Dorothy Hodgkin and the Indian connection

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Dorothy Hodgkin – as crystallographer, scientist and human being far surpasses most and so it is not easy to write about her many-splendoured personality. Instead, in this essay I shall attempt to present the influence she has had on the growth of X-ray crystallography in India, directly through those who worked with her and indirectly by her travelling all over this country. In such an account, one must be pardoned for some personal element creeping in.

In the twenties, India had developed a fairly strong tradition in X-ray physics. The six-week visit of C. V. Raman to Europe in 1921 greatly changed his research interests. On seeing the blue of the Mediterranean he started on his researches on the scattering of light in liquids which finally culminated in the discovery of what is now called the Raman Effect. His encounter with William Bragg and his naphthalene structure started three lines of research in India. (a) Raman fabricated an X-ray tube and was amongst the earliest to use X-ray diffraction as a structural tool to study liquids. He showed that while in large angle scattering the haloes reflected specific molecular sizes and packing shapes, small angle scattering was directly related to the statistical fluctuation of density in a liquid. (b) Raman knew that Bragg's first structure of naphthalene was not consistent with its birefringence, while the second one was. With this as a cue he and his school launched extensive studies on the optical and magnetic anisotropy of organic crystals to get vital information on the arrangements of molecules in the crystalline state. (c) One of his students, Kedareshwar Bannerjee, was amongst the first to probe into the problem of phase determination by direct methods and for this he used Bragg's data on naphthalene. Unfortunately, in spite of this early lead, the first crystal structure was solved in India using Fourier methods by Gopinath Kartha only in 1951. The Indian Institute of Science (IISc) had great hopes of starting a powerful school of X-ray crystallography when G. N. Ramachandran came back from Cambridge. But he went over to Madras and there he established one of the most renowned Schools of Biophysics. With Gopinath Kartha he solved the structure of collagen.

A vacuum was created in Bangalore when Ramachandran went to Madras along with his entire team. R. S. Krishnan (then head of the Physics Department at the Indian Institute of Science, who had a knack of picking young people to lead new scientific groups) asked me in 1951–1952 to be 'in charge of X-ray crystallography' and attempt to grow a group 'worthy of the Physics Department'. The first problem Venkatesan and I took up was to use the novel idea of multiwavelength anomalous scattering (MWAS) to solve the phase problem and we demonstrated its feasibility (1952–1954). Almost immediately I had to spend a year in the United States with I. I. Fankuchen (Fan) working at Brooklyn Polytechnic. My entire outlook towards X-ray crystallography changed when I attended a one-day seminar held there on the phase problem at which David Harker, David Sayre, Herbert Hauptmann and Jerome Karle spoke. At the end of Karle's lucid presentation I remarked to Paul Ewald who was sitting next to me – 'It seems as though this method is going to work' to which Ewald commented, 'Yes it will, and it will take away the excitement from most of the older crystallographers.' It seemed to me as though most techniques connected with the phase problem: the heavy atom and the isomorphous methods, the Patterson synthesis, the vector superposition techniques, approaches through anomalous scattering and finally, direct methods had been formulated. Many details were yet to be worked out but what really remained to be done was to use all the techniques for actually solving crystal structures large and small. At that time (1954–1955) the structures of DNA and collagen had been determined, but one realized that the approach and intuition necessary to solve such structures were very different from those necessary to solve complex single crystal structures.

I discussed this matter in some detail with Fan (who had wisdom and insight. Incidentally, it was he who shortened my name to Siv). We agreed that if X-ray crystallography were to take root in India or indeed anywhere else it must become a 'useful' tool to chemists, biologists and medical people. The centre of gravity of X-ray crystallography must shift from 'Physics Departments' to others. It was in this connection that he mentioned the name of Dorothy Hodgkin.

