WILLIAM THOMAS ASTBURY

1898-1961

WITH the death of WILLIAM THOMAS ASTBURY on 4 June 1961, there passed one of the most characteristic figures of what may be called the heroic age of crystal structure analysis—the first generation to follow the Braggs—but he was more than this. He was a founder of what is now one of the most exciting growing points of science, *molecular biology*. Known to all as Bill Astbury, he was one of the great characters of British science in the twentieth century. Although always associated with Leeds where he worked for thirty-three years, he was born on 25 February 1898, the fourth of seven children, at Longton in the Stoke district where his father, W. E. Astbury, was a potter's turner. Bill Astbury retained to the end of his life the directness and simplicity of the Five Towns. But he early showed his intellectual gifts as well, encouraged by his mother and by a succession of schoolmasters who recognized his promise.

He received all his education by scholarships, a difficult achievement in those days. He won a scholarship to Jesus College, Cambridge, in chemistry, physics and mathematics. He went up in 1917 but his stay in Cambridge was interrupted by the war; he served in the R.A.M.C. in Cork where he met his future wife. In 1919 he returned to Cambridge and completed his course, reading chemistry, physics and mineralogy in Part I and physics in Part II, achieving first classes in both.

Astbury had the good fortune to study under Professor A. Hutchinson a course that was really far the best in crystallography to be given in the United Kingdom. That determined the nature of his career because in 1921 Professor Hutchinson recommended him to Professor Sir William Bragg who was just taking up science again after the war in his physics laboratory at University College, London. It was in that period that he married, bringing his wife over from Ireland. They had two children and for the rest of his life he lived an ideal family life with his children and grandchildren.

In 1923, soon after his marriage, Astbury moved to the Royal Institution with Sir William who was then setting up the Davy-Faraday Laboratory, which was to be for many years a great centre of X-ray crystallography. There Astbury's mathematical training and even more the basic formal crystallography that Professor Hutchinson had taught stood him in very good stead; in fact, he knew more crystallography than either Sir William or Sir Lawrence Bragg.

The period at University College and the Royal Institution was for Astbury a formative one. The band of people who had gathered there were

diverse but all shared in common a lively enthusiasm for the discovery of the new world of crystal structure which they were privileged to share. It was a very happy time: there was no real rivalry because that world was quite big enough for all their work. They were effectively and actually a *band* of research workers, dropping into each other's rooms, discussing informally over lunch and ping-pong and formally in Bragg's colloquia every week. But each developed his own particular interest. There were the seniors, Shearer and Muller, with their development of gas X-ray tubes for photographic purposes and their study of long-chain compounds. There was Miss Yardley, afterwards Mrs Lonsdale, who worked with Astbury in preparing the celebrated Astbury-Yardley tables of space groups (3). There was Gibbs who did the extraordinarily delicate determination of the structures of different forms of quartz and silica. Later were to come J. M. Robertson and Cox: an international gathering too, with Weiss and Mathieu from France—the latter a particular friend of Astbury's—Patterson from Canada, Burgers from Holland and Orelkin from Russia.

Astbury's recollections of this time is given in this unpublished fragment which he intended to contribute to a history of crystallography:

'*Early days at University College, London, and the Davy-Faraday Laboratory of the Royal Institution*

'In sharing out who shall write what in these X-ray diffraction memoirs, the two "oldest hands" available to recall those early days at U.C.L. and the R.I. were obviously Kathleen Lonsdale and myself, but what was not so clear was who should do the actual writing. We could hardly say "we remember" when it was sometimes only one of us who remembered, and anyway we like to think we have distinctive styles, so we compromised—I mean, she agreed to let me do the job. But it is to be understood, though, that it is a joint effort and unless otherwise stated, any particular memory or anecdote may be privy to either or common to both. For the purposes of this article we are to be considered, like the two unresolved heirs in "The Gondoliers", as a single unit.

'I am the older hand of the two, in years and crystallographically, because I joined the staff of the Physics Department of University College in 1921 after graduating two years late through war service, while Kathleen (then Yardley) joined in 1922 after graduating two years younger than most people. I had read chemistry and (classical) crystallography at Cambridge besides physics, and I was also married in 1922, so this experienced old man ventured to take the precocious child under his wing, for a very brief start at least . . .

'It was a case of the blind leading the blind (to mix the metaphor a little), but that of course was the fun of the thing. It has been well said that the greatest asset of scientific research is its naïvety and we must have been a wonderful example of that—all of us, not even excluding Sir William at his own high level. And before going any further let me make it crystal clear that

Sir William—the Old Man, or Bill Bragg, as we called him behind his back—never "led" any of us in the technical sense. That was not his way—if he had a way—and if you were stupid enough you might even claim that you "led" him, since, especially after we migrated in 1923 to the Davy-Faraday Laboratory of the Royal Institution, as often as not when he popped into your room (not terribly often) it was to ask *you* a question in connexion with some lecture that he was due to give. Or you might meet him on the stairs and he would say, "Hello! How's the family?" or some such. He turned up at tea as often as possible, where we rarely talked "shop" in any case.'

Everyone was left free to choose his problems. Methods were more or less predetermined. At first there was only the original Bragg method of the ionization spectrometer, a very precise but incredibly tedious method of working in which hours of observation were necessary to determine the intensity of a single plane, a method quite sufficient, the Braggs had shown, for determining simple structures in the mineral field but, in fact, useless at that stage for complicated organic structures where the essence is to have only relatively accurate measurements on a large number of planes, with which in those days only the photographic methods Astbury did much to perfect, could cope.

Astbury started, rather by coincidence than otherwise, where another great scientist, Pasteur, had started, in the field of the tartaric acids, stimulated by the idea of trying to explain optical rotation by the actual molecular structure. He did not indeed succeed: this was to be left to Beevers (1950) twenty-seven years later. After all, at that time, no one had determined any organic structure more complicated than those of diamond, graphite and simple long-chain crystals.

What the Royal Institution provided was a sharpening of wits in which Astbury gave as much as he took; he had an interest much broader than the fairly straightforward idea of determining the structure of all known crystals. He was, nevertheless, first and foremost a crystallographer. Feeling the need for a regular crystallographic understanding, he collaborated with Miss Yardley in producing the first British tables of space groups.

This was to lead him later, in 1930, to a notable contribution to the whole international correlation of crystallographic results, at the historic meeting called by Ewald at Zurich to consider the possibility of international tables for crystallography which would combine the results achieved by many others in different countries. Among others it was attended by Ewald, Hermann, Mauguin, Niggli, Pauling, Schiebold and Wyckoff. The stamp of its success was the *International Tables* which duly appeared and have been ever since in their improved form the bible of the X-ray crystallographer. And this was due not only to Astbury's and Yardley's mathematical work which had gone into them, but even more to his ability to get them accepted, a very difficult thing to do. It needed all his persuasive powers to get the Astbury-Yardley tables published in the first place: Sir William did not

think they were necessary—any good scientist by common sense could arrive at all the results contained in them. Astbury was able to persuade him that not all people who might be good scientists had his supply of common sense, the weaker vessels might find the tables useful. It was much more difficult when he had to persuade Professor Niggli, a very big name in the crystallographic world, editor of the *Zeitschrift für Krystallographie*, to agree to use a common name for tables which he would have liked to call the Niggli International Tables. We were all in despair and we finally agreed that Astbury should talk to Niggli alone and the result was that he withdrew the demand to include his name. This was due to Astbury's transparent honesty and disinterestedness which were always evident at critical moments.

He showed the fruits of his physical studies in another way by his development of an α-ray absorption intensity gauge (6), one not much used in itself but the basis of a number of devices connected with autoradiography today. At colloquia he was always brimful of ideas but often these were rather difficult to understand. When he spoke, most people thought he was talking nonsense. I found out fairly early that when Astbury was talking it might appear to be nonsense but it always contained a valuable and new idea and I did my best at these meetings to interpret them and, what was much more difficult, to get Astbury's agreement that I had interpreted him correctly.

It would be a mistake to attempt to present the long life work of Astbury in a strictly chronological order, so I will begin with, § 1, the early crystallographic studies which he carried out at the Royal Institution. Then follows his work at Leeds, § 2, the studies on wool and similar fibres, what he called the k–m–e–f group, keratin, myosin, epidermin, fibrin group, in three characteristic forms, α, β and crossed-β or super-contracted. The next section, § 3, will deal with the structure of collagen and its related fibres. The bearing of all this on the textile fibres is dealt with in § 4. Section 5 is the first of his biological studies, that of the arrangement of fibres in cell wall of the alga, *Valonia ventricosa*. Section 6 will deal with his important initial work on nucleic acids; § 7 with various other biological and medical applications and § 8 with his experimental techniques. This is followed by two discussions, the first on the place of Astbury's work in the development of biophysics and molecular biology and, lastly, a further appreciation of his character.

1. *Early crystallographic studies*

The early papers of Astbury on crystal structures were of considerable interest, if not for actual conclusive results. Astbury's first paper (1) was on the crystalline structure and properties of tartaric acid. In the light of modern knowledge it is not very illuminating for the tartaric acid structure but it reveals much more the cast of Astbury's mind and the kind of problem he was likely to treat. The first, or observational, part is admirable and straightforward good crystallography; seen in its very beginning, this is one of the first monoclinic crystals to be studied. He examined 24 faces only,

the simplest that he could find. Although he did not succeed in finding the correct structure, the argumentation is sound, given the fact that at the time very little was known about atomic diameters and what was thought to be known was wrong. It was, however, in the discussion of properties that he shows the widest degree of interest. He sees at once the analogy between the structure of tartaric acid and that of ice—which is indeed true. He notes the possibility of determining the difference between L and D forms. He then goes on to theorize about the origin of the optical activity. Actually, the theory of optical activity of crystals is as yet extremely imperfect and no one would dare to calculate the optical activity of tartaric acid today. He notices that a perfect cleavage is characterized by rupture along the junctions of the hydrogen atoms and hydroxyl groups. This is in fact true. He considers that the crystal growth itself points to an initial grouping on the part of the hydroxyl group towards such an arrangement as holds it in crystalline form and it is fairly safely assumed that the tendency of the molecules to build themselves up into a lattice exists even in solution.

With this paper goes the companion on anhydrous racemic acid (2). This was, practically, quite an achievement because it was the first triclinic crystal to be studied by X-rays and the crystallographic study was admirably done. It involved the study of intensities of 24 planes and their orders, and for only two molecules, one right and one left, per cell. He proceeded to the important conclusion that there was no trace of a molecule of racemic acid, that is, of an inactive molecule, in the cell, a conclusion comparable in importance to chemists to Bragg's original observation that there was no evidence for the existence of a molecule of NaCl in rock salt.

The remaining two papers are studies of metallo-organic compounds, the first to be carried out on basic beryllium acetate (4), in conjunction with G. T. Morgan, who had prepared a long series of similar salts. These are interesting crystallographically because they belong to a lower space group of the cubic system, T_h^4, now written *Fd*3, a type of diamond structure. The second paper (5) is on a similar subject: that of the tervalent metallic acetyl-acetones which occur in two series, the monoclinic and the orthorhombic. There is a third series and it was on a large crystal of the γ form that most of the investigations were carried out. Here he used the photographic method to record the intensities of 256 planes. This greater number, the largest hitherto recorded for a crystal, shows the effective superiority of the photographic method over the ionization spectrometer for organic crystals of any complexity.

Astbury went on to ascertain the disposition of molecules and showed the analogies between the different series. He used advanced methods such as etch figures to determine the symmetry and arrived in the end, by a judicious composition of chemical and X-ray evidence, at a reasonable structure for all the different forms. It was fully confirmed by later observations, a very fine example of Wernerian co-ordination.

These two papers alone would show that Astbury was well on his way to

becoming one of the most effective organic crystal analysts of the rigorous school and he might have made a very great contribution to this field if he had continued on this line. But it would not have been to the same extent either as original or as useful as the one he was to make by going over to the field of imperfect crystals and fibres, particularly that of biological structures.

