

Illustrations from the Wellcome Library

For the Record: The Francis Crick Archive at the Wellcome Library

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History's Occasions

“This is an historic occasion”, announced Francis Crick on 2 June 1966, as he began the opening address of the annual meeting of molecular biologists at Cold Spring Harbor. “There have been many meetings”, he continued, “about the genetic code during the past ten or twelve years but this is the first important one to be held since the code became known.”¹ Such bold pronouncements usually guarantee that an occasion will linger in history’s footnotes and never shine centre-page. But, as the first public presentation of the complete genetic code, the moment had some claim to being historically complementary to the publication of James Watson and Crick’s first paper in *Nature*. In April 1953, in fourteen paragraphs and a diagrammatic sketch (contributed by Odile Crick), they had announced—with a minimalism that came more of urgent certainty than of diffidence or reticence—not just a physical structure for DNA, but something far more. “It has not escaped our notice that the specific pairing [of purine and pyrimidine bases] we have postulated immediately suggests a possible copying mechanism for the genetic material.”² The trajectory begun in 1953 with the suggestion of “a possible copying mechanism” completed its public arc at Cold Spring Harbor in 1966 with a very specific and (almost) complete table showing the genetic code.³ The occasion “marked”, as Crick later judged, “the end of classical molecular biology”.⁴

Students of drama know, however, that actions off-stage can be as important as actions that take place in full view of an audience, if not more so. In Moscow, in August 1961, at the Fifth International Congress of Biochemistry, some 5000 to 6000 delegates gathered over five days.⁵ There, in a seminar-room sideshow, peripheral to the molecular biology main

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¹ F H Crick, ‘The genetic code—yesterday, today, and tomorrow’, *Cold Spring Harbor Symp. Quant. Biol.*, 1966, **31**: 3–9, on p.3.

² J D Watson and F H Crick, ‘Molecular structure of nucleic acids: a structure for deoxyribose nucleic acid’, *Nature*, 1953, **171**: 737–8.

³ What remained of the table to be completed were three codons: “the triplets UAA, UAG, and UGA, had no amino acids assigned to them. One by one, in

experiments in phage genetics by [Sydney] Brenner and independently by Alan Garen at Yale, and then last by Brenner and Crick in 1967, these three triplets were proved to be nonsense codons, whose function was to signal the end of the polypeptide chain.” Horace Freeland Judson, *The eighth day of creation: makers of the revolution in biology*, Harmondsworth, Penguin, 1995, p. 480.

⁴ Francis Crick, *What mad pursuit: a personal view of scientific discovery*, New York, Basic Books, 1988, p. 143 (hereafter, *WMP*). For the genetic code table, see p. 170.

⁵ Judson, *op. cit.*, note 3 above, pp. 463ff.

programme, Marshall Nirenberg, then a young unknown biochemist (described by one delegate as not one of “the club”⁶), reported to a largely empty room that he and Johann Matthaei had succeeded in making a synthetic protein (polyphenylalanine) from synthetic RNA (poly-U), thus establishing the first word in the DNA dictionary: UUU = phenylalanine.⁷ It was as if, through some scheduling embarrassment, history had missed its occasion. The first word of the newly-discovered language of life had been recited to almost no one.⁸ Informed of the presentation, after the event, an excited Crick promptly asked Nirenberg if he would repeat his report, for the record, to the rather larger forum of the main floor, which he did, to the “startlement” of all.⁹

Personal scientific archives are, in many respects, less about end-points, conclusive moments, and a final hammered form of words, than they are about process, the confusion of beginnings, ways and means, drafts, pathways, false turns, actions off-stage, and remarks around- and off-the-record. They offer a body of documentation with an untidy coherence, raw material for histories yet to be written, in contrast to the tidy log of formal scientific record. We value them precisely because they are *not* one and the same as the record to which we have become accustomed. We value their registration of simultaneity—as if time were returned to us in the rich interdependence of the documents they make available—and we value their propensity to disturb that which had seemed settled. The opening of the recently-acquired Francis Crick archive at the Wellcome Library¹⁰ provides an opportunity for re-contextualization and re-evaluation of a body of work that has been central to the emergence of the science of molecular biology in the second half of the twentieth century and central to an accompanying paradigmatic shift in our understanding of the stuff of life. In the following pages, I introduce the collection by way of illustrative passages and some reflections on the nature of archival records and their relationship to received scientific record, as prompted by the process of cataloguing the archive.

Entertaining Dr Crick

The papers now catalogued (PP/CRI) and open to researchers (on-line catalogue at <http://library.wellcome.ac.uk/cat/west_orient_amss.shtml#western>) comprise the first shipment of material to the Wellcome Library, received from California during the summer of 2002. They encompass—in almost 1100 fully-searchable files—all Crick’s work at Cambridge, from postgraduate student (Figure 1) to Nobel laureate and beyond,

⁶ Matthew Meselson, quoted in Judson, *ibid.*, p. 481: “And here was some guy named Marshall Nirenberg; his results were unlikely to be correct, because he wasn’t in the club. And nobody bothered to be there to hear him. Anyway, I was bowled over by the results, and I went and chased down Francis, and told him that he must have a private talk with this man.”

⁷ For Nirenberg’s relevant papers, and a draft of his Moscow presentation, visit: <<http://profiles.nlm.nih.gov/JJ/Views/Exhibit/documents/syntheticrna.html>>.

⁸ Judson, *op. cit.*, note 3 above, p. 480, notes three attendees: “[Alfred] Tissières, [Walter] Gilbert and

[Matthew] Meselson were almost alone.” Crick recalls: “Matt Meselson, whom I ran into in a corridor, alerted me to Marshall’s talk in a remote seminar room” (*WMP*, p. 130).

⁹ *WMP*, p. 130.

