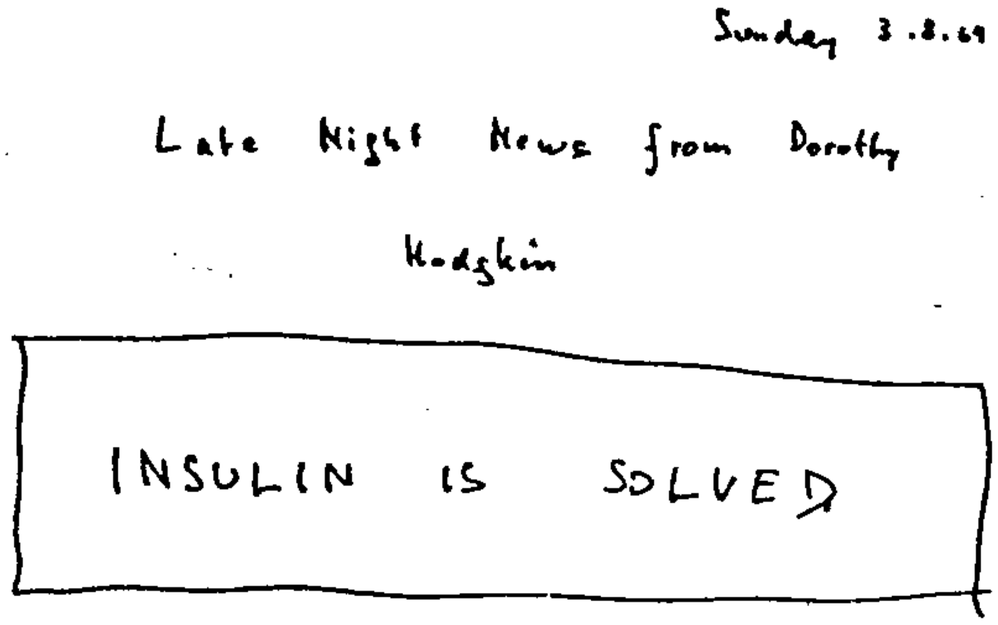

Figure 3. Poster at the Laboratory of Molecular Biology, Cambridge, announcing the great news.

as much to the Swedish crystallographer Gunner Hägg when I ran into him in a tram in Rome. He encouraged me to propose her, even though she had been proposed before. In fact, once there had been a newsleak that she was about to receive the Nobel Prize, but it proved false; Dorothy never mentioned that disappointment to me until long after. Anyway, it was easy to make out a good case for her; Bragg and Kendrew signed it with me, and to my immense pleasure it produced the desired result soon after.

'There are certain letters which I dread to open', Dorothy once told me, 'and when I saw one from Buckingham Palace I left it sealed, fearing that they wanted to make me *Dame* Dorothy'. I suppose it would have made her feel like a *femme formidable*, which she so happily is not. When she eventually opened the letter she was relieved that instead the Queen offered her the Order of Merit, which is a much greater honour and carries no title. She received it in private audience on the same day as Benjamin Britten. Once when they were both getting honorary degrees, Henry Moore said to her: 'It's really very good of them to give the OM to a simple chap like me.' I suspect that this remark echoed some of Dorothy's own feelings.

Dorothy Hodgkin and molecular biophysics in Oxford: A fragment of personal history

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THE Laboratory of Molecular Biophysics had its origins at the Royal Institution, London, in the group that Lawrence Bragg assembled there when he became Resident Professor and Director of the Davy–Faraday Research Laboratory in 1954. During the preceding years in Cambridge, Lawrence's main interest had been in the studies of protein crystals by Max Perutz, John Kendrew, and their colleagues, and he had involved himself deeply in the work of the group during the period when very few crystallographers believed that it was likely to be successful[1]. When he left Cambridge in January 1954, however, the tide had turned dramatically. A few months earlier Max, with David Green and Vernon Ingram[2], had shown how the method of isomorphous replacement could be used in protein crystallography and the way seemed open to the detailed determination of protein structures—starting with Max's haemoglobin and John Kendrew's myoglobin. Even the computational problems no longer seemed insurmountable with the growing power and availability of digital computers[3].

