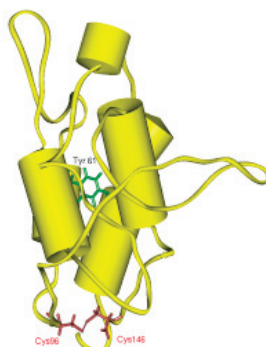


Macromolecular structure determination by X-ray crystallography and NMR spectroscopy

Built upon the widely used programs X-PLOR and CNS

CNX: X-ray Crystallography and NMR Refinement

CNX is the leading software package for macromolecular structure determination from experimental data derived from X-ray diffraction or nuclear magnetic resonance (NMR) spectroscopy.



Built upon the widely used programs X-PLOR and CNS, CNX provides a flexible, easy-to-use system that incorporates leading structure solution algorithms to perform:

- heavy atom searching
- experimental phasing from multi-wavelength anomalous dispersion (MAD) and multiple isomorphous replacement (MIR)
- density modification
- molecular replacement (using AMoRe¹ as an option)
- crystallographic refinement with maximum likelihood targets
- NMR structure calculation using NOEs, J-coupling, chemical shift, and dipolar coupling data

Combined with powerful optimization and statistical cross-validation methods, CNX significantly increases the speed of structure solution, while remaining one of the most reliable and accurate software suites for solving macromolecular structure.

New dihedral angle restraints² and residue-specific B-restraints³ in CNX significantly improve the quality of a refined structure, resulting in up to 3% reduction in R_{free} values.

X-Ray Highlights

Probabilistic MAD Phasing

In addition to MIR and molecular replacement (MR) phasing, CNX can carry out MAD phasing applications, which include data scaling and merging, map calculations, refinement of the anomalous scatterer sites, and phasing⁴.

Anisotropic Displacement Parameters (ADP)

Optimization of atomic anisotropic displacement parameters is indispensable for determining high-quality, high-resolution macromolecular structures from X-ray data. CNX incorporates restraints designed to restrict atomic anisotropic displacement tensors for related pairs of atoms to improve molecular structure during crystallographic refinement.

Torsion-Angle Molecular Dynamics

Torsion groups within a molecule are kept rigid, which increases the radius of convergence during simulated annealing and refinement. Since the number of degrees of freedom in the system is reduced, overfitting is less likely.

SigmaA Weighting for Electron Density Maps With Optional Cross-Validation

Improved electron density maps with reduced bias may be calculated using SigmaA or cross-validated SigmaA weights⁵. The calculation of these types of maps facilitates model rebuilding.

Efficient Energy Minimization Script

CNX offers a powerful and highly automated multi-stage energy minimization tasks file. This is developed to refine crude models using maximum likelihood methodology, the adopted basis Newton-Raphson (ABNR) energy minimization routine, and the Babinet bulk solvent scattering correction.

System Requirements

- Supported on LINUX, IBM, and SGI platforms. For detailed information, please visit the CNX product pages on our website, www.accelrys.com.
- Dial Box is supported for QUANTA on both the Linux and SGI IRIX platforms.

Molecular Replacement with AMoRe and CNX

Task files are provided for carrying out MR searches using AMoRe, in addition to the native CNX functionality. AMoRe is also available from the command line for doing MR searches. Multiple molecules within the crystal asymmetric unit can be placed with each method.

Maximum Likelihood Targets (Amplitude, Intensity, and Phase Probability)

Maximum likelihood targets for refining macromolecular models are considerably more convergent and reliable than the conventional residual target, particularly for incomplete or crude models⁶. Maximum likelihood targets are now standard due to their computational efficiency.

Automated Water Picking Procedure

CNX is able to pick and write out the coordinates of water peaks (corresponding to ordered solvent molecules) from solvent regions close to the protein surface. Task files are provided.

Shared and Distributed Memory Parallelization

CNX uses OpenMP⁷ to allow jobs to be run across several processors in shared multiprocessor machines. This form of parallelism gives better performance for crystallographic systems with larger numbers of atoms and with large FFT grids. In addition, distributed memory parallelization using MPI is enabled in CNX for self- and cross-rotation searches.

NMR Highlights

Time- and Ensemble-Averaged NOE Distance Restraints

With ensemble averaging, an ensemble of conformers is used to satisfy the experimental NMR data⁸. The NOE restraint potential is changed so that NOE derived distance restraints are applied to the time-average of each distance, rather than to each instantaneous distance.

Ensemble-Averaged J Coupling and Cross-Correlated Dipole-Dipole Relaxation Rate Refinement

The three-bond HN-CaH coupling constant potential and the cross-correlated dipole-dipole relaxation rate potential has now changed to allow ensemble-averaged restraints to be used.

Engh and Huber Parameters for NMR Structure Determination

CNX provides a parameter set based on the Engh and Huber parameters for X-ray refinement and NMR structure determination.

Cross-Validation of NOE Distance, NOE Intensity, and Dihedral Angle Restraints

Cross-validation for structure determinations involving NOE distance, NOE intensity, and dihedral angle restraints⁹ is illustrated by scripts used for ensemble averaging.

Structure Calculation With Torsion Angle Dynamics

Torsion angle dynamics, involving both torsion angle and Cartesian dynamics, provides an efficient method for NMR structure determination with a high success rate compared to conventional methods.

Software

- QUANTA environment

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