ARIA Tutorial

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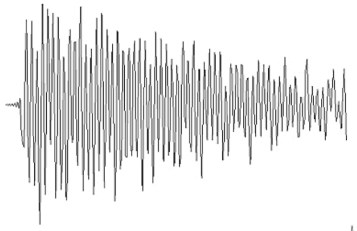
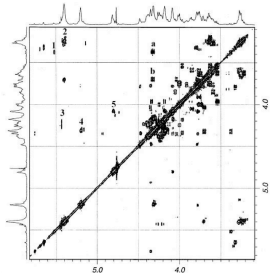
http://aria.pasteur.fr

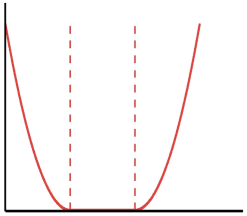
NMR structure determination

data acquisition and processing

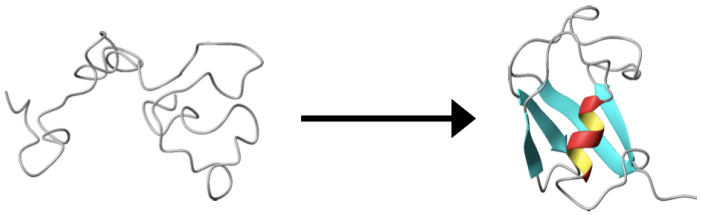




peak picking and assignment



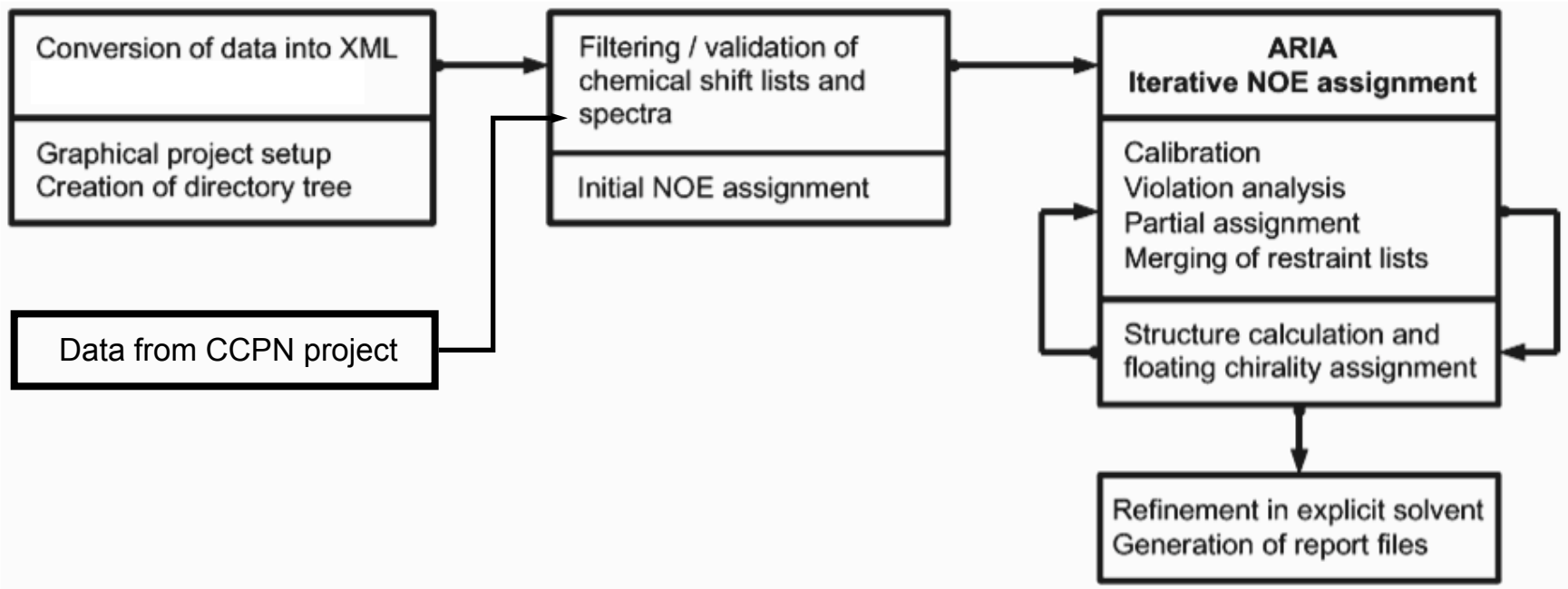
derivation of spatial restraints