Bragg would have liked to take Max and John with him to London to continue the work there, but, at this critical time with so much to be done to exploit the breakthrough, neither was willing to leave Cambridge. But they promised to help Bragg assemble a new group at the Royal Institution and to co-operate closely in its work. At this stage Uli Arndt was already at the Royal Institution, where he had been studying proteins by low-angle scattering with Dennis Riley[4] and developing experimental methods. Early in 1955 he was joined by Helen Scouloudi, who had worked on ribonuclease crystals with Harry Carlisle and now began her study of seal myoglobin. In the autumn, David Green joined the Group from Cambridge and Tony North came from King's College London, where he had worked with J. T. Randall and Pauline (Cowan) Harrison on collagen.

These recruits all had experience of protein work, of one kind or another, but the original team was completed at the end of 1955 by the addition of two more who had not worked directly on proteins. This was Dorothy's doing. Anxious to build up a really strong group at the Royal Institution, Bragg had also asked Dorothy if she would join him there, but she was not prepared to leave Oxford at a time when her family commitments were

heavy and the work on vitamin B_{12} was promising well. Instead, with her inimitable knowledge of crystallographers around the world, she suggested that Bragg should ask Jack Dunitz and me to join him. At this time Jack was, as Dorothy puts it, in an American phase of his transatlantic oscillations – damped, as it has turned out – and I was working with W. H. Barnes at the National Research Laboratories in Ottawa, Canada. So it came about that I joined the Group at the Royal Institution in January 1956 and began to work on diffractometers with Uli Arndt and on sperm-whale myoglobin with John Kendrew—who came from Cambridge to see us nearly every week.

Jack Dunitz also joined the laboratory, but he did not work directly on proteins and stayed only until 1957 when he left for Zurich—again at Dorothy's suggestion. To complete the catalogue of people who are now in the Laboratory of Molecular Biophysics and were at the Royal Institution, I must mention Colin Blake, who came from industry in 1960; Louise Johnson, who began as a graduate student in 1962; and Schaffi (R. Aschaffengurg), our incomparable grower of crystals, who collaborated from his base in Reading from 1955 onwards.

In the mid 1950s there was still quite a sharp division in crystallography between those who worked on proteins and those who did not. Many crystallographers persisted in the view that protein structures could not be solved and the protein specialists sometimes seemed to neglect what was going on in general crystallography, regarding the determination of protein structures as a special problem requiring the development of new methods of analysis. This applied neither to Lawrence nor to Dorothy, who made no distinction between proteins and the rest, though their individual attitudes differed in an interesting way. Lawrence liked best to apply the methods he had developed during the early 1920s for the analysis of mineral structures and he was fond of quoting his paper with West[5] on 'The determination of structures with many parameters'—where 'many' means a dozen or so. Accordingly one of my first assignments, when the earliest semi-automatic diffractometer was ready for operation, was to measure the absolute scale of the seal-myoglobin crystals, using anthracene as the reference crystal to measure the intensity of the incident X-ray beam. Bragg's predilection for considering careful measurements of a few individual reflections is illustrated well by his last research paper, on methods for establishing the positions of heavy atoms in protein crystals[6]. Although he had been the first to demonstrate the value of two-dimensional Fourier syntheses in structure analysis[7], he mistrusted Fourier methods, especially Fourier refinement—which elicited somewhat disparaging remarks about boot straps. Dorothy, on the other hand, is the archexponent of Fourier refinement and her papers are full of Fourier maps—many of which seemed meaningless to most other crystallographers when she first described them. (I remember well the scepticism that greeted her early maps of vitamin B_{12} when she presented them at the Stockholm Conference in 1951.) From penicillin[8] through vitamin B_{12} (ref. 9) to insulin[10] the interpretation of electron-density maps of various kinds has been her principal weapon and delight. Anyone who has seen her at work, surrounded by carefully drawn maps and absorbed in their interpretation, has been privileged to witness an artist in action as, with incomparable insight, she *turns them to shapes, and gives to airy nothing, a local habitation and a name.*

Dorothy came often to see us at the Royal Institution, while we contributed to the work on myoglobin and haemoglobin and then branched out into independent studies of β-lactoglobulin[11] and hen-egg-white lysozyme[12,13], and she never failed to convey a conviction that proteins would eventually follow vitamin B_{12} in submitting to the most detailed and refined study. But her support went far beyond encouragement and advice. As early as 1958 she was discussing with Hans Krebs the possibility of our helping to build up a protein-structure group in the Biochemistry Department in Oxford. In the event this idea was not realized, but it led on to John Pringle's successful campaign for the establishment of a Molecular Biophysics Laboratory in the Department of Zoology. The happy result was that most of us who had worked with Bragg at the Royal Institution were able to move to Oxford, when he retired in 1966, to set up this new laboratory. Even more happily, Dorothy, and the flourishing group she had built up to intensify her work on insulin, joined us there.

