The HYDRO suite of programs for rigid-particle hydrodynamics

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Introduction

The hydrodynamic and other solution properties of rigid macromolecules or particles of arbitrary shapes can be calculated using a methodology that is known as bead modelling. This approach has two variants (1). One of them is bead modelling in a strict sense, in which the particle is represented as an assembly of spherical elements of arbitrary shape, whith the only condition that the overall size and shape of the particle must be as close as possible to that of the particle. The other variant is shell modelling, in which the *surface* of the particle is represented by a shell of small elements ("minibeads"); the results are extrapolated to a zero minibead radius. This procedure is slightly more computing intensive than bead modelling, but it is hydrodynamically more rigorous and avoids problems (like bead overlapping) that had usually troubled the use of the first method.

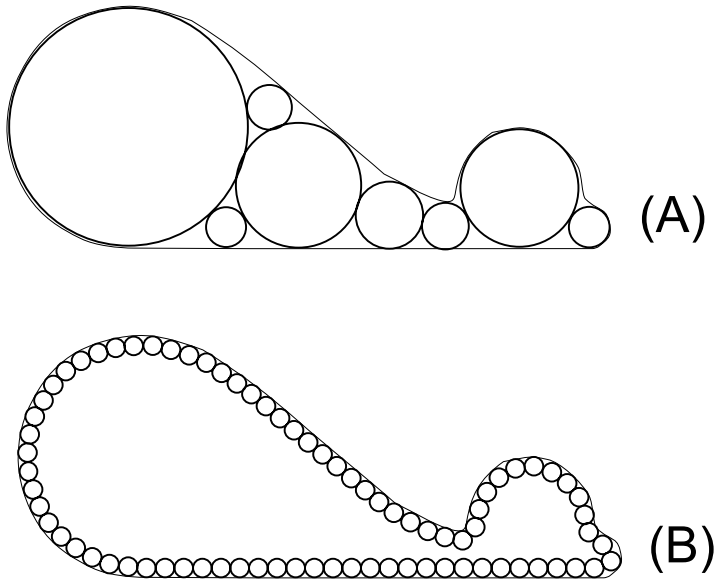

Figure 1. Schematic representation of (A) a bead model in strict sense (B) a shell model.

The computer program HYDRO has been available for a long time, for calculations with bead models. However, an additional problem has been to build the model itself, i.e. the list of Cartesian co-ordinates of the beads which are the primary data for the

hydrodynamic calculations. This is particularly difficult for shell modelling. Therefore, our work in this area during the last few years has been directed to the development of computer programs that, in addition to the hydrodynamic calculation itself, would also include the process of build modelling. These programs consider a variety of situations that are commonly found, like globular proteins, multisubunit structures, etc.

Thus, HYDRO is now a suite that includes a number of computer programs, which is described in this communication.

Computer programs

HYDRO (2) is a program for the calculation of hydrodynamic coefficients and other solution properties of rigid macromolecules, colloidal particles, etc, employing bead models in strict sense, as mentioned above. The user of HYDRO has to build previously the bead model, which will be specified as a list of Cartesian co-ordinates and radii of the beads. An example of a bead model, is given in Figure 2

