SAXS-LabDisk: A centrifugal microfluidic screening platform for protein structure analysis

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SUMMARY

A small angle x-ray scattering (SAXS) screening platform for protein structure analysis based on centrifugal microfluidics is presented. SAXS can be used to reconstruct low-resolution structures of macromolecules directly from solution scattering. This enables screening for conformational changes of proteins due to different environmental conditions. However, for state-of-the art techniques, consumption of the protein samples is still at least 6 µl per condition and the time per measurement is at best 3 min. In most cases this still renders multi-parameter screening impractical. We present a centrifugal microfluidic platform capable of decreasing both, time per measurement and consumed protein volumes in small angle scattering screenings by more than one order of magnitude.
During an automated rotational protocol the presented compact disk prepares 20 different screening conditions for each protein using 2 µl protein solution, 3 µl buffer and 3 µl screening solution. The three input solutions are split into 40 nl aliquots, the aliquots are then combined at predefined ratios, mixed and can be measured on chip. Up to seven independent protein screenings can be performed on one chip. Protein solution (2 µl), screening reagent (3 µl) and buffer solution (3 µl) are pipetted in the disk. During an automated rotational protocol the liquids are split into 120 aliquots of 40 nl each. Then 6 of these aliquots are combined, respectively. This results in 20 mixtures of different predefined ratios. One disk has enough space for seven dilution matrices or 140 experiments, which can be performed on chip within a SAXS beamline. Including positioning within the beam, the expected time per measurement is less than 5 s. The SAXS-LabDisk will enable routine SAXS screening of minute protein volumes.
The performance of the SAXS-LabDisk for protein structure determination will be evaluated at the beamline PETRA-III at EMBL Hamburg, Germany later this year.