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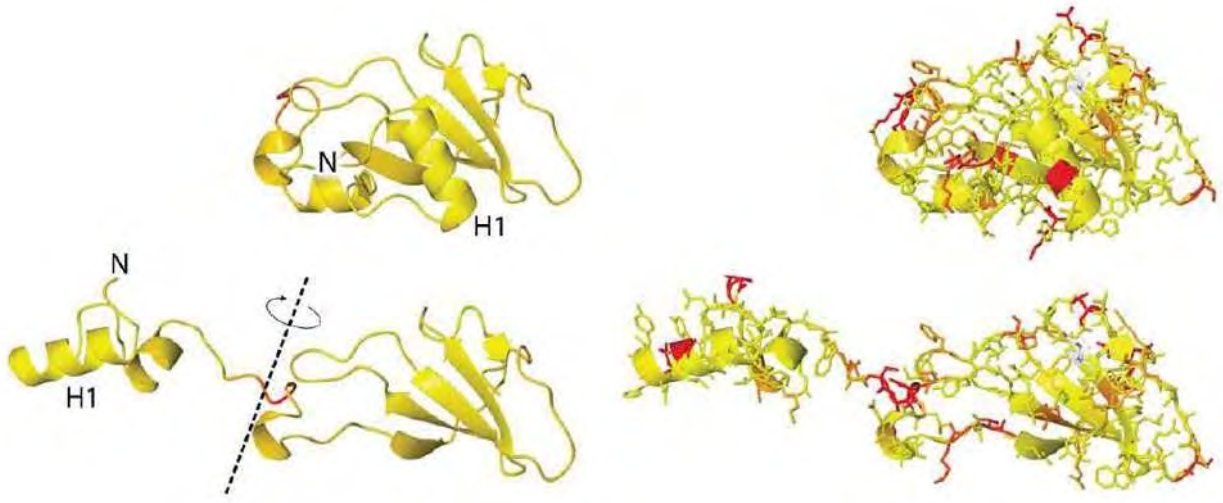
Conformation-independent structural comparison of macromolecules with ProSMART

R. Nicholls[1], M. Fischer[2], G. Murshudov[1]

[1]MRC Laboratory of Molecular Biology, Structural Studies Division, Cambridge, UK, [2]University of Toronto, Faculty of Pharmacy, Toronto, Canada

Structural comparison often aids insight into the function and mechanics of biological macromolecules. To make such analyses more accessible, we present the Procrustes Structural Matching Alignment and Restraints Tool (ProSMART), which is designed to allow fast but detailed comparative analysis of macromolecular structures despite potential dissimilarities in global arrangement, such as domain motion and distortion. Whilst obtaining a residue alignment between structures is a prerequisite for comparative analysis, conventional alignment methods may fail in cases where conformational differences are dramatic. However, ProSMART achieves a conformation-independent structural alignment by focusing purely on local dissimilarities, rather than enforcing chain/domain rigidity. This allows the sensible comparison of protein (or DNA/RNA) structures in the presence of conformational change. ProSMART allows analysis of the structural conservation of local backbone and side chains in a wide variety of scenarios - the method is sensitive enough to allow identification of subtle dissimilarities between structures sharing high sequence homology, whilst being versatile enough to allow identification of local similarities between more distantly-related structures. In addition, ProSMART can be used for the identification of conserved rigid substructures, which may or may not represent functional domains. ProSMART is also used for the generation of external restraints for use in crystallographic refinement. Results from ProSMART can be visualised in either CCP4mg or PyMOL. All residue-based scores are illustrated using intuitive colour gradients, allowing easy visual assessment of local backbone and side chain conservation. Complementary structural comparison tools such as ProSMART can help break the complexity of the constantly growing pool of available structural data into a more readily accessible form, and consequently may aid biological insight into macromolecular structures.

[1] *R. Nicholls, F. Long, G. Murshudov, Acta Crystallographica Section D: Biological Crystallography, 2012, 68, 404-417,* ***[2]*** *R. Nicholls, M. Fischer, G. Murshudov, CCP4 Newsletter on Protein Crystallography, 2012,* ***[3]*** *R. Nicholls, University of York PhD Thesis, 2011*



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