# XFEL Microcrystal Diffraction for Fast and Accurate Small- Molecule Structures

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Serial femtosecond crystallography has quickly become a standard technique for structural biology, but no one has fully realized its potential for determining small-molecule structures from microcrystals. In 2022 we reported the first ab initio small-molecule crystal structures from XFEL radiation, with resolution around 1.2-1.3 Å and datasets collected in several hours. With recent developments at XFEL light sources, including higher-energy X-rays and faster repetition rates, we are now collecting full datasets in 30 min at IUCr-standard 0.83 Å resolution. The resulting structures are approaching SCXRD quality, with R1 values around the 9-12% range.

I will present the technical challenges we solved to deliver these results. To determine unit cells from randomly oriented serial frames, we used a spotfinder to synthesize superresolution powder diffraction patterns that are accumulated one crystal at a time. To index the sparse frames, we use a graph theory approach to find a mutually consistent set of Miller indices. We found it was critical to precisely locate the beam center (within microns) and developed a simple beam center correction using the sharpness of a "powder diffraction" peak.

I will also present a practical overview of the typical SFX data reduction process for small molecules. This will help chemical crystallographers evaluate whether SFX is a viable option for their microcrystal samples.

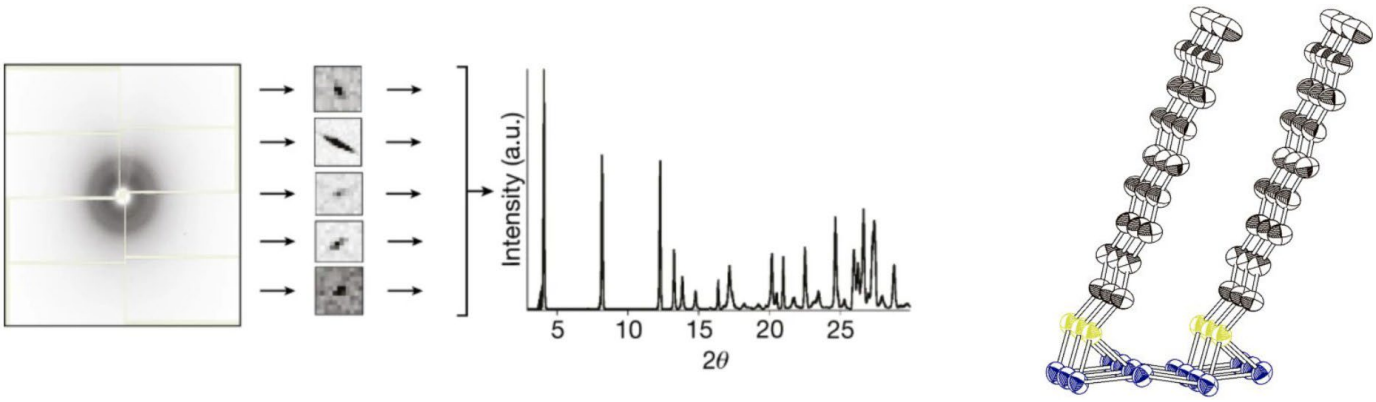


***Figure 1***