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EDITORIAL

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Stereochemistry was born in Paris in the mid-19th century when Pasteur serendipitously observed the spontaneous resolution of racemic tartaric acid. In a spectacular leap of intuition, Pasteur recognized, a quarter of a century before Vant Hoff and Le Bel, that molecular structure and optical activity were related and that common forms like helices and irregular tetrahedra were intrinsically handed. Our present-day understanding of the shapes of molecules and the connections between three dimensionality and chemical function rests to a large extent on the many insights that Linus Pauling had between the 1930s and 1950s. The first triumph of stereochemical thinking in biology was Pauling's realization in 1948, that the non-integral α-helix provided a spectacular solution to the search for folded polypeptide structures. The Watson–Crick double helical structure of DNA appeared in 1953; clearly the pre-eminent example of a three-dimensional model that instantly reveals the basis for biological function. In 1954, the structure of collagen, the most abundant protein of connective tissue was described by G. N. Ramachandran and G. Kartha, working at the University of Madras. The structure, an intertwined three chain triple helix, elegantly accounted for the limited experimental data and provided a compelling rationale for the unique amino acid composition of collagen. It also marked the emergence of a new star, in the fledgling field of structural molecular biology, G. N. Ramachandran.

When G. N. Ramachandran died at Chennai (formerly, Madras) on 7 April 2001 the curtain was rung on one of the most remarkable chapters of modern science in India. Ramachandran began his journey in science when he joined the Indian Institute of Science, Bangalore in 1942, as a student in the Electrical Engineering Department. He realized very quickly that his interests lay in physics, a subject then overwhelmingly dominated at Bangalore by the presence of the legendary C. V. Raman. In retrospect, it appears almost inevitable that Ramachandran would desert electrical engineering and embrace physics; an event that appears to have been accompanied by Raman's soothing words to the Professor of electrical engineering: 'I am admitting Ramachandran into my department as he is a bit too bright to be in yours'. Ramachandran was to eventually become the most distinguished of Raman's students. At Bangalore he first submitted a thesis entitled 'Optics of Heterogeneous Media' for an M Sc degree of the University of Madras and later a doctoral thesis in 1947, which contained some of the earliest applications of X-ray diffraction to the study of crystal perfection. He spent two years in Cambridge, obtained a Ph D degree working with W. A. Wooster and returned to Bangalore in 1949 to begin an independent career as an assistant professor of physics, working in the X-ray diffraction laboratory that he was instrumental in building as a student. He did not stay long. Madras University beckoned with a Professorship and the responsibility to head the Department of Physics. Ramachandran moved to Madras when he was just 30, to begin an extraordinary burst of scientific activity. At Madras, he flourished under the benign and supportive influence of an enlightened Vice-Chancellor, A. Lakshmanaswamy Mudaliar; a relationship reminiscent of that between Asutosh Mukherjee and C. V. Raman in Calcutta. J. D. Bernal visited Madras in 1952 and in a casual conversation suggested that the structural proposals for collagen were unsatisfactory. The Central Leather Research Institute was next door to Ramachandran's laboratory. He soon had a sample and X-ray diffraction photographs. The triple helix emerged in two papers in *Nature* in 1954 and 1955, introducing the coiled coil concept, a fundamental advance in the understanding of polypeptide structures. But, in a sharp critique, Francis Crick, fresh from his DNA success, together with Alexander Rich argued that the Madras structure was 'stereochemically unsatisfactory'. Out of the brewing collagen controversy was to emerge what is undoubtedly Ramachandran's finest contribution to structural biology. Spurred by the criticism of unacceptably short interatomic contacts in his collagen structure, Ramachandran set out to investigate the criteria for describing stereochemically acceptable structures for polypeptide chains. Using the simple hard sphere model for atoms and driven by the insight that each residue in a polypeptide chain is allowed only two degrees of torsional freedom, Ramachandran together with his colleagues C. Ramakrishnan and V. Sasisekharan laid the foundations for the conformational analysis of polypeptide chains. Their seminal paper published in the *Journal of Molecular Biology* in 1963, circumspectly titled 'Stereochemistry of polypeptide chain configurations', introduced the famous two-dimensional map, which was to eventually bear Ramachandran's name. Today, for beginning students of biochemistry, protein structures

are introduced with a discussion of the Ramachandran map, which also forms the cornerstone for many discussions of protein folding. The simple concept of reducing the 'structure space' of protein chains to two-dimensions with dihedral (torsional) angles serving as the variables had a profound impact on stereochemistry and structural biology. In the late 1960s and early 1970s a flood of important papers appeared from Ramachandran's laboratory, which addressed key issues in the structural chemistry of proteins and peptides; chain reversals, *cis*-peptide bonds, hydrogen bonding, non-planar amide distortions and novel helices in polypeptides with alternating L and D-residues.