¹⁰ In December 2001, the Wellcome Trust purchased, with the assistance of the Heritage Lottery Fund, the scientific papers of Francis Crick for the sum of US\$2.4 million, beating-off a rival bid from a private source(s). For the circumstances surrounding the purchase, and issues raised, see Rex Dalton, ‘The history man’, *Nature*, 2001, **411**: 732–3; Alison Abbott and Rex Dalton, ‘Wellcome bid sees



Figure 1: Physics research students, Cavendish Laboratory, Cambridge (June 1952). James Watson and Francis Crick are in the first row standing, sixth and seventh from the left, respectively (PP/CRI/A/1/2/1).

and include some transitional material—correspondence and notes from meetings attended—approximately to 1980. Notwithstanding his having moved to the Salk Institute for Biological Studies, at La Jolla, in 1976, with a declared intention to explore neuro-biological pastures new, it took some time for the wider academic community to accept that he had embraced different research interests. Invitations to lecture, peer-review, and act as the DNA theoretical sounding-board of old continued to arrive with regularity. Indeed, as Crick acknowledged: “It took me several years to detach myself from my old interests, especially as in molecular biology surprising things were happening all the time”.¹¹ New discoveries such as retroviruses, recombinant DNA, rapid DNA sequencing, gene-splicing, introns and the notion of parasitic or “selfish” DNA were threads that proved impossible to ignore completely. Consequently, much of the transitional material from 1976–80 that has been catalogued still retains a DNA focus.

The arrangement of PP/CRI reflects an order revealed rather than an order imposed. Specifically, the titles of the two largest Sections—Travels and Meetings (PP/CRI/E) and Notes and Drafts (PP/CRI/H)—are Crick’s. Whilst not all files now placed in these two PP/CRI Sections were so kept, a sufficiently large proportion of them were for the application of Crick’s headings—backwards and forwards in time as required—to be enforced and practical. Together with the Correspondence file sequences (arranged as found), Travels and Meetings, and Notes and Drafts, provide a chronological spine to the archive, documenting closely the matters and the occasions that occupied Crick’s attention over time. It is envisaged that papers as yet uncatalogued—a second shipment of approximately equal bulk to the first, and a final shipment yet to be received—will be accommodated without strain within the existing arrangement.¹²

Enlivened by charm, wit and strength of personality, the archive is far from dry. In the abundance of material gathered—particularly, the correspondence—there is a richness of detail that will be of considerable interest to researchers tracing the many-stranded history of molecular biology. It would be a mistake to conclude that Crick’s influence as a theoretical driving-force derived solely from the many papers he has published over some fifty years. The impact of the written word—in formal papers, in the informal papers of the RNA Tie Club, and through the constant letters—must have been given considerable added force by Crick’s presence and eloquence—direct and beguiling, by all accounts in the archive—at conference after conference, through formal lectures, extempore summaries, informal meetings and individual conversations. Indeed, one has the impression that it was through these frequent persuasive moments of personal delivery and purposive conversations that Crick was most influential.

To judge from the flurry of the files, Crick’s desk operated at times as an unofficial molecular biology communications headquarters. Here is Crick’s guiding hand, on 29 April

Crick archive return home’, *Nature*, 2001, **414**: 678, and the conference paper by Julia Sheppard, ‘Molecular biology: the issues surrounding the purchase of the archives of leading molecular biologists by an American collector’, available at: <http://www.bath.ac.uk/ncuacs/FP_Sheppard.htm>. See also, for subsequent developments, ‘Auction of DNA archive cancelled’, *Nature*, 2003, **422**: 102.

¹¹ *WMP*, p. 146.

¹² PP/CRI is arranged as follows: A/Personal Material, B/Medical Research Council, C/Salk Institute for Biological Studies, D/Correspondence, E/Travels and Meetings, F/Doctorate, G/Notebooks, H/Notes and Drafts, I/Publication.

1965, writing to Watson and Nirenberg, a little over a year before the “historic” conference moment with which we began, just before the DNA arc completed its trajectory:

I am writing to you both because you are the two Chairmen of the Informal Exchange Group on Nucleic Acids and the Genetic Code. I want to suggest that at the end of the Gordon Conference on Nucleic Acids a statement be issued on the state of the Genetic Code. As you know I have found myself involved in this, but as a collater [*sic*] of information rather than a producer. I am constantly having to provide copies of my private version of the code to interested people . . . This year’s Gordon Conference should provide an ideal opportunity, not to present a final version of the code, but the best version of most of it. It will also be of value since it will show what remains to be established.¹³

And here, to give another example, is Crick writing (7 January 1965) to Alexander Rich, then working on the direction of RNA-messenger reading: “It would be nice to have the direction of messenger reading cleared up. Sydney and the others are working hard trying to discover the codon for amber and ochre mutants. We have a good idea what they are and perhaps by the time I reach MIT we shall know rather more definitely”.¹⁴ News travelled with the man as well as in his letters, and quickly became one very good reason for his being invited to campuses. Indeed, the letters sometimes give the impression that the ostensible purpose of a visit—a lecture, a seminar—was secondary to the conversations that it funded. Thus, on 7 December 1965, at the University of Wisconsin, Madison, Crick lectured (again) on ‘The structure of the genetic code’ to the delight of all who attended, but the primary focus of the visit was news and catch-up with Gobind Khorana, who had organized the visit. Crick wrote (22 November 1965) to Khorana:

Thank you for your very interesting letter of 17th November. It is so full of fascinating news that I can hardly wait to come to Madison to hear more about it all. We seem to be getting closer to the altered sRNA in amber suppression, but I doubt if we will have anything very definite before I leave here . . . I was especially fascinated by your remarks about GAA and about binding and wobble, and I am sure we shall find plenty of time to discuss all these topics fairly thoroughly.¹⁵

The regular flow of information through Crick provided him with constant access to the experimental data that nourished theory.¹⁶

Many “Cricks” are visible in the papers. There is Crick the mentor, Crick the atheist, Crick the free-thinker, and Crick the playful. There is petulant Crick, and disingenuous Crick. There is inspirational Crick. And there is always the Crick who does not suffer fools. Pity Mrs K S Wu, who, in 1973, had sent Crick her manuscript: “Dr Crick”, wrote “(Miss) Sue Barnes” (Crick’s secretary at the time) “has asked me to return to you your manuscript entitled ‘The I-Ching, The Unravalled Clock’ as it appears to him to be complete nonsense from beginning to end”.¹⁷ The sting is all the sharper for being delegated. To add further

¹³ PP/CRI/D/2/45.

