone illustration – the now immortal double stranded DNA structure, represented in diagrammatic form. The base pairs are shown as horizontal lines on a spiral, ladder like structure. The text introduces the selective base recognition scheme, now taught even in high school. The concluding sentence has been imitated by many authors, who hope to invest their findings with an importance that is invariably exaggerated: 'It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material' (Watson, J. D. and Crick, F. H. C., *Nature*, 1953, **171**, 738). The final sentence of the paper on the double helix is a masterfully, understated conclusion, avoiding the need to 'write at length about the biological implications' (*The Double Helix*, Watson, J. D., Touchstone Edition, 1996, p. 120). In an introduction to the 1996 reissue of Watson's 1968 account of the drama behind the discovery of the DNA structure, Sylvia Nasar, author of *A Beautiful Mind*, compares the scientific impact 'to the breakthroughs that led to the splitting of the atom and the invention of the computer'. What of the papers that accompanied the Watson–Crick note in *Nature* sixty years ago? The first by Maurice Wilkins and his colleagues, titled '*Molecular Structure of Deoxypentose Nucleic Acids*' presents an X-ray fiber diffraction pattern and an interpretation in terms of a helical-structure and notes that 'in general there appears to be reasonable agreement between the experimental data and the kind of model described by Watson and Crick' in the preceding communication (Wilkins, M. H. F., Stokes, A. R. and Wilson, H. R., *Nature*, 1953, **171**, 738). The second by Rosalind Franklin and her student R. G. Gosling, titled '*Molecular Configuration in Sodium Thymonucleate*', presents the fiber diffraction photograph that provided the key clues to the model building exercise of Watson and Crick. A reading of the paper by Wilkins *et al.* reveals the importance of 'the exceptional photograph obtained by… R. E. Franklin and R. G. Gosling from calf thymus deoxypentose nucleate'. The authors themselves interpret their data cautiously and note that their 'general ideas are not inconsistent with the model proposed by Watson and Crick in the preceding communication' (Franklin, R. E. and Gosling, R. G., *Nature*, 1953, **171**, 740). Franklin died of cancer in 1958, four years before the award of the Nobel Prize in Physiology or Medicine to Watson, Crick and Wilkins. The unkind portrait of Franklin in Watson's 1968 book has been the subject of much discussion in the years since. Seven authors were involved in the three papers that appeared in *Nature* in 1953, of whom only Raymond Gosling and Watson survive. Gosling was the Ph D student who 'wrapped DNA around a paperclip to keep the molecule's fibres stretched taut in front of an X-ray source so that he could analyse their structure'. In an editorial titled, 'Due credit', *Nature* notes that 'the result was the celebrated "photograph 51" – the image that told James Watson that DNA strands curl around each other like a twisted ladder, and that the specific pairings in the rungs are key to the mechanism of inheritance' (*Nature*, 2013, **496**, 270). 'All three papers appeared with no peer review' – a tribute to the powers of persuasion that could be brought into play in the cloistered environment of London's 'gentleman's clubs', an English institution of undisputed influence. Gosling, now 86, can be heard in an interview on a *Nature* podcast (termed a 'pastcast'), recounting the events of 1953.

The journal *Genome Biology* presents in its 25 April 2013 issue a wonderfully readable account titled, 'Raymond Gosling: the man who crystallized genes' (Attar, N., *Genome Biology*, 2013, **14**, 402). My curiosity was aroused by the concluding sentences of the *Nature* editorial (18 April 2013): 'Discoveries take ego, genius, conflict, inspiration and fierce ambition. But they also need the hard graft of Ph D students who beaver away late into the night and improvise with what they find in a stationery cupboard. They do not always receive the recognition that they deserve. Raymond Gosling is a good place to start to reverse the trend.' The DNA story is set in two locales, Cavendish Laboratory at Cambridge with Lawrence Bragg as the presiding deity and King's College, London, where John Randall put together a group to apply the methods of physics to the problems of biology. In recognizing the importance of interdisciplinary research, Randall was, in Gosling's words, 'ahead of the curve'. The young Gosling was fleeing from the prospect of doing research on 'viscosity' at University College

