

Indonesia. However, the issues discussed are also true of the majority of the Third World countries.

The postscript almost summarizes the contents of some of the chapters. At the end of each chapter, a list of scrupulously selected references useful to research

workers are given. Bold letters and lucid figures enhance the layout of the book. Public health workers cannot afford to ignore this book. However, it is not a book for casual readers but for those genuinely interested in medical sociology, practice of public health and decision making. The

volume is moderately priced and should find a place on the shelves of libraries in colleges and research institutions.

T.C. RAGHURAM

National Institute of Nutrition
Hyderabad 500 007, India

HISTORICAL REMINISCENCES

We wanted to start as a part of our Historical Section, articles covering reminiscences by our scientists. With this in view, through a member of our editorial board we approached Prof. G. N. Ramachandran enquiring whether he could write an article on his growing the remarkable Biophysics Department which he established in Madras. We were overjoyed when we heard that he would be willing to write not one but more articles. Unfortunately there seems to be little chance of this happening, although we are keeping our fingers crossed that it would. Meanwhile when the lecture (published below) was given, many suggested that this could well be published in the Historical Reminiscences Section. The article was read by three referees and rewritten twice.

We invite our scientists (especially the senior ones) to write Historical Reminiscences which contain also interesting anecdotes (the articles will of course be refereed!).

— Editor

Four decades in anomalous scattering – Some reminiscences*

S. Ramaseshan

Indian scientists have played a significant role in developing techniques for using anomalous scattering in X-ray crystal structure analysis. This talk is a personal view of one aspect of its history. We were amongst the earliest to establish the multiwavelength method for phase determination. With the coming of the intense X-radiations from tunable synchrotron sources this method has had a remarkable revival in recent years. Many aspects of our forgotten work have been rediscovered and are used routinely for structure determination.

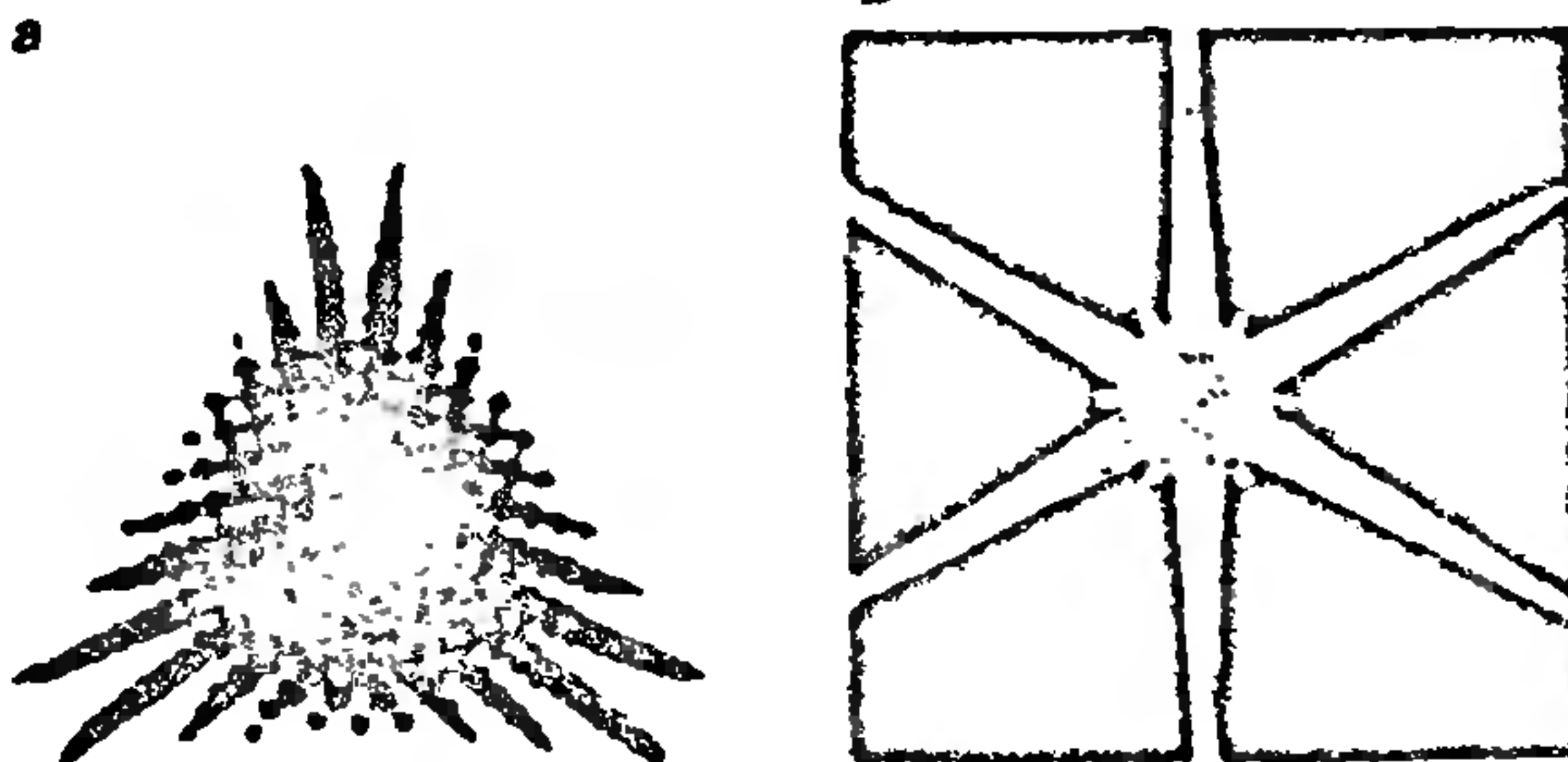


Figure 1. Diffraction patterns of a triangular aperture (ref 29): (a) Fresnel, (b) Fraunhofer

Friedel's law and its violation

X-ray diffraction takes place in the Fraunhofer regime which introduces a centre of symmetry into the diffraction pattern. This is strikingly illustrated in the case of optics (Figure 1) which shows that

while the Fresnel diffraction of a triangular aperture has a threefold axis of symmetry, its Fraunhofer pattern displays sixfold symmetry. The implication of this for X-ray diffraction is that a non-centrosymmetric (hemihedral) crystal will display a (holohedral) centrosymmetry in its X-ray pattern. This is the Friedel law and is expressed as by $I(hkl) = I(\bar{h}\bar{k}\bar{l})$.

