A Centrifugal Microfluidic Platform Using SLM Extraction for combined sample clean-up and enrichment of trace analytes

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

Publication date: 2016

Document Version
Publisher’s PDF, also known as Version of record

Link back to DTU Orbit

Citation (APA):
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 rare analytes, in an easy to use and highly efficient device.

**Working principle: Separating & trapping of weak acids (or bases)**

**EXPERIMENT START:** Non-porous extraction of analyte; only small molecules, on their neutral form, can pass through the oil film, separating the donor flow from a stagnant acceptor buffer. The oil is kept in place by 25 µm thick nanoporous polypropylene membrane.

**EXPERIMENT ONGOING:** By choosing a pH above (below) the pK_a of the acid (base) in the acceptor buffer, the analyte is trapped. While continuing to escalate the donor, both separation and enrichment of the target analyte is possible.

**Real application:** Screening production of genetically modified bacteria strains:

- E. Coli bacteria genetically modified to convert tyrosine to p-coumaric acid (an important precursor for a number of drugs) to increase the yield of drug yield at a separation by the SLM.

**Example:** pH trapping of p-coumaric acid

![image](image_url)

**On-disc flow control: A challenge!**

In order to have efficient and reproducible SLM extractions a good and reliable control of the microfluidic flow is needed. The centrifugal pumping can not be controlled directly, but only indirectly, through the rotational speed of the disc, which affects the desired flow-rate. For instance, the centrifugal induced pressure needs to overcome the surface tension of the liquid. This is an inherent problem, where a certain centrifugal speed is necessary to start a flow, but as soon as the flow has finally started the flow should be as slow as possible (see figure 3).

**Flow chips for testing extraction during flow:**

- To achieve a high uniformity of the SLM extraction on-disc, a high flow rate is needed. The flow rate is important for two reasons: (1) the mass transport from the donor to the acceptor side, through the oil membrane, is diffusion controlled and thus delay time. (2) The amount of donor liquid volume that can be put on a 10–12 µm diameter disc is limited. However, with our flow we have been able to the volumes around 0.5–1 mL, and achieved enrichment factors of ~4 (as well as the purification of the sample).

**On-disc extraction w. enrichment:**

- The microfluidic platform is used to separate the analyte from the background fluid (by choosing a pH above the pK_a of the analyte) and enrichment factors are achieved.

**Other small molecules tested and used for SLM extraction (Neutral (no charge) at low pH):**

<table>
<thead>
<tr>
<th>Compound</th>
<th>pH (at low pH)</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin</td>
<td>&gt;7</td>
<td>Do-protonates here</td>
</tr>
<tr>
<td>Theophylline</td>
<td>7.4</td>
<td>(and acquire charge)</td>
</tr>
</tbody>
</table>

Alternative tactics for achieving even more specific trapping:

- Immuno-SLM
- Chemical binding