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Continuous laminar evaporation: micron-scale distillation†

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A procedure for the continuous purification of volatile liquids within microfluidic systems is reported.

Distillation remains, with liquid/liquid extraction, one of the few truly continuous methods of purification. Its use on an industrial scale is extensive, ranging from the production of fine chemicals to the bacchanalian joys of single malt whiskies. As an applied process, however, it is not without its drawbacks. Many substances decompose before they reach their boiling points. Others may undergo polymerisations or explode under distillation conditions. On the small to medium scale the development of techniques such as bulb-to-bulb distillation or wiped-film distillation has extended the application of this venerable approach.[1] On the fine to bulk scales distillation is always undertaken with caution on new processes because of the inherent risks.

In recent years, microfluidic devices have been used in a variety of applications including molecular biology, small-molecule organic synthesis, immunoassays and cell manipulations.[2,3] Such systems have been shown to have advantages over their macroscale analogues, including improved efficiency with regard to reagent consumption, response times, analytical performance, integration and throughput. When performing chemistry on the microscale, gains in terms of safety, reaction specificity, product yield and throughput can be realised.[4] Most of these gains can be attributed to the high surface to volume ratios and low working volumes encountered on the microscale. Exothermic or endothermic processes can by potentiated by the concomitantly highly efficient heat transfer and side reactions minimised by the thermal flatness of the reacting environment. Despite the wide interest in the 'microworld', little attention has been paid to demonstrating microfluidic components for continuous purification of reaction mixtures. Reactions performed on the microscale are often worked up in bulk, leading to difficulties of integration. Driven by these considerations we present herein a microfluidic distillation technique for continuous purification of fluid streams.

Most distillation techniques operate by generating a vapour above a liquid through boiling and forcing this vapour into a cooling device where it can condense. In this sense the vapour acts as its own transport medium, *i.e.* generation of more vapour forces vapour through the cooling device. This is made possible by controlled boiling (effected by gravitational damping of liquid motion) in a liquid reservoir. In microfluidic environments controlled boiling of this nature is not possible. Gravitational forces are less significant and effects such as surface tension and viscosity predominate. The extent of gravitational effects can be assessed through use of the Bond number (Bo). The Bond number is a measure of the relative effects of gravitational forces and surface tension. Gravitational forces are significant when $Bo >> 1$. For water in a channel of approximately 100 microns Bond numbers are typically < 0.01, indicating the domination of surface tension over gravity. Boiling on this scale is, therefore, inherently uncontrollable due to the lack of a significant damping factor on liquid motion.

To develop a distillation technique for the microscale, it is thus necessary to develop a method of making and transporting the vapour of a volatile without boiling it. Utilising a carrier gas for vapour transport is an established technique for low-pressure distillation and indeed, steam distillation can be considered in this respect. Consequently, in the current studies a carrier gas is used to effect evaporative transport. It should also be noted that the compressible nature of the gas stream coupled with its motion across the liquid surface functions as a shock absorber for any sudden liquid motion,[5] encouraging uniform flow and allowing for easy stream separation

Microfluidic devices for the pre-concentration of solutions have previously been demonstrated.[6] These function by the forced evaporation of solvent, caused by the passage of a gas over a porous membrane behind which the solution flows. In the current approach physical flow separation is not required and flow integrity is maintained through the control of surface affinities and fluid flow dynamics. The greater surface affinity of the liquid for the duct walls, and the cushioning effect of the central gas lamina damp liquid motion and encourage laminarity.

The fluidic channel pattern was designed using CAD software (AutoCad 2002) and microchannels were fabricated using standard photolithographic, wet chemical etching and bonding procedures. Briefly, the channel design was transferred to a positive photoresist coated chrome/glass substrate (Nanofilm, Westlake Village CA.) using a direct write laser lithography system. The exposed regions of the photoresist were removed using a resist developer (Microposit 351, Shipley Europe Ltd, Coventry, UK.) The chromium layer was then removed using a chrome etchant (Lyodyne, Microchem Systems Ltd., Coventry). Channels were then etched into the substrate using a buffered oxide etching solution ($HF–NH_4F$) at ambient temperature. The remaining photoresist was then removed using dimethylformamide (DMF) and the chrome layer removed using chrome etchant. Once complete, the etched substrate was washed sequentially in methanol, DMF and then immersed in H_2SO_4 for 1 hour. The substrate was washed with ultra-pure water at ambient temperature, and dried with N_2 gas. Finally, a cover plate was thermally bonded to the substrate by heating the assembly at 550 °C for 1 h, 580 °C for 5 h and 555 °C for 1 h. The complete device was then allowed to cool for at least 8 h. Holes drilled in the top plate allow access to the fluidic network below. The structured microchannels were 50 μm deep and between 100 and 500 μm wide.

Fig. 1 shows a schematic of a microfluidic device for continuous laminar evaporation. The device consists of three sections. In the first (section i), gas and liquid streams are brought together and rapidly heated. The streams are then split, so that liquid and some carrier gas is diverted back to the feedstock, and vapour-saturated carrier gas is then motivated through a long condensation channel which allows heat transfer to encourage condensation (section ii). The final section consists of a separation module allowing depleted carrier gas and condensate to be separated, and the condensate collected.

