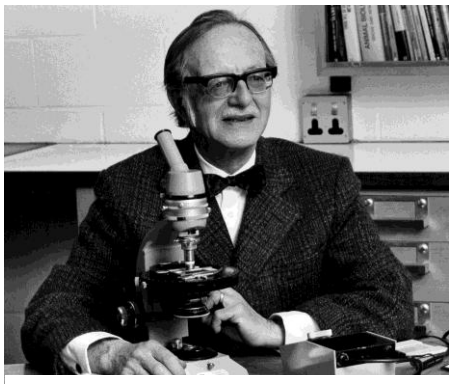
**History of the Astbury Department of Biophysics and Astbury Centre for Structural Molecular Biology**

## Background

Professor William Bragg, who with his son Lawrence had laid the foundations of X-ray crystallography while Professor of Physics in Leeds, said that he regretted that, while in Leeds, he had been unable to do more to help local industry. The opportunity came some years later in 1928 when he supported the application of his protégé William Astbury for the post of Lecturer in Textile Physics in Leeds. Astbury had already helped Bragg with his studies of the structures of 'natural things' at the Royal Institution and, arrived in Leeds, he embarked on detailed studies of the structures and functional consequences of the natural materials of concern to the textile industry – wool, hair, cotton and silk. These innovative studies led to Astbury's group becoming internationally renowned – in the words of Max Perutz, the 'X-ray Vatican' of the developing subject of 'molecular biology'. That term, probably first used by Warren Weaver of the Rockefeller Foundation, which had given Astbury financial support, was defined by Astbury as *'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 the large-scale manifestations of classical biology for the corresponding molecular plan. It is ... predominantly three-dimensional and structural, which does not mean that it is merely a refinement of morphology – it must at the same time inquire into genesis and function'.*

Following the premature death of Astbury in 1961, the University decided to amalgamate his Biomolecular Structure unit with the Plant Biophysics unit, so forming the Astbury Department of Biophysics under Professor Reginald Preston, head of the latter unit. The formation of the new department came at an auspicious time for university funding, enabling the creation of a number of new staff appointments, including the existing members of the two units, and the construction of a new building, part of the complex designed by Chamberlain, Powell and Bon. The building included a lecture theatre and two teaching laboratories. At that time, the University Grants Committee supported the construction of new buildings by providing substantial grants towards equipping them, so that the new Astbury building contained a large workshop, climate-controlled research rooms, several electron microscopes and X-ray diffraction equipment together with photographic facilities. It was world class for the 1970s.



Professor R D Preston, FRS

With the appointment of A C T North as Professor of Molecular Biophysics in 1972, the department comprised 2 Professors, a Reader, 3 Senior Lecturers and 7 lecturers, although it was agreed that Professor North would succeed Professor Preston when he retired at the end of the 1972/3 session. Unfortunately, the early 1970s saw the buoyant university expansions of the 1960s replaced by financial restrictions which initially limited the intention to build strength in protein crystallography; consequently, no new appointments could be made until

the UGC's introduction of its 'New Blood' scheme in the 1980s, which created an opportunity for the appointment of Simon Phillips in 1985.

The Biophysics academic staff were supported by secretarial and technical staff, not least 4 workshop staff, one of whom was paid by a local industrial firm with which Professor Preston had collaborated.

The Astbury department of Biophysics was merged with the Department of Biochemistry in 1990, to form the new Department of Biochemistry and Molecular Biology, while retaining biophysics teaching and research. Over the next few years, research in protein structure and function grew rapidly, with the appointments of Peter Stockley, Sheena Radford, Alan Berry, Peter Henderson and Stephen Baldwin. This led to the formation of the Leeds Centre for Molecular Recognition in Biological Sciences in 1996, a research centre that also attracted members from other departments, most notably Chemistry. The Astbury Centre for Structural Molecular Biology (ACSMB) was founded in 1999, re-establishing the Astbury name in a formally constituted university research centre. Simon Phillips was appointed the first director, and as the Astbury Professor of Biophysics, maintaining the established chair carrying Astbury's name. ACSMB was notable as a multidisciplinary research centre that bridged across departments, with over a third of its members from departments outside Biological Sciences, such as Physics and Chemistry. Since that time, ACSMB has grown into a major centre with an international research reputation, with a very wide range of activities and its own PhD programme.

