DROP KINETIC ANALYSIS IN REAL TIME BY OPTICAL SPECTROSCOPY
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ABSTRACT
The spatio-temporal correspondence between microchannel position and reaction ‘time’ permits the study of kinetics of (chemical and physical) processes with unprecedented time resolution and dynamic range [1]. Monitoring reactions in real-time with non-invasive probes remains, hitherto, a major shortcoming of microchemical drop reactors due to the minute sample volumes (pL-nL) and fast travel speeds (1-1000 mm/s). We evaluate the potential of novel microdevice fabrication via frontal photopolymerisation (FPP) [2] integrated with Cavity Ring-Down Spectroscopy (CRDS) [3] for the online analysis of individual reaction travelling droplets.

KEYWORDS: Cavity ring-down spectroscopy, Frontal Photopolymerisation, Thiolene microfluidic devices

INTRODUCTION
FPP is a rapid prototyping microfabrication approach that generates cross-linked polymer networks with broad solvent resistance and 3-dimensional control. This approach allows the fabrication of organic-resistant microfluidic devices to be fabricated within approximately 1hour, capable of carrying out reactions in organic droplets. Online detection allows for the kinetics of organic reactions to be determined within a microfluidic device, resolved in time, allowing for facile reaction optimisation. Online detection is, however, challenging because of the minute sample volumes and the fast response time required. Ideally, one would increase the detection sensitivity without increasing the sample volume probed. We are investigating and evaluating the use of CRDS in online, real-time drop metrology. CRDS is a highly sensitive analytical technique based on measuring the decay of a light pulse within an optical cavity. In the presence of an absorbing species the cavity losses are increased, leading to a reduction in the time constant for the measured exponential decay and providing a mechanism for spectroscopic absorption measurements. The technique owes its sensitivity to the dramatically increased spectroscopic path length achievable when the sample is positioned within an optical cavity, usually consisting of a pair of mirrors, and is most commonly used for measuring absolute concentrations of trace gas species. The approach can be adapted for absorption measurements on pL liquid samples using an optical fibre-loop cavity [3]. CRDS meets the requirements for online detection within microfluidics as it increases the path length travelled by the light without increasing the path length of the sample.

THEORY
The integration of stationary optical fibres in polydimethylsiloxane (PDMS) and polymethylmethacrylate (PMMA) devices for single-pass absorption experiments is relatively straightforward as high losses in the sample region are acceptable [4]. However, in CRDS experiments, the baseline loop losses must be minimized in order to maximise the sensitivity of the technique. As a consequence, sample regions tend to be smaller, and alignment is much more critical when combining CRDS with microfluidic devices [5]. Mobile integration of optical fibres is desirable as it allows for interrogation of the whole reaction space within a microfluidic device. Additionally, the use of organic-resistant microdevices would allow for online kinetics analysis of reactions in organic droplets. The operating principles of CRDS [3] and the frontal dynamics underlying microfabrication via FPP [2] have been reviewed elsewhere.

EXPERIMENTAL
The fabrication of a thiolene microfluidic chip (Figure 1) combines micropatterning with SU8 and FPP replication and sealing using photosensitive copolymer networks between glass sheets [2].

Figure 1 Microchip produced by frontal photopolymerisation (60 µm channel depth, confined by thin borosilicate glass sheets)
Initial CRDS measurements have been made using pulsed, frequency-doubled Nd:YAG laser light (532 nm). Light is coupled into and out of a closed loop of 50 μm-core-diameter-multimode optical fibre, typically 5 – 15 m long. Light circulates in the loop, undergoing low losses. Breaking the fibre-loop and aligning the fibre ends with a small end separation of only a few tens of microns allows for direct absorption measurements to be made on pL liquid sample volumes (Figure 2).

![Diagram of fibre-chip integration](image)

**Figure 2** Methods of fibre-chip integration. Top left: direct absorption with small end separation between fibre ends. Top right: fibre ends integrated along the chip axis. Bottom left: fibre ends inserted through a chip. Bottom right: Whole chip inserted between fibre ends.

Coupling the fibre-loop CRDS set-up with a microfluidic chip can be achieved in three ways (Figure 3); firstly, integration along the chip axis, secondly, inserting fibre ends perpendicularly through a hole drilled through the chip and thirdly, inserting the whole chip between the fibre ends. The first method is problematic because of the tight alignment tolerances; alignment structures will be needed to implement this in a CRDS experiment. The second method requires the use of a micro-diamond drill, to fabricate a hole that is size matched to the inserted fibre. The last method is most attractive for two reasons; it does not require inserting fibre ends into the chip or channel (thereby removing the potential problem of fibre ends enhancing droplet mixing), and, most importantly, the whole reaction space of the chip can be interrogated simply by translating the chip while keeping the fibre ends fixed. The challenge here is to reduce the overall thickness of the microfluidic chip, and to increase the fibre end separation, so that the chip can be inserted between the fibre ends with minimal loss.

**RESULTS AND DISCUSSION**

The small fibre separation allows for the analysis of pL drops on the fly (ringdown times < 10 μs). Preliminary ringdown experiments have been carried out to determine whether the technique has the sensitivity required for integration in a microfluidic device. In these experiments, the fibre-loop was broken, and the cleaved fibre ends were aligned with a small end separation of about 25 μm. Droplets of water and an organic dye were then placed alternately between the fibre ends. A detection limit of about 50 μM of rhodamine 6G was obtained. A comparison of ring-down traces for water and 0.1125 mM rhodamine 6G is shown in Figure 3.

![Graph of ring-down traces](image)

Water

Ring-down time = 224 ns
These experiments show that fibre-loop CRDS does have the sensitivity required for online detection of reactions carried out in microfluidic channels. Work is currently underway to integrate this fibre-loop CRDS set-up with a microfluidic chip in all of the three set-ups described in Figure 3.

In order to integrate fibre-loop CRDS and microfluidic device in a mobile manner, the chip must be thin enough to fit between the fibre ends without causing too high light loss in the gap between fibre ends. As a guideline, the fibre end separation should not exceed the core diameter of the fibre. Currently, we have fabricated a microfluidic device that has an overall thickness of 250 μm (using two coverslips and thiolene, with 50 μm channels). This can be placed between optical fibres with a core diameter of at least 200 μm. However, the current fibre-loop CRDS set-up has been optimised for use with 50 μm core diameter optical fibre. We are currently working on optimising the set-up for larger core diameter optical fibres, in order to integrate this larger core fibre-loop CRDS set-up with a thin microfluidic chip.

CONCLUSION

Fibre-loop CRDS is clearly a suitable online detector for microfluidic devices as it overcomes the problem of making sensitive absorption measurements on small liquid samples by increasing the sample volume probed by the light, without increasing the sample volume itself. The use of thiolene microdevices allows for organic reactions to be carried out in microfluidic channels. Preliminary fibre-loop CRDS experiments have been carried out to determine the sensitivity of this technique. Currently, we are evaluating the facile and accurate the integration of fibre-loop CRDS with a microfluidic chip to allow for online reaction analysis and feedback.

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REFERENCES


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