Introduction to fibre studies

At the Royal Institution, Astbury found the general direction of the work for the rest of his life almost by accident. One of Sir William Bragg's most subtle ways of directing research—because less of a Director you could hardly imagine—was casually to ask one of the research workers to help him in preparing some photographs or material for a lecture. We did not like this too much, actually, at the Davy-Faraday because it took time off our work and, in fact, the preparation of the children's lectures occupied the whole of the autumn term. Nevertheless, though we did not know it, it often proved the most valuable and instructive part of our research training.

Sir William had the idea of going beyond well-formed crystals and giving a lecture on *The imperfect crystallization of common things*, which included among others, fibres (1926). Work on fibres had already started, mostly at the Kaiser Wilhelm Institut in Dahlem, Berlin, where Meyer and Mark had already been studying X-ray patterns given by simple textile materials, ramie, cotton, silk. Bragg asked Astbury in 1926 to help in getting photographs of fibres like wool. Simple substances like silk and ramie gave beautiful fibre diagrams, but others were very blurred and anyone else but Astbury would have been rather dissatisfied with them compared with the very beautiful clear pictures given by crystals. Astbury, on the contrary, took to them from the beginning and it was clearly his interest to go beyond the regular crystals to the fibrous state which he made his own particular field.

He was already fascinated by the biological implications of the work and he had a clear idea from the start of what he was trying to do but very few believed that he would succeed in doing it. It may have been an accident that he went into wool but it was no accident that he went into organic substances, because he felt this was his real vocation. He said this years afterwards in his Harvey Lecture of 1950 (93):

'The name "molecular biology" seems to be passing now into fairly common use, and I am glad of that because, though it is unlikely I invented it first, I am fond of it and have long tried to propagate it. It implies not so much a technique as an approach, an approach from the viewpoint of the so-called basic sciences with the leading idea of searching below large-scale manifestations of classical biology for the corresponding molecular plan. It is concerned particularly with the *forms* of biological molecules, and with the evolution, exploitation and ramification of those forms in the ascent to higher and higher levels of organization. Molecular biology is predominantly

three-dimensional and structural—which does not mean, however, that it is merely a refinement of morphology. It must of necessity inquire at the same time into genesis and function.'

Thus it was that when an opening occurred in Leeds, Bragg's former university, for a lecturer in textile physics, Astbury was a natural choice. He did not want to go at first but Bragg had a habit of throwing out his best people in order to start off new centres of research and in this case he greatly exceeded his expectations, for the school at Leeds was for at least fifteen years the major centre of fibre research in the whole world. Being Leeds and not Manchester, it was wool that was studied rather than cotton which had been the basis of most of the older fibre structure work. I remember well, at the time, how shocked some of us were at Astbury going into this completely complex and very mundane field. We felt that it was very premature —let us find the structure of regular things first before we tackle the irregular ones. But he proved to us how wrong we were. There he showed his essentially pioneering spirit, moved by an impulse to wander into the unknown and not to give a very precise account of what he does because he is in so much of a hurry to get on to the next place.

2. *Work on the k–m–e–f fibres in their α, β and crossed-β form*

Astbury at Leeds

Astbury's arrival in Leeds is best accounted for in his own words, in part of a report he wanted to give for the book *Fifty years of X-ray diffraction*:

'As an adjunct to Speakman's physico-chemical investigations on the wool fibre commenced in 1926, the University of Leeds asked Sir William whether he could supply someone to carry out complementary investigations in textile physics. I wanted to stay on at the Davy-Faraday, of course, but I accepted the post of Lecturer in Textile Physics in 1928 and set about building up a Textile Physics Research Laboratory based chiefly, in the first place, on X-ray diffraction studies of wool. H. J. Woods was appointed Research Assistant and I had two Ph.D. students and an apparatus allowance of £150 p.a.; otherwise the room provided was quite bare and all we knew was that certain clothes were made of wool, and that wool in turn was composed of an "amphoteric colloid" called keratin—a biochemically lifeless and uninteresting protein which was some kind of polypeptide. Except for a Hyvac pump we constructed all our own apparatus . . . For over 15 years from the early 30's our work was supported principally by the Rockefeller Foundation (no help of any significance ever came from the wool textile industry*) . . . After the war, the biological implications of our work having long outgrown the merely textile, the University inaugurated the

* Though this remark of Astbury is strictly true, it should be noted that it only applies to the pre-war period and to the wool *textile* industry. To give a fairer picture it would be necessary to add that the International Wool Secretariat, which makes a levy on raw wool, did contribute very generously to wool research and it is from this source that most of Astbury's early assistants received their grants. After the war more help did come from the wool textile industry (see p. 17).

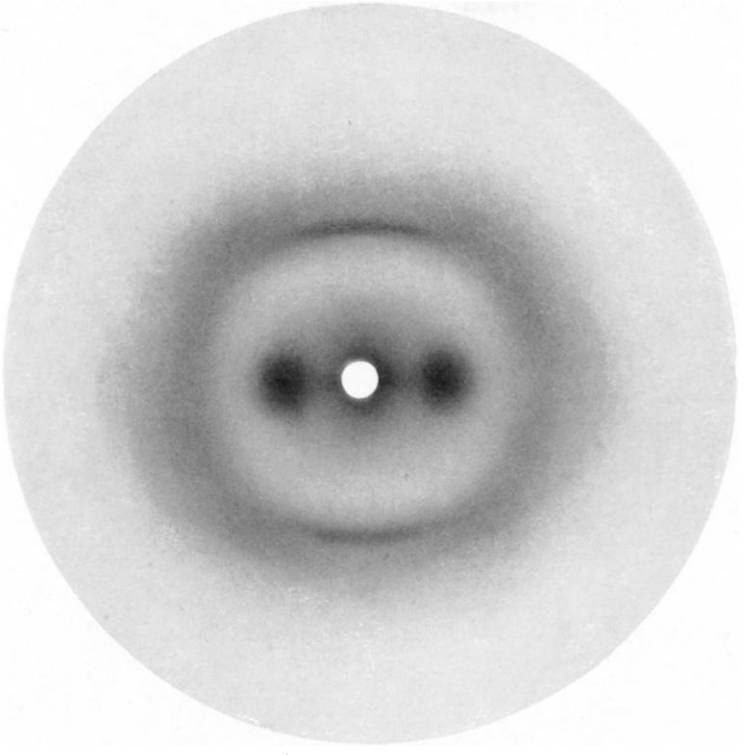
present Department of Biomolecular Structure and appointed me to the Chair. (The title I wanted was "Molecular Biology", the name I myself had first propagated, but the committee thought it was asking too much to describe me as any sort of biologist.)'

Astbury certainly had to start research the hard way but actually he had to keep it up the hard way for the rest of his thirty-three years at Leeds. The Rockefeller grants only enabled him to buy a little apparatus and pay the salaries of a few additional research workers. They could do nothing to help him with building, nor could the University. To the very end, after he had acquired an international reputation and many honours, Astbury's new Laboratory of Biomolecular Structure was really the rooms of an old house acquired by the University and in every way unsuitable for the work he had to do. Like many others of us, he never, in the course of a long scientific life, had a new building made for the purpose of research. Nevertheless, in view of his temperament, this did not dishearten him, although in his latter years I know he felt it acutely as an index of the lack of value that was put on science in this country.

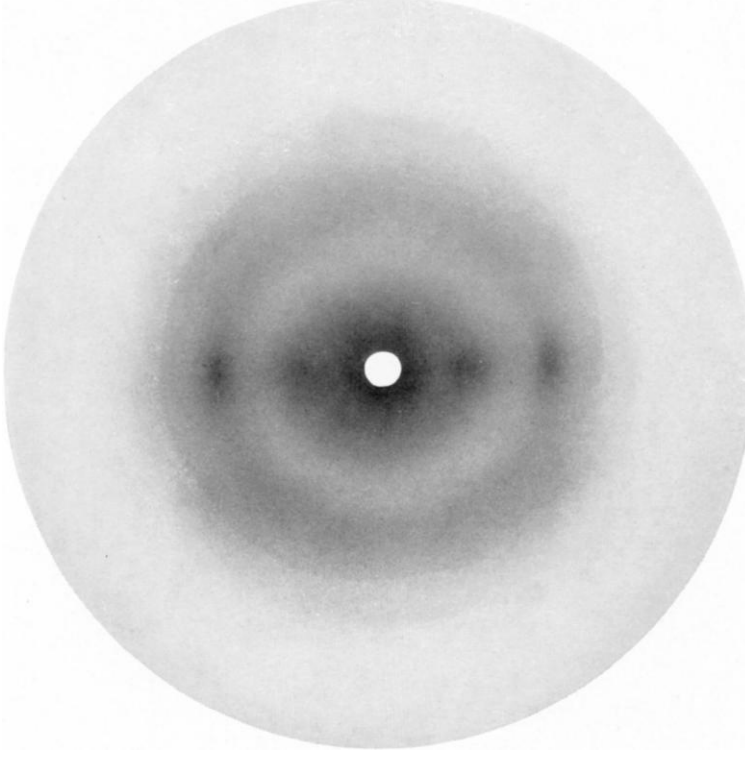
I think it was the very ignorance about wool as a scientific subject that really stimulated him. The two lines of 'amphoteric colloid called keratin, biochemically lifeless and uninteresting', were just enough to start him on a violent attack on this area of ignorance.

Astbury's main work at Leeds was done right at the outset and published between 1931 and 1935 in three key papers, two in the *Philosophical Transactions of the Royal Society* and one in the *Proceedings* (11, 19 and 25), referred to as I, II and III. Of these I, published with Street, is most important, it might indeed be taken as the key paper of all Astbury's work and well repays reading because it provides the kernel of his discoveries and also gives an explanation as to why he was reluctant to abandon his original ideas. Astbury's work drew on two previous sources, early fibre photographs, the first on wool by Hertzog & Jancke as early as 1921 and, secondly, from that of his colleague at Leeds, J. B. Speakman, who had studied particularly the elastic properties of wool fibres (1926, 1927).

What Astbury was trying to do was to repeat and improve the X-ray photographs of wool and to interpret them in the light of the data derived from the study of its extension properties. His first discovery was that the structure of unstretched wool and hair, effectively with only two features, an equatorial spacing at 10Å and the meridian spacing at 5·1Å, with a vague halo surrounding them, was in fact an interpretable structure not of a straight chain but of some kind of folded chain. Secondly, that this was reversibly interchangeable with another. In this pattern (plate 1 (*a*)) there was the same 10Å spacing with the addition of stronger reflexion at 4·65Å on the equator, but the 5Å streak on the meridian had disappeared; it was replaced by a layer line corresponding to a repeat unit of 3·4Å. Such a picture indicated a structure more recognizably fibrous, the β structure, and in fact substantially identical with that of silk. All this, he saw, could be interpretable only



a



b

PLATE I.
Early photographs by W. T. Astbury of the α—β transformation.
(*a*) Cotswold wool, unstretched showing α reflexion.
(*b*) Cotswold wool, stretched 90%, showing β reflexion.

[*Facing page 8*

in terms of a single polymerized type of molecule which must, according to the seminal theory of Emil Fischer in 1901, be a polypeptide. At the date of Astbury's arrival at Leeds, 1928, the Fischer hypothesis was not by any means universally accepted by biochemists, at least not for all proteins. Astbury's work was to put it on a much sounder physical basis. In the paper he further identified the peculiar properties of wools and mammalian hair with the extremely rich content of the sulphur-containing double amino-acid, cystine, an amino acid which had to link together two peptide chains through the S—S link and was thus susceptible to breaking by agents like Na_2S. According to this view the hardness of keratin was like, in many ways, the process of vulcanization of rubber, also carried out through S—S bonds.

Astbury's general approach to the interpretation of the wool structure was characteristic. First he got it by physically altering the material and hence the X-ray patterns and, secondly, by finding other examples of similar patterns among other forms of proteins.

He showed that wool in extension in water could stretch by 30%, but in steam by 90%, giving a much cleaner β photograph (plate 1 (*b*)). The reversibility of this change convinced him that there had been no alteration in the chemical structure and the chain in its α form had to be unfolded (or rather untwisted) to yield the β form. It was the first example of a mechanical polymorph. He favoured the unfolding pattern and in this paper first published his celebrated α-fold (figure 1), the consequence of another study slightly later and reported in *Nature* (51).