¹⁴ PP/CRI/E/1/13/4.

¹⁵ PP/CRI/E/1/13/19.

¹⁶ Crick later made the generalization: “If elegance and simplicity are, in biology, dangerous guides to the correct answer, what constraints can be used as a guide through the jungle of possible theories? It seems to me that the only really useful constraints are contained in the experimental evidence. Even this

information is not without its hazards since . . . experimental facts are often misleading or even plain wrong. It is thus not sufficient to have a rough acquaintance with the experimental evidence, but rather a deep and critical knowledge of many different types of evidence is required, since one never knows what type of fact is likely to give the game away” (*WMP*, p. 141).

¹⁷ PP/CRI/D/1/2/17.

insult, the letter to Mrs Wu—more correctly, as is apparent from her covering letter, Dr Wu—was copied to Dr Joseph Needham and Dr Dennis Gabor. But, if Dr Wu had thought that Crick was likely to be impressed by the proposal of an elaborate scheme of correspondence between the sixty-four DNA codons and the sixty-four hexagrams of the I Ching, she had not done her homework. Nor was homework done when the venue was arranged for Crick's three John Danz Lectures ('Is vitalism dead?'), delivered at the University of Washington (February and March 1966) and immediately published as *Of molecules and men* (1966), his most extensive statement of his views on the relationship between science and atheism. On discovering the nature of the proposed venue, Crick wrote (14 December 1965):

The lectures will be concerned with the impact of biological ideas, both present and future, on our concept of the world. They will not be *militantly* anti-Christian, but nevertheless will be directed against the sort of ideas at present held by many religious people. You may not know that I am an atheist and a few years ago resigned my Fellowship at Churchill College because they threatened to build a College Chapel. I myself have not the slightest objection to lecturing in the Presbyterian Church, but I think the Church Authorities might conceivably not be too keen that their building should be used for what they might regard as anti-Christian propaganda.¹⁸

Crick's advice was swiftly acted upon and the University Presbyterian Church was abandoned in favour of Roosevelt High School Auditorium in North Seattle.

The personal attention that accompanied the award of a Nobel Prize in 1962 (Figure 2) did not fade with time. On the contrary, Crick became (for want of a better term) *fashionable*, and invitations to lecture were increasingly supplemented by a host of non-academic invitations, many from the media, most declined. Responding to an invitation from Sir Lawrence Bragg to give a discourse at the Royal Institution, Crick wrote (25 March 1963): "I am overwhelmed with invitations to give talks and as far as I possibly can I am refusing them all, otherwise I should end up by talking in my sleep".¹⁹ The demand was such that sleep-talking may have sufficed for some. "We can guarantee a large and enthusiastic audience, even if you wish to lecture on the construction of steam-heated swimming pools", wrote one enthusiastic professor on learning that Crick would soon be in town to deliver a lecture at a neighbouring American institution. Crick replied (8 December 1964): "Of course I realise that people do not listen any more to what I say but I like to give the appearance of novelty even if the substance is lacking".²⁰ Good jokes are repeated. Nearly thirteen years later, Thomas Jukes remarked (9 May 1977) after a visit by Crick to Berkeley: "You drew large and enthusiastic crowds at your lectures, and I suppose that you could hold the close attention of an audience even if you were talking about what the weather was like last week . . ." ²¹

A response strategy Crick adopted in the 1960s to cope with an enormous post—and to make a serious point playfully—was the (occasional) use of a pre-printed postcard offering a number of reply options. The seventeen listed (see Figure 3) are a faithful reflection of the requests he regularly received, and one could add more (unsolicited solutions to "the coding problem" were quite common). One way of getting in under the radar of the reply-card might be to acknowledge it as an opening gambit. Thus, perhaps, thought Dr Robert

¹⁸ PP/CRI/E/1/14/5.

¹⁹ PP/CRI/E/2/2.

²⁰ PP/CRI/E/1/13/4.

²¹ PP/CRI/E/1/25/13.