I had, of course, heard of her and read her papers. I did have a slight confusion in my mind – her randomly oscillating between the names Crowfoot and Hodgkin. Her range of interests was perplexing. Proteins – pepsin (1934) and insulin (1935); steroids (the famous paper with Bernal and Fankuchen, 1940). The cholesteryl iodide paper (1945) was a classic, from which I learnt how to use the Patterson and the heavy atom methods; penicillin (1949); pernicious anaemia factor (1950), etc. Every paper was a gem in which she used some new technique and made it work. She wrote with such facility that the reader felt that it was all so very easy.

Fan then said that inspired by her mentor J. D. Bernal and through her sheer genius she was demonstrating the power of X-ray crystallography to the world and 'was thus freeing chemists and biologists to do greater things' (although they themselves were resenting it, as children often do). It was later that I realized what she meant when she said – 'There our scientific world ceased to know any boundaries.'

I also met Dorothy Wrinch at Smiths College and Patterson in Philadelphia. Again Dorothy was mentioned with great respect and affection. Two of their comments struck me. Dorothy introduces her collaborators into problems in crystallography which they could never have even dreamt of and persuades them to use techniques that were absolutely new. They would scarcely know that they were going through a regimen of training not only in crystallography but also in scientific attitudes. The other was that Dorothy was such an internationalist that she welcomed having colleagues from every part of the world and always insisted on their going back to their own countries and working there. All this heartened me for the exodus of our better brains had already started and it attained serious proportions later. I felt it would be ideal if Indian crystallographers could hitch their wagons to this star. I started making preliminary attempts but strangely they only crystallized later on.

Venkatesan and cobyric acid

After his work with me on MWAS, Venkatesan took up the structures of a few organic molecules (for I felt that he should become the nucleus in India for taking crystallography to organic chemists). It was therefore fortunate that Jack Dunitz (who was Venkatesan's thesis examiner) offered him a Fellowship to work in ETH, Zurich. In 1961 at Jack's suggestion, Venkatesan joined Dorothy's group and was promptly christened *Van* by her. Dorothy suggested that he work on the structure of the nucleus of vitamin B_{12} – cobyric acid, the orange red crystals isolated from sewage sludge. She also said that while it should not be difficult to solve its structure by the heavy atom method, with his earlier experience in anomalous scattering, 'it may be fun to try the anomalous dispersion method' and with a twinkle in her eye she added 'it would, of course, mean measuring visually the intensities of thousands of reflections'.

Van writes 'It was clear to me that Dorothy was very interested in seeing the power of the Bijvoet method applied to a largish molecule, and so David Dale and I took it up immediately. I enjoyed greatly working on this structure – continually getting valuable ideas from Dorothy, often crucial to the successful application of this method'. All of us were so happy when his work was dealt with in such detail in her Nobel Prize discourse.

'Today our best evidence of the structure of the nucleus of B_{12} comes from the X-ray analysis of cobyric acid. By measuring the intensities of both Fhkl and Fhkl, Dale and Venkatesan were able to assign rather accurate phase angles to 1994 reflections . . . in the 3-dimensional Fourier map even many hydrogen atom positions appear as peaks, – leaving almost no doubt of the correct formulation of the chemical structure.'

It was in Zurich and Oxford that Van's complete conversion to organic chemistry took place. 'I consider myself extremely fortunate to have worked in two world-renowned centres of chemical crystallography . . . . A week before I left Oxford, Dorothy advised me to visit Chemistry Departments in India and make it a point to discuss their chemistry.'

A year of enjoyable activity

On Van's return, I went to Oxford for a year (1964–65) ostensibly to 'look after' Dorothy's doctoral students when she was to be away in Ghana with her husband Thomas. I arrived in Oxford with my wife and three young daughters. Dorothy then suggested I look into a recalcitrant structure – vitamin B_{12} monoacid which Clive Nockolds had been tackling for some time. A subtle error in indexing was detected and from the visually estimated intensities of about 6500 reflections almost 3000 Bijvoet pairs could be accurately phased. We got the immense satisfaction of picking atom by atom from the first 3-dimensional map till the entire structure unfolded itself in all its glory.