**Biophysics Teaching**

By 1972, no fewer than 4 degree schemes had been started. The major one was a 4-year 'single-subject' scheme in Biophysics; the reason for this length was that it was felt that, while biophysics was not at that time a well-known subject, it was desirable that our graduates should have a firm grounding in physics for the sake of their career opportunities; consequently, these students had 2 years of courses from the Department of Physics, together with subsidiary Chemistry and Mathematics courses, embarking on the Biophysics for their 3$^{rd}$ and 4$^{th}$ years. The department also offered Combined Studies courses, with Genetics, Mathematics and Zoology, Computer Science being added later.

Starting with only 4 single-subject students, numbers gradually built up, eventually reaching 20 admissions per annum. University applicants were expected at that time to offer 5 choices in their UCCA applications, and it was always a problem that there were never 5 different universities offering biophysics degrees, so that potential students had to include a variety of alternatives. While several other universities did start to offer biophysics, including King's College London, York, Liverpool John Moores and Portsmouth, numbers in Leeds remained buoyant, but they started to decline in the late 1980s for no very apparent reason and York, for one, closed its biophysics course. Eventually, although the Leeds Biophysics single honours course had been reconstituted as a 3-year scheme, it became clear that the Leeds courses were no longer viable at a time when the university scrutinised the costs of undergraduate teaching. With the move to amalgamation of departments into larger units, Biophysics was merged with Biochemistry and Genetics and the teaching of specific

biophysics courses was abandoned. It is rather strange that this occurred at a time when the biophysical approach and methodology had become increasingly important in research and applications in the life sciences.

**Biophysics Alumni**

A number of Leeds Biophysics graduates have obtained senior positions in biomolecular structural laboratories throughout the world in universities and industry; we can note especially:

Tony Watts, Professor of Biochemistry, University of Oxford
Geoff Kneale, Professor of Biomolecular Science, University of Portsmouth
Teresa Attwood, Professor of Bioinformatics, University of Manchester
Lynne Howell, Professor of Biochemistry, University of Toronto
Jeremy Smith, Director of Centre for Molecular Biophysics, Oak Ridge National Laboratory
Carrie Wilmot, Associate Head of Biochemistry, Molecular Biology and Biophysics, University of Minnesota
Will Somers, Vice-President of Global Biotherapeutic Technologies at Pfizer, Boston

Several have moved to senior administrative posts in universities, including Helen Grindley (Sheffield) and Mike Joynson (Cardiff)

Others have made their names in business and publishing, including:
Danuta Gray, Executive Chairman of Telefonica Europe and several charities
Helen Gavaghan, Publisher and author of science and technology papers and founder of *Science, People and Politics*
David Parry-Smith, bioinformatics consultant and founder of ChiBio
Christopher Surridge, Chief Editor *Nature Protocols*

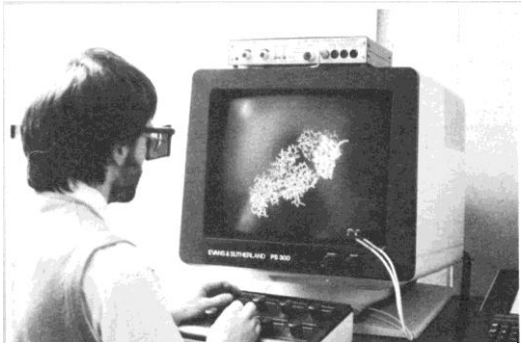
**Biophysics Research**

Sandy Geddes building a model of the cross-beta structure (1968)

Astbury's interests in fibre diffraction had continued with the elucidation by A J (Sandy) Geddes and others of the 'cross-beta' structure of proteins. They had obtained X-ray diagrams of the fibre-like egg-stalk pedestal of the lacewing fly *Chrysopa;* model-building showed that the stalk comprised transverse protein chains with the beta structure zigzagging across its width. Originally thought just to be a curious result from an obscure biological organism, such zigzag arrangements also occur in the amyloid fibrils associated with many human diseases, an important field of current research by Sheena Radford's group in the Astbury Centre.