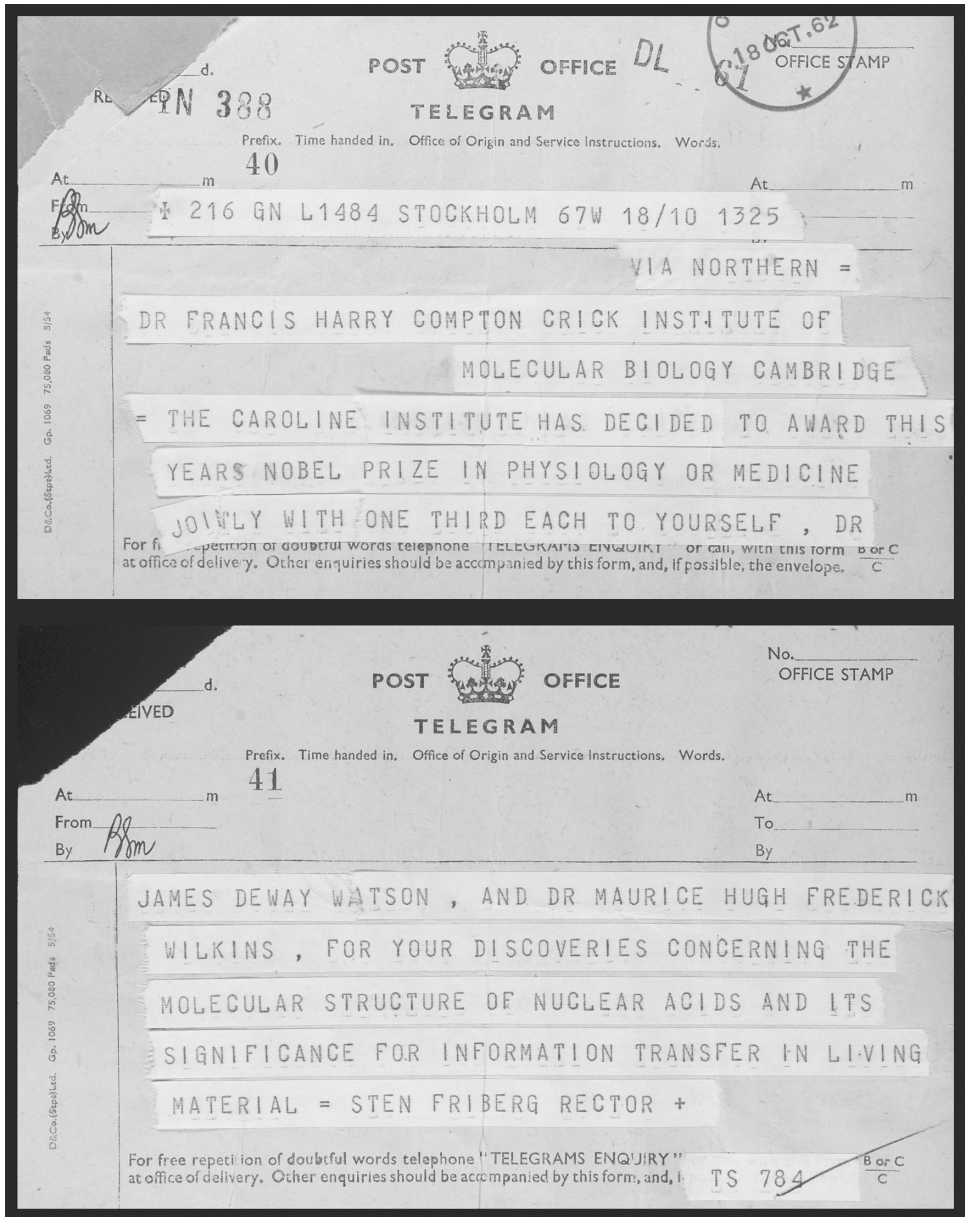


Figure 2: Telegram (18 October 1962, in two parts) from Sten Friberg, Rector, Karolinska Institutet, informing Francis Crick of the award of the Nobel Prize in Physiology or Medicine, shared with James Watson and Maurice Wilkins (PP/CRI/A/3/1/1).

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From:
M.R.C., Laboratory of Molecular Biology, Hills Road, Cambridge.

Dr. F. H. C. Crick thanks you for your letter but regrets that he is unable to accept your kind invitation to:

send an autograph	read your manuscript
provide a photograph	deliver a lecture
cure your disease	attend a conference
be interviewed	act as chairman
talk on the radio	become an editor
appear on TV	contribute an article
speak after dinner	write a book
give a testimonial	accept an honorary degree
help you in your project	

Figure 3: Francis Crick reply card, used, on occasion, in the 1960s (PP/CRI/E/2/1).

Langridge (22 October 1964): “I realise that the following request will make me eligible for receiving one of your all purpose cards with a number of items checked, nevertheless as a somewhat unwilling organizer of the Biophysics Seminars at Harvard this year. . .”²²

To read such remarks is to see some of the brush-strokes that add to a shared portrait of a public Crick, a portrait never quite finished, owned by many, and painted by many hands. Indeed, many of the boldest additions are in Crick’s own hand, such as the entry in *Who’s Who* (no longer current) in which he famously noted his favourite recreation as conversation with pretty women. One reply, call it an answering stroke, came in the form of a telegram (stamped 14 September 1966): “I am a pretty woman who would very much like to interview you for American Vogue as soon as possible stop please contact me at Grosvenor 9080 . . .”²³ Unable to attend a forthcoming Crick lecture, Hans Noll (22 November 1966) wrote a long suspended clause with a footnote flourish: “Although there is good precedence”, he began, “that playing host to Francis Crick is sufficient cause for being excused from any other obligations . . .”, and thereby invoked what might be termed the Crick Excuse. The “precedence” referred to (footnoted in the letter) is that of a colleague who had been scheduled, on a previous Crick occasion, to deliver a lecture himself but had sent “a stand-in with the excuse that he was being visited by Francis Crick! This sounded”, concluded Noll, “like an event that a certain clause in insurance contracts defines as an ‘Act of God’.”²⁴ Once, a public exposition of this recurring conceit—famous atheist and/as

²² PP/CRI/E/1/13/4.

²³ PP/CRI/E/2/4, an ‘Invitations Refused’ file. Another bold Crick brushstroke was as signatory to the SOMA full-page statement which appeared in *The Times*, Monday, 24 July 1967, suggesting to the Home Secretary that he implement a five point programme of cannabis reform. For the statement, visit:

<<http://www.drugtext.org/library/articles/TimesAd.html>>

²⁴ PP/CRI/E/1/15/3. Noll’s next fulsome paragraph is all news, the information that nourishes theory: “We have what I consider definitive evidence that there are at least three classes of ribosomes . . .”.



Figure 4: Crick wall-graffiti. Location and date not indicated (PP/CRI/A/1/2/8).

God—took the form of wall-graffiti: “CRICK FOR GOD”. It is recorded in a sepia photograph in the archive (Figure 4), in which Crick jostles for wall-space (perhaps in Cambridge) with the British Conservative Party politician “ENOCH” [Powell] and “THE LEFTIES”.²⁵

As if deification were not enough, the public portrait was also honoured with a putative knighthood. There are many examples in the archive, over a number of years, of letters wrongly addressed to “Sir” Francis Crick, for which Dr Crick had many graceful responses. James Watson, for one, wrote him a mock-congratulatory letter (8 September 1966) when the knighthood mistake accompanied an article by Crick in the *Saturday Review* for 3 September 1966.²⁶ However, the entertaining apotheosis came when the title appeared in the answer to a newspaper crossword clue in the *New York Times*,²⁷ thereby firmly endorsing the urban legend.

Although the Crick archive at the Wellcome Library is not an archive of personal papers (those are now destined for the University of California), the scientific papers nevertheless bear the stamp of personality and record a scientific career within a manifest social and cultural context.

