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New development in ILMILIONE package: two computational tools for H/D determination in protein structures from neutron data. Dritan Siliqi, Rocco Caliandro. *Institute of Crystallography, CNR, Bari, Italy*.
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X-ray and neutron crystallography technique provide complementary information on the structure and function of biological macromolecules. However, the dependences of X-ray scattering on atomic electron number makes H atoms difficult to locate in experimental electron density maps. Neutron crystallography is a powerful technique for locating hydrogen and can readily provide information on protonation states of amino-acid residues and ligands, the identity of solvent molecules and the nature of bonds involving hydrogen [1]; however the strong incoherent scattering from H introduces significant noise into the data, leading to interference between the negative density associated the hydrogen and the positive density associated carbon atoms. This problem can be circumvented by producing fully-deuterated samples. Recently, there has been a great increase in the application of neutrons in biology, mainly owing to improvements in instrumentation and data-collection and sample preparation methods.[2]
In response to these problems and opportunities, we are developing methods for H/D determination in protein structures. The methods are an evolution of those applied also in X-ray crystallography, the extrapolation beyond observed resolution [known as FreeLunch procedure[4]) and DEDM-EDM [5] (Difference Electron Density Modification technique in combination with Electron Density Modification technique] included in our package ILMILIONE [6]. Two new methods dedicated to neutron crystallography have been developed and successfully tested, called *n-FreeLunch* and *DNDM-NDM*. It was shown that both the methods are complementary with each other and are effective in finding the positions of hydrogen and deuterium atoms in neutron density maps. Both tools in combination with neutron refinement procedure [7] can increase the success rate for the protein structure determination.

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Dynamic Re-definition of Variable-Space in Structure Solution from Diffraction Data. Zhongfu Zhou[a,b], Kenneth D.M. Harris[a]. [a]*School of Chemistry, Cardiff University, Park Place, Cardiff CF10 3AT, Wales.* [b]*Now at the Centre for Advanced Functional Materials and Devices, Institute of Mathematics and Physics, Aberystwyth University, Aberystwyth, SY23 3BZ, Wales.*
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Structure determination of organic molecular solids from powder X-ray diffraction data is nowadays carried out widely, in particular using the direct-space strategy for structure solution [1]. In this approach, the structure solution process involves the exploration of a hypersurface (in which the powder-profile R-factor (R_{wp}) is expressed as a function of the set of variables that define trial structures) in order to find the structure that corresponds to the global minimum of R_{wp}. In principle, any technique for global optimization may be used, and our own current work in this field is focused on the use of a Genetic Algorithm (GA) [2], implemented in the program EAGER [3]. Conventionally, the set of structural variables comprises, for each molecule in the asymmetric unit, the position and orientation of the whole molecule and a set of variable torsion angles, and the definition of variable-space remains the same throughout the calculation. Here we introduce an alternative approach in which the variable-space is transformed dynamically to an alternative variable-space of the same or lower dimensionality during the evolutionary progress of GA calculations, and we assess the feasibility of the new approach in comparison to the standard approach. Structures containing flexible molecules defined by a significant number of torsional degrees of freedom represent a particularly challenging case for direct-space structure solution [4], and stagnation of the population during the evolutionary process can be particularly problematic in such cases. We demonstrate that problems of stagnation may be alleviated by altering the definition of variable-space dynamically during the GA structure-solution calculations.

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