The Argand diagram of the scattering vectors (Figure 2a) shows how the modulus of the resultant amplitude for the two inverse reflections is the same while their phases are opposite ($\alpha(hkl) = -\alpha(\bar{h}\bar{k}\bar{l})$).

In 1928 S. Nishikawa and K. Matukawa demonstrated for the first time that Friedel's law can fail under some

*Talk delivered at the seminar held on the retirement of Prof. K. Venkatesan (19 July 1992)

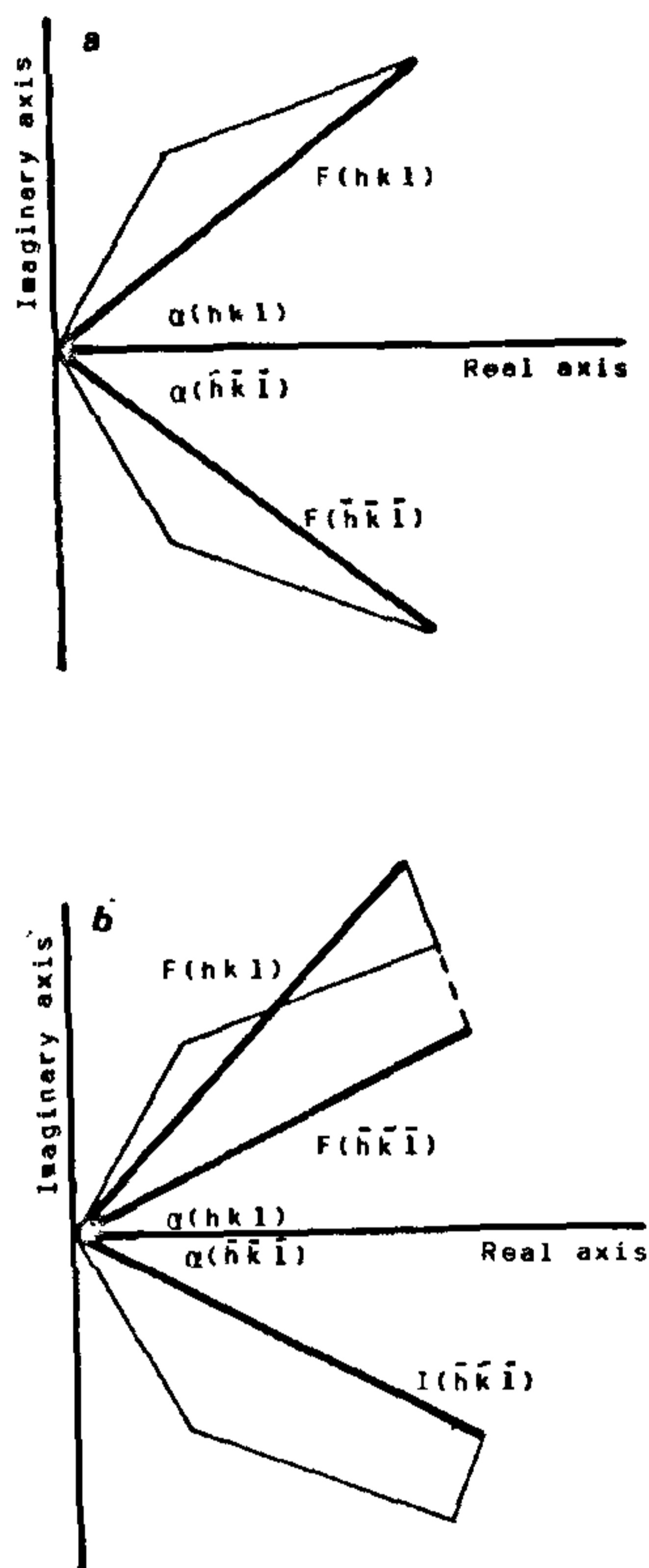


Figure 2. Argand diagrams illustrating (a) Friedel's law, (b) and its violation when f'' is present.

special circumstances¹ (see note 1). They illuminated a crystal of ZnS (which is non-centrosymmetric and piezoelectric) with X-rays having a wavelength close to the critical absorption of the Zn atom, on its shorter wavelength side. Under this condition the Zn atom scatters the X-rays with a phase difference which is independent of its position in the lattice. This results in the violation of Friedel's law (Figure 2b). This work, in effect, showed that the structure of positive and negative piezoelectric crystals can be distinguished by this method

J. M. Bijvoet's contributions

The important application of this work lay dormant for two decades till Bijvoet³ showed how it could be used to determine

the absolute configuration of optically active molecules; it is interesting that Bijvoet was from the laboratory of van't Hoff, who 75 years earlier (along with Le Bel) introduced into organic chemistry the concept of the asymmetric carbon atom! ZnK α radiation was used to determine the absolute configuration of dextro sodium rubidium tartarate: it is a coincidence that the absolute configuration proved to be the same as that chosen purely by chance by Emil Fischer. I had not read this paper by Bijvoet but G. N. Ramachandran discussed it in our Tuesday Physics Club ($\tau\pi\chi$) at the Indian Institute of Science (IISc), when V. Chandrasekharan and he⁴ had to use this method to determine the absolute configuration of optically active NaClO₃ crystals for their photoelastic studies. Ramachandran left IISc in late 1951 to occupy the chair of physics at the

Madras University. All his students (including Gopinath Kartha) also went to Madras. It fell upon me to build, almost from scratch, a group in X-ray crystallography at IISc and to erect and put to use all the equipment that had been ordered for Ramachandran.

In 1952 I saw, what I consider to be, the path-breaking paper of Bijvoet and his collaborators⁵. The basic idea developed in this paper was: (a) if one had data on two isomorphous crystals, the phases of the reflections can be determined but with a bimodal ambiguity. (b) With data on three isomorphous crystals, the phase angles can be determined uniquely provided the third substitution is at a location different from that for the second (see note 2). When I read this paper I could see that if one had data on two isomorphous crystals and also that on the

violation of Friedel's law, the phase ambiguity could also be resolved. I was certain that this must have been quite obvious to Bijvoet himself. In 1952 when I enquired of him, his clarification in a letter to me was unequivocal: (i) My first paper on this subject was entitled 'The phase determination in direct Fourier synthesis of crystal structures' and published in 1949 in the *Proceedings of the Royal Academy of Netherlands* wherein I gave the method of determining the phases uniquely^{3a}, (ii) and it is this that led me on to the idea of determining the absolute configuration of optically active compounds^{3b}. This method of determining absolute configuration was really nothing new as it had been done for piezoelectric crystals² in 1930 (see also note 1), and (iii) the actual calculation of the unique phase angle is just a matter of algebra (a part of which I had indicated in my 1949 paper).

