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Sample delivery methods for serial protein crystallography

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Invited lecture
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11:30-12:00

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Instrumentation and method development is crucial in overcoming the technical challenges when solving fundamental scientific questions. This cannot be overstated, in the advent of the next generation synchrotrons as well as X-ray free electron lasers (XFELs), where new sample manipulation and delivery techniques are necessary to utilise the full power of these X-ray sources in the field of structural biology. In my presentation, I will review sample delivery methods for serial protein crystallography whereby each crystal sample must be replenished before the subsequent X-ray exposures. These include liquid jets, high-viscosity extrusion (HVE) injectors, fixed target supports and acoustic 'drop-on-demand' systems[1-2].

I will highlight the activities of the Time-Resolved Crystallography group based at Paul Scherrer Intitut. In particular, I will describe how we developed and implemented the HVE injectors at the SLS and SwissFEL establishing serial synchrotron[3,4] and serial femtosecond crystallography[5,6]. By including time as a fourth dimension, we are able to study protein-ligand interactions and resolve transient conformational states important for function[5-7]. As one of our latest developments, I will describe the multi-injector device[8], shown in the figure, which constitutes an important step towards automation and efficient sample delivery system for XFEL beamlines. Finally, I will present our most recent project at the next generation synchrotrons (in collaboration with MAX IV), where we achieved 1ms time resolution studying dynamics of membrane proteins rhodopsin 2 (*Krokinobacter eikastus*) by employing the 2kHz Jungfrau X-ray doctor developed at PSI.

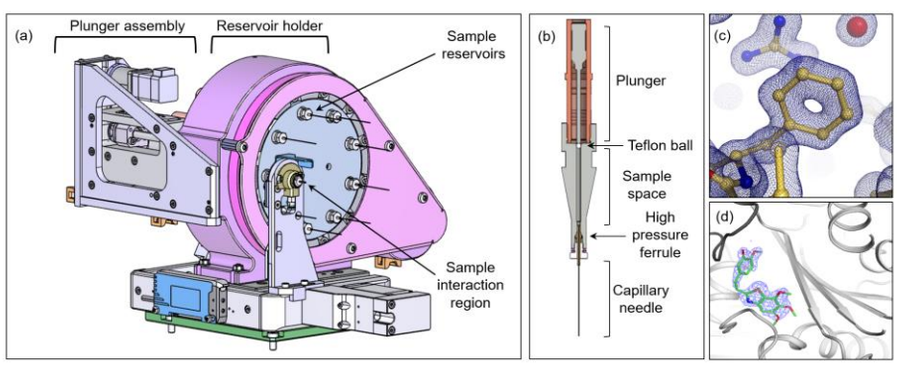

Figure 1. (a) Multi-reservoir high viscosity extruder. The temperature-controlled rotating drum contains slots for nine individual sample reservoirs. (b) Single 130 µL sample reservoir with supporting components. (c) High resolution map (1.43 Å, $2F_o$-F_c at 1.5σ) of lysozyme focused on PHE34 in lipidic cubic phase (LCP). (d) High resolution map (1.65Å, $2F_o$-F_c at 1.5σ) of α-β tubulin bound SBTubA4 for *in vivo* photo control of microtubule dynamic.

References

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