G. N. Ramachandran and the beginnings of structural molecular biology in India

The origins of structural molecular biology may be traced in the 1930s to Linus Pauling's wide ranging researches at Caltech, to W. T. Astbury's work on diffraction studies on fibrous proteins at Leeds and to J. D. Bernal's optimistic and prophetic work on crystals of proteins and viruses at London. The term molecular biology, anticipating a happy fusion of physics, chemistry and biology, was presumably coined by Warren Weaver of the Rockefeller Foundation but in later years was adopted to describe the dramatic revolution in molecular genetics. The first major structural triumph was to come in the late 1940s when Pauling, ironically enough while visiting Oxford, discovered the alpha-helical structures of polypeptides and set the stage for our present day understanding of protein structure. Molecular biology's most celebrated event was of course, Watson and Crick's discovery of the double-helical structure of DNA, heralding in one of the major scientific revolutions of the century. Structural molecular biology in the 1950s was a field in its infancy and England and California were its focal points. Happily enough, there developed in India, at Madras in the 1950s, a vibrant and original school of structural biology, fuelled by the imagination of G. N. Ramachandran.

In papers published between 1954 and 1956 in Nature, with Gopinath Kartha, Ramachandran was to develop the triple-helical coiled-coil structure for collagen, the most abundant connective tissue protein in animals. The collagen triple helix was a logical progression in the complexity of fibrous helical structures, beginning with the alpha-helix in proteins, followed by the DNA double helix. As so often happens in science, a closely related triple-helical structure for collagen was also proposed in 1955, by Alexander Rich and Francis Crick in Cambridge and P. M. Cowan and collaborators at Kings College, London, setting in motion a debate, between the Madras and English groups, on the precise details of the collagen structure. Out of this ferment was born a new idea to analyse the stereochemistry of polypeptide chains based on the elegantly simple concepts of torsional freedom about single bonds, hard sphere atoms and steric contacts, leading to a major simplification in the analysis of complex three-dimensional folding patterns of polypeptides and proteins. Later, these ideas were to develop further in the analysis of polynucleotides and polysaccharides, providing the foundation for present day molecular mechanics calculations on biopolymers. The ideas on biopolymer stereochemistry developed at Madras in the 1950s and 1960s have come to be embodied in the famous Ramachandran map, now a common feature of textbooks of biochemistry and molecular biology.

This issue of Current Science presents a collection of papers in the area of peptide and protein structures, which will hopefully provide a glimpse of the field, over a quarter of a century after the publication of Ramachandran's seminal work and also pay a tribute to a great pioneer of molecular biophysics in India.

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