Seven years were to pass before Ramachandran and Raman⁶ did this algebra and gave the explicit expression for $\alpha(hkl)$ in terms of the measured values $|F(hkl)|$ and $|F(\bar{h}\bar{k}\bar{l})|$ and published it in *Current Science*. An important suggestion made in this paper was that when a crystal is used with an anomalous scatterer the bimodal ambiguity may, to a large extent, be resolved by using the phases closest to that of the anomalous scatterer whose position is determined from the Patterson map. This proved to be a pioneering paper in that it initiated much activity in the determination of the structures of noncentrosymmetric crystals and is also much quoted. It is to be noted that two papers published in 'obscure' journals were to revolutionize X-ray crystal structure determination!

The beginnings of the multiwavelength method

One recalls that the dispersion correction consists of two parts, the imaginary part f'' which is scattered with a phase difference of 90° and the real part f' which modifies the value of the atomic scattering factor f_0 and both f'' and f' were functions of incident wavelength (see note 3) (Figure 3 a). When I saw Bijvoet's paper in 1952, I remembered the suggestion once made by my thesis adviser C.V. Raman that one must read the writings of such scientists like

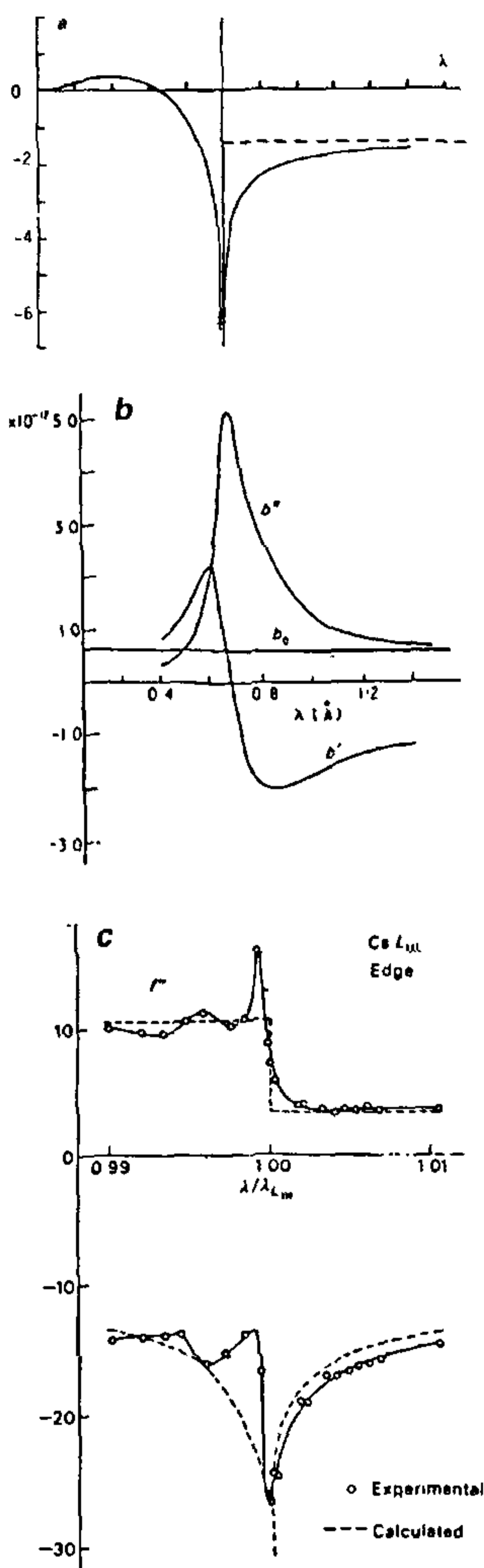


Figure 3. a, Typical curve of the variation of f' with wavelength near the absorption edge; b, Variation of b' and b'' in neutron scattering near the resonant wavelength of ^{113}Cd ; c, Variation of f' and f'' for L_{III} absorption edge of Cs

Wyckoff (see note 4), one of the great pioneers of X-ray crystallography, as he had much insight into X-ray physics. Wyckoff and his students had made a

thorough study of anomalous dispersion. Their measurements⁸ showed that f' in some cases can be as high as 4 to 5 electrons and also it did not decrease with the angle of scattering as did f_0 .

The idea then flashed across my mind that if one changed the incident wavelength of the X-rays (thus introducing new values of f') one changed, in effect, the number of electrons that scatter from the absorbing atom. This was equivalent to generating a series of isomorphous crystals. If this is done, all the deductions of Bijvoet for isomorphous crystals would be applicable *mutatis mutandis*: (i) using two wavelengths, one near the absorption edge is equivalent to collecting data on two isomorphous crystals - which would give the phase angle with a bimodal ambiguity; (ii) by collecting data at three appropriate wavelengths the phases can be determined uniquely; (iii) with only one anomalous scatterer and two wavelengths on either side of the absorption edge and measuring quantitatively the Friedel inequality one can determine the phases uniquely; (iv) the percentage changes in intensity will be much higher at larger scattering angles because while f_0 decreases with the angle of scattering, f' does not; for a typical case these changes can be about 50% at $\sin \theta/\lambda = 0.3$ and 200% for $\sin \theta/\lambda = 0.6$, the absolute values of the changes however will be small, and (v) finally the change in wavelength method has a distinctive advantage in that it represents *perfect isomorphism*. I presented all these ideas at the annual meeting of the Indian Academy of Sciences at Trivandrum in December 1952 when by chance I got an opportunity to speak⁹.