Just before she left for Ghana, in a vague manner (which some of us feel she adopts when talking of very serious things) she asked me whether I could look into the anomalous scattering effect Petersen (who had worked with Bijvoet) and Smith had discovered in neutron scattering in CdS. Having lectured only recently to the undergraduates in Madras, I had some familiarity with nuclear physics, reactors, cadmium absorbers (which Fermi used), of Breit–Wigner formalism of neutron scattering and the Kramers–Kronig relations in optical dispersion. I could see that in ^{113}Cd the dispersion corrections b″ and b′ would be 500% to 1000% of normal scattering amplitude b_o (as against 5% to 10% in the case of X-ray scattering); that b′ would actually change sign (from say $+5b_o$ to $-5b_o$). Introducing special isotopes ^{113}Cd, ^{149}Sm, ^{157}Gd and ^{151}Eu and choosing an appropriate neutron wavelength is equivalent to introducing a very heavy atom in the structure, a concept completely unknown in neutron diffraction; and finally by using the multiwavelength method one could even solve structures with 5000–10000 atoms! The implications of these ideas were so unexpected that Dorothy took me to talk to J. D. Bernal. He heard me with great patience and said that all my ideas were basically

right – but they can become practicable and routine only if the intensities of the neutron beams increased by at least one order of magnitude. The oracle had spoken. In spite of the fact that a few structures were solved using this method, and Dorothy herself put a Cd insulin in the neutron beam the verdict was – 'unfortunately Ramaseshan's suggestion (1964) of using anomalous dispersion of neutrons could not be used to solve the then unknown structure of insulin due to limitations of flux'.

It was wonderful to be with Dorothy's doctoral students, who were an international lot. There was Tony Cooper (USA) who worked on a derivative of fusidic acid and who was one of the earliest to combine photographic methods with automatic microdensitometers and computers for the quick collection and indexing of data. This work, in my view, paved the way to the later sophisticated developments in this field. Mike James (Canada), who displayed all the makings of the outstanding crystallographer he became later, solved a crystal which had a non-crystallographic symmetry in it; Mannan from Pakistan whose thesis I had the pleasure of correcting, Eli Schefter who worked on drug molecules. Tom Blundell who was to join the insulin group later had already started working for his part two – and many others. One was busy but I had enough time to participate in the insulin programme. Working with Guy Dodson – who was the mainstay of Dorothy's insulin team – was always exciting – with the mandatory cricket game one had to play in the lab with a rolled up Fourier map as bat and a crinkled paper as ball. The insulin team consisted of Guy and Eleanor Dodson, Margaret Adams, myself and Dorothy. The major attack of introducing heavy atoms into insulin started then – removing zinc by soaking crystals in EDTA solution and introducing lead and cadmium, testing for isomorphism, collecting data on anomalous dispersion in 2 (or 3) Pb insulin, in 2 (or 3) PCMBS insulin as also in 4 Zn insulin containing HgI_4 (which had to be cooled by blowing cold air as we had done in Bangalore and Brooklyn to prevent the denaturing of the crystal). It became clear to us that having so many strong anomalous scatterers in a cluster was not very useful. It was also at that time that the methods of calculating contribution of the heavy atoms alone using anomalous scattering (and isomorphous) data were evolved. Eleanor started writing the computer programs which played a major role in the final solving of the insulin structure. One also came to the conclusion that the Phillips linear diffractometer (which broke down often giving us cause for much fun and laughter) must be replaced by a four circle one.

It was a magnificent year. Dorothy was awarded the Nobel Prize. As she could not be reached in Ghana by the Nobel Committee we were the first to announce it to her! When she was elected to the 'Order of Merit' we celebrated it in the lab with an old case of Danish beer which lay hidden in the cupboard amongst the Fourier Maps. When lysozyme was solved by David Phillip's group she took us to the Royal Institution. I was flattered when Lawrence Bragg recognized me as the person from Madras who also arranged for his seeing some of the beautiful birds there.