structure calculation

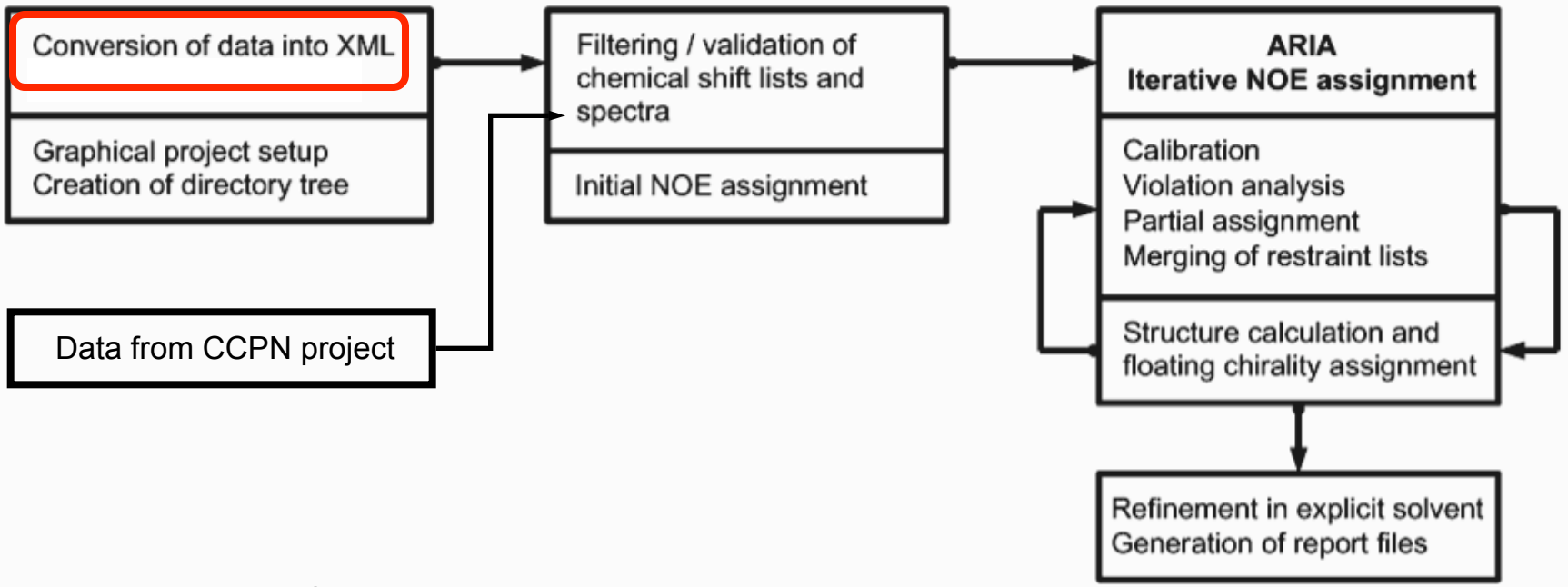
ARIA

- **A**mbiguous **R**estraints for **I**terative **A**ssignment



ARIA

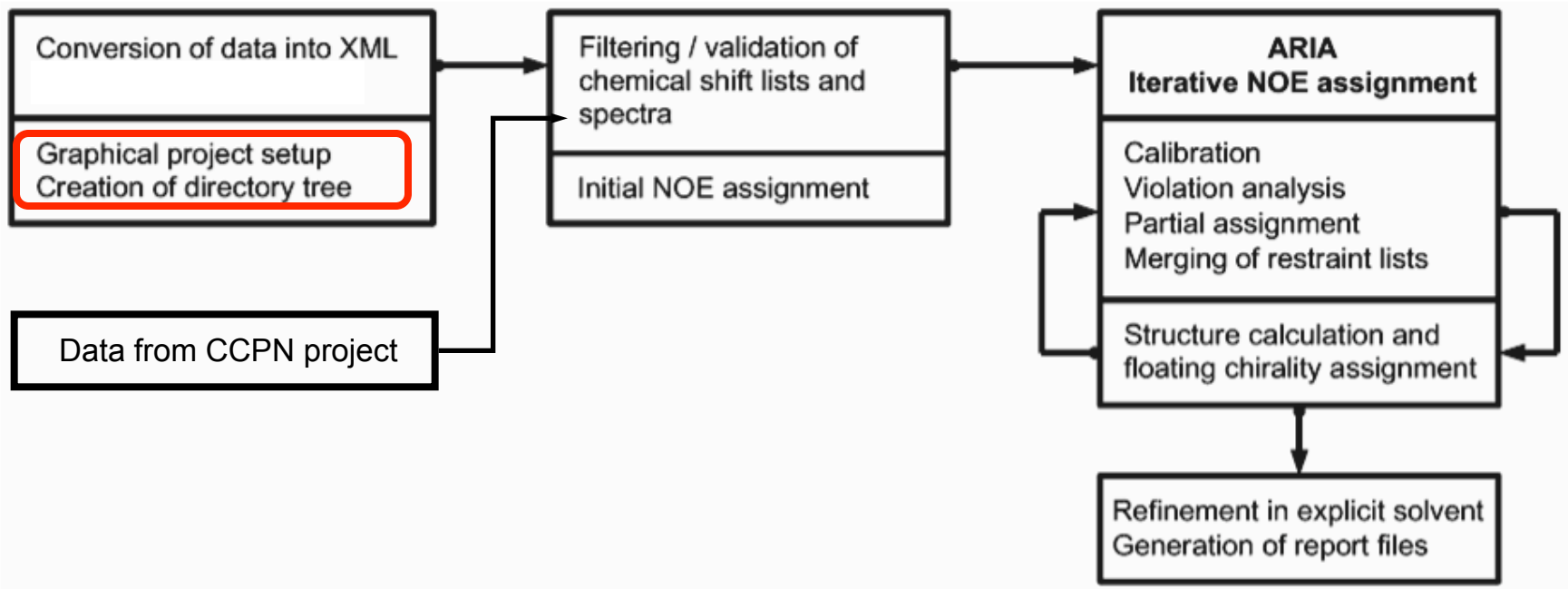
- **A**mbiguous **R**estraints for **I**terative **A**ssignment



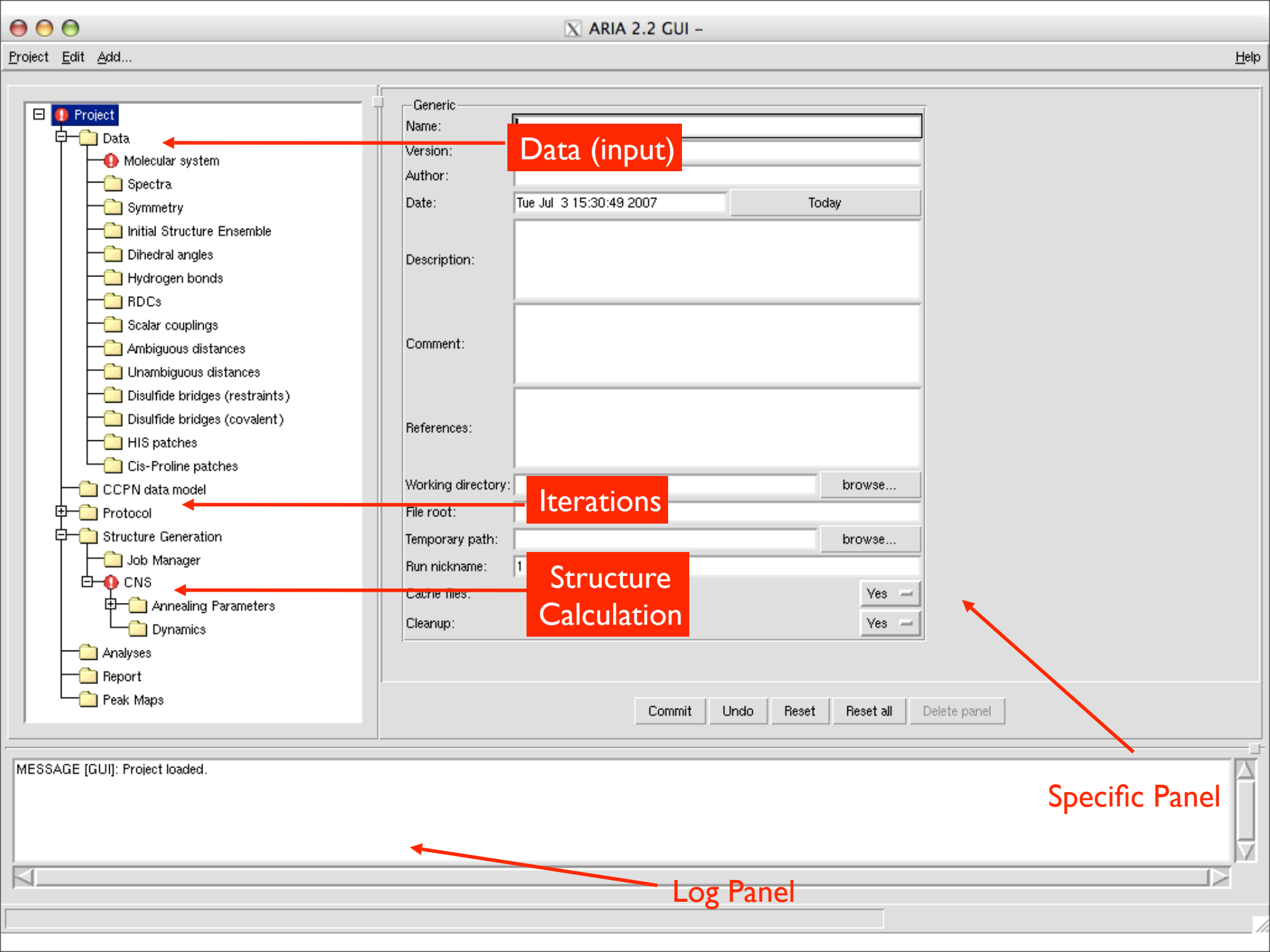
ARIA uses XML format to store the data
(sequence, chem. shifts and spectra)
=> conversion step is required