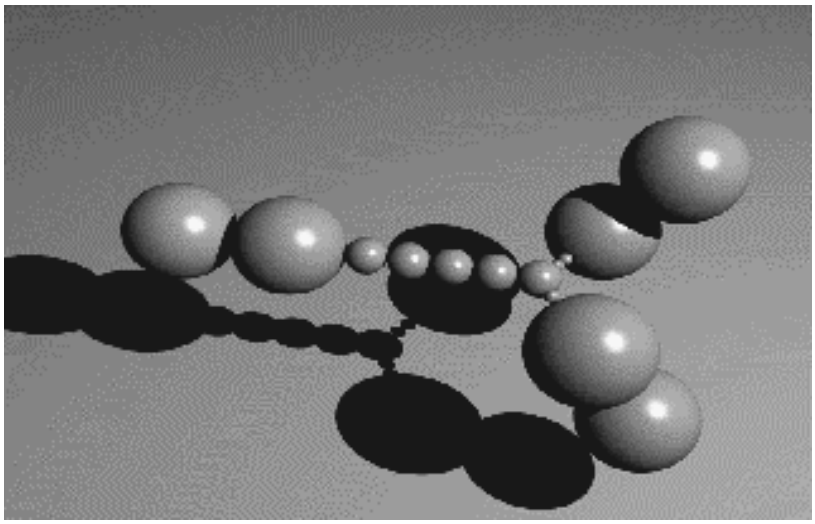

Figure 2. A bead model for the human antibody molecule IgG3

HYDROPRO (3) computes the hydrodynamic properties of rigid macromolecules (globular proteins, small nucleic acids, etc) from their atomic-level structure, as specified by the atomic coordinates taken from a PDB file supplied by the user, from which the proper hydrodynamic model is built by the program itself. The HYDROPRO calculation comprises was the basic hydrodynamic properties: translational diffusion coefficient, sedimentation coefficient, intrinsic viscosity, and relaxation times, along with the radius of gyration. Optionally, HYDROPRO computes also other solution properties such as the covolume (related to the second virial coefficient) and scattering related properties such as the angular dependence of scattering intensities and the distribution of intramolecular distances.

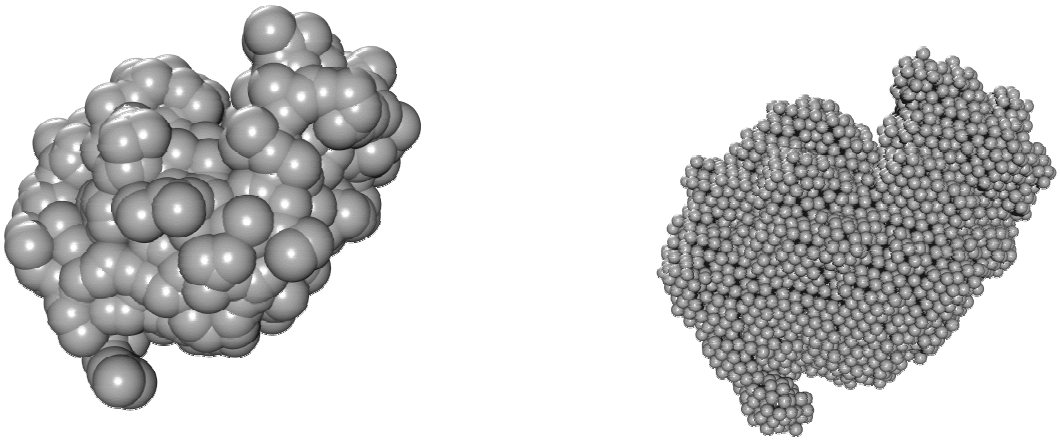

Figure 3. Left: A primary bead model of lysozyme, showing bead overlap. Right: A shell model, produced by HYDROPRO or HYDRONMR

HYDRONMR (4) is a computer program intended for the calculation of NMR relaxation of small, quasirigid macromolecules for structures, with atomic resolution. Like in HYDROPRO, the atomic coordinates are taken from a PDB file. The basic hydrodynamic quantities that are involved in dynamic NMR are evaluated in the same fashion as in the closely related HYDROPRO program. Thus, HYDRONMR calculates NMR quantities like the longitudinal and transversal (spin-spin and spin-lattice) relaxation times, T1, T2, NOE, etc. for each residue of a globular protein (the 15N-H and 13Cα -H vectors are calculated by the program itself). Alternatively, an user-supplied list of vectors can be given. HYDRONMR also reports the translational diffusion coefficient, which is available, among other sources, from some NMR experiments.

HYDROMIC (5) is a computer program for the calculation of solution properties of macromolecular or supramolecular structures determined by cryo-electron microscopy