I also knew at the time I left Oxford that cobyric acid and vitamin B_{12} monoacid were really stepping stones for using anomalous scattering to solve the insulin structure. The base camp had been firmly established for the final assault and the clouds were clearing up and Dorothy could see the top of the peak.

Viswamitra and use of the Patterson

M. A. Viswamitra joined me as a research student in 1955. He was one of the most talented of my earlier students, very independent, with remarkable experimental skills and one who could choose his problems with great discernment. It is of him that Dorothy says, 'Viswamitra, – an Indian research worker visiting our laboratory who has a charmed hand as far as crystals are concerned'. It is of interest that the first problem I set him was to grow single crystals at low temperatures by freezing liquids – which he did with great ease. He joined Dorothy in 1965 just before I left Oxford and worked on the structure of thiostrepton – a large antibiotic molecule with a wide spectrum of activity against gram positive bacteria, comparable with that of penicillin. It crystallized in the tetragonal form, which presented many problems. Mitra by changing the solvent got a more convenient monoclinic form with two molecules per unit cell. Even here the determination of the chemical structure was difficult because of the variability of its hydrolysed products and nor was its chemical formula known: No heavy atom derivative could be obtained. The molecule was alleged to have 5 sulphur atoms and their numbers and positions were quite uncertain. Viswamitra and Bryan Anderson boldly attempted to solve the structure using the Patterson superposition vector shift and Buerger minimum function methods. Writes Mitra (rather flatteringly to the present author) 'The vector shift method was rather new at that time. And I acquired a good background in it when I worked with Ramaseshan, my thesis adviser. The confidence and training I had received with him made me hope that the method would prove successful'. And successful it was. Dorothy Hodgkin in her celebrated Patterson Memorial Lecture gives this as the supreme example of the power of the Patterson technique. Says she: 'They set out with the three-dimensional Patterson drawn on transparent sheets and superposition from every peak in the map (was made) looking for 4 to 5 five-membered rings which should be thiozole rings . . . I never knew how in the end the

structure was solved. The first map that Viswamitra calculated was one of the ones that make me laugh, . . . if it does not make me cry – to think of. But still in the end they got the structure out – a very remarkable feat indeed.'

Mitra also worked on ferroverdin, the green iron-containing pigment (isolated by Chain and his group) which showed extremely interesting magnetic and chemical properties (*Nature*, 1969, **224**, 589).

Vijayan and insulin

Immediately after Mitra left Oxford, M. Vijayan joined Dorothy in January 1968. Vijayan's thesis adviser was Viswamitra. Dorothy was one of the thesis examiners and I was also on the panel. Dorothy informed me that she would like a crystallographer to join the insulin group as Margarat Adams was finishing her thesis and would almost certainly leave. With this new addition she hoped to make a serious attempt to solve insulin. Therefore, when she was to be in India (in 1967) she would like to meet Vijayan. Dorothy met Vijayan and offered him a position. Writes Vijayan: 'Most of my well wishers asked me *not* to join the insulin group. Dorothy had been working on insulin for decades and the solution was not at all in sight. But I decided to work on insulin, primarily as I wished to start a protein group in India; and I could not imagine any other place than Dorothy's to learn the subject. I joined in 1968. The group finally consisted of Guy and Eleanor Dodson, Tom Blundell and myself – the division of labour was not watertight – everybody did a bit of everything – not perhaps the most efficient way – but an excellent strategy in the long run, as each worker far from being a narrow specialist became a well-rounded protein crystallographer. Tom and Guy prepared many heavy atom derivatives. My task was to collect the data on the newly installed four-circle diffractometer and Eleanor did much of the computing. Dorothy decided that the anomalous scattering approach would be the most effective route.' Eleanor and Vijayan developed many techniques for the effective use of this method. All these are described in their paper (*Acta. Cryst.*, 1971, **B27**, 2402). When the structure was clearly coming out there arose a problem. Vijayan had promised Kalyani that he would come back early in 1969 to India to marry her. To keep the team intact – 'the mountain was brought to Mohamed' – Kalyani was brought over to Oxford on a fellowship and their wedding took place at the height of the fever of insulin being solved. Obviously there was no time for a honeymoon. Instead Vijayan had the thrill of seeing along with Guy in the first phased map of insulin, the stretch of alpha helix (10–19). Wrote Vijayan: 'Insulin was solved and Max Perutz came to Oxford with a huge bottle of champagne. Although the champagne turned out be somewhat flat, the atmosphere was nonetheless intoxicating.' The structure was announced at the IUCr Congress at Stony Brook (in August 1969). It was characteristic of Dorothy to ask the youngest member of the team – Tom Blundell to present the structure. I happened to be there to see the crystallographers marvel at this achievement and the stamina and persistence of Dorothy Hodgkin over 34 years. None of Dorothy's colleagues in the insulin group which was involved in the final solution of the structure in 1969 was born when the first photographs of insulin were taken by her (*Nature*, 1935, **135**, 591). Says Vijayan, 'Although one was pleased and excited when insulin was solved – that in some sense one was participating in a piece of history dawned on me only much later'. At Stony Brook Dorothy reminded me of our meeting Vijayan in Bangalore just two years previously. 'I feel so happy that Vijayan did join the insulin group. In Sanskrit I am told Vijayan means the Victorious: Truly he did finally bring us victory'. A rich tribute indeed.