ARIA

- **A**mbiguous **R**estraints for **I**terative **A**ssignment

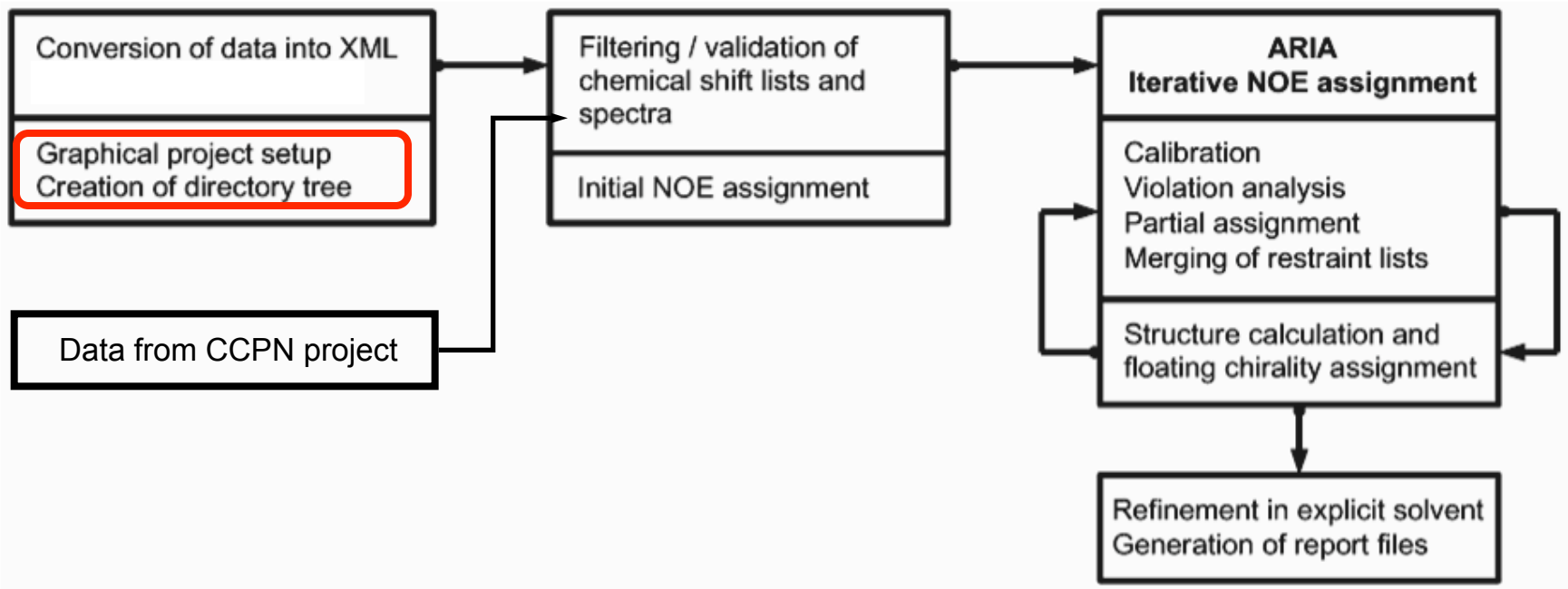



```
aria2 -g
```


ARIA 2.2 GUI –
Project
Edit
Add...
Help
Project
Data
Molecular system
Spectra
Symmetry
Initial Structure Ensemble
Dihedral angles
Hydrogen bonds
RDCs
Scalar couplings
Ambiguous distances
Unambiguous distances
Disulfide bridges (restraints)
Disulfide bridges (covalent)
HIS patches
Cis-Proline patches
CCPN data model
Protocol
Structure Generation
Job Manager
CNS
Annealing Parameters
Dynamics
Analyses
Report
Peak Maps
Generic
Name:
Version:
Author:
Date:
Tue Jul 3 15:30:49 2007
Today
Description:
Comment:
References:
Working directory:
browse...
File root:
Temporary path:
browse...
Run nickname:
1
Cache files:
Yes
Cleanup:
Yes
Commit
Undo
Reset
Reset all
Delete panel
Data (input)
Iterations
Structure Calculation
Specific Panel
MESSAGE [GUI]: Project loaded.
Log Panel

ARIA

- **A**mbiguous **R**estraints for **I**terative **A**ssignment



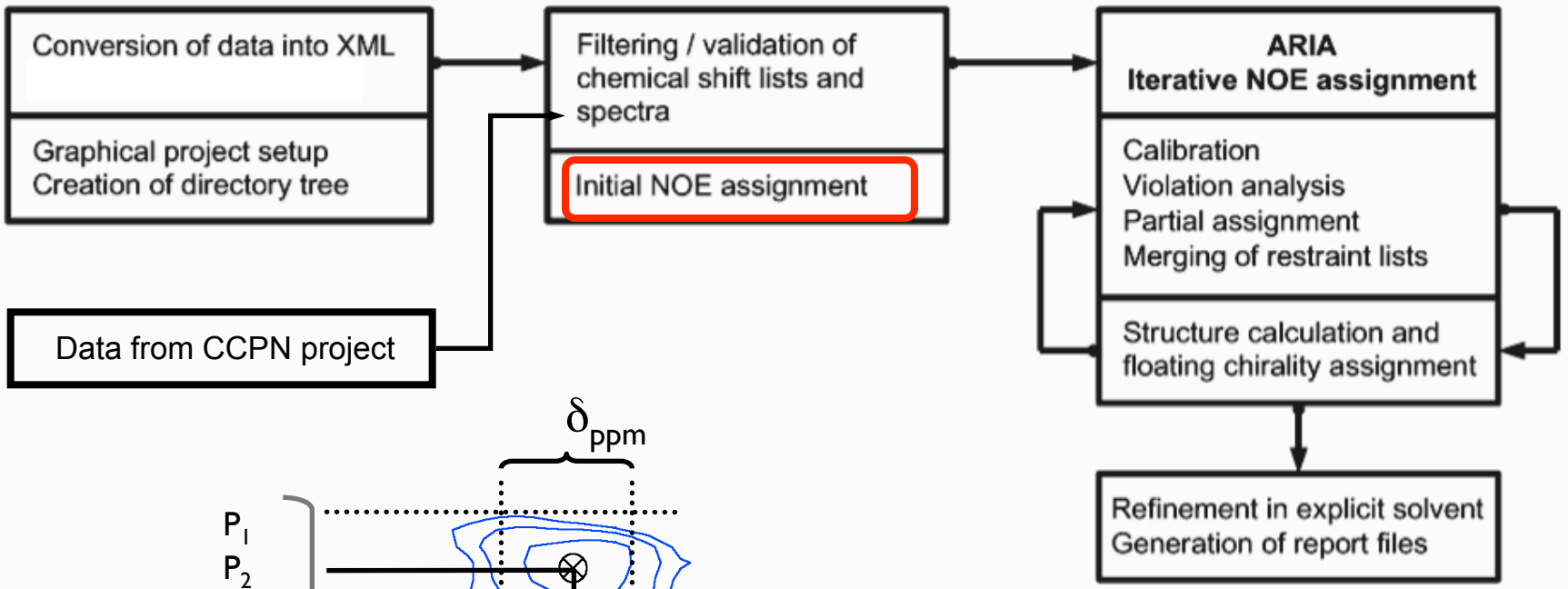

```
aria2 --setup project.xml
```

ARIA

```
run1
|-- cns
|    |-- begin
|    |-- data
|    |    |-- dihedrals
|    |    |-- distances
|    |    |-- …
|    |    |-- sequence
|    |    `-- ssbonds
|    |-- protocols
|    |    `-- analysis
|    `-- toppar
|-- data
|    |-- begin
|    |-- dihedrals
|    |-- distances
|    |-- …
|    |-- sequence
|    |-- spectra
|    |-- ssbonds
|    `-- templates
`-- structures
     |-- it0
     |    `-- graphics
     |-- it1
     |    `-- graphics
     |-- refine
          |-- analysis
          `-- graphics
```

