File:hydrosub7c-sub.doc

HYDROSUB

Version 7c, December 2005

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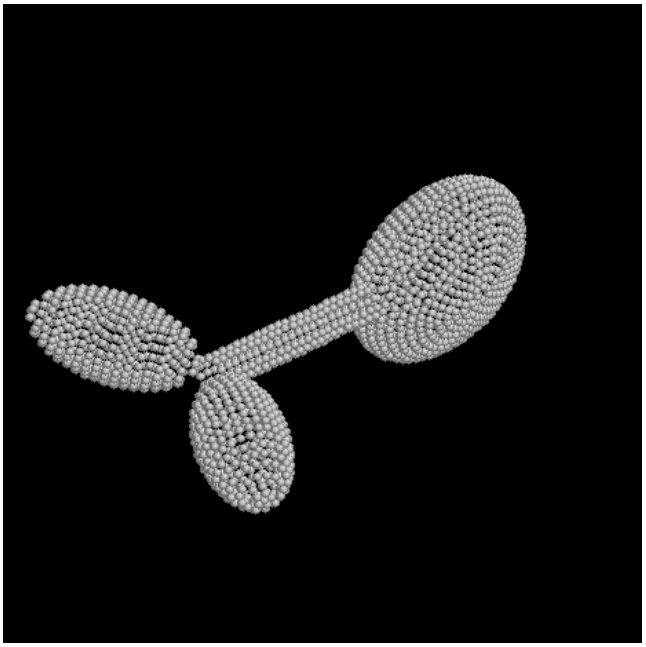
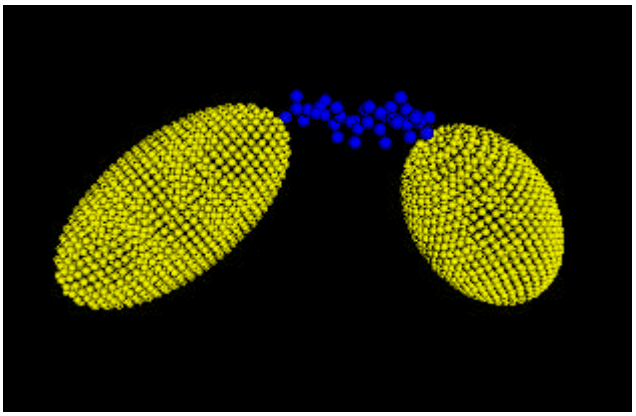
1. Introduction to HYDROSUB

HYDROSUB is a computer program for the calculation of solution properties of a macromolecular or supramolecular structure modeled as an assembly of *subunits* having ellipsoidal (prolate, spherical or oblate) and/or cylindrical shapes. The model may also contain *spheres* that may represent linkers, connectors, protuberances, etc

For instance, the next figure shows the hydrodynamic model for an antibody molecule with two prolate Fab subunits, an oblate Fc subunit, and the hinge, which is represented by another, cylindrical subunit (alternatively, it could be represented by a string of beads)



As an example with subunits connected by strings of beads, we present the following model, which was treated in our *Eur Biophys J* 2003 paper (see below). The model has been chosen by the Journal to illustrate its habitual cover.



2. Literature

The primary reference for HYDROSUB is:

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

If you wish to cite also the theoretical work on which the bead modeling procedure is based, a proper cite is our 1981 review in *Quarterly Reviews of Biophysics*. In our 1999 paper in *Biophysical Journal*, you can find an update of the theory, and a discussion on bead and shell modeling methodologies:

- J. Garcia de la Torre and V.A. Bloomfield, "Hydrodynamic properties of complex, rigid, biological macromolecules. Theory and applications". *Q. Rev. Biophy.*, 14, 81-139 (1981)

- 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).

The possibility of employing HYDROSUB for the Monte Carlo calculation of solution properties of flexible structures has been described recently. It is based on a piece of source code named MONTESUB. If you employ this feature, in addition to the *Biopolymers* paper, the following reference should be considered:

- J. García de la Torre, H.E. Perez Sánchez, A. Ortega, J.G. Hernández, F.G. Diaz and M.C. Lopez Martinez, " Calculation of the solution properties of flexible macromolecules: Methods and applications", *Eur. Biophys*. J. 32, 477-486 (2003).

3. Running HYDROSUB. Input data files

As in all the HYDRO family of programs, you will have to supply two input data files: (a) the main input data file, which will specify primary data such as temperature, solvent density, etc.; and (b) a structural data file, which will contain the information about the structure or geometry of the macromolecule or particle that you are considering.

In the case of HYDROSUB, the structural information will contain information on the size and shape of each subunit and its placement within the whole particle. This will be provided by the user in an ASCII file whose strucuture and contents are given in section 3.d.

The name of the main input data file for HYDROSUB will be `hydrosub.dat,` and it will contain the following lines:

3.a. First part of the input file.