Dorothy in India

Dorothy has visited India often, twice as Raman Professor of the Indian Academy of Sciences. She gave the Gandhi Memorial Lecture and the Azad Memorial Lecture and spoke at the Pugwash Conference in Madras. There was a time when we thought she could spend a part of each year in India as a visiting professor to escape the winters of England which greatly affected her arthritis. But this was not to be, as Thomas's health would not permit it. Unlike most distinguished scientists who came to India just to attend a conference or two and to visit a few very sophisticated centres of research, Dorothy travelled to every nook and corner of India, inaugurated conferences, gave tens of keynote addresses, scores of lectures, seminars to audiences – large and small, visited laboratories, universities and colleges, discussed with groups and individuals. On one memorable occasion she gave an unforgettable lecture when Thomas was seriously ill and was actually fighting for his life. She travelled to Cochin and Trivandrum in Kerala, visited the southern tip of the subcontinent where the three seas meet, Madurai (the great temple city), its university and its excellent biology department, Madras, Bangalore (IISc, RRI, NAL), Hyderabad, Bombay (BARC and TIFR), Delhi, Lucknow, Cawnpore and Calcutta. We travelled to Gauhati in the eastern corner of India where she inaugurated a Congress of scientists and addressed thousands of students and had at least 5 to 6 engagements each day for 4 days. We then drove to Kaziranga on the evening of the Krishna festival. In the twilight each of the hundreds of villages we passed were lit up with oil lamps and were celebrating the festival – with music and dance – she said that it was so beautiful, so graceful

and so enchanting. At Kaziranga, the home of the Indian one-horned rhinoceros, she spent a restful day seeing many of these incredible creatures for the first time and also thousands and thousands of birds. The day we left Assam the famous/notorious 'Assam Agitation' started and myriads of citizens and students took to the streets. She was not perturbed at all, spoke to the students, although I was (on her behalf). We then went to North Bengal, famous for its Naxalite movement. At its epicentre she addressed the students and staff of the Siliguri University which was courageously starting crystallographic research. She gave many talks and had many discussions. I knew she was straining herself too much – 'How can I say no when so many of the young and enthusiastic are eager to listen to me, talk to me and even just see me', she said.

