CYANA 2.1 - New Features

Cyana 2.1 is an update of Cyana 2.0 that provides a number of enhancements and bug fixes. It is recommended to upgrade to Cyana 2.1.

- **CYANA under Windows XP:** CYANA is now fully supported on Windows XP systems with Cygwin, using the free g95 Fortran compiler.
- **Output of restraints in X-PLOR/CNS format:** Distance restraints and torsion angle restraints (with unambiguous assignment) can be saved in files in the format used by the programs X-PLOR and CNS. The new value 'pseudo=3' of the system variable 'pseudo' produces output for a pseudoatom QX in the form HX* used by X-PLOR and CNS.
- **Automated NOESY assignment:**
  - Offsets between different chemical shift lists are taken into account when matching peaks from different spectra. This improves the power of network-anchoring when NOESY spectra recorded under slightly different conditions are used simultaneously.
  - The new option 'changevol' of the 'noeassign' command allows to correct peak volumes based on the changes of upper distance limits by "elasticity".
  - Non-intraresidual distances are only used for network anchoring if they are restricted to less than 5 A by the covalent structure.
- **Assignment statistics for individual peak lists:** The new option '-l' of the 'cyanafilter' shell script provides detailed assignment statistics for each peak list used for automated NOESY assignment.
- **RMSDs to a reference structure in overview files:** The new 'reference=...' option of the 'overview' command allows to include RMSDs to a reference structure in overview (.ovw) files.
- **Residue library:** To conform with IUPAC recommendations, the Arg sidechain amide protons HH11 and HH12, and HH21 and HH22 have been exchanged in the standard residue library file, 'cyana.lib', and 'cyanasmall.lib'. The standard CYANA 2.1 atom names follow exactly the IUPAC recommendations. - Likewise, the atom names HB1/HB2 in HIST and HIS+ have been changed to HB2/HB3 in the residue library file 'special.lib' to be consistent with IUPAC nomenclature.
  - Lines in a residue library (.lib) file that are indented by 8 or more characters are treated as comments. This allows reading of previous libraries that containt comment blocks.
  - The correction of van der Waals radii that is applied to 1-4 interactions is written on the 'ATOMTYPES' line of the residue library file.
  - A 'README' file in the 'cyana-2.1/lib' directory describes the various residue libraries that come with Cyana 2.1.
- **Symmetric dimers:** Two new types of restraints have been introduced that improve the treatment of symmetric dimer structures. Identity restraints are harmonic potentials on the difference between corresponding torsion angles in the two molecules. They help to ensure identical structures of the two monomers. Symmetry restraints are harmonic potentials on the difference symmetry-related interatomic distances and can help to maintain the symmetry of the homodimeric structure. Various other problems relating to symmetric dimers have been resolved.
- **Large molecules:** The output of files for molecules with residue numbers > 999 (or < -99) is now possible. Bugs related to very large molecules have been fixed.

