Research Highlights

DOI: 10.1039/b710975j

Microfluidic dye laser

The integration of photonic components in microfluidic devices is of central interest for the development of functional stand-alone systems. Due to the high popularity of optical detection methods, particularly fluorescence spectroscopy, the realization of on-chip light sources are the focus of many studies. For these purposes, optofluidic dye lasers have been developed, which integrate photonics and microfluidics. Compared to bulky conventional laser systems, simpler liquid handling and optical settings are provided in micrometre dimensions. Recently, a novel type of microsized dye laser has been reported by S. I. Shopova *et al.*[1] The laser system is based on liquid core optical ring resonators (LCORRs). It is made of a glass capillary with thin walls that is filled with liquid of low refractive index (RI) (Rhodamine 6G dye solved in ethanol). The system is pumped by a pulsed laser that is focused onto the side of the LCORR through a cylindrical lens. Due to the light total internal reflection along the curved interface between the high and low RI media, the cross section of the capillary forms a ring resonator which supports whispering gallery modes (WGM). One important benefit of this configuration is the option to simply couple the laser light out through tapered fibres which are in touch with the ring resonator, thus providing the possibility for easy laser delivery. Characterisation of the laser light proved that the novel dye laser provides WGMs of high Q-factors (10^7), which results in low lasing thresholds of 1 $\mu J\ mm^{-2}$. The optofluidic dye laser requires no further optical feedback components and alignment, hence it is insensitive to small vibrations. The laser wavelength can be changed by supplying a new dye solution to the LCORR. Moreover, an array of ring resonators could be created along the capillary, so that multiple independent light sources are formed.

Determination of phase behaviour of aqueous solutions

The generation and manipulation of aqueous droplets by means of microfluidic platforms has been shown in an impressive number of studies during the last few years. The formation of such small aqueous compartments with highly homogeneous size distribution is particularly attractive for high throughput applications. The droplets can be generated independently with alterable content, while there is no cross-contamination between consecutive droplets. Many useful applications have been demonstrated, such as particle formation, protein crystallization, polymerase chain reactions, kinetic studies of enzymatic reactions, cell-free protein expression and single cell encapsulation. In a recent study, Jung-uk Shim *et al.* have added another application to this list.[2] They present a microfluidic chip (''Phase Chip'') that is designed to determine the phase diagram of multicomponent fluid mixtures in micro-sized droplets (Fig. 1). A number of functional modules are integrated on the microchip to formulate droplets, to mix, transport and store the droplets. First, the droplets are formed by hydrodynamic focussing of a water/solute mixture inside a continuous oil stream. Thereby, the composition of the mixture is varied sequentially. A novelty in this work is the guidance of droplets into storage wells using surface tension forces, which is achieved by having different aspect ratios of the microfluidic transport channel and the adjacent storage wells. While a droplet is flattened during transport through the microfluidic channels with a large width but narrow height, it is less confined in the storage wells. The deeper and wider geometry of the storage wells allows a reduction in the surface area of the droplets, *i.e.* the droplet has a more spherical shape in the well. Thereby, a change in the interfacial energy is created, which generates a force on the drop driving it out of the confining channel into the deeper well. In a second innovation of the Phase Chip, the authors exploit the permeability of poly(dimethylsiloxane) (PDMS) to water—the material which is used to manufacture the device—to controllably vary the concentration of solutes in the droplets. The storage wells are separated from a reservoir by a thin PDMS layer, which allows diffusion of water from the storage well to the reservoir that is filled either with dry air or with an aqueous salt solution. The permeation of water through the PDMS layer is theoretically simulated, and experimentally measured by determination of swelling and shrinking of saline droplets in the storage reservoir.

Two applications of the Phase Chip are presented. First, the phase diagram of a salt in water (ammonium sulfate), and a polymer (poly(ethylene glycol), PEG) is measured, and validated by measuring the phase diagram off-chip. Second, the microchip is employed for protein crystallisation. It is demonstrated that the crystallisation rates are enhanced through the manipulation of the kinetics of crystal nucleation and growth. Since the Phase Chip facilitates control over the key parameter, concentration, it is an ideal tool for optimisation of protein crystallisation.