The Spur of Priority

Intellectual priority occupies a special place in the social conventions that govern the communication of scientific ideas, and the establishment of public reputation. The dissemination of scientific information derives from a fundamental characteristic of scientific endeavour, that it is founded upon and advanced by a shared understanding of the world. There can be no private science (other than in alchemy’s alembic). However, it has long been recognized that this characteristic exists in tension with the claim of an individual scientist to priority and, in appropriate cases, to invention, as became rapidly apparent during the emergence of modern scientific practice in the latter half of the seventeenth

²⁵ PP/CRI/A/1/2/8.

²⁶ ‘The computer, the eye, the soul’, *Saturday Review*, 3 Sept. 1966, pp. 53–5.

²⁷ PP/CRI/D/1/4/18.

century. The founding of the Royal Society (1660) and its journal, *Philosophical Transactions* (1665), established a conventional framework which gave an agreed means of resolving dispute whilst simultaneously providing for the dissemination of scientific knowledge through the open practice of publication and the introduction of a form of peer-review. In his Royal Society Anniversary Address for 1999, Sir Aaron Klug, then President, referred to the desire to receive personal credit and the esteem of peers as an important motivating influence on scientists.²⁸ Recent debate about the legitimacy of granting patents in the context of human genome research illustrates very well that the tension is an enduring one.

Whilst the rhetoric appropriate to public occasions, such as the opening address of the annual meeting of molecular biologists at Cold Spring Harbor, 2 June 1966, with which we began, may lead to such occasions being described as “historic”, it is through publication that the scientific record is established and maintained. When Crick returned from the Fifth International Congress of Biochemistry in Moscow, in August 1961, following the surprise of Nirenberg’s presentation, he took particular care with his own contribution to the record, as the archive shows. The Moscow conference had fallen in the midst of a series of genetic experiments that Crick and his colleagues had been conducting with acridine mutants, designed to determine whether the genetic code had a triple ratio. This work, which had been the cause of some excitement to all concerned,²⁹ had been the primary news that Crick bore with him from Cambridge, that had been heralded in letters, and was to be published in *Nature* at the very end of the year, to considerable attention, as ‘General nature of the genetic code for proteins’.³⁰

On 16 November 1961, Crick wrote, with scrupulous precision, to Marshall Nirenberg:

I enclose an account of our genetical work which we have submitted to *Nature*. We had the basic idea in the summer, before your epoch-making discovery, and reported it at the Col de Voza DNA meeting in June, but we only got the triples after I returned from Moscow. Your PNAS papers arrived here the day before we sent off our MSS, so I was able to add the reference. I didn’t put in your footnote about poly C and proline as I felt I had made the point sufficiently well. I expect by now you will have experimental data to show that the coding ratio is 3 rather than 6. We had considered looking at the average length of polypeptide chains produced by a polynucleotide of known average length, but it seemed to us rather difficult.³¹

The detail that is offered here is an exact mapping of the chronological event and its correlate, the published record. It presents what is, in effect, an anatomy of scientific record creation, and differentiation, through the medium of archival record (the letter itself). The sequential pattern of their independent work is here implicitly submitted to the higher authority of the conventions that govern priority. The footnote detail that is Crick’s reference to Nirenberg’s PNAS paper³² illustrates very well the function of the footnote in the

²⁸ Sir Aaron Klug, ‘Anniversary address 1999’, *Royal Society News*, Dec. 1999, p. 1. Sir Aaron Klug was President of the Royal Society from 1995 to 2000.

²⁹ “Carefully we double-checked the numbers on the petri dishes to make sure we had looked at the correct plate. Everything was in order. I looked across at Leslie [Barnett]. ‘Do you realise,’ I said, ‘that you and I are the only people in the world who know it’s a triple code?’” (*WMP*, p. 133).

³⁰ FH Crick, L Barnett, S Brenner, R J Watts-Tobin, ‘General nature of the genetic code for proteins’, *Nature*, 1961, **192**: 1227–32.

³¹ PP/CRI/D/1/1/14.

³² M W Nirenberg and J H Matthaei, ‘The dependence of cell-free protein synthesis in *E. coli* upon naturally occurring or synthetic polynucleotides’, *Proc. Natl. Acad. Sci. USA*, 1961, **47**: 1558–602.

rhetorical conventions that comprise the scientific paper.³³ As may be seen, Crick's report to the meeting in June at Col de Voza is presented as a very important marker in the sequence of events outlined. Crick wants to be sure that an accurate note will be published, and writes on the same day (16 November 1961) to Dr R Latarjet, organizer of the 11th Annual Meeting of the Société de Chimie Physique at Col de Voza, 26–30 June, 1961:

You may recollect that I reported our basic idea in the discussion at the Col de Voza conference, though not the bit about the coding ratio being 3. At the end of the conference I handed in a short written account. Could you tell me when and where it is likely to be published? It is the only simple means I have of establishing that we had the idea before Nirenberg's astonishing discovery that poly U codes for polyphenylalanine.³⁴

A few weeks later, Crick is writing (4 January 1962) to Nirenberg, "The English papers have made rather a fuss about our Nature paper, which was published on Saturday, but as far as I have been able I have stressed that it is your discovery which was the real breakthrough".³⁵ Later in the year, the circumstances of publication of a review article for *Scientific American* are cause for concern. Both Crick and Nirenberg had been commissioned to write articles for *Scientific American*. Crick's article was to be published first. He writes (3 September 1962) to the editor about matters of presentation:

About Nirenberg's article: I am sure you realise that this field has unfortunately been disturbed by personal conflicts and questions of priority. I am therefore taking particular trouble that it should not appear to anyone that we wish to claim more than is our due. However ingenious and elegant our experiments are it must be realised that it is the biochemical work on the cell-free system which will be crucial, and moreover that Nirenberg's and Matthaei's basic discovery was made before we have [*sic*] obtained our triple mutants . . . Now the effect of publishing my article as it stands will make it appear (however unjustly) that I am giving only passing credit for the biochemical work. Moreover it will undoubtedly be said that by some subtle manoeuvre I persuaded you to publish my article before Nirenberg's! It is not simply a question of what Nirenberg himself feels about it (he is a very reasonable person, and we are on very good terms)—but what other people in the field will say. I need not tell you that almost all of them read *Scientific American*.³⁶

