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Towards a better understanding of the nucleation process and advanced detection of nanocrystals

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At synchrotron (SR) and Free-Electron-Laser (FEL) beamlines micro-sized crystals are preferred for diffraction data collection. Therefore, advanced and reliable methods to prepare and score 3D micro- and nano-crystal suspensions need to be established in time. A better understanding of the nucleation process is of fundamental importance in this context. Till now the nucleation process is discussed in theory and experiment differently. In order to obtain more insights about the process and to obtain supporting evidence for the tow-step nucleation mechanism we investigated the nucleation process and early crystallization events applying complementary biophysical methods [1,2]. *In situ* dynamic light scattering, small-angle X-ray scattering and transmission electron microscopy experiments were performed. Data obtained strongly support the existence of a two-step mechanism of nucleation. However, the early process is governed by the formation of liquid dense clusters as initial step [3], followed by the transition to higher order assemblies inside these clusters. The desired size for SFX experiments is preferably in the upper nanometer or lower micrometer regime. This guides to a strong demand to develop and establish new methods to analyze, score nano- and micro crystal suspensions for serial crystallography. To support and facilitate this demand we recently designed and constructed a microscope setup based on detecting second harmonic generation (SHG) signals of crystalline particles. This method and setup enhances the already available signal sensitivity to such extend that detection of small crystals and crystals with higher symmetry, known to produce rather weak signals, is now possible and distinguishing between amorphous and crystalline particles is possible as well. The instrument is equipped with additional channels, which are capable to detect the third harmonic generation signal and three-photon excited UV-fluorescence, all in parallel, to provide complementary information about the crystalline sample suspension. Details and experimental data will be presented.

References:

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