# An *in vacuo* Microfluidic Mixer for Biological X-Ray Solution Scattering


**CNF Project Number: 1940-10**

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*Primary Source(s) of Research Funding: National Institutes of Health GM-103485*

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*Primary CNF Tools Used:*


## Abstract:

**Small angle x-ray scattering (SAXS) is an important tool for probing the structure and interactions of biological molecules under realistic physiological-like conditions. Fabrication of plastic microfluidic chips for time resolved small angle x-ray solution scattering (TR-SAXS) involves embedding various thin, fragile x-ray transparent window materials within a polymer matrix. This continuous-flow mixer utilizes chaotic laminar flow that is designed to reach multiple timescales down to a millisecond. High flow rates of water-based samples though the cell induces high pressures that present design challenges. Our current cell design utilizes relatively deep 500 µm channels for fluid flow combined with either polyimide or synthetic mica x-ray windows. Synthetic mica is more rigid than polyimide, resulting in less flexing of x-ray windows under pressure. Mica also has the advantage of fewer x-ray scattering artifacts and its hydrophilic nature lends itself to bonding.**


## Summary of Research:

Biological small angle x-ray solution scattering (BioSAXS) is a popular technology for extracting structural information from biomolecules under realistic physiological-like solution conditions. Given that many studies in structural biology today rely heavily on crystalline and/or frozen samples, the ability to probe solution behavior is more critical than ever. Many important biological phenomena change on times scale ranging from 1 ms to several seconds [1]. Time-resolved SAXS methods have been developed in the literature that can reach these timescales, but the techniques are difficult to implement and still require intensive effort by specialists in the field. High-volume, repeated experiments required for use in a general user facility are currently impractical. The focus of this work is to make TR-SAXS more easily accessible to the general biology community by developing disposable microfluidic mixing cells that can be easily replaced to handle the high-volume, continuous duty of a user facility.

Our fabrication method uses the recently developed SUEX film (DJ Microlaminates, Sudbury, MA) to create a 500 µm thick layer containing deep microfluidic channels (Figure 1a). The x-ray window is bonded to a poly(methyl methacrylate) (PMMA) base using epoxy then overlaid with SUEX, exposed and developed by standard photolithography techniques. A second x-ray window (4, in Figure 1B) covering all the liquid channels, is sandwiched between the underlying SUEX layer and an outer PMMA support. While thin 7 µm polyimide has been used for some time in x-ray work, it is easily deformed resulting in irreproducible scattering absorption and undesirable scattering background. High quality synthetic mica is now available with superior rigidity and low background scatter (fluorophogopite, Great Wall Mineral, Shijiazhuang, China). Bench testing subjected layers to pressures of approximately 4500 bar, though pressure downstream of the mixing zone was estimated to be much lower (130-70 mbar).

## References:


[1] Panine, P., S. Finet, T. M. Weiss and T. Narayanan (2006). "Probing fast kinetics in complex fluids by combined rapid mixing and small-angle x-ray scattering." Advances in Colloid and Interface Science 127(1): 9-18.

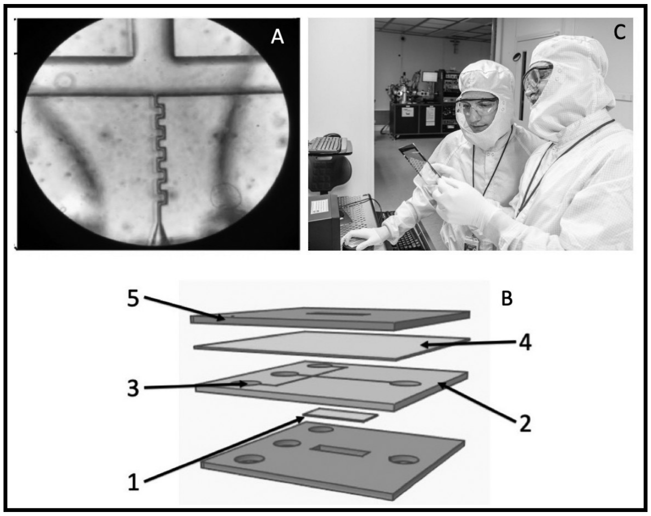


*Figure 1: Microfluidic TR-SAXS chip. (A) Closeup view of mixing region. (B) Schematic of layer design: 1. x-ray window, 2. SUEX layer, 3. Input port, 4. x-ray window, 5. PMMA layer. (C) Christopher Flynn, Fort Lewis, Colorado, SunRise program for Summer students, together with CHESS scientist Richard Gillilan examining their latest photolithography mask.*