

Liquid Microjets in XFELs: Last Train to Molecular Heaven

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High intensity, coherent X-rays (X-ray free electron lasers, XFELs) have become the current paradigmatic tool in high resolution molecular analysis of biological samples. X-ray scattering of a molecule is possible at the Angstrom resolution with a sufficiently strong radiation input (Doniach 1996, *J. Synchrotron Rad.* 3, 260-267). However, the first word storming one's mind when hearing about the interaction of a normally fragile biological molecule and an ultra-high intensity energy input is destruction. A pioneering but hardly recalled work (Solem 1986, *J. Opt. Soc. Am. B* 3, 1551-1565) anticipated for the first time "the remarkable fact that, at sufficiently high intensity, an image of diffraction-limited resolution can be captured before the specimen is obliterated". In the year 2000, Hajdu and co-workers (Neutze et al. 2000, *Nature* 406, 752-757) made the first precise prediction on the energy strength and short pulse time needed to image a protein (lysozyme) before destruction. A time lapse of about 10 years was necessary to build an XFEL with a sufficiently short pulse rate (10-20 fs.) and make experiments with biological samples (protein crystals) (Chapman et. al. 2011, *Nature* 470, 73-78). The enormous success of this achievement, reflected by the explosive interest raised in the scientific literature, was brought in a humble but crucial engineering vehicle (see figure 1 in Chapman et al. 2000): a Flow-Focusing® microjet (Ganan-Calvo 1998, *Phys. Rev. Lett.* 80, 285-288; DePonte et al. 2008, *J. Phys. D: Appl. Phys.* 41, 195505) acting like a ultra-smooth, high-speed micro-train carrying the samples towards their glorious last station destiny: an ultra-high intensity, ultra-short X-Ray spot getting an image of their molecular structure. Here, we provide an overview of current sample introduction strategies in XFELs, their stringent demands and challenges, and how liquid microjets produced by strongly focused hydrodynamic or electrohydrodynamic means deliver.