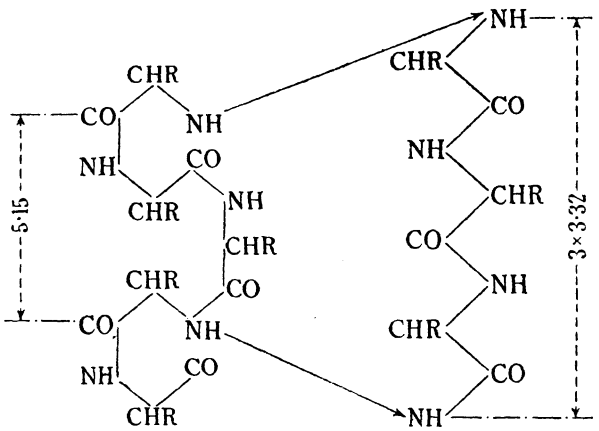


FIGURE 1.

Paper II consists essentially of an elaboration and simplification of these observations in the light of more detailed measurements of the elastic properties, carried out in conjunction with Woods. Here there is an attempt to account for some of the anomalies by pointing out that hair is not

a homogeneous structure but has marked biological differentiations between cortex and medulla and individual cells, and a recognition that hairs are made with different structures in different parts. Astbury himself considered this the most important of his early papers because it brought together, for the first time in the study of X-rays, the anatomical structure, the physical properties and the molecular structure of a natural material. He used to refer to it as the 'wool bible'.

In paper III, Astbury followed another track, the attempt to impose a second orientation on the keratinous fibres, that is, two different orientations at right angles to each other and to the length of the fibre. This he succeeded in doing particularly in the case of horn. To obtain the second orientation he realized that it was necessary to break down the structure for he states categorically:

'In no case has it been found possible to impose preferential orientation on keratin in the α form and only in the β form in the presence of steam or hot water.'

Undoubtedly, however, as his subsequent work shows, he was influenced by the second orientation to prefer the two-dimensional fold to a three-dimensional helix which could not allow for any secondary orientation. In fact, the explanation of secondary orientation is still very obscure.

He also at that time began the study of another variety of keratin, that of feather and reptile-scale keratin, at first sight very different from mammalian keratin but later assimilable to a type of β structure with long period repeats (15) (126). Astbury first used this observation in a biological sense to show the basic difference between reptiles and birds on the one hand and mammals on the other. This was one of the first cases in which it was shown that the systematic differences were effective right down to the biochemical level. This helped to generate the idea in his mind of a 'master plan' of nature (127)—a polypeptide fibre that could adopt a great variety of secondary configurations determined by the different branches of evolution.

As time went on, he turned to other forms of protein. Of very great importance was his study of myosin (50), at that time considered to be a single protein, responsible for muscle in all forms of animals, invertebrate and vertebrate. Astbury studied muscle intensely from his first observations that 'muscle gave a characteristic α protein photograph' but this did not, somewhat to his surprise, change into any kind of super-contraction when the muscle contracted. In the end he came to consider myosin as the generalized α protein or living protein from which the specialized structural proteins were derived by cross linking. Astbury did an enormous amount of work on muscles of various kinds from the byssus retractor muscle of the mussel, *Mytilus*, which contracts and stays contracted, to the frog's muscles with their rapid extension and contraction (72). Later he seized on his friend Szent-Györgyi's discovery by biochemical means of the other component in mammalian striated muscle, actin, to show that here were two different proteins in different states (70). But it was clearly quite impossible for him to give a

serious account of muscle contraction before the elementary structure of muscles was known and that had to wait for the development of the electron microscope.

Finally, he came to study other elastic fibres, such as the epidermin of skin, first systematically studied by Rudall, and fibrinogen and its product fibrin which form the clots of the blood (56). These were the main constituents of his k–m–e–f series of proteins all of which could exhibit according to the circumstances, α, β and cross-β structures.

Astbury's studies of the k–m–e–f group led him naturally into a consideration of the significance of denaturation. He showed (26) that most forms of denaturation did not lead to an amorphous mass but to a definite structure which was nearly always of the β type, normally unoriented, which could be oriented by means of stretching. One of his most characteristic experiments was the formation of a layer of stretched boiled egg white which he showed formed very well oriented β fibres with meridian and equatorial reflexions interchanged, the so-called cross-β type.

Astbury's brilliant idea about the k–m–e–f structure was that the same chain can exist in contracted and expanded state. The fault of his particular interpretation lay in too close an analogy to planar rather than three-dimensional thinking, inspired in this case by the structure of cellulose. The original form of Astbury's fold was much criticized but it was not, however, until 1940 that he made his first serious modification of his explanation of the α fold.* In a paper with Bell (51), he made another proposal, which so to speak, crystallized his ideas on it. It was clear by then that the tide of evidence was running strongly against the original form, where the change α—β involves the opening of the hexagonal rings. This was the consequence of the first use of models showing that there would be no room for side chains in this configuration. In this paper he summarizes the conditions that the α—β transformation must satisfy:

'(1) The α form must be half as long as the β form.

(2) The density must remain practically constant.

(3) The folds must repeat at a distance of about 5·1Å.

(4) The side chains must stand out alternately on one side and the other of the plane of the fold.

(5) The folds must be nowhere so sharp as to leave insufficient room for the side chains.

'Is it feasible to devise an intramolecular fold satisfying all these conditions that could conceivably, pending complete chemical analysis, be adapted equally well to the constitution of myosin as to that of keratin? We believe that it is; and what is more, the proposed solution hints at a principle fundamental for all proteins.'

* Dr MacArthur informs me that this followed the receipt of a letter from H. Neurath (see Neurath 1940).

To satisfy condition (2) he draws the inference that all proteins must have a structure similar to that shown in figure 2. He finds the universally occurring distance of 5·1Å is just about the shortest distance at which it is possible to fold a polypeptide chain so as to leave the side chains alternately on one side and the other of the fold and goes further to say that the side chains are grouped in close-packed triangular columns, first on one side of the fold and then on the other. This modified fold, shown in figure 3, from then on became Astbury's major idea as to the structure not only of fibrous but of crystalline proteins.

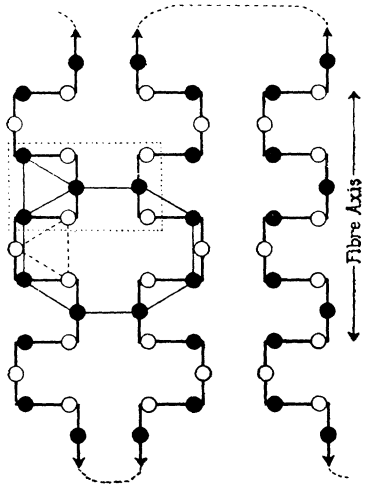


FIGURE 2. Illustrating the close packing of side-chains in the α-fold of keratin and myosin. — represents the direction of the main-chain; ● represents a side-chain pointing *up* from the plane of the diagram; ○ represents a side-chain pointing *down* from the plane of the diagram.

'In order to meet the dimensional requirements', he goes on, 'it has been found necessary to postulate hydrogen bridges between adjacent folds.'

This concept of the intra-chain hydrogen bridges was the basis of the subsequent development of the Pauling α helix.

This idea particularly appealed to Astbury because it showed that the whole structure of proteins depended on the side chains acting not as main linking chains—as he originally considered—but essentially as packing elements which put together the hydrophobic side chains and separated them from the hydrophilic elements. The doubling of the length of the α form on stretching becomes no longer an accident but an inevitable consequence of the close packing of side chains in a simple regular pattern. The new, what we may call the crenellated, form had other advantages. Astbury saw that two of these crenellations together might make a cross-β structure and this he thought was the key to structure of the crystalline globular proteins, that all globular proteins could be denatured and all gave about the same kind of residual structure. But he saw also that in this residual structure the fibres

could be arranged in parallel bundles (figure 3). One of his most characteristic and important discoveries was the observation that the single crystal of the seed globulin edestin could be turned into a set of parallel β fibres which were oriented according to the pre-existing crystal orientation (24). This was the basis of the process of the manufacture by I.C.I. of the artificial fibre 'Ardil' from the crystalline protein arachin derived from groundnuts.

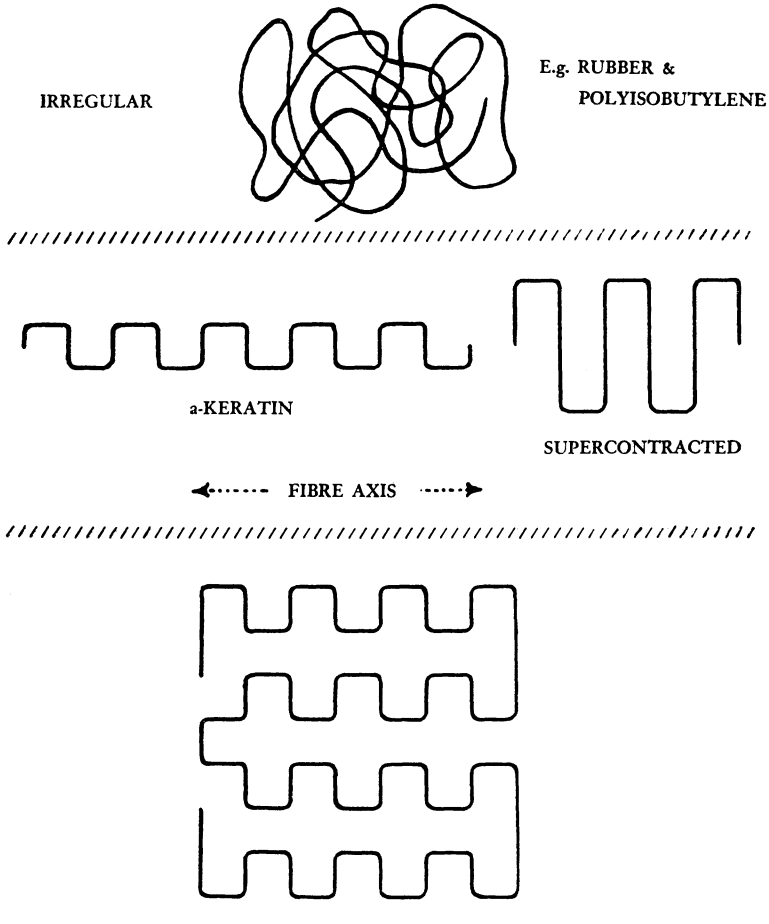


FIGURE 3. Diagrammatic illustration of states of chain-folding.

The notion of the structure of globular proteins fitted in with his own observations and those of Waugh (1946) and Schmitt (1947), on insulin and paramyosin which can be produced in a fibrous form. It has been the leading idea in all the early work on the interpretation of structure of globular

proteins and was in the end to lead to its true solution in the case of myoglobin by Kendrew although the arrangement of the α helices was not to be parallel, as Astbury and others of us thought at the time.

3. *Collagen*

There was an important group of proteins that could not be fitted into Astbury's k–m–e–f group. These were inextensible the fibres related to collagen, the main connective tissue protein and also of industrial importance in the leather industry and in the form of gelatin in photography. He recognized from its X-ray pattern that this was some radically different kind of protein fibre.

His study of collagenous fibres was to last all through his life. It was interesting that he gave the first and ninth Procter Memorial Lectures on them, separated by an interval of twenty-one years, in 1939 and 1960. These lectures are of special interest because they represent what might be called the primitive early and the sophisticated later work of Astbury. In the first he recognized as collagenous the white fibres of connective tissue, tendons, cartilage, scales and fins of fishes, the ichthyocol of swim-bladders, the byssus threads of bivalves, as well as the so-called ovo-keratin of the egg-capsule of the skate, and filaments ejected by the sea-cucumber and jelly-fish. This is some indication of the wide net which Astbury threw over the biological world to find the identical molecular patterns.

