History of Biophysics in Leeds

Biophysics in Leeds after Astbury and the Braggs

Reginald D Preston, having graduated from Leeds with a Physics degree, decided to apply his physics to the study of the organisation of plant cells with reference to problems associated with plant growth. For his PhD and later work, carried out in the Leeds Department of Botany in which he spent much of his career, he used optical microscopy on plant cell walls, mainly of the xylem of higher plants and of the alga Valonia ventricosa. The use of polarised light showed patches of birefringence in the cellulose wall of Valonia which suggested the presence of ordered arrays of 'single cellulose crystals'. Preston then examined these using the X-ray facilities in Astbury's laboratory. He subsequently obtained his own X-ray equipment and electron microscopes. He studied the structure and growth of cellulose and other polysaccharides in a wide range of plant systems, work that was summarised in his 1974 book "Physical Biology of Plant Cell Walls", from which the figures below are taken.

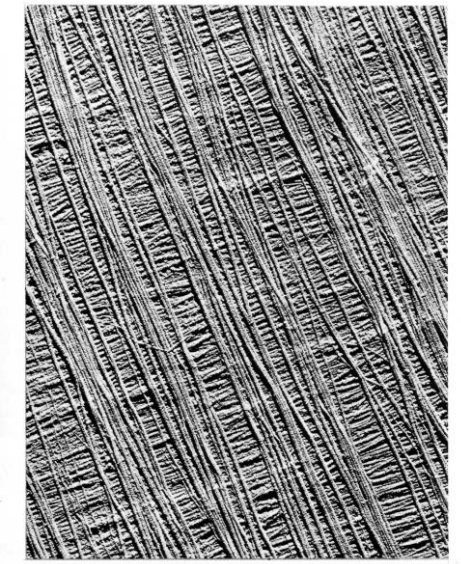

Figure 1: Electron micrograph of lamellae from the side wall of Ch. melagonium from outside the cell - the cell axis runs vertically.

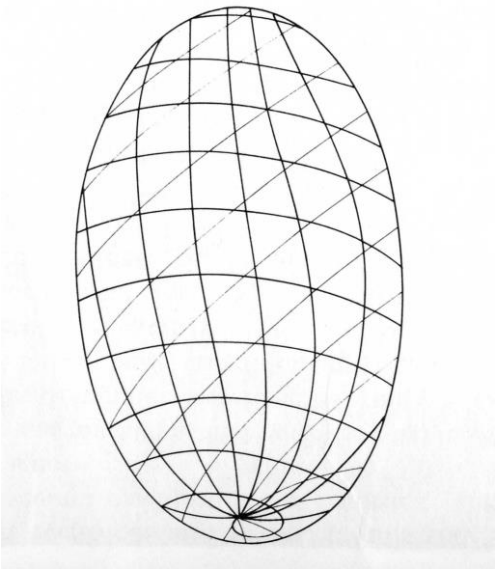

Figure 2: Schematic diagram of the run of the cellulose crystallites (i.e. the microfibrils) in a vesicle of the cellulosic alga Valonia

Electron microscopy revealed the sub-microscopic structures of plant cells and aspects of fibre rheology and development, leading to an understanding of cell wall biosynthesis and growth and showing that the primary cell wall was in fact a complex system produced under delicately balanced regulation. Preston was given a Personal Chair in Plant Biophysics in 1953 and was elected FRS the following year. While there had already been some discussions about merging the two Leeds Biophysics groups, Astbury's early death precipitated matters and in 1962 Preston was appointed Head of the newly-formed Astbury Department of Biophysics. In the next few years, he established undergraduate courses in Biophysics, always with a substantial 'backbone' of Physics.

