Laser-Induced Crystallization: Enhanced predictability of urea crystallization by optimized laser repetition rate

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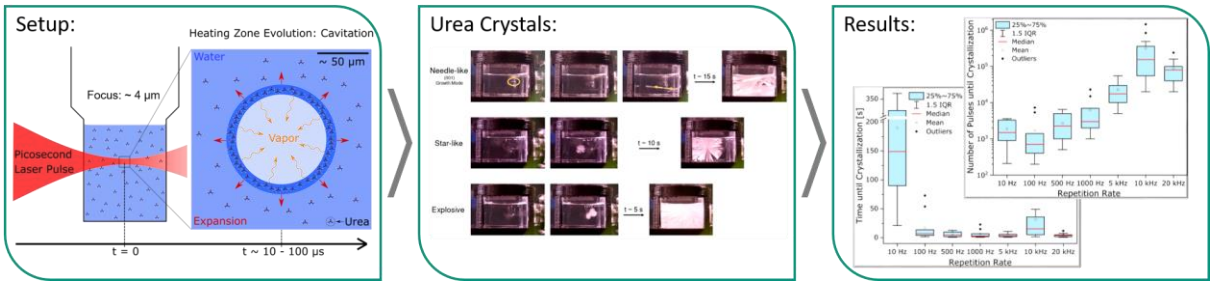
The crystallization of small molecules and proteins is an important technique, relevant in the structural determination process of proteins, purification of molecules, and overall in pharmaceutical research. Furthermore, organic crystals are in great demand for new technologies in materials science and are already on the consumer market. To keep up with the increasing importance of organic crystals, research into fast and reliable crystallization methods is required.[1] New challenges are to be addressed through the combination of spatial and temporal control of the process, and laser-induced crystallization offers a route to such spatiotemporal control.[2]

For this study, the molecule of interest is urea. The pulsed laser system with maximum 8 Watts of output power is focused in a supersaturated urea-D2O solution. The intensity of 1E14 W/cm2 per pulse generates a thermo-cavitation bubble by multiphoton absorption. Evaporation during the bubble growth phase increases the concentration of urea molecules in the shell region. In this shell-layer, a seed crystal can be induced (See Figure). Not each laser pulse generates the perfect cavitation bubble for nucleation. Therefore, this nucleation method is depend on long exposure times or high repetition rates to overcome the low probability to nucleate. Long exposure times are critical, because thermal stress on the molecule should be avoided, especially with regard to protein crystallization. Hence, we investigated the influence of laser repetition rate on the induction time to reduce the exposure time.

The hypothesis of a reduction in induction time with increasing repetition rate was confirmed. At 1 kHz repetition rate the induction time reduced to a median value of 2-5 seconds. Higher repetition rates lowered the induction time to one second. Furthermore, we found additional effects that influence nucleation, such as the interaction of a laser pulse with the previous generated cavitation bubble. This interaction lowers the probability to crystallize. The high repetition rate in the kHz range compensates for this.



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