He noted the high proline and glycine content of collagen. Afterwards he said: 'The real puzzle concerns the amino-acid sequence and the average dimensions of the residue in the direction of the chains.' The indications were that it was 2·9Å against the 3·5Å for β chains of polypeptides, suggesting in some way a change of folding though to a much smaller degree. The first explanation he could find for this difference was that the collagen represented an arrangement of protein chains in *cis*-configuration as against the *trans*-configuration of the fully extended β chain, but even then this conclusion was based on too little evidence. This was his first exercise into following the actual sequence residues in a fibrous protein and it is very interesting how close he came to the subsequent explanation. This paper is a very fine example of Astbury's semi-technical work because it contains the first analysis by X-rays of varieties of a tanning process.

The ninth Procter Memorial Lecture gives a full account of the Ramachandran structure of collagen which shows that the slight twist which Astbury had considered twenty years before, was really a twining of three simple polypeptide groups of glycine, proline and hydroxy-proline (1954, 1955 and 1956). The advance was due to the first stage of work on artificial polypeptides, particularly on the polyglycine II structure itself. From now on it would be necessary to take account of twined as well as of extended single-chained polypeptides.

This Procter Lecture completes the account of collagen to date by the study of a number of further biological structures which involve collagen in

interesting ways, for instance, in the earthworm's cuticle, and Astbury makes the first hypothesis on the relation between collagen and its characteristic internal product, crystalline calcium phosphate—apatite—the beginning of the formation of bone.

Astbury's work on collagen was to have a number of consequences beyond general biological and evolutionary implications. It had applications technically in the practice of tanning. When later it was combined with electron microscope studies, he found many medical uses for it particularly those connected with rheumatism and dentistry, both of which are involved with well- or ill-ordered collagen either in the joints or in the actual structure of bones and teeth. Astbury here showed his ability to combine the theoretical basis of molecular structure with its practical implications and not in textiles alone (94) (117) (119).

4. *Textile fibres*

Astbury always remained much more than a crystal analyst. True he wanted to use the whole of X-ray crystallographic technique to solve his structures, but he was interested in their physical properties to an almost equal extent and this was perhaps spurred on also by his profound technical interest in fibres. He was not a Reader in Textile Physics for nothing. In his remarkable little book *Fundamentals of fibre structure* (128), originally given as lectures to textile students and operatives, Astbury had shown over and over again the clear analogies between the spinning operations which were performed on large fibres and the intricate binding of molecular fibres together. One of his most striking analogies in the book was to describe a globe about 10 inches across, made of silk, and to point out that if it were magnified to the size of the earth, the silk molecules would appear as ropes some 10 feet long and 1 inch thick. Further analogies between molecular twisting and textile twisting were striking and complete and so, as Astbury was to show later with the electron microscope, were the weaving which was shown so beautifully in his structure of *Valonia ventricosa* cell wall and earthworm cuticle.

Astbury had a clear view from the start of the analogy between his biological studies and his technical studies. As he said in his Harvey Lecture (93):

'Nature herself has built up a textile business that far transcends any man-made effort, and really the only thing new that has come out of modern textile science, itself one of the triumphs of the century, is the discovery of how very old it all is. Fibres, visible and invisible, are the principal structural components of all biological tissues, and the fibre concept is as old as life.

'That well-worn figure of speech, "the fabric of life", has thus taken on a substance in fact. It now means literally what it says, and goes moreover right down to the molecular level. Just as textile yarns are constructed from more or less parallel fibres, so the fibres themselves are constructed from

chain-molecules: they are "molecular yarns". The science of fibres is therefore essentially the science of chain-molecules, and molecular biology for the present is mainly the study of the tremendous thing living nature has made of it.'

This is in many ways the key to Astbury's mentality throughout the whole of his career. He recognized from his multiple experiments that nature worked only with a small number of patterns using them over and over again with adaptations to fit various needs. He goes on to say:

'I have come to feel that my adventures, lucky as they seem and as I grant they have been, do indeed represent a method of approach that can hardly be improved upon. . . . All I have had to do has been to trace out and systematize the development and inevitable broadening of my own interests as the panorama unrolled itself to my innocent gaze. The line I propose to adopt thus starts from structure, goes on to properties, then seeks out the underlying plan, and lastly tries to delve down into the origin of things.'

From the moment that Astbury started studying the wool fibres he kept the industry fully informed of what he was doing and not only the wool industry or the allied textile industries but he even used his work on the super-contracting and setting of protein chains to explain the properties of the permanent set of human hair with the example of α—β transformation which, if kept on one side of the hair will produce a curl, and on both sides alternatively a wave. He also saw to it that the ideas should be used as fully as possible. Expressed in a little jingle of A. L. Patterson's:

'Amino acids in chains
Are the cause, so the X-ray explains,
Of the stretching of wool
And its strength when you pull,
And show why it shrinks when it rains.'

Astbury even illustrated his point by putting a permanent wave into a cow's horn. But here he was not as original as he thought he was, for Pliny recalls the use by cattle thieves of this method to change the shape of cow's horns so that even their owners could not recognize them.

When it became possible to make synthetic polypeptides, it was soon found that the types of fibres produced under various conditions follow exactly the patterns which Astbury had first found in wool and in the k–m–e–f series. More, however, than any direct effect of his theories was the effect of the propaganda for introducing X-ray methods as an obligatory part of any textile developments and even more in artificial than in natural textile fibres. Wherever new polypeptides or other polymers are introduced into industry, the methods of Astbury are used and in fact it would be impossible to develop the full possibilities of such structures as nylon without using them. The idea of elastic nylon, for instance, is based on Astbury's contractile hypotheses. It is here that Astbury's propaganda work is most clearly seen. He hammered and hammered at the textile industry and the

artificial-fibre industry until he had got them fully indoctrinated with the idea of the value of X-ray photographs and their interpretation.

And Astbury did not limit his work to exhortation. He took an active part on councils of the textile industry and was a leading scientific member of the Wool Working Party after the war. There, according to another member of the Party, he showed a complete grasp not only of the technical problems but also of the managerial problems of the industry. One result of this work was that he persuaded the industry, one of the oldest and least scientific-minded of all, to adopt a policy of support for research on wool and related subjects in the University and technical college which was a model to all other industries. What he had felt about it is shown in his remark about the state of research finance in the inter-war period (p. 7).

5. *Cell wall structure*

The remainder of Astbury's work to be discussed here is his more purely biological contribution, which is connected neither with wool nor with the textile industry. Astbury had always as a central aim the exploration of biology. He himself quotes in his Harvey Lecture one of his predecessors, Hooke, who in his *Micrographia* wrote:

'So that knowing what is the form of Inanimate or Mineral bodies, we shall be the better able to proceed in our next Enquiry after the forms of Vegetative bodies; and last of all, of Animate ones, that seeming to be the highest step of natural knowledge that the mind of man is capable of.'

One slightly minor field of his researches in this respect concerns the laying down of cellulose fibres in the vegetable cell wall.

As he worked at Leeds and not at Manchester, he was more interested in wool than in cotton. But he did make one very interesting and successful invasion of the field of plant cell structure, choosing a most remarkable organism, the cell of the sea-grape, *Valonia ventricosa* and the related simple alga, *Cladophora*. These are remarkable as some of the largest single cells in the biological kingdom, often as much as an inch in diameter, and their skin or cell wall can therefore be treated as if it were a piece of paper. Astbury (48) found it showed a very beautiful precise crossed pattern of cellulose fibre structure and he had the curiosity to trace this all over the cell showing that the angle between the cross patterns varied. The publication with Preston of the structure of the cell wall of *Valonia* (32) was a classic which lies between Naegli's first efforts to solve this problem by means of very fine optical microscopy in 1844 and the later precise studies by the electron microscope, which did not exist when Astbury started his work. He showed the fibres were arranged in a complex set of double or sometimes treble spirals around two poles at the end of the cell. I was able to add a confirmation in the form of optical polarization studies. Astbury surmised that the laying down of the cell wall was really a highly ordered process and must have some kind of biological, probably protein, lead-in and directing mechanism. One other excursion of Astbury's work in the field of algae

was his X-ray study of alginic acid, a soluble fibre produced from seaweed (63).

What Astbury had achieved in his first ten years' work at Leeds is best summed up in his own words in the Spiers Memorial Lecture in 1937 (37):

'There was first the adventure of the fibre, made from straight polypeptide chains, then that of the fibre made from regularly folded chains; and after that came the globular proteins with their multiple folds. Then came the unfolding of the globular proteins by denaturation and the recovery once more of straight polypeptide chains. Now we would like to fold these chains up again or at least find out how they were folded before we undid them. For the moment, though, we can only unwrap a mysterious protein parcel in the most untidy manner—so untidy that we still cannot see what is inside before it comes undone. But one thing we may be sure of, is that it is something that holds the secret of our health and happiness—our very life itself.'

6. *Nucleic acids*

Perhaps Astbury's greatest contribution to molecular biology were the first steps he took in unravelling the structure of nucleic acids. This was no accident. Astbury was convinced of its importance as was shown in a quotation from his Harvey Lecture (p. 38):

'The proteins lie at the corner of the business, we may be sure of that, and the attack on them must go on unceasingly; but they are not, or have not come to be, entirely self-acting, and it is little less urgent—it is a parallel problem—to concentrate also on their collaborative macromolecules, notably the polysaccharides and nucleic acids, especially the nucleic acids. Many investigations in recent years have brought out and emphasized the importance of the nucleic acids in biosynthesis; as far as we can see, they are absolutely essential components in chromosomal processes and cell multiplication and in virus reproduction, and in fact it is largely believed now that the nature of the interaction of the proteins and nucleic acids is probably the supreme issue of all in the chemistry and physics of life.'

When it is remembered that this was written in 1950, when the concept of the helical structure to which Astbury himself contributed was still not understood, it will be seen with what general grasp and percipience on the biological field Astbury worked all through the latter years of his life.

By 1938 Astbury had come to be regarded as a person to whom one would refer for any kind of fibrous substance and he tackled the newly purified nucleic acid which had been prepared in viscous solution by Hammarsten and Caspersson (1938), as he tackled the other fibrous structures (38). But he noticed at once that there was a fundamental difference in their optical properties. True to the old crystallography, he noted the strongly negative birefringence of the nucleic acid fibres and knowing that their composition included the flat purine and pyrimidine bases, he concluded that these must lie at right angles to the fibre length, with the spacing 3·4Å which occurs over and over again in aromatic substances, notably in the simplest of all of

them, graphite. Here Astbury made a happy use of his analogy with distances. In the first case this was quite correct but he also noticed a number very nearly that of the period 3·2Å of β-type protein structures and knowing there was a close relation between proteins and nucleic acids and, in fact, some basic proteins form apparently homogeneous compounds with nucleic acids, to wit, nucleo-proteins, he assumed that the two chains of the nucleic acid and the protein were parallel. They are not, as we now know thanks to Furberg (1950) and Wilkins (1951), but at right angles.

Astbury was from the very beginning, in his study of tartaric acid, inclined to judge that two distances that were the same must have some common origin. They did in some cases, they did not in others. It was, for instance, this numerical coincidence that led him for so long to defend the concept of fold in the α structures.

Astbury's very pioneering spirit was in the end to be an actual disadvantage to him. He found solutions long before anyone else had, but he stuck to them long after other people had abandoned them. That he himself was not to find out the precise details of the double spiral of *DNA* was not surprising (see below); but he certainly must have the credit for indicating that the nucleic acids were a fruitful subject for X-ray analysis.

7. *Other biological and medical studies*

It would be difficult without reducing this study of Astbury's work to a catalogue to note all the contributions he made to the different parts of biology. One is outstanding and was of greater interest to him as well, the study of flagella from the bacteria, plant cells and protozoa. In the first place, relying on the work of Gard (1944), and Weibull who made the preparations, he was then to examine the extremely minute flagella on bacteria (86), studies which in Astbury's own words:

'have accorded us more molecular biological joy, I should say, than anything else I can remember since the first great days with the α—β transformation.'

