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DESY building 25b, seminar room 109

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## Femtosecond nanocrystallography of membrane proteins opens a new Era for Structural Biology

Femtosecond nanocrystallography provides a novel concept for structure determination, where X-ray diffraction "snapshots" are collected from a fully hydrated stream of nanocrystals, using femtosecond pulses from the world's first high energy X-ray free-electron laser, the Linac Coherent Light Source. Photosystem I, which is the most complex membrane that has been crystallized to date, consisting of 36 proteins and 381 cofactors, was used as the model system.

The experiments show the proof of concept that diffraction of nanocrystals that contain only 100-10 000 Photosystem I molecules can be observed using femtosecond pulses that are  $10^{12}$  stronger than 3rd generation synchrotron sources and destroy any material that is placed in

its focus. Over 3 million diffraction patterns from individual nanocrystals (100nm- 2  $\mu$ m in size) were collected and evaluated. (*Nature*, 470, 73-77) By using femtosecond pulses briefer than the time-scale of most damage processes, femtosecond nanocrystallography overcomes the problem of X-ray damage in crystallography. Data collected at the CXI LCLS beamline at higher energy (8keV) showed that the concept of fs crystallography extends to atomic resolution. Data will be presented that show that nanocrystals of membrane proteins, which are notoriously difficult to crystallize, have extremely low mosaicity and can be grown from a large set of membrane proteins and can be characterized by dynamic light scattering and SONICC.

The talk will also report first results on fs nanocrystallography of membrane proteins grown in lipidic cubic phases. Femtosecond crystallography also opens a new avenue for determination of protein dynamics. First experiments on time resolved X-ray crystallography have been performed on Photosystem I-ferredoxin and Photosystem II nano-crystals. The first results are very promising and pave the way for a new avenue in X-ray crystallography that may allow the determination of molecular movies of the dynamics of membrane proteins "at work" in the future.

