Networked Lab-on-Chips: Enhancing LoCs through microfluidic communications and networking

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I. Applications scenario and design challenges

Microfluidics is an emerging field which deals with the study of the behavior, control and manipulation of fluids at the sub-millimeter scale. Microfluidic systems transport volumes of fluid that vary from microliters (10^{-6} l) to femtoliters (10^{-15} l) in channels that are usually embossed in the surface of a polymer, glass or silicon. One of most promising applications of microfluidics is the lab-on-chip (LoC) technology. LoC devices are used to perform typical laboratory operations with low consumption of reagents and short reaction times. One subcategory of microfluidics is droplet-based microfluidics. Unlike continuous flow systems, droplet-based systems focus on dispersing discrete volumes of liquids (*dispersed phase*) into another immiscible fluid (*continuous phase*). The droplet in a microfluidic system can be seen as an isolated reactor encapsulating samples and reagents, used to accomplish biomedical tasks, such as DNA sequencing, drug delivery, blood analysis [1], [2], etc. In LoCs several operations can be performed on droplets: generation, sorting, splitting, merging and mixing. Currently, most LoC systems are realized through monolithic devices. Samples encapsulated into droplets are processed by passing them through a preset sequence of fixed microfluidic channels. Modularity of individual elements and interconnectivity among them would be needed in the view of developing general purpose microfluidic processors performing more complex programmable laboratory operations. Programmable droplet based LoCs have been already introduced [3]; however they rely on use of active control, such as microvalves, electric fields, laser, electowetting-on-dielectric (EWOD) or dielectrophoretic (DEP) forces requiring a complicated fabrication process or off-chip controllers that imply additional power costs. In addition, some of these methods may be not suitable for some biological scenarios due to biocompatibility of electrical signal on some cells or biomolecules [4].

II. Basic Idea

In this poster we propose a droplet-based programmable microfluidic device exploiting only hydrodynamic droplets manipulation, which uses channel geometries and hydrodynamic forces to steer droplets along the channels. This microfluidic device implements interconnectivity among LoCs, in such a way that several specialized LoC elements can be coordinated and dynamically addressed. In order to allow the programmable LoCs to interact and exchange samples in a flexible and dynamic way, we take inspiration from the telecommunications theory for proposing appropriate methodologies to support communications and switching among those devices. Accordingly, we introduce a new paradigm, called Networked-Lab-on-Chip (NLoC), that brings communications and networking concepts into LoC systems, by supporting flexibility and programmability; this would, consequently, reduce the device costs.

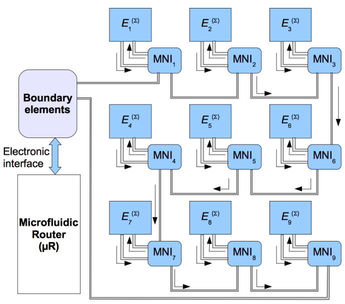

Fig. 1. Microfluidic system architecture.

In the following we illustrate the NLoC reference architecture. Let us consider a microfluidic system that includes a number M of elements each denoted as $\mu f E_i$, $i \in 1, 2, ..., M$, respectively. In our network a *microfluidic element* $\mu f E_i$ is a microfluidic chip which performs one or more microfluidic operations on liquid samples. Similarly to what is done in the network-on-chip domain, we assume that a networking element – called *Microfluidic Network Interface* (MNI) – is attached to each element to perform the operations required for efficient and reliable exchange of droplets with the other elements. The simplest model of interaction is the request/response model in which a central intelligent element requests to a given other element an operation to be executed on a single droplet or, more in general, on a set of droplets. When such operation is completed, the element will respond by sending back the processed droplet(s) to be elaborated by the central device. We have chosen to consider a physical ring topology architecture implementing a logical star topology, because of its simplicity. In fact, a central unit, denoted as *microfluidic router* (μR), performs both packet dispatching and job scheduling functionalities. It is evident that the μR is connected to other boundary elements, e.g. pumps, by using standard electrical/electronic interfaces, in order to control the injection of reagents into the system.

In order to support addressing of a microfluidic device

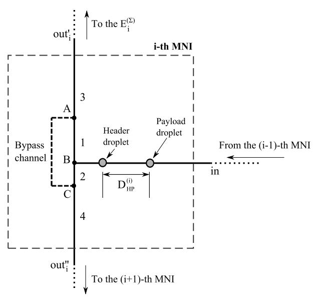

Fig. 2. Distance-based receiver circuit.

in a NLoC, we suppose that the samples which should be chemically treated or analyzed by the NLoC are included in a *payload droplet*. In order to route the payload droplet appropriately, our NLoC addressing scheme exploits another droplet, called *header droplet*, that is used for network signaling only. The *destination address* of the i-th MNI (i.e. the information about the intended destination of the payload droplet) is encoded in $D_{HP}^{(i)}$, that is the distance between the header and the payload droplet. The design of this MNI, showed in Fig.2, exploits the fundamental result that droplets flow along the path with minimum istantaneous hydrodynamic resistance.