Lipocalin chain fold, comprising a barrel of beta strands and 2 short helices

Small molecule crystallography (B. Sheldrick), spectroscopy (P F Knowles), liquid crystal studies (J E Lydon) and light-scattering (D B Sellen) also continued within the department, but research on crystalline proteins crystallography took rather long to flourish, partly because of unlucky choices of substances to study. Eventually, there was success in studies of the insulin-like hormone relaxin, the enzyme dihydrofolate reductase and the lipocalin family of binding proteins, including the mouse and rat urinary-binding proteins and their relationship to β-lactoglobulin. These projects involved collaboration by North with Dodson's group in York, Sawyer's in Edinburgh and several industrial firms.



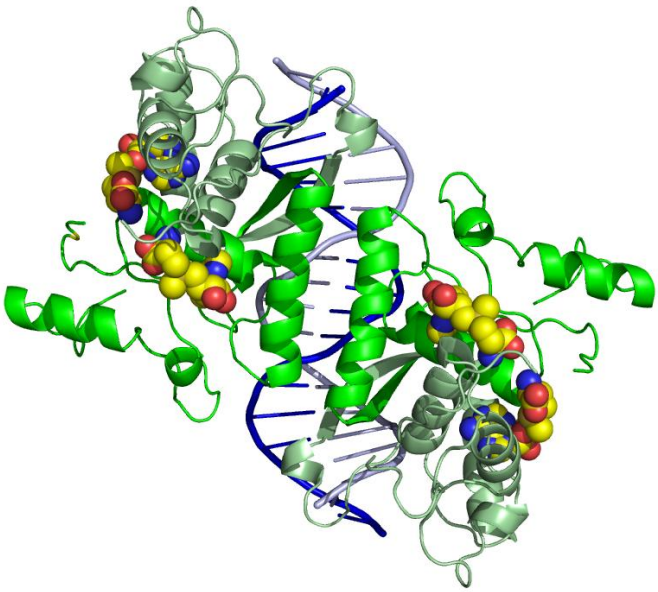
Mark Harris using the stereo-viewing system designed in the Astbury Dept. and marketed by Millennium Ltd

The use of computer-driven CRT display systems, developed by North and Geddes in the Astbury department, led to significant advances in molecular graphics and its use for interpretation of X-ray crystallographic results, the modelling and comparison of molecular structures and the energetics of interactions between molecules, such as the structures of drugs and protein/drug interactions. The first meeting of the Molecular Graphics Society (now the Molecular Graphics and Modelling Society) took place in Leeds as a result.

William Waldegrave (British Science Minister) presents a British Computer Society award in 1993 for databases and software for the study of protein sequences and functions. From L to R:
BCS President, David Perkins, William Waldegrave, Teresa Attwood, Tony North, Donald Akrigg

Research was stimulated by Research Council-funded projects including the Protein Engineering Club (supporting collaboration with other academic groups and industry) and the Molecular Recognition Initiative (supporting inter-departmental research). The use of computer methods initiated in collaboration with J C Wootton (Genetics) and continued with J B C Findlay (Biochemistry) resulted in the production and widespread use of several databases concerned with establishing structural and functional relationships between proteins on the basis of sequence comparisons that lead to the identification of characteristic features.

The arrival of Simon Phillips drove the development of protein crystallography into the areas of antibody recognition, the structure of protein-nucleic acid complexes and structural enzymology. This led to the determination of the first structure of an antibody bound to its protein antigen, which helped to seed the revolution in the use of engineered antibodies as therapeutic agents, and novel structures of proteins that recognize DNA, such as the Met Repressor and Bgl1 restriction enzyme. Rapid expansion followed into virus structure (Peter Stockley), protein folding (Sheena Radford), structural enzymology (Mike McPherson, Peter Knowles, Alan Berry) and membrane protein structure and function (Peter Henderson, Stephen Baldwin, John Findlay), forming the core for the ACSMB. The instrumentation and techniques also developed, with the establishment of high resolution electron microscopy (John Trinick), NMR spectroscopy (Stephen Homans) and a wide range of new biophysics techniques. ACSMB today has facilities and researchers equal to the best in the world, and is a fitting tribute to the legacy of William Astbury.



Met Repressor / DNA complex