- **Calibration:** The new option 'iterative' of the 'calibration.cya' macro can improve automated calibration results when a large number of weak (predominantly artifact) peaks are present. This option can be particularly useful in conjunction with automated peak picking.
- **RMSD calculation:** A serious bug has been resolved in the 'rmsd' command. RMSD values to a reference structure were often not calculated correctly in Cyana 2.0.
- **Peak lists:**
  - Problems with the automatic recognition of peak list dimensions have been resolved.
  - Peak list specific chemical shift matching tolerances, as given by a '#TOLERANCE...' statement are written into output peak lists, if necessary.
  - The command 'peaks volumecal' has been replaced by 'peaks set ... volume=upl'.
  - The command 'peaks filter' to filter 3D peak lists based on a 2D peak list has been added.
  - The command 'peaks set ... w1=...' has been replaced by 'peaks set ... ppm1=...' etc.
  - The command 'peaks exclude' has been removed.
- **Chemical shift lists:**
  - Unreadable lines in an input chemical shift list can be skipped rather than triggering an error if the option 'unknown=warning' is set.
  - The 'read_all' command has been extended to allow for the reading of several chemical shift lists. This possibility is useful for chemical shift consolidation.
  - Minor bugs when working with a reference chemical shift list, and when working with peak list specific chemical shift tolerances have been corrected.
- **Consensus chemical shifts:**
  - When comparing results of chemical shift consolidation with a reference chemical shift list, differences within the same or nearby residues can be distinguished from "serious" errors by which no nearby chemical shift value matches. A new parameter 'nearby=...' has been added to the 'shift consolidate' and 'shift assign' commands.
  - If an assignment is different from the reference assignment, the atom with the closest matching reference assignment is indicated.
  - A statistics of the assigned, identical, different, non-neighboring, incompatible and additional assignments is made.
  - Bugs when transferring consolidation results into the chemical shift list have been resolved.
- **Selections:**
  - A bug with long (> 40 character) selections has been eliminated.
  - The new keyword 'WITHCOORD' selects atoms for which coordinates are available
  - Distance restraints can also be selected by peak number (option 'numbers=...').
  - Peaks can be selected by ppm values (options 'ppm1=...' etc.).
  - Peaks can be selected based on their deviation from the diagonal (options 'diagonal=...').
  - Minor bugs with random selections of peaks and distance constraints have been corrected.

- **Stereopair swapping:** In Cyana 2.0 chemical shift values but not their errors were exchanged when swapping a stereopair. This bug has been eliminated.
- **New or modified system functions:**
  atomlong - long atom descriptor (replacement of the former function 'Atom')
  ipel - order number of nucleus detected in a given dimension of a peak list
  narmsd - number of atoms superimposed for RMSD
  ndim - This function gives now an error message if no peak list(s) have been read yet.
- **New system variables:**
  weight_ide - weight for identity restraints
  weight_sym - weight for symmetry restraints
- **cyanafilter:** The new '-S' option of the 'cyanafilter' shell script allows to select peaks from a given input peak list.
- **Incomplete structures:** Various bugs related to structures with missing atoms, i.e. coordinate files that do not provide coordinates for all atoms that are expected based on the residue library, have been fixed.
- **Gradient check:** The command 'gradient' to numerically check the accuracy of the gradient calculation now shows an error message when applied to a "rigid" structure that cannot be modified by the program because it does not adhere to the standard geometry in the library.
- **Macro files that self-invoke Cyana:** Lines in a macro (.cya) file that start with 'exec' are ignored by Cyana. This allows macro files to be started from the command line by invoking Cyana from within the macro file.
- **g95 Fortran compiler:** Compilation with the g95 Fortran compiler is supported on Linux, Windows XP with Cygwin, and on MacOSX systems. Please note that the program runs significantly slower when compiled with 'g95' than with the Intel Fortran compiler.
- **Crash on SGI systems:** A bug, specifically on SGI systems, that was related to the "flushing" of files has been resolved.

CYANA 2.0 - New Features

This is an (incomplete) list of the new features of Cyana 2.0 compared to Cyana 1.x. Please see also the hints for a smooth migration from earlier Cyana versions.

