Development of serial crystallography methods, which are complementary to efforts currently taken at hard X-ray free electron laser (XFEL) facilities have an extremely high impact on structural biology. Where single molecule and nano-crystal diffraction is out of reach at conventional synchrotron sources, fast room temperature experiments on large ensembles of micron sized crystals could benefit from certain advantages over the XFEL approach.

First approach to develop serial crystallography of membrane proteins is to perform lipidic cubic phase (LCP) microjet-based serial millisecond crystallography at synchrotrons[1], similar to XFELs[2]. The main advantages of this method are: crystal injection using LCP-jet combined with a micro-beam allows diffraction data to be collected at room temperature, without crystal freezing and difficult crystal handling steps; thousands of crystals can be screened in a short time with less than a milligram of protein and the method is well suited for time-resolved diffraction studies. The LCP-jet method has been recently demonstrated by solving a structure of the bacteriorhodopsin at a resolution of 2.4 A[3].

Second approach is based on scanning micro-crystals, which are deposited on solid supports. First successful results have already been obtained using lysozyme micro-crystals[4]. This approach, relying rather on controlled spatial distribution and subsequent scanning, allows to overcome severe limitations of available sample volumes (in particular for membrane proteins) and also it has further opportunities for optimization.

The other approach is to use special crystallization plates[5]. This system is based on a new crystallization plate that allows growing crystals on very thin films that can then be excised with a laser beam to recover the crystalline material. Due to their design, plates allow to collect diffraction data in-situ with very low background and to reduce mechanical stress for the crystals.

References
[1] - collaboration with U. Weiherstall (ASU, USA) , R. Neutze, J. Standfuss, I. Moraes Marie-Curie ITN ‘NanoMem’

Keywords: serial crystallography, membrane proteins, nanobeam, microbeam, LCP-injector