Revealing Protein Binding Dynamics Using Time-Resolved Diffraction Experiments at SwissFEL

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The creation of molecular movies of "biomolecules in action" based on time-resolved diffraction experiments has come within reach thanks to the availability of X-ray-Free-Electron Lasers (XFELs), such as SwissFEL, the new large scale facility at PSI. This project targets the development of XFEL-based methods for dynamic studies of protein-binding events, using the binding of photo-cleavable derivatives to streptavidin as a versatile model system.

The successful applicant for this project will work at the PSI and at the University of Basel and will be supported by teams at both places. As protein crystallographic data collection critically depends on the sample preparation, we will first concentrate on the fabrication of sample holders to accommodate the crystalline samples, enclose them between ultrathin X-ray transparent films and provide access for the optical laser which are used to trigger the binding of a caged cofactor to the protein of interest. For typical measurements, we will need a few hundreds of support structures, which means that they must be mass-fabricated using silicon or polymer technologies. The nanotechnology lab at PSI will support the student in designing and fabricating the holders used for this specific study. Furthermore, the PSI nanotechnology lab is well linked to Macromolecular Crystallography Group at PSI with access to the PX beamlines and to SwissFEL. The PhD student will be involved in measurement campaigns in order to learn all the measurement techniques and data evaluation strategies before his/her own experiments at SwissFEL. With the help of the team at Uni Basel, the student will synthesize photocaged derivatives, and perform their characterization, crystallization and co-crystallization experiments. In the later phase of the project, he/she will design and produce and optimize by directed evolution new variants of the cofactor that allow addressing specific characteristics of streptavidin binding.

For this highly interdisciplinary project, we are seeking for a PhD student holding a master's degree in science or engineering, with experience in protein crystallography, nanofabrication technology and/or peptide synthesis and modification, and with keen interest in method development for experiments at state-of-the art large scale facilities in order to address fundamental biochemical questions.

For further information, please contact the PIs of this project:

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