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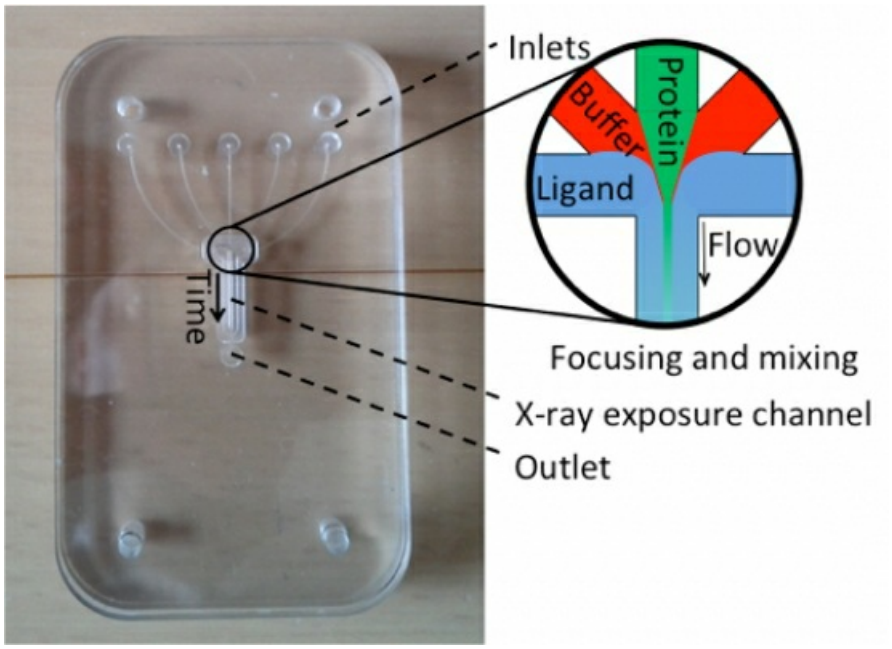
Combined SAXS and Microfludics for time-resolved structural studies of bimolecules

Lise Arleth[1], Grethe Vestergaard Jensen[1], Pie Huda[1], Soren Skou[2], Weifeng Shang[3], Srinivas Chakravarthy[3]
[1]*Niels Bohr Institute, University Of Copenhagen, Copenhagen, Denmark,* [2]*SAXSLAB ApS , Denmark, Skovlunde, Denmark,* [3]*BioCAT, Advanced Photon Source, Argonne National Laboratory, Argonne, United States*
E-mail: arleth@nbi.ku.dk

A microfluidic mixing chip for time-resolved SAXS studies has been developed, aimed at investigations of structural transitions of proteins in solution. Whereas ligand induced structural transitions are an important aspect of the functioning of numerous proteins, only limited knowledge on these processes is currently available. By introducing a microfluidic platform in combination with microfocus synchrotron SAXS, it will be possible to obtain sub-millisecond time resolution with a minimal sample consumption, which is crucial for studies of many biological systems.
In the chip, protein and ligand solutions enter inlet channels in a continuous flow, and are merged at a mixing point. A structural transition of the protein is triggered by the ligand diffusing into the protein sheet, and any position downstream of the mixing point represents a certain time after mixing, which can be probed by SAXS. The chip is based on the same principle as the design suggested by Lois Pollack et al. [1,2].
Using the recently developed compund refractive lens microfocus setup at the BioCAT beamline at APS, it was possible to characterise the profile of the protein sheet. Sheet widths down to 5 micro-m were successfully obtained, which corresponds to typical mixing times of ca. 1 ms (full diffusion of ligand into the sheet). Various protein systems were then initially tested and we showed that the chip indeed allows for triggering structural transitions of proteins in solution and for obtaining time-resolved structural data in solution with time-resolutions down to a few ms.
[1] H.Y. Park et al. (2006), Anal. Chem., 78, 4465-4473.
[2] L. Pollack et al. (2001), Phys. Rev. Lett., 86, 4962-4965.



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