When bits get wet: introduction to microfluidics networking

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Most of experimental pictures in this presentations are complimentary from Prof. Mistura (Univ. of Padova)
1. Introduction to microfluidics networking

2. Research challenges

3. Grow the interest on the subject... and increase my citation index 😊
MICROFLUIDICS...

WHAT IS IT ALL ABOUT?
Microfluidics is both a **science** and a **technology** that deals with the control of small amounts of fluids flowing through microchannels.

**Droplet microfluidics**

- Droplets (dispersed phase) encapsulating samples and reagents are dispersed into an immiscible fluid (continuous phase) and carried throughout microchannels.
MACROSCALE: inertial forces >> viscous forces

microscale: inertial forces ≈ viscous forces
Advantages

- Optimum flow control
  - Accurate control of concentrations and molecular interactions

- Very small quantities of reagents
  - Reduced times for analysis and synthesis
  - Reduced chemical waste

- Portability
Microfluidic research: Tunable filters, Optical Switches,…


Switching Fiber-Optic Circuits with Microscopic Bubbles John Uebbing, Agilent Technologies
Market

- Inkjet printheads
- Biological analysis
- Chemical reactions
- Pharmaceutical analysis
- Medical treatments
- ...

Source: Yole Développement (www.micruxfluidic.com)
The origins and the future of microfluidics
GM Whitesides - Nature, 2006 - nature.com
Abstract The manipulation of fluids in channels with dimensions of tens of micrometres—microfluidics—has emerged as a distinct new field. Microfluidics has the potential to influence subject areas from chemical synthesis and biological analysis to optics and

Cited by 5291 Related articles All 25 versions Web of Science: 3226 Cite Save More

Microfluidics: Fluid physics at the nanoliter scale
TM Squires, SR Quake - Reviews of modern physics, 2005 - APS
Abstract Microfabricated integrated circuits revolutionized computation by vastly reducing the space, labor, and time required for calculations. Microfluidic systems hold similar promise for the large-scale automation of chemistry and biology, suggesting the possibility of

Cited by 3261 Related articles All 27 versions Web of Science: 2047 Cite Save More

Engineering flows in small devices: microfluidics toward a lab-on-a-chip
Abstract Microfluidic devices for manipulating fluids are widespread and finding uses in many scientific and industrial contexts. Their design often requires unusual geometries and the interplay of multiple physical effects such as pressure gradients, electrokinetics, and

Cited by 2697 Related articles All 17 versions Web of Science: 1776 Cite Save More

Developing optofluidic technology through the fusion of microfluidics and optics
D Psaltis, SR Quake, C Yang - Nature, 2006 - nature.com
Abstract We describe devices in which optics and fluidics are used synergistically to synthesize novel functionalities. Fluidic replacement or modification leads to reconfigurable optical systems, whereas the implementation of optics through the microfluidic toolkit gives

Cited by 1448 Related articles All 21 versions Web of Science: 988 Cite Save More
Currently, most LoC are special-purpose devices

Attention is now on **LoC internetworking**

- **Versatility**
  - same device for different purposes

- **Capability**
  - Can concatenate multiple LoCs to realize more complex analysis/functionalities

- **Economy**
  - Cost saving
  - Energy saving
Today’s commercial available programmable microfluidic devices (PMS) exploit active manipulation methods (es. Agilent, Advanced Liquid Logic).

Active Droplets handling (Electrowetting on Dielectrics)

- relies on integrated valves and electrodes
- requires a complex and costly multilayer microfabrication process for the chip
Expensive fabrication process

Biocompatibility of electrical signals on cells and biomolecules

Bubble logic is a first attempt to design a passive PMS

Passive droplets handling

• exploits only pure hydrodynamic forces to control the droplets through an appropriate design of microchannels
• cheap and simple fabrication process

M. Prakash, N. Gershenfeld
Microfluidic Bubble Logic, Science, 315(5813), 2007
Pure hydrodynamic switching principle

1. Droplets flow along the path with minimum hydraulic resistance
2. Channel resistance is increased by droplets

Two close droplets arrive at the junction

First drop “turns right”

Second drop “turns left”
Droplet microfluidics systems can perform basic Boolean logic functions, such as AND, OR, NOT gates.

