Time-resolved SAXS using continuous-flow microfluidic mixers

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Characterization of the structural changes accompanying biomolecular reaction kinetics in the microsecond time regime is important for understanding many biochemical processes such as protein folding, protein-protein, protein-DNA, protein-RNA and protein-ligand interactions. Small-angle x-ray scattering (SAXS) offers a number of advantages for probing kinetics because it is label-free, sensitive to a wide range of length scales and also sensitive to the oligomeric state of macromolecular complexes. The interfacing of efficient and robust microfluidic devices with SAXS concomitant with microsecond time resolution will facilitate these efforts. We will present experimental and computational results aimed toward designing turbulent/chaotic mixers that improve the current time resolution and reduce sample consumption in continuous-flow SAXS experiments. Specifically, the applicability of various turbulence models to these flow regimes will be addressed by comparison with direct numerical simulations. Guided by these simulations, we have fabricated single-piece quartz microfluidic devices with thinned windows and tested their suitability for time-resolved SAXS measurements. The capabilities of these mixers and experimental strategies for optimizing the duty cycle of continuous-flow time-resolved SAXS studies will be discussed. The experimental strategy is used to study the properties of the protein chain under folding conditions.