The process of parallel aggregation enabled him to take photographs of flagella which showed that each flagellum is effectively a single macromolecule about 120Å thick. He regarded them as monomolecular hairs or muscle. He showed they belonged to the k–m–e–f group but, rather curiously, combining α and cross-β characters. In that respect they resemble actomyosin. Astbury, however, found that the protozoal and protophy flagella were of a different character from those of bacteria (107), recognizing that the form was multiple and in fact that this needed an electron microscope to elucidate. They had a characteristic arrangement of nine fibrilla in a ring and two at the centre, but he was unable to make much more out of them; actually, this structure although universal is still a mystery.

In the medical field, Astbury was really able only to start new methods of research. He worked on various aspects of rheumatism which involved studies of decomposed collagen (94), and on various cancers particularly breast cancer of mouse, then known to be virus induced (89) (91).

The programme he laid down in 1950 (93) has been followed more effectively since. It consists of '(*a*) classical histology, (*b*) X-ray diffraction analysis, (*c*) electron microscopy and (*d*) microbiochemistry; in relation to the whole clinical observations besides'. Apart from the use of tracers, of micro-autoradiography and of magnetic resonance methods, which were only introduced later, this is now the new line of what might be called biochemical or functional cytology.

8. *Experimental techniques*

Astbury was primarily an experimentalist working in the field of most unpromising material indirectly derived from animal tissue or produced by rather messy biochemical reactions of the day; he had virtually to devise all his own methods. Although trained on the ionization spectrometer, he soon turned to photographic methods and developed a number of extremely simple fibre cameras for both simple examination and that under various conditions of tension and pressure, which gave him the photographs (plate 1) from which he was able to make such extensive deductions. In the process he had to face the problem of how to get clear and sharp photographs in a reasonable time, so that he produced an original type of rotating anode tube on a Torricellian vacuum, an idea far too simple to get wide application. He had also, in the early days, used radioactive methods for measuring intensities.

In his work on fibres and later on various biological preparations, Astbury showed his genius by the understanding of material and arranging it so as to give the best information for X-rays. Used by him, these methods led to the remarkable results already discussed and they were adapted by other workers and are really the basis for most molecular biology outside the crystalline phases today. But his great success was to see in his photographs (129), good or bad as they were, more than anyone else could see in them and he is undoubtedly the father of all those who since then interpreted other types of fibrous structure, particularly the nucleic acids, and who can recognize types of twist from the pattern of blurs on rather obscure fields.

9. *The effect of Astbury's work on the general progress of biomolecular studies*

The greatest achievement of mid-twentieth century science will undoubtedly be that of the unravelling of the central problems of molecular biology. Such decisive discoveries could not in any case have been the task of a single man or of a single discipline. It is an example of the convergence of a number of disciplines which have come from different sources to deal with what gradually appeared ever more clearly as the central problem, the production and the function of the protein molecules and especially their *reproduction* which was found to be the essential task of nucleic acids. All this was not seen in 1925, which we may take as the point of departure of Astbury's biological work. The knowledge of proteins was extremely primitive and wrapped up with practical considerations, nutritional as far as the

chemistry of proteins was concerned, mechanical as far as the properties of the protein fibres. Another aspect of fibres was the opening of the era of artificial fibres which inevitably led to procedures which threw light on the natural fibres as well. It was not even certain until the late thirties that enzymes, which had been studied as such for their chemical properties and as the basis of modern biochemistry, were necessarily proteins, although they were largely accompanied by proteins.

The other line of approach, of purely biological character, was through genetic analysis and the realization, due to Muller, that the visible chromosomes in cell division were essentially the carriers of genetic information.

Astbury's function was often—and most of all in the earlier stages of this period—that of bringing these different lines of research together. He was able to profit from in the first place the new chemical approach to proteins of very much greater accuracy and rapidity than the methods available in 1925. At that time the analysis of a single protein might take as much as a year and even more, and only the gross proportions could be determined. The next stage which was needed came before any chemical analysis could become significant, the chemical preparation and purification. In order to study biochemical reactions quantitatively, it was necessary to have purified enzymes and in the early thirties, following the pioneer work of Sumner on urease in 1926 and largely thanks to Northrop & Kunitz (1948), it became possible to purify enzymes to such an extent that they could be crystallized. The activity of enzymes led to the possibility of assaying their concentration and thus much more readily to their purification than for other proteins.

The fibrous proteins which could not be crystallized or purified or be assayed for activity would obviously be the last. Nevertheless, it was the fibres which were to provide the clue to the whole of the protein analysis. In 1925, the original hypothesis of Fischer and Hofmeister that proteins were hetero-polypeptides, though in general accepted, was not universally so and many other ideas such as cyclic peptides and diketopiperozine aggregates were postulated as alternative structures, or as the structures of at least some proteins. It was the fibrous nature of proteins that led first to the general acceptance of the Fischer view and then to the understanding of their structure. As the early X-ray analysis of known fibres, such as cotton and silk, showed, it was clear that the polymer chain lay parallel to the fibre direction. Consequently, at least some of the fibrous proteins must be simply polypeptides of indefinite length.

Astbury's first great contribution was therefore to show that in their basic structures these polypeptides belonged to relatively few types, in fact only two in number, for he had shown that the natural fibrous proteins, the keratin of hair, the myosin of muscle, the elastic fibres of tissue and the rapidly created fibres of blood clotting, fibrin, had all essentially the same set of structures, for all the different fibre structures which he had called the β and cross-β were reproducible in every single one of these proteins. The other series, those of the inextensible fibres of collagen and fish elastoidin, equally

widespread, belong to another series. This enormously simplified the problem of protein structure and also showed that the intermediate or secondary structure of proteins, the interrelation of neighbouring amino-acid residues would be key to all kinds of protein structure. This result, as we have seen, was fully achieved by 1932.

The problem of the crystalline protein appeared at first to be radically different, though a very crystalline character showed in principle that they must be composed of identical molecules. For a long time the practical difficulty of proving this by X-rays held up advance until I achieved it in 1934 with the measurement of the cell size of pepsin, to be followed by my pupils Fankuchen, Perutz, Crowfoot and Carlisle for other crystalline proteins. Meanwhile, the same identity of molecules had been proved quite independently for crystalline proteins in solution by Svedberg (1926, 1940), who sorted them out by their mass, and by Tiselius who sorted them out by their electro-phoretic mobility. A crystalline or globular protein molecule was therefore a definite and quasi-identical unit.

But what could such a unit contain? This could be approached in two ways, chemical and X-ray, and it is interesting that the two ways, so to speak, overlapped: complete chemical analyses with the full order of amino-acids were known for some proteins and complete X-ray structures were known for others before detailed structures were known in both ways for any one protein. The chemical approach started, curiously enough, with the analysis of wool, for which normal methods were quite inadequate, and led to the rapid improvement in chemical methods based on a very old principle of paper chromatography by Martin & Synge (1941). This led first of all to a much more accurate gross analysis of amino-acids in proteins which enabled the actual number of each amino-acid to be counted from the knowledge of the molecular weight, and then through the almost incredibly laborious work of Sanger (1945) and his followers, to the actual order of the amino-acid residues. This gave us what is now called the primary structure of protein but this, naturally, was only available for the crystalline or globular proteins.

The second great contribution by Astbury was to show that there was no radical difference between the fibrous and the crystalline proteins. By a study of denaturation and, particularly, by the study of the oriented fibres which can be detected in denatured crystals, Astbury showed that the intimate structure of the fibrous and globular proteins must be the same. The work went further and it was possible to show that the actual transformation between the globular proteins and the fibrous proteins was a reversible one, as shown in insulin, actin and tropo-myosin. In a sense, this fact has been used long before it was understood, ever since the juices of the caterpillar's mouth glands or the spider's spinnerets had turned into silk, observations which were to have many practical applications in the production of artificial fibres.

There were still problems outside this main line to be found in the structure

of other kinds of fibres, such as supporting fibres of collagen, problems which Astbury opened up but did not terminate, and also in the fibres of muscle, where Astbury started off with the realization that he was dealing here with an α protein chain but was in no position to approach the extreme complexity of the molecular architecture which was not to be revealed until the development of the electron microscope.

By the time the second world war came, the next stage of the problem of crystalline protein structure was fairly clear. What was not clear yet was along which line of research would the solution first be found. The chemical method had not yet yielded, but was clearly bound to yield, the *primary* structure of a protein polypeptide. X-ray study of the globular proteins in a crystalline form showed an enormously rich mine of information but it was, apart from molecular size, uninterpretable; either a hypothesis of a structure had to be made or a new method of finding the phases of the X-ray diffraction had to be developed.

The former approach was the first to be tried and led to a long and ultimately fruitless search for a structure, although it contained in itself a fundamental truth. Astbury had already claimed that the double folding found in super-contracted α proteins consisted of folds which were repeated in layers and thus built up a protein molecule as a kind of bundle of sticks. This Perutz, Kendrew, Crowfoot and Carlisle all tried on different proteins, a very tedious work which was ultimately to prove completely wrong. I had then said that if the structure of protein were simple we should soon find it out; in fact, it was not, and took about twenty to twenty-five years to work out. It was Crick (1952) who first decided that the game was not worth the candle and showed that no arrangement of parallel rods of protein, whatever their structure, could possibly do it. Meanwhile, a much slower, surer but more roundabout approach was being developed by Pauling and his crystallographic collaborator, Corey (1952). Pauling was shocked by the freedom with which the X-ray crystallographers of the time, including particularly Astbury, played with the intimate chemical structure of their models. They seemed to think that if the atoms were arranged in the right order and about the right distance apart, that was all that mattered, that no further restrictions need be put on them. Pauling, inspired by his theory of resonance, realized that the freedom of rotation of single bonds could not possibly apply to polypeptides and that the amide group had to be effectively planar. That this was the case was confirmed by the very detailed and accurate analysis of the different amino-acid crystal structures by Corey (1953).

Meanwhile, others had not been satisfied with the peptide chain arrangements which Astbury proposed in the early and later folded α models. Huggins (1943) postulated that instead of a two-dimensional zigzag arrangement, the arrangement of polypeptides in the α proteins was helical. Later Bragg and Perutz (1950) worked out all the crystallographically possible helices compatible with 2-, 3-, 4- and 6-fold screw axes. None of these quite

fitted, although the 4-fold helix fitted the α structure best. It was at that point that Pauling's criticism again became valid. None of the helices preserved the planarity of the amide groups and the only way of preserving it and maintaining its continuous polypeptide thread was to break with the crystallographic rules and introduce an irrational helical arrangement. At the time, this was thought to be a very daring thing to do, although now it is very easy to see by mere logic that in fibre structure, which is lacking in three-dimensional order, that is, which does not show any cross or pyramidal planes, that no rationality should be expected. Nevertheless, it was a novel idea to crystallographers and its full implication took a long time to take in, though when they were they proved to be of enormous power and range. Accordingly, in 1951, when the Pauling helix explanation of the secondary structure of polypeptides was put forward, it was immediately accepted by most workers in the field, and ultimately by Astbury himself.

In a sense it was here also that Astbury helped in a negative way. It was largely as a criticism of Astbury's fold in both its forms that this work had been done. Nevertheless, the acceptance of the α helix left the problem of protein structure still only half solved. The protein analysts knew, or assumed, for it was by no means necessarily true for all proteins, that the peptide chains were arranged in α helices, but even when curled up in this way there was too long a rod to fit into the limited space of 20 to 30Å of actual crystalline protein molecule. It was now necessary to work out the tertiary structure, the way in which the α helical rods were bent and fitted together. Eventually, this is a problem of packing but one which has to be very precisely solved because one thing that is very clear is the quasi-identity of the same protein molecules, even in different crystalline forms.