See: Microfluidic bubble logic, M Prakash, N Gershenfeld - Science, 2007
OUR APPROACH

Purely hydrodynamic LoC internetworking

- **Simple fabrication**
  - No mixed materials
  - 3D printer-made circuits

- **Simple control**
  - Act only at board periphery (mainly, syringes/pumps)

- **Bio compatibility**
  - No electronics → no undesired biological interactions
  - Possibility to implant in living tissues
Droplets behavior is affected by various intertwined factors:

- Flows in each channel depend on the properties of the entire system:
  - Topology & geometrical parameters
  - Fluids characteristics (density, viscosity, …)
  - Obstacles, imperfections, …

Time evolution of a droplet-based microfluidic network is also difficult to predict:

- The speed of the droplets depends on the flow rates, which depend on the hydraulic resistance of the channels, which depend on the position of the droplets…
OUR GOALS

Microfluidic networking

Microfluidic communication systems
OUR GOALS

Microfluidic networking
Our contributions

① Derive simple "macroscopic models" for the behavior of microfluidic systems as a function of the system parameters

② Define a simple Microfluidic Network Simulator framework

③ Apply the method to study the performance of a microfluidic network with bus topology
“Macroscopic” models

Prakash and Gershenfeld, Science ’07
Basic building blocks

① Droplet source

② Droplet switch

③ Droplet use (microfluidic machines structure)
**Capillary number**: captures the relative magnitude of the viscous shear stress compared with the interfacial tension

\[ C_a < C_a^* \approx 10^{-2} \Rightarrow \text{Squeezing regime} \Rightarrow \text{droplet formation} \]
Droplets generation

\[ L_d = w \left( 1 + \xi \frac{Q_d}{Q_c} \right) \]

\[ \delta = L_d \frac{Q_c}{Q_d} + \frac{\pi w^3}{6} - \frac{w^2 h}{Q_d \omega h} (Q_d + Q_c) \]

- By changing input parameters, you can control (average) droplets length and spacing, but NOT independently!
Droplets' effect on fluidic resistance

When a droplet is injected into a duct, the friction generated with the carrier fluid and the forces produced by the inhomogeneity between the dynamic viscosity of continuous and dispersed phases determine an increase of the fluidic resistance of the channel [15, 16, 17]. For our purposes, we need to define a simple model to approximate the resistance's variation produced by a droplet in a microchannel. To this end, we consider the case exemplified in Fig. 1, where a droplet with dynamic viscosity $\mu_d$ occupies a segment of length $\ell_d$ of the channel, otherwise filled by the continuous phase with dynamic viscosity $\mu_c$.

According to (1), the fluidic resistance of a channel of length $L$ without droplets is $R(\mu_c, L)$. The variation of resistance produced by a droplet of length $\ell_d$ injected into such a channel can then be approximated as

$$\Delta R = R(\mu_c, L) - R(\mu_d, \ell_d)$$

Note that, according to our model, the presence of a droplet increases the hydraulic resistance of the channel only if $\mu_d > \mu_c$, whereas in the contrary case, the resistance is actually decreased by the droplet. An intuitive explanation is that the greater the viscosity ratio $\kappa = \frac{\mu_d}{\mu_c}$, the greater the resistance of the droplet to flow. This behavior is consistent with the outcome of OpenFOAM simulations, though it is in contrast with some experimental results where it was observed an increase of the channel resistance even with $\kappa < 1$. A possible explanation for such inconsistency is that neither our model, nor the OpenFOAM simulator take into account friction's sources different from viscous force (e.g., the pressure exerted to the droplet by the thin films of continuous phase that wrap the dispersed fluid). Consequently, the proposed model may fail when viscous forces are not the dominant friction contribution and, hence, it is mainly applicable when $\kappa > 1$.

Junction crossing

A typical microfluidic junction consists of a channel that forks into two branches, usually with T or Y shape. The pattern followed by droplets across a junction may either be regular or chaotic, depending on a number of factors. Furthermore, droplets may collide, coalesce or split when crossing a junction, as observed in several studies [15, 16, 17, 18].

Figure 2: Droplet length (left) and inter-droplet distance (right) vs dispersed over continuous flow ratio, for different values of continuous phase velocity. Lines refer to eq.s (5) and (6), marks to simulative results.
Experimental results

- Varying $Q_d$ for each 4 values of $Q_c$
- $Ca \sim 10^{-4}$
- $\sim 150$ droplets
When crossing a junction a droplet can break up...

