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Synergistic Application of X-Ray Crystallography and NMR Data for Studying of the Supramodular Protein Structures. T. Cierpicki, J.H. Bushweller, Z.S. Derewenda, Dept. of Molecular Physiology, Univ. of Virginia, Charlottesville, VA 22908.

X-ray crystallography is a method of choice for determination of protein structures at high resolution. However, crystallization of multidomain proteins and protein-protein complexes is a major challenge. Furthermore, supramodular protein structures may be affected by the crystal packing forces. In this context NMR spectroscopy might be a useful technique for acquiring structural information in solution, but accuracy of standard NOE-based methods is typically lower relative to high resolution crystal structures. However, the recently introduced measurements of residual dipolar couplings (RDCs) will significantly impact on biomolecular NMR methodology. RDCs provide very accurate structural information, and can be used in conjunction with crystallographic data.

To address the question of the supramodular structure of a two-domain protein, syntenin, we applied synergistic approach combining data derived from X-ray crystallography and RDCs. We show that the two PDZ domains form a compact unit, but their mutual disposition clearly differs from that seen in the crystal structure. Simultaneous application of RDC and crystal structures may become a very useful methodology to study structures of multidomain proteins and protein complexes.