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

Andreasen, Sune Zoëga; Burger, Robert; Emnéus, Jenny; Boisen, Anja

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**A Centrifugal Microfluidic Platform Using SLM Extraction**

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

_Sune Z. Andreasen, Robert Burger, Jenny Emneus & Anja Boisen. DTU Nanotech, Technical University of Denmark_

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 patient samples, found as a trace of asthma and other lung conditions, and is therefore theophylline is also a common drug used in treatment.

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## 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 7 with sulphuric acid) slowly over 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 ($pK_a \sim 8$), neutral in the donor phase, but charged in the acceptor phase:

- **Donor liquid (sample) flowing over membrane**
- **Acceptor 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 acceptor**
  - **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:

1. **Raw image**
2. **Grey scale**
3. **Inverted**
4. **Threshold/binary**

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