HYDRO: A Computer Program for the Prediction of Hydrodynamic Properties of Macromolecules

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ABSTRACT HYDRO is a program for the calculation of sedimentation and diffusion coefficients, rotational relaxation times, and intrinsic viscosities of rigid macromolecules of arbitrary shape that are represented by bead models. Actually, HYDRO contains various FORTRAN callable subroutines that can be linked to the user's own programs to account for variability of shape or flexibility. Some hints are given for the use of HYDRO in various situations.

INTRODUCTION

Hydrodynamic properties, such as sedimentation or diffusion coefficients, rotational relaxation times, and the intrinsic viscosity are simple and commonly employed sources of information about the overall structure and dynamic behavior of biological and synthetic macromolecules in solution. In particular, biological macromolecules usually exhibit very peculiar shapes that cannot be represented by the few geometries, like ellipsoids or cylinders, for which hydrodynamic properties can be calculated from simple, analytical formulas. For the calculation of hydrodynamic properties of particles with an arbitrary shape, bead modeling was proposed by Bloomfield et al. (1967). The rationale is that an arbitrary shape can be modeled using spherical beads of varying size, either filling the space of the particle or covering its surface. A more rigorous treatment was presented some years later (Garcia de la Torre and Bloomfield, 1977) and since then, continuing work has been devoted to improvements to make the hydrodynamic treatment more exact and the computational procedure more efficient. A standard reference for the description of theory and applications is the review by Garcia de la Torre and Bloomfield (1981), with further details covered in subsequent reviews (Garcia de la Torre, 1989, 1992).

PROGRAM DESCRIPTION

HYDRO is a computer program for the calculation of hydrodynamic properties of rigid macromolecules or particles that embodies all the theoretical and computational advances. It actually consists of a suite of FORTRAN-callable subroutines that can be linked to user programs. Actually, HYDRO is the name of the highest-level subroutine. It accepts the geometry of the bead model as determined by the Cartesian coordinates of the centers of the beads and their Stokes radii. Other data regarding the solvent and the solute may be required such as the temperature, the solvent viscosity, and, if available, the molecular weight of the macromolecule and the buoyancy factor. Then HYDRO yields the following physical properties: translational diffusion coefficient, sedimentation coefficient, rotational relaxation times (up to five, for a general body), intrinsic viscosity, Scheraga-Mandelkern parameter, radius of gyration, and volume of the model.

The molecular weight is required for the calculation of the intrinsic viscosity. If it is unknown, the program will report the product of the these two quantities. The buoyancy factor, and the molecular weight are required for the calculation of the sedimentation coefficient. If any of them is unknown, this coefficient will not be computed. We also note that the rotational coefficients, the intrinsic viscosity, and the radius of gyration include a correction that accounts for the finite size of the beads (Garcia de la Torre, 1989).

At the core of the theoretical treatment and numerical procedure there is the inversion of a "supermatrix" of dimension $3N \times 3N$ (where N is the number of beads in the model) that accounts for hydrodynamic interactions between beads. The formalism in our early publications (Garcia de la Torre and Bloomfield, 1981) was later modified in order to handle a symmetric form of the supermatrix, which is equivalent to the diffusion tensor of the system (Garcia de la Torre, 1989). The advantage is that the numerical inversion of a symmetric matrix consumes less computer time and memory. For this step we have found very convenient the use of subroutine LINV1P of the IMSL library. Following the protocols of this library, the symmetric supermatrix is arranged within HYDRO as a monodimensional array. If that subroutine is not available, the user can easily modify the source code to adapt it for another specific matrix inversion subroutine.

We also provide a self-contained version of HYDRO in which a general-purpose matrix inversion subroutine, which is indeed used in various stages of the calculation, is employed also to invert the $3N \times 3N$ supermatrix, thus avoiding the need for access to the IMSL library or rewriting code. The file containing this version is distinguished with a different name, HYDROX. As the matrix inversion does not take advantage of the symmetry of the supermatrix, the CPU time may be several times longer than with the other version.

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Within the package there is a lower-level subroutine, TRV (which is actually called by HYDRO), that handles quantities in a reduced, dimensionless form. Although calculation at this level is not so straightforward, it may be useful in some cases in when one wants to avoid reference to a particular solute/solvent system, or when one wishes a closer control of details of the hydrodynamic treatment. This may be suitable also for calculations intended for theoretical purposes. At this level the only data required are the number of beads and their coordinates and radii, expressed in some unit of length. The main results are, as before, the hydrodynamic coefficients and the size of the model, but now are given in reduced, dimensionless forms. TRV also allows the user to control the type of hydrodynamic interaction to be used in the calculations, including the cases with Oseen interaction, modified-Oseen interaction, and without interaction. The no-interaction case is only interesting for some theoretical purposes, and the modified Oseen type is the recommended choice for practical purposes (this is actually the option when HYDRO calls TRV).

In addition to the main properties listed above, other interesting quantities are the components of the translational, rotational and coupling diffusion tensors. Their values are not given by the HYDRO subroutine but they can be obtained, in reduced form, at the level of TRV. The characterization of the rotational dynamics of macromolecules is usually made by means of optical, electro-optical or spectroscopic techniques, such as dynamic light scattering (Berne and Pecora, 1976), transient electric birefringence or dichroism (Wegener et al., 1979), and fluorescence anisotropy decay (Belford et al., 1972). The pertinent time correlation or decay function contains up to five components whose time constants are the relaxation times that have been described above. The complete prediction of such decay curves requires, furthermore, the amplitudes associated to each component. The calculation of the amplitudes is made in terms of the components of some electro-optic or spectroscopic tensors or vectors referred to the principal axes (eigenvectors) or the rotational diffusion tensor, yielded by TRV.

We finally give some hints for the use of HYDRO. A simple situation in the use of HYDRO would be that in which a main program takes the coordinates and radii from an input file and a single call to HYDRO is made to calculate the properties. In more typical situations, some geometrical parameters of the model may be variable. Then, the program calling HYDRO would calculate coordinates and radii and next it would call HYDRO for each set of those parameters. Another common case is that of models having some type of flexibility, for which the so-called "rigid body" procedure can be used. In this approach, the hydrodynamic properties are calculated as conformational averages over values obtained for a number of conformations, which are regarded as instantaneously rigid particles. The conformations are generated by Monte Carlo simulation or other procedures. Typically, a higher program would call first a subroutine that generates the conformation. The coordinates are stored in the pertinent common block. Then, subroutine HYDRO would calculate the properties. This is done many times, and the final values are the averages over the sample of conformations. Examples of this scheme can be found in the literature (Hagerman and Zimm, 1982; Garcia Bernal et al., 1991; Freire and Garcia de la Torre, 1992).

Program files. The ASCII file HYDRO.FOR contains the FORTRAN code for all the required subroutines except IMSL's LINV1P subroutine. HYDRO.EXE is an executable for PCs under MS-DOS. HYDRO.DAT contains a sample of input file and the corresponding output. A long write-up User's Manual is contained in the PostScript file HYDROMAN.PS. This file will be available at the Biophysics Internet Server or from the authors, who can also provide a printout of the manual.

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