Improving Data Collection Efficiency In Small-Molecule Serial Femtosecond Crystallography at X-Ray Free Electron Lasers

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Small-molecule serial femtosecond crystallography (smSFX) at an X-ray free electron laser has become a proven method for high quality, *de novo* structure determination from small- molecule microcrystals. In our initial study published in *Nature*, we solved three structures from smSFX datasets, and have since followed with 12 more at atomic resolution. In smSFX, microcrystals are suspended in a carrier medium and then delivered to the XFEL interaction region via liquid jet injection; this allows for rapid crystal delivery that is synchronized to the ultrafast XFEL pulses. Compatibility of carrier medium with both the microcrystals and liquid jet injector system is a key component in an smSFX experiment. Small molecules often interact with surfaces and only suspend in volatile organic solvents that are incompatible with the jet injectors, making it difficult to find adequate carrier mediums. As a result, data collection efficiency suffers from clogging in the injector lines and low crystal hit rates. smSFX stands to benefit greatly from Megahertz high-repetition rate XFEL sources, where complete datasets could be obtained in minutes. We cannot make full use of these facilities if we cannot collect data efficiently. Here, we present the current state of smSFX and introduce new methods for improving smSFX data collection efficiency to prepare for next generation XFEL capabilities.

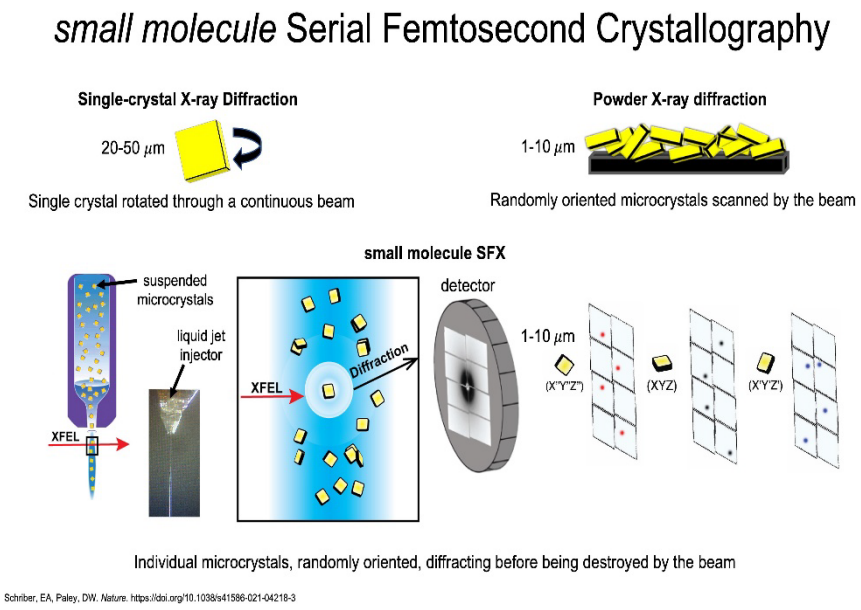

Figure 1