European XFEL Workshop

Opportunities for microfluidic devices at Free-Electron Lasers

Microfluidic crystallography: sample preparation and delivery

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There is no guarantee that a given protein has a crystalline phase, but even existence of an equilibrium crystalline phase is not sufficient for a crystal to form because the transformation of a protein solution to a crystal is governed by two non-equilibrium processes: nucleation and growth. Consequently, supersaturation kinetics play an essential role in crystallization and we argue that the optimal crystallization strategy should involve variables such as depth of supersaturation, duration of supersaturation, and sample volume.

Protein crystallization is a stochastic process; we experimentally optimize crystal nucleation and growth by generating hundreds of different kinetic paths simultaneously by varying both temperature and concentration of the protein solution. We have developed a phase chip technology based on emulsion microfluidics in which nanoliter volumes of protein solution are encapsulated in oil and stabilized by surfactant. This entails finding conditions on-chip for which one crystal is grown per drop and then isolating hundreds of drops for serial crystallography using an x-ray semi-transparent microfluidic device or via liquid jet injection.

Reliable sample delivery is essential to biological imaging using X-ray Free Electron Lasers. Continuous injection using the Gas Dynamic Virtual Nozzle (GDVN) has proven valuable, particularly for time-resolved studies. Yet, many important aspects of GDVN functionality have yet to be thoroughly understood and/or refined due to fabrication limitations. We use 2 high-resolution 3D printing to fabricate high-fidelity GDVNs with submicron resolution. This technique allows rapid prototyping of a wide range of different types of nozzles from standard CAD drawings and optimization of crucial dimensions for optimal performance.