Centrifugal Microfluidic Platform Using Supported Liquid Membrane Extraction for Combined Sample Clean-Up and Enrichment of Trace Analytes

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A Centrifugal Microfluidic Platform Using SLM Extraction

- for combined sample clean-up and enrichment of trace analytes

Here we present a pump-less microfluidic platform which performs sample clean-up and enrichment in a single step, by integrating Supported Liquid Membrane (SLM) extraction. Our platform offers a simple, yet very efficient, method for achieving sample pre-treatment and enrichment of trace analytes in an easy to use and highly efficient device.

A proof-of-principle experiment

As a model compound to investigate the technique we used theophylline extracted from green tea. Theophylline is also a common drug used in treatment of asthma and other lung conditions, and is therefore found as a trace analyte in blood samples from such patients. Samples were based on 15 minute extractions of 1 ml sample, followed by analysis using standard HPLC equipment.

The HPLC made it possible to distinguish theophylline from other analogue compounds normally found in tea, especially the other xanthines, caffeine and theobromine:

SLM extraction explained:

1) At the start of the experiment:
The sample clean-up and enrichment is achieved in a single extraction step, as shown in the following two figures, by simply passing a donor liquid (in this case 1 ml of tea, adjusted to pH 2 with sulphuric acid) slowly on top of the acceptor solution (30 µl of ammonium buffer, pH 10.3), separated by an oil soaked nanoporous polymer membrane, the SLM. Once in the acceptor phase the target analyte is trapped. In this case the trapping mechanism is the pH difference, which renders the theophylline, a weak acid (pK\textsubscript{a} \\textapprox 8), neutral in the donor phase, but charged in the acceptor phase:

Donor liquid (sample)
flowing over membrane

Accepter stationary - no flow.

2) After a while:
Since charged molecules are practically insoluble in the organic phase, the theophylline is trapped, and as it cannot diffuse back into the donor phase, the concentration gradient is unaffected. In this way both sample clean up and high enrichment can be obtained:

Charged and big molecules pass through → Clean-up

Target analyte gets trapped in the accepter → Enrichment

Centrifugal pumping & flow analysis:

Since the extraction itself is basically diffusion controlled, the whole extraction process is depending on two things: 1) How much liquid (donor, the sample) is pumped through the system, and 2) how long time does it take. Furthermore, since the pumping in a centrifugal microfluidic system is not directly controlled, but only indirectly through how fast the disc is spinning, it is imperative to understand how this flow-rate behaves during the pumping process, and whether the process is reproducible. In other words:

How does the flow-rate of a centrifugal microfluidic system behave when a constant spin-rate is applied?

To investigate this the discs were filled with black ink and analyzed as the pumping took place, using an optical spin-stand capable of acquiring still images of the moving disc.

Subsequently the individual images of the image series was analyzed using the following steps, automated into a batch process:

Centrifugal pumping

Flow-rate as a function of the time the centrifugal system has been pumping (example):

Fabrication:
The SLM discs were fabricated using laser cut PMMA (figure a, grey) bonded together with pressure sensitive adhesive (PSA) (figure a, yellow/brown). A 25 µm thick nanoporous polypropylene membrane (figure a, white) is sealed between two pieces of PSA.

The design consists of two partly overlapping microfluidic systems; a donor channel on top, and an acceptor channel at the bottom. The nanoporous membrane works as a support for an oil phase (di-hexyl ether + 5% TOPO) which separates the donor and acceptor at the extraction sites (figure b, red stippled line).

Conventional microfluidic systems used for SLM extraction are usually based on single units, with just a single extraction taking place at any given time. Consequently the number of extractions per hour from such a setup is very limited, and since the extraction in it self is depending on diffusion (the extractions used in this work was running for 15 minutes), the possibilities for decreasing the time for each extraction is also limited. One way to decrease turn around is therefore to implement parallelization, which is easily achieved using a disc platform and centrifugal microfluidics.