Project acronym: **MATCHIT**

Project title: Matrix for Chemical IT

**Deliverable n. 5.5.1: Demonstrator, restricted (RE) M12**
**"Demonstration of chemtainer generation in microsystem with electronic control"**

***Temporary only for restricted circulation****

Due date of deliverable: **31.01.2011**

Actual submission date: **31.03.2011**

Start date of project: **01.02.2010**

Duration: **3 years**

Organisation name of lead contractor for this deliverable: Ruhr-Universität Bochum, BioMIP

* Because this document contains novel and not yet published scientific results, it can only be freely distributed to the MATCHIT Consortium Members, the MATCHIT reviewers and within the European Commission. This information embargo should be respected until all pertinent scientific results are published in the open literature.

# 1. Deliverable n. 5.1: Demonstration of chemtainer generation in microsystem with electronic control

## *1.1 Choice of carrier fluids*

Diverse aspects must be considered when choosing an appropriate carrier fluid in which to create digital droplet flows. First, the fluid must be hydrophobic so that the aqueous droplets are well encapsulated by a layer of a carrier fluid and transported through the microchannels. Second, the fluid should be biocompatible and not show any interactions with biomolecular reagents. Third, the liquid should not diffuse into PDMS, which is the material of the microfluidic layer. This is a well-known problem in microfluidics that PDMS swells in contact with nonpolar (hydrophobic) solvents. Good alternatives are polar fluids, which are immiscible with water. Examples for such a system are Fluorocarbons, which do not swell PDMS[1] although they may have a small dipole moment and a solubility parameter similar to PDMS. They have often been used as a carrier fluid in microdroplet systems[2]. We investigated Fluorinert™ (FC-40, 3M Corp.) in our labs, a fully fluorinated dielectric fluid, which has low thermal conductivity, low miscibility to water and a high density. Additionally, in earlier experiments we found out that oleic acid shows good properties as a separating fluid for droplet formation in connection with low PDMS interaction. The disadvantages of fluorocarbons and oils like oleic acid in terms of compatibility with our chemical microprocessor are the non-conductivity as well as the hydrophobic interaction (covering/insulation) with the surface of the gold electrodes.

For these reasons, we initiated an investigation of ionic liquids (figure 1) as a carrier fluid for droplet formation in microfluidics. We found out that butylmethylpyrrolidinium bis(trifluoromethylsulfonyl)imide [MeBu][NTF] as well as 1-ethyl-3-methylimidazolium bis(trifluoromethylsulfonyl)imide [EMIM][NTF] (Solvent Innovation GmbH, Merck) show a good compatibility with PDMS material and are successful candidates as carrier fluids regarding droplet formation performance.

