



*Nanoscienze & Nanotecnologie  
& Strumentazione*

## ***Seminario***

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***Titolo:***

**Science at Free Electron Lasers  
Femtosecond X-ray Protein Nanocrystallography**

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**Science at Free Electron Lasers**  
**Femtosecond X-ray Protein Nanocrystallography**

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The advent of free electron lasers (FELs) has opened up new opportunities to probe the structure of matter and the dynamics of ultrafast processes with unprecedented spatial and temporal resolution. New methods are therefore being developed to exploit these possibilities.

One interesting application is the use of intense femtosecond X-ray pulses generated by FELs to perform crystallography on systems not accessible with the conventional radiation sources. X-ray crystallography, indeed, provides the vast majority of macromolecular structures, but the success of the method relies on having crystals of sufficient size. Unfortunately, it is often only possible to grow protein crystals up to the micrometer range or smaller and this is a large bottleneck in structure determination.

The high brilliance of FELs sources gives the possibility to acquire diffraction patterns from nanocrystals. Although the pulses are intense enough to cause molecular disintegration, it is possible to record ‘damage-free’ diffraction patterns because the pulses are sufficiently short such that the diffraction process is completed before the molecules undergo significant structural change. In order to solve a structure, thousands of single nanocrystal patterns have to be acquired, indexed and then combined to give a 3D map of the structure factors that can be phased using conventional single-crystal techniques.

An experiment [1] performed at the Linac Coherent Light Source (LCLS) allowed the structure of the membrane protein Photosystem I to be solved using the method described above. A 1.8 keV energy beam hitting a suspension of crystals smaller than 2  $\mu\text{m}$  allowed the reconstruction of an 8.5 Å resolution structure. Most recent experiments were carried out at a photon energy of 9.3 keV, with  $2 \times 10^{11}$  photons per pulse focused to 10  $\mu\text{m}^2$  (manuscript in preparation). Another interesting FELs application is the imaging of non-periodic objects. Coherent X-ray pulses can be used to outrun key damage processes and obtain a diffraction pattern from a single object before the sample explodes and turns into plasma. This idea has first been demonstrated at FLASH, where coherent diffraction patterns were acquired from nanostructured non-periodic objects before destroying them [2]. A recent paper [3] has shown that high-quality diffraction data with a single X-ray pulse can be obtained from a non-crystalline biological sample, namely a single mimivirus particle, which was injected into the pulsed beam of the LCLS.

[1] H.N. Chapman et al., *Femtosecond X-ray protein nanocrystallography* Nature **470**, 73-77 (2011)

[2] H.N. Chapman et al., *Femtosecond diffractive imaging with a soft-X-ray free-electron laser* Nature Physics **2**, 839-843 (2006)

[3] M.M. Seibert et al., *Single mimivirus particles intercepted and imaged with an X-ray laser* Nature **470**, 78-82 (2011)