She had never seen the 'Abode of Snow' (the Himalayas) from close quarters. We motored up to Darjeeling and saw from there the snow-covered mountains forming a colossal amphitheatre. I was getting worried about her health. Even so, at 4 AM we drove miles and stood on top of Tiger Hill. Before the sun rose, its rays hit the world's highest peak, Mount Everest, which stood there in solitary splendour against a dark background: In succession the lower peaks, hundreds of miles apart, all above 25000 ft appeared one by one – the heavenly spotlight picking them out – pink dressed ballerinas that adorned the magnificent mountain stage – till finally the great 'Kanchanjunga' exposed herself in the yellow fiery light – truly a pyramid of gold. When the sun was finally up Dorothy spoke: 'It was truly magnificent. I would not have missed it for the world – Thank you, Siv, for not cancelling this visit.'

By that time I knew she was quite unwell. We flew to Calcutta and then on to Delhi. I shall never forget the help I received from Anna Mani, one of our distinguished women scientists. She arranged for two young doctors ((Ms) Sharma and her husband) to examine her and later (Ms) Padmavathi, one of the best heart specialists we have, who after careful examination declared that one need not be too alarmed. 'The pills and some rest will quieten the fibrillation of the heart and then she can board the plane for England.' For almost ten days I stayed with her at the IPCL guest house (courtesy its Chairman, S. Varadarajan). It was then that I heard about her childhood, her father in Sudan, her mother the textile expert – about her sisters and nephews, her first interest in science. Her chance meeting with Lowry and Joseph which took her to Cambridge and to J. D. Bernal – her interest in insulin and penicillin, steroids, B_{12}, etc. Her meeting with Patterson, Kathleen Lonsdale and a hundred others. It was all so exciting and I felt like writing her biography.

I cannot end this section without a few words about Thomas Hodgkin. I knew him well and we spent hours together conversing and arguing. He had a sharp tongue – but there was absolutely no malice. A scholar with a deep knowledge of History, with a sense of humour that kept you laughing all the time, a most loveable man. In 1982 we got a letter from Dorothy saying that Thomas died. It was sad. When we saw her next, there was a change, something was missing and she appeared far more pensive and serene. In 1984 Kausalya and I made a visit to the place where Thomas died, Tolon in Greece – a country he loved, whose language and art he respected and from whose mythology he often quoted, the day he died commemorated the day on which Greece was declared independent – that too at a place close by. He came out of the house on a beautiful sunny day and just before he fell down dead he saw the indescribable beauty of the bay of Argolis. Yes, in spite of our great sorrow one could not but envy him.

Growth of crystallographic laboratories in India

Dorothy was unhappy about Gopinath Kartha – one of our best crystallographers, settling down in the United States. When Van said that this was probably because of the lack of facilities in India she told him with her characteristic modesty that the greatest satisfaction she derived was when she carried out her investigations under the most difficult and adverse circumstances. Again to Vijayan she said 'Modern facilities are often necessary; however it is really the people who make science'.

Each one of her Indian collaborators knew that she would like them to go back to India, work, and establish groups and laboratories. And they to a large extent succeeded; perhaps they were driven by the fact that they could not fail her. In this process one must be grateful to Satish Dhawan the farsighted Director of IISc who not only brought G. N. Ramachandran back to Bangalore but also appointed many of the younger crystallographers into different departments.

Van joined the Organic Chemistry Department and established one of the better X-ray laboratories for organic and drug chemistry. He tells us the story of when he heard Leslie Leiserowitz of Israel giving a lecture in solid state photochemistry in Oxford, how he told Dorothy that he would like to go to Israel to get exposed to this area. Dorothy's immediate reaction was 'Van, you don't have to go there. You can do it all in India itself'. This gentle but 'firm' advice had its effect. He did start studies of solid state photochemistry along with a very bright young photochemist Ramamurthy who had worked earlier on liquids. He always wonders whether I, who had heard the earlier conversation, had anything to do with getting Ramamurthy to Bangalore when I was director of IISc. Venkatesan describes how

they had to preorganize crystal packing so that they got the photoproducts they required, a process Schmidt called crystal engineering. This team did much work on coumarins, dynamic photochemistry and gas solid reactivity of thioketones, host systems with cavities and reaction in cavities. Gautam Desiraju who was at IISc left for Hyderabad and is doing good work in this field there.

