Controlled samples for single-particle x-ray diffraction

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Synopsis Single-particle diffractive imaging at x-ray free-electron lasers requires the efficient delivery of isolated, reproducible target particles into the x-ray beam. Here, we report on our efforts to push existing control methodologies for small molecules to much larger systems, such as peptides, proteins or viruses. This will enable not only efficient sample delivery, but also the selection of, e.g., structural isomers of biological samples.

Recent years have seen the development of advanced techniques to control and confine various degrees of freedom of neutral molecules. We can now routinely select single structural isomers of small molecules, disperse rotational quantum-states, and in certain cases create single-quantum-state samples [1]. Here, we report on the COMOTION project, which aims to extend the available approaches to significantly larger systems, from (poly-)peptide molecules to entire cells or viruses and, furthermore, to develop methods to inject these controlled samples into the interaction region of x-ray free-electron lasers (XFELs) to enable truly single-species single-particle diffractive imaging.

One of the primary bottlenecks in realizing single-particle diffractive imaging at XFELs is the efficient delivery of isolated, reproducible target particles into the x-ray beam. This contains two important challenges that need to be overcome; (i) vaporisation of (often biological) samples whilst maintaining their native state and (ii) delivery of these into the x-ray focal spot of only a few 100 nm diameter, i.e., in a very dense particle beam. We are working on overcoming the first challenge through the development of novel soft vaporisation techniques. Working with laser or acoustic desorption processes allows the production of large volatile (bio)molecules in the gas-phase, and we have recently shown the production of internally cold, dense molecular beams of intact dipeptides in a setup suitable for future XFEL studies [2]. For even larger, nanoparticle-sized systems, we are applying vaporization methods based on tightly focused liquid jets and electrospray ionisation, which produce nanodroplets that can be evaporatively dried to yield isolated particles. The combination of these techniques with buffer-gas cooling for internally-cold samples is currently being setup in our laboratory. Cold beams can then be further manipulated and controlled, for example through the use of electric fields to spatially separate conformational states [1].

Aerosolized samples are transferred into tightly focused or collimated particle beams using novel aerodynamic lens stacks [3] and convergent-nozzle focusing injectors [4]. We have developed a numerical simulation infrastructure that allows the quantitative simulation of isolated particles within complex aerodynamic lens setups. This is used to build aerosol injection systems optimized for a specific particle size and producing the highest density particle beams to optimize XFEL hit rates. Produced particle beams can subsequently be further manipulated using optical techniques, such as hollow-core vortex laser beams [5, 6].

The produced cold and controlled samples of large (bio)molecules and nanoparticles will not only benefit diffractive imaging experiments at XFELs, but furthermore are of interest in studies of ultrafast electron dynamics across extended biological systems, or in testing the fundamental size-limits of quantum mechanics.

References

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