Microfabricated Mixers for Experiments with Proteins

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Abstract
We are constructing a new generation of rapid mixers to study the reactions involving biological macromolecules. Prototypes will be built and tested to address concerns about mixing efficiency and flow homogeneity.

Summary of Research
This project focuses on the continued development of microfluidic mixers for use with a variety of experimental probes of macromolecular interactions. In the past we have used both x-ray scattering and fluorescence microscopy to study protein and ribonucleic acid (RNA) folding in addition to protein conformational dynamics [1-3]. Our past experimental work employed CNF-fabricated mixers that relied on hydrodynamic focusing to achieve rapid mixing. Several generations of focusing mixers were built, characterized and used for experiments with biomolecules.

In these mixers, the large macromolecules were focused into an ~ micron-wide jet that flowed down the center of a wider channel. This jet was flanked on either side by buffer containing a small molecule; the rapid diffusion of these small molecules across the focused jet triggered the conformational change of interest. Since the mixing time scales with the squared width of the jet, the mixer operates most efficiently when thin jets are employed. Thin jets are highly compatible with laser microscopy, where micron sized focal or detection volumes are easily achieved [2]; however, use in conjunction with probes, such as x-rays, is challenging because the small size of the jet limits signal strength. If we increase the width of the jet, the mixing time increases dramatically.

This year, we have initiated a project to construct a three channel or ‘T’ mixer that operates by turbulent mixing, based on designs from other groups [4]. Larger probe beams will easily interface with these mixers, without the loss of signal to noise. Due to concerns about the uniformity of mixing, and, more specifically, the transition from laminar to full turbulent flow regimes, we are constructing prototype mixers with varying dimensions for characterization. Mixers will be fabricated and tested, to ensure that flow conditions are optimized for experiments.

To date, three port, or ‘T’ mixers have been successfully fabricated by imprinting zeonor [5] from a fabricated silicon master. One such device is shown in Figure 1. The devices must be well-sealed to avoid leakage at the high pressures involved in creating turbulent flow within the channels. This turbulent flow is required to achieve rapid and uniform mixing of solutions. Mixer characterization is in progress.

References
Figure 1: A photograph of the ‘T’ mixer being fabricated.