Molecular Replacement in NMR Structure Determinations

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Protein structure determination by NMR spectroscopy has become an essential tool in biological laboratories and so new methods are necessary, to perform 3D-structure determinations automatically. In view of the larger number of sequences becoming available, for example, from genome projects, the structural determination on a large scale is required, which could not be carried out without a high degree of automation. One of the most time-consuming steps in protein structure determination is the spectral assignment procedure. This involves two main phases: a) sequence specific resonance assignment of the nmr signals; b) assignment of the NOESY spectra with collection of a list of distance constraints: the crucial step. Advanced iterative approaches have been suggested to automate the assignment of NOESY spectra and 3D-structure calculation.[1,2] We suggest an approach that simulates "molecular replacement methods" now currently in use in crystallography. A structure, obtained for instance from homology modelling or x-ray coordinates, may be used as template to automatically provide an initial guess. This structure can be then routinely refined against the experimental NMR data. We have applied this approach to determine the structure of Phl p II allergen, a protein of 96 residues with an immunoglobulin-like fold, of which both nmr and x-ray structures were available.[3]

REFERENCES

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