- **Examples and Demos:** An updated and expanded collection of example files and demos are provided in the 'demo' subdirectory of the cyana-2.0 distribution.
- **Automated NOE assignment algorithm:** A new algorithm for automated NOE assignment replaces the former Candid method. All criteria for assignment are consistently formulated as probabilities. The new algorithm can in general tolerate larger uncertaincies in chemical shift values and peak positions, and is faster. In general, a higher number of NOEs can be assigned with the new algorithm. The 'cyanatable' script provides a quick overview over a running or completed automated structure calculation.
- **Violation confinement:** Violation confinement offers a new alternative to constraint combination in order to reduce the impact of erroneous restraints on the resulting structure in the initial cycles of structure calculations using automated NOE assignment. With violation confinement each assigned NOE yields a corresponding distance restraint for which the maximal contribution to the target function is limited to that of that of a given, maximal violation. The latter can be set globally with the variable 'viocut', or for individual distance restraints.
- **Calibration elasticity:** The standard calibration method for automated structure calculations is simplified in that the upper distance limits are dependent only on the peak volume or peak height (not also on the initially unknown assignment). To account for small errors in the peak intensity NOE upper distance bounds that are consistently violated to a limited extent can automatically and individually be treated in a more conservative manner by "elastically" increasing the distance limit.
- **Chemical shift assignment during NOE assignment:** The NOE assignment algorithm can handle a significant number of unassigned chemical shifts. These can be entered into the calculation with the random coil value and a large uncertainty, letting the program find the chemical shift if sufficient NOESY data is available. In this way, structures can also be obtained with auotmated NOE assignment from less complete chemical shift lists.
- **NMRView peak lists:** Cyana 2.0 can handle NMRView peak lists with the new 'read xpk' and 'write xpk' commands.
- **Standard amino acid residue library:** The amino acid library has been completely revised. It is now based on the geometric parameters of Engh and Huber (Acta Crystallogr. A47, 392-400, 1991) instead of the ECEPP/2 force field. The atom nomenclature follows strictly the IUPAC recommendations. Van der Waals radii for the repulsive term of the target function have been increased significantly in order to produce structures with better packing.
- **Residue library handling:**
  - The library file has "free" format.
  - Residue definitions can be read from several different library files.
  - The command group 'library' has been added (see below).
- **Standard simulated annealing schedule:** The standard simulated annealing schedule has been improved in order to achieve better convergence of the structure calculations, especially when larger van der Waals radii are used.

- **PDB and BMRB submission:** The preparation of coordinate files for submission to the P[rotein Data Bank](#) (PDB) and of chemical shift lists for submission to the [BioMagResBank](#) (BMRB) is straightforward with the 'deposit' macro. Conformers in a file for PDB submission are superimposed and sorted such that the first conformer is closest to the average coordinates.
- **Some new commands (very incomplete list, to be completed):**
  library check - check library for inconsistencies (e.g. duplicate atoms)
  library mirror - create the mirror image of residue library entries (e.g. to handle D-amino acids)
  library new - create a new residue library entry based on an existing one
  library remove - remove selected residues, atoms, angles, atom types from a residue library
  library rename - rename selected residues, atoms, angles
  library replace - replace selected coordinates in the library with those of the current structure
  read xpk - read NMRView peak list file
  read bmrb - read chemical shift list in BMRB format
  shifts - commands related to chemical shifts (formerly 'atom shifts')
  write bmrb - write chemical shift list in BMRB format
  write lib - write residue library
  write seq - write sequence file
  write xpk - write NMRView peak list file
- **New standard macros:**
  calibration - NOE calibration with automatically determined or user-defined parameters
  coco - invoke the external [Coco](#) program for covalent geometry checking
  deposit - prepare coordinate and chemical shift lists for PDB and BMRB deposition
  garant - invoke the external [Garant](#) program for automated assignment
  karplus - Karplus curve definitions (that were previously in the residue library file)
  noeassign - automated NOESY assignment (replaces the former 'candid' macro)
  prolinebond - create restraints to close flexible proline rings
  ramaaco - create angle restraints to favor allowed Ramachandran plot regions
  renumber - consistently renumber a group of chemical shift and peak lists
  rmsd - convenient RMSD calculations
  rotameraco - create angle restraints to favor staggered side-chain rotamers
  structcalc - perform structure calculation
- **Short read/write commands:** The file type specification is now optional if the file name has the default extension for the given type of file. For instance, 'write demo.seq' can be used as a short-hand form of 'write seq demo.seq'.
- **PDB coordinate files:** The standard format for coordinate files is now that of the PDB (.pdb) rather than the (still supported) DG (.cor) format. A (compatible) variant that makes uses of the B-factor column to store an additional digit for each of the three Cartesian coordinates provides a higher accuracy than default PDB files.
- **Nomenclature conversion:** Transparent name translation includes now residue, atom and angle names, and applies to all kinds of input and output files. It is, for instance, straightforward to use the nomenclature of the PDB throughout a calcluation without explicitly changing names in the residue library. The 'translate' macro provides prefined translation tables for IUPAC, Cyana 1.x/Dyana Xplor/CNS, PDB, BMRB and NMRView. Importing/exporting data from other programs is much simplified in this way.

