

This Week's Citation Classic®

Rees D A. Conformational analysis of polysaccharides. Part V. The characterization of linkage conformations (chain conformations) by optical rotation at a single wavelength. Evidence for distortion of cyclohexa-amylose in aqueous solution. Optical rotation and the amylose conformation. *J. Chem. Soc. B* 1970:877-84; and, **Rees D A & Scott W E.** Polysaccharide conformation. Part VI. Computer model-building for linear and branched pyranoglycans. Correlations with biological function. Preliminary assessment of inter-residue forces in aqueous solution. Further interpretation of optical rotation in terms of chain conformation. *J. Chem. Soc. B* 1971:469-79. [Chemistry Department, University of Edinburgh, Scotland]

The first paper suggests a relationship between the optical rotation measured at a single wavelength for a di-, oligo-, or polysaccharide, and the conformation at the glycosidic linkage as expressed in torsion angles about the C-O and O-C bonds. In the second paper, computer models are used to explore the influence of local and remote contacts on the stereochemistry of polysaccharides in various glycosidic linkages and the relationship of this to properties including their optical rotations. [The *SCJ*[®] indicates that these papers have been cited 140 times each.]

Linkage Rotation—Testing a Formula

David A. Rees
Medical Research Council
20 Park Crescent
London W1N 4AL
England

I have already described in another *Citation Classic*¹ the beginnings of my work to understand the physical properties and biological functions of polysaccharides in terms of their chain conformations. The aim of these *Classic* papers was to test my formula for the mathematical dependence of "linkage rotation" on the torsion angles, ϕ and ψ , at the glycosidic and aglycone bonds, respectively, by applying it to the di- and oligosaccharides.

In part V, I took the few crystal structures available for di- and oligosaccharides and used these with my formula to predict optical rotations. Good agreement was indeed obtained with experiment for the β -1,4 series in water and the α -1,4 series in organic solvents! The α -1,4 series in water was anomalous, leading to the interesting possibility of hydrophobic interactions. I suspect that the citation rate for this paper is at least as much due to interest in the relevance of this to cyclodextrin and starch inclusion complexes as to interest in the optical rotation method itself.

In part VI, Bill E. Scott and I used computer model-building in an attempt to establish simple rules for conformational interactions across gly-

cosidic bridges of pyranoglycans, and explore the mutual consistency of these predictions and the optical rotation calculations. The degree of consistency was in fact amazingly good. We proceeded to extend the computer model building to long range interactions and overall secondary structure. This led to the proposal that polysaccharides can be regarded as belonging to different conformational families. The paper is probably cited most for this idea.

Returning to a problem from our original work, I was able to apply the method to the iota carrageenan double helix and show that the sign and magnitude of the optical rotation shift were entirely consistent with the double helix model that we had derived by X-ray diffraction.² Much later, Gene S. Stevens, State University of New York, Ed R. Morris (my research colleague over many years), and I traced the spectroscopic origins of the coil and helix rotations using vacuum ultraviolet circular dichroism.³

Despite this and other successes with the method in my own laboratory, the optical rotation method has largely fallen into disuse. I think this is partly because its application is quite difficult and tortuous. Largely, though, it is due to the subsequent development of the powerful method of determining solution conformations by measurement of nuclear Overhauser effects by NMR spectroscopy and relating these to interatomic distance through space. This is being used for carbohydrate chains in glycoconjugates.⁴ Stevens, however, has now (partly based on our collaboration) formulated a model linked much more firmly and satisfactorily to the fundamentals of theoretical spectroscopy which, when applied to several disaccharides successfully correlates optical activity with conformation.⁵ This is a promising development since further physical methods independent of NMR are needed to move the field forward on secure foundations. For example, some systems for which my own method worked, NMR is still hardly applicable. This is because the rod-like double helices are rigid, making line broadening so severe that spectra cannot be measured with conventional methods.

1. Rees D A. Citation Classic. Commentary on *Advan. Carbohydr. Chem.* 24:267-332, 1969.

Current Contents/Life Sciences 29(47):25, 24 November 1986.

2. Rees D A, Scott W E & Williamson F B. Correlation of optical activity with polysaccharide conformation. *Nature* 227:390-3, 1970.

3. Morris E R, Stevens E S, Frangou S A & Rees D A. Total optical activity of agarose: relation to observable transitions in the vacuum ultraviolet. *Biopolymers* 25:959-73, 1986.

4. Carver J P, Michnick S W, Imberty A & Cumming D A. Oligosaccharide-protein interactions—a 3-dimensional view. *CIBA Foundation Symp.* 145:6-26, 1989.

5. Duda C A & Stevens E S. Trehalose conformation in aqueous solution from optical rotation. *J. Amer. Chem. Soc.* 112:7406-7, 1990.

Received March 13, 1991