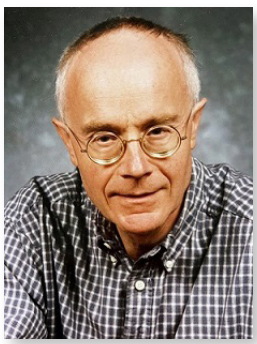
E. James Milner-White, 1945–2023



The passing, last May, of James Milner-White took from us one of the truly original thinkers in British protein science.

James grew up in the village of Sutton Green, near Guildford, Essex, and attended Sherborne School, following a curriculum appropriate to his initial intention of becoming an architect. However, he changed his mind after the fifth year and transferred to Guildford Technical College, where intensive courses prepared him for a career in science. He was accepted to study biochemistry at Aberdeen University, after which he obtained a PhD under the supervision of D. C. Watts at Guy's Hospital Medical School in London. In 1972, he joined the Biochemistry Department at Glasgow University where he spent his entire career, achieving the position of titular professor. After his retirement, he continued working and publishing as an honorary senior research fellow until his death.

One might say that James' milieu was the Protein Data Bank, where the accumulation of protein co-ordinates in the second half of the last century made it possible to determine whether relatively small structural features found in individual proteins occurred more widely. James had an eye for such features and was able to appreciate the significance of the context in which they occurred. In particular, he realized that the backbone, as well as the side-chains, had chemical properties that facilitate a functional as well as a structural role in proteins.

A recurrent aspect of James' work was an engagement with small hydrogen-bonded motifs. Some of these, such as the Schellman loop (or 'paperclip', as he called it), involved hydrogen bonds between the backbone carbonyl and imino groups of peptide bonds and were of interest because of a role in terminating ('capping') α-helices or, in the case of the β-link, providing an entry to a β-sheet. Others — the asx- and ST-turns identified by him and his students — were similar to the previously described β-turn, but with a side-chain oxygen substituting for the main-chain carbonyl group while maintaining the hydrogen bonding. His term for this, 'molecular mimicry', has a slightly anthropomorphic flavour, which is perhaps why it never gained currency, but the underlying concept of molecular variation within basic structural patterns was original and important. Other motifs — the 'niche', 'nest' and the 'crown' — are defined solely by combinations of dihedral angles. However, these angles result in geometric arrangements in which several backbone carbonyl or imino groups are positioned so that together they can bind non-protein molecules such as metal ions (in the case of the niche) or phosphate groups and iron–sulphur clusters (in the case of the nest and the crown). Such motifs are of considerable interest from an evolutionary perspective because — being dependent only on the backbone — they would have enabled fundamental biochemical processes to be performed by primitive proteins lacking the contemporary repertoire of side-chains.

In some of James' work, his quantitative approach is more evident. Together with Peter Maccallum, he showed how coulombic interactions between main-chain atoms can explain the right-handed twist of most β-strands and how they contribute to the stability of the α-helix. He demonstrated that the conventional explanation of the planar peptide bond resulting from a resonance form with a partial positive charge on the imino nitrogen atom was inconsistent with quantum mechanical calculations and bond lengths and suggested that it is preferable to think of the peptide bond as a dipolar unit with a positive charge on the carbon of the carbonyl group and a negative charge on the nitrogen. This leads to a better understanding of the binding sites for inorganic ions at the N-termini of α-helices in certain proteins.

Although driven by curiosity, most us believe that our scientific research can, directly or indirectly, benefit humanity. As well as contributing to studies of the transport system in multi-drug resistant bacteria and of mutant *ras* proteins, James derived particular satisfaction from his work with Steven Hayward on the possible mechanism of interconversion between a transient intermediate α-sheet and the final β-sheet typical of the amyloid found in Alzheimer's and other diseases.

The genomic revolution at the turn of the millennium stimulated the growth of bioinformatics teaching in universities. James was assigned to develop such a Master's degree in Glasgow University, ensuring that the more established areas of computational biology were not drowned in a sea of nucleotides. The course that he constructed was on the smörgåsbord principle of different constituents in appropriate portions, rather than as a bento box with rigid equal-sized compartments. Such an alfresco approach would certainly give today's educational bureaucrats indigestion.

That typified James' relaxed outlook. Although the theoretical nature of his research spared him the stress of writing grant applications, he had the same commitments to teaching and administration as the rest of us. But he made time in his daily routine for lunchtime conversation with colleagues from different disciplines, a recital in the university chapel or a reflective stroll by the river Kelvin. James also had a

keen interest in the lichens native to the semi-rural outskirts of Glasgow where he and his wife Morag lived and had brought up their family, and he was an active member of the Glasgow Natural History Society. His curiosity extended from the sub-microscopic world of proteins to the living world around him. He clearly regarded them as part of the same organic whole. ■

Parts of this obituary are adapted, with permission, from one published in the journal, Proteins.

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