Basically this part provides the information on the structure of the macromolecule. It contains the following lines (the FORTRAN types are specified):

- TITLE(`CHARACTER*20`) Title of the calculation

- FILENAME (`CHARACTER*30`)Name to be used for the various output files corresponding to each subcase in a many-cases execution. The various files produced will have names of the form `filename.xxx`, where xxx is an extension depending on the file type (see section 4 below). This name would eventually include the path for the files.

- INPUT (`CHARACTER*30`) Name of the strucutural file, eventually including its path.

HYDROSUB employs the shell-model methodology. The primary hydrodynamic model is not used in the hydrodynamic calculations. Instead, a shell model , composed of 'minibeads' of radius sigma is employed to represent each ellipsoidal or cylindrical *subunit*, and extrapolation to the shell model limit of sigma=0 is carried out. The *additional spheres* that compose the optional connectors, protuberances, etc are not shell-extrapolated; they remain as beads of fixed size in the successive iterations of the shell-model extrapolation. For the purpose of shell-modeling, the following information has to be supplied next in the main input data file

- NSIG (`INTEGER`) Number of values of the radius of the minibead. This radius will range from SIGMIN to SIGMAX. It must be greater than 2 (typically 5 to 8). There is also the possibility of letting to the program the task of estimating the two extreme values of sigma; this will be indicated giving the value –1 for NSIG, and in this case you will omit the two following lines with the values of SIGMIN and SIGMAX.

- SIGMIN (`REAL`) Lowest value of sigma, the minibead radius

- SIGMAX (REAL) Highest value of sigma, the minibead radius

The smaller the size of the minibeads, the larger the number of them needed to cover the surface of the particle. The present version of the program works with a maximum of 2000 minibeads. If SIGMIN is too small, an error message will be obtained and the program will stop. The value of SIGMAX should be taken such that the number of minibeads is not too small, say in the range 200-400.

3.b. Second part of the input file.

This part provides information on some basic properties of macromolecule and solvent. It contains the following lines:

- T (REAL) Temperature, Kelvin
- ETA (REAL) Solvent viscosity, poises
- RM (REAL) Molecular weight .
- VBAR (REAL) Partial specific volume, cm^3/g
- RHO (REAL) Solution (approx. Solvent) density, g/cm^3

3.c. Third part of the input file.

This part is intended for the calculation of some non-hydrodynamic properties that, in previous versions of our software, were considered separately in the computer program SOLPRO. This properties are the scattering form factor (Debye expression), the distribution of intramolecular distances, and the covolume, and are calculated from the coordinates of the spheres.

For bead models, this calculation is made from the bead coordinates and sizes.

The data that you have to supply are:

- NH(INTEGER), the number of values of the scattering (angular) variable, h. If you wish to omit the scattering calculation, the value given here should be 0, and the following line (HMAX) is omitted.
- HMAX (REAL), the largest value of h (cm^{-1}), so that the scattering variable will range from 0 to HMAX
- NS(INTEGER), the number of intervals for the distribution of distances. The values of the intramolecular distances will be varied between 0 and the longest distance, which is determined by the program. If you wish to omit the calculation of the

distribution of distances, the value given here should be 0, and the following line (RMAX) is omitted.

- RMAX (REAL), the maximum length for the calculation of the distribution of distances (in cm). If you give any negative value, it is understood that RMAX will be the longest distance in the model, which is calculated by the program. The value will be given in the same units as the coordinates and dimensions in the structural file.

- NTRIALS (INTEGER) is the number of trials or MonteCarlo moves in the calculation of the covolume. Set this value to 0 if you wish to omit the covolume calculation. Recall that this calculation is very time-consuming, and must be restricted to models with not too many beads.

The most important quantities related to translational and rotational diffusion are the translational and rotational diffusion coefficients and the rotational relaxation times. The program will give you these quantities. For some special purposes you may also want the full 6x6 diffusion tensor, which contains the 3x3 translational diffusion tensor, rotational diffusion tensor, and the translation-rotation coupling tensor, as well as the center of diffusion.

- IDIF is a flag that indicates (if IDIF is 1) that you wish a detailed report of the diffusivity of the particle, including the full (anisotropic) translational, rotational and coupling tensor, and the position of the hydrodynamic (diffusion) center.

3.d. End of calculation or next case

- Next or final line: If this case is the only or the final one, in the next line you will put an asterisk followed by 19 spaces.

3.e. The structural file for HYDROSUB.

Prior to the HYDROSUB calculation, you have to build a structural file that specifies the size and shape of the particle that you are considering. Positions and orientations of the subunits are referred to an arbitrarily chosen system of Cartesian axis. You have to specify, for each subunit:

- The type of the subunit, given by ITYPE (INTEGER) which can take the following values: 1(prolate), 2(uncapped cylinder), 3(oblate), 4 (capped cylinder or disk)
- The subunit sizes, in Angstroms, given by SEMILONG and SEMISHORT (both REAL). For ellipsoids, SEMILONG and SEMISHORT are, respectively, the longest and shortest semiaxes. For cylinders, SEMILONG and SEMISHORT are, respectively, **half** of the length and the radius. A disk is a cylinder for which SEMILONG is half of the height or thickness.
- The Cartesian coordinates, in Angstroms, XCEN, YCEN, ZCEN (all REAL)of the geometric center or each subunit
- The spherico-polar angles THETA and PHI in degrees(both REAL), that specify the orientation of the main (revolution symmetry) axis of the ellipsoid or cylinder. THETA is the angle subtended by the main particle axis and the Z Cartesian axis.