It was at this point that Perutz, abandoning his previous efforts at *a priori* solutions, made the daring assumption that it would be possible to use the isomorphous replacement method, long familiar in ordinary crystal structure analyses, for protein crystals. The reason it was daring was because it implies that adding one atom of a heavy metal to several thousand atoms of protein will allow its presence to be detected. More than that, from that detection the phases of the structure could be determined and hence actual structure independent of any hypothesis. It happened that of all the proteins examined, those of the haemoglobin-myosin groups proved to be most suitable. And when this was first done in sperm whale myoglobin by Kendrew (1958), rods similar to those postulated by Pauling immediately appeared, leading after many more years of arduous work to a pretty complete tertiary structure of protein. This was done, incidentally, in advance of any knowledge of sequence of amino-acids. Subsequently the structure proposed was found to fit very well with that derived from the full chemical evidence. The basic postulate of Astbury here found its justification in principle if not in detail. The molecules of crystalline proteins are built of segments of α chains.

Before this, as we have seen, Astbury had turned his attention to nucleic acids. This was because of his realization of their biological importance.

Caspersson (1947) had shown the nucleic acids appeared in organisms exactly where protein was being very rapidly produced. Purification of nucleic acid led to the concept, by then familiar to polymer chemists, that viscous solution of nucleic acid must contain long fibrous elements. Astbury examined these elements and came to the conclusion that they consisted of the flat bases held at right angles to the axis, essentially the correct structure. He missed the actual structure of *DNA* for two reasons, first because the X-ray analytic procedure for helical structures was not developed—that was to be the indirect consequence of the study of the α helix for proteins mostly due to the work of Cochran, Crick & Vand (1952)—and secondly because the strategic double coil model of *DNA* could hardly have been guessed at in advance of the chemical equalities between the quantities of the purines and the pyrimidines established by Chargaff (1950). Nevertheless, we may count his work on nucleic acid as Astbury's fourth and greatest contribution to the analysis of biomolecular structures.

There is no need to go further here to study the ultimate achievements of this method of analysis. The complete picture of a protein structure with its primary, secondary, tertiary and higher structures were found in haemoglobin itself. Next came the entry and fusion of the genetic approach with that of the double spiral structure in the Crick-Watson hypothesis, where the properties of the virus-like bacteriophage could be used to find the actual code by which proteins can be made. Last have come the triumphs of tracer technique combined with the electron microscope which showed up the detailed mechanism of messenger and soluble nucleic acids in the synthesis of proteins, a kind of super automated mass production of virus. Now we can see in many of these that the earliest ideas came from Astbury and if he was not to see the end of the race, for the race has not ended yet, he certainly will have for ever the credit of having started it.

When the history of molecular biology comes to be written it will be seen that the work of Astbury from its beginnings in 1926 was, so to speak, the main line of progress of molecular biology. It started with his appreciation of the α fold, as he called it, the α helix as we call it now. All the way through he was guided by a profound sense of analogy, on the one hand with biological principles and on the other with textile techniques.

There is one more thing to be said before leaving an account of Astbury's influence on molecular biology and that is a negative one. With all his abilities and intuition, why did some of the principal discoveries in the field, nevertheless, elude him? Why he discovered so much, why he had so sure a sense of direction and why he did not discover more; why he adhered to peculiar attitudes and techniques which prevented him seeing what other people on the basis of his original work were able to see so easily? This applies particularly to the relation between the fold which he assumed to be the basis of the α-β transformation and the coil which was afterwards the principle of Pauling's helix. It is an interesting contradiction, for both men were basically of the same generation, they both had very similar training

as chemists, but Pauling had the advantage of having absorbed and largely created the new quantum chemistry and he had more sense of quantitative metrical properties, particularly stereo properties, than Astbury had.

Astbury, however, was more isolated and tended to go on what might be called an ortho-dromic course of research; not that he stuck to one thing, his enormously wide interests in biological structures ranged all the way from the vegetable to the animal cell. Very peculiar animal structures, such as the structure of the insect egg cases and egg stalks. These he interpreted continuously as he went along but always in terms of his previously formed theories (116).

We are apt to neglect the importance of Astbury because so much of what he discovered has now become the commonplace of molecular biology. But it became so not only because he discovered it but because he propagated it so thoroughly. It was part of his personality to be so excited and delighted with the things he was finding out, to want to tell everyone about them and to publish them in all kinds of journals in all countries. To appreciate the work of Astbury is for that reason very difficult. At first sight it appears that he has published the same paper over and over again, but this is not so: you only have to look at the papers to find the trace of a new idea appearing in a paper apparently identical with another and being developed later into other ideas. Many of these ideas were not recognized at the time but only appreciated later, such as the idea of the *g–f* transformation.

10. *An appreciation*

Astbury was the recipient of many honours. He was elected a Fellow of the Royal Society in 1940, gave the Croonian Lecture in 1945 and was on the Council 1946-1947. He was elected Honorary Life Member of the New York Academy of Sciences in 1950, Corresponding Member of the Istituto Lombardo di Scienze in 1951, Foreign Member of the Swedish Royal Academy of Sciences in 1956, and Honorary Founder-Member of the British Biophysical Society in 1961. In addition to being a Sc.D.(Cantab.), he was made Doctor *Honoris Causa* of the University of Strasbourg in 1946. He served on the Food Investigation and Forest Products Research Boards between 1946 and 1955. He gave many lectures to scientific and technical societies, including the Harvey, Procter, Mather, Spiers and Sylvanus Thompson Memorial Lectures.

Fully to appreciate the whole work of Astbury is difficult because we are so apt to look at things in the light of present knowledge and not sufficiently in the light of knowledge when Astbury actually undertook the work. There can be no doubt that the work itself, the whole study of the marvellous mechanisms of protein synthesis and use owe enormously to the pioneer work of Bill Astbury. His failures as well as his successes were characteristic of the man.

Part of his difficulties stemmed from his innate or traditional extreme independence. He really belonged to the great sealing-wax and string tradition. I competed with him in an application for a post in Cambridge in

1927 and when he was asked in the interview by two eminent scientists of the time what his view was on collaboration, he answered very rudely: 'I am not prepared to be anybody's lackey'—and he never was. In that sense Leeds gave him an ideal job. No one told him what to do, no one *could* tell him what to do. And, conversely, he did no empire building. He was in his own way too proud to seek for influence or many colleagues. Nevertheless, he was an extremely social and co-operative person but it was a free co-operation and he did not fit into any organization. Consequently his highly original and personal research ideas never secured the support they deserved. A year after his death, however, the Astbury Department of Biophysics was established at Leeds University, where his work will be continued.

Perhaps the man who had the greatest influence on Astbury at the outset of his career at Leeds was Dr Speakman, an imaginative textile chemist who was initially responsible for interesting Astbury in the physical properties of materials which was to be one of the major channels of discovery of the nature of the polypeptide fold. It seems to have been an ideal collaboration. Of his other collaborators, MacArthur was longest associated with him but MacArthur had a temperament very different from Astbury, critical where Astbury was intuitive, refusing to be led along the paths which Astbury's genius often indicated or into the traps into which he so often fell. He got on better with the biological colleagues, with Rudall, Preston and Bailey. Some of his most interesting work was done with the physiologist Dr Sylvia Dickinson, also with a character very complementary to his, extremely self-critical. The traits in his character that were to be most harmful to him were his lively scientific imagination and his rashness and lack of self-criticism.

Rutherford's dictum for success in science was 'Never attempt a difficult problem'. It is unfortunately an attribute of genius to see which of the problems are not really difficult; but although this is a necessary, it is clearly not a sufficient condition. There are plenty of easy problems, the question is to find out which of the easy problems is likely to be vitally important. This is the kind of sense that Astbury had pre-eminently. His introduction to fibre structure may well appear fortuitous but from the moment he started taking photographs for Sir William Bragg in 1926, he saw that he was on to something big and important and he never let go of it.

It may be argued that he started to study these substances prematurely: not enough was known in the first place about proteins in any form, chemical or physical, at the time he started the work and tools did not exist, neither the optical tools in the form of the electron microscope and the infra-red spectroscope, nor the chemical tools in the form of tracers and chromatographic analysis. If Astbury could have waited to start for another twenty years he would no doubt have been able to make use of these tools, but he was born too early and did not know he had to wait. Astbury worked on intuitions, but, however remarkable his intuitions, he had always a scaffolding of theory which unfortunately he did not alter often enough to fit the

facts. But apart from the accuracy or inaccuracy of his schemes, the basic notions which he propagated were to be the foundation of our knowledge of proteins and nucleic acids.

It is ideally possible to construct a rational strategy for any scientific discovery, even for such a complicated investigation as protein structure. Its actual history is full of strategic mistakes, but we can only see these by means of hind-sight. We should, no doubt, be able to plan our researches with this rational strategy, that is, not to advance from one position to another until the time is ripe and the tools have been properly accumulated. Yet few even of the greatest of scientists achieve this. Most lie on a kind of spectrum of scientific approach—often more a measure of the scientist's temperament than of his problems—whether to dash at a problem the moment it presents itself and try to take it by assault or whether to sit down in front of it and to prepare elaborate trenches and investments and take it by a slow siege, advancing securely from position to position. There is no doubt at all that Astbury belonged to the first type: not that he was unwilling to take pains—he took all kinds of pains on the experimental side—but he absolutely refused to step back from his immediate subject to tackle quite simple structures in order to understand much more complicated ones. The people who are willing to do this and carry out siege warfare also make strategic mistakes. If they had the essential quality of tenacity and endless patience they are likely, if they live long enough, to get there. But they also might be advised to wait their time.

Certainly, until the Stockholm meeting in 1951, when the fructifying ideas of Pauling on the α-helix mixed with the analyses which Perutz was carrying out on haemoglobin crystals, all the other work on protein structure was largely wasted—and would have to be—because until much later still, about 1956, in the absence of computers, the tasks which would really be necessary, indeed essential, to the unravelling of protein down to atomic dimensions, just could not be carried out. It was, so to speak, like undertaking a siege with siege guns without sufficient range or accuracy.

Nevertheless, the risks run by being too early are by no means as bad as those run by being too late. Science is full of examples of problems which could have been attempted with success at least thirty years before they were but no one dared to do so. There is a kind of Aristotelian mean about scientific research; if you do it with too much dash you are likely to be wrong and you are also likely to come across obstacles which you are not yet prepared to overcome. If you proceed methodically you may succeed, but do so at such expense of time and labour that you are limited in what you do. By sticking patiently to one approach you cannot get on with another, and the range of the work of a scientist may be more limited by patience and taking pains than by jumping in with inadequate means. We badly need a critical history of science which points out these things, and this would not just be an academic exercise because it would lead to a theory of scientific strategy which might be really useful.

Astbury's character carried what would often be considered the incompatible aspects of being very English and being very un-English. His bluff and simple style he took straight from his native Potteries. He had an easy access to people, whether drinking, playing chess or ping-pong or in listening to or playing classical music. Many scientists use their social gifts to conceal their interests in science, which is not supposed to be a very gentlemanly thing to show. Astbury would have none of this. He considered science, and particularly the science he was doing or was interested in, was really important, exciting and amusing and he never failed to bring this out. But he was anything but a bore. We shall probably never know the extent of his influence on the people who were inspired by his many lectures to take up scientific subjects, particularly in fields which previously had seemed very dry and technical.

Astbury was, especially at the very beginning of his work, somewhat isolated from the scientific world. Nevertheless he conspicuously avoided the fate that occurs to so many brilliant people when they are in this position of becoming embittered and sterilized. By his enthusiasm and by the way in which he communicated it to his co-workers, the Leeds School maintained a continuous production of exciting and interesting papers. As one of his colleagues wrote of him:

'He had the capacity to hold together a comparatively small team for so long with very little material inducement. To us "the lab." was an organic whole; Astbury was, of course, our inspiration and we were content to let him be our mouthpiece, but every paper which was published, no matter whose name was on it, was felt to be in a large degree a corporate achievement.'

It is true that to some of his colleagues his bluff approach was irritating and his successes caused envy. They even went so far as to call him 'a card'—which is not too far from the truth.

Nevertheless Astbury was loved by most of those who knew him and there were thousands who did, all over the country, because he gave freely of himself in all kinds of meetings and participated actively in the life of scientific societies. He radiated a kind of confidence, not so much a confidence in the actual results but confidence in what he called 'the adventure of science' in which he never, in spite of his last illness, lost the excitement and interest. He was genuinely equally interested in the success of others, a much rarer feature in the scientific world. Each new discovery made by the Cambridge or the London or the American school gave rise to expressions of frank delight.