And yet, notwithstanding the sensitivity to priority illustrated by these examples and the evident care and time taken to ensure the veracity of record, insofar as that could be ensured, Crick subsequently came to reflect upon the historical import of the painstaking work with

³³ "While many a general reader . . . may regard the lowly footnote or the remote endnote or the bibliographic parenthesis as a dispensable nuisance, it can be argued that these are in truth central to the incentive system and an underlying sense of distributive justice that do much to energize the advancement of knowledge." Robert K Merton, 'The Matthew effect in science. II. Cumulative advantage and the symbolism of intellectual property', *Isis*, 1988, 79: 621. Consider, in this regard, the troublesome drafting of the penultimate sentence of the first Watson and Crick paper (effectively, a footnote), in which the authors express their indebtedness to the King's College team. See PP/CRI/H/1/11 (for first paper typescripts) and PP/CRI/H/1/42/4

(Maurice Wilkins to Crick [18 March 1953], headed "Suggested modification to your MSS").

³⁴ PP/CRI/E/1/9/5. Amongst the other delegates at Col de Voza were James Watson, Maurice Wilkins, Jacques Monod, Gunther Stent, Seymour Benzer, François Jacob, Arthur Kornberg, Erwin Chargaff, and Gobind Khorana. For Crick's "report", see 'Genetic studies concerning the lysozyme of phage T4', Société de Chimie Physique, *Deoxyribonucleic acid: structure, synthesis and function: proceedings of the 11th Annual Reunion of the Société de Chimie Physique, June 1961*, Oxford, Pergamon Press, 1962, p. 188.

³⁵ PP/CRI/E/1/10/4/2.

³⁶ PP/CRI/H/3/9.

acridine mutants in doubtful terms: “I think you could have deleted the whole work and the issue of the genetic code would not have been very different. It would not have affected Nirenberg’s discovery and most of the other work. This I think is the test, you know, that historians should apply. If you delete a bit of work, would it make a difference?”³⁷ A similar deterministically-framed question is advanced in *What mad pursuit*: “what would have happened if Watson and [Crick] had not put forward the DNA structure[?]” As if historical enquiry were akin to problem-solving, or akin to deleting or adding a DNA base, Crick remarks that this is the sort of question historians should be able to answer, or “I do not see what historical analysis is about”.³⁸

From an archivist’s perspective, the difference that deletion would make, albeit hypothetical, is the diminution of the archival record. The primary archival impulse is not deletion but inclusion, to thicken, so to speak, the historical record, such that more is more. The loss of material, whether irretrievable physical loss or whether the loss of public access (through the practice of private collection), is a keen reminder of the fragility of the historical record.

There is good reason to suppose, from the rather slim body of early Crick material extant, that an unquantifiable amount of material has been lost from the late 1940s and early 1950s. Crick confirms as much in a letter to Watson (16 July 1975). On learning that Watson was considering publishing something on the RNA Tie Club,³⁹ he notes that “almost all my own early correspondence was unfortunately thrown away without my knowledge by an over-efficient Secretary but Sidney still has some letters from [George] Gamow and other relevant papers”.⁴⁰ On the subject of loss, researchers should also note that there are currently (at least) two missing Crick laboratory notebooks. Since the notebooks in question—one from 1952 and the other from 1961—are cited, quoted and referenced in secondary literature, they have been listed in PP/CRI as *wanting*. It is very much hoped that they will appear amongst the materials that remain to be catalogued. PP/CRI/G/1/7 is a laboratory notebook for the period July–August 1952, and contains notes of Crick’s attempts to prove base-pairing experimentally.⁴¹ The second (PP/CRI/G/1/16) is a loose-leaf notebook containing details of the genetic experiments that the Moscow meeting of 1961 had interrupted—ironically, the very work that did not pass Crick’s deletion test.⁴²

Models and Metaphors

If Watson had had his cautious way, the first Watson and Crick paper would have omitted its most far-reaching “suggestion”:

I was keen that the paper should discuss genetic implications. Jim was against it. He suffered from periodic fears that the structure might be wrong and that he had made an ass of himself. I yielded to his point of view but insisted that something be put in the paper, otherwise someone would certainly

³⁷ Judson, *op. cit.*, note 3 above, p. 486.

³⁸ *WMP*, p. 75.

³⁹ Watson gave the first George Gamow Memorial Lecture, on 17 April 1978, at the University of Colorado at Boulder, with the title ‘The RNA Tie Club’.

⁴⁰ PP/CRI/D/2/45.

⁴¹ Cited in the bibliography to Robert Olby, *The path to the double helix*, London, Constable, 1994, p. 467.

⁴² For the period Feb. to June 1961, cited in Judson, *op. cit.*, note 3 above, p. 457. See note p. 657: “notebook entries, 8 May 1961 and after—Laboratory notebooks, in Crick’s hand, and in his files.”

write to make the suggestion, assuming we had been too blind to see it. In short, it was a claim to priority.⁴³

Although the title declared its subject to be the structure of a particular molecule (too unfamiliar to be abbreviated), the paper's true weight was to rest upon, as Crick correctly surmised, the structure's functional implications. There are six typescripts of this paper (PP/CRI/H/1/11) but there is otherwise little direct documentation concerning the identification of the double helix structure. This may be, in part, only a reflection of the circumstances and the manner—some have called it *style*—in which the structure was identified (familiar enough not to need re-telling here), but it may come as a surprise to researchers that there are not more recorded traces of the processes of thought that led to discovery. On the other hand, Crick's PhD thesis ('Polypeptides and proteins: X-ray studies')⁴⁴ is a thorough exposition of originality, preparation and readiness for an assault upon the black box of DNA, for, in Maurice Wilkins' words, "a general offensive on Nature's secret strongholds".⁴⁵ Available in the archive as draft chapters (PP/CRI/F/1) and as a bound volume (PP/CRI/F/2), the thesis includes both the innovative work with Vladimir Vand and William Cochran to determine the Fourier transform of a helix and the hypothesis of a coiled coil structure for α -keratin.⁴⁶ The only other substantial prior material directly relevant to the double helix is the important manuscript (in Crick's hand) with the title 'The structure of sodium thymonucleate: a possible approach' (PP/CRI/H/1/42/1). It is important because it was Watson and Crick's first attempt to address, in writing, the structure of DNA. It makes particular reference to Rosalind Franklin's presentation (21 November 1951, attended by Watson) of her first year's work at King's College London. Within a week of the colloquium, Watson and Crick had built their ill-fated first model and drafted this note of "general principles upon which the structure of DNA might be based". With the four bases on the *outside* of the structure, their erroneous model had *three* chains and insufficient water.⁴⁷

