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## **In Situ Stopped-Flow SANS Study of the Growth of Poorly Water-Soluble Drug Nanoparticles Prepared by Antisolvent Precipitation**

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Using the stopped-flow technique for classical in situ small-angle neutron scattering (SANS) experiments enables to study fast structure formation processes like the formation and growth of organic nanoparticles (NPs) with a temporal resolution in the regime of milliseconds. The statistics of short time frames can be enhanced during the post processing by adding the detected neutrons of each frame for a high amount of repetitive mixing processes of the stopped-flow technique.

First in situ experiments at the KWS-2 instrument (MLZ, Garching) show the reliability of the combination of the stopped-flow technique with SANS. The early growth of poorly-water soluble active pharmaceutical ingredients (APIs) NPs during the antisolvent precipitation process has been studied. The SANS data has been acquired with a high temporal resolution of 2 ms during the first 2 s and by performing up to 400 mixing processes for each sample system. To further enhance the statistics for the analysis, the frames have been binned to a final temporal resolution of 20 ms.

The influence of three structurally different and commonly used surfactants on the growth kinetics and the ripening of the model API fenofibrate has been studied and first analyses reveal an early beginning of ripening already after 250 ms for all surfactant systems and increased growth kinetics combined with inhibited ripening for fenofibrate NPs solubilized by micelles.

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