Enter Venkatesan - and the US visit

There is a difference between having ideas and making them work. I was fortunate in that K. Venkatesan joined me as a doctoral student in July 1953. He was a steady and careful experimenter, very studious and as he still is, four decades later, never uttered an unnecessary word. To test out these ideas we tried to get a noncentrosymmetric crystal with an appropriate anomalous scatterer but whose structure had already been solved, unfortunately we failed to get such a crystal (see note 5). Since our main purpose was to show that the f''

isomorphous method did work, we started on KMnO_4 – a centric crystal. We had at our disposal an old continuously evacuated Shearer tube with replaceable water-cooled anticathodes. The targets used were Cu ($k_\alpha = 1.541 \text{ \AA}$), Fe ($k_\alpha = 1.936 \text{ \AA}$) and Co ($k_\alpha = 1.789 \text{ \AA}$). The absorption edge of Mn was at 1.895 \AA , the latter two anticathodes were prepared by electroplating a copper target. We worked with an old and wobbly Debye Scherrer oscillation camera. By 1954 we did observe all the effects we were looking for and as predicted the percentage changes in intensities were larger at larger $\sin \theta/\lambda$. We were able to achieve many 'firsts' (i) the anomalous difference Patterson $(F\lambda_1^2 - F\lambda_2^2)_{hkl}^2$, (ii) the synthesis $(F\lambda_1 - F\lambda_2)_{hkl}^2$ and (iii) we could recover the structure from these by many methods including the Buerger minimum function methods etc. In all this we used two-dimensional visual data. We had, in short, demonstrated the experimental feasibility of the multiwavelength method.

At this stage at the end of 1954 I had to go to USA for a year to work on low temperature physics (especially crystallography). I took the opportunity of lecturing on our multiwavelength method at many places – Brooklyn Polytechnic (Fankuchen, Ewald), Smiths College (Dorothy Wrinch), Pittsburgh (Jeffreys), Bell Labs (Burbank) and State College Pennsylvania (Pepinsky). I also visited Philadelphia (Patterson). In these lectures I discussed the many experimental difficulties we had faced – the filtering out of the fluorescent radiation, the problem of visual estimation using calibrated film strips, the film-to-film ratios, the scaling problems for different sets of oscillation pictures, the absolute scale factor, the problem of absorption correction – all of which were greatly enhanced when different incident wavelengths were used. We had established without any doubt that the multiwavelength method did work. I ended the lecture with the statement 'In this work which posed many experimental problems I was ably assisted by Mr K. Venkatesan my young and diligent doctoral student'. All the senior scientists in this audience will recognize that *assisted* is just a euphemistic way of saying that all these difficult problems (which sometimes appeared almost insurmountable) were tackled and solved by Venkatesan.

I came back from US in late 1955. Instead of publishing all our results and

maps immediately we thought that we would gather much more accurate data with the Hilger instruments and Phillips (Muller) X-ray tubes which had arrived. We erected the equipment, regathered all the data and N.V. Mani, who had also joined me as a student, helped to do some of the Fourier summations. We published¹⁰ the paper only in 1957, three years later than what we could have and should have done.

A digression – three stories

When I was at Brooklyn Poly I found myself (by chance) sitting at the same lunch counter as Hermann Mark, the renowned polymer chemist. He told me of his search for long-chain molecules to make stronger and stronger fibres (a field I got interested in 20 years later!) and in my turn I told him of our work on anomalous scattering. With a puckish smile he said: 'you obviously do not look at ancient literature. In science, this happens again and again and it may happen even to you!' It was Mark and Szillard¹¹ (another great name) who detected the f' effect first in 1925!, the reflection with odd indices of rubidium bromide, normally absent, appear when one of the atoms scattered anomalously. He congratulated me on the progress we had made and suggested that we should really try L radiation where the f' effect would be much greater and he concluded by saying, 'why are you wasting your time here; go back and perfect this technique. It is sure to become very important' (all prophetic statements).

Years later at Bell Labs when Bill Batterman and I tried to see whether ferroelectric domains could be detected using anomalous scattering I met Ray Pepinsky (who was also a visiting scientist there) in the xeroxing room. He had moved from State College to Florida and in the intervening 15 years he had put on weight (whereas I had not), and he did not recognize me. When we introduced ourselves he said, do you know you have the same name as an old Indian crystallographer who lectured at State College long long ago and who produced many new ideas on the multiwavelength method and even made them work. To say I was flattered would be an understatement.

David Harker, who was also working at Brooklyn Poly, asked me if I could recommend anyone from India who could

work with him on ribonuclease. I suggested the name of Gopinath Kartha who I consider one of the most outstanding amongst Indian crystallographers. Kartha along with Ramachandran had solved the structure of collagen in Madras and he had asked me to be on the lookout for a suitable position for him in USA. Harker showed me his lab and also the precession photographs of ribonuclease into which uranium atoms had been introduced. I could clearly 'see' the breakdown of the Friedel law in these pictures. When I came back to India Kartha asked my advice about two offers he had received – one from Cambridge (not in the protein group) and another from David Harker. I told him 'Go to Harker; by combining the isomorphous and anomalous scattering techniques you may be the first to solve a protein structure and probably win a Nobel Prize'. Kartha did go to Harker; did work on ribonuclease; played a major part in solving its structure; and he did use anomalous scattering for doing this. Unfortunately due to various delays ribonuclease was not the first protein structure to be solved – the first ones did get the Nobel award. Kartha's premature death was a great loss to crystallography.

The Oxford phase

There were suggestions that I should go over to Oxford to apply the anomalous scattering technique to larger molecules. I felt Dorothy Hodgkin could do nothing better than offer Venkatesan a fellowship as his stint in Switzerland with Jack Dunitz was coming to an end. She did and Venkatesan went to Oxford. There along with David Dale (and Dorothy Hodgkin) Venkatesan¹² solved the structure – the aqua cyanide of vitamin B12 also called cobyrinic acid (factor V(I)a) – $\text{C}_{46}\text{H}_{66}\text{O}_9\text{N}_{11}\text{Co}_{11}\text{H}_2\text{O}$ using only the anomalous scattering technique. It had 78 non-hydrogen atoms and the phasing was done using visually measured intensities of the 1994 Bijvoet pairs. I felt rather proud when this work was mentioned¹³ in some detail in Dorothy Hodgkin's Nobel Lecture in 1964.