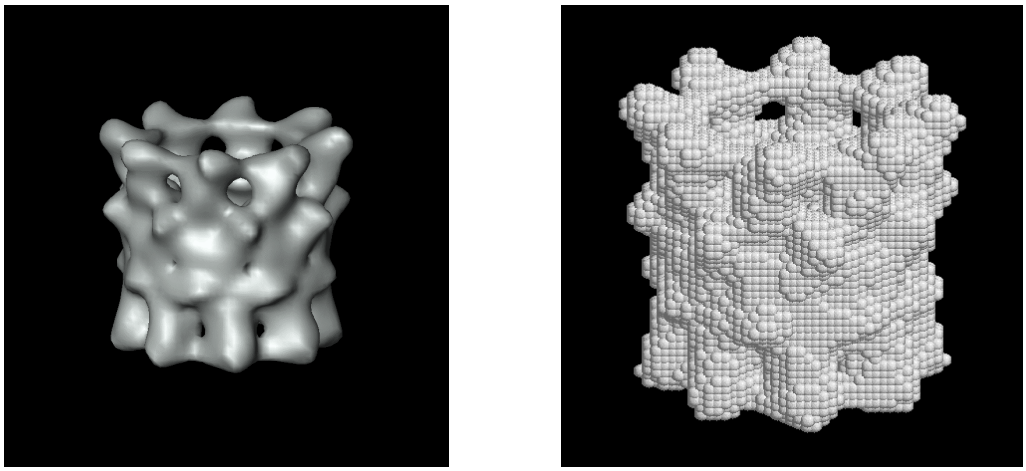

Figure 4. The cryoelectron-microscopy (spider file) reconstruction of the apo form of CCT chaperonin and its shell model

or related techniques. The structure is specified by a so-called *spider* file, which is a file format quite common in electron microscopy. Structures of large macromolecules, and macromolecular complexes may be available in this file. In this mode, HYDROMIC reads a *spider* file, builds from it an appropriate hydrodynamic model, and proceeds with the calculation of properties, including hydrodynamic coefficients, scattering-related quantities, etc.

HYDROPIX (6) is a computer program for the calculation of solution properties of macromolecular or supramolecular structures having an arbitrary shape, using bead-shell models. The task of building and specifying the hydrodynamic model is left to the user, but for this purpose we provide an ancillary FORTRAN program, MAKEPIXB, which just requires some extra lines of FORTRAN code that specify the dimensions and shape of the structure.

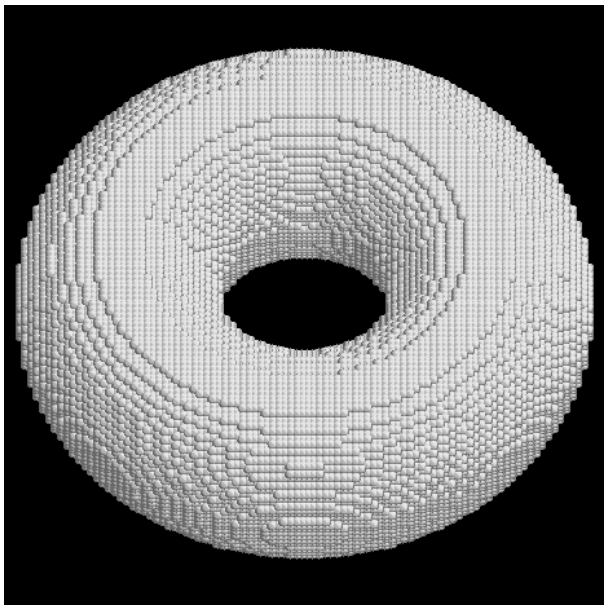

Figure 5. Shell model for a toroid, used in the HYDROPIX calculation

MAKEPIXB produces an intermediate, structural file which is read by HYDROPIX for the hydrodynamic calculations.

HYDROSUB (7) is intended for the calculation of solution properties of a macromolecular or supramolecular structures modelled as an assembly of subunits having ellipsoidal (prolate, spherical or oblate) and/or cylindrical shapes. The subunits are represented using a variation of the bead-shell method, which is particularly suitable for symmetric structures. The user just has to specify, for each subunit, the coordinates of their centers and the polar angles of their symmetry axis.