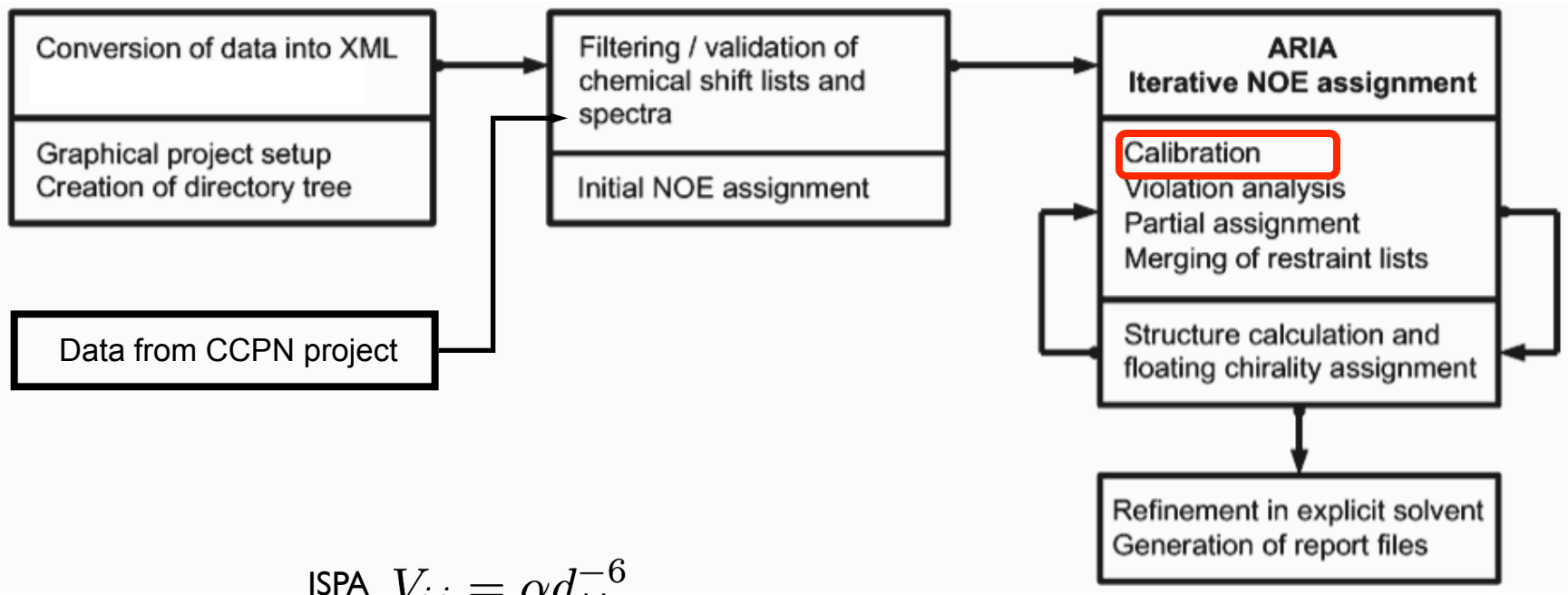
ARIA

- **A**mbiguous **R**estraints for **I**terative **A**ssignment



ARIA

- **A**mbiguous **R**estraints for **I**terative **A**ssignment



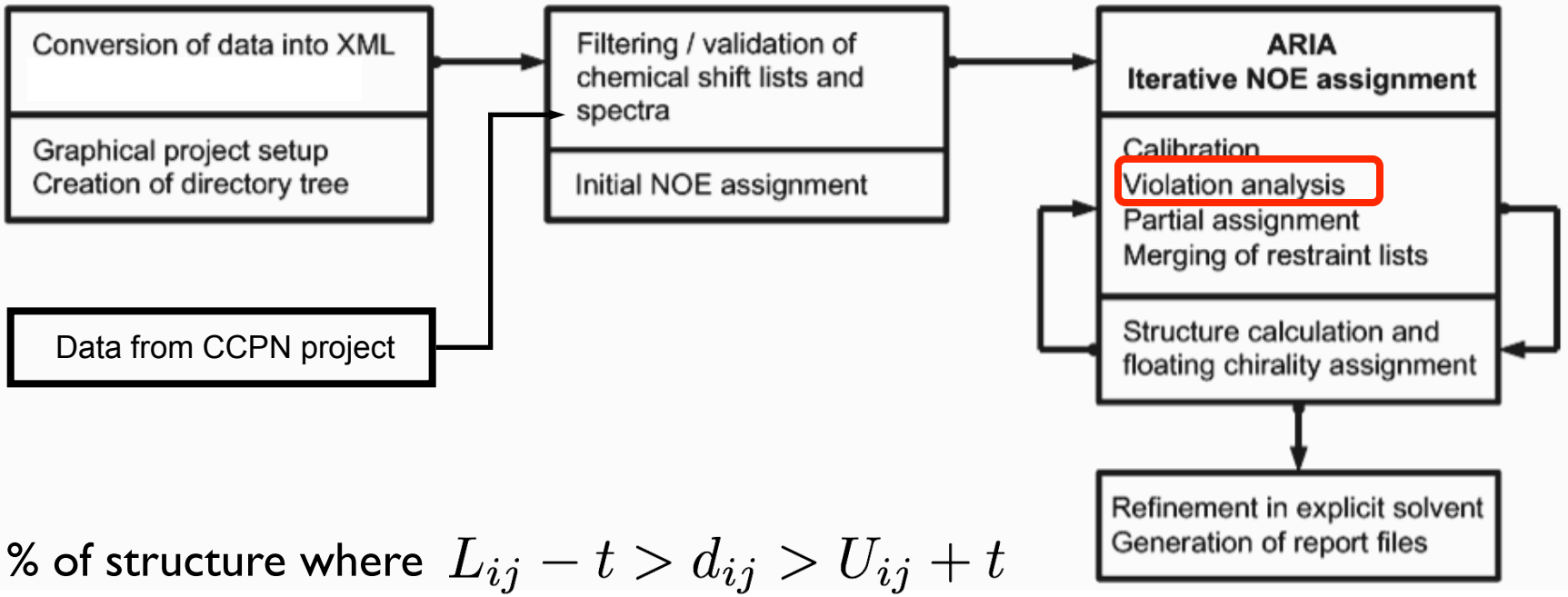
ISPA $V_{ij} = \alpha d_{ij}^{-6}$

Relaxation Matrix Analysis $V_{ij}(\tau_m) = \alpha V_{ij}(0)(\exp(-R\tau_m))_{ij}$

→ Evaluate α

ARIA

- **A**mbiguous **R**estraints for **I**terative **A**ssignment



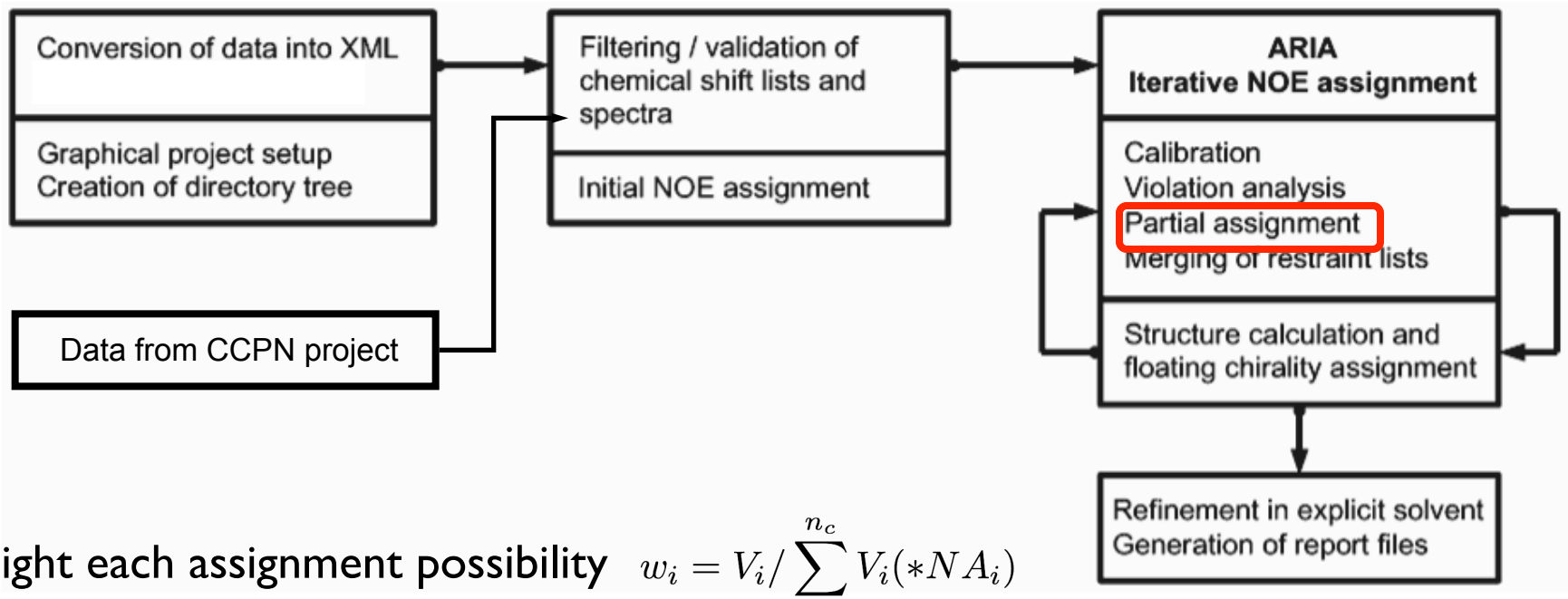
F = % of structure where $L_{ij} - t > d_{ij} > U_{ij} + t$

