PREFACE

Preface

There are two basic approaches for determining the gross conformation of a biological macromolecule in solution. One is to assume a structure (generally an array of spheres of varying sizes) and then calculate its hydrodynamic properties, for example the intrinsic viscosity, sedimentation coefficient, translational diffusion coefficient, and then see how much these predicted properties differ from the experimentally determined properties for the unknown structure. The model is then successively changed or 'refined' until the predicted properties converge to agree with the actual properties. This method has been developed by Bloomfield, Garcia de la Torre and co-workers (Bloomfield et al, 1967, Garcia de la Torre & Bloomfield, 1977a,b,c, 1978, Wilson & Bloomfield, 1979a,b, Garcia Bernal & Garcia de la Torre, 1980). There is however a serious drawback in that the final calculated structure may not be the only one which gives these properties.

The alternative approach is to calculate the structure directly from the known hydrodynamic properties. Some general model must of course be assumed, but although the models available from this approach are less precise (the most general before the commencement of this study being an ellipsoid with two equal axes) it does not suffer from the uniqueness problem. This approach was first developed by Stokes (1851, 1880) in terms of a simple spherical model calculated from the translational frictional property and the rotational frictional property and again for a spherical model by Einstein (1906 - with a correction in 1911) from the viscosity property. Although the current state of theoretical, experimental and data analysis techniques allows use of the '2 equal axes' ellipsoid ("ellipsoid of revolution"), it is clear from a simple perusal of

crystallographic models that for many biological structures this model is a very poor approximation to the true structure.

The aim of this thesis is thus twofold: the first is to review all the current ellipsoid of revolution shape functions (in which some new, hitherto unpublished functions are given) and the second is to develop the current theoretical and data analysis techniques to show that with current experimental precision the restriction of two equal axes on the ellipsoid model can now, in principle at least, be dispensed with to allow use of the more general "tri-axial ellipsoid" model.

I would like to take this opportunity to express my deepest gratitude to Dr. A.J. Rowe for his expert guidance and supervision during the course of this study.

I would also like to thank the following people for their help and advice on specific parts of this study: Dr. M.D. Dampier of the Mathematics Department for helping me derive the viscosity increment for tri-axial ellipsoids, Dr. K. Brodlie of the Computing Advisory Services for helping me with the programming, particularly in the early stages; Drs. J. Rallison & J. Hinch from Cambridge for helpful discussions on suspension rheology; Professor B. Jennings and Drs. V. Morris and A. Foweracker of Brunel University, Dr. Houssier of Liege University and Dr. J. Jost of the Union Oil Company, California for discussions and communications on electric birefringence, Dr. R. Dale of the Patterson Laboratories on the limitations of fluorescence depolarization, and Mr. A. Pancholi of this laboratory for permission to use his viscosity data for hemoglobin.

I am grateful to the Science Research Council for a Research Studentship and also Fisons Pharmaceuticals Limited for financial assistance during this study.

I would like to thank my friends and colleagues in this Department for making my stay here an enjoyable one, and finally my Mother for her great patience whilst typing this manuscript.