GENERATION OF MULTIPLE DROPLETS WITH DENSLY PACKED SEGMENTS FOR STUDYING CHEMICAL SIGNALING IN DROPLET NETWORKS

Jan Guzowski[1], Piotr M. Korczyk[2], Sławomir Jakieła[1], Piotr Garstecki[1]
[1]*Instiutute of Physical Chemistry, Polish Academy of Sciences, Warsaw, Poland*
[2]*Institute of Fundamental Technological Research, Polish Academy of Sciences, Warsaw, Poland*

ABSTRACT
This paper reports a microfluidic system for automated generation of multiple droplets of various previously unattainable architectures in view of applying them to study chemical signaling in compact droplet networks.

KEYWORDS
Multiple droplets, surfactant bilayers, surface tension, self-assembly.

INTRODUCTION
Lipid bilayers form when aqueous droplets covered by monolayers are brought into contact [1] and can serve as models for biological membranes. Accordingly, droplet networks can be viewed as simple artificial tissues and possibly find application in synthetic medicine [2]. Recently, it has been shown [3] that multiple droplets with segments separated by lipid bilayers with incorporated membrane proteins (ion channels) are capable of electrochemical communication with the surrounding environment upon changing pH or temperature. In the present work we show that the architecture of multiple drops and thus the topology of droplet networks can be precisely controlled by using automated microfluidic devices.

EXPERIMENT
One of the most unique and promising applications of microfluidic systems is in controllable and reproducible generation of multiple droplets. Such droplets, composed of multiple immiscible segments find important applications in encapsulation of cells, drugs and other active compounds, as well as in synthesis of functional microparticles of various , often complex but predictable morphologies [4]. Multiple drops are usually generated by using passive flow-focusing devices in which the segmentation of liquids into droplets occurs spontaneously under constant rates of flow. Here we demonstrate application of active control over liquids by using external valves to formation of multiple drops on-demand. Our technique enables achieving previously unattainable volume fractions and timing of droplet generators which lead to novel morphologies. In this paper we describe formation of multiple drops (i) of various architectures, which might be predicted theoretically based on conditions of mechanical equilibrium and (ii) with arbitrary number and size of cores separated by surfactant (also lipid) bilayers.

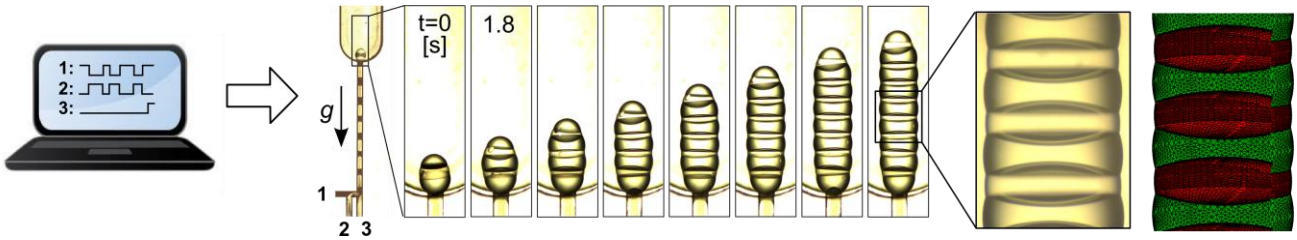

Figure 1: Multiple drops are generated according to a prescribed protocol. Snapshots from formation of a multiple drop stretched by buoyancy and rendering from a corresponding Surface Evolver calculation. The width of the channels supplying the liquids is 200 μm.

At μTAS 2011 we presented an automated system for generation of chains of droplets of arbitrary lengths with segments in shapes of interchanging biconvex and biconcave lenses. Such linear multiple droplets form under buoyancy of the segments when the two immiscible droplet phases-controlled by valves-are supplied from a narrow channel to a wide chamber oriented vertically (Figure 1). Similar droplet architectures have also been obtained in a passive system and polymerized in view of applying them as optical lenses by Ando et al. [5]. Here, we take advantage of the exquisite control given by automation to quantify the details of the morphology of the lenses, which goes beyond both above-mentioned presentations [6]. We also compare the experimental results with the theoretical stability diagrams expressed in terms of contact angles and ratio of volumes of the segments (Figure 2). It turns out that the stability of the chains is controlled by the sum of the contact angles $\theta_A+\theta_B$ such that when the sum approaches π the segments become discs and the whole chain becomes unstable against coalescence of the segments. On the other hand when the sum approaches 2π the segments become more and more spherical and finally detach from each other and the chain decomposes into individual droplets. For the intermediate sums the chains are most stable and the segments attain the shapes of lenses whose thickness and curvature can be controlled by changing the ratio of volumes and one of the contact angles (keeping the sum constant). In our experiment, the latter could actually be changed to some extent by heating the system, which owed to the apparent strong dependence of the interfacial tensions on the temperature. Surprisingly, in the studied system (we used silicone and sunflower oils in water with SDS) the sum of the contact angles remained approximately constant independently of the

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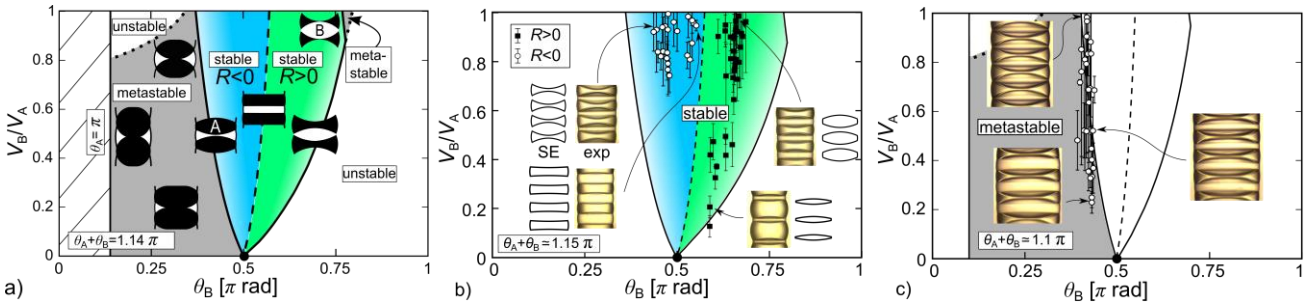

Figure 2: (a) Stability diagram for a chain of droplets in terms of the ratio of volumes and one of the contact angles for a fixed sum of the contact angles. (b) Comparison with experimental results (liquids as in Fig. 1) in the case of stable chains. (c) Micrographs of the metastable states.