If F > *viol. threshold*, restraint *ij* is considered as violated

t: 1000.0 A to 0.1 A

ARIA

- **A**mbiguous **R**estraints for **I**terative **A**ssignment

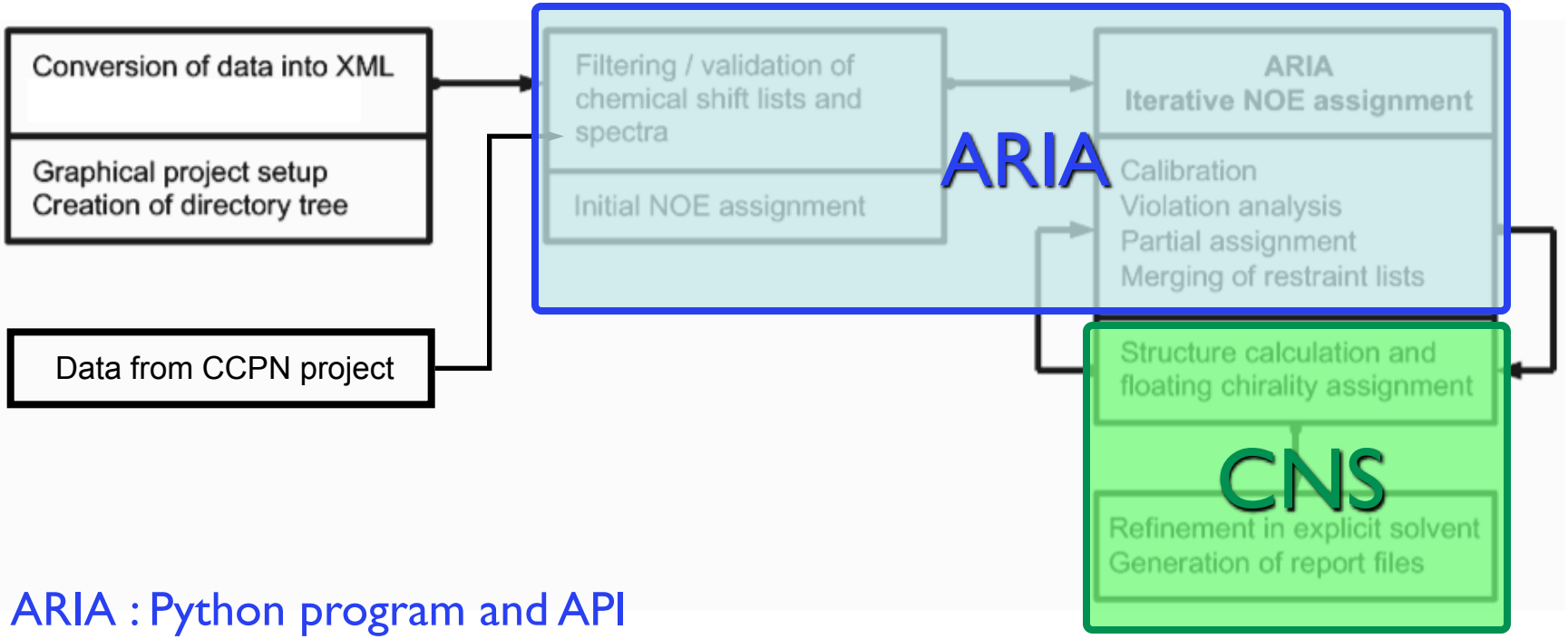


Weight each assignment possibility $w_i = V_i / \sum^{n_c} V_i (*NA_i)$

Keep *m* possibilities satisfying $\sum^{m} w_i \geq w_c$

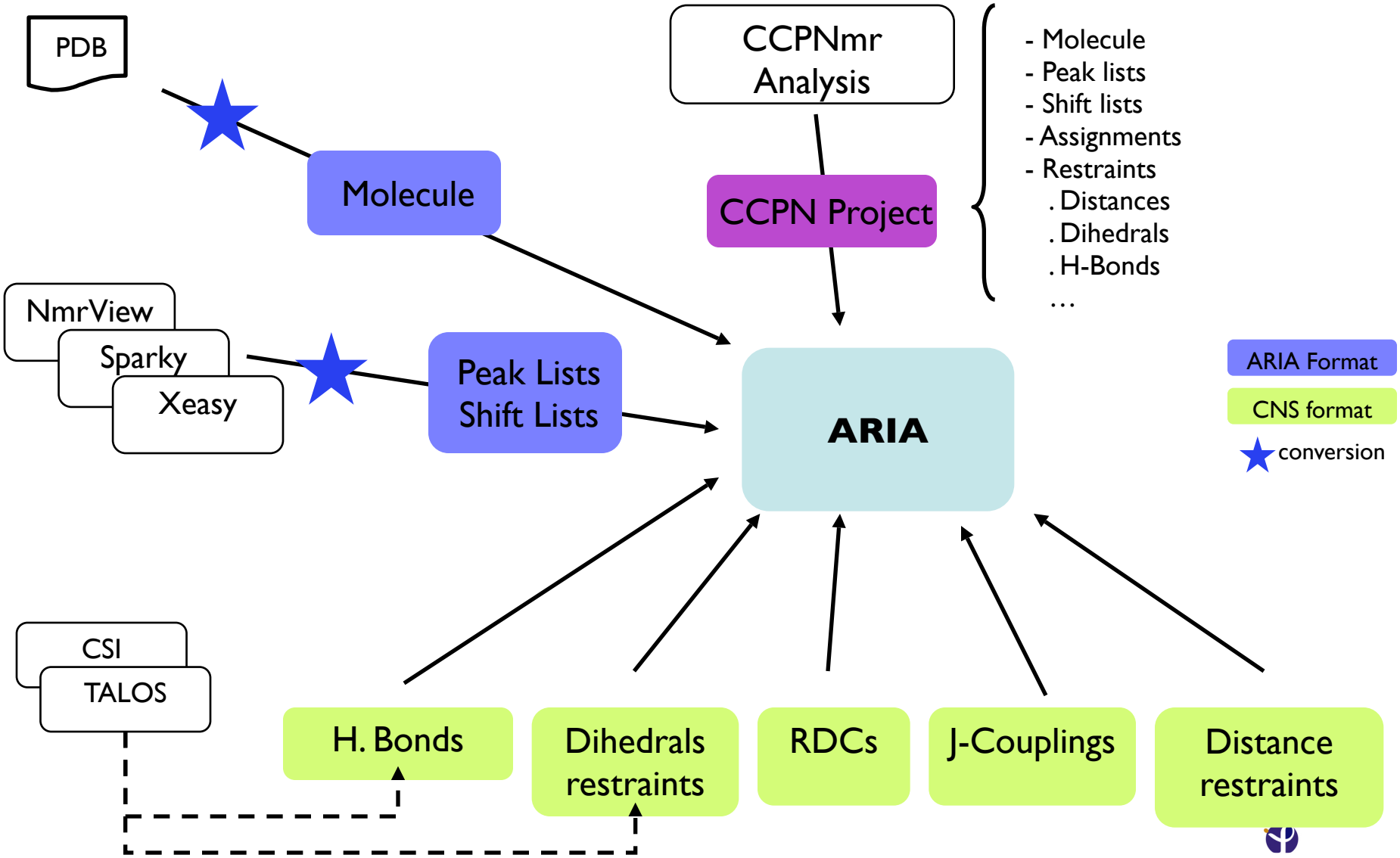
w_c: 0.9999 to 0.8

ARIA/CNS



- ARIA : Python program and API
- CNS : CNS scripts

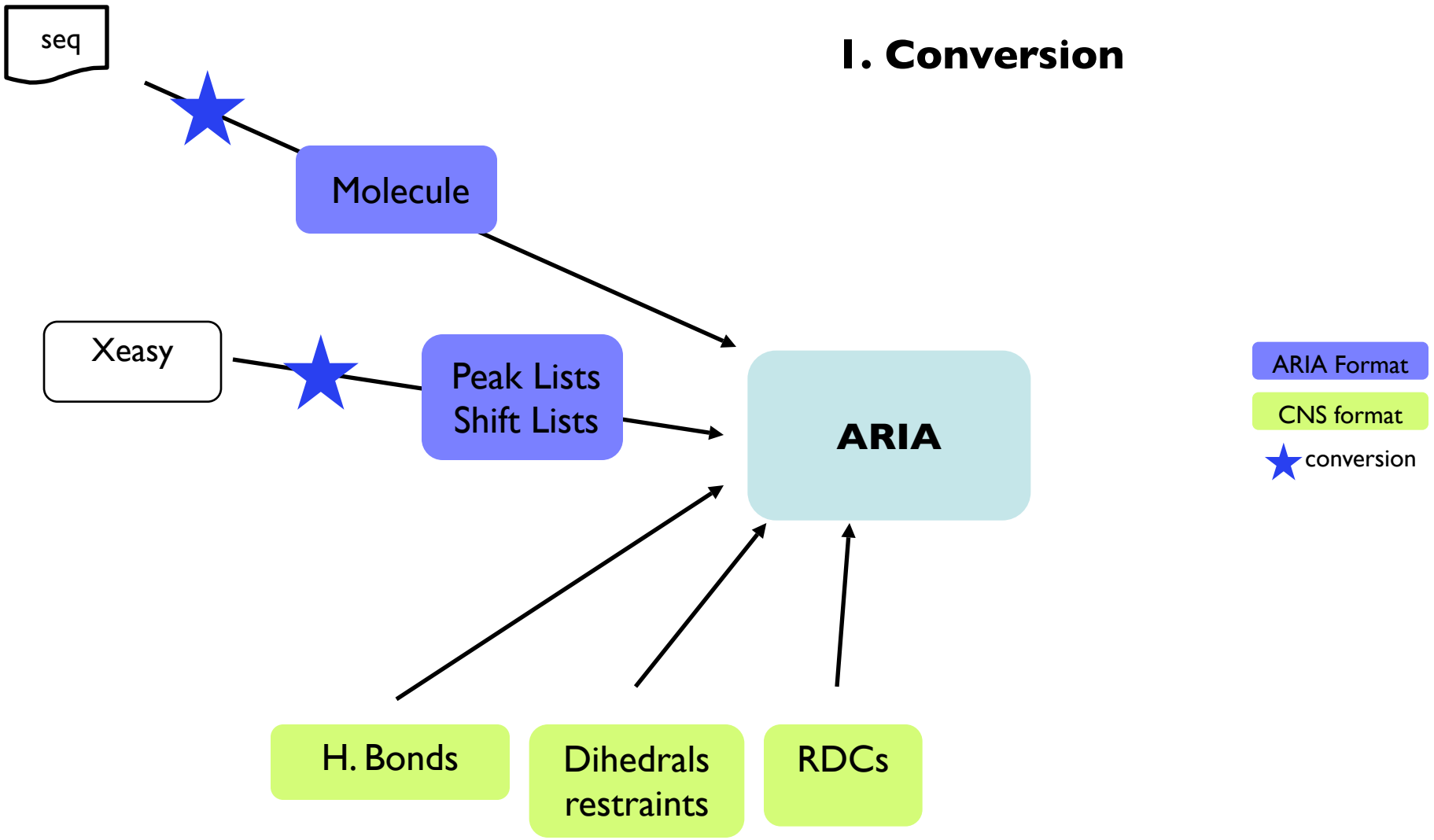
ARIA Inputs


PDB
Molecule
CCPNmr Analysis
CCPN Project
- Molecule
- Peak lists
- Shift lists
- Assignments
- Restraints
. Distances
. Dihedrals
. H-Bonds
…
NmrView
Sparky
Xeasy
Peak Lists
Shift Lists
ARIA
ARIA Format
CNS format
conversion
CSI
TALOS
H. Bonds
Dihedrals restraints
RDCs
