ARIA Practical

EMBO Practical Course, Basel 2007

Benjamin Bardiaux
Aymeric Bernard
Michael Nilges

http://aria.pasteur.fr
NMR structure determination

- data acquisition and processing
- peak picking and assignment
- derivation of spatial restraints
- structure calculation
ARIA

- Ambiguous Restraints for Iterative Assignment
• Ambiguous Restraints for Iterative Assignment

Conversion of data into XML using the CCPN package
Graphical project setup
Creation of directory tree

Filtering / validation of chemical shift lists and spectra

Initial NOE assignment

ARIA Iterative NOE assignment
Calibration
Violation analysis
Partial assignment
Merging of restraint lists

Structure calculation and floating chirality assignment

Refinement in explicit solvent
Generation of report files
• **Ambiguous Restraints for Iterative Assignment**

### Flowchart

- Conversion of data into XML using the CCPN package
- Graphical project setup
  - Creation of directory tree
- Filtering / validation of chemical shift lists and spectra
- Initial NOE assignment

#### ARIA Iterative NOE assignment

- Calibration
- Violation analysis
- Partial assignment
- Merging of restraint lists
- Structure calculation and floating chirality assignment
- Refinement in explicit solvent
- Generation of report files

### Equations

**ISPA**

\[ V_{ij} = \alpha d_{ij}^{-6} \]

**Relaxation Matrix Analysis**

\[ V_{ij}(\tau_m) = \alpha V_{ij}(0)(\exp(-R\tau_m))_{ij} \]

Evaluate \( \alpha \)
**Ambiguous Restraints for Iterative Assignment**

\[ F = \% \text{ of structure where } L_{ij} - t > d_{ij} > U_{ij} + t \]

If \( F > \text{viol. threshold} \), restraint \( ij \) is considered as violated

\( t: 1000.0 \text{ A to } 0.1 \text{ A} \)
• **Ambiguous Restraints for Iterative Assignment**

Weight each assignment possibility  \( w_i = V_i / \sum_{i} V_i(\ast N A_i) \)

Keep \( m \) possibilities satisfying  \( \sum_{i} w_i \geq w_c \)

\( w_c: 0.9999 \) to 0.8
• ARIA : Python program and API

• CNS : CNS scripts
ARIA Inputs

- Molecule
- Peak lists
- Shift lists
- Assignments
- Restraints
  - Distances
  - Dihedrals
  - H-Bonds
  ...

ARIA Format
CNS format
conversion

ARIA Practical - Basel 2007
Practical

- Calculation of Tudor Domain (56 res.)
- ARIA 2.2 / CNS 1.1
- Available data:
  - 13C and 15N edited NOE spectra
  - Chemical Shifts Assignments
  - Hydrogen Bonds
  - Torsion angles from coupling constants
  - Residual dipolar couplings
- Conversion of data from Xeasy format to ARIA XML format
- CCPN Project
ARIA Inputs

1. Conversion

- seq
- Molecule
- Xeasy
- Peak Lists
- Shift Lists
- ARIA
- H. Bonds
- Dihedrals
- restraints
- RDCs

ARIA Format
CNS format
conversion

ARIA Practical - Basel 2007
Practical

- Calculation of Tudor Domain (56 res.)
- ARIA 2.2 / CNS 1.1
- Available data:
  - $^{13}$C and $^{15}$N edited NOE spectra
  - Chemical Shifts Assignments
  - Hydrogen Bonds
  - Torsion angles from coupling constants
  - Residual dipolar couplings
- Conversion of data from Xeasy format to ARIA XML format
- CCPN Project
ARIA Inputs

2. CCPN Project

- Molecule
- Peak lists
- Shift lists
- Assignments
- Restraints
  - Distances
  - Dihedrals
  - H-Bonds
...

CNS format
CCPN Project

- CCPN Data Model
  - Project (XML file) group together sequence, shifts, spectra, assignments and restraints.
  - /home/unilogon/nilges/course/example/tudor_ccpn.xml
  - Can be read by different programs (FormatConverter, Analysis, ARIA….)

http://www.ccpn.ac.uk
Preparing ARIA Project

- Follow the tutorial
  - (Data conversion to ARIA XML)
  - Start ARIA GUI
    
    $ aria2 -g
  
  - Fill in specified information
    
    - Data, parameters, CNS path
  
  - Setup the project
    
    $ aria2 --setup run1.xml

- Run the calculation
  
    $ aria2 run1.xml
ARIA Parameters

Filtering / validation of chemical shift lists and spectra
Initial NOE assignment

ARIA
Iterative NOE assignment
Calibration
Violation analysis
Partial assignment
Merging of restraint lists
Structure calculation and floating chirality assignment

Refinement in explicit solvent
Generation of report files

chemical shift tolerances
Filtering of diagonal peaks
ARIA Parameters

Spin diffusion corr., cutoff, bound correction

Violation tolerance, violation threshold

Ambiguity cutoff, max nb of contributions network-anchoring

# structures
# steps
force constants
Parameters impact

- Parameters of major impact:
  - Network-anchoring parameters
  - Use of spin-diffusion correction [1]
  - Assignment window size and max. number of contributions [2]
  - Number of cooling steps [3]
  - Number of calculated structures
  - Water refinement [4]

ARIA report

- ARIA result analysis

  - Text files: run1/structures/itX/
    - report
    - noe_restraints.unambig, noe_restraints.ambig
    - noe_restraints.violations
    - noe_restraints.assignments
    - noe_restraints.merged

  - Quality report:
    - run1/structures/it8/quality_checks.*
    - run1/structures/refine/quality_checks.*

  - Graphics:
    - run1/structures/itX/graphics/rms_analysis.ps
    - run1/structures/it8/graphics/whatif_profiles.ps
    - run1/structures/refine/graphics/whatif_profiles.ps

  - GUI: Peak Maps
Repeated ARIA runs

Correction of input data
- Completion of NOE assignments
- Removal of noise peaks
- Adjustment of frequency windows
- Setup of a new run

ARIA
- Automated NOE assignment
- Conversion of data into XML
- Graphical project setup

Inspection of report files and analysis of proposed assignments

Investigation of quality indices of final solvent-refined structure ensemble