Whilst there is little specific material immediately prior to discovery of the double helix, there is a considerable amount on its reception thereafter and its survival as a structure over time. Robert Olby has recently written about the double helix's "quiet debut",⁴⁸ and Crick has observed that "the double helical structure of DNA was . . . finally confirmed only in the early 1980s".⁴⁹ During that period the archive records a number of challenges to its correctness—some structural, some more philosophical—most of which involved Crick's response, either through detailed correspondence or in the form of a published note. Surprisingly, when crystallized DNA was first seen, in 1979, it was a left-turning helix,

⁴³ *WMP*, p. 66.

⁴⁴ Crick's PhD thesis (Gonville and Caius College, University of Cambridge) was submitted in July 1953.

⁴⁵ Wilkins, letter to Crick, 7 March 1953 (PP/CRI/H/1/42/4).

⁴⁶ See Robert Olby, 'Francis Crick, DNA and the central dogma', *Daedalus*, 1970, **99** (4): 950.

⁴⁷ In Watson's account of his and Crick's presentation of their incorrect model (to Maurice Wilkins, Rosalind Franklin, William Seeds and Ray Gosling), he notes: "Most annoyingly, [Franklin's] objects were not mere perversity: at this stage the

embarrassing fact came out that my recollection of the water content of Rosy's DNA samples could not be right. The awkward truth became apparent that the correct DNA model must contain at least ten times more water than was found in our model . . . As soon as the possibility arose that much more water was involved, the number of potential DNA models alarmingly increased." (*The double helix*, London, Weidenfeld & Nicolson, 1997, pp. 79–80.)

⁴⁸ Robert Olby, 'Quiet debut for the double helix', *Nature*, 2003, **421**: 402–5.

⁴⁹ *WMP*, p. 73.

christened Z-DNA, and not the familiar right-turning helix of the first Watson and Crick paper. “More ordinary DNA sequences were soon crystallised. This time the resulting structures looked very much like those predicted by the X-ray fibre data, though there were small modifications and the helix varied somewhat depending on the local sequence of the bases”.⁵⁰

A retrospective critique of “classical” molecular biology has been gathering momentum for some years, a process to which the resources of the newly-opened Crick archive will inevitably contribute. Particular attention has been given in such retrospective readings to “the sequence hypothesis” and “the central dogma”, first presented at a symposium held at University College London, September 1957, on ‘The biological replication of macromolecules’ (PP/CRI/E/1/5/4), and subsequently incorporated in ‘On protein synthesis’.⁵¹ Re-addressed by Crick, in the light of new experimental data, in ‘Central dogma of molecular biology’,⁵² it appeared once again, in Appendix A to *What mad pursuit*.⁵³ The “central dogma” was embraced by molecular biologists as the canonical statement of a widely-shared understanding of how a strand of DNA corresponds to the amino acid sequence of a protein. An additional attractive aspect of the “dogma” was its Darwinian character, in that the formulation did not permit the inheritance of acquired characteristics. As well as indicating the direction in which sequence information usually travels, the “dogma” also implied the direction in which sequence information *cannot* travel. “The so-called central dogma is a grand hypothesis that attempts to predict which transfers of sequence information *cannot* take place”.⁵⁴ The triangular figure that Crick used consistently to present the “dogma” visually, with DNA, RNA and Protein at each point of the triangle, and arrows indicating the direction in which the genetic information travels, was revised in ‘Central dogma of molecular biology’ to accommodate both the RNA→RNA transfer of certain viruses such as flu and polio, and the RNA→DNA transfer (reverse transcription) used by RNA retroviruses, such as the AIDS virus. Crick’s correspondence with Howard Temin (who shared a Nobel Prize in 1975 for his work on discoveries concerning the “interaction between tumour viruses and the genetic material of the cell”)⁵⁵ is of some interest in this regard, particularly Crick’s letters of 3 August and 17 September 1970. Evidence accumulated to substantiate Temin’s view that RNA→DNA transfer “is more general than just in RNA tumour viruses, and in fact that the RNA tumour viruses arise from normal elements with this mode of transfer”.⁵⁶ Today, we know from sequencing data that the human genome is dominated by retro-elements, that there are “more copies of sequences encoding reverse transcriptase than sequences encoding all other proteins combined. Half of our genome is devoted to retroelements and their remnants, compared with only a few percent devoted to gene coding regions.”⁵⁷

⁵⁰ Ibid.

⁵¹ F H Crick, ‘On protein synthesis’, in *The biological replication of macromolecules*, Symposia of the Society for Experimental Biology, vol. 12, Cambridge University Press, 1958, pp. 138–63. For an earlier typescript, see ‘Ideas on protein synthesis (Oct. 1956)’ (PP/CRI/H/2/6).

⁵² F H Crick, ‘Central dogma of molecular biology’, *Nature*, 1970, **227**: 561–3.

⁵³ *WMP*, p. 168.

⁵⁴ Ibid.

⁵⁵ <<http://www.nobel.se/medicine/laureates/1975/press.html>>

⁵⁶ Temin to Crick, 27 July 1970, PP/CRI/D/1/1/19.

⁵⁷ Steven Henikoff, ‘Beyond the central dogma’, *Bioinformatics*, 2002, **18** (2): 223–5.

