Present tributes to achievements past

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Perspectives in Structural Biology: a volume in honour of GN Ramachandran (Editors M Vijayan, N Yathindra & AS Kolaskar), University Press (India), Hyderabad & Indian Academy of Sciences, Bangalore, 1999. £20.95 (paperback) ISBN 81 7371 254 9.

This volume contains a wealth of data in approximately 54 papers that cover almost the whole of structural biology. The topics encompass the following: the structure and action of proteins; collagen structure; analysis of protein structures; protein folding and stability; carbohydrates and carbohydrate-binding proteins; membrane proteins; molecular assemblies; peptide conformation and function; structure and interaction of nucleic acids; and methods and algorithms. It is a volume for dilettantes that are interested in all aspects of protein structure and in the relationship between protein structure and function. The volume is dedicated to GN Ramachandran on the occasion of the Congress of the International Union of Pure and Applied Biophysics held in New Delhi in September 1999.

GN Ramachandran was the founding father of structural biology in India. He was born in 1922 in Kerala in southern India. He joined Nobel Prize winner Sir CV Raman at the Indian Institute for Science at Bangalore for his graduate work obtaining his doctorate in 1947. G Venkataraman [1] has commented 'While Raman occupied himself with surveying the various manifestations of optical phenomena …, he left Ramachandran the task of developing a formal treatment. Ramachandran provided the perfect foil to Raman in that respect. Given his natural bent of mind to mathematical topics he enjoyed furnishing the analytical backups to Raman's explorations.' With the help of an 1851 Exhibition Scholarship, Ramachandran then went to the Cavendish Laboratory in Cambridge where he worked with WA Wooster and obtained a second doctorate in 1949. He returned to India and in 1952 moved to Madras (now Chennai) to establish the Department of Physics at the age of 30. There he made his first major contribution to structural biology; the structure of collagen. As Sasisekhararan and Yathindra describe in this volume, the Ramachandran and Kartha model for collagen (based on X-ray diffraction fibre photographs and proposed in 1954 [2,3]) involved a coiled-coil structure of three parallel peptide chains that are related by a threefold axis of symmetry and held together by interchain hydrogen bonds. The model explained the presence of glycine at every third residue and the necessity for the frequency of proline and hydroxyproline residues. The model postulated the possibility of two hydrogen bonds for every three residues so as to provide maximum stability for the three-stranded collagen structure. There was also a possibility of a C–H ...O hydrogen bond. In the following years, several other structures were proposed for collagen based on a triple helix but most incorporated only one hydrogen bond. Later, in 1968, Ramachandran and Chandrasekharan [4] slightly modified their model by proposing that a water molecule mediated the second hydrogen bond. It is rewarding that the recent structures of collagen-like peptides confirm the model proposed by Ramachandran and, as described here by Kramer and Berman, support the water-mediated hydrogen-bonding interactions. There is also an interesting follow-up paper by John Kuriyan that describes the role of the polyproline Type II helix in the regulation of the c-Src protein kinase.

The Madras group focussed on the X-ray determination of amino acids, peptides and their derivatives. The information derived from these structures and the problems in stereochemistry that Ramachandran wrestled with in the structure of collagen, led to the second outstanding achievement of Ramachandran in 1963, the Ramachandran plot [5] . The stereochemical contact map of a system of two linked peptide units is one of the most useful aids in understanding the complexities of protein structure and in an updated form is used widely in the validation of protein structures. The Ramachandran plot shows that only 23% of the available conformational space generated by rotation about single bonds is available to polypeptide chains because of steric criteria. The allowed regions correspond to three areas that encompass the secondary structural elements of the right-handed α helix, the extended β conformation and the polyproline helix, and a third smaller area corresponding to a left-handed helical conformation. In the same year Ramachandran, Ramakrishnan and Sasisekeharan [6] applied a similar conformational analysis to the structures of β-(1–4)-linked glucosyl polymers. They showed that the glucopyranose ring had a standard conformation that varied little among the eight different monosaccharide and disaccharide structures that were known at that time, and that β-(1–4) polymers exhibited a restricted preferred conformation that resulted in an intrahydrogen bond.

The analysis of polysaccharide conformation played an important role in the studies by David Philips and his team on lysozyme. I remember a visit by Ramachandran to the Royal Institution around that time. I was a junior graduate student and I had to operate the projector for the great man's seminar.

In 1970 Ramachandran moved to the Indian Institute of Science in Bangalore and set up the Molecular Biophysics Unit that continues today as a centre of excellence both in its research and in the quality of graduate students that it trains. The Institute of Science had been the brainchild of JN Tata, a distinguished member of the Parsi community who had introduced modern steel technology to India. He had become convinced that India's problems in the long run could be solved by the large scale introduction of science and technology. With the help of the Maharajah of Mysore, who donated 300 acres of land in Bangalore and provided an annual subsidy, the Institute was founded in 1911. Tata had died in 1904 before his dream was realised; the delays were caused by the then British Government of India. Ramamachandran has received many honours both from India and abroad. He was elected a Fellow of the Royal Society in 1977. More recently, in 1999, the International Union of Crystallography awarded him the Ewald Prize. Sadly, because of his long-term illness he was not able to attend and M Vijayan received the prize on his behalf.

The volume contains a wealth of information. Most authors have chosen to review their own results in terms of conformational analysis, often bringing in gems of information that had been excluded in the original publications. It is invidious to single out a paper but one that I enjoyed much was that by Kumar, Ævarsson and Hol on multiprotein assemblies with point group symmetry. The paper starts with an appreciation of the five Platonic solids and comments that symmetry is a rich treasure trove in macromolecular structure; it then illustrates this point with definitions of perfect, pseudo, temporal, partial and linked symmetry in nature. Restricting themselves to assemblies that exhibit point group symmetry and to those of which the structures have been determined by X-ray crystallography, they summarise examples of structures with cyclic point group symmetry (C_n where n = 2, 3, 4, 5, 6, 7, 8, 9, 11, 17), with dihedral point group symmetry (D_n where n = 2, 3, 4, 5, 6, 7), and with cubic symmetry (tetrahedral 23, octahedral 432 and icosahedral 523). Like Monod, Wyman and Changeux, they note the frequency of assemblies with point group symmetry and speculate on the advantages.

The volume is a fine tribute to Ramachandran, who achieved so much with limited equipment and hard thinking. The editors are to be congratulated on their splendid collection of papers.

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