I did finally go to Oxford, mainly 'to look after' Dorothy's doctoral students so that she could spend a year in Ghana with her husband Thomas. As soon as I arrived she suggested that I first look into the rather recalcitrant structure of vitamin B12 mono acid (cyanocobalamin)

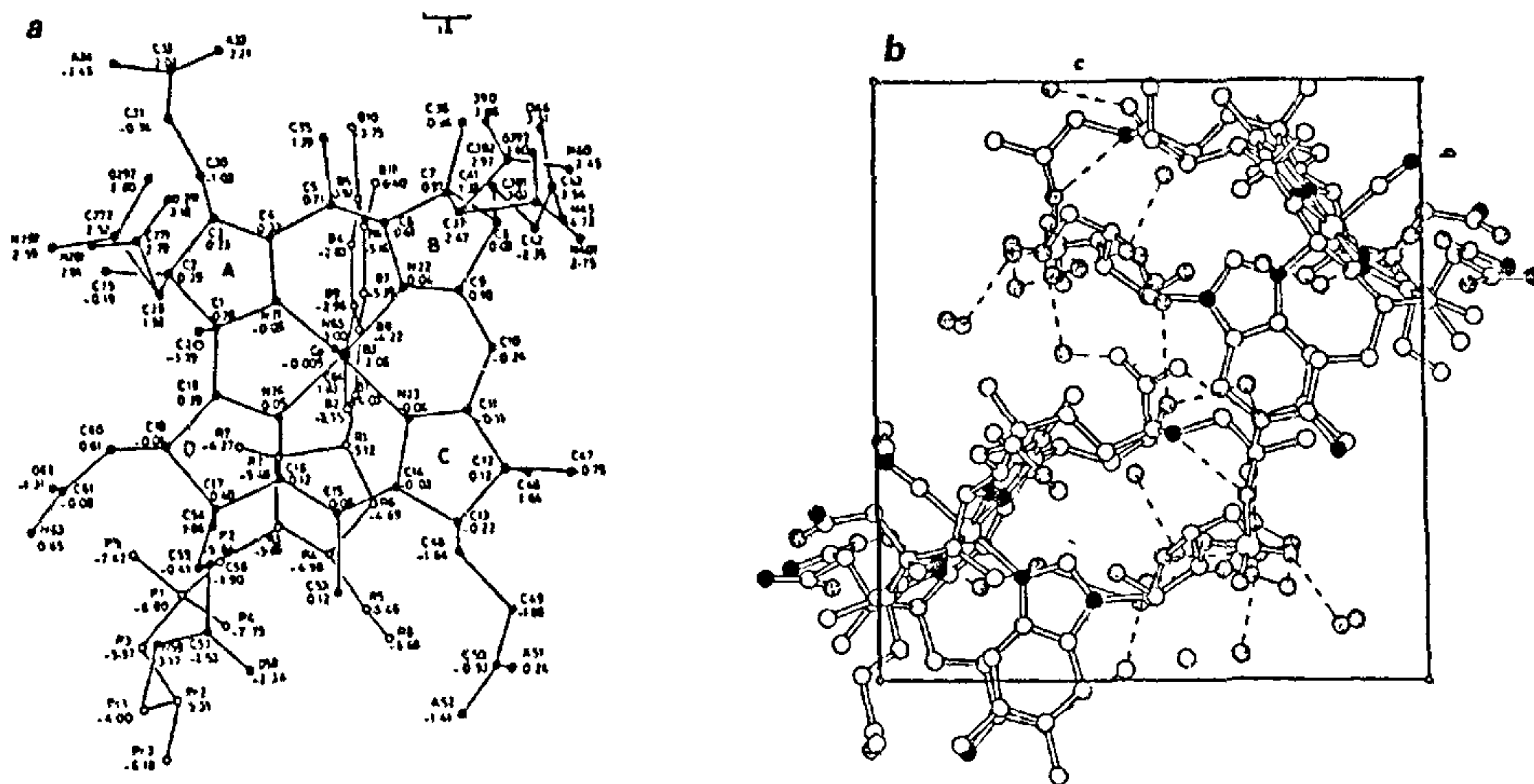


Figure 4. a, The molecule of vitamin B₁₂ monoacid. b, Atomic positions projected along the *a* axis.

C₆₃H₈₇O₁₅N₁₃ (Figure 4a) on which Clive Nockolds was working and which seemed to evade solution. 6323 reflections had been recorded of which almost 3000 were Bijvoet pairs. On the first sitting I was fortunate in discovering a rather subtle error in indexing. When this was rectified, phases could be determined for the 2875 Bijvoet pairs. In the first 3D synthesis the complete structure came out without any problems (Figure 4b)¹⁴. The structure of not only the dry crystals but also the wet ones was solved using X-rays and neutron diffraction.

Working with Guy Dodson, who was the main pillar of Dorothy's insulin group, was great fun. It was mandatory to play cricket inside the lab when Dorothy was not there with rolled up Fourier maps as a bat using crinkled paper balls. We tried to get the anomalous scattering data of insulin with HgI₄ in it¹⁵. Since all the five atoms exhibit large anomalous scattering for CuK_α radiation one thought that phasing would be easy. The crystals deteriorated on exposure to X-rays (more than most normal insulin crystals did). We therefore cooled the crystals by blowing cold air (in a manner similar to the one used in Bangalore¹⁶). The 'life' of the crystals increased three-fold. Unfortunately we found that having anomalous scatterers in a close cluster was not profitable.

Collecting data with a diffractometer was a time-consuming process as the intensities are measured sequentially. In a discussion in 1964 in Dorothy's lab one concluded that for large molecules the photographic method may prove to be the ultimate solution as the reflections were recorded simultaneously. This was followed up by Toni Cooper, a PhD student who used small oscillation photographs – programmed a computer for indexing the reflections, measuring their intensity on an automatic microphotometer, reduced the data, etc. Even the Bijvoet differences could be measured and printed. This pioneering work of Cooper, in my opinion, paved the way for the later more sophisticated developments in this field.

Neutron anomalous scattering

Dorothy left for Ghana within three weeks of my reaching Oxford. In the last week – in a very vague manner (which she often uses when dealing with very serious matters) – she said that Peterson¹⁷ (who phased lysine hydrochloride using anomalous scattering when he worked with Bijvoet) had discovered the violation of Friedel's law in neutron diffraction in a crystal with cadmium atoms in it, and that Terry Willis and David Dale were trying

some experiments at Harwell on CdS; could I possibly look into this problem? It took me a very short time to perceive the importance of this. I was fresh from lecturing to undergraduates at the Indian Institute of Technology, Madras on nuclear physics and nuclear reactors. Cd is used as a moderator for nuclear reactors and its isotope ¹¹³Cd had an exceptionally high absorption. It therefore must scatter neutrons anomalously with very high imaginary components *f''* (called *b''* in the case of neutron scattering) and *b'* must also be large (a consequence of the Kramer–Kronig relation that one learns from as mundane an area as the dispersion of the refractive index). Since nuclear scattering is governed by the Breit–Wigner formalism the dispersion curve near the absorption line would resemble that of optical dispersion. Hence *f'* would take both positive and negative values on either side of the absorption frequency (Figure 3b). I told Dorothy immediately that I felt all these had tremendous consequences to neutron crystallography and that I would work them out. A few days later Terry Willis gave me the reprint of the paper of Peterson and Smith¹⁸.