- **Pseudoatom handling:**
  - Coordinate files do by default no longer include pseudo atoms. The positions of pseudoatoms are calculated internally by the program if the variable 'pseudo' is set to 0, its default value. Traditional behavior can be restored with 'pseudo=1'.
  - As an alternative, a simplified naming scheme can be used interchangeably with the traditional 'Q...' names for pseudo atoms. In the simplified system the name of a pseudoatom is obtained from the names of the hydrogen atoms that it represents by removing the last (or the two last) digits. For instance, in the case of Val methyl protons HG11, HG12, HG13, HG21, HG22, HG23 the pseudo atoms are called QG1 --> HG1, QG2 --> HG2, and QQG --> HG. To use the simplified pseudo atom naming scheme on output, set 'pseudo=2'.
- **Multiple angle restraints:** A new type of multiple angle restraint is available that simultaneously involves several torsion angles and yields a violation only if all its individual torsion angle restraints are violated. Multiple angle restraints are useful, for example, to implement a Ramachandran plot potential that puts a penalty on "forbidden regions of the Ramachandran plot.
- **Temporary angle restraints:** It is now possible to apply angle restraints only temporarily during certain phases of the simulated annealing schedule.
- Ramachandran and rotamer angle restraints: Angle restraints that favor allowed regions of the Ramachandran plot and staggered rotamer positions for side-chain torsion angles can be used automatically during the initial phases of simulated annealing.
- **Symmetric dimers:** The automated NOE assignment algorithm has been extended to make explicit use of the dimer symmetry, if necessary, and the new command group 'molecules' has been added to treat symmetric dimers.
- **Fortran 90 implementation:** The program has been rewritten in Fortran 90 making use of the dynamic memory allocation features of Fortran 90. There are no longer any hard-coded limitations on the numbers of atoms, peaks, restraints etc.
- **INCLAN command language improvements:**
  - Fortran 90 implementation without memory limitations.
  - Possibility for Inclan macros (.cya files) to be started as shell scripts at the Unix prompt that automatically invoke Cyana.
  - Macro names given as a parameter on the command line that starts Cyana can, optionally, contain the .cya extension. E.g. the command 'cyana CALC.cya' given at the Unix prompt will start Cyana and execute the CALC.cya macro.
  - New command 'cd' or 'chdir' to change the current working directory.
  - New intrinsic character function 'getcwd' to obtain the name of the current working directory.
  - New intrinsic logical function 'master' that is true for the master process in parallel execution, and false otherwise.
- **Additionally supported systems:**
  - Full support for the Mac OS X operating system.
  - Experimental support for Windows XP using Cygwin and the Intel Fortran compiler.
  - Experimental support for the free 'g95' Fortran compiler.
  - File systems that do not distinguish upper from lower case letters are supported.

- **Parallelization:** Setting up parallel structure calculations on Linux cluster systems with MPI is straightforward with the 'cyanajob' script.
- **New system functions:**
  anamlib(i) - original name of atom i in the residue library
  dnamlib(i) - original name of angle i in the residue library
  rnamlib(i) - original name of residue i in the residue library
  cyanadir - directory in which cyana is installed (=libdir)
  nmol - number of molecules (e.g. 2 for a symmetric dimer)
  nlol - number of lower distance limits
  rmsd - calculate RMSD value to the average coordinates
  rmsdcurr - calculate average RMSD value of selected structure with respect to current structure
  rmsdpair - calculate average pairwise RMSD value
  rmsdstd - standard deviation of RMSD values
  rmsdmin - maximal individual RMSD value
  rmsdmax - maximal individual RMSD value
  iccoa(j,i) - j-th atom of scalar coupling constant i (j=1,2)
  dcosel(i) - is distance restraint i selected?

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