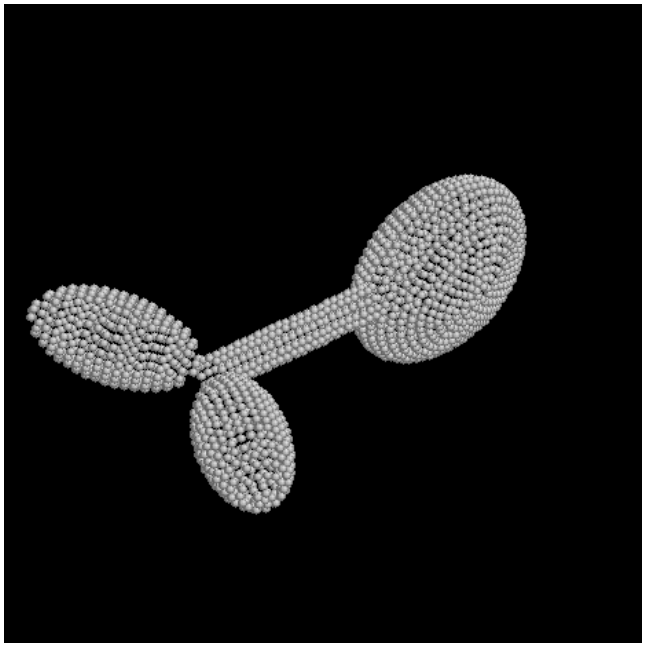

Figure 6. Shell model for a IgG3 molecule, generated with HYDROSUB, showing the two prolate Fab subunits, the oblate Fc subunit and the long (nearly rodlike) hinge. The molecule is the same as that in Figure 2; note the difference between a bead model and a shell model

Finally, the HYDRO suite is completed with the ancillary program SOLPRO (8,9). The programs of the HYDRO collection (HYDRO, HYDROPRO, HYDROMIC, HYDROSUB, HYDROPIX,...) provide the basic solution properties, including hydrodynamic coefficients, radius of gyration and covolume, scattering-related properties, etc. SOLPRO takes the results produced by those programs and performs the calculation of two other classes of solution properties:

- Time dependent properties, including (1) Fluorescence anisotropy decay; (2) Electric birefringence and electric dichroism decay (3) Decay of the function <P2(t)> for a particle-fixed vector, <P2(t)> being a shorthand notation for the time-dependent function $<(3\cos^2(\vartheta)-1)/2>$, where is ϑ the angle subtended by two orientations of that vector separated by time t.
- Shape-dependent, size-independent quantities, like the Perrin parameter P (also known as f/f_0), the viscosity increment (Einstein-Shima parameter), the Flory parameters for translational diffusion and intrinsic viscosity, and many, many others.

Availability

All these programs are freely available. We have produced executables for a variety of plataforms, including MS DOS/Windows, Linux, Silicon Graphics and Compaq (Digital) Alpha. Each program has its corresponding User Guide, as well as sample

input and output files. All this material will be available from our web site, whose present address is http://leonardo.fcu.um.es/macromol . Further help can be obtained from jgt@um.es

Acknowledgment

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References

(1) B. Carrasco and J. Garcia de la Torre, "Hydrodynamic properties of rigid particles. Comparison of different modeling and computational strategies". *Biophys. J.* 76, 3044-3057 (1999).

(2) J. Garcia de la Torre, S. Navarro, M.C. Lopez Martinez, F.G. Diaz, J. Lopez Cascales. HYDRO. A computer software for the prediction of hydrodynamic properties of macromolecules. *Biophys. J.* 67, 530-531 (1994).

(3) J. Garcia de la Torre, M.L. Huertas and B. Carrasco, "Calculation of hydrodynamic properties of globular proteins from their atomic-level structure. *Biophys. J.* 78, 719-730 (2000)

(4) J. García de la Torre, M.L. Huertas y B. Carrasco. "HYDRONMR: Prediction of NMR relaxation of globular proteins from atomic-level structures and hydrodynamic calculations", *Journal of Magnetic Resonance* B, 138-146 (2000).

(5) J. García de la Torre, J.M. Valpuesta and J.L. Carrascosa, "HYDROMIC: Prediction of hydrodynamic properties of rigid macromolecular structures obtained from electron-microscopy images" *Eur. Biophys. J.*, 30, 457-462 (2001).

(6) J. García de la Torre, "Building hydrodynamic bead-shell models for rigid bioparticles of arbitrary shape" *Biophys. Chem.*, 94, 265-274 (2001).

(7) J. García de la Torre and B. Carrasco, "Hydrodynamic properties of rigid macromolecules composed of ellipsoidal and cylindrical subunits", *Biopolymers* 63, 163-167 (2002).

(8) J. Garcia de la Torre, B. Carrasco and S.E. Harding. "SOLPRO: theory and computer program for the prediction of SOLution PROperties of rigid macromolecules and bioparticles". *Eur. Biophys*. J. 25, 361-372 (1997)

(9) J. Garcia de la Torre, S.E. Harding and B. Carrasco. "Calculation of NMR relaxation, covolume and scattering of properties of bead models using the SOLPRO computer program". *Eur. Biophys. J.* 28, 119-132 (1999)