Normally neutron scattering lengths of most atoms are of the same order of magnitude. Neutron crystallography therefore suffers from a problem similar to that

of solving light atom structures in X-ray crystallography. That is why neutron crystallography was always considered a handmaiden to X-ray crystallography and is used mainly to determine water, hydrogen bonds, etc. If, however, the isotopes ^{113}Cd , ^{149}Sm , ^{157}Gd or ^{151}Eu can be introduced into the structure and appropriate wavelengths chosen, the value of b'' would be 10 times greater than b_0 which is equivalent to having an exceptionally heavy atom in the structure. Hence for the first time in neutron crystallography one could use the heavy atom technique. Further the multi-wavelength method can also be used with ease to phase the reflections particularly as b' changes sign with wavelength.

With f''/f_0 only 10% a structure of about 106 non-hydrogen atoms could be solved with ease¹⁴. In the above isotopes b''/b_0 can be as high as 500% to 1000% and so one gets the astounding result that with such isotopes present a structure with 5000 to 10,000 atoms can be phased and solved¹⁹.

These ideas were so new and revolutionary that Dorothy felt that I should first present it at the American Crystallographic Association meeting at Gatlingburg (July 1965). The paper was quite well received. More importantly she arranged for me to meet her mentor J. D. Bernal. She was also present at the meeting. He heard me very patiently and finally said that all my arguments were correct and he saw no reason why the method should not work. However he had one serious reservation: that the neutron beam intensity of the present reactors must increase by at least one to two orders of magnitude if this method is to become practical and routine! Dorothy saw disappointment on my face and she, the very personification of kindness, said, 'In any case I shall put Cd-doped insulin in the neutron beam and let us make observations'. But the oracle had spoken and his verdict proved correct. The following paragraph by S. A. Mason really summarizes the situation.

Following the suggestion of Ramaseshan (1964), work was begun immediately at Harwell on insulin crystals by Moore and McDonald and later by the present author along with Hodgkin, Willis and Fues. In the beginning it was thought that the potential power of the anomalous dispersion of neutrons would contribute to the solution of the then unknown crystal structure of insulin. However, the limitation of flux did not permit this objective to be reached

In spite of this a few neutron crystallographers did follow up this idea and solved a number of structures - for list see, ref. 20. However, before I turned my attention to other applications one rather nice piece of work came out. The determination of the position of the anomalous scatter (AS) or heavy atom (HA) helps greatly in solving structures. Unfortunately in large structures this is by no means easy. If, however, one could obtain the specific contributions to scattering by the anomalous scatterer or the heavy atom from the experimental data on anomalous or isomorphous crystals, a straightforward Patterson would do, as only the AS/HA vectors would appear without the cluttering effect of other atoms. My student Singh²¹ derived an exact formula for this. This formula has become very useful with the coming of synchrotron radiation.

Application of anomalous scattering to physical problems

When I read G. Venkataraman's PhD thesis I got interested in binary liquids and amorphous solids. These binaries are characterized by three atomic distributions of A-A, B-B and A-B vectors which are known as partial structure factors. A knowledge of each of these is necessary for calculating or predicting many of the properties of such systems, particularly for calculating the electrical resistivity of alloys. Unfortunately, it is impossible to separate these partial structure factors from one scattering experiment. The idea suggested itself that the simple answer to this was to use multiwavelength anomalous scattering. My student Ramesh was able to derive the detailed formulae required. This method has been extensively used for studying many binary molten alloy systems. Because of its use in technology this has become one of our well-quoted papers²².

When mixed crystals are prepared, because of the differences in the atomic or ionic radii, there are small displacements of the atoms from their normal (ideal) positions. A knowledge of these 'static displacements' is necessary from the point of view of various applications/properties, dislocation movement, strength, etc. Again, Ramesh was able to show that the multiwavelength anomalous scattering can provide a simple method of getting all the information on these important parameters²³. Our method is

being used systematically these days using tunable synchrotron radiation.

The third application is a novel but recondite application to lattice dynamics and lattice waves in crystals. This was done in collaboration with K. S. Viswanathan (who is an authority in lattice dynamics) and Ramesh. It was shown that the multiwavelength method provides an effective tool for extracting the components of complex eigenvectors of a lattice wave propagating along a general direction in a crystal. Here we discovered a law similar to Friedel's law, the violation of which leads to the solving of the initial relative phases of the elliptic motions of atoms in a crystal²⁴.

Perhaps, the most elegant application of these ideas was the explanation by Ramesh of the variation of resistivity in liquid caesium with pressure. Solid Cs which is a fcc crystal transforms at 42.5 kb isostructurally (i.e. it continues to remain fcc) but with a drastic volume change. This was attributed by Fermi to the electronic collapse of the Cs atom from the 6s to the 5d state. Due to statistical fluctuations in the liquid state some of the distances between Cs atoms may be closer than the interatomic distance in Cs in the collapsed solid state. This may induce the collapse of some Cs atoms so that there are two species of atoms in the liquid. While considering how this two-species model can be experimentally established by anomalous scattering, Ramesh brilliantly suggested that the collapsed caesium atom in its virtual bound state would scatter the free electrons 'anomalously' and change the resistivity. He then applied the theory we had developed for X-ray anomalous scattering for binary liquids and explained in a most convincing manner the change of electrical resistivity of liquid Cs with pressure lending much credence to the two-species model²⁵.

The coming of the synchrotron

Years passed. Our work on the multi-wavelength method appeared to be just a curiosity. The picture changed spectacularly with the advent of the intense tunable synchrotron X-ray sources. Large 'anomalous dispersion corrections' were discovered in the L radiation²⁶. For example, in caesium values as large as $f' = -26.7$ and $f'' = 16.1$ were found (Figure 3c) (shades of Hermann Mark's perceptive remarks in 1955). The multiple

wavelength method became a viable alternative for determining phases and is now becoming more and more popular. Three to four decades had passed and all the work that Venkatesan and I did was forgotten. But not quite.

