Towards X-FEL based dynamic studies on 2D and 3D nanocrystals of membrane proteins on solid supports.

Dr. Celestino Padeste
Lab. for Micro- and Nanotechnology, and
Dr. Xiao-Dan Li, Biomolecular Research
Paul Scherrer Institut
5232 Villigen PSI
www.psi.ch/lmn
www.psi.ch/lbr

Prof. Dr. Henning Stahlberg and
Dr. Thomas Braun
Center for Cellular Imaging and
NanoAnalytics (C-CINA)
Biozentrum, University of Basel
Mattenstrasse 26, 4058 Basel
www.c-cina.unibas.ch

Background

To understand the relation of structure and function of specific proteins, insight into dynamic processes is highly desired. The current development of free-electron laser sources (XFELs) adds a new dimension to the power of X-ray based protein structure determination. It has been demonstrated that using the extremely short, coherent, and intense X-ray pulses produced in XFELs, diffraction patterns from nanometer-sized protein crystals can be collected before the crystal is destroyed by the enormous energy of the pulse ("probe-before-destroy"). This opens the way towards dynamic measurements, e.g., by sending an optical laser pulse to crystals of photoactive proteins shortly before the X-ray pulse produces the diffraction pattern.

To obtain a reasonable dataset, a large number of crystals need to be probed by X-ray pulses. This can for instance be achieved by deposition of nanocrystals on supports consisting of grids with thin windows. The protein-loaded supports are then scanned through the beam. First measurements at the LCLS in Stanford revealed the great potential of this type of protein crystallography, in particular in view of dynamic experiments. However, they also pointed out the importance of well-adapted sample preparation and treatment methods, on which this project will focus.

Your Project

The main aim of this project is the further development of sample preparation methods for XFEL based protein nano-crystallography in three ways, (1) the development of supports optimized for protein crystal preparation, (2) adaptation of a liquid handling system for minimized sample consumption, and (3) developments towards pump-probe experiments on the solid supports. You will work at the PSI and at the University of Basel and will be supported by both teams. The Lab. for Micro- and Nanotechnology at the PSI provides equipment and know-how for sample preparation based on silicon and polymer replication technology. The group of Dr. T. Braun in the lab of Prof. H. Stahlberg has established technologies for automated deposition on grids for transmission electron microscopy. Furthermore, you will participate in measurement campaigns at the Swiss Light Source and at XFEL facilities, in collaboration with the group of Dr. X.-D. Li (PSI), who is focused on membrane proteins, including structure determination of 2D crystals using electron microscopy and X-ray/XFEL-based methods.

Your Profile

You are physicist, chemist, engineer, nanoscientist or (protein)crystallographer with an interest in instrument and method development. You are highly motivated to work on a project between engineering and basic research in a highly interdisciplinary research team.