

Sundaralingam M. Stereochemistry of nucleic acids and their constituents. IV. Allowed and preferred conformations of nucleosides, nucleoside mono-, di-, tri-, tetraphosphates, nucleic acids and polynucleotides. *Biopolymers* 7:821-60, 1969. [Department of Chemistry, Case Western Reserve University, Cleveland, OH]

Conformational analysis based on single crystal X-ray data of nucleic acid constituents and model compounds, and fiber diffraction data of nucleic acids and polynucleotides, revealed that the nucleoside is constrained to two predominant conformational classes, which generate two favored families of nucleic acid double helices. A comprehensive conformational nomenclature for polynucleotides was developed. [The SC[®] indicates that this paper has been cited in over 620 publications since 1969.]

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"After obtaining my PhD with G.A. Jeffrey in Pittsburgh, I joined Lyle H. Jensen in Seattle in 1962 where I carried out a high precision X-ray analysis of the nucleotide 3'-CMP. A conformational analysis of this molecule led me to think about the stereochemistry of nucleic acids. At that time, the conformational analysis of polynucleotides was regarded as highly complex because of the rotations around the numerous single bonds in the polynucleotide chain. The Watson-Crick base pairing principle was the foundation of nucleic acid secondary structures, but the stereochemical principles governing (a) nucleotide conformation, (b) internucleotide phosphodiester, and (c) their relation to chain folding were fragmentary. I started to build a unified picture^{1,2} of the structural principles governing nucleic acid conformations based on crystallographic studies of nucleotides and molecular modeling. I recognized the crucial role of the sugar in the determination of the conformation of the nucleotide unit, and, ultimately, the polynucleotide sugar-phosphate backbone.

"After a brief spell with Robert Langridge in Boston, I moved in 1966 to Case Western

Reserve University where I continued my systematic investigation of the structures of the nucleic acid constituents. Although my detailed paper was submitted to *Biopolymers* in 1968, I had already presented the basic concepts and much of the data in 1966 at the International Symposium on DNA, Jena, German Democratic Republic, and the University of Madras, India, and in 1968, at the ACA summer meeting, Buffalo.

"I found that the restricted rotations about the single bonds (conformational wheels) and the correlations among them (two-dimensional pairwise conformational correlation maps between adjacent bond rotations) greatly reduced the number of conformations preferred for the nucleotide building blocks and the configurations accessible to polynucleotides. In the absence of 3',5'-dinucleoside monophosphate structures, I constructed the internucleotide phosphodiester map (ω, ω) from model phosphodiester compounds. This map gave the favored regions for both right- and left-handed helices as well as for loop-forming phosphodiesters. I found that the helical conformation was an intrinsic property of the sugar-phosphate backbone, and that the energetics of the sugar-phosphate backbone are important, in addition to base stacking and base pairing interactions, in determining polynucleotide architecture.

"I think this paper is frequently cited because it provided (a) a comprehensive conformational nomenclature for polynucleotides, (b) a foundation for the conformational analysis of nucleotide and polynucleotide structures, and (c) a basis for future theoretical and physicochemical studies of polynucleotides including dynamics in nucleic acids.

"Since the publication of this paper, scores of crystal structures of nucleic acids, including oligonucleotides and transfer RNA have been determined by numerous able colleagues in my group as well as in other laboratories. It is satisfying to see that these studies have amplified and placed on a firmer basis the structural principles of the nucleic acids developed in this paper."^{3,4}

1. Sundaralingam M. Conformations of the furanose ring in nucleic acids and other carbohydrate derivatives in the solid state. *J. Amer. Chem. Soc.* 87:599-606, 1965.
2. Sundaralingam M & Jensen L H. Stereochemistry of nucleic acid constituents. II. A comparative study. *J. Mol. Biol.* 13:930-43, 1965.
3. Sundaralingam M. Nucleic acid principles and transfer RNA. (Srinivasan R, ed.) *Biomolecular structure, conformation, function & evolution*. Oxford: Pergamon Press, 1980. Vol. 1. p. 259-82.
4. Sundaralingam M & Westhof E. The nature of the mobility of the sugar and its effects on the dynamics and functions of RNA and DNA. (Sarma R H, ed.) *Biomolecular stereodynamics*. New York: Adenine Press, 1981. p. 301-26.