

# HYDRONMR and Fast-HYDRONMR

Version 7c, September 2004

## Index

1. Introduction to HYDRONMR
2. Literature
3. Running HYDRONMR. Input data file
4. Output files
5. Notes and hints
7. Release notes

## 1. Introduction to HYDRONMR and Fast-HYDRONMR

HYDRONMR is a computer program intended for the calculation of NMR relaxation of small, quasirigid macromolecules whose structure, with atomic resolution, is taken from a PDB file of atomic coordinates. For this purpose, the basic hydrodynamic quantities that are involved in dynamic NMR are evaluated in the same fashion as in the closely related HYDROPRO program. Then, HYDRONMR calculates NMR quantities like T1, T2, NOE, etc. for each residue of a globular protein (the  $^{15}\text{N}$ -H and  $^{13}\text{C}\alpha$ -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.

Fast-HYDRONMR is a version of the same program which employs an approximate, but much faster hydrodynamic treatment. With the cost of a small loss in accuracy, the Fast-HYDRONMR is much faster: less than one second of CPU time, compared with about 3 minutes with HYDRONMR. If CPU times of the order of minutes are acceptable for you (as we expect to be the case for most users), we advise to employ HYDRONMR. The use of Fast-HYDRONMR can be advantageous in situations where calculations have to be done for many structures. We recall that the T1/T2 values obtained with the two programs may be slightly different; however the two procedures give practically the same results for  $\nabla$  values of the residues.

## 2. Literature

The primary reference for HYDRONMR is:

- 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*, 147, 138-146 (2000).

If you employ Fast-HYDRONMR, in addition to the primary reference you also should cite:

- A. Ortega and J. García de la Torre, “Efficient, accurate calculation of rotational diffusion and NMR relaxation of globular proteins from atomic-level structures and approximate hydrodynamic calculations”, *J. Am. Chem. Soc.* 127, 12764-12765 (2005).

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. Biophys.*, 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).

### **IMPORTANT: HYDRONMR vs. Fast-HYDRONMR**

- The procedures to run both programs are identical. Thus, hereafter we mention just HYDRONMR.
- The “clever” corrections that make the approximate hydrodynamics in Fast-HYDRONMR quite accurate are not valid for translational diffusion. Thus, although the present version of the program still report the translational diffusion tensor and coefficient, these results must be ignored. For the calculation of the translational diffusion, please use HYDRONMR or, if you just want translational diffusion, you may simply employ HYDROPRO.

### **3. Running HYDRONMR. Input data files**

**IMPORTANT:** HYDRONMR and Fast-HYDRONMR are used identically. Hereafter we mention just HYDRONMR.

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 HYDRONMR, the structural file is just the PDB file containing the atomic

coordinates. The name of the structural file will be one of the data in the main input data file. The name of the main input data file for HYDRONMR will be `hydronmr.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 PDB file with the atomic coordinates, eventually including its path.
- `AER ( REAL )` Effective radius (angstroms) of the atomic elements *[a]*, *[b]*

HYDRONMR 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 derived from it, and extrapolation to the shell model limit of  $\sigma=0$  is carried out. For this purpose, 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. It must be greater than 2 (typically 5 to 8). The radius will range from `SIGMIN` to `SIGMAX`. 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

### 3.c. Third part of the input file.

This part is specifically intended for calculation of NMR-related quantities. Presently, this includes: (1) anisotropy of rotational diffusion ; (2) spectral densities and relaxation times for specific dipoles. The first line is:

- IFLAG (INTEGER) Flag that indicates the source of the vectors (dipoles) for which NMR relaxation parameters and dipolar couplings will be calculated. The possibilities are:
  - \* = 0 No calculations for dipoles; only anisotropy of rotational diffusion [c].
  - \* = 1 N-H bonds, implicit hydrogens, not given in pdb [d].
  - \* = 2 N-H bonds, explicit hydrogens, given in pdb.
  - \* = 3 C-H bonds, implicit hydrogens, not given in pdb [d].
  - \* = 4 C-H bonds, explicit hydrogens, given in pdb
  - \* = 9 Dipoles taken from an user-supplied file

If IFLAG=0 the following lines will be omitted. Go to section 3.d.

- (Only when IFLAG=9) (CHARACTER\*30) Name of a (separate) file containing the vectors. The first line will contain NDIP, the number of dipoles (INTEGER, I3) . The following NDIP lines will contain the three components of the unitary vectors (REAL, space or comma-separated)
- GAMMAX (REAL) Gyromagnetic ratio of the X nucleus.
- RHX (REAL) Distance X-H in angstroms.
- DIFSIG (REAL) Chemical shift anisotropy, in p.p.m.
- NFIELD (INTEGER) Number of values of the magnetic field. This line will be followed by a number of lines equal to NFIELD, containing:
  - FIELD (REAL) magnetic field, in Teslas

### 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.

## 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 main results, with the name specified in the input file
- `.t12` Output file containing only the values of T1/T2 and Nabla, ready to be read or imported by other program. Contents is : 1<sup>st</sup> line: title; 2<sup>nd</sup> line: AER; next line: FIELD; following lines, for each residue, residue number, T1/T2 and  $\nabla$  ; next line, eventually, another FIELD; ... and so on.
- `-pri.bea` is a pdb-formatted file representing the primary hydrodynamic model, that can be viewed with RASMOL
- `-pri.vrml` is a VRML-formatted file containing the coordinates of primary hydrodynamic 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.

Other files are:

NOTE: Do not forget to specify: Display / SpaceFill in the RasMol menu to see the visualization files.

## 5. Hints and notes.

*[a]* At the present time a value of 3.2 Angstroms is recommended.

*[b]* The program will take into account all non-hydrogen atoms contained in the ATOM records of the PDB file, including non-protein atoms (HETATM records) except water oxygens.

*[c]* The option IFLAG=0 still produces a complete analysis of the fully anisotropic rotational diffusion tensor, reporting its components, eigenvalues and eigenvectors, etc.

*[d]* In the case of implicit hydrogens, the program will read the coordinates of either the alpha carbon (CA) or the amide nitrogens (N), and their two neighboring atoms in the polypeptide chain. Thus the coordinates of the missing hydrogen will be calculated, and from them the components of the CH or NH vector.

## 6. Release notes

The previous released version of HYDRONMR was `hydronmr5A-XXX.exe`. The main changes in this new version are:

- `.t12` and `-pri.vrml` files
- The previous version worked with the so-called estimated extrapolation method for the shell model calculation, intended for a bit faster calculation, which was activated with `NSIG=1`. Presently, this procedure is being reconsidered. Indeed, Fast-HYDRONMR provides now a much faster procedure. Then the estimated extrapolation is not present in this version.
- However, both HYDRONMR and Fast-HYDRONMR have we also include the convenient special case of “automatic” estimate of sigmas. (particular case with `NSIG=-1`).
- The number of dipoles (C-H or N-H vectors has been redimensioned to 2000).
- We recall, as noted in Section 2, that Fast-HYDRONMR is not adequate for translational diffusion. The program still reports translational diffusion tensor and coefficient, just because we have not removed the corresponding instructions. If you need translational diffusion, you must use HYDRONMR or HYDROPRO.

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. Executables of this program will be available for other platforms; please consult our web pages