When David Sayre held a conference in 1981 I was invited to be the first speaker of the session²⁷ on anomalous scattering. One flattered oneself that our pioneering work was not completely forgotten. At this meeting I touched upon many things including the work done by another of my PhD students – Ramesh Narayan. The question we tried to answer was whether the phase errors are to be minimized in the multiwavelength method: (a) how many wavelengths must one use? (b) are there any advantages in using specific wavelengths in relation to the absorption edge? and (c) the actual duration of each observation in different wavelengths so that the synchrotron time is conserved²⁷

A walk with J. B. S. Haldane

My meeting Haldane was an accident and I had the opportunity of walking with him (at a very fast and tiring pace) from IISc to the Lalbagh gate. We talked of a hundred things, the biology of cashew plants, of custard apples (Seethaphal), the great triangular survey of the Indian subcontinent which started long long ago at Bangalore, the upthrust of the Himalayas and the Tibetan plateau, the magnetic equator and the big bang! His mind was always fresh and original; he was so quick; his knowledge was encyclopaedic; his perception in science, in literature and religion was remarkable. When we were discussing the handedness in nature, noticing my special interest, he suddenly asked me what I was doing. I told him, amongst other things, that a student of mine and I had developed a method which, we thought can solve the phase problem of X-ray crystallography. He was greatly interested and asked me to explain. I talked to him of anomalous scattering, the violation of Friedel's law, of absolute configuration of molecules and Bijvoet's isomorphous replacement method and finally I also explained the multiwavelength method Venkatesan and I had used in solving the phase problem. I then remarked that since the intensity of the X-radiation was quite low – this technique may just be a curiosity – and that probably X-ray and electron microscopes may soon be devised to 'see'

large molecular structures directly. He listened to all this with great concentration.

He said 'My reputation as a prophet is at present at its lowest' (he probably was referring to the errors he had made with regard to predicting space flights). But he was certain that in two decades with the great big electron accelerators (or with laser bombardment) X-ray intensities must become 5 to 6 orders greater: He was pessimistic that in this period X-ray microscopes and electron microscopes could 'see' large molecular structures.

He suddenly got excited and asked me if one crystal with a 'marker' atom (as he called it) with two appropriate wavelengths would be enough to solve a structure and when I replied in the affirmative, he exclaimed: 'that is indeed very clever – do you know what I would do – the secret of intelligent research is to make nature do your work'. I will feed an organism a chemical with 'the marker' so that the organism itself gets it into the molecule when it synthesizes it. All that we will have to do is to extract the substance, crystallize it and use the method you have described – and lo and behold, the structure will be revealed.

Looking back almost three and a half decades one realizes what a visionary he was. He predicted the coming of the synchrotron radiation and the method he suggested is now being regularly used by Wayne Hendrickson²⁸.

1. Nishikawa, S. and Matukawa, K., *Imp. Acad. Jpn.*, 1928, 4, 97.
2. Coster, D., Knol, K. S. and Prins, J. A., *Z. Phys.*, 1930, 63, 345.
3. a. Bijvoet, J. M., *Proc. Konink Ned. Acad.*, 1949, 52, B13; b. 1951, 54, 16 and *Nature*, 1951, 168, 271.
4. Ramachandran, G. N. and Chandrasekharan, V., *Proc. Indian Acad. Sci.*, 1951, A33, 199.
5. Bokhoven, C., Schone, J. C. and Bijvoet, J. M., *Acta Crystallogr.*, 1951, 4, 275.
6. Ramachandran, G. N. and Raman, S., *Curr. Sci.*, 1956, 25, 348.
7. Ramaseshan, S. and Abrahams, S. C., *Anomalous Scattering*, International Union of Crystallography, Munksgaard, Copenhagen, 1974.
8. Wyckoff, R. W. G. and Armstrong, A. H., *Z. Kristallogr.*, 1929, 72, 319; *Phys. Rev.*, 1939, 35, 215 and 583; 1930, 36, 1116.
9. Ramaseshan, S., 18th Annual Meeting of the Indian Academy of Sciences, December, 1952.
10. Ramaseshan, S., Venkatesan, K. and Mani, N. V., *Proc. Indian Acad. Sci.*, 1957, A46, 95; Ramaseshan, S. and Venkatesan, K., *Curr. Sci.*, 1957, 26, 352; Ramaseshan, S.,

Advanced Methods in Crystallography (ed. Ramachandran, G. N.), Academic Press, 1964.

11. Mark, H. and Szillard, L., *Z. Phys.*, 1925, 33, 658; Bradley and Rogers, J. W., *Proc. R. Soc. (London)*, 1934, A144, 340; Jones, F. N. and Sykes, C., *Proc. R. Soc. (London)*, 1937, A161, 440.
12. Dale, D., Hodgkin, D. C. and Venkatesan, K., *Crystallography and Crystal Perfection*, Academic Press, 1963, p. 237; Venkatesan, K., Dale, D., Hodgkin, D. C., Moore, F. H. and Oconnor, D. H., *Proc. R. Soc. (London)*, 1971, A323, 455.
13. Hodgkin, Dorothy Crowfoot, *Nobel Lecture*, 1964, *Le Prix Nobel*, Royal Academy, Stockholm, 1965.
14. Nockolds, C., Ramaseshan, S., Hodgkin, D. C., Waters, T. N. M. and Waters, J. N. M., *Nature*, 1967, 214, 129.
15. Adam, M., Coller, E., Dodson, G., Hodgkin, D. C. and Ramaseshan, S., *Acta Crystallogr. 21st Suppl.*, 1966, A156.
16. Viswamitra, M. A. and Ramaseshan, S., *Rev. Sci. Instrum.*, 1960, 31, 456; *Z. Kristallogr.*, 1963, 119, 79.
17. Petersen, S. W., *Nature*, 1955, 176, 395.
18. Petersen, S. W. and Smith, H. G., *Phys. Rev.*, 1961, 6, 7.
19. Ramaseshan, S., *Curr. Sci.*, 1966, 35, 87.
20. Ramaseshan, S. and Narayan, R., *Structural Studies on Molecules of Biological Interest* (Hodgkin Festschrift), Clarendon Press, Oxford, 1981, pp. 233–245.
21. Singh, A. K. and Ramaseshan, S., *Acta Crystallogr.*, 1966, 21, 279.
22. Ramesh, T. G. and Ramaseshan, S., *J. Phys.*, 1971, C4, 3029.
23. Ramesh, T. G. and Ramaseshan, S., *Acta Crystallogr.*, 1971, A27, 569.
24. Ramaseshan, S. and Viswanathan, K. S., *Acta Crystallogr.*, 1970, A26, 364; Ramaseshan, S. and Ramesh, T. G., *Acta Crystallogr.*, 1971, A27, 332.
25. Ramesh, T. G. and Ramaseshan, S., *Phys. Lett.*, 1972, A39, 308.
26. Templeton, D. H., Templeton, L. K., Phillips, J. C. and Hodgkin, K. O., *Acta Crystallogr.*, 1980, A36, 436.
27. Ramaseshan, S., *Computational Crystallography* (ed. Sayre, D.), Clarendon Press, 1982, p. 281.
28. Hendrickson, W. A. et al., *Proc. Natl. Acad. Sci. USA*, 1989, 86, 2190; *Nature*, 1981, 290, 107.
29. Raman, C. V., *Lectures on Physical Optics*, Indian Academy of Sciences, Bangalore, India, 1959.