Multistep carbamate synthesis

Microreactors provide many advantages for chemical synthesis, such as reduced reaction volumes, fast heat and mass transfer, and protection from air and moisture. However, for multistep continuous-flow operation, integration of continuous workup procedures with microreactors, *e.g.* modules for solvent exchange and separation, is still needed. Klavs F. Jensen and co-workers from the Department of Chemical Engineering at MIT are developing microfluidic techniques for separation of immiscible fluids such as gas–liquid and organic–aqueous phases. In a current article they describe the integration of these extraction systems in a continuous microreaction

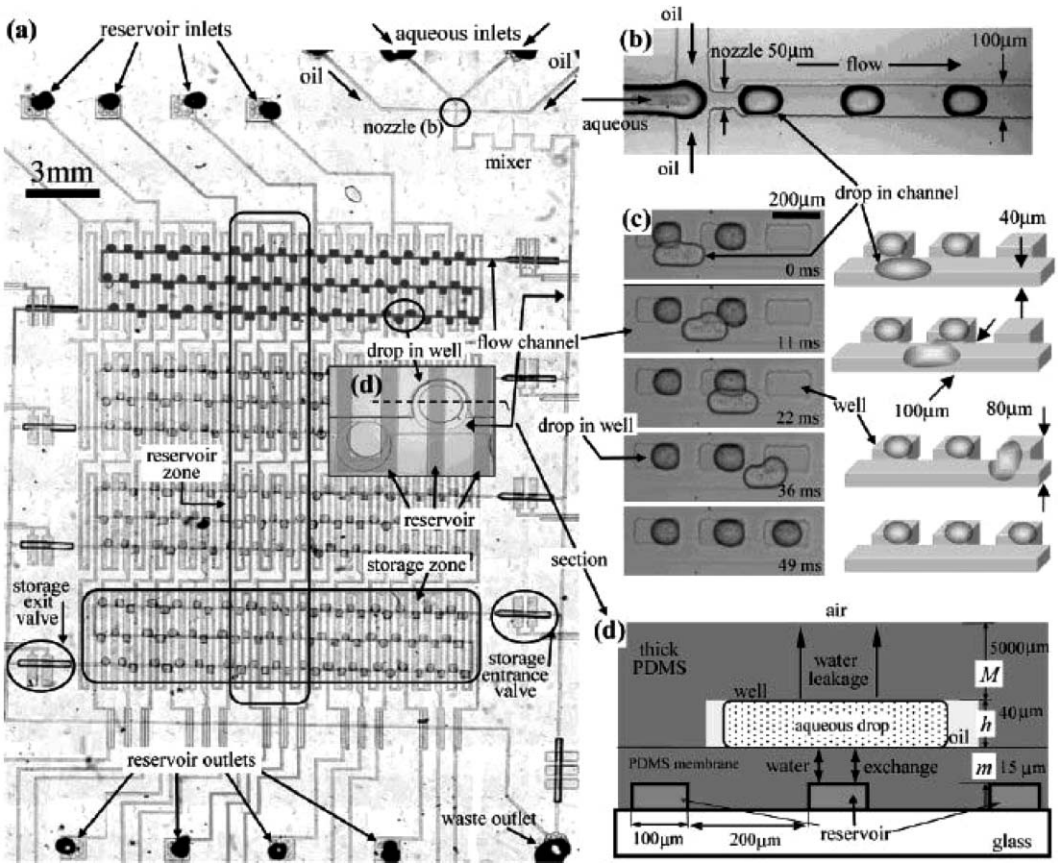

Fig. 1 (a) Design of the microfluidic device (''Phase Chip'') to determine the phase diagram of multicomponent fluid mixtures in micro-sized droplets. (b) Droplets are formed by hydrodynamic focusing of an aqueous solution into two streams of hydrophobic carrier fluid (oil). (c) Surface tension guided storage of droplets into wells. (d) Vertical section of the storage wells. (Reprinted from Shim *et al.*[2] Copyright 2007 American Chemical Society.)

