Integrated sample-handling and mounting system for fixed-target serial synchrotron crystallography

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Serial synchrotron crystallography (SSX) is enabling the efficient use of small crystals for structure-function studies of biomolecules and for drug discovery. An integrated SSX system has been developed comprising ultralow back-ground-scatter sample holders suitable for room and cryogenic temperature crystallographic data collection, a sample-loading station and a humid 'gloveless' glovebox. The sample holders incorporate thin-film supports with a variety of designs optimized for different crystal-loading challenges. These holders facilitate the dispersion of crystals and the removal of excess liquid, can be cooled at extremely high rates, generate little background scatter, allow data collection over >90° of oscillation without obstruction or the risk of generating saturating Bragg peaks, are compatible with existing infrastructure for high-throughput cryocrystallography and are reusable. The sample-loading station allows sample preparation and loading onto the support film, the application of time-varying suction for optimal removal of excess liquid, crystal repositioning and cryoprotection, and the application of sealing films for room-temperature data collection, all in a controlled-humidity environment. The humid glovebox allows microscope observation of the sample-loading station and crystallization trays while maintaining near-saturating humidities that further minimize the risks of sample dehydration and damage, and maximize working times. This integrated system addresses common problems in obtaining properly dispersed, properly hydrated and isomorphous microcrystals for fixed-orientation and oscillation data collection. Its ease of use, flexibility and optimized performance make it attractive not just for SSX but also for single-crystal and few-crystal data collection. Fundamental concepts that are important in achieving desired crystal distributions on a sample holder via time-varying suction-induced liquid flows are also discussed.

Figure 1. Integrated sample-handling and mounting system for fixed-target serial synchrotron crystallography