His monument will be found in the whole of molecular biology, a subject which he named and effectively founded. But to those who knew him and had the good fortune to work with him he will always be remembered as Bill Astbury, someone who made you glad to be alive.

I cannot do better than close with the lines of Shakespeare which Astbury himself quoted to open the Ninth Procter Memorial Lecture and which

express, with rare percipience, what he himself conceived was his function in science:

> 'The which observ'd, a man may prophesy,
> With a near aim, of the main chance of things
> As yet not come to life, which in their seeds
> And weak beginnings lie intreasured.'
>
> *King Henry IV*, Pt. 2, III, i.

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BIBLIOGRAPHY

Papers

(1) 1923. The crystalline structure and properties of tartaric acid. *Proc. Roy. Soc.* A, **102**, 506.
(2) 1923. The crystalline structure of anhydrous racemic acid. *Proc. Roy. Soc.* A, **104**, 219.
(3) 1924. (With K. YARDLEY.) Tabulated data for the examination of the 230 space-groups by homogeneous X-rays. *Phil. Trans.* A, **224**, 221.
(4) 1926. (With G. T. MORGAN.) Crystal structure and chemical constitution of basic beryllium acetate and its homologues. *Proc. Roy. Soc.* A, **112**, 441.
(5) 1926. The structure and isotrimorphism of the tervalent metallic acetylacetones. *Proc. Roy. Soc.* A, **112**, 448.
(6) 1927. A simple radioactive method for the photographic measurement of the integrated intensity of X-ray spectra. *Proc. Roy. Soc.* A, **115**, 640.
(7) 1928. Photography and photometry in X-ray crystal analysis. *Phot. J.* **68**, 500.
(8) 1930. (With H. J. WOODS.) The X-ray interpretation of the structure and elastic properties of hair keratin. *Nature, Lond.* **126**, 913.
(9) 1931. (With H. J. WOODS.) The molecular weight of proteins. *Nature, Lond.* **127**, 663.
(10) 1931. The structure of fibres. *Ann. Rep. Chem. Soc.* **28**, 322.
(11) 1931. (With A. STREET.) The X-ray studies of the structure of hair, wool, and related fibres. I.—General. *Phil. Trans.* A, **230**, 75.
(12) 1932. (With H. J. WOODS.) The molecular structure of textile fibres. *J. Text. Inst.* **23**, T17.
(13) 1932. (With T. C. MARWICK and J. D. BERNAL.) X-ray analysis of the structure of the wall of *Valonia ventricosa*—I. *Proc. Roy. Soc.* B, **109**, 443.
(14) 1932. The X-ray diffraction photographs of vegetable and animal fibre. *Phot. J.* **72**, 318.
(15) 1932. (With T. C. MARWICK.) X-ray interpretation of the molecular structure of feather keratin. *Nature, Lond.* **130**, 309.

(16) 1933. Some problems in the X-ray analysis of the structure of animal hairs and other protein fibres. The structure of the keratins. *Trans. Faraday Soc.* **29**, 193.
(16a) 1933. X-ray analysis of fibres. *Nature, Lond.* **132**, 193.
(17) 1933. The X-ray interpretation of fibre structure. *J. Soc. Dyers and Colourists*, **49**, 169; *Sci. Progr.* No. 110, 210.
(18) 1933. (With W. R. Atkin.) X-ray interpretation of the molecular structure of gelatin. *Nature, Lond.* **132**, 348.
(19) 1933. (With H. J. Woods.) X-ray studies of the structure of hair, wool and related fibres. II.—The molecular structure and elastic properties of hair keratin. *Phil. Trans.* A, **232**, 333.
(19a) 1934. Aspects of growth. *Cold Spring Harbor Symp.* **2**, 15.
(20) 1934. The constitution of animal hairs. I.—X-ray interpretation. *J. Soc. Dyers and Colourists, Jubilee Issue*, p. 24.
(21) 1934. (With R. D. Preston.) A mercury-sealed water-cooled rotating X-ray target. *Nature, Lond.* **133**, 460.
(21a) 1934. The molecular structure of wool and hairs of animal origin studied by means of X-ray diffraction diagrams. *Chim. et Ind.* Spec. Number April, p. 186.
(21b) 1934. Röntgenoskopie von Proteinfasern. *Koll.-Zeitschrift.* **69**, 340.
(21c) 1934. (With R. Lomax.) X-ray photographs of crystalline pepsin. *Nature, Lond.* **133**, 795.
(22) 1935. (With S. Dickinson.) α-β intramolecular transformation of myosin. *Nature, Lond.* **135**, 95.
(23) 1935. (With S. Dickinson.) α-β transformation of muscle protein *in situ*. *Nature, Lond.* **135**, 765.
(23a) 1935. (With R. D. Preston and A. G. Norman.) X-ray examination of the effect of removing non-cellulosic constituents from vegetable fibres. *Nature, Lond.* **136**, 391.
(24) 1935. (With S. Dickinson and K. Bailey.) X-ray interpretation of denaturation and the structure of seed globulins. *Biochem. J.* **29**, 2351.
(25) 1935. (With W. A. Sisson.) X-ray studies of the structure of hair, wool and related fibres. III.—The configuration of the keratin molecule and its orientation in the biological cell. *Proc. Roy. Soc.* A, **150**, 533.
(26) 1935. (With R. Lomax.) An X-ray study of the hydration and denaturation of proteins. *J. Chem. Soc.* p. 846.
(26a) 1936. Recent advances in the X-ray study of protein fibres. *J. Text. Inst.* **27**, 282.
(27) 1936. The X-ray interpretation of protein structure. *Chem. Weekblad*, **33**, 778.
(27a) 1936. X-ray interpretation of protein structure. *J. Soc. Dyers and Colourists*, **52**, 306.
(28) 1936. X-ray studies of protein structure. *Nature, Lond.* **137**, 803.
(29) 1936. (With S. Dickinson.) X-ray study of myosin. *Nature, Lond.* **137**, 909.
(30) 1937. (With D. M. Wrinch.) Intramolecular folding of proteins by keto-enol interchange. *Nature, Lond.* **139**, 798.
(30a) 1937. The keratin fibres. *Chem. and Ind.* **15**, 1076.
(31) 1937. Relation between 'fibrous' and 'globular' proteins. *Nature, Lond.* **140**, 968.
(32) 1937. (With R. D. Preston.) The structure of the wall of the green alga *Valonia ventricosa*. *Proc. Roy. Soc.* B, **122**, 76.
(33) 1938. (With F. O. Bell, E. Gorter and J. Van Ormondt.) Optical and X-ray examination and direct measurement of built-up protein films. *Nature, Lond.* **142**, 33.
(34) 1938. Protein structure from the viewpoint of X-ray analysis. *C.R. Trav. Lab. Carlsberg, Ser. Chim.* **22**, 45.
(35) 1938. Röntgenstrahlen-Abentenuer unter den Eiweisskörpern. *Koll.-Zeitschrift.* **83**, 130.
(36) 1938. (With F. O. Bell.) Some recent developments in the X-ray study of proteins and related structures. *Cold Spring Harbor Symp.* **6**, 109.

(37) 1938. X-ray adventures among the proteins (4th Spiers Memorial Lecture, 1937). *Trans. Faraday Soc.* **34**, 377.
(37a) 1938. An X-ray study of the dyeing of wool. *J. Soc. Dyers and Colourists*, **54**, 6.
(38) 1938. (With F. O. Bell.) X-ray study of thymonucleic acid. *Nature, Lond.* **141**, 747.
(39) 1939. Crystallography—proteins. *Ann. Reps Chem. Soc.* **35**, 198.
(40) 1939. Evidence from the X-ray study of fibrous proteins. *Proc. Roy. Soc.* A, **170**, 69.
(41) 1939. The molecular structure of the fibres of the collagen group. (1st Procter Memorial Lecture.) *J. Internat. Soc. Leather Trades' Chemists*, **24**, 69.
(42) 1939. (With F. O. Bell.) Structure of proteins. *Nature, Lond.* **143**, 280.
(43) 1939. (With F. O. Bell.) X-ray data on the structure of natural fibres and other bodies of high molecular weight. *Tabul. Biol., Hague*, **17**, 90.
(43a) 1939. X-ray studies of the structure of compounds of biological interest. *Ann. Rev. Biochem.* **8**, 113.
(44) 1939. X-ray study of proteins and related structures. *Sci. Progr*, No. 133, 1.
(45) 1940. (With R. G. Harrison and K. M. Rudall.) An attempt at an X-ray analysis of embryonic processes. *J. Exp. Zool.* **85**, 339.
(46) 1940. The hydrogen bond in protein structure. *Trans. Faraday Soc.* **36**, 871.
(47) 1940. (With F. O. Bell.) Molecular structure of the collagen fibres. *Nature, Lond.* **145**, 421.
(47a) 1940. Proteins under the X-rays. *Chem. and Ind.* **18**, 129.
(48) 1940. (With R. D. Preston.) The structure of the cell wall in some species of the filamentous green alga *Cladophora*. *Proc. Roy. Soc.* B, **129**, 54.
(49) 1940. (With F. O. Bell and C. S. Hanes.) X-ray comparison of natural and synthetic starch. *Nature, Lond.* **146**, 558.
(50) 1940. (With S. Dickinson.) X-ray studies of molecular structure of myosin. *Proc. Roy. Soc.* B, **129**, 307.
(51) 1941. (With F. O. Bell.) Nature of the intramolecular fold in α-keratin and α-myosin. *Nature, Lond.* **147**, 696.
(51a) 1941. Proteins. *J. Soc. Dyers and Colourists*, **57**, 336.
(52) 1941. Proteins (Jubilee Memorial Lecture). *Chem. and Ind.* **60**, 41, 491.
(52a) 1941. Röntgenologische Untersuchung von Proteinen. *Die Methoden der Fermentforschung*, **1**, Leipzig.
(53) 1942. Sir William Bragg. (Obituary.) *Nature, Lond.* **149**, 347.
(54) 1942. Textile fibres under the X-rays. *Endeavour*, **1**, No. 2, 70.
(55) 1942. X-rays and the stoicheiometry of the proteins, with special reference to the structure of the keratin-myosin group. *J. Chem. Soc.* p. 337.
(56) 1943. (With K. Bailey and K. M. Rudall.) Fibrinogen and fibrin as members of the keratin-myosin group. *Nature, Lond.* **151**, 716.
(57) 1943. X-rays and the stoichiometry of the proteins. *Advanc. Enzymol.* **3**, 63.
(58) 1944. (With M. M. Davies.) Structure of cellulose. *Nature, Lond.* **154**, 84.
(59) 1944. Types of man-made fibres. *Endeavour*, **3**, No. 11, 95.
(60) 1945. Artificial protein fibres: their conception and preparation. *Nature, Lond.* **155**, 501.
(61) 1945. The forms of biological molecules. *Essays on growth and form.* Oxford Univ. Press.
(62) 1945. (With I. Macarthur.) A simple moving-anode X-ray tube. *Nature, Lond.* **155**, 108.
(62a) 1945. The structural properties of the cell. *Biochem. J.* **39**, lvi.
(63) 1945. Structure of alginic acid. *Nature, Lond.* **155**, 667.
(64) 1945. The X-ray examination of plastics. *Chem. and Ind.* No. 15, 114.
(64a) 1945. X-ray interpretation of wool. *J. Roy. Soc. Arts*, **43**, 613.
(65) 1946. Fibres and fabrics, old and new. *Proc. Roy. Inst.* **33**, 140.
(66) 1946. Progress of X-ray analysis of organic and fibre structures. *Nature, Lond.* **157**, 121.
(67) 1946. (With C. J. Brown.) Structure of terylene. *Nature, Lond.* **158**, 871.
(68) 1946. X-ray studies of the structure of plastics. *J. Soc. Dyers and Colourists*, **62**, 3.