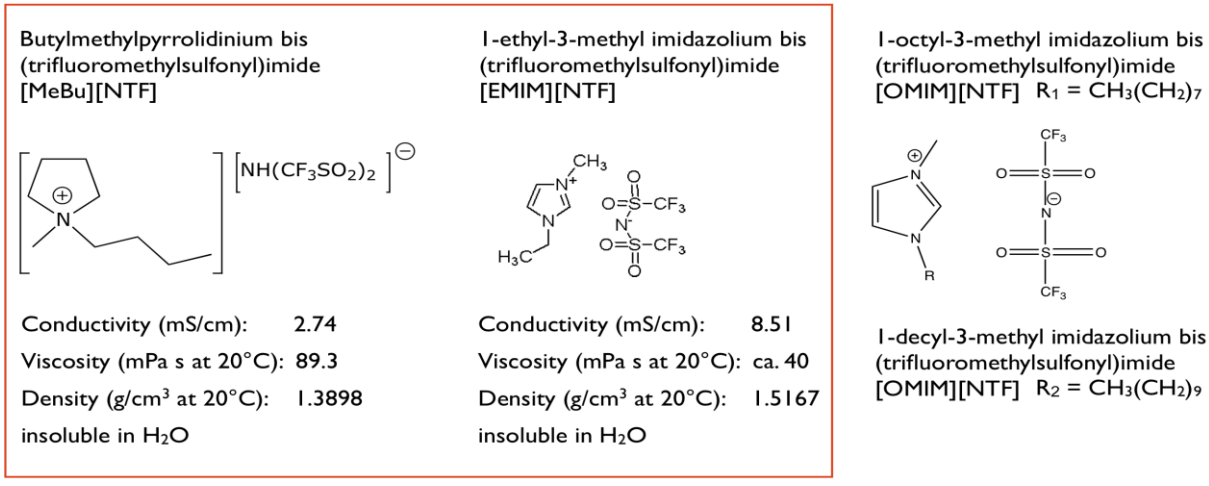


**Figure 1: Overview of commercial (in a red box) and synthesized (right) ionic liquids.**

[1] Deng, T.; Ha, Y.-H.; Cheng, J. Y.; Ross, C. A.; Thomas, E. L. Langmuir 2002, 18, 6719-6722.

[2] H. Song, J.D. Tice, and R.F. Ismagilov, "Reactions in Droplets in Microfluidic Channels," Angew. Chem. Int. Ed., vol. 42, pp. 768-772, 2003

## *1.2 Performance tests in microchannel tubes*

To test the stability of droplets with various carrier fluids in hydrophobic (FEP, PTFE, PE) as well as in hydrophilic ($SiO_2$) microchannel environments we investigated the droplet properties and flow dynamic stability in different microchannel tubes. The experiments, summarized in table 1, show that ([MeBu][NTF] and [EMIM][NTF] are well suited as a separating carrier material for droplet formation in a microfluidic environment.

| tube material / carrier fluid | FEP [ID 200µm] | PTFE [ID 300µm] | Polyethylene [ID 400µm] | $SiO_2$ [ID 500µm] |
|---|---|---|---|---|
| Fluorinert® FC40 | o | o | + | + |
| FC40 + 1% Perfluordecan | o | o | - | + |
| FC40 + 3% Perfluordecan | - | + | o | o |
| [MeBu][NTF] ionic liquid | + | + | + | + |
| [EMIM][NTF] ionic liquid | + | o | + | + |
| oleic acid | - | - | o | o |

**Table 1: Droplet stability in microchannel tubes (+ droplets are stable, no droplet breaking, no residues at channel walls/ o droplets are stable but residues at channel walls etc./ – no monodisperse droplets, formation of droplet satellites, residues of the aqueous solution at the channel walls)**

## *1.3 Compatibility of ionic liquids with vesicles, oil droplets as well as the formation of reverse micelles (SDU cooperation)*

BioMIP sent two probes of ionic liquids ([MeBu][NTF] and [EMIM][NTF] to SDU labs to test the interaction of these liquids with vesicles and oil droplets at the phase interface as well as in reverse micelle formation.

According to a published paper from Moniruzzaman et al.[3], the carbon chain on the nitrogen in the imidazole ring needs to be longer than 4 carbon atoms to form stable reverse micelles using Dioctyl sodium sulfosuccinate (AOT) as. For this reason, the two ionic liquids [$C_8$MIN] [$Tf_2$N] and [$C_{10}$MIN] [$Tf_2$N] (see also figure 3, right) were synthesized according to the procedure of Huddleston et al.[4].

By using 75mM AOT as surfactant and 1-hexanol (10 vol%) as co-surfactant (procedure adapted from Moniruzzaman et al.) it was possible to produce reverse micelles in ionic liquid. With a water-to-surfactant molar ratio ($w_o$) 3 and 4 we have achieved a diameter of the reverse micelles of 220 nm, which is somewhat larger than stated in the work of Moniruzzaman et.al. (140-180 nm). The aqueous phase in the experiments was a 5mM pyranine solution in 100 mM Trizma® buffer. At the above-mentioned conditions, a clear and colourless solution is obtained.

[3] Moniruzzaman et al., „Formation of Reverse Micelles in a Room-Temperature Ionic Liquid“ Chem. Phys. Chem., 2008, 9, 689-692.

[4] Huddleston et al., Green Chemistry, 2001, 3, 156-64.