To avoid breakup, droplets shall not be too long [1]

\[ \ell_d < \ell^* \approx \chi W C^{-0.21}_a \]

To increase droplet length you must reduce capillary number $C_a \rightarrow$ reduce flow rate $\rightarrow$ droplets move more slowly!

$C_a = \frac{\mu_c Q_c}{\sigma w h}$

- Junction breakup
- Non breakup
- Breakup regime
Microfluidic Network Simulator

Prakash and Gershenfeld, Science '07
## Microfluidic/electric duality

<table>
<thead>
<tr>
<th>Microfluidic domain</th>
<th>Electric domain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volumetric flow rate $Q$</td>
<td>Current intensity $I$</td>
</tr>
<tr>
<td>Pressure difference $\Delta P$</td>
<td>Voltage drop $\Delta V$</td>
</tr>
<tr>
<td>Hagen-Poiseuille law $\Delta P = RQ$</td>
<td>Ohm law $\Delta V = RI$</td>
</tr>
<tr>
<td>Flow and energy conservation $\Sigma Q = 0; \Sigma \Delta P = 0$</td>
<td>Kirchhoff laws $\Sigma I = 0; \Sigma \Delta V = 0$</td>
</tr>
</tbody>
</table>

**Flow and energy conservation laws:**
- Hagen-Poiseuille law: $\Delta P = RQ$
- Ohm's law: $\Delta V = RI$

**Kirchhoff's laws:**
- $\Sigma I = 0$
- $\Sigma \Delta V = 0$
Microfluidic/electrical analogy (I)

Syringe pump \(\rightarrow\) current generator

Pneumatic source \(\rightarrow\) voltage generator
Microfluidic/electrical analogy (II)

- Microfluidic channel filled only by continuous phase
  ↓
  resistor

- Bypass channel (ducts that droplets cannot access)
  ↓
  resistor with negligible resistance

- Microfluidic channel containing a droplet
  ↓
  series resistor
Example

$R_1 < R_2 \rightarrow$ First droplet takes branch 1

$R_1 + \delta > R_2 \rightarrow$ Second droplet takes branch 2
$G(t) = (V,E)$

$V = \{v_1, \ldots, v_{N_{nodes}}\}$

$E = \{e_1, \ldots, e_{N_{edges}}\}$
Parallel with electrical network

- Static MN graph is mapped into the dual electric circuit
  - flow generator
  - pressure generator
  - microfluidic channel
  - bypass channel
Simulation cycle

1. **Compute the flow rates using Kirchhoff laws**
2. **Compute the motion of each droplet**
3. **Update the resistance of each channel depending on droplets position**
4. **Determine the outgoing branch when droplets enter junctions**
Simulation vs experimentation
Bus Network analysis

Prakash and Gershenfeld, Science '07
Case study: microfluidic network with bus topology
Microfluidic bus network with bypass channels
Performance

- **Throughput**
  - *volume* of fluid conveyed to a generic MM per time unit ($S \ [\mu \text{ m}^3/\text{ms}]$)

- **Access strategy**
  - “exclusive channel access”: one header-payload at a time!
Bus network with simple T-junctions

Throughput (N=10)

$S^{\text{opt}}(3)$

$S^{\text{opt}}(4)$

$S^{\text{opt}}(7)$

Payload length [mm]

Flow rate $S$ [µm$^3$/ms]
Bus network with bypass channels

![Graph showing throughput (N=10) with different target values (3, 4, 7)]
**Conclusions and future developments**

- **Addressed Issues:**
  - Definition of a **totally passive** droplet’s switching model
  - Design of a macroscopic droplet-based **Microfluidic Network Simulator**
  - Analysis of **case-study: microfluidic bus network**

- **Looking further ahead:**
  - Joint design of network topology and MAC/scheduling protocols
  - Design and analysis of data-buffer devices
  - Proper modeling of microfluidics machines
  - Characterization of microfluidics traffic sources
  - Information-theory approach to microfluidics communications
  - ...
Microfluidic communication systems
Our contribution

- Add communication capabilities in microfluidic systems
- Transmit information in a microfluidic channel by means of a PAM like modulation
- Use droplet length/interdistance to code the information
- Evaluate system performance on a real case scenario
Bit string

<table>
<thead>
<tr>
<th>00</th>
<th>01</th>
<th>10</th>
<th>11</th>
</tr>
</thead>
<tbody>
<tr>
<td>↓</td>
<td>↓</td>
<td>↓</td>
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</tbody>
</table>