J-Couplings
Distance restraints

Practical

- Calculation of Tudor Domain (56 res.)
  - http://aria.pasteur.fr/documentation/courses/brisbane_0810/tudor_example.tgz
  - http://aria.pasteur.fr/documentation/courses/brisbane_0810/tudor_results.tgz (5MB)
  - http://aria.pasteur.fr/documentation/courses/brisbane_0810/aria.pdf
  - http://aria.pasteur.fr/documentation/courses/brisbane_0810/practical.pdf
  - http://aria.pasteur.fr/documentation/courses/brisbane_0810/handout.pdf
- ARIA 2.2 / CNS 1.1
- Available data:
  - 13C and 15N edited NOE spectra
  - Chemical Shift 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

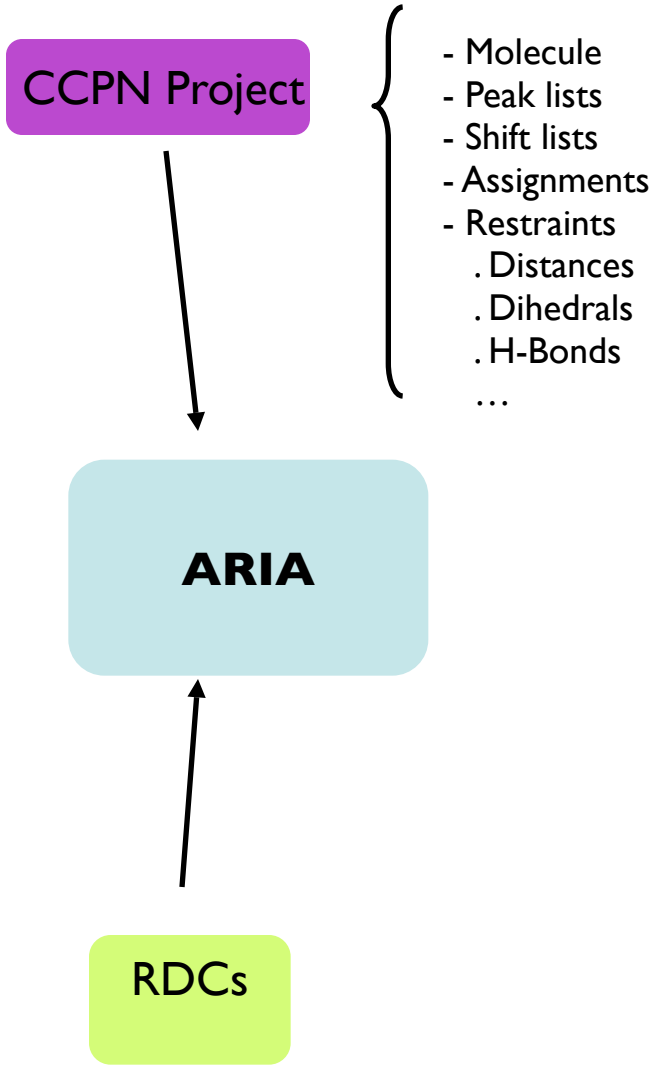

seq
Molecule
Xeasy
Peak Lists
Shift Lists
ARIA
H. Bonds
Dihedrals
restraints
RDCs
1. Conversion
ARIA Format
CNS format
conversion