It is the concept of “information”—as an assumed but unexamined given term at the heart of molecular biology’s conceptualization of its project—which has recently been the object of much discussion. The term makes an early appearance in the second Watson and Crick paper for *Nature*, published only one month after their first: “it therefore seems likely that the precise sequence of the bases is the code which carries the genetical information”.⁵⁸ Was this usage of “information” only a convenient heuristic device to aid thought, or was “information” intended more literally? Crick conceived it as “specificity”: “information means here the *precise* determination of sequence, either of bases in the nucleic acid or on amino acid residues in the protein.”⁵⁹ It has, however, been forcibly argued recently that in this context the term is best interpreted as a metaphor, rather than as a literal reference to biological phenomena. Sahotra Sarkar, for example, sees “no clear technical notion of ‘information’ in molecular biology. It is little more than a metaphor that masquerades as a theoretical concept and . . . leads to a misleading picture of the nature of possible explanations in molecular biology”.⁶⁰ The central charge of the case is that molecular biology has been engaged in “reductionism” in focus and practice, and this has led to a “hegemony of genetics over other approaches to biological problems” and to “the extreme position . . . that all or most human disease and human behaviour can be ascribed to genes”.⁶¹

Some indication of the scientific distance travelled since the structure of DNA was proposed in 1953 is given in several review papers in the fiftieth DNA anniversary issue of *Nature*. It is a changed world in which the double helix is less exclusively dominant (though not in its enduring iconic form), and even fleeting: “What you find instead in the cell nucleus is, apparently, a tangled mess. And don’t think that this will, on closer inspection, turn out to be woven from that elegant, pristine double helix. Rather, the threads are chromatin—a filamentary assembly of DNA and proteins—in which only very short stretches of the naked helix are fleetingly revealed.”⁶² Furthermore, there is recognition of epigenetic inheritance. “At its simplest level, chromatin should be viewed as a single entity, carrying within it the combined genetic and epigenetic codes.”⁶³ The next physical DNA frontier is the difficult middle ground of mesobiology: “We know about molecules, we know about cells and organelles, but the stuff in between is messy and mysterious.” At this difficult level of magnification (“perhaps a few to several hundred nanometres”),

⁵⁸ “The phosphate-sugar backbone of our model is completely regular, but any sequence of the pairs of bases can fit into the structure. It follows that in a long molecule many different permutations are possible, and it therefore seems likely that the precise sequence of the bases is the code which carries the genetical information.” J D Watson and F H Crick, ‘Genetical implications of the structure of deoxyribonucleic acid’, *Nature*, 1953, **171**: 964–7. See PP/CRI/H/1/12 for seven drafts of the paper.

⁵⁹ Crick, *op. cit.*, note 51 above, p. 153.

⁶⁰ Sahotra Sarkar, ‘Biological information: a skeptical look at some central dogmas of molecular biology’, in Sahotra Sarkar (ed.), *The philosophy and history of molecular biology: new perspectives*,

Dordrecht, Kluwer Academic Publishers, 1996, p. 187. See also Jesper Hoffmeyer, ‘The central dogma: a joke that became real’, *Semiotica*, 2002, **138**: 1–13: “In the absence of any rigid definition of the term ‘information’ the instructional conception of this word imperceptibly slid into the matrix of tacit metaphors nourishing the minds of modern biologists” (p. 6).

⁶¹ Jon Beckwith, ‘The hegemony of the gene: reductionism in molecular biology’, in Sarkar (ed.), *op. cit.*, note 60 above, p. 171.

⁶² Philip Ball, ‘Portrait of a molecule’, *Nature*, 2003, **421**: 421–2, on p. 421.

⁶³ Gary Felsenfeld and Mark Groudine, ‘Controlling the double helix’, *Nature*, 2003, **421**: 448–53, on p. 452.

scientists expect to see “DNA on a scale where it flexes and twists like a soft rod” revealing “how the mechanical and the molecular interact.”⁶⁴ It is a world for which “the central dogma”—bravely predictive⁶⁵—was a point of entry but now ill-fits a post-genomic mesobiological world that is ready for new models and new metaphors to match its bewildering complexity. A systems approach to biology is one methodology now being advocated, one which recognizes “two types of biological information: the digital environment of the genome, and environmental information, such as metabolite concentrations, secreted or cell-surface signals from other cells or chemical gradients”. By this view, the end of a journey begun in 1953 is projected as “the grand unification of the biological sciences in the emerging, information-based view of biology”.⁶⁶ In this new, enlarged and defined information set, DNA is recontextualized, placed amongst a range of processes—many unseen, and many, it is recognized, not yet understood—that comprise heredity.

Whatever future direction molecular biology takes, and whatever historical interpretations of its development are advanced, the work of Francis Crick will remain a formative and central episode. Crick scholarship is in its infancy. There is, as yet, no published edition of his scientific papers. Their variant drafts, now available for the first time, are ripe for scholarly attention, as is the substantial correspondence.⁶⁷ The archive captures, in its responsive and detailed chronicle of the period, much of the process through which molecular biology came to define the scope of its project and thus itself. Much of what is to be discovered in the Francis Crick archive is the rich and “untidy” log of that process.

⁶⁴ Ball, *op. cit.*, note 62 above, p. 421.

⁶⁵ Crick, *op. cit.*, note 52 above, p. 561: “The central dogma was put forward at a period when much of what we now know in molecular genetics was not established. All we had to work on were certain fragmentary experimental results, themselves often uncertain and confused, and a boundless optimism that the basic concepts involved were rather simple and probably much the same in all living things. In such a situation well constructed theories can play a really

useful part in stating problems clearly and thus guiding experiment.”

⁶⁶ Leroy Hood and David Galas, ‘The digital code of DNA’, *Nature*, 2003, **421**: 444–8, on pp. 446, 448. See also, for an overview, Tom Sgouros Jr, ‘Figure and ground: translating the genome’, available at: <<http://www.as220.org/tomfool/meta/dnachap.html>>

⁶⁷ In 1977, Horace Judson proposed editing a selection of papers, including correspondence extracts, but Crick declined (PP/CRI/D/2/15).