PAM symbols

<table>
<thead>
<tr>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>↓</td>
<td>↓</td>
<td>↓</td>
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</table>

Droplet length

$L_d^{(0)}$ $L_d^{(1)}$ $L_d^{(2)}$ $L_d^{(3)}$

<table>
<thead>
<tr>
<th>$L_d^{(0)}$</th>
<th>$L_d^{(1)}$</th>
<th>$L_d^{(2)}$</th>
<th>$L_d^{(3)}$</th>
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<tr>
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</table>

Dispersed phase flow

<table>
<thead>
<tr>
<th>0.5</th>
<th>1</th>
<th>1.5</th>
<th>2</th>
<th>[μl/min]</th>
</tr>
</thead>
<tbody>
<tr>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td></td>
</tr>
</tbody>
</table>

Continuous phase flow

<table>
<thead>
<tr>
<th>5</th>
<th>[μl/min]</th>
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<td></td>
<td></td>
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</table>
Experimental setup
Frame processing

- Camera frame
- Binary image
- Lowpass Wiener filter
- Median filter
- Connected components identification
Droplet lengths

\[ L_d(i) \]

\[ \bar{L}_d \]

\[ \sigma_d(i) \]
We assume that the length (interdistance) can be modeled as a Gaussian RV. The assumption can be validated comparing the empirical and theoretical CDFs.
Symbols PDFs

The diagram shows PDFs for different values of $L$ and $l_{th}(m,n)$. The PDFs are plotted against $L_d [\mu m]$ with thresholds indicated at specific $L_d$ values.

- $thr_{L}^{(0,1)}$
- $thr_{L}^{(1,2)}$
- $thr_{L}^{(2,3)}$

Thresholds are marked with ✔️ for success and ✗ for failure.
Assuming equally likely symbols

\[ e = \frac{1}{4} \sum_{i=0}^{3} P(E|s^{(i)}) \]

### Table: Error Probability for Droplet-length PAM and Inter-droplet distance PAM

<table>
<thead>
<tr>
<th>i</th>
<th>(\bar{L}_{d}^{(i)})</th>
<th>(\sigma_{d}^{(i)})</th>
<th>thr(_{L}^{(i,i+1)})</th>
<th>(\bar{\delta}^{(i)})</th>
<th>(\sigma_{\delta}^{(i)})</th>
<th>thr(_{\delta}^{(i,i+1)})</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>184.52</td>
<td>2.26</td>
<td>193.29</td>
<td>769.65</td>
<td>14.04</td>
<td>679.5107</td>
</tr>
<tr>
<td>1</td>
<td>202.05</td>
<td>2.56</td>
<td>215.26</td>
<td>589.37</td>
<td>15.30</td>
<td>513.0877</td>
</tr>
<tr>
<td>2</td>
<td>228.47</td>
<td>3.08</td>
<td>243.85</td>
<td>436.80</td>
<td>9.44</td>
<td>397.8275</td>
</tr>
<tr>
<td>3</td>
<td>259.24</td>
<td>2.88</td>
<td>/</td>
<td>358.85</td>
<td>4.09</td>
<td>/</td>
</tr>
</tbody>
</table>

\[ e_{L} = 1.80 \cdot 10^{-5} \quad e_{\delta} = 8.95 \cdot 10^{-7} \]
This work:

- investigated the feasibility of extending communication concept to microfluidics
- implemented basic modulation technique based on length/interdistance
- evaluated system performance with experimental data
  - Both droplet length and inter-droplet distance can carry information bits
  - Inter-distance is generally preferable BUT, in complex network, it can vary as droplets stream along the channels

See Biral & Zanella, NanoComNet 2013
Looking forward…

- Transient characterization
  - Time to change modulated symbol
    - Related to *symbol period*
    - Depends on the physical “distance” between symbols → *symbol-dependent transmission rate*

- more sophisticated modulations
  - Combining length and distance
  - Using other circuits to dynamically change droplet inter-distance

- consider other performance indexes
  - throughput, delay, energy consumption
And YES... you can publish this stuff!


- A. Biral, D. Zordan, A. Zanella, "Simulating macroscopic behavior of droplet-based microfluidic systems" in the Proceedings of IEEE Global Communications Conference Dec. 6-10, 2015, San Diego, CA, USA


Transmitting Information with Microfluidic Systems

Andrea Biral, Davide Zordan, Andrea Zanella

Any questions?