Fourteen years later the traces of Dorothy's influence can be seen everywhere: our biochemical effort under Robin Offord is largely concerned with exploiting the new knowledge of insulin derived from her studies; the study of triose phosphate isomerase came to us from her, since it was naturally to Dorothy that Stephen Waley turned (as have many others) when he first obtained useful crystals of the enzyme; and everywhere, it seems, there are Fourier maps—as larger and larger structures submit to refined analysis just as she knew they would. When I started work on proteins in 1956 not many people expected that we should one day study the apparent thermal motion of the atoms in them[14] or locate their hydrogen atoms[15]. But I do not think Dorothy is surprised. When we met the other week she was chuckling over two additional water molecules she had just seen in the latest map of insulin. Who knows what she may inspire us to see next?

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Meetings with Dorothy

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Dorothy Hodgkin (née Crowfoot) is a remarkable person and an eminent scientist, who has done much for the glory of her homeland, England, and is well-known for her scientific and humanitarian activities throughout the world. Her personal example and extensive contacts have deeply influenced the development of X-ray crystallography of biological molecules in many countries, including Russia.

In the after-war years, John Bernal often visited the Soviet Union in connection with his scientific work and the world peace movement. On these trips he never failed to visit the Institute of Crystallography of the Academy of Sciences. In 1952 he brought Dorothy with him. She was to speak at the seminar conducted by academician A. V. Shubnikov, the founder and the first director of the Institute. What the audience saw was a woman with a beautiful and intelligent face, who was rather awkward at first, but then went on to speak with mounting enthusiasm about her remarkable work on penicillin and vitamin B_{12}. Whisper went among the audience – it was she who was the first to obtain, together with Bernal, an X-ray pattern from a protein crystal (Bernal, Crowfoot – Pepsin, 1934). Since then, scientists from the Institute of Crystallography and other Institutes of the Academy often met Dorothy both in Moscow and Oxford, and enjoyed her constant attention and support. Her small laboratory in Oxford received post-graduate students from many countries, including those from Moscow.

At that time I was engaged mainly in electron diffraction studies, and later in diffraction of X-rays by high-polymer molecules. But by the end of the sixties I became increasingly more interested in biocrystallography: we started investigations of amino acids, peptides and proteins. Dorothy suggested an interesting topic – deciphering the structure of gramicidin S, discovered by Soviet scientists. Without X-rays, by just considering the chemical formula of this antibiotic, she predicted the conformation of this cyclic decapeptide based on the interbinding of hydrogen bonds. X-ray patterns from this structure (very complex for that time) were analysed by Galina Tischenko – a scientist from the Institute of Crystallography, first in Moscow and then for some time in Oxford with Dorothy. But gramicidin defied solution. It was achieved only in 1989 in collaboration with Dorothy's pupils from York University, and the molecule was just as predicted by Dorothy, but instead of being planar it turned out to be slightly twisted.

The triumph of penicillin, and then vitamin B_{12}, made Dorothy famous all over the world. In 1964 she became a Nobel Prize Winner.

I have met Dorothy many times during her visits to Moscow and on trips to England, at the International Congresses and meetings. The reports she presented at biochemical and crystallographic meetings, e.g. at the VII International Congress of Crystallographers in Moscow (1966), were always brilliant. I have often visited her at her old and rather long two-storey cottage in Ilmington, a small village about 30 miles from Oxford. This is how they lived, the furniture served till it almost fell apart, dinner was always announced by a gong, all rooms were overfilled with books. In Dorothy's husband Thomas' study, the table could be reached only by complicated maneuvering through mountains of books piled right on the floor.

I remember how Dorothy, sitting on the old sofa, talked about her family and the way its members rose to the heights of academic career from their rather