Viswamitra wrote: 'I was in Dorothy's lab from 1965 to 1968 and this had a much wider significance to me: It led to my fascination for biological molecules and later to my commitment for work on such molecules.' Mitra established at the IISc a reputed school for the study of oligonucleotides. He and his school pioneered studies on the conformational differences between two nucleotide species because of the possible relevance to DNA and RNA structures. It is now agreed that the concept of the DNA double-helix having sequence-dependent variability in its structure came after Mitra's laboratory determined the crystal structure of the tetranucleotide d_p A–T–A–T. The idea of taking up this sequence came from a discussion Mitra had with Francis Crick. Mitra also established a close collaboration with Olga Kennard in Cambridge. In much of this work he again used the Patterson superposition technique. His pursuit of DNA crystallography is continuing and he has with his 'green fingers' crystallized many decanucleotides and has found an alpha DNA structure in some of these.

Vijayan has established a school of small molecule and macromolecular crystallography. Their work on biomolecular interaction, including their implications for chemical evolution and the origin of life is now recognized. His centre has been functioning for some time and it carries out the structure analysis of lectins (peanut, jack fruit, and winged bean). Once when I was able to get funds for the crystallographic groups at IISc I asked Dorothy if some type of organization or direction is called for. Her reply was, 'It is people who matter, once the proper choice has been made it is best to leave them alone and let them organize themselves'. It was sound advice and it paid dividends.

It must not be thought that crystallography in India is confined to those who actually worked with Dorothy. Her inspiration has gone down to the next generation and to the next. I invited Venkatesan's student M. R. N. Murthy (who was working with Michael Rossman in Purdue) to come to the IISc. He came back readily and the first virus structure from his group has appeared recently in *J. Mol. Biol.* Extremely good schools of protein crystallography, neutron crystallography and high pressure crystallography, have been established in Bombay by one of our noted scientists R. Chidambaram (again a product of the IISc and a contemporary of Van and Mitra); his protein group is now being led by T. S. Kannan, Mitra's student. Applied crystallography, has been established in NAL (A. K. Singh and Kalyani Vijayan). Good groups have sprouted out all over the country – not accidentally at places which Dorothy visited. Yes, India owes much to Dorothy and the world at large may never suspect the yeoman service she did for us.

Dorothy's graciousness and humanity

After my return from Oxford I often wondered whether I had justified the confidence she had reposed in me by her inviting me there. I was truly surprised when she wrote some time later. 'In Oxford, we first began to know something of his qualities when he spent a year in the Crystallographic Laboratory. It might have been a difficult year for my research group. I was a great deal abroad. In fact, it was a marvellous experience for them being guided instead by Sivaraj Ramaseshan with his great learning and critical understanding. Complicated structures were solved under his hand, mistakes put right and new approaches to structure analysis developed. It was not surprising to find that the whole group had become his devoted friends and admirers – and had developed great respect for Indian science.' Whether this is true or not is immaterial. It is another example of Dorothy's graciousness and magnanimity; her realizing the need to encourage one from a far-off country where the playing fields of science had not yet been established.

Yes, she is the ultimate in graciousness and kindness. The only manner in which an Indian can describe her is to say that she treated us as members of her own family. The little considerate things she did moved us. Sending a telegram welcoming to Europe my family when we reached Naples by ship from India. Seeing personally that Van had a comfortable place to sit in the lab and one to stay outside; the concern she showed to the families of Viswamitra and Vijayan when they were not well – are just a few of the innumerable examples one could quote. She made us feel that she was giving to each one of us a treatment different from that given to others, that each of us was very special to her. How she found time to look after all her brood, select appropriate presents for each one of them, one would never know. It is good to remember that her brood extended over countries and continents, United States, Canada, New Zealand, Australia, Ghana, Nigeria, Egypt, Sudan, Morocco, China, India, Vietnam and it goes on and on. She became friends with all the children and remembered their names. Once when my wife and I came back to Oxford from London, our children greeted us in the middle of the night shouting, 'Our Dorothy has won the Nobel Prize; we saw it on TV' To 10- and 8-year olds she had become 'Our Dorothy'.