The device is a T-shaped circuit with one inlet arriving from the (i-1)-th MNI and the two outlets connected respectively to the i-th μfE and to the inlet of the next MNI in the ring. The asymmetric branches 1 and 2 of the junction are connected by a bypass channel having a low hydrodynamic resistance. This channel helps to equalize the pressure between the connected points at the two branches, so that the direction taken by the droplets does not depend on the resistance of branches 3 and 4. The direction taken by the payload droplet at the bifurcation B depends on the presence of the header droplet in branch 2, so that the payload droplet goes either into branch 1 (and then to the current element) or 2 (and then to the ring) if the header droplet is in branch 2 or 3 respectively.

III. Experimental activity

A computational fluid dynamic (CFD) analysis along with an experimental approach was used to study the proposed system. In particular, in order to support appropriate switching functionalities, we preliminarily need to characterize the communication channel and, consequently, the achievable channel capacity. In order to characterize the noise statistics in the microfluidic channel we have run a large set of simulations aimed at the characterization of how droplets flow in microfluidic channels. We have used the OpenFOAM simulator to design a T-junction device. We have compared the performance of two simple droplets encoding schemes: 1) presence/absence encoding, in which the presence of a droplet in the channel in a certain time slot represents a bit ’1’, while no droplet represents a bit ’0’; 2) distance encoding, in which information is encoded in the distance between consecutive droplets. In our simulations we measured the inter-arrival time between pairs of consecutive droplets at different boundaries, for many values of the ratio η_r between the viscosities of the dispersed and continuous phases. We have observed that the variance of the droplet inter-arrival time increases as the viscosity of the continuous phase increases if the viscosity of the disperse phase is kept constant. As far as the distance between consecutive droplets is concerned, this does not depend on the boundary where we observe the flux of droplets. Another significant and surprising result is that the variance does not increase significantly as the distance between the beginning of the T-junction and the considered boundary increases. This means that in microfluidic communication channels the “*noise*” does not increase as the distance between the sender and the receiver increases. We have also found a threshold which identifies the convenience regions for the two encoding schemes. It came out that the scheme based on distance between consecutive droplets is convenient when the ratio η_r is around 2 or higher, which is a condition verified in most microfluidic systems scenarios. We also present our experimental results on the design of a reliable receiver able to manage the information about the destination address encoded as distance between droplets. This receiver is indeed the MNI illustrated in Figure 1: we report both the simulation results obtained to assess the MNI receiving functionalities and the preliminary results from the experiments. Primarily the objective of these early experiments was to validate the concept of distance-based switch through a prototype. The device includes a T-shaped junction where the dispersed phase forms the discrete droplets. The two fluids were injected in the micro-channel by syringe pumps and the distance between droplets adjusted by changing the flow rate of the dispersed phase and the continuous phase. In Figure 3 we show how the addressing scheme works when the payload droplet is meant to be directed the i-th MNI.

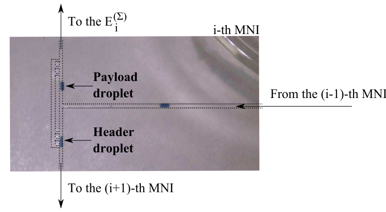

Fig. 3. Experimental results for the case when the payload droplet enters pipe 1.

IV. Work in progress

In order to further develop and deploy our idea we are currently setting up another set of simulations and experimental tests on more complex network architectures involving the interconnection of three or more LoCs. Moreover, to improve this architecture we will design microfluidic components and droplets protocols that realize other basic networking functionalities such as medium access control, channel sensing and buffering.

References

[1] H. Song *et al.*, “Reactions in droplets in microfluidic channels,” *Angewandte Chemie International Edition*, vol. 45, no. 44, 2006.
[2] S.-Y. Teh *et al.*, “Droplet microfluidics,” *Lab Chip*, vol. 8, Jan. 2008.
[3] R. Fair *et al.*, “Chemical and biological applications of digital-microfluidic devices,” *Design Test of Computers, IEEE*, vol. 24, no. 1, jan.-feb. 2007.
[4] R. Fair, “Digital microfluidics: is a true lab-on-a-chip possible?” *Microfluidics and Nanofluidics*, vol. 3, 2007.