(69) 1946-1947. The science of fibres. *J. Bradford Text. Soc.* p. 3.
(70) 1947. (With L. C. SPARK.) An electron microscope and X-ray study of actin. II.—X-rays. *Biochem. Biophys. Acta*, **1**, 388.
(71) 1947. (With R. D. PASSEY, L. DMOCHOWSKI and R. REED.) Electron microscope studies of normal and malignant tissues of high- and low-breast-cancer strains of mice. *Nature, Lond.* **160**, 565.
(72) 1947. On the structure of biological fibres and the problem of muscle. (Croonian Lecture 1945.) *Proc. Roy. Soc.* B, **134**, 303.
(73) 1947. La structure et les propriétés elastique des protéides fibreux du groupe keratine-myosine fibrinogène. *J. Chimie Phys.* **44**, 3.
(74) 1947. Vetenskapen om fibrerna är vetenskapen om oss själva. *Text. och Konfektion*, **9**, 358.
(75) 1947. X-ray studies of nucleic acids. *Symp. Soc. Exp. Biol.* No. 1, 66.
(76) 1947. X-ray study of actin. *Nature, Lond.* **160**, 388.
(77) 1948. (With S. V. PERRY, R. REED and L. C. SPARK.) An electron microscope and X-ray study of the synaeresis of actomyosin. *Biochem. Biophys. Acta*, **2**, 674.
(78) 1948. Science in relation to the community. *School Sci. Rev.* No. 109, 268.
(79) 1948. (With C. E. DALGLEISH, S. E. DARMON and G. B. B. M. SUTHERLAND.) Studies of the structure of synthetic polypeptides. *Nature, Lond.* **162**, 596.
(80) 1948. (With R. D. PASSEY, L. DMOCHOWSKI, R. REED and P. JOHNSON.) Ultra-centrifugation and electron microscope studies of tissues of inbred strains of mice. *Nature, Lond.* **161**, 759.
(81) 1948. (With R. REED and L. C. SPARK.) An X-ray and electron microscope study of tropomyosin. *Biochem. J.* **43**, 282.
(82) 1949. Fibrous proteins. *Nature, Lond.* **164**, 33.
(83) 1949. Structures of α-keratin and synthetic polypeptides. *Nature, Lond.* **164**, 439.
(84) 1949. The structure of biological tissues as revealed by X-ray diffraction analysis and electron microscopy. (Silvanus Thompson Memorial Lecture, 1948.) *Br. J. Radiol.* **22**, 355.
(85) 1949. Structure of polyglycine. *Nature, Lond.* **163**, 722.
(86) 1949. (With C. WEIBULL.) X-ray diffraction study of the structure of bacterial flagella. *Nature, Lond.* **163**, 280.
(87) 1949. X-ray and electron microscope studies, and their cytological significance, of the recently-discovered muscle proteins, tropomyosin and actin. *Exper. Cell Res.* Suppl. 1, 235.
(88) 1950. Applications of the electron microscope. *Proc. Electron Microscopy Conf., Delft*, p. 27.
(89) 1950. Biophysical studies of extracts of tissues of high- and low-breast-cancer strains of mice. *Biochem. Biophys. Acta*, **4**, 391.
(90) 1950. A discussion on muscular contraction and relaxation: their physical and chemical basis. *Proc. Roy. Soc.* B, **137**, 58.
(91) 1950. (With R. D. PASSEY, L. DMOCHOWSKI, R. REED and P. JOHNSON.) Electron microscope studies of normal and malignant tissues of high- and low-breast-cancer strains of mice. *Nature, Lond.* **165**, 107.
(92) 1950. The molecular structure of skin, hair, and related tissues. *Br. J. Derm. and Syph.* **62**, 1.
(93) 1951. Adventures in molecular biology. (The Harvey Lecture, 1950.) *Harvey Soc. Series*, **46**.
(94) 1951. (With J. H. KELLGREN, J. BALL, R. REED and E. BEIGHTON.) Biophysical studies of rheumatoid connective tissue. *Nature, Lond.* **168**, 493.
(95) 1951. (With R. D. PASSEY, L. DMOCHOWSKI, R. REED and P. JOHNSON.) Electron microscope and high-speed centrifuge studies of the milk factor. *Acta Union Int. Contre le Cancer*, **7**, No. 2, 299.
(96) 1951. (With R. D. PASSEY, L. DMOCHOWSKI, R. REED and G. EAVES.) Electron microscope studies of human breast cancer. *Nature, Lond.* **167**, 643.

(97) 1951. Flagella. *Sci. American*, **184**, No. 1, 21.
(98) 1951. Hairs, muscles and bacterial flagella. *Nature, Lond.* **167**, 880.
(99) 1951. How the wool molecule works, and its further significance in biology and medicine. *Internat. Wool Secretariat*, p. 3.
(100) 1951. Some recent adventures among the proteins. *Publ. Staz. Zool. Napoli*, **23**, Suppl. 1.
(101) 1952. (With R. E. TUNBRIDGE, R. N. TATTERSALL, D. A. HALL and R. REED.) The fibrous structure of normal and abnormal human skin. *Clin. Sci.* **11**, 315.
(102) 1952. Hairs, muscles and bacterial flagella. *Proc. Roy. Inst.* **35**, 154.
(103) 1953. A discussion on the structure of proteins. Introduction. *Proc. Roy. Soc.* B, **141**, 1.
(104) 1953. (With L. HOYLE and R. REED.) Electron microscope studies of the structure of the influenza virus. *Nature, Lond.* **171**, 256.
(105) 1953. The great adventure of fibre structure. (The Mather Lecture, 1952.) *J. Text. Inst.* **44**, 81.
(106) 1953. (With J. W. HAGGITH.) Pre-transformation stretching of the so-called 5·1Å and 1·5Å spacings in α-keratin. *Biochem. Biophys. Acta*, **10**, 483.
(107) 1953. (With N. N. SAHA.) Structure of algal flagella. *Nature, Lond.* **171**, 280.
(108) 1954. (With R. D. PRESTON.) Structure of cell wall of *Valonia*. *Nature, Lond.* **173**, 203.
(109) 1955. Introductory review. *Istituto Lombardo (Rend. Sc.)*, **89**, 1.
(110) 1955. Concluding remarks. *Istituto Lombardo (Rend. Sc.)*, **89**, 330.
(111) 1955. Introductory review. *Symp. Soc. Exp. Biol.* No. 9, 1.
(112) 1955. X-rays and the stoichiometry of keratin: a renewed enquiry. *Proc. Int. Wool Text. Res. Conf.* B, p. 202.
(113) 1955. In praise of wool. *Proc. Int. Wool Text. Res. Conf.* B, p. 220.
(114) 1955. Textile fibres and molecular biology. *Ann. Text.* No. 3-9/55 *Molecular Biology*, 22.
(115) 1956. (With F. G. E. PAUTARD.) Extraneous X-ray diffraction patterns from algal flagella. *Nature, Lond.* **178**, 372.
(116) 1958. Configurations and interactions of macromolecules and liquid crystals. II.—Macromolecules. Introduction. *Faraday Soc. Disc.* No. 25, 80.
(117) 1958. Fundamentals of collagen. *Dent. Pract.* **8**, 261.
(118) 1958. Giant molecules. *Nature, Lond.* **181**, 94.
(119) 1958-1959. Fine-structural studies of the collagen-apatite partnership. *Lectures on Sci. Basis of Med.* **8**, 429.
(120) 1959. (With E. BEIGHTON and K. D. PARKER.) The cross-β configuration in super-contracted proteins. *Biochem. Biophys. Acta*, **35**, 17.
(121) 1960. The fundamentals of fibre research: A physicist's story. *J. Text. Inst.* **51**, 515.
(112) 1960. Indications on muscle contraction from X-ray diffraction studies of the fibrous proteins. *Proc. Seminar on Size and Shape Changes of Contractile Polymers*, p. 78
(123) 1960. Some fundamental molecular considerations of the fibrous proteins of the skin. *Ann. Ital. Derm.* **15**, 1.
(124) 1960. X-ray diffraction studies of protein structure. *New Scientist*, **8**, 93.
(125) 1961. Molecular biology or ultrastructural biology? *Nature, Lond.* **190**, 1124.
(126) 1961. (With E. BEIGHTON.) Structure of feather keratin. *Nature, Lond.* **191**, 171.
(127) 1961. The structure of the fibres of the collagen groups and related matters twenty-one years after. (9th Procter Memorial Lecture, 1960.) *J. Soc. Leather Trades' Chemists*, **45**, 186.

Books

(128) 1933. *Fundamentals of fibre structure*. London: Oxford Univ. Press.
(129) 1940. *Textile fibres under the X-rays*, Imperial Chemical Industries.

References

Bragg, W. H. 1926 *Nature, Lond.* **118**, 120.
Bragg, W. L., Kendrew, J. C. & Perutz, M. 1950 *Proc. Roy. Soc.* A, **203**, 322.
Caspersson, T. 1947 *Symp. Soc. Exptl. Biol.* **1**, 127.
Chargaff, E. 1950 *Experentia*, **6**, 201.
Cochran, W., Crick, F. H. C. & Vand, V. 1952 *Acta Cryst.* **5**, 581.
Corey, R. B. & Pauling, L. 1953 *Proc. Roy. Soc.* B, **141**, 10.
Crick, F. H. C. 1952 *Acta Cryst.* **5**, 381.
Franklin, R. E. & Gosling, R. G. 1953 *Nature, Lond.* **171**, 740.
Furberg, S. 1950 *Acta Chem. Scand.* **4**, 751.
Gard, S. 1944 *Arkiv für Kemi*, **19**, A, No. 21.
Herzog, R. O. & Jancke, W. 1921 *Naturwissenschaften*, **9**, 320.
Huggins, M. L. 1943 *Chem. Rev.* **32**, 195.
Kendrew, J. C., Bodo, G., Dintzis, H. M., Parrish, R. G. & Wyckoff, H. 1958 *Nature, Lond.* **181**, 662.
Martin, A. J. P. & Synge, R. L. M. 1941 *Biochem. J.* **35**, 294.
Neurath, H. 1940 *J. Phys. Chem.* **44**, 296.
Northrop, J. H., Kunitz, M. & Herriott, R. M. 1948 *Crystalline enzymes*, 2nd Ed., New York: Columbia University Press.
Pauling, L., Corey, R. & Branson, H. R. 1951 *Proc. Nat. Acad. Sci. Wash.* **37**, 205.
Ramachandran, N. & Karta, G. 1954 *Nature, Lond.* **174**, 269.
Ramachandran, N. & Karta, G. 1955 *Nature, Lond.* **176**, 593.
Ramachandran, N. & Karta, G. 1956 *Nature, Lond.* **177**, 710.
Rudall, K. M. 1946 *Soc. Dyers & Colourists Symp. on Fibrous Proteins*, p. 15.
Rudall, K. M. 1952 *Advance in Protein Chemistry*, **7**, 255.
Sanger, F. 1945 *Biochem. J.* **39**, 507.
Schmitt, F. O., Bear, R. S., Hall, C. E. & Jakus, M. A. 1947 *Ann. New York Acad. Sci.* **47**, 799.
Signer, R., Caspersson, T. & Hammarsten, E. 1938 *Nature, Lond.* **141**, 747.
Speakman, J. B. 1926 *J. Text. Inst.* **17**, T457.
Speakman, J. B. 1927 *J. Text. Inst.* **18**, T431.
Stern, F. & Beevers, C. A. 1950 *Acta Cryst.* **3**, 341.
Steward, F. C. & Mühlethaler, K. 1953 *Ann. Bot.* (N.S.) **17**, 295.
Svedberg, T. & Fåhraeus, R. 1926 *J. Amer. Chem. Soc.* **48**, 430.
Svedberg, T. & Pedersen, K. O. 1940 *The ultracentrifuge.* Oxford: Clarendon Press.
Watson, J. D. & Crick, F. H. C. 1953 *Nature, Lond.* **171**, 737.
Waugh, D. F. 1946 *J. Amer. Chem. Soc.* **68**, 247.
Wilkins, M. F. H., Gosling, R. G. & Seeds, W. E. 1951 *Nature, Lond.* **167**, 759.