In another system we demonstrated possibility of generation of droplets with multiple cores (Figure 3). Automation allows for precise control over the volume and the number of each core as well as over the volume of the shell. We generated droplets in which the volume of the shell was small enough such that the inner droplets get squeezed and start touching each other. Because of confinement the degrees of freedom for the motions of the cores get reduced which leads to their rearrangement until a local mechanical stability is achieved. Usually the final equilibrium configurations are unique but sometimes metastable states can also be observed-usually in the case of larger numbers of cores (more than 7). For generation of multiple drops we used fluorinated oil as the external phase, mixture of hexadecane and silicone oil with SPAN80 as the shell phase and water with 0.014% of SDS with a blue dye as the core phase. Silicone oil in the shell acting as a bad solvent for the surfactant expelled the amphiphilic SPAN molecules towards the interface enhancing formation of surfactant monolayers on the sirface of aqueous cores. In the confinement imposed by the small volume of the shell surfactant bilayers formed at the contact regions between the cores (Figure 3b). Similar experiment has been also successfully repeated with two different cores (Figure 4a) and for lipids instead of SPAN (Figure 4b). We observed formation of lipid bilayers between the aqueous cores. In a prospective experiment we also plan to study diffusion and propagation of reaction fronts in such systems.

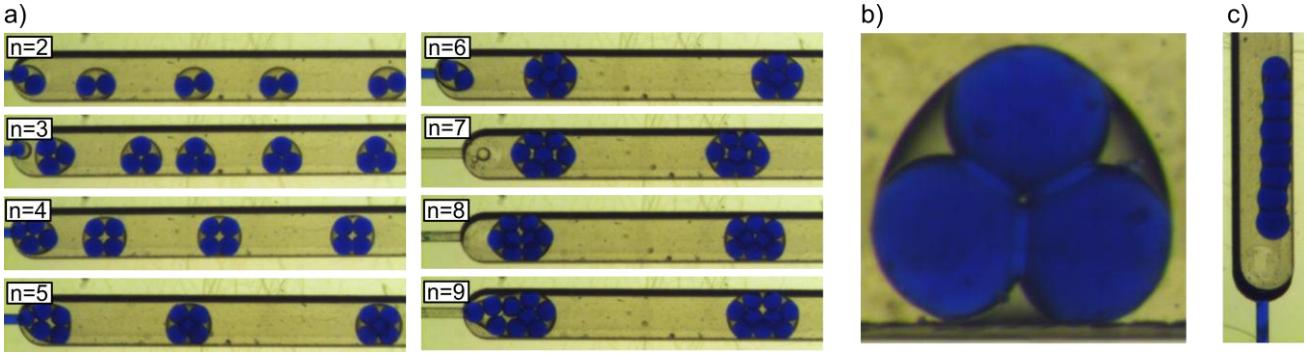

Figure 3: a) Snapshots from generation of completely engulfed close-packed droplets with multiple cores. The fluids are fluorinated oil with PFPE-PEG surfactant as the continuous phase, 7:3 mixture of silicone oil with hexadecane and 1% SPAN80 as the shell and water with SDS as the core phase. b) Close-up view of formation of surfactant bilayers between the aqueous cores. c) Chains form when the device is tilted such that buoyancy acts on the droplets upwards .

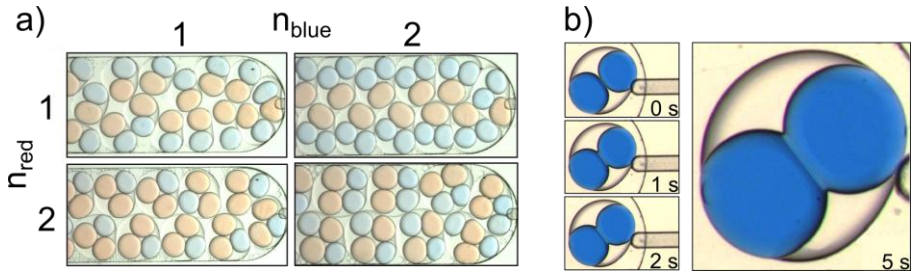

Figure 4: a) Snapshots from generation of completely engulfed close-packed droplets with multiple cores of two different species. The fluids are water with SDS as the continuous phase, fluorinated oil with PFPE-PEG surfactant as the shell and silicone oil with two different dyes as the core phase. b)Formation of a lipid bilayer between water droplets encapsulated by a drop of solution of DOPC lipid in oil (9:1 mixture of silicone and hexadecane oils)with fluorinated oil as the continuous phase.

To our knowledge, the presented work is the first attempt to apply microfluidic techniques to generation of lipid bilayers in multiple droplets. In further perspective such microfluidic techniques offer huge potential for the development of biomolecular sensors and drug screening applications.

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CONTACT

Jan Guzowski jguzowski@ichf.edu.pl
Piotr Garstecki garst@ichf.edu.pl