This arrangement allows a mixture of volatiles to be separated according to their vapour pressures, in a similar way to standard distillation. The condensation channel has an average width of 150 μm, yielding a Reynolds number of 1.4 and a surface-to-volume ratio of 1300 $m^2\ L^{-1}$

Careful design of the microchannel network ensures laminar flow conditions during operation, and thus minimal contamination of distillate. During a standard distillation process residence times

† Electronic supplementary information (ESI) available: Figure S1. See http://www.rsc.org/suppdata/cc/b3/b311697b/

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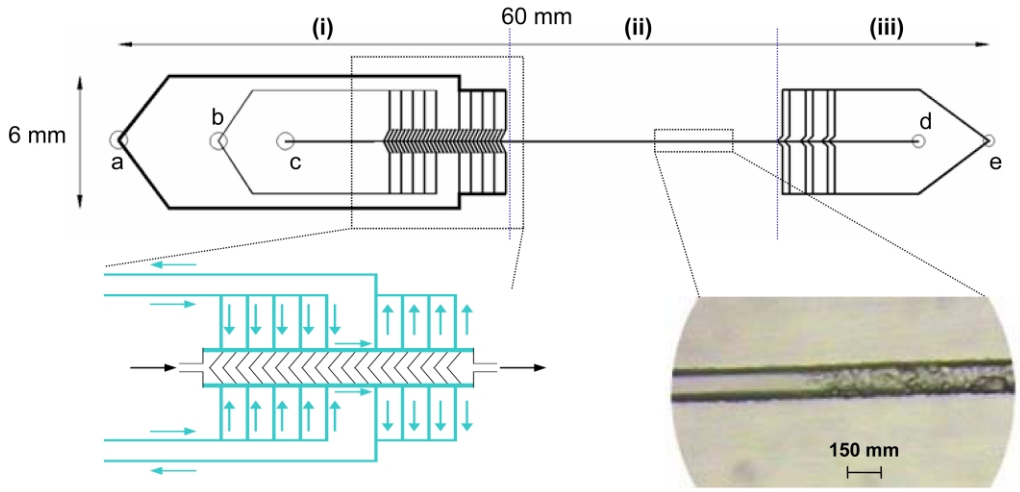

Fig. 1 Schematic of a continuous laminar evaporation microdevice. The flow of carrier gas (Helium, Black arrows) necessary to maintain laminarity varied. For a liquid flow rate of 150 μl min^{-1} a pressure of 30 p.s.i. or less was required. Liquid (blue arrows) laminar widths are approximately 50 μm. The magnified section illustrates condensation of enriched acetonitrile.

for feedstock in the device are on the order of 0.1 s. The operating principles of the devices are straightforward. Gas enters the contact chamber from a central channel at a typical pressure of 25 psi, whilst liquid is introduced through multiple channel inlets using either a syringe pump (Harvard Instruments PHD 2000) or an HPLC pump (Constametric 3, LDC/Milton Roy) at a typical rate of 75 μl min^{-1}. Chevron structures etched into the chamber floor encourage laminar integrity. Any droplet departing from the liquid lamina encounters the chevron structures and experiences an asymmetric viscous drag, the resultant of which encourages recombination with the main lamina.

Heating section i to a temperature of 60 °C (using a flat-bed chromium resistor plated onto the glass substrate) provides an adequately saturated vapour in most cases (it should be noted that bulk scale distillation of acetonitrile requires a temperature of 80 °C or more). After co-running for 10 mm the gas and liquid flows are separated and the gaseous flow diverted through the long distillation channel. Visible dewing occurs in the region from 5–10 mm from the heated zone. (Fig. 1 inset)

A 50:50 mixture of acetonitrile and DMF was used as a trial mixture for separation (Fig. 2). Using the operating conditions described above a ninefold enrichment in acetonitrile concentration could be achieved in a single distillation without recourse to active cooling. This equates to 0.72 theoretical plates per device. Fig. S1† illustrates similar results for the purification of crude pyrrole and a DMF and toluene mixture.

The fact that the system will induce evaporation at a temperature lower than the boiling point of the distillate demonstrates potential applications in the purification of temperature sensitive compounds. The system can also be run at reduced pressure, which would further enhance this effect. The efficiency of the current system could be further improved by the addition of an active cooling device to the condensation channel. This would minimise the evaporation of condensate by carrier gas. Furthermore, as the feedstock is continuously recycled under HPLC pump motivation, the device is well suited for continuous operation. Indeed, if distillate is reintroduced into the device, further enrichment takes place in the expected way. The continuous nature of the enrichment process, and the ability to 'daisychain' such devices, makes the presented concept attractive for microscale purification.

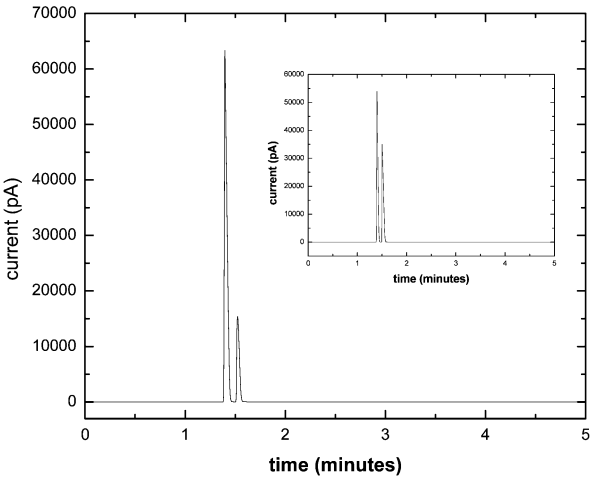

Fig. 2 Gas chromatographic analysis of the distillate from the chip after a single pass. Inset: a GC trace of the feedstock solution. Peaks at 1.4 and 1.5 minutes represent acetonitrile and *N*,*N*-dimethylformamide respectively.

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