PHI is the angle subtended by the projection of the main particle axis on the (X,Y) plane and the X Cartesian axis.

- If there are additional spheres, the number of them, and their coordinates and radii

The structural file can have any name, and its contents will be:

- A first line with the value of NSUB(`INTEGER`), the number of subunits
- A number of lines equal to NSUB, containing (separated by spaces) the values of ITYPE, XCEN, YCEN, ZCEN, THETA, PHI, SEMILONG and SEMISHORT
- Next line, NSPHER, the number of additional spheres (if there are not such spheres, give 0 (zero) in this line
- If NSPHER is not zero, the following NSPHER lines will contain the coordinates, X, Y and Z, and the radius, E of the subunits

4. Output files

Several files are produced at execution time. There will be a set of files for each case included in a single run. All these files will have a common name, given by the filename specified for each case in the input file, and a different extension. The extensions correspond to:

- `.res` Output file containing the mains results, with the name specified in the input file
- `.bea` is a a pdb-formatted file containing the coordinates of the shell model, to be viewed with RASMOL. This is intended for models with identical beads, as in shell models without extra beads. If there are extra beads, with sizes different from those of the shell beads, the extra beads will appear with the same radius as the shell beads. NOTE: Do not forget to specify: Display / SpaceFill in the RasWin menu to see the the visualization files.
- `.vrml` is a VRML-formatted file containing the coordinates of the shell model, that can be viewed with a VRML viewer, like Cortona(for models with only subunits, without additional spheres). See our separate VisualBeads user Guide.
- `.sol` is an ASCII file containing data needed if you wish to run the separate program SOLPRO

Other files are:

- `summary.txt` is a numeric archive containing a line for each case in the calculation.

(a) If there was no distance distribution calculation and no scattering calculation, this file has 13 columns containing (1) first 10 characters of title; (2) translational diffusion coefficient; (3) radius of gyration; (4) volume; (5-9) the five relaxation times; (10) intrinsic viscosity; (11) sedimentation coefficient; (12) longest distance; (13) covolume. (b) If there was either distance distribution

(b) If there was scattering function calculation, *P(h)*, with a number of values NH, with NH not greater than 100, then the above columns will be followed by NH+2 columns containing NH, HMAX, and the values of the distribution function corresponding to the NS intervals (centered at h_i=[i+0.5]HMAX/NH

(c) If there was distance calculation *p(r)*, with a number of values NS, with NS not greater than 101, then the above columns will be followed by NS+2 columns containing NS, RMAX, and the values of the distribution function corresponding to the NS intervals (centered at r_i=[i+0.5]RMAX/NS

As mentioned above, HYDROSUB can be employed to obtain solution properties of flexible structures by the Monte Carlo method. Using a user's program based on our MONTESUB source code (see the Instructions for that program), it is possible to generate the `hydrosub.dat` file for a multi-case execution, along with the structural files. Each case would correspond to a possible conformation of the flexible particle, and in the spirit of the Monte Carlo procedure, the final properties would be the averages of the individual values. The values for each conformation are contained in `summary.txt`, so that you may, for instance, export this file to an Excel spreadsheet in which you can carry out the Monte Carlo averages.

5. Hints and notes

- The molecular weight is used in the calculation of the intrinsic viscosity and the sedimentation coefficient, and the specific volume of the solute and the solution density are only used for the sedimentation coefficient. If you do not know these quantities, you may give then some approximate or estimated values in the data files. HYDROSUB will still be useful, because all the other solution properties (diffusion coefficients, relaxation times, radius of gyration, scattering properties, covolume, etc) will be correct.

6. Release notes

This is the third released version of HYDROSUB (the second one was Version 5b, October 2003). The main changes in this version are:

- Calculation of non-hydrodynamic properties: radius of gyration and volume of the model, scattering function, distribution of distances and covolume
- File `summary.txt` contains the results for the distance distribution and the scattering function.
- Visualization of the model in the VRML format

In future releases this section will contain a description of the main changes.

This program has been developed in a Windows PC. The MS DOS/Windows executable can be started from Windows, but we advise to open a MS DOS session in a window for program execution, while doing the other tasks (editing, visualization, etc) as usually in

Windows.

This program will be available also for other platforms: Please consult our web site:

http://leonardo.fcu.um.es/macromol/

IMPORTANT: *Valuable information on the usage and availability of this and other programs can be found in the FAQs section of our web site. Inquires about other questions not covered in this manual or in the FAQs are welcome, although I do not promise an immediate response.*