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

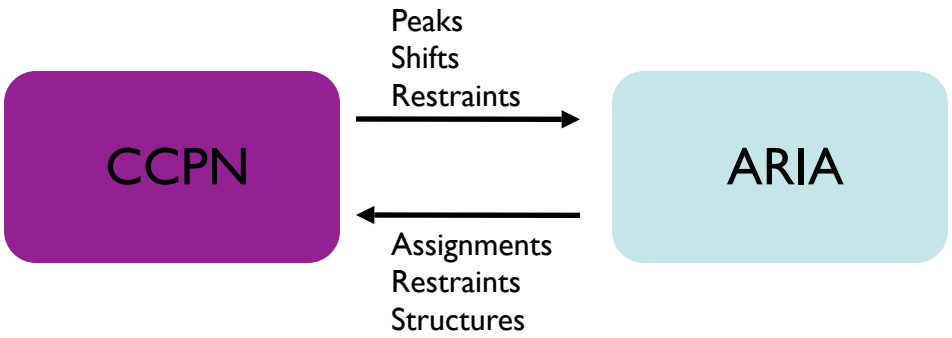
2. CCPN Project



CCPN Project

- CCPN Data Model
  - Project (XML file) group together sequence, shifts, spectra, assignments and restraints.
  - `example/data/ccpn/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

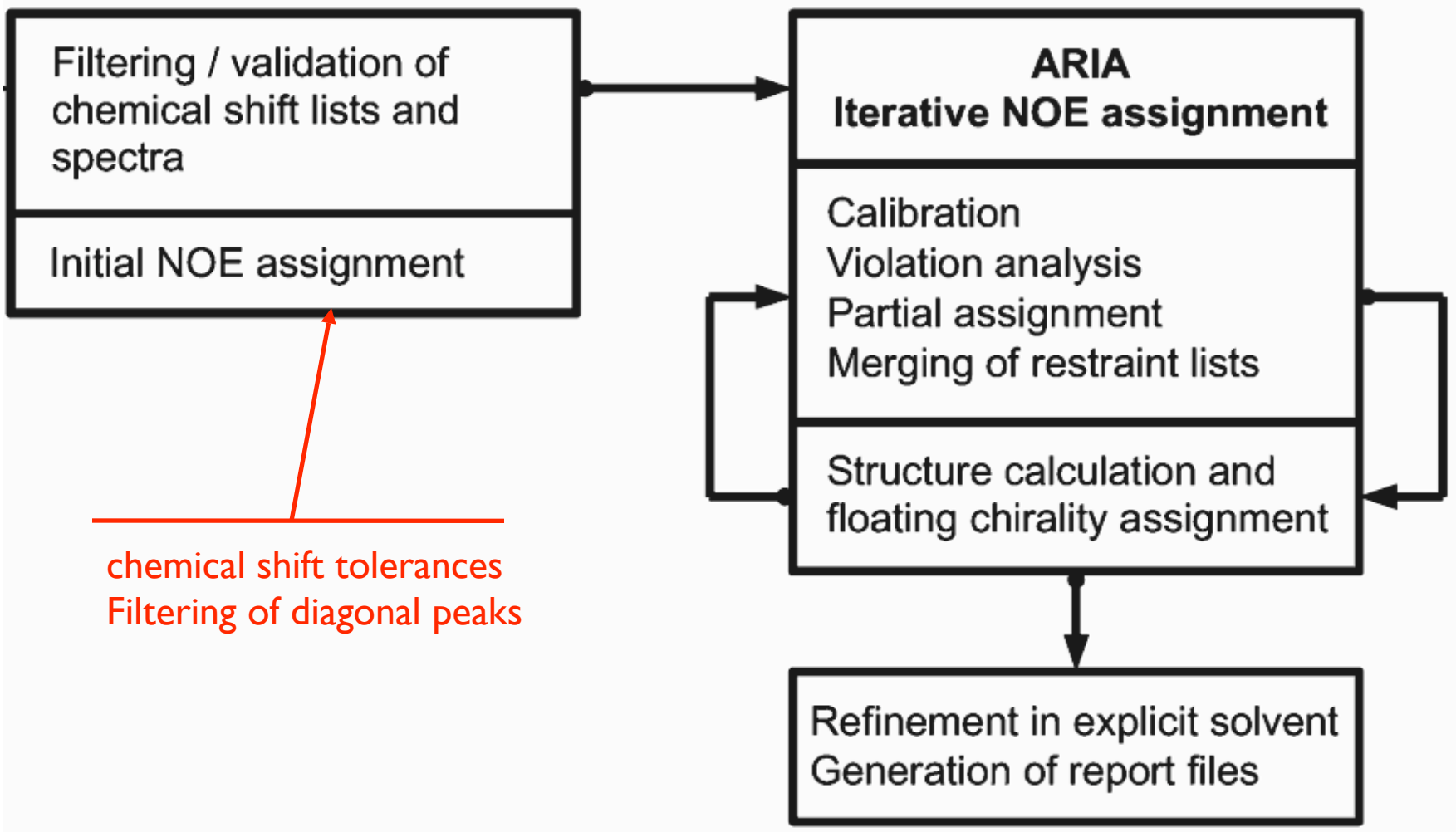
    $ `aria2 -g`
  - Fill in specified information