system (Fig. 2).[3] As a case study, the synthesis of carbamates using the Curtius rearrangement reaction is performed. During the multistep reaction, organic azides and isocyanates are formed, which are important starting compounds in many reactions of synthetic chemistry. Due to the conductance of the reaction in a continuous manner, such hazardous and reactive intermediates are consumed immediately after generation, making the synthesis scheme safer than in conventional batch approaches. The synthesis involves three reaction steps and two separation steps. First, aqueous azide and acid chloride form organic azide in a silicon-based microreactor. Second, the aqueous and organic mixture is separated using a porous fluoropolymer membrane that is selectively wetted by the organic solvent, while the aqueous phase is prevented from passing the membrane pores. In the next reaction step, isocyanate is formed using a solid acid catalyst. The generated nitrogen is removed by liquid wetting of the membrane, while gas transmission is prevented. Finally, the product is formed in a reaction between isocyanate and alcohol.

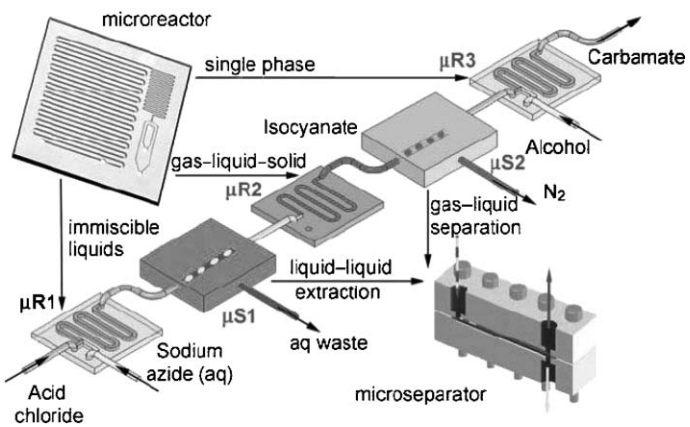

Fig. 2 Microfluidic device for the multistep carbamate synthesis. The process involves three reaction steps, conducted in the modules μR1, μR2 and μR3, and two separation steps, performed in the modules μS1 and μS2. (Adapted with permission from Sahoo *et al.*[3] Copyright 2007, Wiley-VCH.)

Furthermore, the potential of microreactor-based parallel synthesis of a family of compounds is demonstrated. After formation of the hazardous isocyanate, a network of three microreactors is created yielding three different carbamate derivatives.

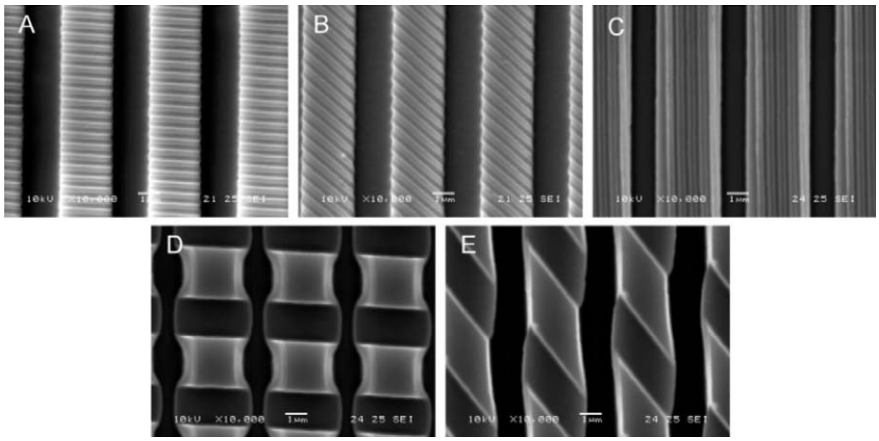

Fig. 3 Tunable anisotropic wettability on polymer surfaces. The figure shows SEM images of polymer films with two-level hierarchical structures that consist of micrometre and submicrometre scale gratings. (Reprinted from Zhang and Low.[4] Copyright 2007 American Chemical Society.)

