Serial crystallography (SX) is a powerful method for structural determination in macromolecular crystallography (MX), especially for samples and experimental conditions not amenable to single-crystal cryocrystallography. Much effort has been put on sample delivery and analysis of diffraction data, to great success. With SX, protein structures can be gleaned from room temperature diffraction with little radiation damage, protein dynamics can be measured, and pump-probe experiments can elucidate biochemical pathways in large biological systems. But from a user service (specifically, storage ring MX beamline) perspective, we find that the largest barrier to getting users interested in trying SX for their own samples is not inertia (users would do it if they knew how to), nor is it infrastructural (nearly every MX beamline nowadays has some capacity to do SX). The hurdle is not making sample preparation and sample delivery accessible to most structural biology laboratories’ MX structure pipelines. Easier access to SX sample delivery systems would enable users to the many possibilities of SX.

With accessibility in mind, we have developed an integrated fixed-target sample delivery system for SX with a target of commercialization and mass production. The sample holders are thin, photopatterned Kapton sheets containing hundreds of wells for samples, with sealable gaskets that can be easily mounted on a standard magnetic base and transported in Unipucks for shipping. In addition, we have developed a portable sample mounting station for room temperature sample preparation, under a humidified atmosphere so sensitive crystalline samples do not dry out. Our new sample delivery system has been commercialized and has already made promising results. We demonstrate the utility of this system on a pair of Glutaminase C-drug complexes, in which an explanation of the large difference in enzyme inhibition could only be determined by room temperature SX analysis.

References

Kapton-based fixed target mount.
Humidor for sample deposition.