London. The prospect of working at a rival institution with Randall, a 'strange bald-headed little man with a Napoleonic complex, who was running the circus in biophysics', sounded wonderfully attractive. In Gosling's telling of the story, Randall's role 'in the pursuit of the double helix cannot be overstated'. The DNA model building work at Cambridge critically depended on fibre diffraction data. Randall skillfully played the two competing groups at King's College, Wilkins and Franklin, in pushing the experimental research forward. Rosalind Franklin's recruitment, in Gosling's version, was a result of Randall's conviction that Wilkins and Gosling would never 'learn enough crystallography to be able to solve this spotty diagram'. Gosling a Ph D student with Wilkins was reassigned to work with Franklin. His assessment of Randall, with the benefit of hindsight: 'He [Randall] subscribed to the divide and rule principle, as lots of people did. He thought it would make them more competitive and improve their work.' Wilkins appears to have been an instinctive experimenter. The DNA sample used to obtain the beautiful diffraction patterns, 'Signer DNA', was accidentally obtained. Rudolf Signer, a Swiss biochemist, delivered a lecture at the Royal Society on his method for producing DNA of a superior quality. In Gosling's words: 'Signer asked at the end of the lecture if anybody would like some of this material and he had a specimen tube full of this freeze dried material. Only two people put their hand up. I'm glad to say that Maurice [Wilkins] was awake enough to put his hand up!' Gosling reveals an interesting contribution made by Wilkins to the first successful experiment to obtain a good diffraction pattern of DNA. In attempting to displace air inside the camera with hydrogen, Gosling struggled with ways 'to prevent the gas from coming out of the collimator tube'. Wilkins, the 'rather shy Assistant Director of the MRC Unit', provided an innovative solution, by producing a packet of condoms, which quickly solved the problem. The *Genome Biology* commentary notes that this 'somewhat unorthodox, and nevertheless essential contribution' to Gosling's first X-ray images of crystalline DNA, was understandably omitted from Wilkins' Nobel lecture. Gosling was a witness to Rosalind Franklin's demolition of the first 'wrong model' – a double helix with phosphates in the middle – built by Watson and Crick. This was the only occasion, as Crick was to note later, that 'he ever saw Jim Watson at a loss for words'. Gosling was an integral part of the King's College effort to extract structural information from their X-ray photographs. They were overtaken by the inspired model building at Cambridge. Would they have finally hit upon the right model? Gosling thinks so: '…we would have got there at King's, but not in one fell swoop, that it would have come out in dribs and drabs about various aspects'.

Gosling's career path immediately after his Ph D illustrates a point that is not very well known today – the DNA papers appearing in *Nature* in 1953 attracted little attention. In a commentary that appeared on the 50th anniversary of the double helix, Bruno Strasser notes: 'We usually think that the double-helix model acquired immediate and enduring success. On the contrary it enjoyed only a "quiet debut"…. So when did it become so immensely popular in the scientific community? The 1960s? 1970s? 1980s? None of these. Not until the 1990s' (Strasser, B., *Nature*, 2003, **422**, 803). A plot of the citations to the Watson–Crick paper of 1953 shows a peak in 1963, following the Nobel prize and a decline thereafter, with rapid growth beginning in the early 1990s. Why should modern day authors cite the 1953 paper? After all, the Watson–Crick double helix is so well known that citation is hardly likely to be necessary. Strasser provides an answer: 'Authors in an unprecedented variety of fields, from neurosurgery to plant physiology cite the 1953 paper in an attempt to appropriate the current prestige of molecular biology for their own speciality by underlining (sometimes far fetched) historical affiliations with the double helix.' The developing pace of the human genome project in the 1990s also stimulated many citations of the 1953 paper. Strasser adds that 'setting the double helix as the highest standard of scientific creativity helped to make the descriptive genome sequencing project less tedious. After all, both were attempts at describing the structure of DNA and would result only in a guess at the possible "genetic implications" as Watson and Crick had put it.'

Whom did Watson and Crick cite in 1953? There are only 6 references in their original report. A notable omission is the absence of any reference to the work of Oswald Avery and his group, establishing the chemical nature of the genetic material as DNA, which appeared in 1944. A historical note appearing in this issue of *Current Science* analyses the citation patterns of the four papers on the double helix published by Watson and Crick in 1953–54 (Kantha, S. S., *Curr. Sci.*, 2013, **104**, 1237). The author draws attention to a paper by W. T. Astbury and F. O. Bell that appeared in 1938, some years before Avery's work, which may have been 'prophetic in recognizing the genetic role of DNA' (*Nature*, 1938, **141**, 747). I read Watson's 1968 account of the double helix in the same year, as a student wondering whether to soldier on towards an advanced degree in science. While I had no knowledge of the nature of DNA or its importance, research, as portrayed by Watson, seemed exciting – almost a game in which the winner takes all. Decades later, Bruno Strasser's assessment seemed to ring true: 'The double helix worked as the marker of an age of (lost) innocence, when youth, intelligence and self assurance were sufficient to make great discoveries in science.' As the origins of the double helix recede into history, periodic anniversaries serve to remind us of the human drama that accompanied the birth of molecular biology.

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