Anisotropic wettability on microsized polymer structures

A surface that is anisotropic in wettability shows non-identical contact angles of a liquid droplet sitting on that surface, when measured from different directions. Such surfaces are beneficial in applications where the direction of liquid flow has to be controlled. Fengxiang Zhang and Hong Yee Low from the Institute of Materials Research and Engineering in Singapore describe the fabrication of polymer structures with tuneable anisotropic wettability without the need for chemical treatment of the polymer surfaces.[4] Inspired by the hierarchical structures reported for lotus leaves, the authors fabricated a series of two-level hierarchical structures on polystyrene (PS) and poly(methyl methacrylate) (PMMA). The structures consist of gratings of micrometre and sub-micrometre dimension (Fig. 3) that are created by using the technique of sequential imprinting, which is based on conventional nanoimprint lithography. Various two-level hierarchical structures are fabricated, and their wetting behaviour is analysed. Characterization of the surfaces by water contact angle measurements revealed that the contact angle of water can be tuned to nearly 120° on both polymer surfaces. Furthermore, the hierarchical structures show a wide range of wettability anisotropy (6° to 54° for PMMA, and 8° to 32° for PS), which is defined by the difference in the contact angles in two perpendicular directions. The authors suggest that this technique may be useful in fields such as anti-fouling, microfluidics or micro- and nano-optics.

Genetic analysis of microbes from the human mouth

Microbes are omnipresent and colonise a wide variety of environmental niches. However, only few bacterial species have been axenically cultured, and even less of the recognized bacterial phyla include cultivated representatives. Although techniques in microbiology have advanced significantly in recent decades, there is poor information about the majority of bacteria, which are still "dark matter" in biology. To reveal the microbial diversity of ecosystems and communities, analysis techniques on an individual cell level are needed. Addressing this demand, Stephen R. Quake and co-workers designed and fabricated a microfluidic device that allows the isolation and genome amplification of individual bacterial cells.[5] The microchip is capable of processing eight samples in parallel. Microbial cells are directed towards individually addressable chambers, in which, in sequence, cell isolation, lysis, neutralisation and whole-genome amplification is performed. The potential of this device is demonstrated by analysing microbes found in the human subgingival crevice. Microbial cells of the sample are selected according to their morphology, *i.e.* only rod-like are further processed. Through this selection, the researchers expected to enrich for the phylum TM7, which is a prominent candidate phyla that has no cultivated or sequenced members. These microbes have been furthermore associated with chronic periodontitis in humans. To identify the isolated cells, PCR is performed on the 16S rRNA gene from amplified genomic DNA, and positive results are obtained for nearly all captured cells. By sequencing of more than 1000 genes, further insights into the TM7 cells are provided. It is shown by sequence similarity-based mapping that most of the TM7 genes are not closely related to genes from representatives of any known phyla.

The presented microdevice has the ability to analyse uncultivated members of any other bacterial biofilm. Using this single-cell genetic analysis approach, deeper insights into complex microbial communities can be expected.

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References

1 S. I. Shopova, H. Zhou and X. Fan, Optofluidic ring resonator based dye laser, *Appl. Phys. Lett.*, 2007, **90**, 221101.
2 J. Shim, G. Cristobal, D. R. Link, T. Thorsen, Y. Jia, K. Piattelli and S. Fraden, Control and Measurement of the Phase Behavior of Aqueous Solutions Using Microfluidics, *J. Am. Chem. Soc.*, 2007, **129**, 8825–8835.
3 H. R. Sahoo, J. G. Kralj and K. F. Jensen, Multistep Continuous-Flow Microchemical Synthesis Involving Multiple Reactions and Separations, *Angew. Chem., Int. Ed.*, 2007, **46**, 5704–5708.
4 F. Zhang and H. Y. Low, Anisotropic Wettability on Imprinted Hierarchical Strucutres, *Langmuir*, 2007, **23**, 7793–7798.
5 Y. Marcy, C. Ouverney, E. M. Bik, T. Lösekann, N. Ivanova, H. G. Martin, E. Szeto, D. Platt, P. Hugenholtz, D. A. Relman and S. R. Quake, Dissecting biological "dark matter" with single-cell genetic analysis of rare and uncultivated TM7 microbes from the human mouth, *Proc. Natl. Acad. Sci. U. S. A.*, 2007, **104**, 11889–11894.