COMPUTER AND INSTRUMENTATION GROUP OF THE BIOCHEMICAL SOCIETY
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'CONFORMATION OF BIOPOLYMERS'

Some Applications of Computer Model-Building in Polysaccharide Biochemistry

By D. A. REES. (*Unilever Research, Colworth/Welwyn Laboratory, Sharnbrook, Bedford, U.K.*)

Our use of model-building calculations began with the particular problem of finding a backbone conformation to account for the main features of X-ray-diffraction diagrams of certain polysaccharides. Diffraction evidence was insufficient for the direct derivation of a structure, and it was therefore necessary to work from the covalent formula by trial and error. Months of model-building by hand had been tedious and frustrating. Thus we turned to computer methods and found them, in this instance, to be satisfying and conclusive; they led to the double-helix model for α -carrageenan (Anderson, Campbell, Harding, Rees & Samuel, 1969; Rees, 1970a).

However, the further use of computer methods soon led us (as it led others, before and since) to recognize serious limitations, especially that the results may be very sensitive to starting assumptions about bond lengths, bond angles and energy functions. It is of the greatest importance that standards of strict realism be imposed on the assumptions that are made in all work of this type. Since the beginning (Rees & Skerrett, 1968) our procedure has been to repeat calculations with a series of assumptions to cover the whole range of reasonable possibilities, and to rely only on results that emerge from them all. Of course, results may then turn out to be too ambiguous to be useful. Even so, independent routes converged on the same model for the carrageenan helix (Anderson *et al.* 1969), L-rhamnose residues in the pectic polysaccharides of plant cell walls were shown to have a 'kinking' function with likely implications for biological function (Rees & Wight, 1971), and there emerged a stereochemical classification of homopolysaccharide types that would appear to correlate with biological function (Rees & Scott, 1971).

If starting assumptions could be made more certain in their details, energy calculations could greatly advance our understanding of polysaccharide conformation and its role in biology. Therefore it is worth while to try to establish methods by which the assumptions can be tested quantitatively against experimental evidence; if a single set of assumptions can then be found to satisfy the evidence for a wide range of carbohydrate systems, we could begin to use this particular set

with some confidence. We are attempting to apply tests based on the calculation of the energies and hence probabilities of all possible conformational states of a series of mono- or di-saccharides, from which we derive the value of a property that can be measured in solution for each compound, such as optical rotation (Rees, Scott & Williamson, 1970; Rees, 1970b) or position of mutarotation equilibrium. The progress of this work will be described.

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Study of Protein Conformations

By A. C. T. NORTH. (*Laboratory of Molecular Biophysics, Department of Zoology, University of Oxford, South Parks Road, Oxford OX1 3PS, U.K.*)

Attempts to predict polypeptide conformation from amino acid sequence have involved several different types of approach: first, theoretical calculations based on appropriate energy functions for rotations about single bonds, non-bonded interactions and hydrogen-bond and dipole-dipole interactions; secondly, experimental studies of the conformations of homopolymers and copolymers of known sequence; thirdly, statistical surveys of the distribution of amino acids or particular di- or oligo-peptides between different types of conformation in proteins whose atomic arrangement is known. Undoubtedly these approaches taken singly or in combination have some predictive value, though at present such predictions are essentially restricted to distinguishing between sequences likely to have compact α -helical type conformations in which near-neighbour interactions are favourable and those in which near-neighbour interactions are unfavourable and relatively extended conformations are probable. For the prediction of tertiary structure, it appears that little progress will be made until methods can be found of achieving a proper balance between the conventional energy terms and solvent or entropic effects. The energy of a hydrogen