Every time we were in England we visited her and Thomas in Crab Mill in Ilmington – their beautiful long house which seemed at first sight all chaos but which

was really a home to all of us. Someone from some corner of the earth was always also there. We could stay there as long as we liked – breakfast, lunch, dinner (Thomas always made vegetarian dishes for us). All sat together and relaxed in the garden; Dorothy showing us some manuscript of hers for an opinion. Thomas having heated arguments on the state of world. Or we would go to dine with Dorothy's remarkable mother-in-law who lived in a beautiful house up the road when she would tell of the naughty things that happened in the early part of the century at the university. Dorothy's greatness does not rest on her having solved cholesterol, penicillin, B_{12} or insulin. True, these are unparalleled achievements. But to many of us her greatness also lay elsewhere which made her spread her science to all parts of the world and also in her concern for humanity. All pay lip services to the cliché, 'We must love humanity'. But Dorothy's method of doing this was like that of Gandhi or Mother Teresa, to have compassion and a personal affection for every fragment of humanity – young and old, wherever and whichever corner of this world it was found in.

Dorothy and insulin crystallographic research in China

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ALTHOUGH only two of us have the privilege to be the authors of this article, we believe that many other Chinese scientists, who know Hodgkin either personally or by her fame as a great scientist, have the same wish to express their respect and esteem. Dorothy Hodgkin is to us a dear friend who has given us help and support in our work. What we express here is only a small part of what Dorothy's many friends in this country wish to say.

One of us, Dong-cai Liang, crystallographer, worked on seeking heavy atom derivatives of insulin crystals in the Department of Zoology, University of Oxford under the guidance of Hodgkin in 1966. 'It was an unforgettable experience in my life, at Oxford with Dorothy' Liang told his colleagues and students. 'There I was, the first scientist from Red China in Dorothy's international laboratory, a man from Canton with black hair and a small pair of hands, thanks to which I was able to mount crystals into the capillaries quickly and accurately, and this impressed Dorothy.'

Last May, Liang was told by Guy Dodson that Dorothy wished to come to China this summer for the 16th International Crystallography Congress. We were delighted at this news and Liang made a great deal of effort to bring her to the meeting in China. Nevertheless, considering her age, we were a little concerned about her health during the long journey from Oxford to Beijing. Furthermore, the big gathering of crystallographers from all over the world would no doubt give her a very busy and exhausting time. How could we fail to understand her? She would go not only to Beijing but even to the ends of the earth. Her age, the hot weather, the long journey, all these are nothing compared to her science. Science is her life! We could not wait to see her again, in China, for the eighth time.

In the 1950s, many Western people knew very little of China, and even less about Chinese science. Dorothy first came to China early in 1959 with her husband, Thomas Lionel Hodgkin, cherishing her intrinsic sense of duty for human progress and civilization and her enthusiasm for people and science in developing countries. In 1965 she visited China again.

In 1967 a group of young Chinese crystallographers started an X-ray crystal structure analysis of insulin in Beijing, stimulated directly by the successful achievement in the total chemical synthesis of bovine insulin with full biological activity in 1965. This was accomplished by a joint group of Chinese biochemists and organic chemists, and also enlightened by the insulin crystallographic research in Dorothy's laboratory. In 1971 and 1973 we obtained the isomorphous replacement electron density maps of insulin in rhombohedral 2 zinc insulin crystals at 2.5 Å and 1.8 Å respectively. In 1972 Dorothy visited China for the third time, this time bringing with her the Oxford electron density map of insulin, as she knew that the Chinese scientists were determining the three-dimensional structure of insulin. Indeed, we compared in detail our electron density maps, as both maps were drawn at a scale of 1 cm to 1 Å, so there would not be many difficulties in cross-checking them. But, there was actually a moment of acute concern when we first put the maps together and found they were not