    - Data, parameters, CNS path….
  - Setup the project

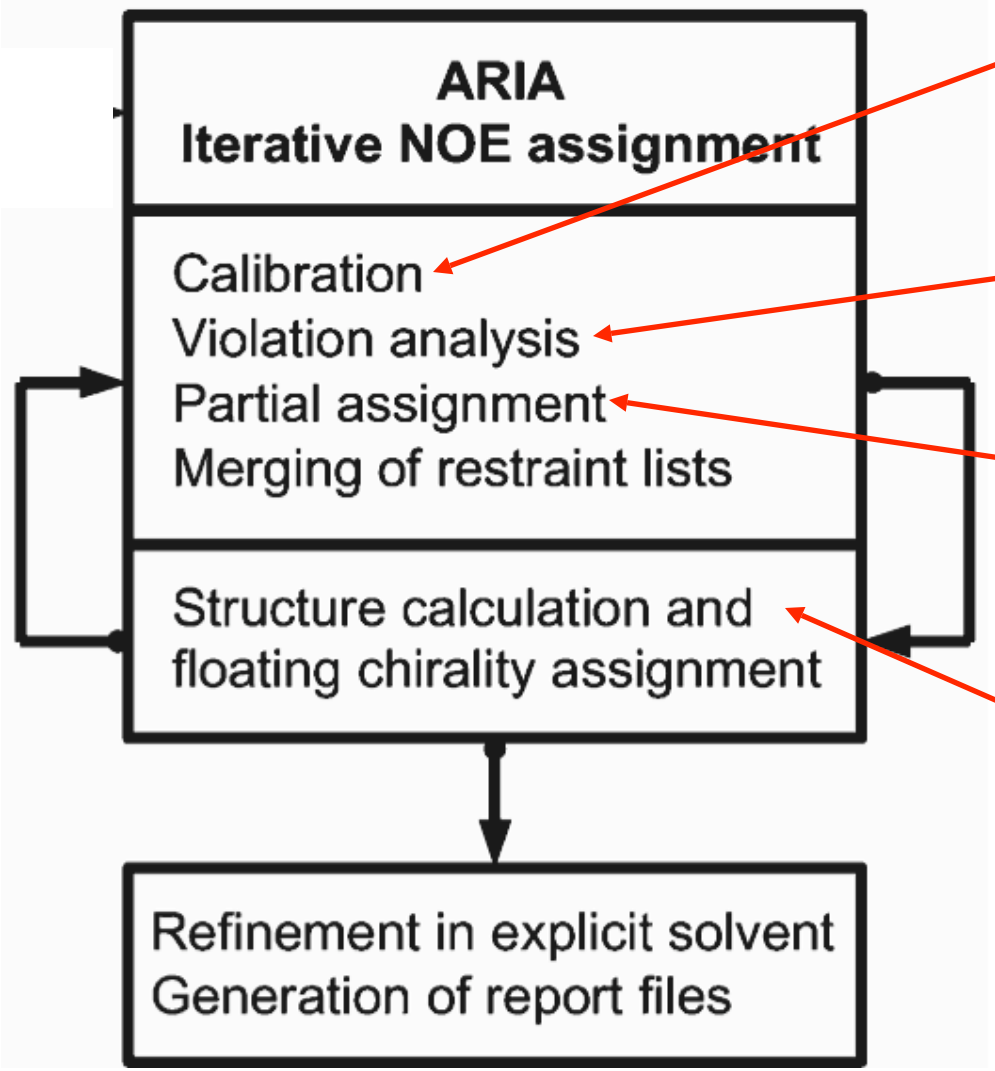
    $ `aria2 --setup run1.xml`
  - Run the calculation

    $ `aria2 run1.xml`

ARIA Parameters



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]

[1] J. P. Linge et al. Correction of spin diffusion during iterative automated NOE assignment. J Magn Reson, 167(2):334–342, Apr 2004.
[2] M. Fossi et al.. Influence of chemical shift tolerances on nmr structure calculations using aria protocols for assigning noe data. J Biomol NMR, 31(1):21–34, 2005.
[3] M. Fossi et al. Quantitative study of the effects of chemical shift tolerances and rates of sa cooling on structure calculation from automatically assigned noe data. J Magn Reson, 175(1):92–102, 2005.
[4] J. P. Linge et al. Refinement of protein structures in explicit solvent. Proteins Struct. Funct. Genet., 20(3):496–506, 2003.

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:

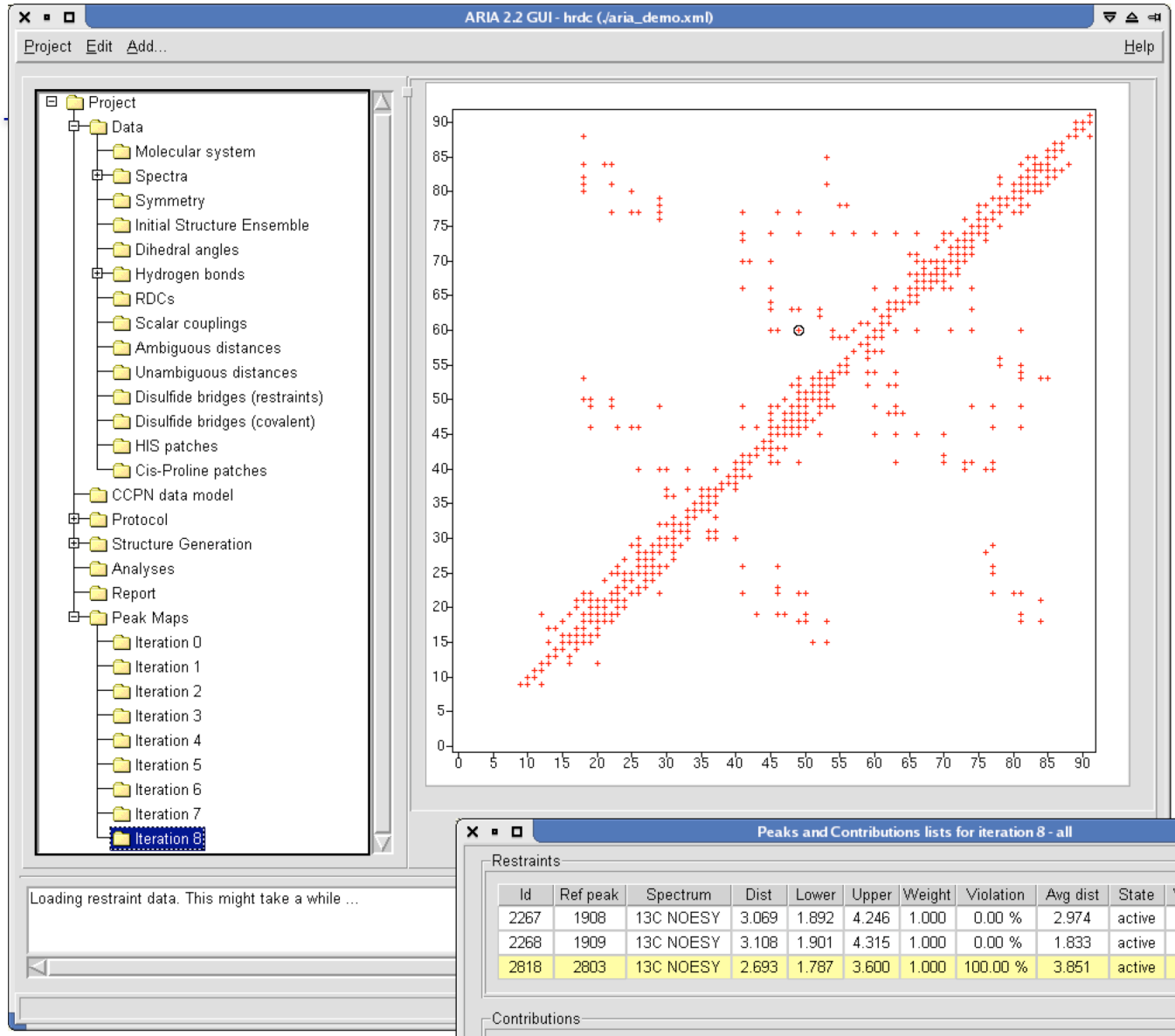
    `run1/structures/it8/quality_checks.*`

    `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



Peaks and Contributions lists for iteration 8 - all

Restraints

Id	Ref peak	Spectrum	Dist	Lower	Upper	Weight	Violation	Avg dist	State	Violated	Type
2267	1908	13C NOESY	3.069	1.892	4.246	1.000	0.00 %	2.974	active	no	unambiguous
2268	1909	13C NOESY	3.108	1.901	4.315	1.000	0.00 %	1.833	active	no	unambiguous
2818	2803	13C NOESY	2.693	1.787	3.600	1.000	100.00 %	3.851	active	yes	unambiguous

Contributions

ariapeak	id	dist	weight	res 1	at 1	seg 1	res 2	at 2	seg 2
2267	16685	2.571	1.000	49	HB*		60	HE*	
2268	16687	2.158	1.000	49	HB*		60	HE*	
2818	20149	3.882	1.000	49	HE*		60	HD*	

Dismiss

Repeated ARIA runs