Lab on a Chip

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Towards an Integrated Chemical Circuit

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"Chip laboratories" or "lab-on-a-chip devices" are catch phrases describing a new technology by which chemical processes and systems are miniaturized using microsystem technologies.[1] Scientists dream of repeating the success of microelectronics in chemistry by shrinking entire chemistry and analysis laboratories to fit on a single microstructured chip. Such microfluidic laboratories are full of promise. As they use only tiny quantities of chemicals, they are more environmentally friendly and economical. Besides the advantages of miniaturization, such as improved portability, safety, and reduced reagent consumption, one of the most promising features of chip laboratories is the accelerated speed of reaction and analysis. The most fascinating perspective of this new technology, however, is the ability to create entirely new systems that surpass the performance of conventional chemical devices, just as in the triumph of microelectronics, where an entire new technology was invented rather than just shrinking or improving main-frame computers.

The key components of a chemical laboratory on a chip are the microfluidic structures, as reactions are performed in microscale channels and cavities rather than in flasks and tubes. There are currently two main subcategories of microfluidics:

A) Continuous microflow systems utilizing miscible solutions in the homogeneous phase. Various well-established macroscopic techniques have been realized in this area, from simple flow-through reactors to commercialized chip-based separation techniques such as chip electrophoresis and chip chromatography.
B) Droplet-based microflow systems, which can be directly generated from two immiscible phases.[2]

In such segmented-flow systems (category B), single droplets floating in an immiscible liquid can serve as discretely addressable microcompartments. Droplet-based systems are especially attractive for chemical reactions owing to the effective convective mixing they allow. In continuous microflow systems with low Reynolds numbers, mixing of reactants is challenging owing to the laminar flows. Other advantages of droplet-based systems are the enhanced heat transfer arising from the high surface-to-volume ratio and the increased throughput, which allows a series of reactions to be performed straightforwardly. Such microdroplets can also be utilized for long-term storage without any diffusive zone broadening. A recent reports describes systems for directed movement and coalescence of discrete addressable droplets by electric potentials,[3] opening fascinating possibilities for multistep reactions.

A combination of these two microfluidic worlds is very attractive[4] and would be an important step towards the development of an integrated "chemical circuit". With such an integrated system it should be feasible to perform a series of reactions in microdroplets with subsequent electrophoretic or chromatographic separation of the reaction products after conversion from a droplet-based system to a continuous-flow system. Realization of this goal requires miniaturized tools to transfer a segmented flow to an homogeneous-flow system[5] and verse visa. Such a hypothetical integrated chip laboratory with an imaginary droplet interface is shown schematically in Figure 1.

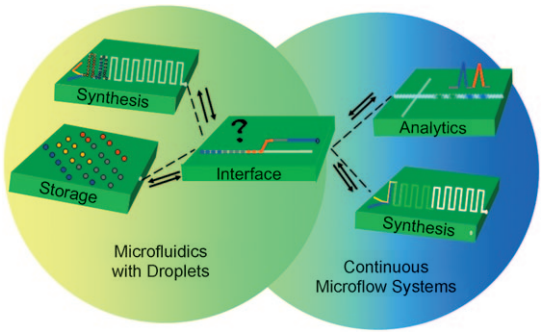

Figure 1. Integration of droplet-based microfluidics with continuous microflow systems utilizing an imaginary droplet interface.

The first step on this path was reported recently by Roman et al.[6] They presented a system that enables the coupling of a droplet-based segmented flow with on-chip electrophoresis. In this approach, a hydrophobic carrier and an aqueous buffer flow parallel to each other to form a so-called virtual wall at the interface. As aqueous droplets in the oil phase come into contact with the virtual wall, coalescence occurs and the sample is transferred to the continuous aqueous phase. Such injected zones can subsequently be transferred to a separation channel in which the electrophoretic separation occurs (Figure 2).

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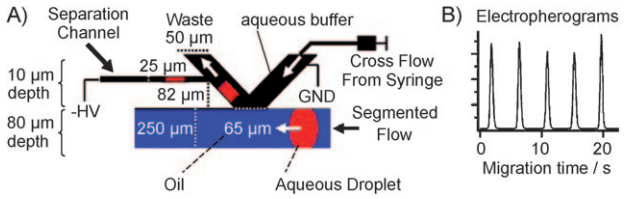

Figure 2. A) K-shaped droplet interface according to Roman et al. for coupling of chip electrophoresis with a droplet-based microflow system. HV = high voltage, GND = ground. B) Serial electropherograms from discrete droplets. Adapted from Roman et al.[6]

The inverse approach, namely the development of a microfluidic tool enabling the subsequent segmentation of an electrophoretic separation, was just realized by Edgar et al.[7] In this work it was demonstrated that electrophoretically separated zones can elegantly be segmented into a series of individual droplets. The concept of this microfluidic design is shown in Figure 3. Analytes are electrophoretically separated

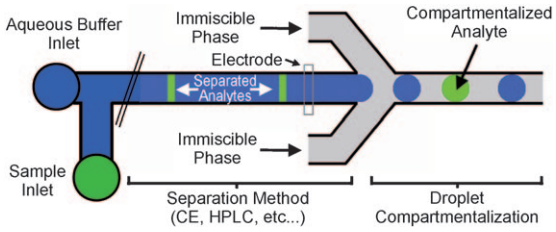

Figure 3. Interface for droplet compartmentalization of electrophoretically separated zones according to Edgar et al.[7]

in a microfluidic channel using a typical aqueous electrolyte. An indium tin oxide electrode on the floor of the microchannel works as the outlet electrode. The droplet formation region behind it is comprised of two oil channels that flank the electrophoresis channel and an exit channel. If an electric potential is applied at the electrolyte channel, droplets are formed at the interface, and a series of droplets floats in the immiscible oil phase towards the outlet.

With this approach, electrophoretically separated zones can be segmented into a series of small microdroplets. It is remarkable that the electrophoresis remains nearly undisturbed by this process. Electropherograms recorded before and after the droplet interface look very similar, with the exception that each analyte signal after the interface consist of many individual peaks (droplets; Figure 4). This subsequent compartmentalization of analytical separations offers interesting possibilities. Discrete droplets of the individual fractions can be stored in microcompartments, for example, for examination with another analytical technique or for subsequent chemical reaction.

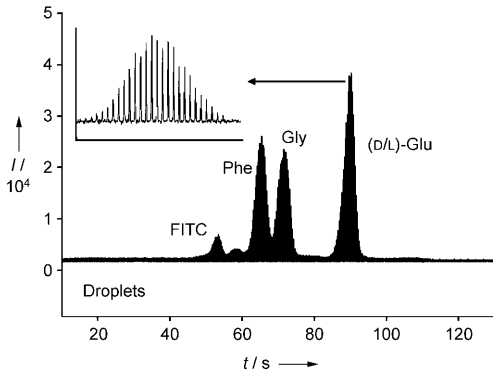

Figure 4. An electropherogram obtained by Edgar et al. after the droplet interface. FITC = fluorescein isothiocyanate.

Looking at the approaches presented by Roman et al. and Edgar et al. in context offers fascinating perspectives for the integration of complex synthetic and analytical chip laboratories. It should be feasible to perform a chemical reaction, separate the products electrophoretically, and then perform an additional synthetic step on the fractions compartmentalized in droplets. The reaction mixture in the droplets could then be analyzed on the chip in a homogeneous aqueous phase using electrophoresis, chromatography, or mass spectrometry.[8]

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