MINIATURIZATION OF AQUEOUS TWO-PHASE EXTRACTION FOR BIOLOGICAL APPLICATIONS

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Aqueous two-phase extraction (ATPE) is a biocompatible liquid-liquid (L-L) separation technique that has been under research for several decades towards the purification of biomolecules, ranging from small metabolites to large animal cells. More recently, with the emergence of rapid-prototyping techniques for fabrication of microfluidic structures with intricate designs, ATPE gained an expanded range of applications utilizing physical phenomena occurring exclusively at the microscale.

Studies of ATPSs at nanoliter-scale are further extending the range of applications of these systems by taking advantage of rapid diffusion times, increased degree of control of individual liquid streams and droplets, continuous flow and the integration of multi-dimensional separation modes. Several examples of microfluidic ATPS platforms are described.
The partition of molecules between two co-flowing liquid streams confined within a microchannel was successfully demonstrated by the on-line extraction of a fluorescein isothiocyanate (FITC) labeled immunoglobulin G (IgG) from a salt rich flow to a PEG rich flow. IgG diffusion to the PEG-rich phase was complete after 16 cm of channel using flow rates of 1 and 0.2 µL/min for the salt and PEGrich phases respectively. Besides proteins, ATPS have also been used to separate other more complex biomolecules in microfluidics such as virus-like particles.
The potential of miniaturization as a high-throughput screening tool has also been explored. The developed setup allowed the screening of a wide range of concentrations inside the microchannel by varying the flow rates of the solutions while using sub-mL volumes for each ATPS-forming system.

As a novel demonstration of the integrative potential of ATPE as a microfluidic sample preparation module, a microfluidic device comprising two modules was developed and used to perform a complex matrix clean-up in-line with an immunoassay.

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