Abstract:
We are developing tools for manipulating and mounting crystals of proteins and other biological macromolecules for structure determination by X-ray crystallography. Some of these tools have been commercialized by Mitegen, LLC, and are now used by academic and industrial researchers in more than 25 countries.

The molecular structures of proteins, viruses and macromolecular complexes are essential to understanding biological function and to the design of new medications to modify those functions. With advances in genetic cloning, expression, and purification on the one hand and in x-ray sources, detectors and analysis software on the other, the difficulties associated with growing and mounting crystals of proteins for structure determination by X-ray crystallography have become important obstacles limiting the rate at which new structures are solved. Existing tools for manipulating crystals after they are grown, and mounting them in cold gas streams for X-ray measurements, degrade achievable data quality and limit overall diffraction throughput. We are developing a family of tools for retrieving crystals from crystallization media, performing post-growth manipulations like cryoprotectant and heavy atom soaks, and holding the crystals in the X-ray beam [1-3]. Some of these tools have been commercialized by Mitegen, LLC of Ithaca (www.mitegen.com).

The tools are fabricated using standard photolithographic techniques from Photoneece PWDC-1000 photoexposable polyimide, which provides excellent mechanical properties and excellent X-ray transparency. Protein crystals can be more than 90% water and are spectacularly fragile, and so the tools must facilitate very gentle handling. We have designed and prototyped more than 50 tools for retrieving small and large crystals from crystallization drops, removing crystals that have adhered to the surfaces of crystallization media, separating crystal clusters, and mounting for flash cooling and data collection crystals with a variety of morphologies and sizes ranging from microns to millimeters.

Summary:
New tools for manipulating and mounting crystals of biological macromolecules for structure determination by X-ray crystallography are being developed. Some of these tools have been commercialized, and are rapidly being adopted by the worldwide structural genomics community.

References:
Figure 1: Tool for mounting roughly 200 µm protein crystals. The crystal rests in the small aperture in the tip. The channel and larger aperture allow excess liquid, which contributes to background X-ray scatter and causes crystal damage during flash cooling, to be wicked away.

Figure 2: Tool for retrieving multiple small crystals from early crystallization trials. By using a small (0.1 mm) X-ray beam, the diffraction properties of crystals can be individually interrogated.