

# This Week's Citation Classic

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**Ramachandran G N & Sasisekharan V.** Conformation of polypeptides and proteins. *Advan. Prot. Chem.* **23**:283-437, 1968.  
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**The three-dimensional architecture of a molecule is very important in deciding its chemical properties and biological activity. The article deals with the rules governing the shapes of proteins, polypeptides and related biomolecules, their internal structure and the nature and origin of the variations which occur, both in solution and the solid state. [The SCF® indicates that this paper has been cited over 580 times since 1968.]**

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"When I joined the University of Madras as a research professor in 1952, I looked out for a new line of work to follow in my future career. The beautiful papers by Pauling and Corey<sup>1</sup> on the helical structure of proteins and polypeptides, which had appeared in 1951, influenced me to take up the field of biomolecular structure as my life interest. Our first studies<sup>2</sup> were on the fibrous protein, collagen, and these led to the first proposal, in 1954, of the chain configuration in the triple helical structure of collagen, which is now universally accepted. The next year, several groups, Kartha and I<sup>3</sup> in Madras; Rich and Crick<sup>4</sup> in Cambridge; and Cowan, McCavin, and North<sup>5</sup> in London, improved the structure to have 3.3 units per turn for collagen, and also showed that the prototype helix occurs for related polypeptides like polyglycine and polyproline. This was extended to polyhydroxyproline by my colleague, Sasisekharan,<sup>6</sup> in Madras in 1959.

"Having been interested in several such structures in specific examples, we worked out a general theory in the early 1960s of the conditions for the conformation of

a pair of peptide units to be stable, in terms of 'contact criteria,' and a short note was published in the *Journal of Molecular Biology* in 1963.<sup>7</sup> This paper is also a widely quoted reference, and as a result of this, we held an International Conference on the Conformation of Biopolymers in Madras in 1967, the first of its kind, and one attended by all the leading workers of that time in the field.

"In 1964, I was elected an honorary member of the American Society of Biological Chemists, and soon after that, J.T. Edsall invited me to write the article under discussion. It contains a detailed account of the description of peptide and polypeptide conformations arising from variations of the dihedral angles phi and psi, and of the consequent phi-psi map, which has now come to be known as the Ramachandran Map. The mathematical technique of making such variations and calculating atomic coordinates, helical parameters, and so on, was presented systematically in that review. It was also one of the earliest to discuss techniques of energy minimization, which has now come to be widely used.

"It is worthwhile commenting on the fact that my colleague, Ramakrishnan, spent some six months with a desk calculator for obtaining the data for the first phi-psi-plot, while this can be accomplished in a few minutes on the present day electronic computers. Thanks to such sophisticated aids, the subject of biopolymer conformation has become explosive in recent years, and conformational analysis (both theory and experiment) has now been accepted as the most important technique for the understanding of biology in terms of physics and chemistry.

"There have been any number of reviews after 1970 on this subject, but two may be mentioned in particular—namely the books by Fraser and MacRae<sup>8</sup> on fibrous proteins and Schulz and Schirmer<sup>9</sup> on globular proteins."

1. Pauling L & Corey R B. Series of papers on the structure and helical configurations of polypeptide chains. *Proc. Nat. Acad. Sci. US* **37**:235, 241, 251, 256, 261, 272, 1951.
2. Ramachandran G N & Kartha G. Structure of collagen. *Nature (London)* **174**:269-70, 1954.
3. .... Structure of collagen. *Nature (London)* **176**:593-5, 1955.
4. Rich A & Crick F H C. The structure of collagen. *Nature (London)* **176**:915-6, 1955.
5. Cowan P M, McGavini S & North A C T. The polypeptide chain configuration of collagen. *Nature (London)* **176**:1062-4, 1955.
6. Sasisekharan V. Structure of poly-L-hydroxyproline A. *Acta Crystallogr.* **12** 903-9, 1959.
7. Ramachandran G N, Ramakrishnan C & Sasisekharan V. Stereochemistry of polypeptide chain configurations. *J. Mol. Biol.* **7**:95-9, 1963. [The SCF® indicates that this paper has been cited over 200 times since 1963.]
8. Fraser R D B & MacRae T P. *Conformation in fibrous proteins*. New York: Academic Press. 1973. 628 p.
9. Schulz G E & Schirmer R H. *Principles of protein structure*. New York: Springer-Verlag, 1979. 314 p.