## *1.4 Demonstration of chemtainer generation with electronic control*

The BioPro Software package has been built up in former projects and is continuously being enhanced to facilitate and operate the controlled Chemical Microprocessor - ChµP, with many different variants of fluidic designs. In addition to control of the electrodes, chip position, temperature, light-sources, filters etc. a further basic functionality is the control of the volume-driven syringe pumps (Micromechatronic Technologies GmbH, Germany) integrated into our microfluidic workstation, which have the unique feature of supporting extreme continuous low flow-rates (less than micro-litres per hour) with a pulse-free flow. The pumps can be individually controlled electronically and syringe diameters and flow-rates can be specified. Using this setup we are able to generate droplet container both on-chip as well as using an external device (e.g. microfluidic Y- and T-junction.). External droplet generation is useful in allowing modular combination with a whole range of downstream processing devices. On-chip droplet generation is useful for achieving smaller droplets and systems with locally different droplet properties.

Figure 2 shows the electronically controlled chemtainer droplet generation using ionic liquids. In this case an external custom-built glass microcapillary Y-junction was used and the fluids transferred first into a FEP microchannel tube with a diameter of 200 µm and then (optionally) into the chemical microprocessor chip. We are able to control the droplet volumes by regulating precisely the flow rate ratio of the reagent/carrier streams with volume-driven flow control.

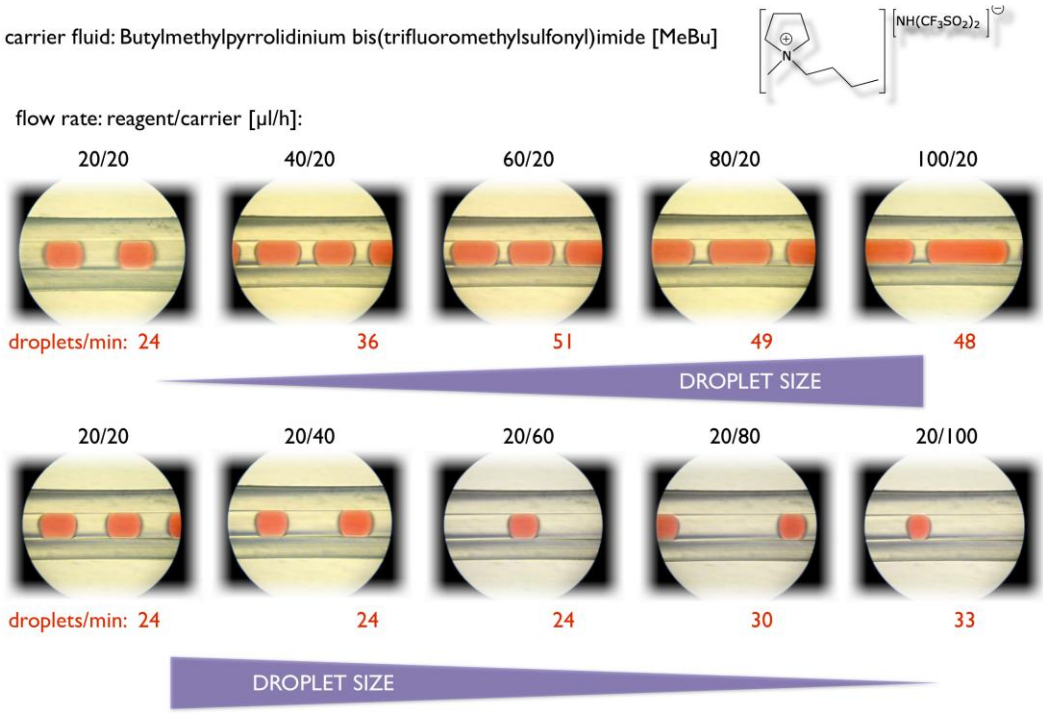


**Figure 2: Chemtainer droplet generation using ionic liquids. The figure shows the (coloured) reagent droplets in the colourless ionic liquid carrier fluid, with droplet sizes being programmed by electronically regulated flow ratios.**

Movies of the demonstrator can be downloaded at:

https://sibelius.biomip.rub.de/bmcmyp/Data/MATCHIT/Movies

**login:** review

**password:** M5Vpim0J

Please use the QuickTime player to view the movies!