While polypeptide stereochemistry was a dominant theme in Ramachandran's career between the 1950s and 1970s, his sharp incisive mind turned often to his first love, X-ray crystallography. Fourier theory fascinated him and he authored, with his colleague R. Srinivasan, an influential book on Fourier Methods in Crystallography. Ramachandran's paper in this journal on a 'A new method for the structure analysis of non-centrosymmetric crystals' was influential in promoting the use of anomalous scattering for solving the crystallographic phase problem. In 1971, Ramachandran together with A. V. Lakshminarayanan published a key paper on three-dimensional image reconstruction, which was to have important applications in Computer Assisted Tomography. Ramachandran had a remarkable ability to cut through unnecessary details and go straight to the heart of a problem. This quality coupled with formidable physical insights and mathematical skills allowed him to make many important contributions in biophysics and crystallography.

Ramachandran was the editor of *Current Science* between 1950 and 1957. This was the only time that the editorial office moved out of Bangalore in the 69 years of this journal's existence. He published several important papers, notably his work on the X-ray topographs of diamond and anomalous dispersion in this journal. In 1990, *Current Science* highlighted his contributions to polypeptide stereochemistry in a special issue. Ramachandran was an excellent teacher and lecturer. His clear grasp of the fundamentals of a problem allowed him to convey to listeners the key elements of a scientific issue, shorn of all the complicating details.

Ramachandran was widely honoured for his work in India and abroad. In recognizing Ramachandran's work most agencies in India honoured themselves and conferred a new lustre on the awards they instituted. A dispassionate analysis of his life and work will reveal that he did not, in large measure, get his due. The Government of India, undoubtedly advised by the scientific establishment, never found it fit to include him in the annual Republic Day honours list. This act of omission in no way diminished his stature; instead it forever dimmed the lustre of these awards. The Royal Society belatedly recognized Ramachandran in 1977, almost towards the end of his active scientific career and over two decades after his remarkable work on collagen. Ramachandran was clearly a 'Nobel class' scientist, to borrow a phrase from Eugene Garfield. But, his active career was all too brief by modern day standards. For the last twenty years Ramachandran was not really visible internationally, reminding us of one of the ironies of modern science; achievement alone is not enough, packaging and marketing play an important role. In India, where administrative positions are often considered a mark of scientific success, Ramachandran was essentially an 'outsider' to the establishment. We have yet to learn that idiosyncratic personalities often make the most original contributions to our science. Ramachandran did all his work in India, following in the footsteps of his mentor, C. V. Raman. In the 1960s and 1970s he did travel regularly to the United States, to the University of Chicago where he held a visiting professorship. At Madras, Ramachandran's work brought an unprecedented level of recognition to the University. The two international conferences he organized in 1963 and 1968, brought to Madras some of the most famous names in molecular biology and biophysics; Linus Pauling, Severo Ochoa, Maurice Wilkins, Stanford Moore, David Phillips, Ephraim Katchalski, Harold Scheraga, Paul Flory, Elkan Blout and John Schellman.

Ramachandran returned to Bangalore to set up the Molecular Biophysics Unit at the Indian Institute of Science in 1971. His move from Madras was catalysed by the deteriorating academic atmosphere of the University. Indeed, Ramachandran's two decades at Madras University clearly showed that the highest levels of research could be practiced within our University system. His departure signaled an impending change. We have all watched, with varying degrees of helplessness, the steady decay of University science in India, over the last three decades. At Bangalore in the period between 1971 and 1979, Ramachandran fashioned a new department, which has grown into a major center of structural biology. Like many extraordinarily gifted individuals, Ramachandran often had an uneasy relationship with his surroundings. It was not easy for him to come to terms with mediocrity. Elevated to the formidable position of a head of department at 30, he grew to be isolated from his colleagues, rarely establishing the easy academic relationships that make science a pleasure. But even at the height of his career Ramachandran most enjoyed scientific discussion; unfortunately his surroundings could rarely rise to the levels he demanded. His last years were troubled. A stroke and the steady onset of Parkinsonism diminished his movements and activities. The loss of his wife Rajalakshmi (Rajam), after 53 years of marriage, in 1998, was a great blow. In many ways, when the end came it was indeed time to go. But, Ramachandran has left behind a rich scientific legacy. His achievements will serve as a source of inspiration for generations to come. Ramachandran was undoubtedly one of the most outstanding scientists of post-Independence India and truly, a jewel in the crown of India's science. For us, it was a very special privilege to have known him.

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