MS3-O5 Automated solutions for fragment screening at the HZB MX beamlines

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X-ray diffraction plays an essential role in fragment-based lead discovery and design to identify target hits, and determine the location and structure of fragments bound to a target protein. Recently, a second beamline at the HZB MX facility [1] has been upgraded with a Pilatus detector and sample changer and is dedicated for fragment screening campaigns, enabling fast high throughput experiments to be performed routinely.

In order to help users cope with the huge amount of data thus created and reliably interpret their results rapidly, we have developed the expert software XDSAPP [2] for the analysis of diffraction images during measurements with minimal effort and time. It mainly uses the diffraction data processing program XDS [3], along with additional software like POINTLESS from the CCP4 suite [4], XDSSTAT [5], SFCHECK [6] and PHENIX.XTRIAGE [7] for automated decision making. An independent refinement pipeline for automated ligand search based on PHENIX and COOT [8] has been developed and can also be used within XDSAPP. In the presentation, the workflow of the pipeline will be described and its application to an example will be discussed.

XDSAPP is available free of charge for academic users from www.helmholtz-berlin.de/bessy-mx.

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MS4. Advances in phasing, refinement, and autobuilding

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MS4-O1 ARCIMBOLDO, an *ab initio* approach to MR phasing

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Ab Initio phasing of macromolecular structures, from the native intensities alone without need of derivatives or previous particular structural knowledge has been the object of a long quest. Currently, both experimental phasing and molecular replacement are going *ab initio*, as in the first case, inherent anomalous signal is succeeding with increasing generality[1] and in the second, the previous structural knowledge required is becoming unspecific[2,3,4]. Our own approach[5,6] relies on the combination of locating model fragments such as polyalanine alpha-helices, libraries of unspecific folds or portions of distant homologs with the program PHASER[7] and density modification with the program SHELXE[8]. Given the difficulties in discriminating correctly positioned fragments, many putative groups of fragments have to be tested in parallel, thus calculations are usually performed in a grid or supercomputer. The method has been called after the Italian painter Arcimboldo, who used to compose portraits out of fruits and vegetables. In the case of our program, most collections of fragments remain a “still-life”, but some are correct enough for density modification to reveal the protein's true portrait. Latest developments, such as the single machine implementation ARCIMBOLDO_LITE, advances on the supercomputer GORDON at the SDSC or the first case of a solution for an unknown all-beta structure will be described. (http://chango.ibmb.csic.es/ARCIMBOLDO_LITE).

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