Belousov-Zhabotinsky droplet mixing on-chip for chemical computing applications

Philip King, Gareth Jones, Hywel Morgan, Maurits R.R. de Planque and Klaus-Peter Zauner
Electronics and Computer Science, University of Southampton

Belousov-Zhabotinsky for information processing

Without an imposed physical structure, even the most complex chemistries are limited in their ability to process information. For example, the Belousov-Zhabotinsky (BZ) oscillating reaction has been shown to have information procession potential,[1] but only if structure is imposed e.g. using physical barriers[2] or light-sensitive catalysts.[1, 3] Recently, separated BZ droplets in oil have been investigated.[4] Another option for aqueous/oil systems is to add lipid into the oil, which self-assembles into a monolayer at the phase boundary. If the lipid-stabilised droplets are brought into contact, a bilayer is formed, separating the BZ droplets into compartments.[5] This technique is more flexible than other methods of imparting structure, allowing for the creation of droplet arrays inspired by biological neuronal networks.

Microfluidic droplet production and merging

Although simple droplet networks can be produced by hand,[6, 7] more complex networks require an automated approach. Microfluidic technologies have been used extensively for the production of droplets, mainly towards biomedical applications.[8] Aqueous droplets are produced into a continuously flowing oil phase. Although it is possible for BZ to be mixed in bulk and formed into droplets using microfluidic devices, we have found the bulk production of CO_2 gas by malonic acid BZ media causes unwanted flow inside the closed microfluidic chips due to gas expansion. Bubbles also block microfluidic channels (see *figure 1a*). Droplets created using normal microfluidic devices are also too small, oscillating only briefly or not at all. This is due to the nL-range volume of the droplets, which are quickly depleted of reaction components, and the presence of inhibitory O_2 dissolved in the oil.[12] Although gasless BZ mixtures exist,[14] they are unsuitable for use on-chip due to long incubation times.

In order to avoid bulk CO_2 production, a number of methods for mixing BZ on-chip have been investigated (*figure 1b-g*). Passive pillar-based structures have been investigated in a number of papers for the passive trapping,[9] arraying[10] and merging[11] of droplets in microfluidic devices. These systems have focussed on droplets in the nanolitre volume range.

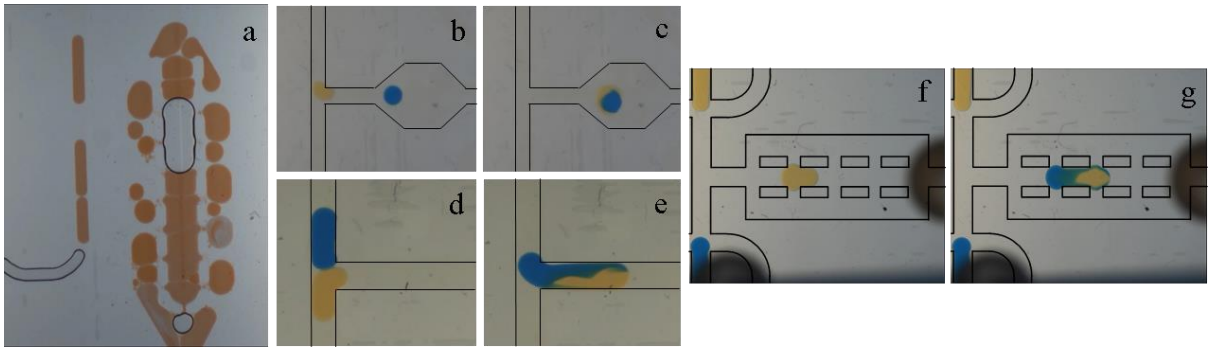

Figure 1 *– Microfluidic merging of large volume droplets. BZ using malonic acid as the substrate produces large amounts of CO_2 when mixed in bulk (a). To avoid this, we evaluated several different methods of droplet merging found in the literature, albeit using much smaller droplet volumes. A simple chamber can be used to reduce the fluidic flow, slowing the initial droplet (b), which is contacted and merged by a subsequent droplet (c). Alternatively, two droplets can simply be brought together at a t-junction (d) and merged (e). Both methods were found to require precise timing and were unreliable. A simpler method involves the use of pillars to trap the initial droplet (f). A secondary droplet is then injected into the array and merges with the first (g). This method also allows the merging of more than two droplets and is not time dependent.*

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In order to produce larger droplets, we have designed microfluidic chips with features in the range of hundreds of micron, an order of magnitude larger than most devices in the literature. We have developed a technique using 3D printing to produce moulds for PDMS soft lithography[13] that would be impossible using conventional photolithographic techniques. It was initially found that the 3DP material (Objet VeroWhite) was incompatible with the curing of PDMS. This was solved by baking the moulds overnight at 80ºC. A number of techniques developed for droplet production and manipulation at smaller scales work with larger droplet volumes. Droplets can be produced on-demand at any volume above 700 nL.

On-chip Belousov-Zhabotinsky droplet production

We have also found that the mixing of active, oscillating malonic acid BZ on-chip is possible using these techniques. Two droplets, each containing 'half-BZ' (see *figure 2* text), are bought together in the absence of lipid. They are merged and mixed, before being stabilised with lipid. BZ production in this manner avoids bubble formation as the volume of BZ is relatively low, and any gas produced can escape into the oil or PDMS material. An initial black precipitate quickly dissolves as the droplet is mixed, and is contained within the droplet. It is hoped that such a system could be expanded to include further droplet input channels, allowing the creation of complex arrays of droplets with variable composition.

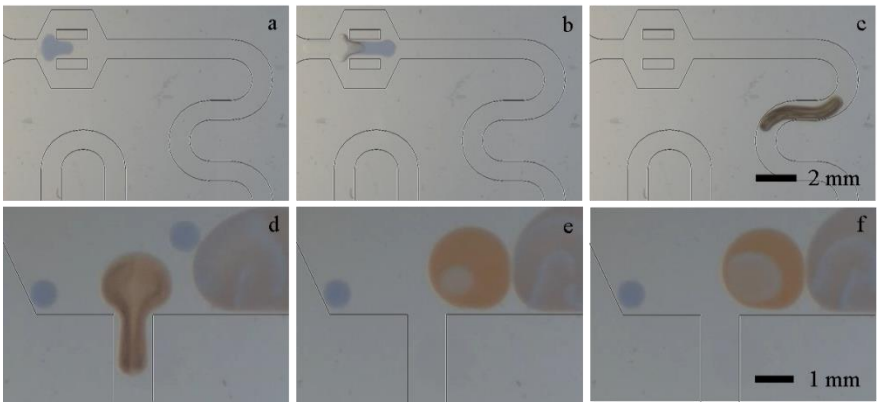

Figure 2 *– Handling BZ in microfluidic chips. To avoid gas production, malonic acid BZ droplets can be produced on chip. Droplets produced in oil without lipid can be captured between pillars (a) and merged with further droplets (b). The composite droplet fills the capture chamber and is ejected by the oil flow (c), mixed (d) and introduced to lipid-containing oil added separately (e). This stabilises the droplets, which are found to oscillate as if mixed in bulk (f-g). The two 'half-BZ' solutions contained* H_2SO_4*,* $NaBrO_3$ *and ferroin (blue) and* H_2SO_4*, malonic acid and KBr (clear).*

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