Preston was succeeded as Head of the Department in 1973 by Anthony C T North, who had been appointed the previous year as Professor of Molecular Biophysics. North too had a first degree in Physics,

followed by a Ph D for X-ray fibre diffraction studies of the protein collagen, carried out at King's College, London. He subsequently spent 11 years in Sir Lawrence Bragg's group at the Royal Institution, first collaborating with Max Perutz in determining the 3-dimensional structure of haemoglobin and then, with David Phillips and others, solving the 3-dimensional structure and mechanism of action of hen egg-white lysozyme, the third protein and first enzyme to be solved at atomic resolution. North's particular role had been in developing the computer software required for automated data collection and analysis, the lysozyme work being the first major crystallographic project for which every stage was carried out by computer.

In 1966, North moved with Phillips to Oxford where he was a pioneer in the use of the 'molecular replacement' method to solve the structure of a protein by use of the known structure of a related molecule, and also in the development of computer graphics for studying molecular structure and analysing crystallographic and NMR data.

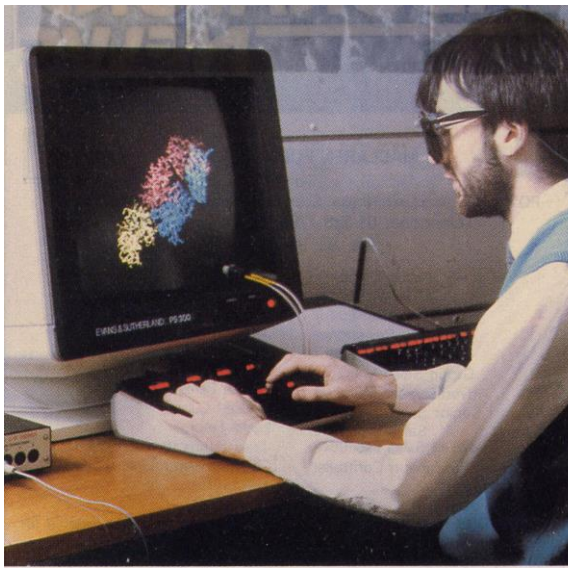

Figure 3: As an aid to the study of 3-dimensional structures of molecules, the group designed and built stereoscopic viewing devices, such as the spectacles used in the above study of a lysozyme/antibody complex.

Figure 4: 3-dimensional diagram of the structure of the milk protein beta-lactoglobulin, showing the calyx-shaped container formed by a pair of beta sheets, providing a pocket for the protein to carry a lipid molecule

In Leeds, he continued the development of computer graphics both for crystallographic work and for the application of structural information to aid the design of novel drugs for pharmaceutical use. He and his colleagues solved the 3-dimensional structures of a number of proteins, including: the hormone relaxin (based on its similarity to insulin); the enzyme dihydrofolate reductase (a target for the development of anti-cancer and anti-malaria drugs, work carried out in collaboration with his colleague Sandy Geddes and pharmaceutical companies); and members of the lipocalin family of lipid-transporting proteins, an example of which is shown above. The 1980s saw the applications of biomolecular structural knowledge, coupled with biochemical and genetic techniques, to the newly developing fields of Biotechnology and Protein Engineering. In Leeds, University Grants Committee funding led to the establishment of the

Biotechnology Unit, followed by the institution of a new first degree course in Biotechnology, both administered jointly by the then-separate Departments of Biochemistry, Biophysics and Genetics. In 1985, the Science & Engineering Research Council, together with 4 major industrial companies, established a pioneering academic/industrial venture called the Biotechnology Club, with the biggest single grant being awarded to a joint Protein Engineering project between Leeds and Birkbeck College; the leaders of the Leeds team were Tony North, John Findlay (Biochemistry) and John Wootton (Genetics), who were jointly responsible for developing computer databases of protein families and structure/functional relationships. Such collaborative ventures in both teaching and research have led naturally to the present-day inter-disciplinary Astbury Centre.

3-dimensional crystallographic studies in Leeds were consolidated with the appointment of Simon E V Phillips in 1985, who succeeded North as Astbury Professor of Biophysics when he retired in 1996.