Notes

1. This work was brought to my notice by S. Hosoya. In 1929 Nishikawa, one of the pioneers of X-ray crystallography (and who greatly influenced R. W. G. Wyckoff), is reported to have shown the photographs to J. A. Prins (who was considered at that time to be the high priest of X-ray physics in Europe). D. Coster, K. S. Knol and J. A. Prins² made quantitative measurements on Zn and wrote a

detailed paper (1930) on this subject. Since then these authors have been credited with this discovery even though they cited Nishikawa's earlier work!.

2. This remarkable suggestion of using multi-isomorphous crystals for unique phase determination was missed out by many crystallographers till it was pointed out by Dorothy Hodgkin and Max Perutz who then

proceeded to use it to solve the haemoglobin structure.

3. In those days the dispersion corrections were designated as $\Delta f'$ and $\Delta f''$. In 1974 at the Madrid conference⁷ it was decided to drop the deltas to call them just f' and f'' .
4. Wyckoff was one of the examiners for my D Sc thesis, the other was C.G. Darwin!
5. This was in early 1953 when extremely few

non-centric crystals had been solved – three years before the appearance of the Ramachandran-Raman paper⁶, which provoked a spate of activity on noncentric structures. It was also very unfortunate that we could not get hold of crystals of strychnine selerate – the structure Bijvoet and his collaborators solved⁵.

PERSONAL NEWS

Dear Anna,

Today is your 75th Birthday (23 August 1993), and since this is the conference season, you are not in India but travelling in Europe and the United States; and as a distinguished meteorologist said of you – 'to be one of the much loved invited speakers at international meetings'. I feel rather odd writing a formal letter to congratulate you on this occasion. For we have known each other for more than five decades; we have worked under the same preceptor, we have shared the same laboratory at the Indian Institute of Science, we have laughed and quarrelled, joked and argued ever since I was 19 years of age.

In 1945 after a stint of about 5 years with Prof. C. V. Raman, you changed your field of activity and went to England 'to train' in meteorological instrumentation. I remember you saying that you enjoyed every moment of your stay in England but you learnt little about meteorological instrumentation as applicable to India; the relevant knowledge on this subject you gathered only after you came back to India. You joined, in 1948, S. P. Venkiteshwaran, who was heroically attempting to build a group on meteorological instrumentation in the India Meteorological Department (IMD), Poona. When he left as Director, Agricultural Meteorology, you led the instrumentation group. You were then a woman in fury because we were importing almost all our instruments. A dilapidated shed and a handful of workers became a magnificent centre for designing, fabricating, testing and calibrating meteorological instruments, manufacturing at least

100 types of instruments, from the simplest to the most sophisticated ones, like radiometer, radiosondes, etc. With great insight you put these instruments to use by installing them in a network of stations, which you helped to set up all over India, to measure the parameters necessary for meteorology.

Your researches on atmospheric ozone are well known. You inspired your students to design and fabricate India's first ozonesondes and to set up many ozone-sounding stations. Little did anyone realize at that time that in a matter of two decades these activities would assume major importance in a global sense. You must have felt truly proud when your student and colleague C. R. Sreedharan set up India's first ozone-sounding station in Antarctica and obtained many exciting results. The International Ozone Commission recognized your important contributions to this field and you were also awarded the K. R. Ramanathan Memorial Medal, which you treasured as Prof. Ramanathan was your other mentor who inspired you into doing ozone research. It was also no surprise to me that because of your respect and affection for him you agreed to edit the selected papers of K. R. Ramanathan. About your instrumentation activities Oliver Ashford said:

My only regret is that with her expertise in such a wide range of measuring devices, radiosondes, ozone, radiation instruments and anemometers – to name only a few – we do not yet have an eponymous instrument; how I would love to make observations on an ANNAMANIMETER.

When you formally retired from IMD, you as a Visiting Professor at the Raman Research Institute used a newly designed infrared spectrometer to assess the precipitable water over several stations, a knowledge essential for setting up millimeter wave radio telescopes. Then started one of the most dynamic phases of

your career. With the moral backing of the Raman Research Institute Trust, with funding from DST and DNES and support from IITM, you set up scores of stations all over India in farflung and inaccessible places and studied the wind climatology in many states of India. Your studies, extending over 15 years, resulted in five monumental volumes which have received rave reviews: 'This set will constitute a bible for engineers and scientists for setting up solar and wind power stations'.

I am one of the many scientists you have influenced. You had set up meteorological facilities for the International Rocket Launching Station at Thumba in Kerala at the request of Vikram Sarabhai. Probably you learnt from him that my group was involved in making Fibre-Reinforced Plastic (FRP) rocket nose cones for his space activity. You then suggested (twisted my arm) that my group get involved in making FRP radomes to protect from fierce cyclonic storms the weather radars you were installing at many places. It was thus that the country got studded with these beautiful radomes. These are the tributes I paid to you and your vision. You literally dragged me to Delhi when a Japanese Airliner crashed, to show me the antiquated imported visibility measuring instruments our airports had. This forced me to initiate activities on better airport instruments. As President of the Current Science Association, much of the improvement that people say has taken place in the journal in recent years is due to the silent encouragement you gave me.

Perhaps the greatest surprise to me was when I recognized you as a character in a Sahitya Academy Award-winning Malayalam/English novel entitled *I Thank You Seismograph* by C. Radhakrishnan. This novel is about science, scientists, research and scientific administration in India and each of these

Text of the letter that was written by Prof. S. Rameshan, Editor to Ms. Anna Mani, President, Current Science Association on her 75th Birthday.