The droplet formation theory involves different physical regimes, depending on the overall flow rate, and whether the droplets are in touch with the walls (slugs). For wall-free systems droplet formation is "a balance between the interfacial tension and the shear force present in the system" [as analyzed by T. Thorsen, M.I.T.]. Here we operate the device in a flow regime where the droplets maintain continuous contact with the walls of the capillary, which is distinct from the theory of wall-free droplets. The slug droplet generation process was analysed and calibrated by measuring chains of droplets at various electronic pump flow rate pairs for the reagent and carrier fluids in a 210 µm inner diameter cylindrical channel (figure 3). The droplet and carrier fluid volumes (A) were calculated from the lengths via the geometric formulae $d^3\,\pi/6 \pm (l-d)\pi d^2$ valid for strong differences in the hydrophilicities (contact angle). Although the dependencies of the slug volumes appear nonlinear and complex (B), the plots of slug volume ratio versus flow ratio (D) and of total complementary slug volume (C) vs flow ratio are roughly linear and can be used as calibration curves for programming droplets with desired volumes. The total complementary slug volume is the slug volume of the reagent droplet for the given flow rates plus the slug volume of the carrier droplet for the swapped flow rates (inverse ratio). The upper and lower curves shown in (C) and (D) are the standard error deviates from the data: these are greatest near balanced flow rates where the system is less stable.

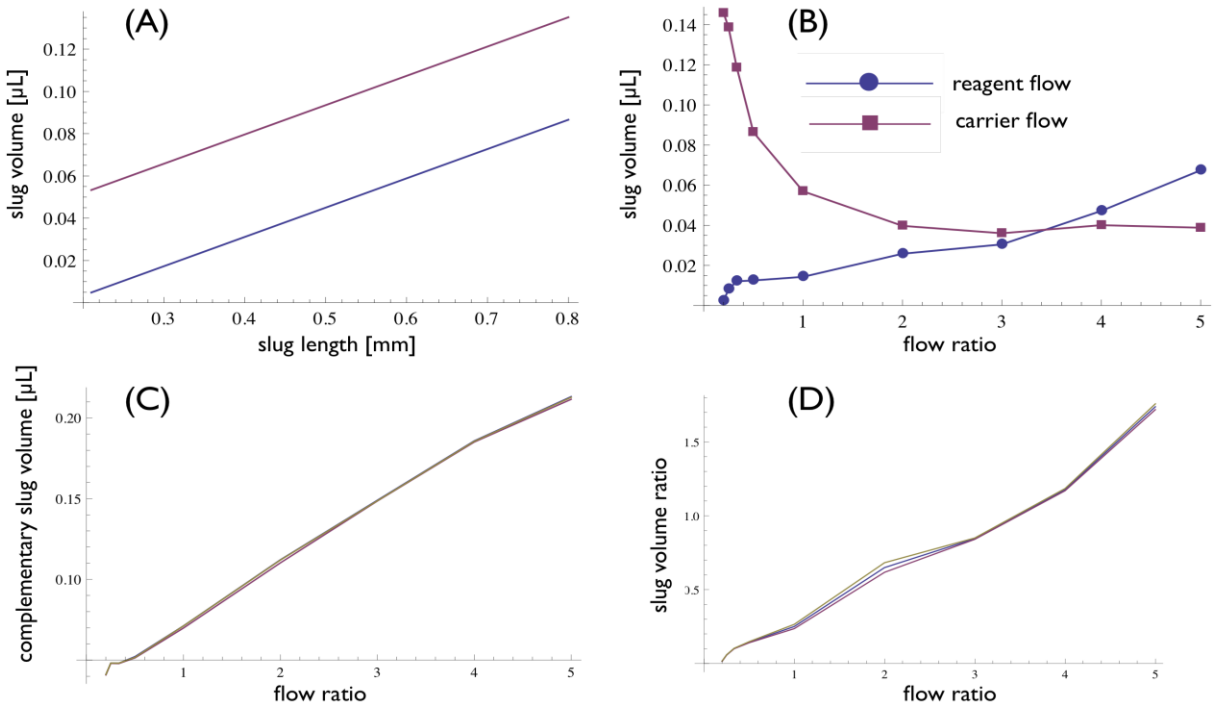


**Figure 3: Microdop analysis (Mathematica)**

## Summary

As a result of this research, we have an electronically programmable and calibrated method of droplet chemtainer generation of various sizes in microfluidic channels. Further work, linked to our microelectrode array development, will attempt in year two to gain local programmable control to manipulate these droplets (e.g. specific loading with substances from the gel phase) at specific sites in the microfluidic system.